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ADAPTATION AND CROSS-ADAPTATION
IN OLFACTION

E. P. KOSTER

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AN EXPERIMENTAL STUDY WITH OLFACTORY
SIMULATIONS OF VARIOUS INTENSITIES

RESUME

THE ADAPTATION OF THE OLFACTORY SYSTEM TO
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AN EXPERIMENTAL STUDY WITH OLFACTORY
STIMULI AT LOW LEVELS OF INTENSITY

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IN OLFACTION

AN EXPERIMENTAL STUDY WITH OLEOXYL
STIMULI AT LOW LEVELS OF INTENSITY

PROMOTOR: PROF. DR. C. F. VAN PARREREN

DATE

FROM PETER ROSSER

DEPARTMENT OF PSYCHOLOGY

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CHAPTER 1

INTRODUCTION

1.1. THE PROBLEM OF OLFACTORY DISCRIMINATION

The sense of smell is a keen sense. It is not only very sensitive, but it also has a fascinating power of discrimination between odorous substances. It is readily agreed upon that man can distinguish thousands (the most conservative estimate being 10,000) of odours. Unfortunately, however, very little is known about the actual receptive processes by means of which this is accomplished.

In a recent survey of the literature on olfaction, Wenzel and Sieck (1966) characterized the situation thus: "There is at present no adequate description of the transducing mechanism for either the quality or the intensity of olfactory sensation; nor, even worse, is there an understanding of what constitutes the critical feature of the olfactory stimulus.

The worker in olfaction therefore does not yet have a stimulus dimension analogous to the visible spectrum or the auditory frequency range to assist him in selecting and specifying stimuli. Intensity can be varied more or less reliably by changing the concentration of most odorous substances, but specific qualities cannot be produced upon demand by manipulation of any recognized characteristics of chemical compounds".

If this is by far the most serious handicap to the study of olfaction, another one is formed by the fact that the perception of odorous substances is by no means always restricted to the olfactory sense alone. Some substances, like ammonia and menthol, stimulate the trigeminal nerve endings and perhaps even the cold receptors in the nose at the same time as the proper olfactory recep-

tors. These sensations may of course contribute to the discrimination between different odorous substances, thus complicating the study of the purely olfactory functions.

The isolation of the critical feature (or features) of the olfactory stimulus and the understanding of the nature of the olfactory transducing mechanism, thus still constitute the major problems in the study of the sense of smell. To make at least some contribution towards a solution of these problems is the object of this thesis.

1.2. ANATOMY AND HISTOLOGY

If still very little is known about the transducing mechanism in olfaction, more information is available on the anatomy and histology of the olfactory epithelium and of the more central parts of the receptive system, especially of the olfactory bulb. Le Gros Clark (1951), Müller (1955), Allison (1953) and more recently Nieuwenhuys (1967) and Lohman (1967) have given detailed descriptions of the morphology in the olfactory system in vertebrates. De Lorenzo (1963) and Reese (1965) have studied the ultrastructure and histology of vertebrate chemoreceptors by means of the electron microscope. Moulton and Tucker (1964) and Ottoson and Shepherd (1967) have provided surveys of the physiology and the functional relationships in the olfactory structures. Schneider (1963, 1964) and Dethier, Larson, Adams (1963) finally have described and investigated the fine structure of the olfactory receptors in insects.

Only a short survey of the most important features of the vertebrate olfactory equipment will be given here. More detailed information is to be found in the articles just mentioned.

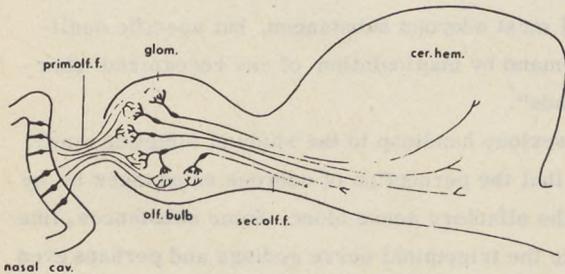


Fig. 1.1. Scheme of the organization of the peripheral and central olfactory system in vertebrates. cer. hem. = cerebral hemisphere; glom. = glomerulus; nasal cav. = nasal cavity; olf. bulb. = olfactory bulb; prim. olf. f. = primary olfactory fibers; sec. olf. f. = secondary olfactory fibers. (After R. Nieuwenhuys)

As is shown in fig. 1.1. the olfactory system in vertebrates can roughly be subdivided into three main parts, the olfactory epithelium with the primary olfactory fibers, the olfactory bulb with the secondary olfactory pathways and the cerebral hemispheres. These three parts will be described here.

a. The olfactory epithelium and the primary olfactory fibers.

In the surface of the olfactory epithelium, which lies in a narrow passage of the nose, somewhat removed from the main respiratory air stream, two types of cells, receptor cells and sustentacular cells, are found.

As is shown in fig. 1.2. the dendritic process of each of the receptor cells is surrounded by the closely packed sustentacular cells. Only the terminal extension of this dendritic process, the bare and unshathed olfactory rod is left free for interaction with the stimuli.

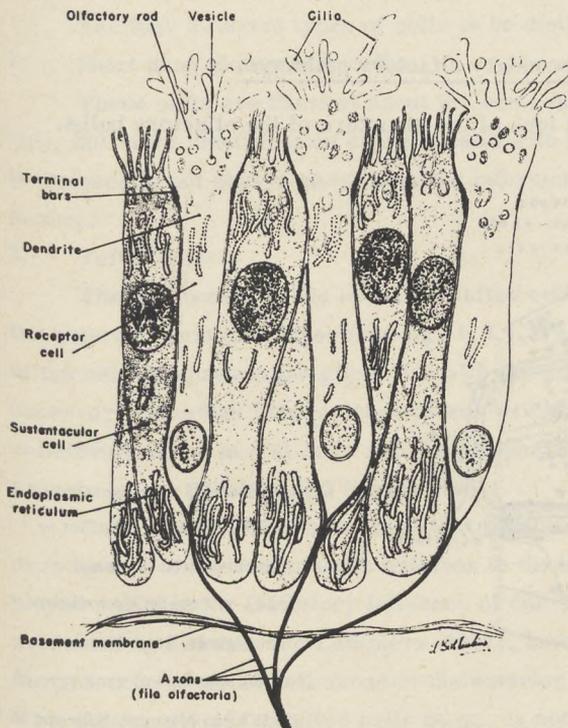


Fig. 1.2. Schematic representation of the olfactory mucosa showing the relationships of the various cell types based upon observations with the electron microscope. (After A. J. D. De Lorenzo)

From the so-called vesicles on the rod a number of hairlike extensions, the olfactory cilia, spread out in the olfactory mucosa. These olfactory hairs, which are generally considered to contain the actual sites of receptor activation, have a structure which is similar to that of the modified cilia of other

sensory cells such as retinal rods, mechanoreceptors of the cochlea, chemoreceptors of flies, etc. According to Ottoson and Shepherd (1967), whose recent discussion of olfaction physiology has provided most of the data presented in this section, the precise location of the receptive sites on the cilia is not known. The cilia lie enmeshed in the microvilli, which are the fingerlike extensions found on the terminal processes of the supporting cells. The resulting feltwork of cilia and microvilli is bathed in the pigmented secretions of the so-called Bowmans glands, which send their ducts through the epithelium. On their way to the olfactory bulbs the unmyelinated axons of the receptor cells form groups of about 15 to 40, which are surrounded by Schwann cells. Several of these fasciculi come together and pass through holes in the cribriform plate of the ethmoid bone (see fig. 1.3.).

As these bundles reach the bulb, the axons spread out over the surface of it and form an intricate network before they penetrate into the deeper layers.

b. The olfactory bulb and the secondary olfactory pathways.

Fig. 1.3. gives a general idea of the structure of the olfactory bulbs.

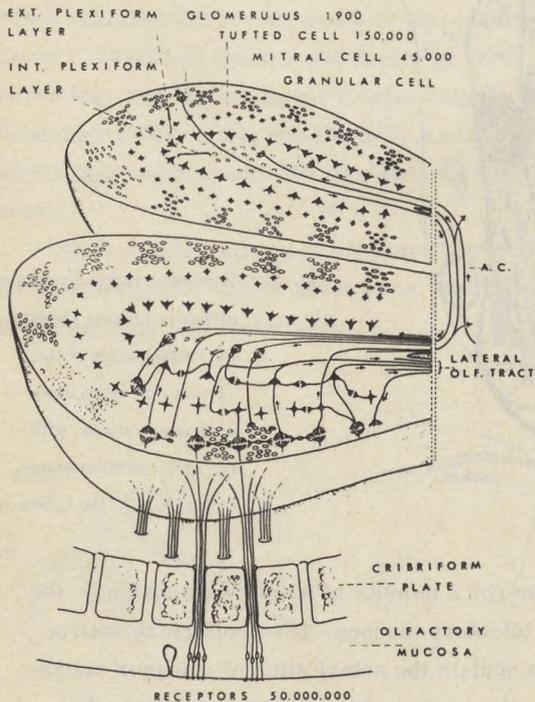


Fig. 1.3. Structure of the olfactory bulbs and their relations to the nerves and mucosa. A. C. = Anterior Commissure. The figures are estimates of the numbers of each type of cell in an olfactory bulb and in the olfactory mucosa lining one nasal cavity of the rabbit. (After Moulton and Tucker's modification of Gastaut and Lammers')

In this figure the four main types of cells that occur in the bulb, their arrangement in different layers and the types of interconnections that seem to exist between them, are shown.

Before discussing the different cell types and their connections separately, attention should be given to yet another feature of the bulb, the olfactory glomeruli. These rounded structures, which are also shown in fig. 1.1. are formed by "the branched terminations of the primary olfactory nerve axons and the bushy dendritic tufts of the nerve cells in the bulb" (Ottoson and Shepherd (1967)). Since the receptor cell axons do not branch before they reach the glomeruli, each glomerulus receives its impulses from a distinct set of receptors. This fact and the fact that the glomeruli contain the only synapses between the receptor and the cerebral cortex in the olfactory system, stress the importance of the study of the function of these bodies for an understanding of the working of the olfactory system as a whole.

The four different types of cells to be distinguished in the bulb are:

1. Short axon glomerular cells.

These cells are found at about the same depth in the bulb as the glomeruli, but since identification of these cells with electrophysiological recording techniques is not always easy, detailed information about their function is still scarce.

2. Tufted cells.

The cell bodies of the so-called tufted cells lie deep to the glomeruli in the external plexiform layer (see fig. 1.3.). The main dendritic process of the tufted cell synapses in the glomeruli with the primary olfactory neurones. Their accessory dendrites form a dense plexus with the dendrites and recurrent axon collaterals of the mitral cells and the peripherally directed processes of the granule cells. (Moulton and Tucker (1964).

Until recently it was believed that the axons of the tufted cells crossed over by way of the commissura anterior to the opposite bulb and that they played a part in the inhibitory influence of one bulb on the other. Evidence presented by Lohman and Lammers (1967), however, casts serious doubts on the presence of tufted cell axons in the anterior commissure.

Where the axons of the tufted cells do go, is not quite clear yet. The axons give off both recurrent collaterals, which synapse in the external plexiform layer with the accessory dendrites of other tufted cells and mitral cells, and "deep" collaterals which terminate in relation to the elements of the internal granular layer (Nieuwenhuys (1967).

According to Ottoson and Shepherd (1967), almost everything about the tufted cells beyond the fact that they have "primary" dendrites ending in the glomeruli, is still obscure and confusing.

3. Mitral cells.

The mitral cells, which lie still deeper in a distinctive layer of one to three cells thick (at least in mammals), are undoubtedly the most important cells found in the bulb, because their axons form the olfactory projection pathways to the secondary centres of the hemispheres.

Each of the mitral cell bodies is connected by a long "primary" dendrite with one of the glomeruli, where the terminal dendritic branches form the only connection of the mitral with the afferent input provided by the axons from the olfactory nerve. Secondary dendrites of the mitral cells, which do not end in glomeruli, ramify freely in the external plexiform layer (Nieuwenhuys (1967). and there is both histological and physiological evidence for the existence of dendro-dendritic synapses between these secondary dendrites and the dendrites of the granular cells (Rall, Shepherd, Reese and Brightman (1966). Before entering the lateral olfactory tract, the axons of the mitral cells, just like those of the tufted cells, give off two types of collaterals, recurrent and deep collaterals, which end in contacts with the dendrites of other mitral cells and tufted cells in the external plexiform layer and with granular elements in the deep layer respectively.

The mitral cell axons in the olfactory tract provide the main projection from the olfactory bulb to the brain. These axons give off a great number of collaterals to the underlying cortex of the olfactory peduncle and prepyriform region. The collaterals make axodendritic connections with the pyramidal and polymorphic cells, the axons of which in turn enter the internal capsule and also send branches into the anterior commissure (Ottoson and Shepherd (1967).

4. Granule cells.

The granule cells, which are found in the deepest layer, are not in direct contact with primary olfaction fibers. They have a number of short processes and a long peripherally directed offshoot which ramifies in the external plexiform layer. None of these processes shows the morphological characteristics of an axon (Nieuwenhuys (1967)). As was indicated earlier, there seem to exist dendrodendritic synapses between the granular cell processes and the secondary dendrites of the mitral cells. Thus, the granular cells can be excited by way of the secondary mitral cell dendrites. The granule cells seem in turn to exert an inhibitory influence on mitral cells. The granule cells do

also receive input from other sources in their deeper lying processes. According to Rall, Shepherd, Reese and Brightman (1966), the granule cell is therefore "strategically situated to enable its inhibitory activity to represent an integration of several inputs".

c. The cerebral hemispheres.

Only the various structures which constitute the "rhinencephalon" will be mentioned here. A more detailed description has been given by Nieuwenhuys (1967).

According to this author the main areas which receive olfactory input are:

1. the nucleus olfactorius anterior;
2. the secondary olfactory areas in the pallium;
3. the striatum;
4. the amygdala;
5. the tuberculum olfactorium;
6. the septum;
7. the area optica and the extra telencephalic regions.

Ottoson and Shepherd (1967) point out, that, in general, there is a close structural relationship between the olfactory pathways and the rest of the brain, particularly those parts related to affective and endocrine functions, like the pituitary. As these authors indicate, this need not surprise us, since olfaction has been shown to play an important part in such behaviours as feeding, mating and reproduction.

Before closing this section on anatomy and histology, some attention should be given to the efferent innervation which reaches the bulbs. Two different types of efferent fiber systems, the thin and the thick fiber system, can be distinguished. The thin fiber system provides a connection between the two bulbs by way of the anterior limb of the anterior commissure, whereas the thick fiber system consists of fibers from the rhinencephalon which run in the lateral olfactory tract and in the anterior limb of the anterior commissure, thus making a projection of each paleocortical field to both bulbs possible (Moulton and Tucker (1964)).

There are no indications of efferent innervation of the olfactory epithelium.

No efferent fibers go below the level of the bulb.

1.3. FUNCTIONAL RELATIONSHIPS IN THE BULB

Only some of the possible functional relationships between the different structures in the bulb have been indicated in the preceding section. Since the bulb is really the first olfactory centre and seems to play an important role in the integration of the olfactory signals, it may be opportune to give a short survey of the excitatory and inhibitory relationships between the different bulbar units. In fig. 1.4., a schematic diagram of the main functional pathways and connections in the mammalian olfactory bulb is given.

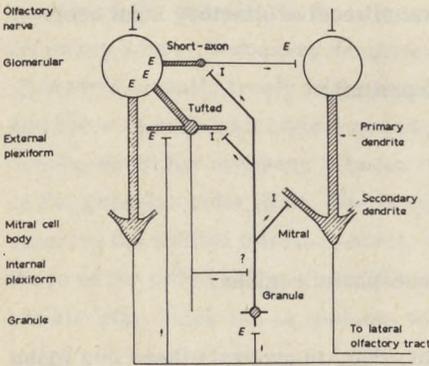


Fig. 1.4. Schematic diagram of the main functional pathways and connections in mammalian olfactory bulb. Presumed excitatory and inhibitory connections labeled E and I, respectively. Histological layers of the bulb indicated at left.
(After Shepherd)

Not shown in this figure are the dendrodendritic synapses between the secondary mitral cell dendrites and the granule cell processes mentioned in section 1.2. under b3. In general, the important role of the granule cell in regulating the input and the excitability of the other cell types will be evident from this figure. This point becomes even more clear in inspection of fig. 1.5., which shows the efferent influences in the bulb.

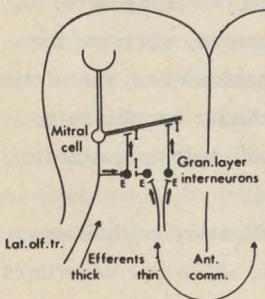


Fig. 1.5. Schematic diagram illustrating functional relation between anterior commissure and granular layer neurons in the olfactory bulb. Excitatory and inhibitory connections indicated E and I, respectively. Main centrifugal pathways to bulb indicated as thick fibers in or near lateral olfactory tract, and thin fibers in anterior commissure.
(After D. Ottoson and G. M. Shepherd)

Here again the granule cells are the first to be excited by the efferent fibers and they in turn exert inhibitory effects on the other cell types. The granule cells may therefore be to a large extent responsible for the occurrence of such phenomena as lateral inhibition and adaptation in olfaction.

1.4. CLASSIFICATION OF ODOROUS SUBSTANCES

Since finding the physical correlate of qualitative difference in odours and understanding the receptive process constitute such major problems in the study of the sense of smell, a lot of work has been done to solve them. Most of this work involved some form of odour classification as a first step towards the isolation of the critical feature of the olfactory stimulus and of the specific property of the receptive system that forms its physiological counterpart. If odours can be classified, it is argued, it seems likely that all substances whose odours are classified together stimulate some specific parts of the receptive system or, if the receptive system should be uniform stimulate all parts in a more or less equivalent way. Arguing along this same line, substances with very different odours would affect different parts of the receptive system or all parts in a different way. Thus, finding the physical or chemical properties of the molecules which are shared by substances belonging to the same class and are not shared or shared to a very different extent by substances belonging to different classes would possibly throw a light on the nature of the receptive process.

Fundamentally, odorous substances have nearly always been classified on the basis of one of the following three classification principles:

- a. Similarity and dissimilarity in the perceptual quality of their odours.
- b. "Common Fate" of their odorous properties under abnormal perceptual conditions.
- c. Differential nervous activity evoked by their odours in parts of the receptive system.

These three ways of classifying odorous substances will be discussed here more extensively in order to evaluate their usefulness for further investigation.

- a. Classification of odorous substances on the basis of similarity and dissimilarity in the perceptual quality of their odours.

Subjective judgement of similarity and dissimilarity between odours has for long been the only basis of odour classification. The classical classifica-

tions like Linne's (1764), Zwaardemaker's (1895), Henning's (1916) and, more recently, Crocker Henderson's (1927), were all obtained in this way, the judgements being made either by the author alone or by a small group of subjects. The results however, were often contradictory, (Ross and Harriman (1949) Findley (1924)) and none of the authors of these classifications succeeded in finding a property of the molecule that could serve as the physical correlate of olfactory quality.

The methods used by these authors were rather primitive and consisted mainly of verbal description of odours and free association techniques.

The value of such semantic methods is to a large extent restricted because of a lack of adequate words to describe odorous sensations.

Later, more sophisticated and semantically less dependent methods for measuring subjective judgements, like similarity rating scales and comparison methods, were used. Some of the recent experiments in this field, like Yoshida's (1962, 1964, a, b, c), give a certain amount of support to old classifications like Zwaardemaker's, and some, like those by Engen (1962), Wright and Michels (1964) and Amoore and Venstrom (1965, 1966), provide evidence for relationships between odour similarity and similarity in molecular properties like chainlength, Raman spectra and molecular shape and size. The fact however, that, in two large scale experiments by Yoshida (1962, 1964, a, b, c) and by Woskow (1968), in which similarities were analysed with a multidimensional scaling technique, by far the most predominant dimension correlated very highly with a category like "pleasant-unpleasant", which, according to Moncrieff (1966), is highly dependent upon cultural influences, indicates that a classification based on similarities reflects perhaps mainly the cultural pattern of odour preferences. If this is true, it does not seem very likely that important inferences on the nature of the transducing mechanism and on the critical feature of the odorous molecules can be made on the basis of such classifications.

In general, it is perhaps too simple to think that there exists a direct relationship between the odorous quality of a substance and the way in which the molecules of that substance affect the receptive system. That this relationship is indeed more complicated, will be shown in the next section in which anosmia, the olfactory analogue of colour blindness, is discussed.

- b. Classification of odorous substances on the basis of the "common fate" of their odorous properties under abnormal perceptual conditions.

Another way of classifying odorous substances is to group them according to the way in which the perception of their odour is affected by changes in the function of the receptive system.

If the perception of some substances is affected in the same way by such a change, whereas the perception of other substances does not share this "fate" or is affected to a much lesser degree, it can be argued that the two groups of odours stimulate different parts of the sensory system or stimulate the same parts in a different way.

The study of partial anosmias provides a good example of the conclusions that can be drawn on the basis of such "common fate" classifications. A person suffering from partial anosmia has lost (either completely or to a large extent) his sensitivity to some odours, whereas his sensitivity to other odours has remained normal. Guillot (1948 a + b) reports that some of his subjects, who were perfectly sensitive to the bitter almond odours of benzaldehyde and furfural, were completely insensitive to the bitter almond odour of cyanic acid. Nevertheless these bitter almond odours are very similar.

In the same way, a subject who could smell neither the strong musk smell of the large cycle ketones, lactones and alcohols, nor the musk odour of Ruzicka's steroids, was perfectly sensitive to the three nitro-musks (musk-xylene, musk-ketone and ambermusk).

Again these odours are very similar and even an experienced observer may have considerable difficulty in distinguishing between the odorous qualities of these three groups of musks.

From these data Guillot draws the conclusion that there exist different mechanisms for the perception of certain odours, which all result in the perception of the same quality, but which are activated by different types of stimuli. In his own words: "The identity of the olfactory sensation is not a criterion for the identity of the sensory and psychophysiological mechanisms involved". If this is true, it is not very surprising that classification on the bases of subjective similarity judgement does not provide a good starting point for the selection of the critical feature of the olfactory stimulus. Since each class of such a classification may contain a number of substances which affect the receptive system in a different way, looking for resemblances in the properties of the molecules of these substances may even be misleading. Amoore (1967) recently described a method for using anosmia in defining primary odour modalities. He distinguishes between partial anosmics, who show a reduced sensitivity to a number of qualitatively different odours and

specific anosmics, who seem to be defective for one odour only or for a small group of very similar odours.

According to Amoore, whose steric odour theory implies the existence of a number of primary receptor types, differing in shape and size in order to fit different odorous molecules, these specific anosmics miss one type of receptor. The odours of the substances which these anosmics do not perceive at all, because, again according to Amoore, the molecules of these substances fit only the specific type of receptor the anosmics are missing, are called primary odours.

Amoore found that about 2% of a group of 400 subjects were specifically anosmic to the sweaty odours of some carboxylic acids and especially to that of iso-valeric acid. From this fact he concluded that this last compound closely approached the ideal molecular configuration for eliciting a sweaty primary odour. This conclusion may still be open to some doubt, however, since it rests heavily on Amoore's theoretical assumptions.

Although the steric odour theory is supported by some experimental data (Johnston (1963), Johnston and Sandoval (1962), Rubin, Apotheker and Luttmer (1962), Amoore and Venstrom (1967, 1966) and Döving (1967), it has also frequently been criticized (Fullman (1963), Döving (1965) and Köster (1965)) and it is still far from being generally accepted.

Although the study of partial and specific anosmia has certainly contributed to olfactory theory, as a scientific tool it has certain disadvantages. Usually very little is known about the nature of the functional change in the receptive system and this functional change can in no way be manipulated as an independent variable. This handicap has been overcome in another type of "common fate" investigation, the study of adaptation and cross-adaptation phenomena. In adaptation experiments changes in the sensitivity can be controlled to a large extent and can be invoked at will by the investigator. Adaptation is a basic phenomenon in all the senses. Upon prolonged stimulation the sensitivity of the receptive system decreases. In cross-adaptation experiments the specificity of this sensitivity decrease is investigated and used as a basis for classification. The usual procedure in such experiments is to measure first the subject's sensitivity to two different substances A and B. After the olfactory thresholds for these substances have been determined independently, the subject is adapted to stimulus A for a given period of time, and the influence of this adaptation period on the threshold for stimulus B is determined directly afterwards. If the threshold of B is raised by previous adaptation to A, it is

assumed that the stimuli A and B both affect a certain part of the receptive system and that the loss of sensitivity to B is due to adaptation processes in that part. The substances A and B seem therefore to belong to a same class of odorous substances. If adaptation to stimulus A has no influence on the sensitivity to B, the two odorous substances seem either to stimulate different parts of the receptive system or the same parts in a different way. In that case they seem to belong to different classes of odorous substances. A number of investigators has used this method. Their work will be discussed extensively in the next chapter. (page 49).

So far, it has not resulted in a complete and new classification, but it has been used to verify older ones and to test specific hypotheses in the transducing mechanism. Ohma (1922) has tried to prove Zwaardemaker's classification with cross-adaptation and LeMagnen (1948) used it as an independent proof of Guillot's data on anosmia.

"Common fate" classification in general, either by the study of anosmia or by cross-adaptation experiments, is a very useful tool in the search for the transducing mechanism. It appears to be more relevant in its approach than similarity classification.

c. Classification of odorous substances on the basis of the differential nervous activity, evoked by their odours in parts of the receptive system.

Perhaps the most direct attack on the problem of cracking the olfactory code and understanding the mechanism of olfaction is made by the electro-physiologists. Ever since Adrian (1951) presented the first indication of spatial differentiation of the receptors in the mucosa, more and more refined recording techniques have been used to find specificity and spatial patterning of response in different parts of the receptive system.

Because of their direct importance for a solution of the problem of olfactory discrimination, these electrophysiological studies will be discussed here in some detail.

1) Differentiation of response in the olfactory bulb.

Adrian (1951, 1953, 1956) inferred from his recordings in the bulb, on which the mucosa is topically represented, that water soluble substances are more effective in the anterior parts of the mucosa, whereas oil soluble substances elicit stronger responses in the posterior parts. Mozell and Pfaffmann (1954), Moulton and Beidler (1967) and Moulton (1965, 1967), working along the same

lines, demonstrated both temporal and spatial differentiation in the activity of the bulb. Again differences in response activity between the anterior and posterior parts of the bulb were found to be relative rather than absolute. Döving (1964, 1965, 1966, 1967) using a vast array of odorous stimuli, studied the activity of bulbar neurons in the frog. For each of the neurons investigated, he recorded whether its activity was raised (excitatory response), was diminished (inhibitory response) or was left unaffected (zero response) by each of a group of olfactory stimuli. A simple chi square method then made it possible to calculate whether the ways in which the different odorants in the group affected the activity of the neurons were independent or not. Instances of both dependency and independency were found. Leveteau and MacLeod (1969), working with rabbits, investigated specificity in the olfactory glomeruli. The responses (slow potentials) of each of 96 glomeruli to twelve different odorous stimuli were recorded.

All the glomeruli responded to one or more of the odorous substances, and nine of them responded indiscriminately to all twelve stimuli. Although all degrees of selectivity seem to occur, the distribution of the glomeruli according to the number of stimuli to which they respond appears to be bimodal with peaks at 33% and 60% of the stimuli. Chi-square values, indicating the amount of dependency, c. q. independency, in the ways in which the odorous stimuli affect the glomeruli, were calculated by Leveteau and MacLeod. The values of Chi-square found range from 11.3 to 0.0 (df = 1).

This indicates that here again both dependency and independency in the ways in which the odorous substances affect the glomeruli, are found.

2) Differentiation of response in the olfactory nerve and the olfactory epithelium.

Mozell (1964a) recorded simultaneously from two widely separated branches of the olfactory nerve of the frog. For each of a number of odorous stimuli a different response magnitude ratio between the two branches was found, indicating some form of spatial localization. Differences in the time lapse between the two nerve responses were also shown to exist, when different chemicals were used.

In a later study (1964b) Mozell demonstrated, by changing the direction of the airflow and noting the resulting shifts in the response ratios found, that spatial separation of vapours by adsorption is probably an important part of the olfactory analysing mechanisms. Ottoson (1956, 1958), in his extensive study on the frog, investigated the relationship between physico-chemical properties

of odorous substances and their stimulating effectiveness as measured by the magnitude of the electro olfactogram (EOG) (a slow potential reflecting a massive response of the olfactory epithelium). Stimulating effectiveness increased with increasing chain length up to a certain maximum in aliphatic alcohols, aldehydes and ketones. With the fatty acids this relation between chain length and stimulating effectiveness was not as clear. Furthermore it was shown that in terms of thermodynamic activities the alcohols of intermediate chain length are equally stimulating while the lower alcohols are less effective.

Shibuya and Shibya (1963) recorded single unit spikes in the olfactory epithelium of the tortoise. They reported that, when three different odorous stimuli (amyl acetate, florida orange (?!) and spike lavender (?!)) were applied to the same single unit, only a difference in the frequency of the spikes was observed, but that no great specificity could be shown.

Gesteland and others (1965) however, working with the frog, found it very easy to demonstrate specificity in single fibers of the olfactory nerve. In fact, for each pair of odorous stimuli, a single unit which responded differently to the two stimuli could be found without much trouble. These authors not only made extensive studies on the specific shapes of the electro-olfactogram (EOG) with different stimuli but also presented a large amount of information on the activity of single receptor units. Some of their conclusions will be reported here.

According to them the EOG is compounded of at least two processes that oppose each other. One of these processes tends to bring the potential back to a certain level or to drive it positive, the other displaces the potential in the negative direction.

The influence of the first process on the potential seems to be dependent on the distance of the potential to its baseline.

The more negative the potential is at a given moment as the result of previous stimulation, the larger will be the positive swing caused by the first process upon renewed stimulation. The extent to which each of the two processes contributes to the potential differs from one odorous stimulus to another.

In so far as the activity of single receptor units is concerned, Gesteland c. s. showed that the fibers of the olfactory nerve can react in four different ways. They can be inhibited by some odours, excited by others, left unaffected by a third kind and may sometimes show a response in which their noisy baseline activity becomes more rhythmic. So far, not enough odorous substances have been used in these studies to group them effectively according to the ways in which they affect the receptor units.

Schneider and his group (1963, 1964) and Dethier (1962) have described many cases of response specificity found in single unit recordings in insect antennae. They used terpeneol, iso-safrole, phenyl ethyl alcohol, cinnamaldehyde, phenyl ethyl acetate, nitrobenzene, oil of clove (eugenol), cinnamic alcohol and other odorous substances.

Boeckh (1965) reported on the stimulative effects of a number of substances on a well defined single unit in *Bombix Mori*. There again the selectivity and functional specificity of a single unit were demonstrated.

From this survey it will be clear that the electrophysiological methods have already contributed much relevant information on specificity in the olfactory system and that along this most promising line of attack much more is to be expected.

Three different ways of classifying odorous substances have been described here, but only one of them - judging qualitative similarity of odours - has resulted in complete odour classifications. As was shown, however, these similarity classifications have only limited relevance to the problem of understanding the olfactory transducing mechanism. The other two methods of classification - the "common fate" principle and the electrophysiological technique - are much more adequate for this purpose. Unfortunately, workers in these fields, including the present author, have nearly always chosen their odorous substances in a rather haphazard way. If, however, a more systematic approach would be chosen in the future and if more investigators using different techniques would cooperate in using the same substances, a solution for the fundamental problems of olfactory discrimination might be found.

1.5. AIM AND OUTLINE OF THIS THESIS

It is the aim of this thesis to provide an exploratory contribution to the knowledge of recovery of olfactory sensitivity after adaptation and cross-adaptation to stimuli of low subjective intensity and to investigate the possibilities of classifying odorous substances on the basis of the cross-adaptational relationships between them. The method will be a psychophysical one and will therefore - by nature - be limited in the answers it can give. At best it may provide a number of general rules and some hypotheses on the underlying

mechanisms to be tested by the electrophysiologists.

It is unlikely that enough data can be collected to provide a valid full scale classification of odorous substances.

Chapter 2 will be devoted to a discussion of olfactory adaptation.

A description of the phenomena of adaptation, recovery and cross-adaptation will be given on the basis of a historical survey of the literature.

The apparatus and the methods used in the experiments treated in chapter 4 and 5 will be described in chapter 3. Some technical and methodological problems will be discussed on the basis of small control experiments in the context of chapter 3.

Chapter 4 has been reserved for experiments on adaptation and recovery.

In all experiments in this chapter the same odorous substance was used both as the adapting stimulus and as the stimulus for testing the sensitivity of the subject (self-adaptation).

Experiments on cross-adaptation, in which the adapting stimulus and the test stimulus consist of different odorous substances, are discussed in chapter 5. Two sets of seven substances have been used in these experiments. The experiments have been performed before most of the experiments described in chapter 4, but they are described later, because the results of the adaptation experiments given in chapter 4 have a certain relevance for the interpretation of the cross-adaptation experiments.

Chapter 6 is a summary.

CHAPTER 2.

ADAPTATION AND RECOVERY OF THE SENSE OF SMELL

2.1. SENSORY ADAPTATION

When a sensory system is exposed to a stimulus, its sensitivity may decrease. This phenomenon is usually called sensory adaptation. An understanding of the processes underlying it is of fundamental importance for an understanding of the functioning of sensory systems.

As Irene Martin (1964) points out, a number of restricted laws and theories have been developed for specific forms of sensory adaptation, but no quantitative laws are known which can be applied to all forms. Nevertheless, some general features of sensory adaptation phenomena should be mentioned here as a background to a more specific discussion of adaptation phenomena in the sense of smell.

Under continuous stimulation the sensitivity of a sense organ drops rapidly at first and then levels off gradually to a new degree of sensitivity which is maintained as long as the stimulation lasts. The point on the intensity scale at which this new level of sensitivity is reached is dependent upon the intensity of the stimulus to which the sense organ is exposed. The higher the intensity of this stimulus, the larger the decrease in sensitivity. Since the threshold intensity (or just perceptible intensity) corresponding with the new level of sensitivity sometimes lies above the intensity of the stimulus used, complete adaptation (i. e. reaching the new level) may result in a cessation of the perception of the stimulus. The time necessary for complete adaptation or for cessation of the perception of the stimulus is dependent upon the intensity of the stimulus. The higher the intensity of the stimulus, the longer it takes

to adapt the sensory system completely.

After cessation of the stimulus itself, the original sensitivity of the sensory system is gradually restored. This phenomenon is called recovery and its temporal curve has the same negatively accelerated shape as the one for adaptation. The time necessary for regaining the original threshold is dependent upon the level of previous adaptation.

A schematic example of adaptation and recovery curves for two stimuli of different intensity is given in fig. 2.1.

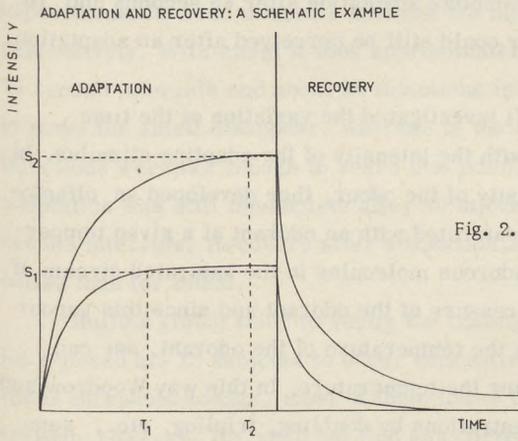


Fig. 2.1. Schematic example of the adaptation and recovery curves for two stimuli of different intensity (S_1 and S_2). Indicated are the points in time (T_1 and T_2) at which the threshold becomes higher than the adapting stimulus. (Complete adaptation)

2.2. OLFACTORY ADAPTATION

Olfactory adaptation is a well known phenomenon. Upon entering a room, a person may at first be overwhelmed by an odour, but his sensitivity will soon decrease and after a few minutes in that room he may not even smell the odour anymore. This is an example of olfactory adaptation.

It is the object of the first part of this chapter to give a description of adaptation phenomena based on a historical survey of previous investigations in olfaction. After this descriptive part, the processes underlying these phenomena will be discussed in a separate section.

a. The adaptation time necessary for cessation of the smell sensation.

Aronsohn (1886) was probably the first to do systematic research on olfactory adaptation. In 1886 he described a series of experiments on "fatigue

and recovery of the olfactory nerve", in which he measured the time necessary for complete disappearance of the olfactory sensation under continuous stimulation. He used eight different substances in undiluted form as adapting stimuli and the times he found ranged from 50 seconds to 12 minutes. The times found for a dilution of eau de cologne were considerably shorter than those found for the same substance in undiluted form. For camphor, which is a substance used by most investigators, he measured times from 5 to 7 minutes.

Vaschide (1902) used camphor, ether and ammonia as adapting substances. For ether and ammonia he found complete adaptation after 85 seconds and 10 minutes respectively, but camphor could still be perceived after an adaptation period of 30 minutes.

Woodrow and Karpman (1917) investigated the variation of the time required for complete adaptation with the intensity of the adapting stimulus. In order to control the physical intensity of the odour, they developed an olfactometer in which a stream of air is saturated with an odorant at a given temperature. Since the concentration of odorous molecules in the saturated stream of air is proportional to the vapour pressure of the odorant and since this vapour pressure is in turn dependent upon the temperature of the odorant, one can change the concentration by changing the temperature. In this way Woodrow and Karpman prepared series of concentrations by doubling, tripling, etc., some rather arbitrarily chosen concentration (indicated as 1 x in fig. 2.2) of each of the adapting substances. Fig. 2.2. summarizes the results they obtained for propanol, camphor and naphthalene respectively.

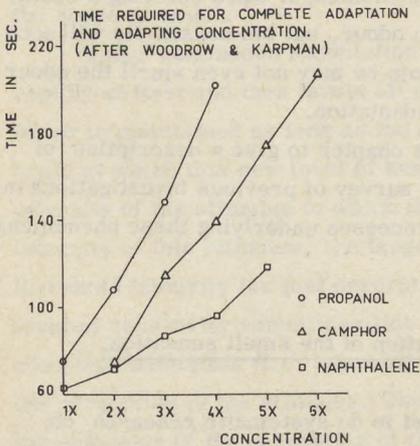


Fig. 2.2. Results of Woodrow and Karpman (1917) on the time necessary for a cessation of the smell sensation (complete adaptation) X = arbitrary concentration.

As the curves in this figure indicate, there seems to exist a linear relationship between the time required for complete adaptation and adapting intensity.

Woodrow and Karpman expressed this relationship with the formula $t = K + k \cdot I$, in which t represents the adaptation time in seconds, K and k are determinable constants and I is the physical intensity.

Elsberg (1935) studied the cessation of the smell sensation by giving repeated injections of odorous air in the nose. The odorous substances used were citral and coffee, both presented at threshold concentration. In his experiments he used intervals between the injections of 15, 20 and 25 seconds respectively. With citral it took approximately 10 injections in the case of the 15 second intervals and about 20 injections in the case of the 20 second intervals to make the smell disappear, whereas in the case of the 25 second intervals 30 injections were not enough to reach this point. With coffee as the stimulus, adaptation was still incomplete after 30 injections, even in the case of the 20 second intervals. Recovery after adaptation seemed therefore to be faster for coffee than for citral.

Mullins (1955) tried to verify the findings of Woodrow and Karpman. He exposed his 23 subjects to odour concentrations which ranged from 1 to 100 times threshold dosage, most of them lower than 20 times threshold concentration, however. He could not find any correlation between the time required for disappearance of the smell sensation and the adapting concentration, but he did find differences in "odor duration" between his three odorous substances, n-butane, n-butanol and pentadecanolide.

He supposes that the results of Woodrow and Karpman were partly due to the fact that they used a very low flow velocity of 1 liter per minute. According to Mullins, this might have resulted in an increase - with time - of the concentration at the olfactory epithelium, since a portion of the odorous material could have been absorbed by the mucous membranes of the nose before the epithelium was reached. It is hard to see why Mullins uses this as an argument, though. Actually, since the increase in concentration would last till the membranes are saturated and equilibrium is reached and since such an equilibrium would be reached earlier with a high concentration than with a low one, it seems that this argument could on the contrary be used to argue that the "odor durations" found by Woodrow and Karpman for low concentrations were relatively too long compared with the ones for higher concentrations. This would mean that the true effect was even more marked than the one found by Woodrow and Karpman. To carry the discussion a step further, the argument could also be

used to explain some of Mullins' own data. He admits having had a technical problem with pentadecanolide, because it showed a tendency to adsorb on glass. This might indicate that the times found by Mullins for low concentrations of pentadecanolide were relatively too long, thus obscuring a true relationship between "odor duration" and adapting concentration. One other point should be mentioned that may explain some of the differences between the results of Mullins and of Woodrow and Karpman. The last two gave a special training to their subjects, whereas Mullins seems to have worked with rather unexperienced subjects. He reports that they had difficulty in deciding when olfactory stimulation had ended and merely trigeminal stimulation was left. It was for this reason that he introduced pentadecanolide which has no trigeminal effect. Nevertheless, the use of inexperienced subjects may have reduced the reliability of his results.

Stuiver (1958), in his thesis, not only gave an excellent survey of the literature on olfactory adaption and recovery, to which the present author is much indebted, but made a substantial contribution to the knowledge of the subject by reporting on a large number of experiments carried out with unprecedented precision.

The stimulus concentrations in his experiments were prepared by means of an olfactometer, similar to the one used by Woodrow and Karpman, but more precise and more flexible as far as rapid changes of concentration are concerned. A detailed description of a modified form of this olfactometer will be given in chapter 3.

In his experiments on the "adaptation time required for cessation of the smell upon prolonged stimulation" (A. T. C. S.), Stuiver used two substances, d-octanol and m-xylene. The concentrations of the adapting stimuli ranged from 1 time threshold concentration to 220 times threshold concentration.

Stuiver discusses largely the necessity of expressing the adapting concentration in the absolute threshold concentration. He states that only when the intensity scale is based on the individual absolute threshold as a unit, one can expect to find the same A. T. C. S. for equal adapting concentrations in different individuals. He criticizes Aronsohn and Vaschide for not meeting this requirement.

Although he is right in denouncing the insufficiency of their stimulus control (one used undiluted substances, the other expressed the intensity in the amount of odorous substance dissolved), it should be remembered that the validity of his own argument for using individual thresholds as the unit, is limited by the fact that there might be individual differences in the rate at which the adaptation

time changes with change in concentration. In fact, the individual results of Woodrow and Karpman's subjects, (let alone the results of Mullins' inexperienced ones) do provide some indication of such individual differences. The results of Stuivers' experiments on the adaptation time required for cessation of the smell sensation upon prolonged stimulation are shown in fig. 2.3

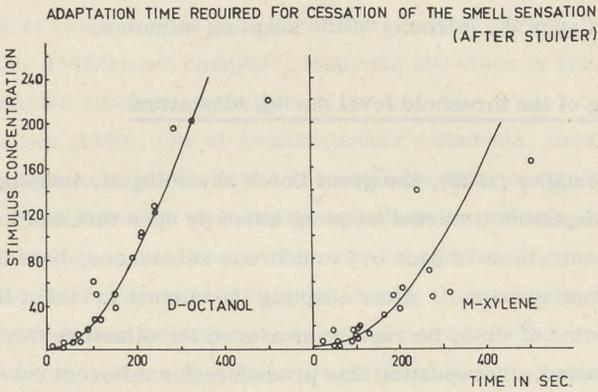


Fig. 2.3. Results of Stuiver (1958) on the time necessary for a cessation of the smell sensation. Stimulus concentration in number of times unadapted threshold.

According to Stuiver the best fitting curves are given by $t = 20 \sqrt{C - 1}$ and $t = 30 \sqrt{C - 1}$ for d-octanol and m-xylene respectively, where t is adaptation time in seconds and C is the adapting concentration expressed in number of times threshold concentration.

Although the relationship between A. T. C. S. and adapting concentration found by Stuiver is obviously not a linear one, his results reconfirm Woodrow and Karpman's findings in that they show that there exists such a relationship.

Furthermore, as Stuiver remarked in the discussion of his results, the curve for d-octanol is approximately linear, when adaptation times larger than 100 seconds are required and this is in accordance with the linearity found by Woodrow and Karpman in this range of times (60 - 220 seconds).

There remain, however, differences in the rate at which the adaptation times increase with increasing adapting intensity.

Stuiver, after some ingenious calculations, estimates that the increase in concentration needed in his own experiments to provoke the same increase in adaptation times as in Woodrow and Karpman's experiments, is at least twice as large.

These differences may have been caused by the use of different odorous substances, as Stuiver himself supposes.

In general, it is clear that these studies of the time necessary for complete adaptation or for cessation of the perception of the stimulus in olfaction yield the same sort of results as were described in the general section on sensory adaptation. In olfaction the time necessary for complete adaptation is also dependent upon the intensity of the adapting stimulus.

b. The raising of the threshold level during adaptation.

Zwaardemaker (1925), the great Dutch physiologist, investigated the influence of adaptation time and adapting intensity upon threshold raising. He used two concentrations of each of two odorous substances, benzoin and india rubber, as adapting stimuli. After adapting the subject to one of these smells for a given period of time, he rapidly measured the olfactory threshold for the substance involved. By repeating this procedure for different concentrations and for different adaptation times, he obtained the data shown in fig. 2.4. In this figure, the threshold concentrations as well as the concentrations are expressed in "olfactics", one "olfactie" being the normal (i. e. unadapted) threshold concentration for a particular odorous substance and a given subject.

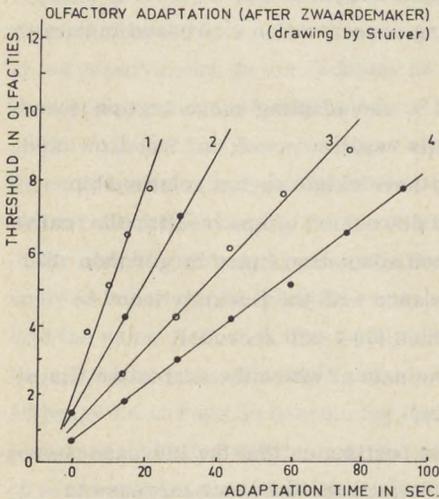


Fig. 2.4. Results of Zwaardemaker (1925) on the raising of the threshold during adaptation. Curves 1 and 2 = two different adapting concentrations of benzoin (9 and 3.5 olfactics) Curves 3 and 4 = two different adapting concentrations of India rubber (14 and 10 olfactics).

As the curves of fig. 2.4. indicate, the threshold rises with an increase of both the duration and the intensity of the adapting stimulus.

Furthermore it will be evident that adaptation rate may vary from one odour to another. Since the curves are linear, it seems reasonable to assume that the level of complete adaptation has not yet been reached in these experiments. Whether there exists, for these substances, such a level at which the threshold reach a constant value can not be concluded from these curves.

Vaschide (1902) used camphor, ammonia and ether in similar experiments and obtained analogous results.

Hermanides (1909), one of Zwaardemaker's students, used isoamyl-acetate, nitrobenzene, valeric acid and scatole as odorous substances and measured reaction times as an indication of adaptation effects. Reaction times were found to be longer as a result of previous adaptation.

Backman (1917) adapted his subjects during 15 minutes to a known concentration of an odorous substance and then measured the threshold. Although the threshold found was nearly always proportional to the adapting concentrations used, the minimum perceptible concentration was for some substances considerably lower than the adapting concentration. Backman considered this to be a confirmation of his theory that the sense of smell was stimulated by a change of concentration, either a positive or a negative one, rather than by the mere presence of a constant concentration. Stuiver however, in his discussion of these data (1958), agrees with Zwaardemaker who explains the fact of these relatively low minimum perceptible concentrations by assuming that in Backman's experiments sufficient time had elapsed between the end of adaptation and the threshold measurement, to allow for considerable recovery of sensitivity.

Komuro (1922), in Zwaardemaker's laboratory, investigated the influence of the intensity of the adapting stimulus on the olfactory threshold for guaiacol, caproic acid and terpeneol. He used four different concentrations of each of these substances as adapting stimuli and presented them during five deep inspirations (total duration about 1 minute) to his subject. After this he determined the threshold with Zwaardemaker's olfactometer. The results given in fig. 2.5. show the rising of the threshold with increasing adapting intensity. Unfortunately, since the threshold measurements for these substances took rather long (about 3 minutes for terpeneol and about 1 minute for the others), here, as in Backman's experiments, some recovery must have taken place during the threshold determination.

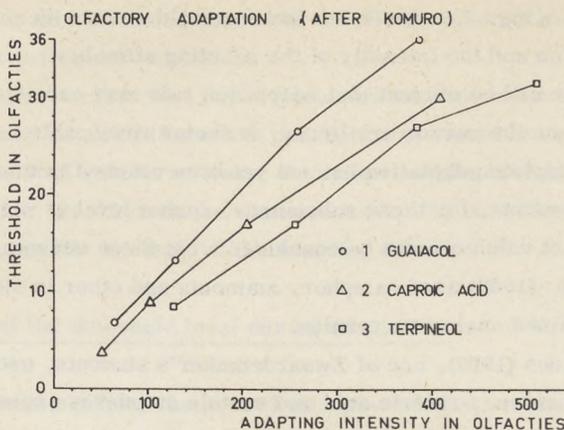


Fig. 2.5. Results of Komuro (1922) on the influence of the intensity of the adapting stimulus on the olfactory threshold.

1 olfactie = normal unadapted threshold concentration.

Adaptation time: 5 deep inspirations.

If this is the case the threshold found by Komuro would be too low compared with the true ones.

Cheesman and Mayne (1953) and more recently Cheesman and Townsend (1956) published the results of adaptation experiments with four substances, dioxan, isopropanol, cyclopentanone and cyclopentanol. They measured the influence of adaptation at different concentrations of the adapting stimulus, using a sniff-bottle method. The adapting stimulus was presented during one deep inhalation only and the adapting concentrations were above threshold value. The results obtained indicate that the threshold of an odour varies in such a way that the logarithm of the threshold is a linear function of the logarithm of the adapting concentration.

The work of Cheesman and his co-workers will be discussed more extensively below in the section devoted to cross-adaptation.

Moncrieff (1957) also investigated the adapting effect of one deep inhalation of an odour on its olfactory threshold. As adapting stimuli he used 22 undiluted odorous substances and series of dilutions of acetone, ethyl mercaptan and isopropanol.

He determined threshold concentrations under two conditions (I, II). Under condition I the subject took a sniff of the undiluted odorant just previously to the threshold determination. The threshold concentration obtained under this condition was indicated as C_1 .

Under condition II the subject only took a sniff of the diluent used in preparing the test stimuli, just before the threshold determination. The threshold concentration thus obtained, called C_2 , had not been effected by previous adaptation.

From these two threshold concentrations, Moncrieff calculated a coefficient $I = C_1 / C_2$, which he considered to be an indication of the intensity of the odour. According to him, the results arrived at seemed to be in good agreement with "everyday experience of odour intensities".

Translated into adaptational terms these findings would indicate that the more intense adapting stimulus has a larger adaptational effect, even when different substances, and not just different concentrations of one substance, are compared.

Stuiver (1958) varied both adaptation time and adapting intensity in his work on the rising of the threshold as a function of adaptation. He used d-octanol and m-xylene as adapting stimuli. His results for d-octanol are shown in fig. 2.6. With m-xylene analogous results were obtained.

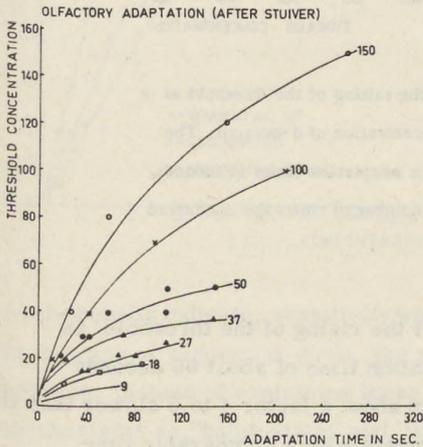


Fig. 2.6. Results of Stuiver (1958) on the raising of the threshold during adaptation to d-octanol. The numbers at the curves indicate the concentration of the adapting stimulus in number of times the unadapted threshold.

As will be seen from these curves, Stuiver's results do not agree with the linear relation between the raised threshold and adaptation time found by Zwaardemaker. Stuiver claims rightly that these curves, which allow for a continuous transition from a rising of the threshold to a constant level of complete adaptation, are probably nearer to the truth. It should be realized, however, that the difference is not such a very great one, as Zwaardemaker used concentrations which were about as low as Stuiver's lowest ones. In that

low range of concentrations even Stuiwer's own curves approach linearity. The results shown in fig. 2.6. can also be used to plot the rising of the threshold for a constant adaptation time as a function of the adapting concentration. Represented in this way (fig. 2.7.) Stuiwer's results can be compared with the curves found by Komuro (fig. 2.5.).

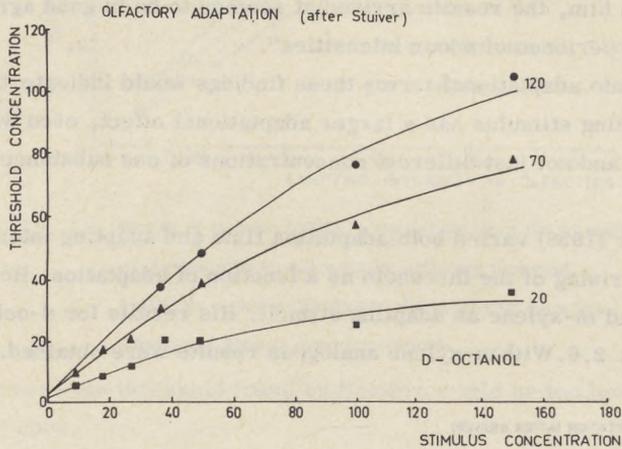


Fig. 2.7. Results of Stuiwer (1958) on the raising of the threshold as a function of the adapting concentration of d-octanol. The numbers at the curve indicate adaptation times in seconds. Concentrations are given in number of times the unadapted threshold.

The curves have about the same shape, but the rising of the threshold as determined by Komuro, who used an adaptation time of about 60 seconds (Stuiver erroneously quotes 15 seconds), is about a factor 4 to 5 slower than the rising of the threshold in Stuiwer's experiments with a comparable time. This difference could, at least in part, be explained by the fact that Komuro's thresholds may have been too low as a result of recovery during threshold measurement. Since this effect would be much stronger for high adapting concentrations than for low ones, the slopes of the curves would indeed be affected. Stuiwer hardly allowed any time for recovery at all. Besides, the two authors used different substances in their experiments.

Pangborn, Berg, Roessler and Webb (1964) quite involuntarily provide another good example of olfactory adaptation. They made a methodological

study of methods of threshold determination and compared the results of three forms of stimulus presentation: sequential-up, sequential-down and randomized. In the first method, each following stimulus is more intense than the one preceding it, the first one being well below the threshold level. In the second method, each following stimulus is less intense than the one preceding it, the first one being well above the 100% detection level. In the third method, stimuli of different intensities are presented in a random order.

The results for 2-heptanone obtained by these three ways of presentation are shown in fig. 2.8.

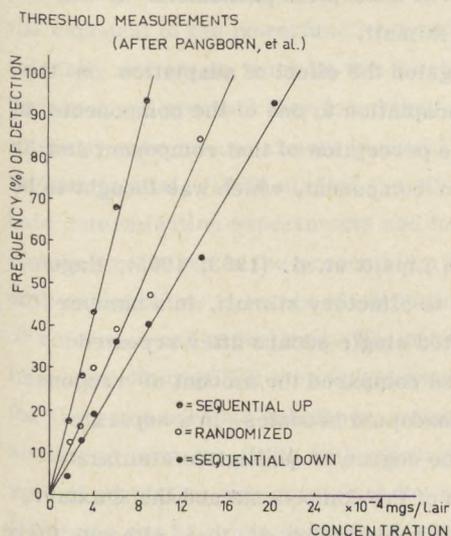


Fig. 2.8. Results of Pangborn et al. (1964) obtained in threshold experiments with three different methods of stimulus presentation: sequential up, randomized and sequential down.

As the results indicate, sensitivity was highest in the case of sequential-up and lowest in the case of sequential-down, the randomized order taking an intermediate position. Instead of explaining these results by invoking such vague psychological mechanisms as "habituation" and "anticipation", these results can be explained by adaptation since the strength of the preceding stimulus and therefore of its adapting effect is minimal with the sequential-up and maximal with the sequential-down method.

Ironically enough, Pangborn, in a recent survey of the literature on olfaction (1965), quotes this article as a piece of conclusive evidence for the absence of adapting effects provoked by stimuli of near threshold concentration. In fact, she refers to another experiment mentioned in the same article, in which stimuli of a near threshold concentration (+) and blank stimuli (-) were pre-

sented in a random order with 15 second intervals. In order to study the effect of a preceding stimulus on the olfactory sensitivity, the percentages correct response to the second members of two stimulus orders ++ and -, i. e. odorous stimulus after odorous stimulus and odour after blank, were compared. The percentages found were 84.8 for the ++ order and 64.9 for the -+ order, indicating that the stimulus was perceived better, when the preceding stimulus contained odour. As will be seen later, however, (page 87), this astonishing result, which seems to contradict an adaptation hypothesis, is almost certainly due to the fact that the concentration of the second odorous stimulus in the ++ order was considerably higher as a result of adsorption phenomena in the olfactometer used for presentation of the stimuli.

Engen and Lindström (1962) investigated the effect of adaptation on the perception of odour mixtures. Previous adaptation to one of the components of the mixture resulted in a decrement of the perception of that component and in an increment in the perception of the other component, which was thought to be the result of a contrast effect.

In later studies, carried out together with Lipsitt et. al. (1963, 1965), Engen studied behavioural reactions of neonates to olfactory stimuli. In a number of very interesting experiments they presented single odours after repeated adaptation to a mixture of these odours and compared the amount of response obtained with the amount of response in unadapted neonates. In a separate experiment with adults they determined the degree of qualitative similarity between the components and between each of the components and the mixture. The results of the experiments with the neonates indicated that, although there was considerable decrement in the response to the successive presentations of the mixture, only the response to the component that resembled the mixture most was reduced after the adaptation series, whereas the response to the other component was not affected.

According to Engen c. s. this seemed contradictory to an explanation in terms of pure sensory adaptation, because in that case both components should have been affected.

Stone (1966) recently reported some experiments on adaptation. His subjects were continuously exposed to a supra-threshold concentration of n-propanol and were asked to indicate the intensity of the stimulus on a 10-point rating scale after fixed intervals of 5, 10 and 15 seconds respectively in different experiments.

Adaptation was shown to be rapid during the first 90 seconds and then to slow

down considerably.

Ekman, Berglund, Berglund and Lindvall (1967) studied adaptation to a supra-threshold concentration of hydrogen sulphide, using a cross-modality matching method for the scaling of the intensities. They found that an exponential function of the general type $R = a + b/c^T$, in which R is the perceived intensity and T is the time measure, whereas a, b and c are individual constants, could be fitted with reasonable agreement to the curves of all of their eight subjects, except one.

Cain and Engen (1969) studied olfactory adaptation at supra-threshold intensities using magnitude estimation. They were able to show that adaptation increases the exponent of the powerfunction and that the increase is dependent upon the intensity and not so much on the duration of the adapting stimulus. Using propanol and pentanol they found that adapting stimuli of matched subjective intensity gave rise to almost identical selfadapting effects.

Steinmetz et al. (1969) studied the effect of interspersed blank stimuli in threshold determination experiments and found that thresholds were lower if more blanks were given in the presentation series. They accounted for this result with explanations in terms of adaptation effects, maintenance of internal frame of reference and expectancy. The substance used was methyl isobutyl ketone. In a later study (1970) they investigated adaptation and recovery (see page 48) for the same odorous substance, using threshold determination and category scaling procedures. With both psychophysical procedures they found that the rate of adaptation was greater at the higher of their two adapting concentrations (10 times and 20 times the individual thresholds of their two subjects).

In a third study these authors (Pryor et al. 1970) tried to overcome some of the difficulties encountered with the use of the category scale and the method of threshold determination. They used an unstructured magnitude estimation procedure to avoid problems with shifts in the position of the reference standard on the internal scale of the subjects and they gave only one test trial after each adaptation period to avoid problems with partial recovery during the test periods. With adapting concentrations of four, ten and twenty times the subjects' individual threshold concentrations, they found in the magnitude estimation study somewhat similar decreases in subjective intensity over time as in the category scaling experiments reported earlier, but the fact that for the higher concentrations the rate of decrease of the magnitude estimates was lower than the rate of decrease in the category scaling experiment, casts some doubt on the greater reliability of the unstructured magnitude estimation procedure with regard to

maintenance of the internal frame of reference of the subject. This last point is further illustrated by the fact that the estimates given for the stimuli of the highest concentration after complete recovery tended to be higher than the estimates given for these same stimuli at the onset of adaptation. Such shifts of the internal frame of reference provide a serious handicap in the use of scaling methods for the assessment of adaptation effects.

Like Cain and Engen (1969) and Cain (1970), these authors demonstrated that the exponents of the power functions obtained in magnitude estimation experiments increase with increasing adaptation.

With regard to the adaptation data collected with the threshold measurement procedure by Steinmetz et al., it should be noted that the times necessary to reach an asymptotic level of adaptation (or complete adaptation in the case of one of the subjects) were at least twice as long as the times found by Stuiver (1958) in his experiments with d-octanol and m-xylene.

This low rate of adaptation may of course be typical for methyl isobutyl ketone, but it may also be that adsorption artefacts, which seem not uncommon in the Stone olfactometer used by Steinmetz, have influenced the results. As was explained earlier (see page 40), such artefacts would lead to a slow rise of the concentration presented to the subject. In view of the extraordinary finding that recovery was faster than adaptation in these experiments (see page 48), this last explanation deserves some attention.

In general, the data reported in this section on adaptation in the sense of smell, are in good agreement with the description of general features of adaptation phenomena given in the first section of this chapter.

In olfaction too, the level of sensitivity at a given moment during adaptation is dependent upon both the duration and the intensity of the adapting stimulus. Furthermore, the decrease in olfactory sensitivity follows a negatively accelerated course with time, like in most other senses.

c. Recovery of the olfactory sensitivity after previous adaptation.

Aronsohn (1886) measured the amount of "recovery of the olfactory nerve" by comparing the times necessary for cessation of the smell sensation, determined after a fixed recovery period had been allowed since the last adaptation trial, with the same times obtained without previous adaptation. He used coumarin and eau de cologne as adapting stimuli and came to the conclusion that even after an interval of 3 minutes the sensitivity to these substances had

not yet been completely restored.

Since the maximal times necessary for complete adaptation with coumarin and eau de cologne were 120 and 65 seconds respectively, it appears that adaptation is a much faster process than recovery.

Elsberg (1935), in his experiments on recovery of the olfactory sensitivity after adaptation, used coffee and citral as adapting stimuli and presented them at a constant concentration for 30, 60, 120 and 180 seconds. He also varied the rate at which the stimulus was injected into the nose of the subject and he compared the effects of bilateral and unilateral injection.

After cessation of the stimulus, he measured the time necessary for complete recovery of the sensitivity by giving every 30 seconds a short injection of the subject's previously determined threshold concentration. These measurements were made either birhinally or monorhinally on each side of the nose. The moment corresponding with the first of three successive positive responses to the threshold concentration was used for calculating the recovery time or "duration of the olfactory fatigue" as Elsberg called it. In his survey of the research on recovery, Stuiver (1958) criticizes the term "duration of the olfactory fatigue" as being misleading. His objections are irrelevant however, since the argumentation shows that he has misunderstood Elsberg's experimental procedure. Some of Elsberg's results on monorhinal fatigue are represented graphically in fig. 2.9. and fig. 2.10.

They show the increase of the "duration of the olfactory fatigue" with increasing adaptation time at two rates of injection for coffee and citral respectively.

RECOVERY TIME AFTER DIFFERENT ADAPTATION TIMES
(AFTER ELSBERG)

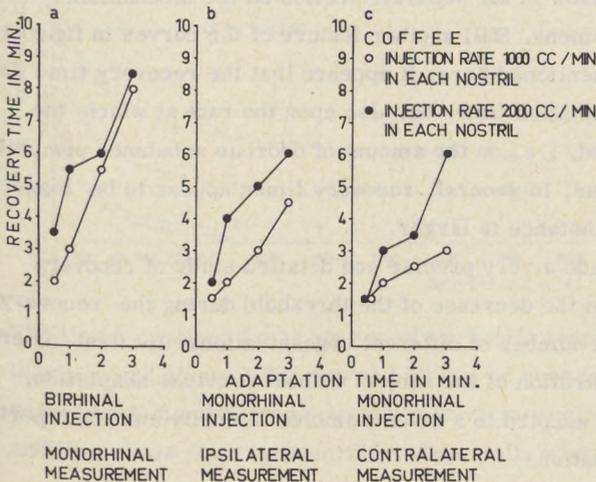


Fig. 2.9. Results of Elsberg (1935) obtained in experiments on recovery after different adaptation times and different injection rates. Injection of the adapting stimulus on both sides of the nose (birhinal) or on one side only (monorhinal). Measurement with a threshold stimulus always monorhinal at either the adapted side (ipsilateral) or the non-adapted side (contralateral) of the nose. Odorous substance: coffee.

RECOVERY TIME AFTER DIFFERENT ADAPTATION TIMES
(AFTER ELSBERG)

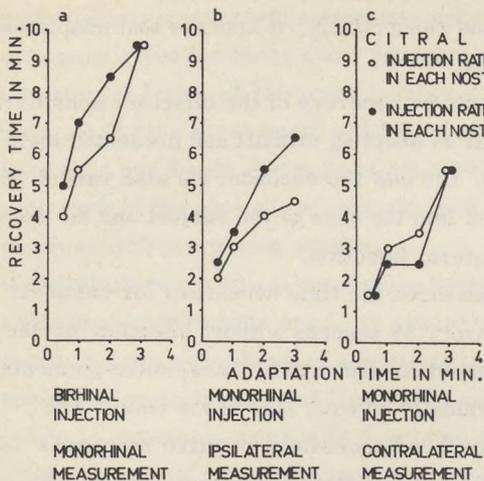


Fig. 2.10. Results of Elsberg (1935) obtained in experiments on recovery after different adaptation times and different injection rates. Injection of the adapting stimulus on both sides of the nose (birhinal) or on one side only (monorhinal). Measurement with a threshold stimulus always monorhinal at either the adapted side (ipsilateral) or the non-adapted side (contralateral) of the nose. Odorous substance: citral.

The curves in fig. 2.9a and fig. 2.10a show the effect of birhinal adaptation on the monorhinally measured recovery time. In the same way the b and c graphs of figures 2.9 and 2.10 show the effects of monorhinal injection on the recovery times of the side of the nose where the injection took place and of the contralateral side.

As would be expected, with monorhinal injection the effect appears to be strongest on the ipsilateral side of the nose. The fact that there is any adaptation at all on the contralateral side, seems to indicate that adaptation is partly due to fatigue of central parts of the olfactory nerves. This possibility will be largely discussed below in the separate section on the mechanisms underlying adaptation phenomena. Still another feature of the curves in figures 2.9. and 2.10. should be mentioned here. It appears that the recovery time is not only dependent upon adaptation time, but also upon the rate at which the adapting stimulus is injected, i. e. on the amount of odorous substance per unit time in the adapting stimulus. In general, recovery times appear to be longer if the amount of odorous substance is larger.

Stuiver (1958) has made a very precise and detailed study of recovery phenomena. He investigated the decrease of the threshold during the recovery period after adaptation to a number of different concentrations. He first determined the threshold concentration of the subject without previous adaptation. After this, the subject was adapted to a given stimulus intensity until he reported cessation of the smell sensation.

Then adaptation was stopped and the subject breathed in pure air. At intervals the subject took an inspiration from a current of odorous air of a concentration below the one he had been adapted to. As soon as this concentration was perceived, the corresponding recovery time was recorded and the concentration of the odorous air was adjusted to a lower level. This procedure was repeated several times until the threshold sensitivity had been restored. The results obtained in this way for a number of different adapting concentrations, ranging from 6 to 200 times the threshold concentration of d-octanol and m-xylene, are given in fig. 2.11 and fig. 2.12.

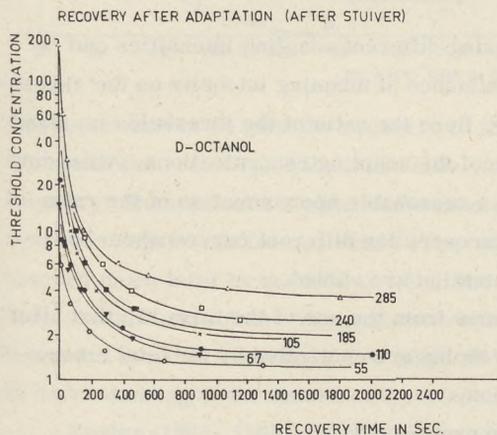


Fig. 2.11. Results of Stuiver (1958) on the relationship between the decrease of the threshold and the recovery time for various adaptation times and adapting intensities. The adapting intensities are equal to the threshold concentrations when recovery begins. At the right of the curves the adaptation times in seconds. Odorous substance: d-Octanol

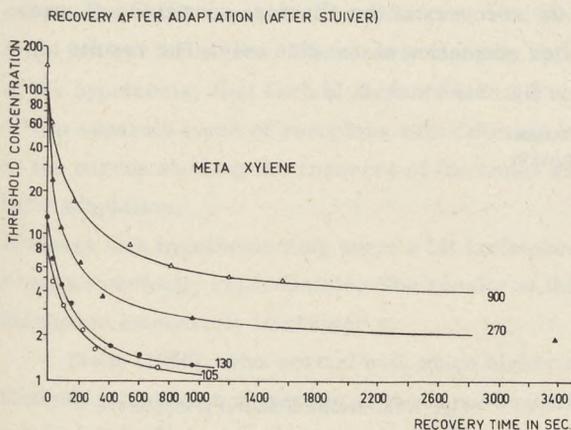


Fig. 2.12. Results of Stuiver (1958) on the relationship between the decrease of the threshold and the recovery time for various adaptation times and adapting intensities. The adapting intensities are equal to the threshold concentration when recovery begins. At the right of the curves the adaptation times in seconds. Odorous substance: m-Xylene.

The times required for cessation of the smell sensation for each of these intensities are given at the curves. As can be seen from these curves, the recovery of the olfactory sensitivity is very rapid during the first few minutes and then slows down considerably. Especially when the adapting concentrations

used are large, the decrease of the threshold during the first 100 seconds is tremendous. After this period the ratios of the thresholds become constant, according to Stuiver, who performed some experiments to study this ratio in more detail.

He adapted his subject to a fixed stimulus intensity during various adaptation times and found that the ratio of the thresholds after about 100 seconds was equal to $T^{1/6}$ or $T^{1/5}$, in which T is the ratio of the adaptation times. As Stuiver puts it, this relation essentially shows "that the increase of the threshold after more than 100 seconds of recovery increases only slowly with the previous adaptation time".

In the same way it is possible, by using different adapting intensities and a fixed adaptation time, to show the influence of adapting intensity on the thresholds after 100 seconds of recovery. Here the ratio of the thresholds is about equal to $I^{1/4}$, in which I is the ratio of the adapting concentrations. According to Stuiver a factor $(IT)^{1/4}$ would be a reasonable approximation of the ratio of the threshold after 100 seconds of recovery for different curves when both adaptation time and adapting concentration are varied.

This would indicate, as will be obvious from the use of the term IT, that after a few minutes of recovery, the thresholds are controlled by the total amount of odorous substance used for adaptation.

Stuiver confirmed this in a separate experiment.

Finally, Stuiver investigated the recovery of the olfactory sensitivity of each of the two sides of the nose after adaptation of one side only. The results of these experiments are given in fig. 2.13 and 2.14.

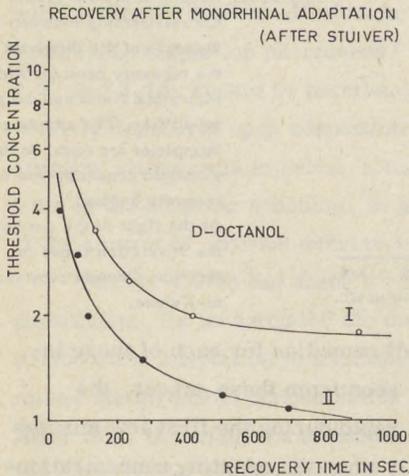


Fig. 2.13. Results of Stuiver (1958) on the recovery of one nose side when the same nose side has been adapted (I) and the recovery of the nose side which has not been adapted (II). A concentration of 50 times the absolute threshold concentration for d-Octanol was given during 100 seconds before the recovery started.

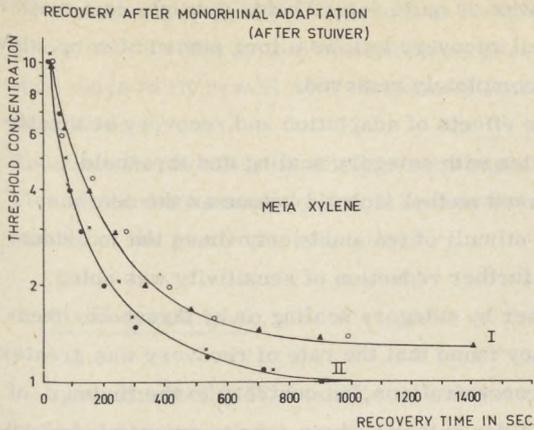


Fig. 2.14. Results of Stuiver (1958) on the recovery of one nose side when the same nose side has been adapted (I) and the recovery of the nose side which has not been adapted (II). A concentration of 70 times the absolute threshold concentration for m-Xylene was given during 80 seconds before recovery was started.

The upper curves (I) give the recovery of the adapted side, the lower ones (II) represent the recovery of the other side. As Stuiver points out, at longer recovery times there is a clear difference between the curves. The unadapted side soon regains its former sensitivity, whereas the original sensitivity is reached much later at the side at which the adaptation has taken place. These results, which are in agreement with the findings of Elsberg, will be discussed more extensively below (page 58) because of their importance for an understanding of the nature of the adaptation processes.

Köster (1965, 1968) drew attention to the irregular shape of the recovery curves found for a number of substances, like m-xylene, dioxan, isopropanol etc., but not for others. The clearly biphasic appearance of these curves led to the hypothesis, that each of them showed the super-imposed recovery curves of two separate types of receptors with different rates of recovery, in analogy to the curves showing the recovery of the cones and rods in the retina after light adaptation.

Although this hypothesis may seem a bit farfetched, the phenomenon itself remains perfectly reproducible. The results of these investigations will be discussed extensively in chapter 4.

Stone (1966), who worked with much higher concentrations and a scaling method, found some indication of the same biphasic shape in his recovery experiment with n-propanol, but did not pay attention to it. Cain and Engen (1969), using magnitude estimation showed that allowing for a recovery period of only three breathes reduces the effects of adaptation sizably. This is in accordance with the findings of Stuiver who showed that recovery is very rapid at the beginning. Whether the generalized conclusion of Cain and

Engen that "recovery from adaptation is quite rapid" holds through, is a matter of definition. After the rapid initial recovery follows a long period of very slow recovery until the sensitivity is completely restored.

Steinmetz et al. (1970) studied the effects of adaptation and recovery at threshold and at suprathreshold intensities with category scaling and threshold measurement procedures. They used methyl isobutyl ketone as the odorous substance and presented adapting stimuli of ten and twenty times the individual threshold concentrations until no further reduction of sensitivity was noted. Then recovery was measured either by category scaling or by threshold measurement. Like other authors, they found that the rate of recovery was greater at the higher of the two adapting concentrations, but contrary to the findings of Stuijver (1958) and of many of the older authors, their results seemed to indicate that recovery occurred more rapidly than adaptation.

The same authors (Pryor et al. 1970) used the same stimuli and an additional one of four times the individual threshold concentration in a study in which magnitude estimation was substituted for the category scaling procedure and in which a safer method for threshold measurement was introduced (see page 41). The results once more showed that recovery was faster than adaptation. However, this result seems to be in contradiction with the results on the effect of blank samples on absolute odour threshold determinations obtained by the same authors (Steinmetz et al. 1969) (see page 41). In that experiment odorous stimuli and blanks were presented at twenty second intervals. The odorous stimuli lasted only 5 seconds. Notwithstanding the fact that in this experiment the time allowed for recovery was at least four times as long as the adaptation time recovery must not have been completed, because it was shown that the threshold decreased as a function of the number of blanks introduced in the presentation series. The conclusion, that in this case recovery is slower than adaptation, seems almost inevitable.

On the other hand, the conclusion reached in the other experiments, that recovery is faster than adaptation, is of course not only dependent upon the rates of recovery found, but also upon the rates of adaptation. As has been discussed before (see page 42) these rates of adaptation are at least twice as low as the ones found by Stuijver for d-octanol and m-xylene. As was pointed out in that discussion, the low rates of adaptation found by Steinmetz et al. may have been the result of artefacts related to adsorption in the olfactometer they used. It seems that more work needs to be done to settle this important point.

Apart from Köster's findings on irregularities in the shape of the recovery curve, all the data in this section on recovery of the olfactory sensitivity seem once more to fit in well with the general features of recovery after sensory adaptation.

Recovery in the sense of smell is very rapid during the first 100 seconds and then slows down considerably. It is dependent on both the duration and the intensity of the preceding adaptation.

d. Cross-adaptation.

Aronsohn (1886), in order to verify a supposed olfactory analogy of Helmholtz's theory of the specific energies of the different fibers of the optic nerve, adapted his subjects completely to one substance and then tested their sensitivity to a number of others. Thus he came to the conclusion that: "Different odorous qualities affect different areas of the olfactory nerve in such a way, that one given class of odorous substances stimulates one area maximally, affects a second area only to a limited extent and does not stimulate a third area at all". Aronsohn used these findings as the basis for a scientific classification of odorous substances, "because", as he puts it, "we are forced, when we find that in the case of decreased sensitivity for one odorous quality another quality is no longer perceived either, to postulate the existence of one and the same perceiving element for these two substances in the fibers of the olfactory nerve and to classify these substances as belonging together in one class".

Unfortunately, however, his odorous substances were not very well chosen. Some of them were just plant extracts, which contained quite a number of unspecified chemicals in unknown proportions.

Nagel (1903) reports that, when a mixture of coumarin and vanillin, which normally has a strong odour of vanillin, is smelt after complete adaptation to vanillin, it can not be distinguished from pure coumarin. He also states that adaptation for a certain odour does not always cause either complete adaptation or no adaptation at all for other odours, but can bring about any amount of sensitivity decrease between these two extremes.

Vaschide (1902) tried to prove the mutual independence of the olfactory sense and the "sense of touch" (trigeminus ?), when he investigated the influence of adaptation with ether on the thresholds for camphor and for ether itself. He used adaptation times of 5, 35, 85 and 180 seconds. For camphor the threshold

was only very slightly raised after 85 and 180 seconds, but for ether itself the rising of the threshold was considerably faster and after 180 seconds the adaptation was complete.

In similar experiments with ammonia and camphor Vaschide also found only a slight impairment of the ability to smell camphor after 20 seconds of adaptation to ammonia, whereas a state of anosmia for ammonia itself was already reached after 10 seconds.

In a third experiment he showed that ammonia and ether reduced the sensitivity for each other to a large extent.

Apart from these "intersensory" investigations, Vaschide performed some experiments with other stimuli, which, although more olfactory in nature, were inadequate because of their chemical impurity, most of them being extracts or composite perfumes.

Backman (1917) performed some experiments with guaiacol, camphor and benzaldehyde as adapting stimuli and phenol, vanillin, mentol and nitroresol as substances used for testing the sensitivity.

He found cases in which cross-adaptation did occur and cases in which it did not. In later studies he used a larger number of substances.

Komuro (1922) used terpineol, guaiacol and caproic acid as adapting stimuli and measured their influence on the thresholds of nine substances. In one experiment four different concentrations of the adapting substances were given for a very short period only, in another experiment the subject was completely adapted to the substances. In both experiments a rising of the threshold after cross-adaptation was found for all substances, but for most of them the increment in threshold was only very small.

Ohma (1922), using six odorous substances, studied the cross-adaptation they caused to each other and to a number of other substances belonging to the same class of odours of Zwaardemaker's classification. The substances used as adapting stimuli were camphor, eucalyptol, eugenol, benzaldehyde, citral and safrol, all of them being representatives of one of the subclasses of the class of aromatic odours in the Linne - Zwaardemaker classification (camphor and eucalyptol belonging to the same subclass).

The main results of Ohma's experiments are given in table 2.1.

Indicated is the number of times the threshold for a given substance is raised after adaptation to another substance. Complete adaptation to stimuli varying from 200 to 440 times the threshold concentration for the different substances, was used.

Table 2.1.

Results of cross-adaptation experiments by Ohma. Indicated is the number of times the threshold for a given substance (left) is raised after to another substance (top)

Substance	Adaptation by:					
	Camphor	Eucalyptol	Eugenol	Benzaldehyde	Citral	Safrol
Camphor	3, 70	2, 47	1, 60	1, 48	1, 30	1, 61
Eucalyptol	3, 00	6, 69	3, 09	1, 68	1, 35	1, 29
Eugenol	1, 53	3, 04	3, 16	1, 74	1, 31	1, 27
Benzaldehyde	1, 43	1, 09	1, 60	0, 91	1, 32	1, 25
Citral	2, 12	1, 50	1, 31	1, 31	2, 15	1, 28
Safrol	2, 40	1, 50	1, 27	1, 28	1, 20	2, 70

On the basis of these and other results Ohma concluded that Zwaardemaker was right in dividing this group of odours into three subgroups. Further inspection of this table shows in all columns, with the exception of the one for benzaldehyde, that the highest amount of threshold increment is found when normal adaptation or auto-adaptation is involved (adapting substance = test substance).

Another important feature of these data is that the adaptation is reciprocal in most of the cases, i. e. that the two members of a pair of different substances raise the threshold of the other member to about the same extent.

In some cases, however, as in the relation between camphor on the one hand and citral and safrol on the other, adaptation is not reciprocal. Camphor seems to have a stronger adapting effect than the other two. These differences cannot be explained by differences in adapting concentration, because the concentration of safrol (440 x threshold concentration) is the largest one in the whole set of stimuli and the difference in concentration of camphor (440 x) and citral (380 x) is only slight.

Hermanides (1909), using prolongation of the reaction times to the odorous stimulus as an indication of adaptation, obtained the results given in tabel 2.2.

Table 2.2.

Results of cross-adaptation experiments by Hermanides.
Measurement of changes in reaction time to odorous
stimuli as a results of adaptation.

After adaptation with;	Prolonged reaction time;	Unchanged reaction time;
Iso-amylacetate	Iso-amylacetate Valeric acid	Nitrobenzene
Nitrobenzene	Nitrobenzene	Valeric acid
Valeric acid	Valeric acid Iso-amylacetate	Nitrobenzene
Scatole	Scatole	Iso-amylacetate Nitrobenzene Valeric acid

Here too, instances of non-reciprocity are found. Adaptation to iso-amyl acetate, for instance, has no influence on the reaction time to nitrobenzene, but adaptation to nitrobenzene does change the reaction time to iso-amyl acetate. Scatole seems to be rather different from the other three and leaves the reaction times for them unaffected.

LeMagnen (1947) has reported the results of a number of experiments on cross-adaptation. He points out that the degree of specificity of the adaptation varies from one pair of odorous substances to another and that the amount of cross-adaptation found in a pair of substances does not always correlate with the amount of qualitative similarity between their odours. Substances with subjectively identical odours like the musks, may show a great specificity in their adapting effects, whereas substances with very different odours, like, for instance, terpineol and vanillin, may adapt very strongly for each other. This is indeed in good agreement with Guillots conclusion, which was based on his studies of partial anosmia (see page 21), that different mechanisms may be involved in the perception of one odorous quality.

LeMagnen also found instances of non-reciprocal cross-adaptation in his experiments and furthermore came to the conclusion that the way in which each of the substances affected the functional parts of the receptive system was complex in nature, each substance stimulating at least a number of different functional receptive units.

Mullins (1955), carried out some cross-adaptation experiments with butane, butanol and acetone. He adapted his subjects completely to concentrations ten times as high as the threshold. His results are shown in table 2.3.

Table 2.3.

Results of cross-adaptation experiments by Mullins

Olfactory Cells adapted at 10 x threshold to	Threshold measured for	Change of threshold %
Butane	Butyl alcohol	0
Butyl alcohol	Butane	0
Acetone	Butane	100
Acetone	Butyl alcohol	500

Butane and butanol do not affect the sensitivity for each other at all, it seems, but the sensitivity to both is affected and to a different extent, by acetone. This complex result led Mullins to the assumption that there are at least three different types of receptors involved in the perception of these substances.

Cheesman and Mayne (1953) and more recently Cheesman and Townsend (1956) published the results of cross-adaptation experiments in which four substances, isopropanol, dioxan, cyclopentanone and cyclopentanol, were used as the odorants.

They measured the influence of cross-adaptation at different concentrations of the adapting stimuli for each of the possible pairs of these substances. As was pointed out earlier (page 36), their results indicated that the olfactory threshold of a substance varies according to the concentration of the adapting stimulus in such a way, that the logarithm of the threshold concentration is a linear function of the logarithm of the adapting concentration. They used the slope of this linear relationship as an indication of the extent of the interaction between the two odours. The adapting stimulus was presented during one deep inhalation only and the adapting concentrations were above threshold value. The results of these experiments are given in table 2.4.

Table 2.4.

Results of cross-adaptation experiments by Cheesman et al. Indicated are the "Communities of Olfactory Property", i.e. the slopes of the linear relationships between the logarithms of adapting and threshold concentrations (see text).

		Test Stimulus			
		Isopropyl Alcohol	Dioxan	Cyclopentanone	Cyclopentanol
Adapting Stimulus	Isopropyl Alcohol	0.67	0.47	0.19	0.70
	Dioxan	0.61	0.88	0.47	0.57
	Cyclopentanone	0.16	0.56	0.62	0.07
	Cyclopentanol	0.66	0.65	0.19	0.66

In his discussion of these data Cheesman stresses the following points.

The values on the diagonal from top left to bottom right, which represent the slopes found with normal adaptation, are all very similar (approximately 0.70 according to a slightly different way of calculating).

The values found with cross-adaptation do not exceed these values.

The two alcohols have almost identical effects when they are used as adapting stimuli. They affect the sensitivity to each other to the same degree as the sensitivity to themselves. Cyclopentanone and cyclopentanol on the contrary, are very different in their adapting effects.

The two reciprocal values found with cross-adaptation are very similar in all pairs.

This last result has not been reconfirmed by Cheesman in later work (1965) with different substances.

Moncrieff (1956) compared the cross-adaptational effects found in pairs of very similar odours with the ones obtained in pairs of different odours. He

found some relationship between the amount of the effect and the subjective likeness of the odours. In these experiments the undiluted odorants were used as adapting stimuli and presented for a period of one deep inhalation. The thresholds obtained before and after adaptation were used for calculating a "coefficient of odour likeness". Self-adaptation proved to be much stronger in nearly all cases. Cross-adaptational effects did not seem to be necessarily reciprocal for each pair.

In a later study, Moncrieff (1957) investigated adaptation and cross-adaptation using acetone and iso-propanol. In these experiments the influence of a number of different adapting concentrations was studied in the same way as in Cheesman's work.

Self-adaptation was again shown to be stronger than cross-adaptation. The cross-adapting influence of acetone on the sensitivity to iso-propanol was stronger than the one of iso-propanol on the sensitivity to acetone.

Engen (1962) published some results of cross-adaptation work with the aliphatic alcohols. He used a number of different psychophysical methods. Cross-adaptation was obtained both at threshold and at supra-threshold intensities. The amount of the effect was not related to the similarity in chain length of the stimuli.

Schutz et. al. (1958) claimed that they could not find any cross-adaptation at supra-threshold levels.

Cain and Engen (1969) did find it, however. They used propanol and pentanol in a cross-adaptation experiment and presented matched subjective intensities of the two substances as adapting stimuli. They showed that the cross-adapting effects are smaller than the self-adapting effects and that pentanol appears to have more influence on propanol than propanol has on pentanol.

From this survey some general features of cross-adaptation phenomena emerge.

Instances of reciprocal and non-reciprocal cross-adaptation are found as well as cases in which no effect is found at all.

Furthermore, there is no clear relationship between the amount of cross-adaptation that two odorous substances cause to each other and the subjective similarity of their odour qualities.

2.3. THE NATURE OF THE ADAPTATION PROCESSES.

a. Hypothetical

Sofar, the term adaptation has been used rather loosely here. Sensory adaptation has been described as a loss of sensitivity due to previous stimulation. In fact however, there is no way of measuring a loss of sensitivity directly and independently from the responses given by the subject or recorded electrophysiologically. What is measured is the decrement of these responses resulting from previous exposure to a stimulus. There are a large number of possible mechanisms and processes which might explain such a response decrement. They will be reviewed briefly in this section.

1. Reflex mechanisms reducing admission of odorous molecules to the olfactory epithelium.

Swelling of the nasal structures may reduce the proportion of the inhaled air which reaches the olfactory epithelium in the olfactory clefts. Both increase of mucus excretion and dilatation of the blood vessels in the nasal cavity may result in such swelling and both these phenomena may be produced by way of a reflex mechanism as a result of trigeminal stimulation. Thus, trigeminal stimulation caused by the adapting stimulus may indirectly influence the response to the test stimulus.

2. Physico-chemical processes in the olfactory mucus.

In order to reach the olfactory sites on the olfactory hairs, the molecules have to pass the olfactory mucus. Therefore, physico-chemical processes in this watery layer of unknown composition might play a role in adaptation phenomena.

In the first place it is known that some substances dissolve more readily in the mucus than others, a fact which seems to account at least in part for the rather big differences in olfactory thresholds found for different substances (Laffort 1970).

In the second place it is known (Tanyolac 1968) that odorous substances change the surface tension of water and that they often do not dissolve uniformly in the mucus, but tend to form mono-molecular layers at the aqueous-lipid interface between the mucus and the receptor. Finally, it is reasonable to accept the idea that some odorous substances leave the aqueous solution more readily

than others, the rate of their evacuation from the contact points with the receptors being an important variable in the recovery of the olfactory epithelium. Although up to now very little is known about these physico-chemical processes and their exact function in the olfactory mucus, it will be evident that they may have a certain relevance for an explanation of the phenomena of response reduction described here as adaptation.

3. Processes at the receptor sites themselves.

The actual transducing mechanism being a mystery, all hypotheses relating adaptation phenomena to possible transducing mechanisms remain extremely speculative. Nevertheless it will be clear, that the mere number of sites available to accept a given odorous substance may influence the response reduction. If the number of sites is small and the evacuation of the molecules after stimulation is slow, the response reduction will be rapid, whereas if the number is larger, the response reduction will be slower at the same evacuation rate. Thus, the relative number of receptor sites available to a substance and the rate at which they are occupied and made free for new stimulation may be of importance for the response reduction observed.

Apart from the number of sites involved, the characteristics of the transduction mechanism might play an important role. If it is true, as Davies (1965) supposes, that the transduction mechanism consists of a puncturing of the receptive membrane by the odorous molecule causing a depolarisation of the membrane potential, the time required for the membrane to heal and to restore its original potential might be of direct relevance for the response reduction observed. If, on the other hand, receptor proteins play the important role in the transduction mechanism ascribed to them by authors like Ash (1969) still other factors may be invoked as an explanation for adaptation phenomena.

4. Processes in the receptor cells.

Adaptation processes in the receptor cells themselves may also be responsible for the response decrement. Receptor cells can be subdivided in two classes: phasic and tonic receptors. The first category adapts fast and under constant stimulation shows a rapid and progressive decrease in generator potential and spike frequency immediately following the peakvalue obtained at the onset of the stimulus. The second category adapts slowly and shows only a limited decrease in generator potential and spike frequency to a level just below the initial peak value.

This level is maintained as long as the stimulus lasts.

5. Processes at the bulbar level.

From the description of the inhibitory mechanisms in the olfactory bulbs (see section 1.2.2.) it will be clear that these mechanisms may contribute substantially to the adaptation phenomena. The granule cells seem to play an important part in this respect and since these cells themselves are stimulated both by collaterals of the afferent mitral cells and by the efferent fibers stemming from the anterior commissure and the lateral olfactory tract, many parts of the central olfactory system may be involved.

6. Processes in higher olfactory centres.

Apart from the efferent control that higher olfactory centres may exert on the transmission of olfactory signals in the bulb, events in the higher centres themselves may also be responsible for the response reduction.

7. Processes in other parts of the brain.

The reduction in the subject's responses may also be the result of events in other, non-olfactory, parts of the brain.

The monotony of the adapting stimulation may lead to loss of attention for the olfactory stimuli. Under such circumstances the responsiveness of the subject will be reduced.

b. Experimental

It is not clear whether the adaptation processes are located in the peripheral or in the central parts of the receptive system.

This problem has been studied with psychophysical methods by Elsberg (1935) and Stuiver (1958) and with electrophysiological methods by Adrian (1953), Ottoson (1956) and Döving (1966).

As was mentioned earlier (page 43), Elsberg investigated the "duration of olfactory fatigue" at both the ipsilateral and the contralateral side of the nose after monorhinal adaptation. As his results indicate (fig. 2.9 b, c and fig. 2.10 b, c), both sides of the nose show adaptation, but to a different degree.

The recovery times are in general a bit shorter at the contra-lateral side than at the ipsilateral side. This finding has been reconfirmed by Stuiver (fig. 2.11 and 2.12 page II, 15) who showed that recovery is quite rapidly completed at

the unadapted side of the nose, but that the adapted side regains its original sensitivity only very slowly after an initial phase of rapid but incomplete recovery.

The results obtained by these authors lead to interesting conclusions on the location of the sensory adaptation processes. For if these processes were restricted to the peripheral level in the receptor cells, monorhinal adaptation should not have affected the sensitivity at the other side at all. Since this is clearly not the case, the contralateral side being affected almost as strongly, it must be assumed that adaptation occurs to a large extent in the more central parts of the receptor system, i. e. in or beyond the first synapse in the glomeruli. The fact however, that the ipsilateral side and the contralateral side are not adapted to exactly the same extent and that the decrease in sensitivity at the ipsilateral side persists after recovery at the contralateral side is completed, indicates that some adaptation process also occurs at the level of the receptor cells. Furthermore, the very slow recovery rate which is typical for this peripheral process, suggests that it is not of the same nature as the central adaptation processes which are followed by rapid recovery.

The idea that there exist two different adaptation processes, one peripheral and one central in nature, is supported to a certain extent by the work of the three electrophysiologists.

Adrian (1956) studied adaptation in the rabbit and came to the conclusion that it was mainly a central phenomenon which ought to be explained by the reappearance of the intrinsic activity of the olfactory bulb. This intrinsic activity is at first suppressed by stimulation but reinstalls itself after a while. Adrian found only a progressive failure in the receptors when a steady current of odorous air was used, but not when the stimulation was intermittent as in normal breathing.

Ottoson (1956), in his extensive study of the electro-olfactogram (EOG) in the frog, investigated adaptation, recovery and cross-adaptation. He came to the conclusion that the olfactory receptors should be classified as slowly adapting end organs. They showed a slow decrement of the height of the response to repeated stimulation. Ottoson obtained very similar results in the rabbit (1959). In his opinion, the disappearance of the odour sensation in man upon complete adaptation is more likely to be due to suppression of the activity induced in the central olfactory pathways than to an inability of the receptors to respond to stimulation.

Döving (1964) simultaneously recorded the EOG and the activity of single units in the olfactory bulb of the frog. He demonstrated that adaptation develops faster

in the bulbar neurons than in the olfactory receptors.

If indeed two distinct forms of adaptation process exist, one central and one peripheral, anyone who wants to study the problem of the olfactory transducing mechanism with a cross-adaptation method will have to realize himself which of the two kinds of adaptation he is measuring. Measuring central adaptation may be quite irrelevant with regard to this problem which is clearly peripheral in nature. It may therefore be necessary to try to measure the peripheral component alone. How can this be done?

In the first place it will be clear from the discussion of Stuiver's findings, that, if sufficient time is allowed for recovery of the central component, only peripheral adaptation is left.

Furthermore, it seems that much depends on the total amount of odorous substance used for adaptation.

As Stuiver pointed out (page 46), the thresholds after 100 seconds of recovery, i. e. the amounts of peripheral adaptation left after recovery of the central parts, vary only with the fourth root of the amount of odorous substances used $((IT)^{1/4})$.

The thresholds measured immediately after adaptation however, are to a much larger degree dependent upon the product of intensity and duration of the adapting stimulus.

This is clearly illustrated in another of Stuiver's graphs which is represented in fig. 2.15.

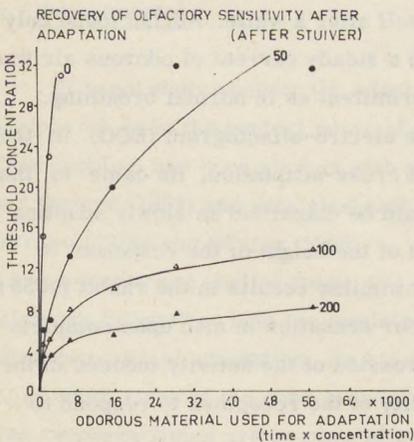


Fig. 2.15. Results of Stuiver (1958) showing the threshold concentration as a function of the quantity of odorous material used for the adaptation, for the same recovery time. The recovery time is given at the curves. Odorous substance: d-Octanol.

When large amounts of odorous material are used, the differences between the thresholds measured immediately after adaptation (0 curve) and the thresholds

measured after 100 or 200 seconds (100 and 200 curve) are extremely large, but when small amounts of odorous substances are used as adapting stimuli, the differences are small and the curves nearly coincide. This indicates that the fast, central component of the adaptation and recovery processes plays a much less predominant role at these low concentrations.

Thus, there are three factors which are relevant if one wants to isolate peripheral adaptation and to reduce the influence of the central adaptation on the measurements as much as possible:

1. Intensity of the stimulus. The lower this intensity, the smaller is the relative influence of the central component.
2. Duration of the adapting stimulus. The shorter this duration, the smaller is the relative influence of the central component.
3. Time allowed for recovery before the measurement is made. The longer this time, the smaller is the relative influence of the central component.

It should be realized, that these factors do not only affect the central component but also influence peripheral adaptation itself, if to a much lesser degree. The requirement that there should remain an absolute amount of peripheral adaptation which is large enough to be measured at all, therefore limits their use to some extent.

Nevertheless, it will be clear that in cross-adaptation experiments intended to study the problem of the olfactory transducing mechanism, relatively short and weak adapting stimuli should be used and that some time should be allowed for recovery of the central component before the adapting effect of these stimuli is measured.

None of the cross-adaptation experiments described in section 2.2.d (pages 49 - 55) meets all of these requirements and only a few meet some of them.

Since the adapting stimuli have not always been specified completely when these experiments were discussed, the details are given here in table 2.5.

In all of the experiments the threshold measurements were carried out as soon as possible after cessation of the adapting stimulus. As far as the total amount of odorous material used for adaptation is concerned, only Cheesman's experiments seem to have been carried out with a reasonably small amount.

Since it is clear that in these cross-adaptation experiments mainly central adaptation has been measured, their relevance for such peripheral problems as the working of the olfactory transducing mechanism and the existence of receptor specificity may be rather limited.

Table 2.5.

Survey of the intensity and duration of the adapting stimuli used by different authors in cross-adaptation experiments.

Author	Adapting stimuli	
	Intensity	Duration
Aronsohn	Undiluted	Complete adaptation
Nagel	Undiluted	Complete adaptation
Vaschide	Undiluted	Normal inhalation during 5, 35, 85 or 180 seconds
Backman	Undiluted	Normal inhalation during 15 minutes
Komuro a	51 - 510 times threshold concentr.	Normal inhalation during 1 minute
b	102 - 128 times threshold concentr.	Complete adaptation
Ohma	200 - 440 times threshold concentr.	Complete adaptation
Hermanides	5 - 20 times threshold concentration	5 - 20 deep inhalations
LeMagnen	Undiluted	Normal inhalation during 10 minutes
Mullins	10 times threshold concentration	Complete adaptation
Cheesman et al.	5 - 10 times threshold concentration	One deep inhalation only
Moncrieff	Undiluted	One deep inhalation only
Engen	Undiluted	One deep inhalation only
Cain and Engen	Sufna-threshold	3-15 inhalations

CHAPTER 3.

OLFACTOMETRIC TECHNIQUE AND EXPERIMENTAL METHOD

3.1. THE OLFACTOMETER

An olfactometer is an instrument for diluting odorous substances and presenting them in known concentrations to the subject.

The requirements to be met by such an olfactometer are determined by the sensitivity of the olfactory sense of the subject and by the type of investigations envisaged. For the human nose, the lowest concentrations which are still just perceptible lie between 1×10^{-5} Moles/liter and 1×10^{-14} Moles/liter. Since the stimuli to be used in the cross-adaptation experiments are to be of threshold concentration, the olfactometer should at least be capable of delivering these concentrations with a high degree of precision. Moreover, it should allow the experimenter to vary the concentration of the stimulus rapidly and to switch from the presentation of one odorous substance to that of another swiftly and without much trouble caused by adsorption of molecules of the first substance. This last requirement seems the most difficult to meet.

Of the many types described in the literature (see Wenzel (1948) and other authors), a modified version of the olfactometer developed by Stuiver (1958) was chosen.

a. The modified Stuiver olfactometer.

As the diagram in fig. 3.1. shows, the olfactometer fundamentally consists of two sections, an air duct (from A to V.S.) and a nitrogenduct (from D to V.S.), the two being connected by a number of capillaries (3_a , 3_b , and 3_c) only.

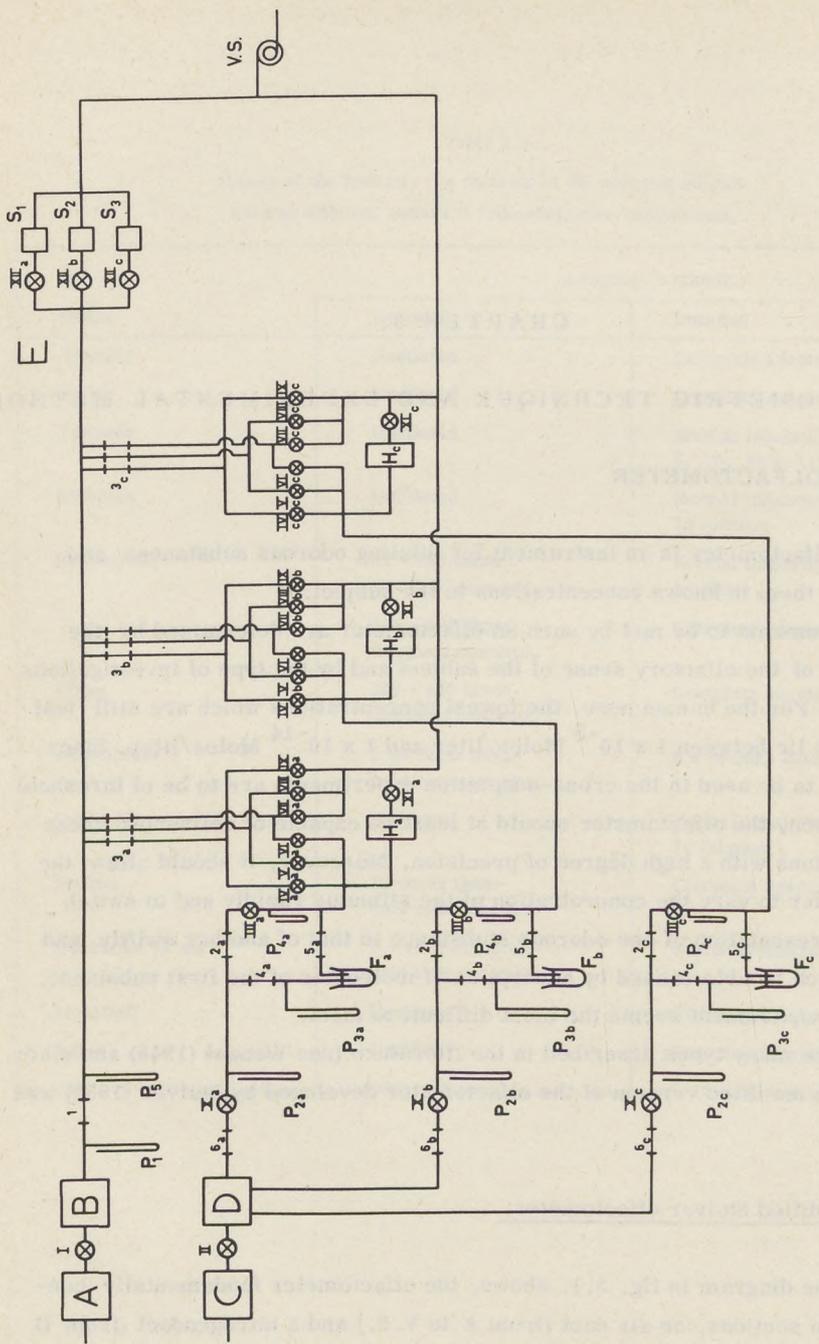


Fig. 3. 1. Schematic drawing of the modified Stuver olfactometer.
 A = Compressor; B = Air conditioning unit; C = Nitrogen bottle; D = Expansion vessel; E = Division point airduct; F = Odour vessels;
 H = Electromagnetic valve; P = manometers; S = Smelling point for subject; V. S. = Ventilation system; I - XII = Stopcocks;
 1 - 6 = Capillaries.

Air drawn in from outside the building is driven through the system by the compressor A, washed in water and brought to constant humidity and temperature (by cooling to 0°C , and subsequent heating to 20°C .) at point B.

After having been conditioned in this way the air passes through capillary 1 at a rate which can be calculated from the pressure between the manometers P_1 and P_5 . The air then proceeds to the point E where it is subdivided into three equal streams (by setting the cocks XIIa, XIIb and XIIc), which pass the three sniffing points (S_1 , S_2 and S_3) before leaving the olfactometer by way of the ventilating system (V.S.).

The flow of air can be controlled between 0 and 900 ml/sec by means of valve I. Normally this valve is set to allow for an airflow of 600 ml/sec. Cocks XIIa, b and c are set in such a way that 200 ml/sec passes each sniffing point.

A stream of nitrogen of about 30-60 ml/sec flows from the nitrogen bottle (C), proceeds to an expansion vessel(D) and is subdivided into three equal streams by means of the capillaries 6_a , 6_b and 6_c . Each of these streams is divided again by the capillaries 2 and 4 into two streams, the flows of which are approximately 10 ml/sec and 1 ml/sec respectively. The smaller of the two in each stream is saturated with an odorous substance in the odour vessel F, which is held at a constant temperature by means of a thermostat bath or by cooling with ice. After having been saturated, the small streams are reintroduced in the larger streams from which they originated by means of the capillaries 5_a , 5_b and 5_c .

In this way a mixture of very constant concentration is obtained in each of the three separate odour lines. For, even if pressure fluctuations occur in the system, the flow ratio between capillaries 2 and 4 will remain virtually constant and therefore the concentration will not change as long as the smell streams remain small enough to be completely saturated with the odorous substance.

In each of the three odour systems the mixture of nitrogen and odour is then fed to the ventilation system via valves IV and IX, while valves V and VI, which are alternatives for valve IV, remain closed. If valve IX is partially closed, the pressure in the system rises. As soon as the pressure in manometer P_4 exceeds the pressure in P_5 , a certain amount of the odour-nitrogen mixture will be injected into the airstream by way of capillary 3. The capillaries shown to the right of each of these capillaries in fig. 3.1 differ in size from the capillaries 3. They can, by means of valves V to VIII, be used to introduce larger quantities of the mixture into the stream or air.

The final concentration of the odorous substance in the airstream can be calculated from the following data:

1. The vapour pressure of the odorous substance at the temperature of vessel F_(a, b or c).
2. The distribution ratio of capillaries 2 and 4 in each system.
3. The flow in capillary 3_{a, b or c} at a given pressure difference between P_{4(a, b or c)} and P₅.
4. The rate of flow of the airstream.

The concentration of each of the three possible odorous substances can be changed rapidly by adjusting valve IX_(a, b or c) (or valves VII_(a, b or c) or VIII_(a, b or c)). If these valves are opened further the pressure in P_{4(a, b or c)} diminishes and the final concentration of the corresponding odorous substance in the airstream becomes lower. In order to automate the olfactometer three electromagnetic valves H_a, H_b and H_c were introduced in the different nitrogen lines. These valves have an effective diameter of 6 mm and a closing time of 0.1 sec. Opening these valves causes a short-circuit in the pressure system with the result that the odour-nitrogen mixture flows directly to the ventilation system instead of passing through the manual valves. By closing the magnetic valves one can restore the original situation. Thus, it is possible to fix valve IX_(a, b or c) in a certain position and to establish the corresponding pressure in the nitrogen line by simply closing the magnetic valve. It is also possible to pass rapidly from one odour to another by opening the magnetic valve of one of the nitrogen lines and closing that of another one.

In the same way a rapid change of concentration for one odour can be made if a number of parallel magnetic valves with different flow settings are used.

In order to prevent the pressure in the nitrogen systems from dropping to the slight underpressure which exists in the ventilation system the cocks XI_a, XI_b and XI_c were introduced. They are closed to such an extent that the pressures in P_{4(a, b or c)} drop only to just below that of P₅. In this way back-flows from the air system to the odour-nitrogen system through capillaries 3_{a, b or c} become negligible.

b. Sniffing device and subjects environment.

According to information obtained from Stuiver and to the results of previous research (1960) by the author, injection of the odour into the nose is

a very unsatisfactory method of stimulation.

The results obtained are improved substantially if the subject is enabled to sniff the odour actively. However, in order to provide a check on the amount inhaled per unit time, the injection apparatus was replaced by a simple device, which is represented schematically in fig. 3.2.

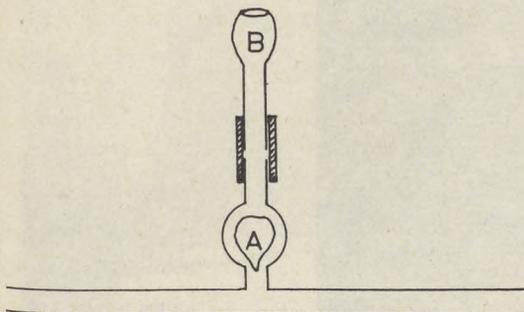


Fig. 3.2. Schematic drawing of the smelling device.

A = Pearshaped wedge; B = Nose piece;

Shaded part = Silicon rubber tubing.

The two horizontal lines are part of the air line between capillary C_3 and the ventilation system. The vertical tube broadens into a spherical chamber in which a pear-shaped wedge (A) is introduced. At the top of the vertical tube is a removable nosepiece (B) which is held in position by a short length of silicon hose (shaded). The weight of the wedge (A) is such that it is lifted from its seat when the subject sniffs through the nosepiece. If, however, the action of sniffing is too vigorous, the wedge shuts off the outlet at the top of the spherical chamber. This arrangement makes it possible to control the rate of inhalation within certain limits. The partial vacuum which occurs in the nostril when the wedge closes the upper hole of the chamber is rather frustrating to the subject, who thus rapidly learns to avoid it by sniffing at a constant and moderate rate. The internal volume of the device is restricted to a minimum in order to limit the disturbing influence of residue on subsequent stimuli. In fig. 3.3. a photograph of the device is shown.

The subjects are seated in odour-free cabins in which one of the sniffing devices just described is mounted. They have also a number of pressbuttons at their disposal. By means of these buttons they can indicate their response. Stale air is continuously removed by exhausters on top of the cabins, while fresh air is being introduced from under the tables.

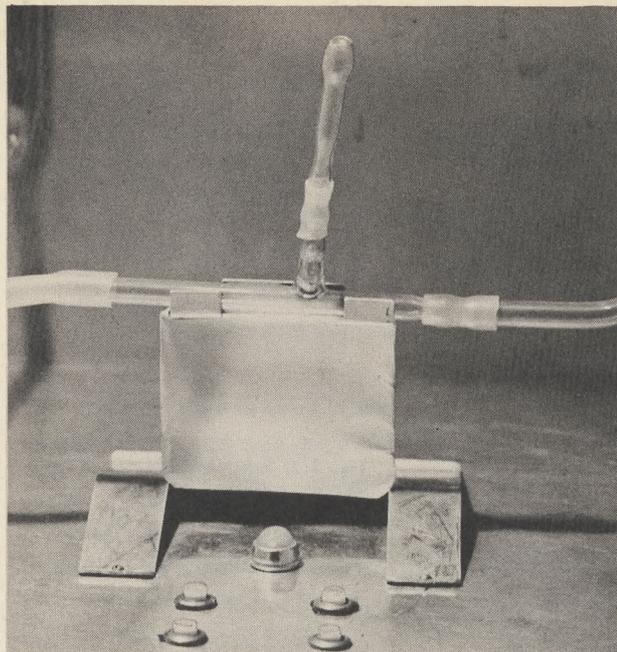


Fig. 3.3. Photograph of the smelling device. Note the signallamp for the subject and the four pressbuttons for encoding the response.

c. Equipment for stimulus programming and recording of responses.

The opening and closing of the electromagnetic valves H_a , H_b and H_c is controlled by a program coded on punch tape. Special circuits enable the experimenter to use the same codes for the manipulation of different combinations of valves and to produce mixtures of various odours in almost any desired ratio. The subjects report their answers by pressing the buttons in front of them (see fig. 3.3.). These responses together with the program code are automatically punched on a new tape. These tapes (one for each subject) are sent to the computer which processes the data, the first statistical treatment consisting principally of serial analyses and counts.

During the experiment a switching device controls the succession of the various stages. At preset intervals (variable between 15 seconds and 3 minutes) a time switch issues an instruction to take a sniff. If the subject fails to respond within a brief period an alarm sounds. As soon as all subjects have reported their responses, the punchtape containing the presentation program is moved on and the apparatus is reset according to the new code read.

Fig. 3.4. gives a general view of the automation equipment.

At the top on the right is the tape reader, on the left are the three punchtape perforators and at the bottom right is the time control unit.

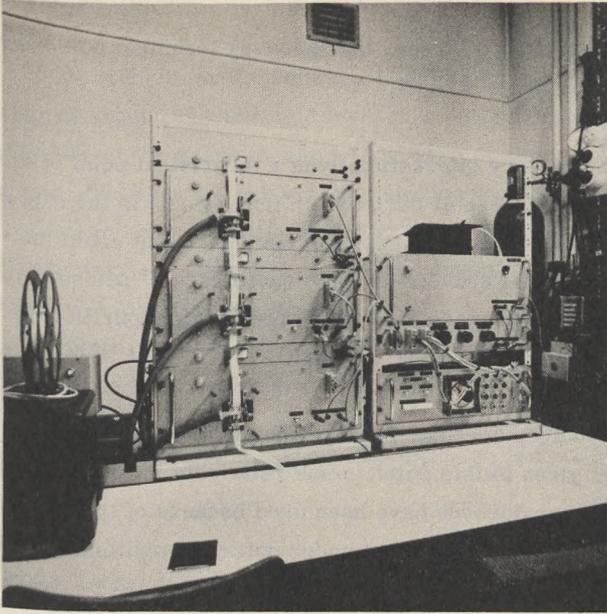


Fig. 3.4. General view of the automation equipment.

3.2. ODOROUS SUBSTANCES AND CONCENTRATIONS

a. Selection criteria.

Nineteen different odorous substances were used in the experiments. The reasons for choosing them were manifold. Some of them were used simply because they had been used by other authors. Thus, *m*-xylene was selected to verify some of Stuiwer's results and to check the functioning of the modified version of the Stuiwer olfactometer. Once interesting results had been obtained with *m*-xylene (see chapter 4), other substances were added on account of their related chemical structures (the xylene-isomers and a number of alkyl benzenes). In the same way cyclopentanone, cyclopentanol, dioxan and isopropanol were used in experiments 27 - 33 to provide a basis for comparison with the results of Cheesman et al. (1953, 1956). Here, cyclohexanone and α -thujone (a cyclic ketone with a complicated ring structure and an isopropyl group) were added on account of the relatedness of their chemical structures. A number of odorous substances were chosen to provide a wider variety of both chemical structure and olfactory quality. This variety seemed important in order to obtain enough diversity in the cross-adaptational relationships investigated. Citral and safrole had also been

used by Ohma (1922) in cross-adaptation experiments.

Apart from these general reasons, the following technical points were taken into account in selecting these stimuli.

1. Availability and purity.

Some substances which may be very interesting from a theoretical point of view, are not readily available in a degree of purity sufficient for use in the experiments. For practical reasons only substances have been used that could be obtained directly from commercial sources with the qualification "purissimum". Gaschromatographic analyses were made of these samples and impurities up to some tenths of a percent were found in some of them.

2. Keeping qualities.

Some substances are hard to keep because they are chemically instable. Although attention has been given to this point, some relatively instable products like for instance citral and benzaldehyde have been used because of their theoretical importance. Such substances were kept under optimal conditions (cooling, dark, under nitrogen if necessary) and they were regularly replaced by fresh samples of the same specification.

3. Adsorption.

Some substances show a strong tendency to adsorb on glass. Since this may be a handicap when one wants to switch rapidly from one concentration to another or from one odorous substance to another, such substances have been avoided as much as possible. That this policy has not been entirely successful will be shown in section 3.5.a.

4. Trigeminal effects.

As it was pointed out in section 1.1. some substances do not only affect the olfactory receptors, but stimulate also the nerve endings of the trigeminal nerve. Although the concentrations used in these experiments were supposedly low enough to remain under the threshold of the trigeminal nerve, such specific trigeminal stimulators like for instance ammonia have been avoided. Some of the substances used would give rise to trigeminal effects when presented in much larger concentrations, however. (See also the discussion in Chapter 4, page 129).

Table 3.1. gives a survey of the nineteen substances that were finally chosen. In this table, the extent to which each of the substances meets the selection criteria just mentioned and other useful data such as chemical composition, commercial source and the names of other authors who have used the same substances in cross-adaptation studies, are indicated.

b. Concentrations.

In order to avoid central adaptation as much as possible, low concentrations of about 70% threshold level (i.e. concentrations that were perceived in only 70% of the cases in which they were presented) were used in the experiments. Since such a subjective criterion was used for selecting the concentration, the concentrations used in different experiments with the same substance were not always the same on account of differences in the average sensitivity of the group of subjects used.

A complete list of the concentrations of the odorous substances used in each of the experiments is also found in table 3.1.

Table 3.1. Specifications of the odorous substances used.

Experiment	Substance	Concentration in Mol./liter	Code	Purity	Keepability	Adsorption	Trigiminal effect	Commercial source	Other authors who have used the same substance
1	m-Xylene	1.28×10^{-8}	B	99.87	+	-	O ^a	Fluka	Stuiver
		2.57×10^{-8}	C						
		3.85×10^{-8}	D						
		5.14×10^{-8}	E						
2	m-Xylene	2.57×10^{-8}	B	99.87	+	-	O	Fluka	Stuiver
		3.85×10^{-8}	C						
		5.14×10^{-8}	D						
3	m-Xylene	9.63×10^{-9}	B	99.87	+	-	O	Fluka	Stuiver
		1.93×10^{-8}	C						
		2.89×10^{-8}	D						
		3.85×10^{-8}	E						
4	m-Xylene	2.57×10^{-9}	X	99.87	+	-	O	Fluka	Stuiver
5	m-Xylene	6.70×10^{-9}	X	99.87	+	-	O	"	"
6	m-Xylene	5.14×10^{-8}	X	99.87	+	-	O	"	"
7	m-Xylene	5.14×10^{-8}	X	99.87	+	-	O	"	"
8	m-Xylene	2.32×10^{-8}	X	99.87	+	-	O	"	"
9	m-Xylene	7.33×10^{-7}	X	99.87	+	-	O	"	"
10	o-Xylene	1.04×10^{-8}	X	99.91	+	-	O	"	"
11	p-Xylene	7.61×10^{-8}	X	98.95	+	-	O	"	"
12	Benzene	4.74×10^{-7}	X	99.35	+	-	O	Merck	
13	Ethyl Benzene	3.80×10^{-9}	X	99.48	+	-	O	Fluka	
14	Cumene	2.05×10^{-9}	X	99.26	+	-	O	"	
15	Toluene	1.49×10^{-7}	X	99.56	+	-	O	"	
16	iso-Propanol	1.07×10^{-6}	X	98.62	+	-	O	"	Cheesman
17	Dioxan	5.09×10^{-7}	X	99.16	+	-	O	"	"
18	Cyclopentanone	3.66×10^{-7}	X	99.37	+	-	O	"	"
19	b-Ionone	5.99×10^{-7}	X	98.92	+	+	O	Naarden	

Experiment	Substance	Concentration in Mol./liter	Code	Purity	Keepability	Adsorption	Trigimimal effect	Commercial source	Other authors who have used the same substance
20	m-Xylene	6.64x10 ⁻⁷	X	99.87	+	-	O	Fluka	Stuiver
	Benzyl Acetate	5.64x10 ⁻⁷	Y	99.12	+	-	O _b	I.F.F.	
	Citral	1.15x10 ⁻⁹	Z	96.83	-	-	+	Naarden	Ohma
21	m-Xylene	6.64x10 ⁻⁷	X	99.87	+	-	O	Fluka	Stuiver
	Safrole	1.83x10 ⁻⁷	Y	98.63	+	+	O	Naarden	Ohma
	Methyl Salicylate	6.47x10 ⁻⁷	Z	99.14	+	+	O	"	
22	m-Xylene	7.52x10 ⁻⁷	X	99.87	+	-	O	Fluka	Stuiver
	Butyl Acetate	1.50x10 ⁻⁵	Y	99.34	+	+	O	"	
	Cyclopentanone	6.73x10 ⁻⁶	Z	99.37	+	-	O _b	"	Cheesman
23	Citral	1.09x10 ⁻⁹	X	96.83	-	-	+	Naarden	Ohma
	Methyl Salicylate	7.34x10 ⁻⁷	Y	99.14	+	+	O	"	
	Butyl Acetate	6.91x10 ⁻⁶	Z	99.34	+	+	O _b	Fluka	
24	Citral	1.27x10 ⁻⁹	X	96.83	-	-	+	Naarden	Ohma
	Safrole	9.61x10 ⁻⁸	Y	98.63	+	+	O	"	"
	Cyclopentanone	5.60x10 ⁻⁶	Z	99.37	+	-	O	Fluka	Cheesman
	Benzyl Acetate	7.06x10 ⁻⁷	X	99.12	+	-	O	I.F.F.	
25	Methyl Salicylate	7.34x10 ⁻⁷	Y	99.14	+	+	O	Naarden	
	Cyclopentanone	4.77x10 ⁻⁶	Z	99.37	+	-	O	Fluka	Cheesman
	Benzyl Acetate	9.06x10 ⁻⁷	X	99.12	+	-	O	I.F.F.	
26	Safrole	1.83x10 ⁻⁶	Y	98.63	+	+	O	Naarden	Ohma
	Butyl Acetate	4.12x10 ⁻⁶	Z	99.34	+	+	O	Fluka	
	Cyclopentanol	4.89x10 ⁻⁵	X	98.16	+	-	O	"	Cheesman
27	a-Thujone	2.27x10 ⁻⁷	Y	98.95	+	-	O	"	
	Cyclohexanone	8.98x10 ⁻⁶	Z	99.23	+	-	O	"	
	iso-Propanol	2.80x10 ⁻⁵	X	98.62	+	-	O	"	Cheesman
28	a-Thujone	2.27x10 ⁻⁷	Y	98.95	+	-	O	"	
	Cyclopentanone	1.33x10 ⁻⁵	Z	99.37	+	-	O	"	Cheesman
	m-Xylene	8.14x10 ⁻⁷	X	99.87	+	-	O	"	
29	a-Thujone	1.25x10 ⁻⁷	Y	98.95	+	-	O	"	
	Dioxan	1.04x10 ⁻⁴	Z	99.11	+	-	O	Merck	Cheesman
	m-Xylene	8.14x10 ⁻⁷	X	99.87	+	-	O	Fluka	
30	iso-Propanol	8.02x10 ⁻⁵	Y	98.62	+	-	O	"	Cheesman
	Cyclopentanol	4.89x10 ⁻⁵	Z	98.16	+	-	O	"	"
	Cyclohexanone	8.98x10 ⁻⁶	X	99.23	+	-	O	Fluka	
31	iso-Propanol	9.03x10 ⁻⁵	Y	98.62	+	-	O	"	Cheesman
	Dioxan	8.74x10 ⁻⁵	Z	99.11	+	-	O	Merck	"
	Cyclohexanone	8.01x10 ⁻⁶	X	99.23	+	-	O	Fluka	
32	m-Xylene	5.77x10 ⁻⁷	Y	99.87	+	-	O	"	
	Cyclopentanone	9.03x10 ⁻⁶	Z	99.37	+	-	O	"	Cheesman
	Dioxan	1.06x10 ⁻⁴	X	99.11	+	-	O	Merck	"
33	Cyclopentanol	1.01x10 ⁻⁴	Y	98.16	+	-	O	Fluka	"
	Cyclopentanone	9.03x10 ⁻⁶	Z	99.37	+	+	O	"	"

3.3. SUBJECTS.

All subjects in the experiments were students at Utrecht University. Both male and female students took part and their ages ranged from 18 till 28 years. They were carefully selected on account of their olfactory sensitivity. In view of the fact that in adaptation experiments each subject is always used as his own control, it seemed more important to have a group of subjects of about equal sensitivity, than to have a group which was representative of a larger population insofar as sensitivity was concerned.

The fact that the olfactometer could not present different concentrations to each of the three subjects that could be handled simultaneously with it, played an important part in deciding in favour of this selection. For if three subjects differed too much in sensitivity, it might have been impossible to find a specific concentration that was perceived in about 70% of the cases by all three of them. Therefore, subjects of either very low or very high sensitivity were omitted. The number of subjects participating in each of the experiments is indicated in chapters 4 and 5 in the direct context of each separate experiment. Most subjects took part in a large number of experiments and some subjects participated in nearly all of them. The subjects were paid per hour. They knew that they might be dropped from the group if they did not perform well enough.

3.4. EXPERIMENTAL METHOD

a. General.

Instead of measuring thresholds and comparing the thresholds obtained before and after adaptation, a somewhat different method of estimating the amount of the adaptational effect has been adopted here. With this method the sensitivity of a subject is not expressed in the concentration which the subject can just perceive in, say, 50% of the cases, but it is expressed in the percentage of positive response which a subject gives when a fixed concentration of the odorous substance is presented to him.

The theoretical implications of this method can best be illustrated by fig. 3.5. The two S-shaped curves in this figure represent the theoretical relationship between detection probability expressed in percentage positive response and intensity or concentration of the odorous stimulus. They can be considered to be the curves found for either two subjects S and S' of different sensitivity or

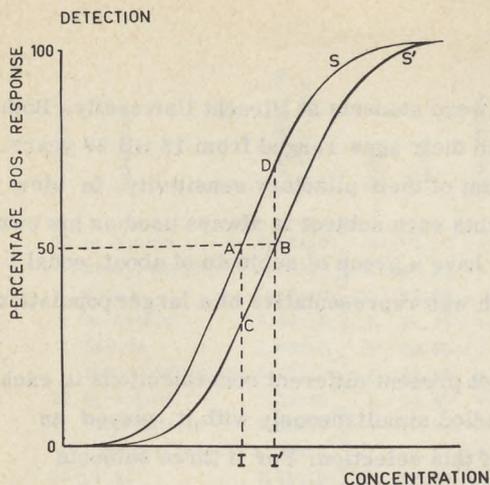


Fig. 3.5. Theoretical curves expressing the relationship between detection probability (percentage of positive response) and concentration of the odorous stimulus. S and S' represent two subjects of different sensitivity or two states of sensitivity of the same subject.

for two different states of sensitivity S and S' in the same individual. Although each of the concentrations I and I' corresponds of course with a different percentage positive response on the two curves, it will be clear that the differences AC and BD found for these percentages, remain almost constant as long as the concentrations fall in the range where both curves are practically linear.

This range lies between the concentrations that yield 20% and 80% of positive response respectively, according to Stuiver (1958), who found almost perfect linearity within these limits for all of a number of different odorous substances. Pangborn et al. (1964) obtained similar results with 2-heptanone in an even wider range. Therefore, within this range of concentrations averaging seems permitted and making comparisons between different percentages of positive response seems possible on a linear basis.

This point is important because with the method described, adaptation and recovery are not, as by most other authors, expressed in a change in threshold concentration (shift from A to B) but in a change of detection probability (shift from A to C).

If the percentages positive response become larger than 80% or smaller than 20% difficulties may indeed arise as it is shown in fig. 3.6.

In this figure the recovery curves for cyclopentanone of three groups of subjects of different sensitivity are represented. For each group the percentages positive response are given after five different recovery times. The group of medium sensitivity consisted of 8 subjects, the other two groups contained 4 subjects each.

H₃ RECOVERY AFTER ADAPTATION
 THREE GROUPS OF DIFFERENT SENSITIVITY
 X = CYCLOPENTANONE

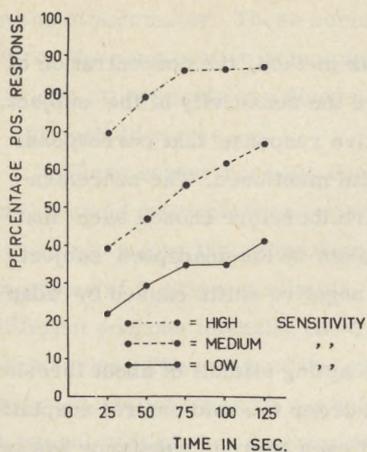


Fig. 3.6. Recovery after adaptation for three groups of subjects differing in sensitivity. Odorous substance: Cyclopentanone.

These results are part of the data on recovery mentioned earlier in section 2.2.c. (page 47).

The flattening of the curve at about 85% of positive response found for the high sensitivity group is probably due to the non-linearity of the detection curves at that level. That such difficulties need not be encountered at concentrations below the 80% level is further illustrated in fig. 3.7, where the same type of curves

H₁ RECOVERY AFTER ADAPTATION
 THREE GROUPS OF DIFFERENT SENSITIVITY
 X = ISOPROPANOL

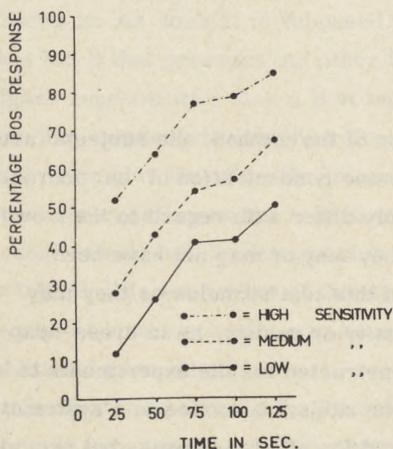


Fig. 3.7. Recovery after adaptation for three groups of subjects differing in sensitivity. Odorous substance: isopropanol.

are given for iso-propanol. Each of the groups of different sensitivity consisted of five subjects. Here the curves are indeed very similar both in slope and in shape. The exceptional shape of these curves will be discussed extensively in chapter 4.

From all this it should be obvious that, with this method, the concentration of the constant stimulus, which is used to measure the sensitivity of the subject, should be chosen such that the percentage positive response that corresponds with it can shift and still remain within the limits mentioned. The concentrations used in the experiments to be described are therefore chosen such that they are perceived in about 60% to 80% of the cases by the unadapted subject. Thus, there is left plenty of possibility for the negative shifts caused by adaptation, to occur.

Since it had been decided earlier to use adapting stimuli of about threshold concentration (see section 2.3, pag 61) in order to avoid central adaptation as much as possible, the same concentration of each odorous substance has been used both as the adapting and as the test stimulus in most experiments. This procedure has considerable advantages from an economical point of view, as it will become clear below when the construction of the presentation series is discussed. It is also of theoretical importance because using the same adapting and test stimuli helps to avoid uncontrolled influences such as novelty effects. All different stimuli are given equally frequent in each series.

In general it can be remarked that the method is both very economical and very sensitive. In cases in which it would be very hard to calculate a shift in threshold concentration with reasonable precision, a change in percentage positive response can already be shown in a reliable way.

b. Presentation series.

As follows from the general description of the method, the subjects are tested for their sensitivity with exactly the same concentration of an odorous substance, a large number of times. They only differ with regard to their own adaptational history at each presentation. They may or may not have been adapted just previously to the presentation of this test stimulus or they may have been adapted to stimuli of varying intensity or quality, as in cross-adaptation. In most of the presentation series constructed for the experiments to be described here, the adaptational history of the subject is varied in a systematic way. Some of the series have been constructed for other purposes, but provide

some useful information on adaptation phenomena. The variation of the adaptational history at each presentation is merely accidental in these series.

Some special series were constructed for checking the influences of adsorption in the olfactometer. These series will be discussed in section 3.5.a.

Here, the construction principles of the different types of series used in the various experiments are discussed. The following types can be distinguished:

1. Threshold series.

These series were not intended for adaptation measurement, but served in threshold determination experiments. Nevertheless, the composition of these series was such, that adaptation effects could be calculated from them. They consisted of 5 different stimuli, a zero stimulus (A) and four odorous stimuli of different odorous intensity ($B < C < D < E$), which each were given 6 times in each series. The order of the stimuli was randomized and the interval between two presentations was 60 seconds.

A typical part of such a series would read:

B C A C D B B D C A E etcetera.

Each odorous stimulus in such a sequence acts both as a test stimulus and as an adapting stimulus for the next one. Thus, the underlined C is a test stimulus of a given concentration. It follows an A stimulus and it can be compared with each of the other two C's in the sequence. If adaptation plays a role at the concentration level used and with the recovery times allowed, it is to be expected that the underlined C will elicit a higher percentage positive response than the other two, because it follows a blank stimulus and is therefore not under the direct influence of adaptation like the others which follow an odorous stimulus. This same C in turn constitutes the adapting stimulus for the D that follows it. As such it is supposed to exert a stronger adaptational influence than the B that precedes the other D in the example, because a C stimulus is of higher concentration than a B stimulus.

One may wonder whether the relevant part of the adaptational history is limited to the stimulus that directly precedes the test stimulus or whether earlier stimuli may influence the sensitivity to the test stimulus too. These "second order" effects will be discussed in more detail below. (page 81).

In total 8 different series of this type were used (series 1a - 1h). In experiment 2 only 3 odorous stimuli were used and the E's in each series functioned as additional zero stimuli.

2. Series for measuring ipsilateral and contralateral adaptation effects.

In experiment 4 the two sides of the nose were stimulated alternately

with intervals of 20 seconds. The special series developed for this experiment contained odorous stimuli (X) of a fixed concentration near the threshold and non-odorous stimuli (O). A typical series would read:

Right: O X O O X X O X X O O X O X X O O X O X O O X O X X

Left: O O X O O X O O X O O O O X O X X O X X O X X X X

In the first half of the series only 3 out of the twelve stimuli at the left side of the nose were odorous stimuli, but in the second half of the series 9 out of 12 stimuli on the left side were odorous. In both halves of the series each of the combinations XX, XOX and XOOX was given twice on the right side of the nose. The adaptational history at the moment the last odorous stimulus of these combinations was presented, differed in two respects.

First, the ipsilateral adaptation differed according to the number of non-odorous stimuli in the combination, the times allowed for ipsilateral recovery being 40, 80 and 120 seconds respectively.

Second, the contralateral adaptation differed depending on whether the combination occurred in the first or in the second half of the series. Thus, the two underlined test-stimuli differ not in ipsilateral adaptation, but have a different contralateral adaptational history.

Four of these series (2a - 2d) were constructed in such a way, that the test combinations XX, XOX and XOOX were presented at the right side of the nose in two of them and in two of them at the left side of the nose, whereas the position of the two halves of the series containing 75% or 25% of X-stimuli was also interchanged systematically.

3. Recovery series.

In experiment 5, three series were used that were not especially made for measuring recovery, but from which data about recovery could be obtained nevertheless. Each of these series contained 20 odorous stimuli of one concentration (A) and 8 blank stimuli (O). Combinations like AA and AOA occurred several times in all three series of this type, but some of them also contained AOOA and AOOOA. The interval between two successive stimuli was always 60 seconds (series 3a - 3c).

Another kind of series has been developed especially to study recovery phenomena. In these series only two different stimuli, a blank stimulus (O) and an odorous stimulus of fixed intensity (X) were used. A typical part of such a series would read:

X O X O O X X O O O X O X O O O O X X O O X etcetera.

Here again each odorous stimulus acts both as an adapting and as a test stimu-

lus. The only thing that changes from one presentation of the test stimulus to another is the recovery time elapsed since the last adapting stimulus. The above sequence contains for instance all of the following combinations of odorous and non-odorous stimuli:

...XX...
...XOX...
...XOOX...
...XOOOX...
...XOOOOX...

The recovery time allowed since the last stimulus differs for each of the underlined X stimuli. The recovery time ($t_{rec.}$) can be expressed as $t_{rec.} = i(k+1)$, where i is the duration of the fixed interval between each pair of successive presentations and k is the number of blank stimuli between the particular X stimulus and the preceding one. In order to change the recovery time, i or k or both may be varied.

In experiment 6, 12 series have been used with a k varying from 0 to 2 and an i of 37 seconds. The three possible combinations, XX, XOX and XOOX were given four, eight and four times respectively in the first five of these series, and six times each in the other seven. Their order was randomized with the restriction that never two combinations without a O stimulus could follow each other. (series 4a - 4b).

In the ten series used in experiment 7, k was varied from 0 to 4 and i was 32 seconds. Here all five possible combinations, XX, XOX, XOOX, XOOOX and XOOOOX were given four times in each series. Their order was again randomized and the same restriction as in 6 was applied. (series 5a - 5j).

In the five series used in experiments 8, 10, 11, 12, 13 and 14, k was again 4 but i was 25 seconds. All combinations, XX, XOX, XOOX, XOOOX and XOOOOX were given 4 times per series. Their order was randomized under the same restriction as in experiments 6 and 7 (series 6a - 6e).

In the experiments 9 and 15 series were used in which not only all "first order" combinations such as XX or XOOX were presented, but all possible "second order" combinations such as XXX, XOXX, XOOXX, XOOOXX, XOOOOXX, XXOX, XOXOX, XOOXOX, XOOOXOX etc., from XXX till XOOOOXOOOOX. Each series contained all 25 second order combinations. The order of the combinations was randomized with the restriction that the last part of a second order combination was always the first part of the next one. (series 7a - 7e).

4. Cross-adaptation series.

In the series used for cross-adaptation measurement, two or three qualitatively different odorous stimuli (X, Y, Z) were presented together with blank stimuli (O).

A typical part of such a series with three different odorous stimuli would read:
 O O Z Y O X Z O O X Y O O Z X O Y Z O O Z Z O X X

Such a series is composed out of the following stimulus combinations:

XX	XY	XZ
XOX	XOY	XOZ
XOOX	XOOY	XOOZ
YX	YY	YZ
YOX	YOY	YOZ
YOOX	YOOY	YOOZ
ZX	ZY	ZZ
ZOX	ZOY	ZOZ
ZOOX	ZOOY	ZOOZ

The series used in the cross-adaptation experiments (exp. 20 - 33) were composed of all of the combinations mentioned above. Four different series were made and were presented about equally often in each of the 16 experiments. The interval between presentations was 30 seconds. The order of presentation was random under the restriction that no two combinations that contained no O-stimulus could follow each other. (series 8a - 8d).

c. Instructions to the subjects.

The subjects were asked to take a sniff from the special smelling device (see page 68) in front of them every time a light signal was turned on. The intervals between these signals were regulated by an automatic reset clock. The subjects had to decide whether an odorous substance was present or not and, in the case of the cross-adaptation experiments, to which of the different odorous qualities it belonged. They made their decision known by pressing one of four differently coloured pressbuttons, according to a code (see table 3.1.) they had learned before the experiment started. They used one nostril only and were not allowed to sniff between presentations.

d. Treatment of data.

The percentages positive response to each test stimulus in the series is calculated for each subject separately and for the group as a whole. Unless stated otherwise, only the data for the total group will be given below. The percentages positive response obtained with the same test stimuli under different adapting conditions and with different test stimuli under the same adapting conditions are compared and differences in percentage positive response are calculated. The Wilcoxon matched-pairs signed ranks test (Siegel, 1956) is used to estimate the statistical significance of these differences.

The different adapting conditions can be subdivided roughly into first order and second order effects. A first order effect is the adapting influence exerted on the sensitivity to a test stimulus by the adapting stimulus that precedes it.

The strength of the adapting influence is likely to be dependent upon the nature of the adapting stimulus and upon the time allowed for recovery between the adapting and the test stimulus. Thus, it is likely that differences in percentage of positive response to the last stimulus of combinations like XX and XOOOOX or ZX and ZOOOOX or ZY and YY are found. In all of these combinations only first order effects are considered. A second order effect is the adapting influence exerted on the sensitivity to a test stimulus by the one but last adapting stimulus that precedes it. Thus the following combinations may differ in their second order effect, whereas their first order effects are kept constant: XXOX, XOXOX, XOOXOX etc.

It is also possible to construct combinations in which the second order effects have been held constant whereas the first order effects are varied. Examples of such combinations are XXOOOX, XOXOOX, XOOXOX and XOOOXX. Careful examination of the results of experiments 9 and 15 showed that effects of higher order than the second order could be neglected completely, since they had no influence.

3.5. EMPIRICAL CHECKS

A number of empirical checks have been carried out to control the reliability of the olfactometer and of the experimental method used.

a. Adsorption

Adsorption is usually the main cause of defection in olfactometers. The molecules of most odorous substances show a strong tendency to stick to the glass walls of the apparatus. This is of no importance in parts of the olfactometer where a constant concentration of an odorous substance is maintained, because in these parts an equilibrium between adsorption and evaporation is reached. In parts in which changes of concentration are needed however, problems may arise. In the olfactometer used here, changes of concentrations occur only in the part of the airline between the point where the mixture of nitrogen and odorous substance is injected in the stream of air and the ventilation system. (see fig. 3.1. page 64). Furthermore, the adsorption phenomena in the last part of this line, beyond the smelling device, will not influence the concentration presented to the subject, provided that the subject does not inhale more odorous air per unit time than the system can supply. Thus, only adsorption and desorption in the part of the airline between the injection capillaries (capillary 3) and the smelling device are relevant.

Two kinds of difficulties can arise from it. In the first place, it may be difficult to lower the concentration of the odorous substance rapidly because of the slow desorption rate. In the extreme case, when one wants to change the concentrations from a given level to zero, as it occurs often in the series described above, it may take considerable time before all the odorous molecules have evaporated. If the time between two presentations is taken too short, this may result in rightly given "false positives". This effect can be reduced in a number of ways. Shortening the part of the airduct involved as much as possible is certainly the best and most effective of all. Furthermore, it is possible to raise the air current in the duct (600ml/sec. in the olfactometer used here) and to reduce the width of the glass tubing in order to have it washed and "scrubbed" by the air as much as possible. The turbulence that almost certainly occurs in such a system at this flow rate is of course much more effective in this respect than laminarity would be.

In order to check on the effect that adsorption may have on the results obtained in the experiments to be described here, a simple experiment has been performed with each of the odorous substances used. During two minutes the maximum concentration that possibly could be produced by the apparatus (at least a hundredfold of the threshold concentrations used in the experiments) was led through the relevant part of the airline. Then the concentration was lowered, either to zero or to a threshold value. Fifteen seconds after this change had

been made an experienced subject was asked to take a sniff and to indicate whether he could smell the odorous substance or not.

This procedure was repeated until each of the two conditions had been given 20 times. If the subject could distinguish the threshold concentration in about 50% of the cases and did not give more than 5% of false positives (1 out of the 20) to the zero stimulus, it was decided that under the normal experimental conditions, in which a far smaller concentration (threshold value) passed the part of the airduct for a far shorter period (40 seconds maximally) and in which an evaporation time of at least 20 seconds was allowed, adsorption of odorous molecules from one stimulus would not influence the results obtained with the next one.

With none of the odorous substances used in the experiments, the subject failed to meet this criterion.

A second check is provided by the percentage of false positives given to the first zero stimulus after each odorous stimulus in the actual experiments. If this percentage is not higher than that obtained with the second zero stimuli, it can again be thought unlikely that adsorption is of influence on the perception of the next stimulus. In none of the experiments such an effect was found in any systematic way.

The second way in which adsorption phenomena may cause difficulties, is of a less obvious kind and has at first been overlooked in the experiments. If the concentration in the apparatus is raised, it may take some time before it comes to full strength because at first a large amount of the surplus odorous molecules tend to adsorb and the new equilibrium is established only gradually. Especially if one wants to change the concentrations from zero to a given level, as it occurs often in the experiments to be described, this may cause difficulties. These difficulties can also be reduced in a number of ways. Again the best way is to make the part of the airduct between the injection capillaries and the smelling device as small as possible.

Furthermore, it may be better to use a smaller air current in this case, because the "scrubbing" of the walls and the turbulence may hinder the rapid establishment of the equilibrium. However, lowering the rate of flow in the air line will most likely reintroduce adsorption difficulties of the first kind.

The effects of the second kind of adsorption phenomena became apparent in the results of the experiments 20 - 26 by the fact that for some substances a concentration that had been present in the airduct of the apparatus for a longer period, was more likely to be perceived than a stimulus that had not passed the airduct very long. Thus the second stimulus of the sequences XX, YY and ZZ

which had been in the airduct for at least 50 seconds was in some cases perceived more often than the second stimulus in OX, OY and OZ, which had been present in the airduct for 25 seconds maximally. This most disturbing fact was of course completely contradictory to the expected first order adaptational effects which should have reduced the percentages positive response to the second stimulus in the combinations XX, YY and ZZ.

In order to check whether this effect was really due to adsorption, another experiment was carried out. In order to provide an equilibrium, a threshold concentration of an odorous substance was led through the airduct for 90 seconds before the subjects were asked for the first time to take a sniff from it and to indicate whether they perceived it or not. After another 30 seconds the subjects were asked to sniff a second time. Thus, they got the same stimulus presented twice with an interval of 30 seconds, just as in the XX combination of the cross-adaptation experiments. In another condition of this experiment pure air was led through the airduct during the 90 seconds before the subjects were asked to take their first sniff. Then, as soon as subjects had answered (within 7 seconds) the same threshold concentration as the one given in the first condition was led through the airduct and again the subjects were asked to take a sniff 30 seconds after the first one. In a third condition the odorous concentration was present in the air line for 90 seconds as in the first condition, but it was reduced to zero as soon as the subjects had answered for the first time. No odorous concentration was led through the airduct when they took their second sniff after 30 seconds.

The three conditions can be characterized schematically as X'X, O'X and X'O, where the X' and O' represent stimuli which have been in the airline for 90 seconds, whereas the O and the X have been there only for 30 seconds.

The average percentages positive response given by six subjects to each of these stimuli are shown in table 3.2.

In each row the percentage of positive response to the underlined stimulus of the combinations heading the row is indicated for each of the seven odorous substances. The odorous substances which in exp. 20 - 26 gave higher percentages of positive response to the last stimulus of the XX combinations than to that of the OX combination, are marked with asterisks in the table.

Table 3. 2.

The influences of adsorption in the airduct of the olfactometer and recovery times allowed to the subject on the percentages of positive response to stimuli of seven different odorous substances.

Conditions :		Substances						
		Safrole *	Butyl Acetate *	Methyl Salicylate *	Benzyl Acetate	Cyclopentanone	Citral	m-Xylene
A	Odour in airduct: 90 sec	60, 4 ^{ab}	59, 2 ^{ab}	61, 3 ^{ab}	41, 2 ^{ac}	57, 7 ^{ac}	52, 9 ^{ac}	40, 4 ^{ac}
	Recovery: 90 sec (<u>X'</u>) $X' = X'X + X'O$							
B	Odour in airduct: 120 sec	55, 7 ^a	38, 8 ^a	56, 3 ^a	26, 4 ^a	47, 1 ^a	44, 3 ^a	29, 9 ^a
	Recovery: 30 sec (<u>X'X</u>)							
C	Odour in airduct: 30 sec	38, 3 ^b	42, 5 ^b	53, 3 ^b	48, 3 ^c	67, 5 ^c	70, 0 ^c	51, 6 ^c
	Recovery: 120 - 150 sec(O' <u>X</u>)							

a = cond. A > cond. B sign. $p < .05$ T = O n = 6 (Wilcoxon two-tailed)

b = cond. A > cond. C sign. $p < .05$ T = O n = 6 (Wilcoxon two-tailed)

c = cond. A < cond. C sign. $p < .05$ T = O n = 6 (Wilcoxon two-tailed)

* Substance which gave a higher percentage pos. response to the last stimulus of the XX combinations than to that of the OX combinations in experiments 20 - 26.

As a comparison of conditions A and B in the table shows, X' was always perceived more often than X in the combination X'X, indicating that adaptation occurred for all substances and that the earlier findings with butyl acetate, methyl salicylate and safrole seemed indeed to be the result of the gradual rise in concentration caused by adsorption. According to the Wilcoxon matched pairs signed rank test, all differences between the two columns were significant at the 1% level.

A comparison of the results obtained under the conditions A and C further confirms the adsorption hypothesis. Only when the three substances mentioned are used, the percentage of positive response to O'X, which has been only 30 seconds in the airline is lower than to X' which has had the opportunity to

saturate the walls of the airline with odorous molecules during 90 seconds. The fact that for the other substances the percentages of positive response given to $O'X$ lies considerably higher than that given to X' , can be explained to a large extent by first order adapting effects. In the case of $O'X$ the time elapsed since the last odorous stimulus is always at least 120 seconds and when the $O'X$ follows a $X'O$ combination it is even 150 seconds. In the case of the X' , the possible intervals allowed for recovery are either 90 seconds, when it follows a $X'X$ combination as it is most frequent in the series, or 120 seconds, when it follows a $X'O$ combination.

The influence of different recovery times upon the percentage of positive response given to the stimuli is illustrated in fig. 3.8. Closed circles indicate stimuli which have been in the airduct for at least 90 seconds (X' and the second stimulus in $X'X$).

The open circles represent the X stimuli in OX .

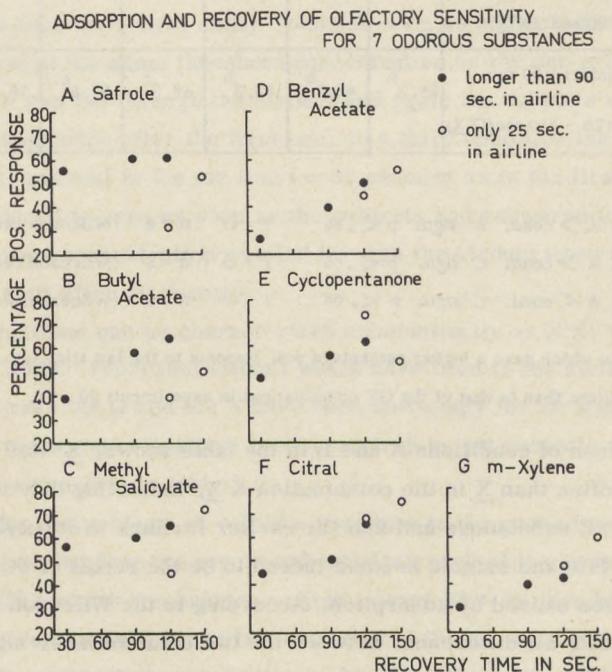


Fig. 3.8. Effect of adsorption in the airduct on the percentages of positive response obtained after recovery from adaptation. (Explanation: see text)

The influence of adsorption is once more clearly demonstrated in the three graphs at the top (see A, B, C) by the fact that the open circles lie lower than would be expected if they represented stimuli of the same concentration as the ones indicated by the closed circles. Three of the other graphs (D, F, G) show a nice fit of the two kinds of stimuli in one recovery curve. Only the results obtained with cyclopentanone, shown in graph E, do not fit too well.

It is likely that adsorption difficulties of this last kind are also responsible for the results obtained by Pangborn et al. (1964) with the Stone olfactometer. As it was mentioned earlier (see page 40), they also found that the second stimulus in a combination in which two odorous stimuli followed each other (++) was perceived more often than the second stimulus in a combination in which it followed a zero stimulus (-+). The interval used between two successive stimuli was fifteen seconds. It is very likely that a sorptive equilibrium has not been established in this short period, especially so, because the part in which the concentration changes occur is by no means small in the Stone olfactometer. This would be a simpler explanation of the results than postulating "that the proximity of odor-containing stimuli in the ++ combination facilitated retention of "odor memory" and reinforced the psychophysical response". Pangborn and her co-workers indicate vaguely the possibility of adsorption in the apparatus but reject it because they do not have any difficulties of the first kind described above (i.e. the second stimulus in their combination +- does not elicit a false positive more often than in --). As has been shown here, however, the two effects do not necessarily go together and one can perhaps shift from one effect to the other by changing the rate of flow of the air current and the turbulence of it.

It should finally be pointed out that the difficulties caused by the slow increase of the stimulus concentration affect only the validity of the results obtained with the XX, YY, or ZZ combinations in the experiments to be described here. In all other cases the stimulus is equally long in the airduct and it may therefore be assumed that the concentrations of these stimuli are alike, even if it is difficult to know their absolute value.

Some substances do show practically no adsorption to glass at all. This is for instance the case with all substances in experiments 27 - 33, perhaps with the exception of a-thujone.

b. Air pollution.

Since the air in the olfactometer is drawn in directly from outside the building and is only washed in water before use, air pollution may constitute a serious problem, especially because the laboratory is situated in the centre of Utrecht. Fortunately there is very little chemical industry in the surroundings of this city. In fact the air is surprisingly pure on most days. Only one factory at the north eastern side of the city was of real importance as a source of pollution as was shown by checking on the relationship between the direction of the wind and the number of series discarded because they contained too many (more than 8%) of false positives. The results of a survey of this kind made during experiment 1 are given in table 3.3. No data on days with northerly winds were available.

Table 3.3.

Relationship between the direction of the wind and the number of series discarded because they contained more than 8% false positives.

Wind	Number of days	Number of series discarded
N	-	-
NE	3	6
E	4	1
SE	3	0
S	4	0
SW	8	2
W	5	0
NW	4	0

It will be clear from this table that only the north-easterly winds caused serious trouble. Since it was known at the time of this experiment that the factory causing the air pollution would stop its activity in Utrecht, no special arrangements were made to counteract the influence of this pollution. At days at which north-easterly winds prevailed (not too often in Holland), the experiments were simply discontinued. After a year the factory stopped working.

c. Inhalation speed.

The rate of inhalation of the subject is regulated by the special smelling device described earlier. In order to check the effect this device has on the constancy of the inhalation speed, a number of measurements have been made with experienced subjects. Both the maximum flow rate and the total volume

inhaled per sniff were measured. Although interindividual differences were rather large (up to 20%) both in flow rate and in volume, the intra-individual variation was really very small (about 1, 5% and never more than 5%).

d. Expectancy effects.

Since the presentation series in the cross-adaptation experiments have been constructed in such a way that never more than two odorous stimuli can follow each other and that two groups of odorous stimuli are separated either by one or by two blank stimuli, it may be suspected that the subject, to whom a number of these series are presented, develops expectations as to whether an odorous stimulus will be present or not. Although no explicit information about the way in which the series were constructed is given, the subject may learn something about them during the experiment. He may either be induced to give a negative response if his two preceding responses were positive or he may be tempted to respond positively after a run of negative answers. In either case this will be reflected in a difference in the number of positive responses given to the blank stimuli which immediately follow an odorous stimulus (first zero stimuli) and to those which follow another blank stimulus (second zero stimulus). If these expectations do influence the subjects response, he will give relatively more positive responses to the second zero stimulus than to the first one.

A study of the false positives given in the experiments 27 - 33 has been made to check this. The experiments 27 - 33 were chosen because the odorous substances used in these experiments hardly show any adsorption to the glass walls of the olfactometer. Therefore, there is no danger that the first zero stimuli elicit an artificially high percentage of positive response due to the slow rate of evaporation of the odorous molecules.

The absolute amounts of positive response to the first and to the second zero stimuli in each of the experiments are given in table 3.4. These amounts are also expressed in percentages. The data have been subdivided according to the odorous stimulus that preceded each particular zero stimulus. Also indicated are the differences in percentage positive response between the first and the second zero stimuli. Negative values indicate that relatively more false positives were given to second zero stimuli.

As will be clear from this table, the second zero stimuli do indeed elicit a slightly higher percentage of positive response, but the difference is far

Table 3.4.

False positives in experiments 27 - 33
(Explanation see text.)

Exp.	Substance	Number of first zero stimuli positive	Number of second zero stimuli positive	% First zero stimuli positive	% Second zero stimuli positive	Difference percentages first - second zero stimuli
27	Cyclopentanol	12	5	1,33	1,11	+0,22
	a-Thujone	9	8	1,00	1,78	-0,78
	Cyclohexanone	13	9	1,44	2,00	-0,56
28	iso-Propanol	12	11	1,33	2,44	-1,11
	a-Thujone	10	10	1,11	2,22	-1,11
	Cyclopentanone	20	9	2,22	2,00	+0,22
29	m-Xylene	14	12	1,55	2,66	-1,11
	a-Thujone	11	6	1,22	1,33	-0,11
	Dioxan	17	9	1,89	2,00	-0,11
30	m-Xylene	19	6	2,11	1,33	+0,78
	iso-Propanol	17	10	1,89	2,22	-0,33
	Cyclopentanol	24	11	2,66	2,44	+0,22
31	Cyclohexanone	17	7	2,26	1,86	+0,40
	iso-Propanol	13	5	1,73	1,33	+0,40
	Dioxan	12	3	1,60	0,80	+0,80
32	Cyclohexanone	16	10	1,78	2,22	-0,44
	m-Xylene	19	9	2,11	2,00	+0,11
	Cyclopentanone	26	13	2,89	2,89	0
33	Dioxan	14	9	1,55	2,00	-0,45
	Cyclopentanol	13	10	1,44	2,22	-0,78
	Cyclopentanone	19	7	2,11	1,55	+0,56
	Total:	327	179	1,77	1,95	-0,18
	N	18450	9225			

from being significant ($T_{\alpha} = 75,5$; $N = 20$ in the Wilcoxon test).

In table. 3.5. the data have been regrouped in such a way that the influence of the preceding odorous stimulus on the amounts of positive response to the first

Table 3.5.

Amounts of false positives after seven different odorous substances.

Substance	Number of first zero stimuli positive	Number of second zero stimuli positive	Total zero Stimuli positive	% First zero stimuli positive	% Second zero stimuli positive	Difference percentages first-second zero stimuli	Intensity of odorous substance in % pos. response
1 m-Xylene	52	27	79	1,92	2,00	-0,08	59,1
2 iso-Propanol	42	26	68	1,64	2,03	-0,40	53,1
3 Cyclopentanol	49	26	75	1,81	1,92	-0,11	50,7
4 a-Thujone	30	24	54	1,11	1,78	-0,67	72,1
5 Dioxan	43	21	64	1,68	1,64	+0,03	69,1
6 Cyclopentanone	65	29	94	2,41	2,15	+0,26	61,9
7 Cyclohexanone	46	26	72	1,79	2,03	-0,24	69,5

and second zero stimuli can be estimated more clearly. The data for each of the seven substances have been taken together in this table.

In the last column of this table the perceived intensity of the odorous stimuli, expressed in the average percentage positive response elicited by them, is given.

The fact, that the only rather large difference occurs with a-thujone which is at the same time the strongest of all the odorous stimuli used may be of some importance. In fact, it can be shown that this large difference is not due to a relatively large amount of positive second zero stimuli, but to a relatively low number of positive first zero stimuli. This suggests that after this strong stimulus, a zero stimulus is by contrast judged more often as being non-odorous. Apart from the check on false positives, the subjects were occasionally asked whether they knew what their last response had been in order to see whether they remembered them. Only very rarely would they know this. This is not surprising, because the subjects were allowed to read between trials and they usually participated for such large numbers of series that they lost interest in the actual circumstances of the experiment.

Therefore, it seems unlikely that their expectations played a major role in their decisions.

CHAPTER 4.

EXPERIMENTS ON ADAPTATION AND RECOVERY

4.1. GENERAL

In this chapter the results of a number of experiments on adaptation and recovery will be presented and the meaning of these results for an understanding of the adaptation processes and of the transducing mechanism will be discussed. Since in this chapter the attention will be devoted to the adaptation phenomena themselves rather than to their implications for odour discrimination, no stress has been laid upon the choice of a representative sample of odorous substances. Therefore, only a few odorous substances have been used in the experiments described here. The experiments on cross-adaptation, which provide data on the specificity of olfactory sensitivity, will be discussed in chapter 5.

In the present chapter, the discussion will center around three specific topics:

1. Adaptation at threshold level.
2. Central and peripheral adaptation.
3. The temporal course of recovery.

The treatment of the results of the experiments will be limited to their relevance to the general discussion of these topics.

The discussion of the results of each separate experiment will be preceded by the relevant details of that experiment, such as substances used, number of subjects, interval between stimuli and number of series per subject. Further details can be found in chapter 3 (table 3.1.).

4.2. ADAPTATION AT THRESHOLD LEVEL

a. Description of the experiments.

It was decided to avoid central adaptation as much as possible by using only low concentrations of about threshold level as adapting stimuli in the experiments. In view of this decision and in view of the statement of Pangborn et al. (1964) that no adaptation whatsoever occurs at or near threshold level, it seemed important to investigate the existence of adaptation effects at these intensities. Although the conclusions of Pangborn c. s. could already be invalidated on the basis of their own results (see page 39) the need for some independent proof was felt.

Fortunately, relevant data could be found by inspection of the results of three experiments on daily threshold fluctuations carried out with a small number of subjects (4 in the total of the 3 experiments).

Experiment 1.

Substance: m-Xylene Total duration in work-days: 31

Number of subjects: 1 Type of series used: $1_a - 1_h$

Interval between stimuli: 60 sec.

Number of series per subject: 120

In this experiment four m-xylene stimuli (B, C, D, E) of increasing concentrations and a non-odorous stimulus (A) were presented in random series and the percentages of positive response given by the subject to each of these stimuli were calculated. By comparing the percentages found for stimuli that differed only in their adaptational history (e.g. a C stimulus after an A, a C after a B, a C after a C, etcetera, an idea could be obtained of the influences of different adapting intensities. The results of these comparisons made for each of the five stimuli, are shown in table 4.1.

TABLE 4.1.

Percentages positive response to 5 different stimuli (A, B, C, D, E) after adaptation to 5 adapting stimuli (A', B', C', D', E')

		A	B	C	D	E
After:	A'	8,7	41,4	64,2	85,7	93,2
	B'	5,2	41,7	74,0	91,7	100,0
	C'	14,3	27,6	69,7	72,0	92,8
	D'	11,6	37,6	57,7	73,3	84,7
	E'	14,5	28,0	47,0	78,4	81,4

The results in this table are represented graphically in fig. 4.1.

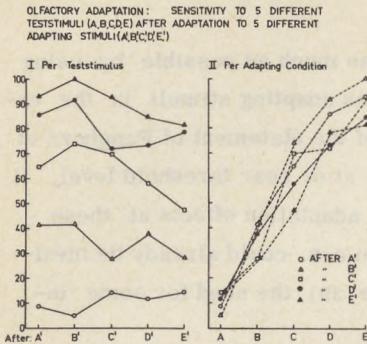


Fig. 4.1. Olfactory adaptation: Percentages of positive response to 5 test stimuli of increasing concentration A, B, C, D, E after adaptation to 5 adapting stimuli A', B', C', D', E'. (same concentrations as A, B, C, D, E; for specifications see table 3.1, page 71; concentration A = A' = 0).

In the left-hand graph of this figure the influence of adaptational history on the percentage positive response is shown. The points connected by the lines (columns in tabl 4.1.) indicate the percentages response given to the same stimulus A, B, C, D or E, when it is presented after an A', B', a C' etcetera. Thus, the upper curve shows that an E stimulus is perceived in 100% of the cases if it is presented after a B', but that the percentage decreases to 92,8 %, 84,7 % and 81,4 % respectively when it follows a C', a D' or an E'.

From these lines it will be clear that in general the amount of reduction in the percentage of positive response to a stimulus increases with an increasing concentration of the adapting stimulus.

In the right-hand graph of fig. 4.1. the same data are arranged in a different way: the points connected by the lines (rows in table 4.1.) indicate the percentages of positive response given by the subject to each of the different stimuli A, B, C, D, E, when they are presented after A', B', C', D' and E' respectively. Thus, the 'upper' line connects the percentages found for A, B, C, D and E, when the preceding stimulus was a B' one. As can be seen, the lines are quite similar in shape, but differ somewhat in slope.

Experiment 2.

Substance: m-Xylene

Total duration in work-days: 24

Number of subjects: 1

Type of series used: $1_a - 1_h$

Interval between stimuli: 60 sec.

Number of series per subject: 140.

Only three m-xylene stimuli (B, C and D) of increasing concentration were used in the second experiment and twice as many zero stimuli were given (E=A). The results are given in table 4.2. and represented graphically in fig. 4.2.

TABLE 4.2.

Percentages positive response to 4 different stimuli (A, B, C, D) after adaptation to 4 adapting stimuli (A', B', C', D').

	A	B	C	D
After: A'	16,0	38,9	80,1	100,0
B'	11,2	40,3	79,2	100,0
C'	13,8	40,0	66,7	89,9
D'	14,1	17,0	40,0	73,4

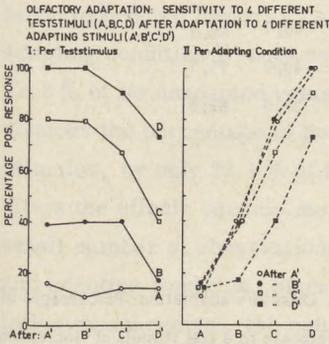


Fig. 4.2. Olfactory adaptation: Percentages of positive response to 4 test stimuli of increasing intensity A, B, C, D, after adaptation to 4 adapting stimuli A', B', C', D', (same concentrations as A, B, C, D, for specifications see tab 3.1, page 71 ; concentration A = A' = O.)

These results confirm the results of experiment 1: The amount of reduction of positive response also increases with increasing adapting concentration. From the graph on the right hand side it may be seen that adaptation may not only alter the slope of the sigmoid curves found, but may also make the whole curve shift to a higher intensity level.

Experiment 3.

Substance: m-Xylene

Total duration in work-days: 25

Number of subjects: 2

Type of series used: $1_a - 1_h$

Interval between stimuli: 60 sec.

Number of series per subject: 130.

In the third experiment the number of m-xylene stimuli of increasing concentrations (B, C, D, E) was again Four. The results of this experiment are shown in table 4.3. and in fig. 4.3.

The data of the two individual subjects have been averaged. The percentages of positive response given to the non-odorous stimuli are not represented in fig. 4.3.

TABLE 4.3.

Percentages positive response to 5 different stimuli (A, B, C, D, E) after adaptation to 5 adapting stimuli (A', B', C', D', E').

	A	B	C	D	E
After: A'	0	11,1	31,9	66,5	87,3
B'	0,7	10,9	32,6	62,1	85,5
C'	0	8,7	20,1	50,7	82,8
D'	0,9	8,8	17,6	49,0	77,7
E'	0,4	6,3	19,9	38,0	68,0

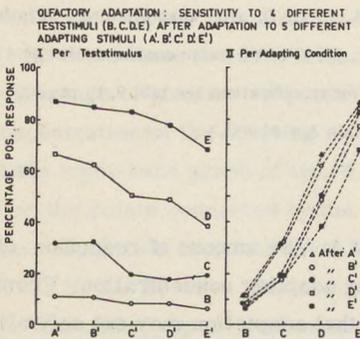


Fig. 4.3. Olfactory adaptation: Percentages of positive response to 4 test stimuli of increasing concentration B, C, D, E, after adaptation to 5 adapting stimuli A', B', C', D', E'. (same concentrations as B, C, D, E, for specifications see table 3.1., page ; concentration A = A' = 0).

The results of this experiment show the same characteristics as those of the other two experiments. The more intense the adapting stimulus, the larger is the reduction in percentage of positive response to the next stimulus. In table 4.4. the amount of the reduction, i.e. the difference between the percentage of positive response found after a given adapting condition and the percentage found for the same test stimulus after A', is expressed as a percentage of the percen-

tage of positive response after A'.

TABLE 4. 4.

Amounts of response reduction by adaptation, expressed in percentages of the unadapted test stimulus (test stimulus after A').

	B	C	D	E
After: A'	0	0	0	0
B'	1,8	-2,2	6,6	2,1
C'	21,6	37,0	23,8	5,2
D'	20,7	44,8	26,3	11,0
E'	43,2	37,6	42,9	22,1

This table shows that the relative adapting effect of a given adapting stimulus tends to become lower as the intensity of the test stimulus rises. Thus, the adapting condition E' cuts down the percentage of positive response to D by 42,8 % of its unadapted value (after A'), whereas the same adapting stimulus reduces the percentage of positive response to E, which is a stronger test stimulus, by only 22,1 % of the unadapted value. With stimuli of lower intensities the effects become more irregular. This is in part due to the relatively small number of observations of some of these combinations of test stimulus and adapting condition. Since the series were not designed especially for adaptation measurement, the combinations do not all occur in the same frequency. It can also be shown that both the slopes and the positions of the ogives representing the relationship between percentage of positive response and concentration of the test stimulus (right hand graph in fig. 4.3), are affected by differences in the adapting conditions. This can be illustrated most clearly by converting the percentages of positive response given in table 4.4 into z-scores and by calculating the best fitting straight line for the data in each row. The equations representing the lines thus obtained are given in table 4.5, together with the sums of the squares of the differences between the calculated and the observed Y-values (ΣW^2), which give an impression of the "goodness of fit" of the lines. In the last column of the table the olfactory thresholds, found for each of the adapting conditions, are given. These thresholds are obtained by simply solving the equations for $Y = 0$.

TABLE 4.5.

Adaptation to m-xylene: Relationships between stimulus concentration in Mol./liter (X) and amount of positive response expressed in z-scores (Y) under different adapting conditions (A', B', C', D', E')

	$Y = mX + k$	ΣW^2	Threshold: (Mol./liter)
A'	$Y = 8,29.10^7 X - 2,031$	0,0066	$2,45.10^{-8}$
B'	$Y = 7,93.10^7 X - 1,985$	0,0004	$2,51.10^{-8}$
C'	$Y = 8,06.10^7 X - 2,250$	0,0434	$2,79.10^{-8}$
D'	$Y = 7,51.10^7 X - 2,195$	0,0505	$2,92.10^{-8}$
E'	$Y = 6,79.10^7 X - 2,190$	0,0090	$3,21.10^{-8}$

The slopes of the five lines vary in an almost perfect way in accordance with the intensity of the adapting stimulus, as will be clear from an inspection of fig. 4.4, in which the lines are represented graphically. The lower the intensity of the adapting stimulus, the steeper the slope of the line. The only exception to this rule is the line found for adapting condition C'. It should be remarked that the fit of this line is rather poor in comparison to that of the other lines (the second largest ΣW^2).

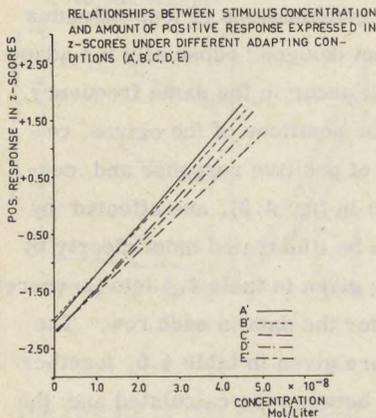


Fig. 4.4. Best fitting straight lines representing the relationships between stimulus concentration and amount of positive response expressed in z-scores under 5 different adapting conditions.

The fact that the k values in the equations of table 4.5, i. e. the cut-off points on the Y-axis for X = 0, are somewhat lower for the last three equations than for the first two, may indicate that also some form of lateral shift takes place, when the adapting stimuli become more intense.

Finally, it should be remarked that there is a clear relationship between the adapting intensity and the olfactory threshold. The stronger the intensity of the adapting stimulus has been, the higher is the threshold. This relationship can be described by the power function $T = 9,89 A^{0,168}$ in which T is the threshold concentration and A is the adapting concentration. The fact that a power function is found is in accordance with the results of Cheesman and Townsend (1956), who claimed that there existed a linear relationship between the logarithm of the threshold and the logarithm of the adapting concentration (see page 36). Whereas the slope of this line expressed by the exponent of the power function was always about .70 in Cheesman's experiments with homogeneous pairs of adapting and test stimuli, the value of the exponent found here is only .17. However, this difference could perhaps be explained by the fact that in this experiment as distinct from those of Cheesman's, a period of 30 seconds has always been allowed for recovery.

b. Conclusions.

On the basis of the data collected in these three experiments it can be concluded that, in general, the influence of adaptation is easily demonstrated with adapting stimuli of threshold concentration, even after a recovery period of 60 seconds. The denial of the existence of these influences by Pangborn and her co-workers can therefore be rejected. It can also be concluded that the adapting effect increases with increasing concentration of the adapting stimulus. Finally, it can be shown that the slopes of the sigmoid curves found for a set of test stimuli of increasing concentrations are affected by differences in adapting conditions and that the height of the olfactory threshold is positively correlated with the intensity of the adapting stimulus that preceded the threshold measurement.

4.3. CENTRAL AND PERIPHERAL ADAPTATION.

a. Description of the experiments.

After having demonstrated that adaptation does occur even with the use of low intensity adapting stimuli, it seemed important to find out whether the adaptation measured in the experiments was mainly central or mainly peripheral in nature.

As has been pointed out in the last sections of chapter 2, (pages 56 - 62) adaptation may occur at very different levels in the receptor system.

One way to estimate the respective contributions of the adapting processes at the level of the receptor cells and the olfactory nerves on the one hand, and of those at the levels above the first synapse in the glomeruli on the other, is to compare the adapting effects of monorhinal adaptation on the olfactory sensitivity at the ipsilateral and at the contralateral side of the nose. If the effects at the two sides of the nose do not differ, the adaptation is purely central in nature or at least, as in the case of changes in the mucus flow, regulated by way of a central mechanism. If, on the other hand, no adapting effect is found at the contralateral side, while still some adaptational effect persists at the ipsilateral side, it is very likely that peripheral adaptation plays an important part. Some experiments along these lines by Elsberg (1935) and by Stuiver (1958) have already been reported (see pages 43 and 46).

However, both these authors used rather strong adapting stimuli and since it was deduced from some other experiments by Stuiver (see page 45) that peripheral adaptation was most likely to be measured in experiments in which the intensity of the adapting stimuli was kept low and the time allowed for recovery was long, the need for some further experimentation was felt.

Experiment 4.

Substance: m-Xylene	Total duration in work-days: 30
Number of subjects: 7	Type of series used: $2_a - 2_d$
Interval between stimuli: 20 sec.	(40 sec. between ipsilateral stimuli)
Number of series per subject: 36	

In this experiment monorhinal stimulation took place alternatingly at the right and at the left side of the nose. Unfortunately, it was not yet possible, at the time of this experiment, to stimulate both sides of the nose simultaneously with different stimuli (odorous on one side and non-odorous on the other). Disturbing factors, like contralateral adaptation by way of retro-nasal stimulation, could therefore not be completely excluded.

The presentation series used in this experiment have been described in chapter 3 (see page 77). They are arranged in such a way, that the same series of odorous stimuli is presented to one side of the nose under two different adapting conditions at the contralateral side of the nose. Under the first of these conditions (A) only 25% of the stimuli presented at the contralateral side of the nose

are odorous stimuli, whereas under the other condition (B) odorous stimuli are present in 75% of the cases on that side. The test stimuli at the original side of the nose follow each other with intervals of 40, 80 and 120 seconds respectively. The percentages of positive response to each of these three types of test stimulus under adapting conditions A and B respectively, are given in table 4.6.

TABLE 4.6.

Percentages positive response to odorous test stimuli after different recovery times under two contralateral adapting conditions.

		Recovery time since last test stimulus (ipsilateral)		
		40	80	120
Condition A (25% adapting stimuli)		47,02	49,01	55,16
Condition B (75% adapting stimuli)		35,52	41,47	44,25
Difference A - B		11,50	7,54	10,91
Significance of difference p :		<.02	n.s.	<.02
Wilcoxon	T :	0	4,5	0
	n :	7	7	7

The fact that differences between the percentages of positive response to the test stimuli under the two conditions are found, indicates that condition B exerts indeed a stronger adapting effect and that the influence of central adaptation has not been ruled out in this experiment.

A further analysis of the presentation series makes it possible to compare the percentages of positive response given to the last stimulus of specific stimulus combinations. In table 4.7 the results of such an analysis are given. The contralateral adapting stimuli are indicated at the left-hand side of each stimulus combination in this table and at the right-hand side one finds the ipsilateral adapting stimulus (top) and the test stimulus (bottom). The percentages of positive response to this last stimulus are given.

In the table an extrapolated value is given in brackets for a combination that does not (and in a strict sense even could not) occur. This extrapolated value has been included so as to make calculation of the means of both rows and columns possible. The extrapolation was made on the basis of the results in the other rows of the table, in which the percentages of the last two combinations hardly differ at all. Analogous to these other rows and on the assumption that the results in these rows prove that the particular adapting condition which is characteristic for the middle column does influence the results in almost the

same way as the adapting condition in the last column, the results of the last combination in the first row are considered to be a fair estimate of the true value of the missing combination.

TABLE 4.7.

Contralateral and ipsilateral adaptation.
 Percentage positive response to the last stimulus of different stimulus combinations (In brackets: extrapolation).

Combination			Mean
X		X	38,0
X		O	
X		X	
29,8	(42,1)	42,1	
X	X	X	49,5
O	X	O	
O	O	O	
X	O	O	
X	X	X	
46,1	51,0	51,5	
X	X	X	55,4
X	O	X	
O	O	O	
O	X	O	
O	O	O	
X	O	O	
X	X	X	
49,8	58,0	58,3	
Mean	41,9	50,4	50,6

Finally, both the first and the last combination of the last row contain an extra contralateral adapting stimulus. Since the interval between this stimulus and the test stimulus is large, it seems unlikely that these extra stimuli influence

the results in a significant way.

The only difference between combinations within the rows that is statistically significant, is the one between the first and the last combination of the first row. Within the columns all three differences between the first and the second row and the middle one between the second and the third row are significant. All differences between the first and the third row are again significant.

b. Conclusions.

The results shown in table 4.7 lead to the following conclusions:

1. Contralateral adaptation does occur.

Combinations in which a contralateral adapting stimulus is given 20 seconds before the test stimulus (first column) yield a lower percentage of positive response than similar combinations in which no contralateral stimulation is given (last column).

2. Recovery from contralateral adaptation is fast.

Combinations in which the contralateral adapting stimulus is presented 60 seconds before the test stimulus (middle column) yield a percentage of positive response that is nearly as high as that of a similar combination in which no contralateral adapting stimulus is presented (last column).

Recovery from the adaptation caused by the contralateral stimulus must therefore have taken place within 60 seconds. This is in accordance with the results of Stuiver, who also found that recovery from contralateral adaptation was fast.

3. Ipsilateral adaptation is stronger than contralateral adaptation.

Combinations in which the ipsilateral adapting stimulus is presented 40 seconds before the test stimulus (upper row) yield a lower percentage of positive response than similar combinations in which the ipsilateral adapting stimulus is given 80 seconds before the test stimulus (middle row) and these last combinations in turn yield a lower percentage of positive response than the combinations in the lowest row of the table in which the ipsilateral adapting stimulus precedes the test stimulus by 120 seconds. The total differences in the mean percentages of positive response to the upper and lower combinations in the columns are at least twice as large as those between the mean percentages of response to the first and the last combinations of the rows.

Furthermore, it should be noted that the test stimuli in the first column

follow the contralateral adapting stimulus after a recovery period of only 20 sec., whereas the test stimuli in the first row follow the ipsilateral adapting stimulus after a recovery period of 40 sec.

The percentages used in the comparison of the ipsilateral and contralateral adapting effects are, therefore, somewhat biased. If equal recovery times had been used, the difference between the effects of these two modes of adaptation would probably have been even larger.

4. Recovery from ipsilateral adaptation is slow.

Whereas recovery after contralateral adaptation seems to be completed within 60 seconds, it takes considerably longer (perhaps even more than 120 sec) to restore the olfactory sensitivity after ipsilateral adaptation. This is again in accordance with the results of Stuiver, who also found that ipsilateral adaptation had a much more lasting effect than contralateral adaptation.

On the basis of these data, which are in agreement with Stuiver's results, one is inclined to accept his interpretation that in ipsilateral adaptation two different adapting processes, one in the central parts of the system and one peripheral in nature, are involved, whereas in contralateral adaptation only the central process (i. e. a process that occurs above the level of the glomeruli) plays a part.

Of course it remains possible to explain the large difference between the amounts of response reduction caused by ipsilateral and contralateral adaptation by assuming that the central parts involved in the perception of the test stimulus are affected more heavily by ipsilateral adapting stimuli. However, the fact that recovery proceeds at a much slower rate after ipsilateral than after contralateral adaptation, makes it more likely that two different processes, a central one allowing rapid recovery and a peripheral one which is much more persistent, are involved indeed.

Before concluding the discussion of the results of this experiment, it should be remarked that the combined effect of the two forms of adaptation (see the percentages on the diagonal from top left to bottom right) is rather large. This proves once more that adaptation plays an important part, even when adapting stimuli of threshold level are used.

4.4. RECOVERY

One of the most remarkable features of the experiments described sofar

is the fact that the adaptational effects caused by these low concentrations are still perceptible after a recovery period of 60 seconds.

The time course of recovery after adaptation has been studied in a number of experiments. Some of these experiments have already been described in other publications (Köster, 1965, 1968), but they will be discussed here again, because of the relevance of their results for an understanding of adaptation phenomena.

a. Recovery experiments with m-xylene.

Experiment 5

Substance: m-Xylene

Total duration in work-days: 30

Number of subjects: 12

Type of series used: $3_a - 3_c$

Interval between stimuli: 60 sec.

Number of series per subject: 90

The first set of data to be shown here was provided by an experiment intended for sensitivity measurement. In this experiment odorous stimuli of only one concentration were presented together with a number of non-odorous stimuli.

The recovery intervals between two odorous stimuli obtained in this way were 60, 120, 180 or 240 seconds.

Table 4.8 gives the percentage of positive response obtained for the first odorous stimulus after each of these intervals. Also included are the differences between the response percentages found and an indication of the statistical significance of these differences.

TABLE 4.8.

Recovery after adaptation (Exp. 5)

Substance: m-Xylene

Recovery time in sec.	60	120	180	240
Percentage pos. response	39,8	46,1	46,8	51,8
Differences		6,3	0,7	5,0
Significance		$p < .005$	n. s.	n. s.
Wilcoxon T :		2	33	12,5
n :		12	12	10

Experiment 7

Substance: m-Xylene

Total duration in work-days: 16

Number of subjects: 2

Type of series used: $5_a - 5_j$

Interval between stimuli: 32 sec.

Number of series per subject: 75

In order to study some parts of the recovery period more carefully an experiment was carried out with stimulus intervals of 32 seconds.

Recovery periods of 32, 64, 96, 128 or 160 seconds were used. Each subject received the odorous stimulus 300 times under each of these recovery conditions and again the percentages of positive response were calculated. The results of this experiment are given in table 4.10.

TABLE 4.10.
Recovery after adaptation (Exp. 7)

Recovery time in sec.	32	64	96	128	160
Percentage pos. response					
Subject D.K.	57	74	76	85	89
Subject J.G.	21	50	56	73	80
Average	39	62	66	79	84,5
Differences	23,0	4,0	13,0	5,5	

The results are represented graphically in fig. 4.5.

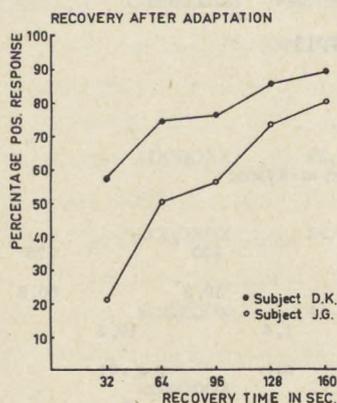


Fig. 4.5. Recovery after adaptation to m-xylene for two subjects.

As the differences shown in tabel 4.10 and the irregular shape of the curve in fig. 4.5 indicate, recovery occurs mainly in two periods between 32 and 64 seconds and between 96 and 128 seconds. Between 64 and 96 seconds and beyond 128 seconds hardly any recovery takes place. The recovery curve has, therefore, a clearly biphasic shape.

When this result was obtained the genuineness of this irregularity was doubted very much at first. However, the shape of the curve is identical for each of the two individual subjects and it proved to be highly reproducible, even when different presentation series were used in order to exclude effects that might have been caused by a lack of true randomness.

Two other possible sources of the biphasity of the curves, expectation effects and third order effects, have been investigated in the next two experiments.

Experiment 8

Substance: m-Xylene

Total duration in work-days: 20

Number of subjects: 7

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 25

A third experiment on the recovery after adaptation to m-xylene was carried out with a somewhat different interval duration of 25 seconds to make sure that the occurrence of the biphasic effect was dependent upon the actual recovery time and not upon the number of intervals between the adapting and the test stimuli. This seemed important, for if the number of intervals proved to be more important than the recovery time, the whole biphasic effect might have been a mere artefact caused by a signal expectancy or a response set of the subject.

The results of this experiment are given in table 4.11.

TABLE 4.11.
Recovery after adaptation (Exp. 8) Substance: m-Xylene

Recovery time in sec.	25	50	75	100	125
Percentage pos. response	21,7	37,1	48,9	50,3	60,9
Differences	15,4	11,8	1,4	10,6	
Significance	$p < .025$	$p < .01$	n.s.	$p < .01$	
Wilcoxon T :	0	0	11,5	0	
n :	6	7	7	7	

As is indicated in this table the sensitivity does rise significantly up to 75 seconds of recovery time and again beyond 100 seconds, but in the period between these two recovery times no significant increase in sensitivity takes place. This is in agreement with the time course found in the preceding experiment. It can therefore be concluded that the biphasic shape of the curve is indeed dependent upon the recovery time elapsed since the last stimulus, and not upon the number of intervals between the adapting stimulus and the test stimulus. In the preceding experiment the flat part of the curve was found in the third interval after the adapting stimulus and in this experiment it is found in the fourth interval. It is therefore very unlikely that expectancy effects or response sets play a part in the occurrence of the biphasic curve.

The possibility that the irregularities in the recovery curves are caused by the influence of second order effects has also been considered.

An analysis of the data of experiment 7 was made and some combinations of 3 odorous (X) and 4 non-odorous stimuli (O) were selected, in which the position of the second odorous stimulus was varied in a systematic way. In table 4.12 the percentages of positive response to the last odorous stimulus of five of these combinations are compared.

TABLE 4.12.

Second order effects in recovery after adaptation.

Selected combinations with constant distance between first and third odorous

stimulus. Substance: m-Xylene (Exp. 7)

Combination	Percentage pos. response	Difference	Recovery time between 2 nd and 3 rd odorous stimulus
XOOOXX	26,8		32
		25,2	
XOOXOX	52,0		64
		- 4,0	
XOOXOOX	48,0		96
		19,2	
XOXOOOX	67,2		128
		8,6	
XXOOOXX	75,8		160

From these results it becomes clear that keeping the second order influences constant only accentuates the biphasic shape of the curve. This even reaches the point at which the difference between the percentages found after 64 and 96 seconds of recovery becomes negative.

That the different second order effects may obscure the biphasic shape to some extent, when the combinations are presented randomly in the series, is understandable if one realizes that for instance each of the odorous stimuli at the beginning of the last combination in table 4.12 may set up a biphasic process, but that these two processes would necessarily be out of phase with each other and would therefore reduce the biphasic aspect of the curve that combines their effects. Thus it seems that the second order effects, instead of causing the irregularities, are more likely to diminish them. In order to reconfirm these findings and to make sure that the same trend could be found at shorter inter-stimulus intervals another experiment was carried out.

Experiment 9

Substance: m-Xylene

Total duration in work-days: 14

Number of subjects: 3

Type of series used: $7_a - 7_e$

Interval between stimuli: 25 sec.

Number of series per subject: 50

In this experiment all possible second order combinations containing from zero to eight non-odorous stimuli were presented to the subjects.

At one extreme in this series one finds the combination XXX and at the other the combination XOOOXOOOX. The percentages of positive response to the last stimulus of each combination are given in table 4.13.

To find a combination like XOXOOX in this matrix one takes the row indicated XOX and looks under XOOX. The underlined stimuli indicate the second or middle odorous stimulus of each combination. In the columns of this matrix one finds combinations in which the distance between the second and the third odorous stimulus is kept constant and the distance between the first and the second odorous stimulus is varied. In the rows the distance between the first and the second odorous stimulus, the "prefix", is kept constant, whereas the distance between the second and the third odorous stimulus is varied. The data of the three subjects have been combined.

TABLE 4.13.

Second order effects in recovery after adaptation.

Substance: m-Xylene (Exp. 9)

Prefix	End-combination:					Total
	<u>XX</u>	<u>XOX</u>	<u>XOOX</u>	<u>XOOOX</u>	<u>XOOOOX</u>	
<u>XX</u>	33,3	51,3	69,3	74,0	80,7	61,7
<u>XOX</u>	32,0	51,3	70,0	70,7	80,0	60,8
<u>XOOX</u>	39,3	68,7	76,7	77,3	81,3	68,7
<u>XOOOX</u>	48,7	61,3	82,7	80,0	86,7	71,9
<u>XOOOOX</u>	48,0	58,0	75,3	80,7	82,7	68,9
Total	40,3	58,1	74,8	76,5	82,3	66,4

As will be seen from the percentages in the lowest row, which indicate the totals regardless of the special "prefixes", the results reconfirm the results of experiment 8. Here also recovery takes place up to 75 seconds of recovery time and again beyond 100 seconds, but the part of the curve between these two recovery times remains relatively flat. Further analysis of the results in the separate rows shows that in all of them except the last the difference between the third and the fourth column is smaller than the difference between the fourth and the fifth column. The occurrence of the biphasic shape of the recovery is therefore not dependent upon the influence of the second order effects.

If the distance between the first and the third odorous stimuli is kept constant, but the position of the second stimulus is varied as in table 4.14, the biphasic shape becomes again more accentuated.

Just as in the results given in table 4.12, one of the differences between the successive percentages of positive response is a negative one. Here, it is the difference between the percentages at 75 and 100 seconds of recovery time, and in the other table it was the difference between the percentages at 64 and 96 seconds. Therefore, it is likely that between 60 and 100 seconds of recovery time a true negative phase occurs in the recovery curve of m-xylene.

Before concluding the description of this experiment some attention should be given to the general influence of the different prefixes (see table 4.13). As can be seen from the total column giving the percentages of positive response fol-

TABLE 4. 14

Second order effects in recovery after adaptation.

Selected combinations with constant distance between first and third odorous stimulus.

Substance: m-Xylene (Exp. 9)

Combination	Percentage pos. response	Difference	Recovery time between 2 nd and 3 rd odorous stimulus
XOOOXX	48,0		25
		13,3	
XOOXOX	61,3		50
		15,4	
XOOXOO	76,7		75
		-6,0	
XOXOOX	70,7		100
		10,0	
XXOOOX	80,7		125

lowing each prefix, irrespective of the end combinations used, the differences in effect of the different prefixes are rather small. Furthermore, there are two groups that can be distinguished. The upper two prefixes (XX and XOX) differ very little in their effect (i. e. in the amount of reduction in positive response caused by them), but their effect is considerably larger than the effects exerted by the other three, which again do not differ very much among themselves. This indicates that beyond a certain period the last stimulus is out of reach of the effect of the first one in a second order combination.

Although on the basis of the results in the total column one would be inclined to set this period at less than 100 seconds, inspection of the individual columns learns that a period of less than 125 seconds is more adequate, because in the first column, where the third stimulus follows the second one immediately, the transition between the two groups is less abrupt and becomes complete only between the third row and the fourth row. (In combination XOOOXX the distance between the first and the third odorous stimulus is 125 seconds.)

An even more interesting conclusion can be drawn from the fact that the percentages of positive response given to the combinations in the second row of

table 4.13 are not higher and in some cases even lower than the percentages found for the corresponding combinations in the first row.

The prefixes OXX and XOX have the same adapting effect. This may mean that maximum adaptation is reached, when two adapting stimuli follow each other within a period of 50 seconds (or at least less than 75 seconds), regardless of the distance of the stimuli within that period. It is argued that, if this is true, inserting another X in the XOX prefix should not increase the adapting effect of the prefix. To check this point, the percentages of positive response to the last stimulus of three combinations which contained XXX as an adapting prefix were calculated. The results of these calculations are shown in table 4.15, where the percentages of positive response of these combinations are compared with the corresponding combinations in which OXX or XOX served as the prefix. (the percentages given for the OXX combinations were recalculated from the original values of the upper row in table 4.13 after subtraction of the combinations with XXX prefixes).

TABLE 4.15.

Comparison of percentages positive response to selected combinations after 3 different prefixes.

Substance: m-Xylene (Exp. 9)

Prefix	End-combination:			Total
	<u>XOX</u>	<u>XOOX</u>	<u>XOOOX</u>	
<u>OXX</u>	51,8	68,7	73,7	64,7
<u>XOX</u>	51,3	70,0	70,7	64,0
<u>XXX</u>	50,0	71,4	74,3	65,2
Total	51,1	70,0	72,9	

As can be seen from this table the introduction of the extra X in the XOX prefix does not affect the percentages of positive response and the conclusion that adaptation is at its maximum, when two adapting stimuli follow each other with an interval of 50 seconds or less, is therefore justified. This means that the results in the two upper rows of table 4.13 show the true recovery curves after maximum adaptation and that the results in these rows are not influenced in any

way by possible third order effects. Obviously, two short separate sniffs of a concentration of m-xylene, which is perceived in about 85% of the cases taken within a period of 50 seconds, suffice to adapt the olfactory sense maximally to this concentration. Though adaptation is extremely rapid, recovery is much slower, for after 25 seconds only 38,3 % of its original sensitivity (32,6 % positive response is 38,3 % of 85 % positive response) has been restored and after 50, 75, 100 and 125 seconds these percentages rise to 60,3, 81,9, 85,1 and 94,5 respectively.

The recovery curves found for m-xylene in the last four experiments are given together in figure 4.6.

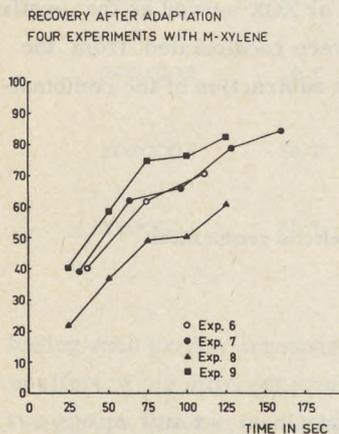


Fig. 4.6. Results on recovery after adaptation to m-xylene obtained in four independent experiments.

As can be seen all curves resemble each other very much, both in shape and in slope. The curve of experiment 6, which is based on only three points, fits in well with the curve of experiment 7.

Both the very fast rate of recovery during the first 60 seconds and the biphasic shape are characteristic of the recovery curve for m-xylene.

b. Recovery experiments with the xylene-isomers (di-methyl benzenes).

So far only recovery experiments with meta-xylene have been discussed. In order to see whether the phenomena found for this substance would also be found when closely related odorous substances, like the isomers ortho- and para-xylene, were used, two experiments of the same type as experiment 8 were carried out.

Experiment 10

Substance: o-Xylene

Total duration in work-days: 20

Number of subjects: 9

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 25

In this experiment, o-xylene has been used as the odorous substance. The results are shown in table 4.16.

TABLE 4.16.

Recovery after adaptation (Exp. 10)

Substance: o-Xylene

Recovery time in sec.	25	50	75	100	125
Percentage pos. response	35,8	43,9	58,5	57,4	64,8
Differences	8,1	14,6	-1,1		7,4
Significance	$p < .025$	$p < .005$	n. s.		$p < .005$
Wilcoxon T :	4,5	0	12		0
n :	9	9	7		9

Just like m-xylene, o-xylene shows a clearly biphasic recovery curve. All differences, except the one between 75 and 100 seconds, which is even slightly negative, are significant.

Experiment 11

Substance: p-Xylene

Total duration in work-days: 20

Number of subjects: 9

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 25

The third of the xylene isomers, p-xylene served as the odorous substance in this experiment. The results are given in tabel 4.17.

Here, all differences are significant and no direct indications of a biphasic shape of the recovery curve are found. Nevertheless, the difference between the percentages found at 75 and at 100 seconds of recovery time is smaller than the one between 100 and 125 seconds. The curves for the three xylene-isomers (exp. 8, 10 and 11) are represented in fig. 4.7.

TABLE 4.17.

Recovery after adaptation (Exp. 11)

Substance: p-Xylene

Recovery time in sec.	25	50	75	100	125
Percentage pos. response	47,1	55,0	62,8	66,8	72,7
Differences :	7,9	7,8	4,0	5,9	
Significance :	$p < .025$	$p < .005$	$p < .025$	$p < .005$	
Wilcoxon T :	4,5	0	3	1,5	
n :	9	9	8	9	

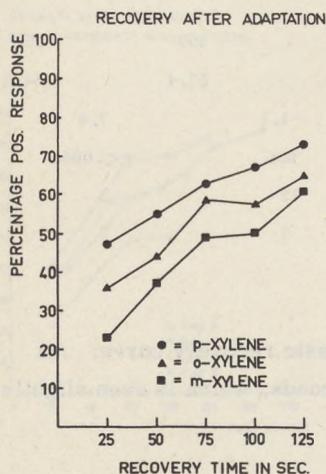


Fig. 4.7. Recovery after adaptation for the three xylene isomers.

The curves resemble each other in general slope, but they differ in their manifestation of the biphasic shape. In passing from para-xylene via meta-xylene to ortho-xylene, the biphasic shape of the curves becomes more evident. One is tempted to relate this change in the curve to the change in the position of the methyl groups. In para-xylene the methyl groups are attached to opposite ends of the benzene ring. Therefore, the molecule is symmetrical in shape. When the methyl groups are in the meta position, the molecule is no more symmetrical and this a-symmetry is even more pronounced in ortho position, where the methyl groups lie together at one side of the molecule.

If, it could be argued, there is some truth in Amoore's steric odor theory and if molecules stimulate receptor sites of different form depending on their own overall molecular shape, it is reasonable to suppose that irregular molecules

like ortho- and meta-xylene fit more different receptor sites than the symmetrical molecules of para-xylene. If furthermore, the different receptor sites have different recovery speeds, the recovery curves of the a-symmetrical molecules can be expected to be more irregular than the recovery curve of para-xylene. Though the curves in fig. 4.7 are in agreement with these hypotheses, it can easily be demonstrated on the basis of the results of the other recovery experiments to be discussed below, that the occurrence of the biphasic shape can not be explained by the degree of symmetry of the odorous molecules. It is interesting to note that subjects have more difficulty in distinguishing qualitatively between the odors of the two isomers with the biphasic curves, o-xylene and m-xylene, than between the odor of each of these and the odor of p-xylene. p-Xylene has a softer somewhat less pungent odor.

c. Recovery experiments with alkyl benzenes.

Following the experiments with the xylenes, similar experiments were carried out with a number of other closely related substances like benzene and some alkyl benzenes. The experiment with toluene (methyl benzene) provides also data on second order effects in the recovery curve. The results of this experiment can be compared directly with those obtained in experiment 9. For this reason the toluene experiment will be treated last in this section.

Experiment 12

Substance: Benzene

Total duration in work-days: 40

Number of subjects: 18

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 25

Benzene was used as the odorous substance in an experiment with a large number of subjects. The results of this experiment are given in table 4.18. Here, all differences are significant, but again the difference between the percentages obtained at 75 and at 100 seconds of recovery is the smallest.

Experiment 13

Substance: Ethyl Benzene

Total duration in work-days: 40

Number of subjects: 20

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 50

TABLE 4.18.

Recovery after adaptation (Exp. 12)					
Substance: Benzene					
Recovery time in sec.:	25	50	75	100	125
Percentage pos. response:	37,7	49,3	61,3	63,9	72,6
Differences:		11,6	12,0	2,6	8,7
Significance:		p<.005	p<.005	p<.005	p<.005
Wilcoxon T :		0	2	15,5	0
n :		18	18	16	17

In the second experiment with a large number of subjects ethyl benzene was the odorous substance. The results of this experiment are given in table 4.19.

TABLE 4.19.

Recovery after adaptation (Exp. 13)					
Substance: Ethylbenzene					
Recovery time in sec.:	25	50	75	100	125
Percentage pos. response:	30,0	41,5	51,6	55,1	63,8
Differences:		11,5	10,1	3,5	8,7
Significance:		p<.005	p<.005	n.s.	p<.005
Wilcoxon T :		1,5	17	64	8,5
n :		20	19	19	19

All differences, except the one between the percentages found at 75 and at 100 seconds of recovery time, are significant. A true biphasic curve is thus found.

Experiment 14

Substance: Cumene

Total duration in work-days: 36

Number of subjects: 17

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 25

Another derivative of benzene, cumene was used in this experiment. The results are shown in table 4.20.

TABLE 4.20.
Recovery after adaptation (Exp. 14)
Substance: Cumene

Recovery time in sec.:	25	50	75	100	125
Percentage pos. response:	26,8	42,8	52,7	57,6	66,2
Differences:	16,0	9,9	4,9	8,6	
Significance:	$p < .005$	$p < .005$	$p < .005$	$p < .005$	
Wilcoxon T :	3	4	19	7	
n :	17	17	16	16	

Here again all differences are significant, but the one between the percentages at 75 and at 100 seconds of recovery is the smallest.

Experiment 15

Substance: Toluene

Total duration in work-days: 45

Number of subjects: 12

Type of series used: $7_a - 7_e$

Interval between stimuli: 25 sec.

Number of series per subject: 50

The last experiment of this series was included mainly to check the results of experiment 9 and to provide more information on the influence of different prefixes in second order combinations. Nevertheless, the results of this experiment can be presented in the same way as those of the preceding experiments

TABLE 4.21.
Recovery after adaptation (Exp. 15)
Substance: Toluene

Recovery time in sec.:	25	50	75	100	125
Percentage pos. response:	43,8	54,9	61,5	67,5	70,9
Differences:	11,1	6,6	6,0	3,4	
Significance:	$p < .005$	$p < .005$	$p < .005$	$p < .025$	
Wilcoxon T :	0	6	0	11,5	
n :	12	12	11	12	

in order to make a direct comparison possible. The odorous substance used was toluene and the results are given in table 4.21.

All the differences are significant and there is no indication of a biphasic recovery curve on the basis of the data presented in this table.

There is some indication of biphaticity, when the results are analysed in more detail as they are in table 4.22. There the results of the combinations with a constant distance between the first and the third odorous stimulus are shown. These results seem to give a recovery curve with a biphasic shape. However, none of the differences between the pairs of successive combinations, except the last one, is significant.

TABLE 4.22

Second order effects in recovery after adaptation.

Selected combinations with constant distance between first and third odorous stimulus.

Substance: Toluene (Exp. 15)

Combination	Percentage pos. response	Difference	Significance	T	n	Recovery time between 2 nd and 3 rd odorous stimulus
XOOOXX	51,2					25
		3,3	n.s.	9,0	8	
XOOOXOX	54,5					50
		6,7	n.s.	20,5	12	
XOOXOOX	61,2					75
		1,3	n.s.	31,0	12	
XOXOOOX	62,5					100
		7,1	$p < .025$	13,5	12	
XXOOOOX	69,6					125

Inspection of the results in the individual rows of the table that gives the data for all second order combinations table 4.23 does not give support to the idea of of biphasic recovery curve for toluene either.

TABLE 4. 23.

Second order effects in recovery after adaptation

Substance: Toluene (Exp. 15)

Prefix	End-combination:					Total
	<u>XX</u>	<u>XOX</u>	<u>XOOX</u>	<u>XOOOX</u>	<u>XOOOOX</u>	
<u>XX</u>	37, 2	53, 6	56, 7	63, 5	69, 6	56, 1
<u>XOX</u>	37, 9	51, 9	57, 7	62, 5	67, 1	55, 4
<u>XOOX</u>	45, 8	53, 6	61, 2	69, 8	70, 1	60, 1
<u>XOOOX</u>	47, 1	54, 5	65, 3	68, 8	72, 4	61, 5
<u>XOOOOX</u>	51, 2	60, 8	66, 6	73, 4	75, 2	65, 5
Total	43, 8	54, 9	61, 5	67, 5	70, 9	59, 7

A comparison of the general features of the results in table 4.23, with those obtained for m-xylene in experiment 9 (see table 4.13) shows that the adapting influence of the first stimulus of a combination on the sensitivity to the last one lasts much longer here than in the case of m-xylene. The differences in percentage of positive response to two combinations like XOOOXOX (54, 5 %), in which the first stimulus precedes the third by 150 seconds, and XOOOXOX (60, 8 %), in which the difference between first and third stimulus is 175 seconds, prove that with toluene the influence of the first stimulus lasts at least 150 seconds. This is reconfirmed by the differences found between XOOXOOX (61, 2 %) and XOOOXOOX (65, 3 %), between XOXOOOX (62, 5 %) and XOOXOOOX (69, 8 %) and even between XOOOXOOOX (68, 3 %) and XOOOXOOOX (73, 4 %). When m-xylene is the odorous stimulus the influences of the first stimulus do not last longer than 125 seconds.

Therefore, it can be concluded that recovery after adaptation is much slower for toluene than for m-xylene.

On the other hand, adaptation is at least nearly as fast for toluene as for m-xylene, which can be demonstrated by the fact that here, as in experiment 9, there is no difference between the adapting effects of the prefixes XX and XOX. This means that also for toluene successive stimulation with two stimuli within a period of at least 50 seconds results in maximum adaptation. This is further illustrated in table 4.24 where the percentages of positive response to three

combinations are given after the prefixes OXX, XOX and XXX.

TABLE 4.24.

Comparison of percentages positive response to selected combinations after 3 different prefixes.

Substance: Toluene (Exp. 15)

Prefix	End-combination:			Total
	<u>XOX</u>	<u>XOOX</u>	<u>XOOOX</u>	
<u>OXX</u>	53,8	57,3	63,1	58,1
<u>XOX</u>	51,9	57,7	62,5	55,4
<u>XXX</u>	52,7	55,0	63,8	57,2
Total	52,6	56,7	63,1	

Again it can be shown that even the introduction of the extra X in the XOX combinations does not substantially alter the adapting effect. (Again, the values given for the OXX prefix have been recalculated from the data in the XX row of table 4.23 after subtraction of the XXX cases).

The recovery curves found for the four substances discussed in this section are shown together in fig. 4.8.

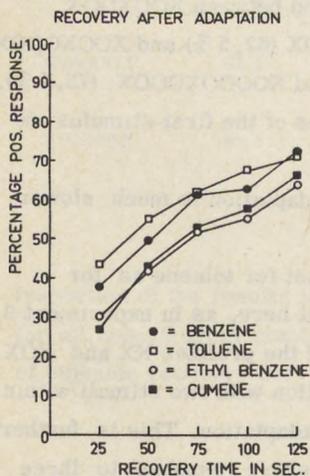


Fig. 4.8. Recovery after adaptation for four alkyl benzenes.

The fact, that benzene, which has the most symmetrical molecule of all four substances, most clearly shows the biphasic shape of the recovery curve, illustrates that symmetry of the molecules is not the functional variable which determines whether the curve will be irregular or not.

Among these four substances, only toluene does not have a biphasic curve. Its curve resembles the curve of p-xylene in two respects. It is monophasic and the initial rise is not as steep as in the curves found for the other substances. As was indicated before (page 121), recovery for toluene is rather slow. It is tempting to ascribe the resemblance of the curves of toluene and p-xylene to the relatively free position of the methyl group in both molecules. Qualitatively both substances have a more pleasant and somewhat softer smell than the other substances discussed, which may indicate that these two substances cause less trigeminal stimulation than the other substances. Although the concentrations used in the experiments are very low, the possibility of trigeminal stimulation can not be ruled out completely. This possibility will be discussed more extensively in section 4.3.e.

Notwithstanding the differences in the biphasic appearance of the four curves in fig. 4.8, they resemble each other very much in general slope and shape.

d. Recovery experiments with odorous substances of diverse molecular structure.

So far only odorous substances with molecules containing a benzene ring have been used in the experiments. In order to check on the generality of the types of recovery curves found, it was decided to use a number of substances of different molecular structure. The substances chosen were iso-propanol, dioxan, cyclopentanone and b-ionone.

Experiment 16

Substance: iso-Propanol

Total duration in work-days: 25

Number of subjects: 14

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 25

In the first experiment of this section iso-propanol was the odorous substance. The results of this experiment are given in table 4.25.

TABLE 4. 25.

Recovery after adaptation (Exp. 16)

Substance: iso-Propanol

Recovery time in sec.:	25	50	75	100	125
Percentage pos. response:	28,5	42,5	55,4	57,3	65,9
Differences:	14,0		12,9	1,9	8,6
Significance:	$p < .005$		$p < .005$	n. s.	$p < .005$
Wilcoxon T :	2		0	18	1,5
n :	14		14	12	14

All differences in percentage of positive response, except the difference between the percentages at 75 and 100 seconds of recovery time, are significant at the 1% level. Therefore, the biphasic shape of the recovery curve is also found, when iso-propanol is the odorous substance.

Experiment 17

Substance: Dioxan

Total duration in work-days: 24

Number of subjects: 13

Type of series used: $6_a - 6_e$

Interval between stimuli: 25 sec.

Number of series per subject: 25

The second experiment was carried out with dioxan as the odorous substance. The results are given in table 4.26.

TABLE 4. 26.

Recovery after adaptation (Exp. 17)

Substance: Dioxan

Recovery time in sec.:	25	50	75	100	125
Percentage pos. response:	32,3	42,4	58,0	58,3	64,5
Differences:	10,1		15,6	0,3	6,2
Significance:	$p < .005$		$p < .005$	n. s.	$p < .005$
Wilcoxon T :	5		0	43,5	3
n :	13		13	13	13

Here all the differences in percentage of positive response are significant. The recovery curve of the sensitivity for dioxan shows the same biphasic shape as those for iso-propanol and m-xylene.

Experiment 18

Substance: Cyclopentanone Total duration in work-days: 30
 Number of subjects: 16 Type of series used: $6_a - 6_e$
 Interval between stimuli: 25 sec.
 Number of series per subject: 25

In this experiment the odorous substance was cyclopentanone.
 The results are represented in table 4.27.

TABLE 4.27.
 Recovery after adaptation (Exp. 18)
 Substance: Cyclopentanone

Recovery time in sec. :	25	50	75	100	125
Percentage pos. response:	43,1	51,0	58,4	61,5	65,3
Differences :	7,9	7,4	3,1	3,8	
Significance:	$p < .005$	$p < .005$	$p < .025$	$p < .025$	
Wilcoxon T :	11	5,5	20,5	21,5	
n :	14	16	15	15	

All differences are significant in this experiment. Therefore, it can not be concluded that the recovery curve of cyclopentanone has the same type of bi-phasic shape as the recovery curves of the substances mentioned so far. It should be remarked, however, that the difference between the percentages of positive response at 75 and 100 seconds of recovery time is the smallest difference found.

Experiment 19

Substance: b-Ionone Total duration in work-days: 15
 Number of subjects: 5 Type of series used: $6_a - 6_e$
 Interval between stimuli: 25 sec.
 Number of series per subject: 25

If b-ionone is used as the odorous substance the results are quite different, as will be seen from table 4.28.

TABLE 4.28.

Recovery after adaptation (Exp. 19)

Substance: b-Ionone

Recovery time in sec.:	25	50	75	100	125
Percentage pos. response:	40,3	41,5	42,3	46,5	54,3
Differences:	1,2		0,8	4,2	7,8
Significance:	n. s.		n. s.	n. s.	$p < .025$
Wilcoxon T :	6,0		6,0	9,0	0
n :	5		5	6	6

Only the last difference in this recovery curve is significant. Not only that there is, of course, no sign of biphasity in this curve, but proper recovery does not even start before 75 seconds of recovery time. It can be concluded therefore that the recovery curve for b-ionone differs from those described so far (both in shape and in slope).

The results of these four experiments are shown together in fig. 4.9.

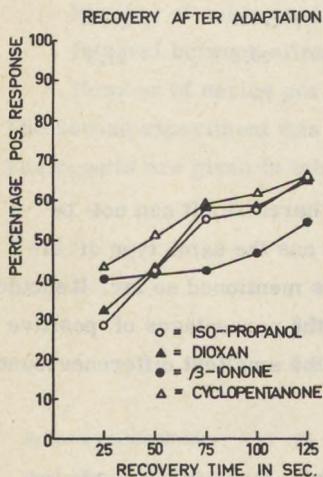


Fig. 4.9. Recovery after adaptation for four odorous substances of diverse chemical nature.

It will be clear, that the curves in this figure are more different in appearance than the curves in the two preceding figures, where the results of substances with more similar molecular structures were given. The recovery curves for iso-propanol and dioxan are clearly biphasic and show the fast initial

rise in sensitivity that is common to the curves of this type. The recovery curve of cyclopentanone resembles the curves found for toluene and p-xylene. It is monophasic and it rises slowly, especially in the beginning.

The curve of b-ionone has a completely different shape. As has already been remarked, recovery starts very late for this substance.

Differences in molecular structure seem to lead to differences in the shape of the recovery curve. In this connection it is interesting that b-ionone which has the most exceptional curve of the substances studied so far, also has an odour that is most markedly different. Presented in high concentrations it has a woody smell, but when it is diluted to near threshold concentrations (as in this experiment), it smells like violets.

Unfortunately, no other floral odours have been used in the recovery experiments. Therefore, it can not be concluded whether the shape of the recovery curve of b-ionone is just specific for that substance or whether it is representative for a class of odours like the floral ones. The odours of the two substances with the biphasic curves are again somewhat more pungent, whereas cyclopentanone has a much softer smell.

e. Recovery experiments: conclusions.

The shape of the recovery curve varies with various odorous substances. The recovery of the sensitivity is slow for some substances and faster for others. For some substances the recovery takes place in different phases, an initial fast one and a slower one.

Perrin (1965) found the same biphasic recovery curves for m-xylene and dioxan in her experiments concerning the recovery of the amplitude of the electro-olfactogram (EOG) in the rabbit after adaptation. Her curves for citral showed no biphasity whatsoever. On the other hand she found not only biphasic shapes in the m-xylene and dioxan curves, but also signs of a true negative phase between the two positive ones. In the experiments described here there are some signs of a negative phase, although none of them is strong enough to provide solid evidence. It will be remembered that the percentage of positive response found for o-xylene at 100 seconds of recovery time is lower than the one at 75 seconds (see table 4.16 page 115) and that the same is true for m-xylene data when the second-order effects are kept constant (see table 4.12 + 4.14 pages 109+112). The same might be true for dioxan, if the second-order effects were kept constant, because the difference between the percentages of

positive response at 75 and 100 seconds is already very small (0.3 %, see table 4.26 page 124) in the present experiment and because keeping the second-order effects constant usually accentuates these effects. The existence of a true phase of negative recovery or loss of sensitivity during the recovery period can not be excluded. In fact, all signs of biphasity might be the result of the occurrence of such a negative phase.

To a certain extent, the recovery curves of the different substances can be used to characterize them.

4.5. WHAT MECHANISMS MAY EXPLAIN THE DIFFERENCES IN RECOVERY FOUND?

Several alternative hypotheses can be mentioned.

1. Specific olfactory receptors.

One way of explaining the different recovery curves would be to assume the existence of a number of different olfactory receptors, each with their own specific sensitivity and their own characteristic rate of recovery. The biphasic shape of the recovery curve of some substances could then be interpreted as the result of the stimulation of two receptor types with clearly different recovery rates. The analogy with the recovery curve of the rods and cones during dark adaptation is obvious. This hypothesis has already been discussed in earlier work (Köster, 1965, 1968) and it has been mentioned again in section 4.4.b. where the possible influence of symmetry of the odorous molecules and Amoore's theory were treated.

Several objections can be raised against it. Thus, it is hard to explain the occurrence of a true negative recovery phase, like the one found by Perrin and perhaps also in this work (see experiments 7, 9 and 10, tables 2.12, 2.14 and 2.16), in terms of recovery of specific receptors. Nevertheless, it is possible that some receptors responsible for the perception of a given odorous compound act as inhibitors to other receptors involved. Gradual recovery of these inhibiting receptors might lead to a reduction of the total amount of excitation and thus to a negative phase in the recovery curve.*

Apart from this objection, the plausibility of the hypothesis is greatly reduced by the fact that in recent electrophysiological studies on single receptor cells Gesteland (1970) did not find any signs of receptor specificity. He comes to

* The author is much indebted to Prof. Dr. J.J. Groen for this suggestion.

the conclusion: "That receptor cells in the frog's nose are organized in such a way as to look at the odor world in as many different ways as possible. The code appears to be holistic".

Although an explanation in terms of different receptor types becomes unlikely on the basis of Gestelands' findings, the same author provides another possible explanation at the peripheral level by pointing out that there are two different processes, an excitatory and an inhibitory one, that contribute to the E.O.G.. After describing a number of different E.O.G. waveforms Gesteland comes to the conclusion that: "As stimulus intensities are changed the relative amplitudes of various components of the E.O.G. can vary in complicated ways. This does not necessarily mean that the cells are behaving in such complicated ways, only that the nonlinear combinations of the external signs of inhibition and excitation processes with different time constants are very complicated".

It will be clear, that the processes described may account for the multiphasic shape of the E.O.G. recovery curves obtained by miss Perrin. They may also be the cause of the biphasic shape of the psychophysical recovery curves discussed in this chapter.

2. Trigeminal and olfactory receptors.

Another possibility to explain the irregular shapes of the recovery curves has already been suggested in section 4.3.c., where it was pointed out that the substances which show the biphasic curves tend to have more pungent odours. It was suggested that trigeminal receptors play an additional part in the perception of these substances.

Until a few years ago the trigeminal sensitivity was generally considered to be much lower than the olfactory sensitivity. Therefore, it seemed unlikely that trigeminal factors influenced the perception of the weak threshold stimuli used in the experiments described here. However, in recent years Beidler and Tucker (1955) and Tucker alone (1962) demonstrated that for some substances the trigeminal nerve endings may be more sensitive than the olfactory receptors.

Beidler (1965) summarizes the findings as follows: "Psychologists often report that phenylethyl alcohol (with its pleasant odor) is one of the few substances that can excite the olfactory receptors without exciting the free nerve endings. However, the recording of neural activity (in the rabbit) shows that in most cases the free endings of the trigeminal nerve respond to lower concentrations of phenylethyl alcohol than do olfactory receptors. This has also been found true of substances that one would normally class as noxious as well as others

possessing pleasant odors. The responses to the vast majority of substances that have been studied, however, do indicate that the olfactory receptors are more sensitive than the free nerve endings. Furthermore, the olfactory receptors are extremely sensitive to certain well-defined odors as the mercaptans".

Now if stimulation of the trigeminal nerve endings played a part in the perception of some of the odorous substances used in the experiments, what effect would this stimulation have on the recovery curves found for those substances?

Does the trigeminal sensitivity decrease under adaptation at the same rate as the olfactory sensitivity and does it recover in a similar way? Here again, Beidlers' findings are very elucidating:

"During successive odor inspirations, the olfactory response is present during the inspirations and declines rapidly during each expiration.

The response is usually of greatest magnitude during the first inspiration and if high concentrations are used, will steadily decline with each successive inspiration. Free nerve endings, on the other hand, increase their response during each inspiration until the response becomes so large it is carried over during expiration to maintain a rather constant level of activity throughout successive inspirations.

The trigeminal response to high odor concentrations often reaches maximum levels when the olfactory response has already completely adapted.

The complete role of the trigeminal nerve is not known, although it is usually thought to be of great importance in various reflexes. One of these reflexes involves the odorous stimulation of free nerve endings, which in turn increases the sympathetic activity in the nasal region. This restricts the nasal passage and limits the amount of odor reaching the olfactory receptors and free nerve endings. The response to some odors is great enough so that the animal may stop breathing for short periods."

Two facts stand out from this survey:

- a. Repetitive stimulation tends to increase the response of the trigeminal nerve rather than to decrease it as would be expected in the case of adaptation.
- b. Stimulation of the trigeminal nerve gives rise to a reflex mechanism that limits the accessibility of the olfactory cleft and in doing so reduces the chance of renewed stimulation of both the olfactory and the trigeminal receptors.

The two mechanisms described are contradictory in nature, the one having a positive effect on the perception of repeated stimuli, the other a negative effect. On the other hand, it will be clear that as the interval between the stimuli

increases, the influence of these effects on the perception of the repeated stimulus decreases. This would result in a decrease of the perceptibility due to the loss of the influence of the first mechanism and in an increase in perceptibility due to a renewed accessibility of the olfactory cleft. These two mechanisms combined with the recovery of the olfactory receptors may provide a reasonable explanation of the biphasic shape of the recovery curve. Thus, the initial fast rise of the recovery curve may be due to the combined effect of the widening of the olfactory cleft (fast) and the recovery of the olfactory sensitivity (slow). Furthermore, the early points of the recovery curve might all be shifted upwards by the increased irritability of the trigeminal receptors. Now, if the widening of the cleft is completed after about 60 sec recovery time and if the summative effect of repetitive trigeminal stimulation is greatly reduced for stimuli that are more than 75 seconds apart, the occurrence of a plateau or even a negative phase in the recovery curve between 75 and 100 seconds becomes understandable.

Unlike the foregoing hypothesis, this one can provide an explanation of the negative phase in the recovery curves, but there also are some objections to it. The fact that the negative phenomena are also found in the electro-olfactogram could be such an objection if one supposed the E.O.G. to be exclusively dependent on the response of the olfactory receptors. Since the fibres and nerve endings of the trigeminus are not lying in one direction they will not give rise to a slow potential and it is indeed hard to see how the stimulation of these endings could influence the E.O.G. in a direct way. Since the question of the nature of the E.O.G. is still not settled, the validity of this objection remains uncertain.

It will be clear that only electrophysiological studies can demonstrate the influence of the trigeminal receptors. As long as no data are available on the time constants involved in the summative trigeminal effects caused by repeated presentation of low stimulus concentrations, and in the reversal of the vascular reflex, the hypothesis remains very speculative.

That the odours of the substances that produce biphasic curves are a bit more pungent is in fact the only behavioral argument in favour of it. Although Beidler has raised some doubt on the relationship between pungency and trigeminal irritability by showing that trigeminal stimulation in the rabbit may also occur with substances that have pleasant odours, he does not mention any substances with noxious odours that do not stimulate the trigeminal nerve endings.

This one argument may remain valid therefore.

3. Changes in vaso-constriction and vaso-dilatation.

Even without any trigeminal stimulation to trigger off sympathetic activity, changes in blood supply may perhaps occur in the nasal region.

Kottmeyer (1957) demonstrated that such changes can be provoked by olfactory stimulation and Schneider and Wolf (1960) studied the effects of different degrees of vaso-dilatation on olfactory sensitivity.

These last authors come to the conclusion that vasodilatation and mucus secretion favour the olfactory perception as long as they do not result in nasal obstruction. It seems unlikely that the effects of the low intensity stimuli used here are large enough to lead to such obstructions.

4. Adsorption and solubility properties.

The different shapes of the recovery curves found for the different odorous substances may be due also to adsorption and solubility phenomena. Although relatively little is known about these phenomena in general and about the specific properties of the surfaces in the epithelium and the composition of the mucus, it is very likely that differences in adsorption and solubility properties may influence the rate of recovery.

Moncrieff (1955) studied the adsorption properties of the olfactory membrane using tissue from the olfactory receptive region of sheep. He showed not only that by adsorption this tissue can reduce the intensity of different odours to a different degree (grass odour being reduced very fast), but also that this tissue reduced the intensities of benzaldehyde and ethyl acetate considerably faster than did other tissues in sheep or even activated carbon.

Thus, the very slow rate of initial recovery found in the case of b-ionone may be related to its strong tendency to adhere to surfaces and to a special receptivity of the mucous membrane for this substance. b-Ionone shows a more pronounced adsorption to glass walls than any other of the substances used here.

It will be clear that none of the four hypotheses mentioned can be either accepted or rejected without further investigation. In most cases only electrophysiological data can bring a definite answer nearer.

CHAPTER 5.

CROSS-ADAPTATION

5.1. GENERAL

In each of the experiments described in chapter 4, the same odorous substance was used both as the adapting stimulus and as the stimulus for testing the sensitivity (test stimulus). In this chapter experiments on cross-adaptation, in which the effect of an adapting stimulus of a given odorous substance on the sensitivity to a test stimulus of another odorous substance is measured, will be discussed. In all experiments the roles of the adapting stimulus and the test stimulus have been interchanged so as to provide complete reciprocity in the measurement of adaptational effects.

Fourteen experiments were carried out with a total of 12 substances. These substances were arranged in two groups of seven, two of them (m-xylene and cyclopentanone) being represented in both groups.

In each group of seven all possible forty-two cross-adaptational relationships were determined.

It was the aim of these experiments to study the types of cross-adaptational effects (reciprocal, non-reciprocal, large, small, no effect) that might be found in a group of diverse substances and to get a first idea of the possibility of odour classification on the basis of cross-adaptation.

First, the results of the separate experiments will be described (5.2. a.) and then the general outcomes will be discussed (5.2. b.).

5.2. DESCRIPTION OF THE EXPERIMENTS.

The general form of these experiments has already been pointed out in chapter 3 (see page 80).

Experiment 20

Substances: m-Xylene
Benzyl Acetate
Citral

Total duration in work-days: 36

Type of series used: 8_{a - d}

Number of subjects: 10

Interval between stimuli: 30 sec.

Number of series per subject: 40

The results of this experiment are given in table 5.1. In the table the percentages of positive response to the last stimulus of each combination of odorous stimuli (XX, XY, XZ, YY, YX, etc.) are given. These percentages can be compared with those obtained in combinations which contain also non-odorous stimuli (XOX, XOOX, YOX, YOOX, YOY, YOOY, etc.). In these combinations the recovery times allowed are 60 and 90 seconds respectively, whereas the recovery time is only 30 seconds in those combinations in which the odorous stimuli follow each other directly.

In the table all results are given twice. In the top half of the table they are grouped according to the test stimulus (last stimulus of the combination). This makes it possible to compare the adapting effects of the different odorants on the sensitivity to this stimulus directly. In the bottom half of the table the same data have been grouped according to the adapting stimulus used. Here, one can compare the adapting effect of a particular stimulus on the different test stimuli.

As can be seen from the differences in percentage of positive response at 30 sec. and 90 sec. of recovery time, the sensitivity to m-xylene is reduced to a considerable degree by adaptation to both benzyl acetate and citral. The fact, that the percentage positive response to m-xylene at 30 seconds after auto-adaptation (XX) is not lower than the percentage found after 90 seconds of recovery is due to an artefact caused by a pressure rebound in the automatic system, which was only discovered and overcome after this first experiment of the series was completed. The relatively high percentage of positive response at 30 sec. of recovery time after self-adaptation found for citral (ZZ) can be explained in the same way. The curves obtained for self-adaptation of m-xylene

in experiments 21 and 22 and of citral in experiments 23 and 24, give a better idea of the adapting effects in these combinations.

TABLE 5.1.

Experiment 20 Cross-adaptation.

x = m-Xylene

y = Benzyl Acetate

z = Citral

Percentages of positive response after 30, 60 and 90 seconds of recovery time.

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	65.4	67.2	64.9
yx	51.0	61.1	67.1
zx	48.4	64.0	68.4
yy	41.7	48.6	51.7
xy	54.4	61.9	56.8
zy	57.5	53.0	61.6
zz	66.5	55.7	66.9
xz	60.3	66.0	65.8
yz	64.5	66.0	65.3

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	65.4	67.2	64.9
xy	54.4	61.9	56.8
xz	60.3	66.0	65.8
yy	41.7	48.6	51.7
yx	51.0	61.1	67.1
yz	64.5	66.0	65.3
zz	66.5	55.7	66.9
zx	48.4	64.0	68.4
zy	57.5	53.0	61.6

If benzyl acetate has a relatively large adapting effect on the sensitivity to m-xylene (YX), the degree in which the sensitivity to benzyl acetate is affected by the previous presentation of the m-xylene stimulus (XY) is much lower. Nevertheless, m-xylene has more adapting influence on benzyl acetate than citral.

It is of some interest to note that the percentage of positive response to benzyl acetate is higher at 60 seconds after m-xylene than at 90 seconds. This is in agreement with the findings about the biphasic recovery curve of m-xylene which have been reported in the preceding chapter. Looking at the adapting effects on citral one sees that, whereas m-xylene has some influence, the reduction in percentage of positive response caused by benzyl acetate is virtually nil.

Experiment 21

Substances: m-Xylene	Total duration in work-days: 38
Safrole	
Methyl Salicylate	Type of series used: 8 _{a-d}

Number of subjects: 12

Interval between stimuli: 30 sec.

Number of series per subject: 40

The results of this experiment are shown in table 5.2.

Here, a normal recovery curve is found for m-xylene after self-adaptation. The fact, that the same m-xylene stimulus, which is perceived in 58,6 % of the cases after 90 seconds of recovery time in the XX-combinations, is perceived in 77,1 % of the cases if it is preceded with a 90 second interval by the methyl salicylate stimulus, indicates that the recovery from self-adaptation is not yet completed after 90 seconds. Therefore, the flattening of the recovery curve of m-xylene between 60 and 90 seconds of recovery found here, seems to be a reflection of the flat part of the biphasic recovery curve mentioned earlier in chapter 4 (see page 108), rather than a sign of complete recovery.

If one considers 77,1 % of positive response to the m-xylene stimulus (the highest percentage found in this experiment) to be the best approximation of the sensitivity of the subjects after complete recovery, the actual reduction in percentage of positive response caused by a preceding m-xylene stimulus (XX) is emphasized dramatically. Even after 90 seconds of recovery from this stimulus the reduction is still 18,5 % (77.1 - 58.6) and at 30 seconds of recovery it is even 36.9 % (77.1 - 40.2). Since there is no direct evidence from these data that complete recovery has indeed been reached at 77.1 percent, the real reductions

may be larger still.

TABLE 5.2.

Experiment 21 Cross-adaptation

x = m-Xylene

y = Safrole

z = Methyl Salicylate

Percentages of positive response after 30, 60 and 90 seconds of recovery time.

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	40.2	56.6	58.6
yx	65.6	64.8	70.0
zx	65.5	66.4	77.1
yy	68.1	47.9	55.9
xy	47.3	53.0	53.9
zy	51.6	46.8	54.5
zz	67.4	50.3	51.8
xz	32.3	42.3	46.8
yz	42.1	43.8	44.8

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	40.2	56.6	58.6
xy	47.3	53.0	53.9
xz	32.3	42.3	46.8
yy	68.1	47.9	55.9
yx	65.6	64.8	70.0
yz	42.1	43.8	44.8
zz	67.4	50.3	51.8
zx	65.5	66.4	77.1
zy	51.6	46.8	54.5

It is quite obvious, that neither the safrole nor the methyl salicylate stimulus has such a large effect on the sensitivity to m-xylene. Nevertheless, they definitely reduce the percentage of positive response to the m-xylene stimulus. The adapting effect of the safrole stimulus seems to be a bit more

long lasting than that of the methyl salicylate one, because after 90 seconds of recovery the percentage has risen to 70.0 %, which is still 7.1 % below the 77.1 % obtained after methyl salicylate.

If this experiment did not suffer from the artefact which influenced the percentages at 30 seconds of recovery after self-adaptation for m-xylene and citral in the last experiment, here, another artefact has distorted the results obtained for self-adaptation of safrole and methyl salicylate after 30 seconds of recovery. As was pointed out already in chapter 3, adsorption to the glass walls of the olfactometer slows down the build up of concentration of some substances. These substances do not reach their full concentration in the 25 seconds allowed between the subjects last response and the presentation of the new stimulus. However, if the substance stays longer in the airduct as is the case in the XX, YY and ZZ combinations where the stimuli are left on for a full 55 seconds, the concentration of the stimulus will become higher and, consequently, will be perceived more often.

In a special experiment (see chapter 3, pages 82-87), in which all seven substances used in this group of cross-adaptation experiments were tested, it was shown that the adsorption influences the results of safrole, butyl acetate and methyl salicylate, but not those of benzyl acetate, cyclopentanone, citral and m-xylene.

Therefore, the three substances that are affected show relatively high percentages of positive response at 30 seconds of recovery time after self-adaptation or, to make a more correct statement, artificially low, but equally affected, percentages of positive response in all other combinations.

From the results of this experiment it will be clear that safrole and methyl salicylate have very little cross-adaptational effect upon each other, whereas adaptation to m-xylene affects the sensitivity to both of them.

Experiment 22

Substances: m-Xylene
Butyl Acetate
Cyclopentanone

Total duration in work-days: 39

Type of series used: 8_{a-d}

Number of subjects: 12

Interval between stimuli: 30 sec.

Number of series per subject: 40

The results of this experiment are presented in table 5.3.

TABLE 5.3.

Experiment 22 Cross-adaptation

x = m-Xylene

y = Butyl Acetate

z = Cyclopentanone

Percentages of positive response after 30, 60 and 90 seconds of recovery time.

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	40.4	50.6	51.3
yx	54.0	60.6	63.4
zx	57.3	59.7	71.7
yy	72.7	58.4	57.4
xy	46.6	62.8	61.4
zy	57.2	56.6	65.7
zz	59.8	58.8	64.8
xz	63.9	62.1	68.6
yz	64.4	68.3	69.5

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	40.4	50.6	51.3
xy	46.6	62.8	61.4
xz	63.9	62.1	68.6
yy	72.7	58.4	57.4
yx	54.0	60.6	63.4
yz	64.4	68.3	69.5
zz	59.8	58.8	64.8
zx	57.3	59.7	71.7
zy	57.2	56.6	65.7

In this experiment all stimuli affect the sensitivity to each other, although the sensitivity to cyclopentanone is affected less than the sensitivity to the other two substances.

The self-adaptation to butyl acetate (YY) shows the artefact described in the discussion of the last experiment. Here again, there is a relatively high percentage of positive response at 30 seconds of recovery.

Once again, it can be shown here that the recovery after self-adaptation to m-xylene is in no way completed after 90 seconds, for again the same m-xylene stimulus is perceived much more often if it is presented 90 seconds after another substance (ZX). Ninety seconds after the presentation of a butyl acetate stimulus the sensitivity to m-xylene is also still reduced. (63.4 % against 71.7 % after cyclopentanone.)

On the other hand recovery of the sensitivity to cyclopentanone seems to be very rapid after adaptation to butyl acetate, since the percentages of positive response at 60 and 90 seconds of recovery hardly differ any more and are at the same time among the highest percentages found for the cyclopentanone stimulus.

Experiment 23

Substances: Citral	Total duration in work-days: 26
Methyl Salicylate	Type of series used: 8 _{a - d}
Butyl Acetate	
Number of subjects: 9	
Interval between stimuli: 30	
Number of series per subject: 25	

The results of this experiment are shown in table 5.4.

Here again, the artefact mentioned in the description of experiment 21 shows up in the methyl salicylate and butyl acetate data at 30 seconds of recovery after self-adaptation. All three substances used in this experiment have adapting effects on each other. The strongest effects are perhaps those exerted by citral and methyl salicylate on butyl acetate (XZ and YZ: ZZ at 90 sec = 63.8 %), but the differences in effect are rather small.

Experiment 24

Substances: Citral	Total duration in work-days: 25
Safrole	Type of series used: 8 _{a - d}
Cyclopentanone	
Number of subjects: 9	
Interval between stimuli: 30 sec.	
Number of series per subject: 25	

The results of this experiment are shown in table 5.5.

The sensitivity to citral is not yet fully recovered at 90 seconds of recovery time after self-adaptation, as can be deduced from the higher percentage of positive response to the citral stimulus in the ZX combination after 90 seconds of recovery time. Cyclopentanone has a rather slow rising recovery curve with a late start. This is well in line with the data on the recovery of

TABLE 5.4.

Experiment 23

Cross-adaptation

x = Citral

y = Methyl Salicylate

z = Butyl Acetate

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	40.9	53.2	48.1
yx	55.8	55.4	61.3
zx	51.1	52.9	58.1
yy	53.8	38.5	51.2
xy	51.3	64.6	61.1
zy	50.2	52.1	62.7
zz	85.1	59.9	63.8
xz	47.8	56.5	55.6
yz	45.5	55.2	58.5

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	40.9	53.2	48.1
xy	51.3	64.6	61.1
xz	47.8	56.5	55.6
yy	53.8	38.5	51.2
yx	55.8	55.4	61.3
yz	45.5	55.2	58.5
zz	85.1	59.9	63.8
zx	51.1	52.9	58.1
zy	50.2	52.1	62.7

cyclopentanone discussed in chapter 4 (page 125). The percentage of positive response to the YY combination at 30 seconds of recovery time is of course artificially raised again due to the artefact.

All substances influence the sensitivity to each other. In the combinations YX and XY the percentages of positive response at 60 seconds of recovery are higher than those found at 90 seconds. This may be another sign of a biphasic recovery curve.

TABLE 5.5.

Experiment 24 Cross-adaptation

x = Citral

y = Safrole

z = Cyclopentanone

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	45.3	46.9	55.1
yx	50.2	59.5	53.1
zx	54.0	57.0	63.5
yy	75.3	50.0	61.2
xy	50.9	62.9	57.2
zy	51.6	46.6	56.3
zz	51.8	48.6	57.7
xz	48.9	57.5	60.9
yz	54.0	59.1	60.3

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	45.3	46.9	55.1
xy	50.9	62.9	57.2
xz	48.9	57.5	60.9
yy	75.3	50.0	61.2
yx	50.2	59.5	53.1
yz	54.0	59.1	60.3
zz	51.8	48.6	57.7
zx	54.0	57.0	63.5
zy	51.6	46.6	56.3

Experiment 25

Substances: Benzyl Acetate
 Methyl Salicylate
 Cyclopentanone

Total duration in work-days: 24

Type of series used: 8_{a - d}

Number of subjects: 9

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment are shown in table 5.6.

TABLE 5.6.

Experiment 25 Cross-adaptation.

x = Benzyl Acetate

y = Methyl Salicylate

z = Cyclopentanone

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	32.0	40.6	49.4
yx	53.3	60.2	54.7
zx	50.0	57.0	65.7
yy	56.4	44.1	45.6
xy	47.3	61.2	56.0
zy	50.9	49.1	62.7
zz	60.9	56.6	65.6
xz	63.1	71.0	70.9
yz	69.6	64.9	74.1

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	32.0	40.6	49.4
xy	47.3	61.2	56.0
xz	63.1	71.0	70.9
yy	56.4	44.1	45.6
yx	53.3	60.2	54.7
yz	69.6	64.9	74.1
zz	60.9	56.6	65.6
zx	50.0	57.0	65.7
zy	50.9	49.1	62.7

Both benzyl acetate and methyl salicylate recover rather slowly from self-adaptation. The sensitivity to cyclopentanone recovers somewhat faster after a late start, but it is still not back to the highest possible level at 90 seconds after self-adaptation.

All substances reduce the sensitivity for the other substances, if to a varying degree. The percentage of positive response to methyl salicylate at 30 seconds after self-adaptation is again relatively high due to the artefact mentioned earlier.

Experiment 26

Substances: Benzyl Acetate
Safrole
Butyl Acetate

Total duration in work-days: 25

Type of series used: 8_{a-d}

Number of subjects: 9

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment are shown in table 5.7.

The percentages at 30 seconds of recovery after self-adaptation for safrole and butyl acetate are again influenced by the adsorption artefact. The cross-adaptational effects found in this experiment are rather small, with the exception of the effect of butyl acetate on the sensitivity to benzyl acetate and vice versa. The influence of butyl acetate is the larger of the two.

Experiment 27

Substances: Cyclopentanol
a-Thujone
Cyclohexanone

Total duration in work-days: 21

Type of series used: 8_{a-d}

Number of subjects: 6

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment, which is the first one of the second set of seven experiments to be discussed here, are shown in table 5.8.

Cyclopentanol has a strong self-adapting effect as can be seen from the fact that it is perceived only in 23.0% of the cases when it follows itself by 30 seconds, but in 53.7% if it follows a-thujone and 90 seconds are allowed for recovery. However, the sensitivity to cyclopentanol is substantially reduced by the other two substances. This can not be said of a-thujone, since the sensitivity to this substance is hardly affected by previous adaptation to cyclohexanone and

TABLE 5.7.

Experiment 26 Cross-adaptation.

x = Benzyl Acetate

y = Safrole

z = Butyl Acetate

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	24.7	33.8	38.4
yx	42.9	38.4	46.0
zx	26.9	34.1	42.7
yy	81.3	59.3	56.8
xy	55.6	61.8	63.9
zy	57.3	50.9	60.3
zz	70.7	58.4	62.4
xz	57.8	67.8	66.5
yz	65.0	64.3	69.9

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	24.7	33.8	38.4
xy	55.6	61.8	63.9
xz	57.8	67.8	66.5
yy	81.3	59.3	56.8
yx	42.9	38.4	46.0
yz	65.0	64.3	69.9
zz	70.7	58.4	62.4
zx	26.9	34.1	42.7
zy	57.3	50.9	60.3

not at all by adaptation to cyclopentanol. The relative weakness of the cyclopentanol stimulus which is perceived in only 53.7% of the cases at its best, may have been a factor in the low cross-adaptational effect of this substance on the sensitivity to the much stronger (78.2%) α -thujone.

Finally, the sensitivity to cyclohexanone is reduced by cyclopentanol, but not

TABLE 5.8.

Experiment 27 Cross-adaptation

x = Cyclopentanol

y = a-Thujone

z = Cyclohexanone

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	23.0	31.4	40.8
yx	33.3	37.5	53.7
zx	34.0	40.1	48.1
yy	60.7	65.6	74.1
xy	77.7	77.0	74.7
zy	73.7	74.6	78.2
zz	59.3	52.2	67.7
xz	60.0	71.0	68.2
yz	66.3	66.9	62.2

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	23.0	31.4	40.8
xy	77.7	77.0	74.7
xz	60.0	71.0	68.2
yy	60.7	65.6	74.1
yx	33.3	37.5	53.7
yz	66.3	66.9	62.2
zz	59.3	52.2	67.7
zx	34.0	40.1	48.1
zy	73.7	74.6	78.2

by a-thujone. Here the weaker stimulus has more cross-adaptational effect than the stronger one.

The results of this experiment give a good impression of the non-reciprocity that occurs in many cross-adaptational relationships.

Experiment 28

Substances: Iso-propanol
 a-Thujone
 Cyclopentanone

Total duration in work-days: 20

Type of series used: 8_{a - d}

Number of subjects: 6

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment are shown in table 5.9.

TABLE 5.9.

Experiment 28 Cross-adaptation.

x = Isopropanol

y = a-Thujone

z = Cyclopentanone

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	25.7	40.9	47.4
yx	37.7	43.4	44.8
zx	37.0	38.1	51.6
yy	47.3	47.8	69.3
xy	65.3	76.0	66.7
zy	72.0	69.4	80.9
zz	47.3	56.9	69.0
xz	57.0	60.9	69.5
yz	62.3	65.4	66.2

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	25.7	40.9	47.4
xy	65.3	76.0	66.7
xz	57.0	60.9	69.5
yy	47.3	47.8	69.3
yx	37.7	43.4	44.8
yz	62.3	65.4	66.2
zz	47.3	56.9	69.0
zx	37.0	38.1	51.6
zy	72.0	69.4	80.9

All three substances exert cross-adaptational influences on each other. The effects exerted by *a*-thujone and cyclopentanone on iso-propanol are relatively large. The relatively weak iso-propanol stimulus has more influence on the sensitivity to *a*-thujone than the much stronger cyclopentanone stimulus. A similar situation is found in the effects on cyclopentanone where the weak iso-propanol stimulus again causes more reduction of the sensitivity than the stronger *a*-thujone one.

Experiment 29

Substances: *m*-Xylene
a-Thujone
Dioxan

Total duration in work-days: 22

Type of series used: 8_{a - d}

Number of subjects: 6

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment are shown in table 5.10.

For none of these three substances the recovery from self-adaptation is completed after 90 seconds as can be seen from the fact that each of these stimuli is perceived in a much larger percentage of the cases when it follows another stimulus by 90 seconds than when it follows itself. Both *a*-thujone and dioxan reduce the sensitivity to *m*-xylene. The influence of dioxan is clearly the larger of the two. The effects of *m*-xylene and dioxan on *a*-thujone seem to be almost equal, although the effect of *m*-xylene lasts somewhat longer.

m-Xylene has a larger and also more lasting influence on the sensitivity to dioxan than *a*-thujone. It should be noted that the sensitivity to *a*-thujone and to dioxan is higher at 60 seconds of recovery time after adaptation to *m*-xylene than at 90 seconds. This and the fact that there is no difference between the percentage of positive response at 60 and at 90 seconds in the recovery curve of *m*-xylene after self-adaptation, is in agreement with the earlier findings on the biphasic recovery curve of *m*-xylene, described in chapter 4.

Experiment 30

Substances: *m*-Xylene
Iso-propanol
Cyclopentanol

Total duration in work-days: 21

Type of series used: 8_{a - d}

Number of subjects: 6

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment are shown in tabel 5.11.

TABLE 5.10.

Experiment 29

Cross-adaptation.

x = m-Xylene

y = a-Thujone

z = Dioxan

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	38.3	52.3	52.7
yx	60.0	68.9	69.9
zx	50.0	60.1	73.7
yy	53.7	45.6	62.1
xy	69.0	72.3	64.9
zy	70.0	74.1	78.3
zz	49.0	54.1	64.4
xz	58.4	66.1	63.5
yz	64.4	63.8	71.5

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	38.3	52.3	52.7
xy	69.0	72.3	64.9
xz	58.4	66.1	63.5
yy	53.7	45.6	62.1
yx	60.0	68.9	69.9
yz	64.4	63.8	71.5
zz	49.0	54.1	64.4
zx	50.0	60.1	73.7
zy	70.0	74.1	78.3

TABLE 5.11.

Experiment 30 Cross-adaptation
 x = m-Xylene
 y = Isopropanol
 z = Cyclopentanol

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	36.3	45.1	54.8
yx	51.0	51.5	55.8
zx	55.0	56.9	62.4
yy	35.0	45.0	62.5
xy	52.0	64.4	59.4
zy	51.7	51.4	63.6
zz	41.0	35.1	53.3
xz	46.7	55.7	57.1
yz	43.3	50.5	49.3

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	36.3	45.1	54.8
xy	52.0	64.4	59.4
xz	46.7	55.7	57.1
yy	35.0	45.0	62.5
yx	51.0	51.5	55.8
yz	43.3	50.5	49.3
zz	41.0	35.1	53.3
zx	55.0	56.9	62.4
zy	51.7	51.4	63.6

Again, the recovery from self-adaptation to m-xylene is not completed after 90 seconds, but this time there are no direct signs of a biphasic shape of the recovery curve. However, the fact that the percentage of positive response to the iso-propanol stimulus is again higher at 60 seconds than at 90 seconds after the m-xylene stimulus and that the difference in the perception of cyclo-

pentanol at 60 and 90 seconds after m-xylene is very small, points again in the direction of the biphasic shape.

All three substances reduce the sensitivity to each other to some extent. The strongest effect is perhaps the one exerted by iso-propanol on the sensitivity to cyclopentanol (57, 1% - 43, 3%).

Cyclopentanol has relatively little effect on the sensitivity to m-xylene.

Experiment 31

Substances: Cyclohexanone
Iso-propanol
Dioxan

Total duration in work-days: 20

Type of series used: 8_{a - d}

Number of subjects: 5

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment are shown in table 5.12.

The cyclohexanone stimulus is relatively strong in this experiment. Ninety seconds after adaptation to dioxan it is perceived in 82.1% of the cases. Both iso-propanol and dioxan affect the sensitivity to this stimulus. On the other hand, adaptation to cyclohexanone has considerable influence on the sensitivity to iso-propanol, but very little effect on the sensitivity to dioxan. The sensitivity to iso-propanol is also reduced considerably by adaptation to dioxan, but iso-propanol itself has very little effect on dioxan.

Experiment 32

Substances: Cyclohexanone
m-Xylene
Cyclopentanone

Total duration in work-days: 22

Type of series used: 8_{a - d}

Number of subjects: 6

Interval between stimuli: 30 seconds

Number of series per subject: 25

The results of this experiment are given in table 5.13.

The sensitivity to none of the three substances is fully recovered from self-adaptation after 90 seconds. Both m-xylene and cyclopentanone reduce the sensitivity to cyclohexanone. Recovery seems to have a late start in these cases. Cyclohexanone and cyclopentanone influence the sensitivity to m-xylene. The reduction in percentage of positive response is more marked at 60 seconds than at 30 seconds of recovery after adaptation to cyclopentanone. The sen-

TABLE 5.12.

Experiment 31 Cross-adaptation.

x = Cyclohexanone

y = Isopropanol

z = Dioxan

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	59.6	67.7	62.6
yx	72.0	67.8	74.1
zx	74.0	68.8	82.1
yy	24.4	27.3	50.8
xy	39.2	48.1	45.6
zy	44.0	42.3	61.5
zz	47.2	51.4	62.8
xz	63.6	67.0	67.7
yz	64.0	69.0	63.2

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	59.6	67.7	62.6
xy	39.2	48.1	45.6
xz	63.6	67.0	67.7
yy	24.4	27.3	50.8
yx	72.0	67.8	74.1
yz	64.0	69.0	63.2
zz	47.2	51.4	62.8
zx	74.0	68.8	82.1
zy	44.0	42.3	61.5

sitivity to cyclopentanone itself is affected by previous exposure to cyclohexanone, but suffers very little from adaptation to m-xylene.

TABLE 5.13.

Experiment 32 Cross-adaptation.

x = Cyclohexanone

y = m-Xylene

z = Cyclopentanone

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	43.3	61.8	62.3
yx	68.0	66.2	67.4
zx	59.3	60.9	77.2
yy	27.7	28.9	49.0
xy	47.7	53.6	58.3
zy	52.3	44.3	49.1
zz	44.0	55.5	64.2
xz	54.7	60.5	58.2
yz	68.0	71.3	72.4

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	43.3	61.8	62.3
xy	47.7	53.6	58.3
xz	54.7	60.5	58.2
yy	27.7	28.9	49.0
yx	68.0	66.2	67.4
yz	68.0	71.3	72.4
zz	44.0	55.5	64.2
zx	59.3	60.9	77.2
zy	52.3	44.3	49.1

Experiment 33

Substance: Dioxan
 Cyclopentanol
 Cyclopentanone

Total duration in work-days: 23

Type of series used: 8_{a - d}

Number of subjects: 6

Interval between stimuli: 30 sec.

Number of series per subject: 25

The results of this experiment are shown in table 5.14.

TABLE 5.14.

Experiment 33

Cross-adaptation.

x = Dioxan

y = Cyclopentanol

z = Cyclopentanone

Percentages of positive response after 30, 60 and 90 seconds of recovery time

a. Grouped according to teststimulus

Recovery time	30	60	90
xx	57.7	68.2	71.7
yx	70.0	68.0	78.5
zx	73.0	76.8	77.9
yy	27.7	37.1	48.4
xy	33.7	50.8	45.1
zy	48.0	55.6	62.3
zz	43.4	39.5	44.6
xz	43.4	45.6	57.6
yz	53.3	45.3	53.6

b. Grouped according to adapting stimulus

Recovery time	30	60	90
xx	57.7	68.2	71.7
xy	33.7	50.8	45.1
xz	43.4	45.6	57.6
yy	27.7	37.1	48.4
yx	70.0	68.0	78.5
yz	53.3	45.3	53.6
zz	43.4	39.5	44.6
zx	73.0	76.8	77.9
zy	48.0	55.6	62.3

The adapting effects exerted by cyclopentanol and cyclopentanone on dioxan are only small, the effect of the weaker stimulus cyclopentanol being the larger of the two. The influences of dioxan and cyclopentanone on the sensitivity to cyclopentanol are rather large, especially the influence of dioxan. Finally, the sensitivity to cyclopentanone is reduced to some extent by dioxan, but decreases only very little under the influence of cyclopentanol. The sensitivity to none of the three substances has fully recovered from self-adaptation within 90 seconds.

5.3. GENERAL OUTCOMES AND GENERAL RULES

Before trying to extract some general rules concerning adaptation and cross-adaptation from the data in the first part of this section, it is perhaps best to provide a survey of the most important outcomes.

The amounts of response reduction caused by cross-adaptation have been calculated for each test stimulus by subtracting the percentage of positive response at 30 seconds after an adapting stimulus from the highest percentage of positive response found for that same test stimulus after 90 seconds of recovery in the same experiment. These amounts of response reduction, which are considered to be the best approximations of the cross-adaptational effects caused by the adapting stimuli, are shown in table 5.15 for each of the two groups of seven substances.

From this table, it can be seen that previous presentation of citral as an adapting stimulus has a much larger cross-adaptational effect on the sensitivity to cyclopentanone (12.0% reduction) than on the sensitivity to benzyl acetate (4.1% reduction), whereas the sensitivity to benzyl acetate for instance suffers most of all from previous exposure to butyl acetate (19.1% reduction). Thus, all cross-adaptational relationships are represented. The data of table 5.15 are illustrated in figures 5.1. and 5.2.

TABLE 5. 15.

Amounts of response reduction caused by cross-adaptation

Experiments 20 - 26	Test stimuli						
	1	2	3	4	5	6	7
Adapting stimuli							
1 Citral	-	12.0 ^a	4.1	10.3 ^{xb}	20.0 ^a	11.4	16.0 ^b
2 Cyclopentanone	9.5	-	15.7 ^b	9.6 ^b	14.4 ^a	11.8	8.5 ^c
3 Benzyl Acetate	2.4	11.0 ^c	-	8.3 ^c	17.4 ^a	15.4 ^c	12.1 ^{yc}
4 Safrole	13.3 ^{xb}	6.9 ^c	3.1	-	18.5 ^c	9.7 ^c	4.9 ^z
5 m-Xylene	6.6 ^c	5.6 ^b	7.2	8.6 ^a	-	19.5 ^a	19.1 ^a
6 Methyl Salicylate	5.5	4.5	12.4	4.3	11.6 ^a	-	18.5 ^a
7 Butyl Acetate	10.2	5.1	19.1 ^{ya}	6.6 ^z	17.7 ^a	12.5 ^a	-
Experiments 27 - 33							
Adapting stimuli							
1 Dioxan	-	14.2	8.1	8.3	23.7 ^c	17.5 ^c	28.6 ^c
2 Cyclopentanone	5.5	-	17.9	8.9	6.0	14.6 ^c	14.3
3 Cyclohexanone	4.1	17.7 ^c	-	4.5	10.6	22.3 ^c	19.7 ^c
4 a-Thujone	7.1	7.2	1.9	-	13.7 ^c	13.9 ^{xc}	20.4 ^c
5 m-Xylene	13.1 ^c	4.4	9.2	9.3	-	11.6 ^c	10.4 ^c
6 iso-Propanol	3.7	12.5 ^c	10.1	15.6 ^{xc}	11.4	-	13.8 ^c
7 Cyclopentanol	8.5 ^c	4.3	8.2	0.5	7.4	11.9 ^c	-

x, y, z : Larger influence of a substance with a lower position in the rank order on a substance with a higher rank order position

a : Response reduction significant at the $p < .005$ level
 b : " " " " " $p < .01$ level
 c : " " " " " $p < .05$ level

A number of general rules concerning adaptation and cross-adaptation can be extracted directly from table 5.15 or can be obtained by comparing the data in this table with other data.

1. No adapting substance enhances the sensitivity to another substance.

Inspection of table 5.15 shows that all substances when used as adapting stimuli reduce the sensitivity to other substances to some extent. These reductions may be very small and at times negligible and statistically not significant, but it is meaningful that no substance enhances the sensitivity to another substance in any of the 84 relationships investigated.

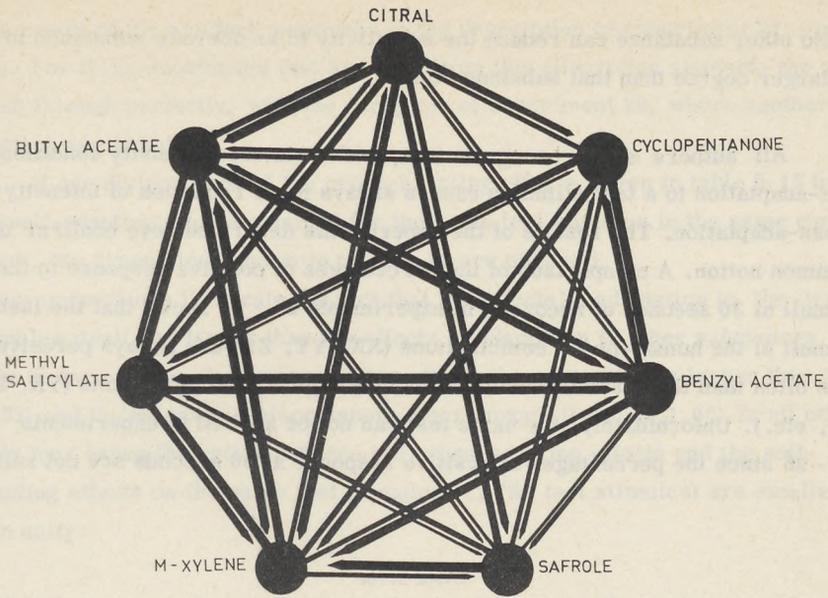


Fig. 5.1. Cross-adapting effects found for the seven odorous substances of experiments 20 - 26. Thickness of lines indicates strength of the effect, arrows show direction of the effect.

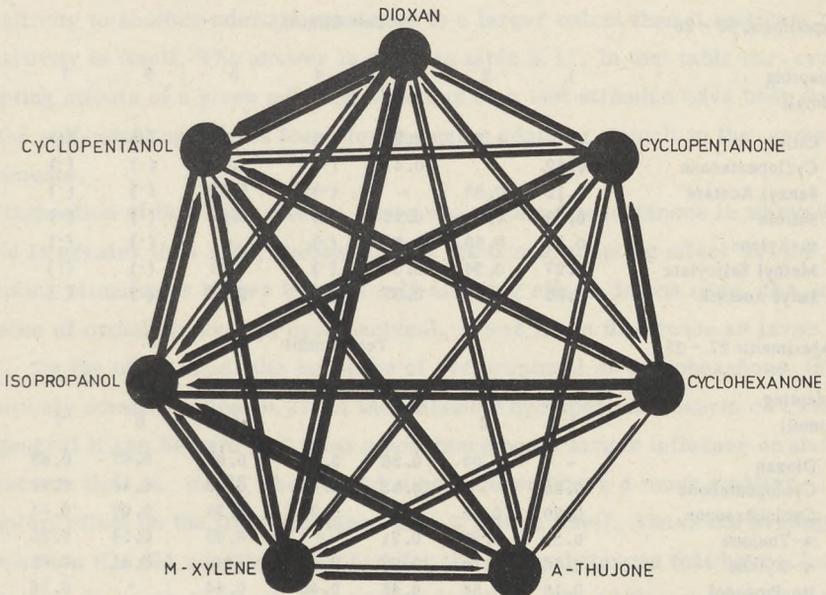


Fig. 5.2. Cross-adapting effects found for the odorous substances of experiments 27 - 33. Thickness of lines indicates strength of the effect, arrows show direction of the effect.

2. No other substance can reduce the sensitivity to an odorous substance to a larger degree than that substance itself.

All authors seem to agree that, under matched intensity conditions, self-adaptation to a test stimulus causes always more reduction of intensity than cross-adaptation. The results of the experiments described here confirm this common notion. A comparison of the percentages of positive response to the test stimuli at 30 seconds of recovery in experiments 27 - 33 shows that the last stimuli of the homogeneous combinations (XX, YY, ZZ) are always perceived less often than those same stimuli in the heterogeneous combinations (YX, ZX, XY, etc.). Unfortunately, the same test can not be applied to experiments 20 - 26 since the percentages of positive response at 30 seconds are not reliable

TABLE 5. 16.

Cross-adapting effects expressed as proportions of the self-adaptation of the test stimulus (CA/SA test stimulus)

((-)=no data on self-adaptation available)

Experiment 20 - 26		Test stimuli						
Adapting stimuli	1	2	3	4	5	6	7	
1 Citral	-	1.32	0.21	(-)	0.61	(-)	(-)	
2 Cyclopentanone	0.52	-	0.47	(-)	0.46	(-)	(-)	
3 Benzyl Acetate	0.12	0.83	-	(-)	0.53	(-)	(-)	
4 Saffrole	0.73	0.76	0.15	(-)	0.50	(-)	(-)	
5 m-Xylene	0.34	0.58	0.36	(-)	-	(-)	(-)	
6 Methyl Salicylate	0.27	0.34	0.37	(-)	0.31	(-)	(-)	
7 Butyl Acetate	0.50	0.53	0.90	(-)	0.56	(-)	(-)	

Experiments 27 - 33		Test stimuli						
Adapting stimuli	1	2	3	4	5	6	7	
1 Dioxan	-	1.00	0.36	0.34	0.67	0.47	0.83	
2 Cyclopentanone	0.26	-	0.53	0.26	0.20	0.56	0.41	
3 Cyclohexanone	0.20	0.62	-	0.26	0.35	0.60	0.64	
4 α -Thujone	0.32	0.32	0.21	-	0.39	0.54	0.66	
5 m-Xylene	0.58	0.15	0.27	0.38	-	0.41	0.65	
6 iso-Propanol	0.18	0.56	0.45	0.46	0.44	-	0.86	
7 Cyclopentanol	0.41	0.30	0.92	0.03	0.28	0.42	-	

as a result of the artefact mentioned in the description of experiment 21 (page 136). For those substances that are free from this adsorption artefact, the rule holds through perfectly, with the exception of experiment 20, where another artefact was found.

If one divides each of the cross-adapting effects shown in table 5.15 by the self-adapting effects obtained for the same test stimulus in the same experiment, the proportions shown in table 5.16 are obtained.

These proportions illustrate the fact that the effects of adaptation to the test stimulus itself are larger than the effects of adaptation to other substances. Only in one case (cyclopentanone after citral) the proportion is larger than 1.00 (1.32) and in one case (cyclopentanone after dioxan) it equals 1.00. In all other sixty four cases the ratios between the cross-adapting effects and the self-adapting effects on the same test stimulus (CA/SA test stimulus) are smaller than unity.

3. A substance may have a larger adapting effect on another substance than it has on itself.

One can ask the question whether a given odorous substance may reduce the sensitivity to another odorous substance to a larger extent than it reduces the sensitivity to itself. The answer is given in table 5.17. In that table the cross-adapting effects of a given adapting stimulus on a test stimulus have been divided by the self-adapting effects found for the same adapting stimuli in the same experiments.

As inspection of this table shows, there are quite a few instances in which the ratio is greater than 1.00, indicating that the cross-adapting effect of the adapting stimulus is larger than its self-adapting effect. In one case, the influence of cyclohexanone on cyclopentanol, it was more than twice as large.

On the other hand, the influence of cyclopentanol on cyclohexanone is a relatively small fraction (0.27) of the influence cyclopentanol exerts on itself. In general it can be said that when a substance has a larger influence on another substance than on itself, the second substance will have a much smaller adapting effect on the first substance than it has on itself. Thus, the average proportion (CA/SA adapting stimulus) for the nine substances that have a larger effect on other substances than on themselves is 1.29 and the average proportion for the nine stimuli that form their counterparts in the same pairs is only 0.27 (the highest one being 0.66). Therefore, there seem to be "strong adaptors" and

TABLE 5.17.

Cross-adapting effects expressed as proportions of the self-adaptation of the adapting stimulus (CA/SA adapting stimulus)
 ((-)= no data on self-adaptation available)

Experiments 20 - 26	Test stimuli						
	1	2	3	4	5	6	7
Adapting stimuli							
1 Citral	-	0.66	0.21	0.57	1.04	0.56	0.78
2 Cyclopentanone	1.04	-	1.19	1.05	1.48	0.89	0.88
3 Butyl Acetate	0.12	0.33	-	0.39	0.87	0.46	0.57
4 Safrole	(-)	(-)	(-)	(-)	(-)	(-)	(-)
5 m-Xylene	0.20	0.18	0.22	0.23	-	0.53	0.60
6 Methyl Salicylate	(-)	(-)	(-)	(-)	(-)	(-)	(-)
7 Butyl Acetate	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Experiments 27 - 33	Test stimuli						
Adapting stimuli	1	2	3	4	5	6	7
1 Dioxan	-	0.68	0.40	0.37	1.05	0.85	1.38
2 Cyclopentanone	0.39	-	0.63	0.40	0.21	0.66	1.01
3 Cyclohexanone	0.18	0.52	-	0.51	0.31	0.99	2.21
4 α -Thujone	0.29	0.21	0.11	-	0.56	0.41	1.17
5 m-Xylene	0.37	0.14	0.30	0.26	-	0.44	0.40
6 iso-Propanol	0.10	0.48	0.27	0.60	0.40	-	0.48
7 Cyclopentanol	0.25	0.12	0.27	0.02	0.46	0.74	-

"weak adaptors" among the odorous substances. If there exist "strong adaptors", it should nevertheless be remembered that most substances do exert less cross-adapting than self-adapting influence. Furthermore, it has been shown that no other substance exerts a larger adapting influence on a given substance than that substance itself (rule 1). Table 5.18 gives a general survey of the frequencies of occurrence of proportions of different magnitudes in the tables 5.15 and 5.17.

As can be seen from the second column in this table, 40 of the 66 ratios expressing the cross-adaptation undergone by a test stimulus as a proportion of its self-adaptation are .50 or lower, indicating that the self-adaptation was at least twice as large as the cross-adaptation. The median of these proportions lies at .447 and the semi-interquartile range is .138.

The last column of the table shows that when the cross-adaptation is expressed as a proportion of the self-adaptation of the adapting stimulus 36 out of 66

proportions are .50 or lower, indicating that the self-adaptation exerted by the adapting stimulus was at least twice as large as the cross-adaptation exerted.

TABLE 5.18.

Frequency of occurrence of different classes of cross-adapting effects expressed as proportions of the self-adaptation of the test stimulus (CA/SA test stimulus) and of the self-adaptation of the adapting stimulus (CA/SA adapting stimulus).

	CA/SA test stimulus		CA/SA adapting stimulus	
	frequency	cumulative freq.	frequency	cumulative freq.
.01 - .10	1	1	2	2
.11 - .20	6	7	7	9
.21 - .30	9	16	11	20
.31 - .40	12	28	10	30
.41 - .50	12	40	6	36
.51 - .60	12	52	9	45
.61 - .70	5	57	4	49
.71 - .80	2	59	2	51
.81 - .90	4	63	4	55
.91 - 1.00	2	65	1	56
1.01 - 1.10			5	61
1.11 - 1.20			2	63
1.21 - 1.30				
1.31 - 1.40	1	66	1	64
1.41 - 1.50			1	65
1.51 - 2.00				
2.01 - 2.50			1	66
Md	.447		.445	
$\frac{Q_3 - Q_1}{2}$.138		.279	

Here, the median lies only slightly higher at .455, but the semi-interquartile range is more than twice as large (.279) as for the data in the first two columns of the table. This larger semi-interquartile range is probably due to the presence of the "strong" and "weak" adaptors mentioned earlier.

4. Within pairs of odorous stimuli the cross-adaptation effects the stimuli exert on each other are usually not reciprocal.

If there are "strong" and "weak" adaptors among the odorous substances used, it is to be expected that the cross-adaptation effect exerted by the stronger of two stimuli on the weaker one is larger than the effect of the weaker on the stronger one. This has been shown to be true for a number of pairs already (page 159), but the question can be asked how general a phenomenon this non-reciprocity of the cross-adapting effects within pairs is. The results of table 5.15 (page 156) provide an answer to this question.

In this table, the odorous substances within each set of seven have been put in such an order that of each two substances, the one which is higher on the list has the strongest cross-adaptational effect. Thus, the influence of citral on cyclopentanone leads to a response reduction of 12.0%, whereas the percentage of positive response to citral after cyclopentanone is only reduced by 9.5%. Likewise, cyclopentanone has a stronger influence on benzyl acetate, on safrole, on m-xylene, etc., than these substances have on cyclopentanone.

There are only a few exceptions to this general rule. Safrole reduces the sensitivity to citral by 13.3%, whereas citral causes only a reduction of 10.3% when safrole is used as the test stimulus. Butyl acetate has a larger adapting influence on the sensitivity to both benzyl acetate and safrole than these substances have on butyl acetate. In the bottom part of table 5.15 there is only one exception. The adaptation caused by a-thujone reduces the sensitivity to iso-propanol less than iso-propanol affects the sensitivity to a-thujone.

Apart from these exceptions, it is possible to arrange the seven odorous substances in each group almost perfectly in a "pecking order" on the basis of their cross-adaptational effects. This fact provides a good illustration of the frequent lack of reciprocity of cross-adaptation effect.

In some pairs of substances the differences in cross-adapting effects are only slight. That almost perfect reciprocity does certainly occur is illustrated by the results obtained for such pairs as cyclopentanone-cyclohexanone and m-xylene-iso-propanol in the bottom part of table 5.15.

In these cases the response reductions do not differ more than 0.2%. Table 5.19 gives a survey of the differences in response reduction within pairs.

It will be clear from this table, that about half of the pairs differs less than 5% in their cross-adapting effects. On the other hand, there is quite a group of pairs in the second series of experiments with differences of 10% and larger.

TABLE 5.19.

Frequency of occurrence of differences in percentage of response reduction within pairs

Percentage response reduction	exp. 20 - 26 frequency	exp. 27 - 33 frequency	total frequency	cumulative frequency
0.0 - 0.9	0	2	2	2
1.0 - 1.9	3	6	9	11
2.0 - 2.9	2	3	5	16
3.0 - 3.9	3	0	3	19
4.0 - 4.9	1	2	3	22
5.0 - 5.9	4	0	4	26
6.0 - 6.9	1	0	1	27
7.0 - 7.9	3	0	3	30
8.0 - 8.9	1	1	2	32
9.0 - 9.9	1	0	1	33
10.0 - 10.9	1	2	3	36
11.0 - 11.9	0	1	1	37
12.0 - 12.9	0	1	1	38
13.0 - 13.9	1	1	2	40
14.0 - 14.9	0	0	0	40
15.0 - 15.9	0	0	0	40
16.0 - 16.9	0	0	0	40
17.0 - 17.9	0	0	0	40
18.0 - 18.9	0	0	0	40
19.0 - 19.9	0	1	1	41
20.0 - 20.9	0	1	1	42

The fact that the differences in this second series are so marked is of particular interest, because some of the substances used in these experiments were taken from an early study of Cheesman et. al. (1956) in which they claimed to have found only reciprocal cross-adaptational relationships. These substances were iso-propanol, dioxan, cyclopentanone and cyclopentanol. In table 5.20 the reductions of positive response obtained with these substances in experiments 27 - 33 are shown once more in a way which makes it easy to compare them with Cheesman's results in table 2.4 (page 54).

TABLE 5.20.

Cross-adapting effects obtained in experiments 27 - 33 for the four substances used by Cheesman et al. (see page 54)

Adapting stimuli	Test stimuli			
	1	2	3	4
1 iso-Propanol	-	3.7	12.5	13.8
2 Dioxan	17.5	-	8.1	28.6
3 Cyclopentanone	14.6	5.5	-	14.3
4 Cyclopentanol	11.9	8.5	4.3	-

Inspection of this table immediately shows, that a number of non-reciprocal relationships is found. The amounts of response reduction can of course not be compared directly with the slopes obtained by Cheesman c. s. , but one can rankorder both the slopes of Cheesman and the effects in table 5.20 and one can calculate the rank correlation between the two sets of data. Since a steep slope and a large amount of response reduction both mean a high degree of cross-adaptational effect, one would expect a relatively high positive correlation between the two sets of data.

In fact, the correlation found is very low ($Rho = +.07$). This may be due to the fact that Cheesman used higher adapting concentrations and measured the sensitivity immediately after adaptation. If earlier speculations about the role of central and peripheral adaptation are correct, central adaptation components should have played a much larger part in his work than in the work described here. The influence of central adaptation might also explain the predominance of reciprocal relationships in his results. If this is true, the results obtained by the method used here are more relevant to problems of receptor mechanisms than the results of Cheesman.

5. The members of some pairs of odorous stimuli have more cross-adapting effect on each other than those of other pairs.

Although the relationships within pairs are often not reciprocal, it may well be that in some pairs the members have a lot more influence on each other than in other pairs. Thus, citral reduces the sensitivity to m-xylene by 20%, whereas m-xylene reduces the sensitivity to citral by only 7%. Therefore, the

two substances can not be said to be reciprocal in their effects, but they do influence each other to a much larger extent than for instance, citral and benzyl acetate, which have cross-adapting effects of 4% and 2% respectively.

In order to check whether such differences between pairs occur in a systematic way, the influence exerted by the stronger members of the pairs, which can be found in table 5.15, have been correlated with those exerted by the weaker ones. The correlations were $Rho = +.75$ for experiments 20 - 26 and $Rho = +.38$ for experiments 27 - 33. Both correlations are positive, but one of them is not very high.

Therefore, it can be concluded that there is a certain reciprocity in the general level of cross-adaptation which the stimuli exert on each other, notwithstanding the lack of reciprocity within pairs.

6. The cross-adapting effects found are related to the self-adapting effects of the test stimuli, but not to those of the adapting stimuli.

If one expresses the cross-adaptation effects as proportions of the self-adaptation of the test stimulus as in table 5.16, the correlations between the highest proportions and the lowest proportions in the pairs are $Rho = +.83$ for the 6 pairs of experiments 20 - 26 for which data on self-adaptation are available and $Rho = +.48$ for the 21 pairs of experiments 27 - 33. Expressing the cross-adapting effects in this way seems to enhance the correlation somewhat. On the other hand, expressing the cross-adapting effects as proportions of the self-adaptation of the adapting stimulus as in table 5.17 reduces the correlation to $Rho = +.24$ for the 6 pairs of experiments 20 - 26 and to $Rho = -.08$ for the 21 pairs of experiments 27 - 33. In this case the correlations are virtually annihilated.

The fact that the correlations are enhanced in the first case, whereas they are virtually annihilated in the last one, suggests that the cross-adapting effects are related to the self-adapting effects of the test stimuli rather than to the self-adapting effects of the adapting stimuli. The most direct way of verifying this suggestion is of course to correlate the cross-adapting effects found in table 5.15 with the self-adapting effects found in the same experiment for the test stimuli and the adapting stimuli respectively.

Table 5.21 gives the correlation coefficients found.

TABLE 5.21.

Rank-correlations between cross-adapting effects and self-adapting effects of the stimuli (A) and between cross-adapting effects and self-adapting effects of the adapting stimuli (B)

	A	B
experiments 20 - 26	+ .56	+ .01
experiments 27 - 33	+ .64	- .20

As can be seen from this table the correlations with the self-adapting effect of the test stimuli are positive and quite large for both sets of experiments and the correlations with the self-adapting effects of the adapting stimuli are very small indeed.

7. The differences between the cross-adapting effects which the members of a pair exert on each other seem to rise only slightly with the general level of the cross-adapting effects exerted by the pair members.

One can ask the question whether the differences in cross-adapting effect between pair members discussed earlier under rule 4 are dependent upon the general level of the cross-adapting effects mentioned in the discussion of rule 5.

It is evident that the higher the general level of the cross-adapting effects of a pair is, the more room there is for differences in cross-adapting effect between the members of the pair. Stated in another way, the differences can never be larger than the sum of the cross-adapting effects and therefore the possibilities of obtaining large differences in pairs with a low general level are very limited.

In order to check whether the differences are indeed dependent upon the general level, the sums of the cross-adapting effects of the pair members found in table 5.15 have been correlated with the differences of their cross-adapting effects. The resulting correlation coefficients are $Rho = +.28$ for experiments 20 - 26 and $Rho = +.27$ for experiment 27 - 33. Both correlations are positive but low, indicating that on the whole there is a slight tendency in the differences to grow with the general level of cross-adaptation.

8. The perceived intensity of an adapting stimulus is not a predominant determinant of its cross-adapting strength.

When trying to explain the existence of a cross-adaptational "pecking order" (see table 5.15 and discussion under point 4) an explanation in terms of differences in intensity of the adapting stimuli prompts itself. As has been shown in chapter 4 (page 99) the amount of response reduction caused by an adapting stimulus is positively related to its strength, but in these cross-adaptation experiments much has been done to reduce differences in intensity of the adapting stimuli. In principle, all concentrations were chosen such that the stimuli were perceived in about 70% of the cases when the subjects were not adapted. However, in practice the highest percentages of positive response found in the experiments (best approximation of the unadapted state) varied from 46.0% to 82.1%. Therefore, it was supposed that differences in intensity might have been responsible for the differences in cross-adaptation effects that led to the establishment of the "pecking order".

TABLE 5.22.

Highest percentage of positive response found for each stimulus per experiment

Experiments 20 - 26

Other stimuli present in the same experiment

stimuli	1	2	3	4	5	6	7
1 Citral	-	63.5	66.9	63.5	66.9	61.3	61.3
2 Cyclopentanone	60.9	-	74.1	60.9	69.5	74.1	69.5
3 Benzyl Acetate	61.6	65.7	-	46.0	61.6	65.7	46.0
4 Safrole	61.2	61.2	63.9	-	55.9	55.9	63.9
5 m-Xylene	68.4	71.7	68.4	77.1	-	77.1	71.7
6 Methyl Salicylate	62.7	62.7	62.7	51.8	51.8	-	62.7
7 Butyl Acetate	63.8	65.7	69.9	69.9	65.7	63.8	-

Experiments 27 - 33

Other stimuli present in the same experiment

stimuli	1	2	3	4	5	6	7
1 Dioxan	-	78.5	67.7	71.5	71.5	67.7	78.5
2 Cyclopentanone	57.6	-	72.4	69.5	72.4	69.5	57.6
3 Cyclohexanone	82.1	77.2	-	68.2	77.2	82.1	68.2
4 a-Thujone	78.3	80.9	78.2	-	78.3	80.9	78.2
5 m-Xylene	73.7	58.3	58.3	73.7	-	62.4	62.4
6 iso-Propanol	61.5	51.6	61.5	51.6	63.6	-	63.6
7 Cyclopentanol	62.3	62.3	53.7	53.7	57.1	57.1	-

Table 5.22 gives a survey of the perceived intensities of the adapting stimuli as expressed in the highest percentages of positive response found for them in the same experiment.

When the data in this table are correlated separately for each group of seven experiments with the cross-adaptational effects caused by the same stimuli in table 5.15, rank correlation coefficients of $+ .12$ and $+ .24$ are found for experiments 20 - 26 and 27 - 33 respectively. Both these correlation coefficients are positive, but low and statistically not significant. When the cross-adapting effects are expressed as proportions of the self-adaptation of the test stimuli or as proportions of the adapting stimuli, the correlations with the perceived intensities are even lower ($Rho = + .10$ and $Rho = - .04$ respectively for experiments 20 - 26 and $Rho = + .15$ and $Rho = + .13$ for experiments 27 - 33.) Therefore, the relative intensity of the adapting stimuli does not seem to be a major source of the differences in their cross-adapting effects.

9. Recovery from self-adaptation is not yet completed after 90 seconds.

Some authors claim that stimuli of low intensity have only a negligible adapting effect. Therefore, they consider threshold procedures using repeated stimulation with 15 second intervals to be legitimate. As was pointed out earlier in chapter 4, this view has to be rejected because all data from the experiments described so far show clearly that even when stimuli are involved which are only just above threshold level, sensitivity has not recovered completely after 90 seconds. This can be illustrated by the data in the first column of table 5.23, which gives a summary of the average differences between the percentage of positive response at 90 seconds after self-adaptation to each stimulus and the highest percentage of positive response found for that stimulus after the same recovery period in the heterogeneous combinations of the same experiment. This difference is some indication of the state of recovery after the 90 second period. The larger the difference, the less complete is recovery from self-adaptation. However, the absolute values of these differences at 90 seconds of recovery have only a relative meaning since they remain dependent upon the completion of the recovery from cross-adaptation to the substances that happen to be in the same experiment.

TABLE 5.23.

Differences between the percentages of positive response at 90 seconds of recovery after self-adaptation and after adaptation to the stimulus that reduces least (A) and differences between the percentages of positive response at 90 seconds and 30 seconds after self-adaptation (B)

Experiments 20 - 26

	A	B	
1 Citral	6.7	8.5	
2 Cyclopentanone	5.8	5.2	
3 Benzyl Acetate	11.3	13.7	
4 Safrole	0.6	(4.7)	
5 m-Xylene	14.1	14.7	
6 Methyl Salicylate	7.9	(5.0)	
7 Butyl Acetate	3.3	(20.4)	$Rho_{A-B} = +.36$

Experiments 27 - 33

	A	B	
1 Dioxan	6.3	15.0	
2 Cyclopentanone	5.9	14.4	
3 Cyclohexanone	11.6	10.1	
4 α -Thujone	10.6	14.5	
5 m-Xylene	12.6	18.5	
6 iso-Propanol	5.3	25.2	
7 Cyclopentanol	10.2	16.9	$Rho_{A-B} = -.12$

10. The sensitivity at 90 seconds after self-adaptation does not seem to be dependent exclusively upon the rate of recovery.

In table 5.23, the average differences between the percentages of positive response to each stimulus at 30 seconds and at 90 seconds of recovery after self-adaptation are given also. This is an indication of the rate of recovery after self-adaptation. The larger the difference, the faster is recovery. Unfortunately, the percentages of positive response at 30 seconds of recovery after self-adaptation to safrole, methyl salicylate and butyl acetate can not be used for this purpose, because they are influenced by the adsorption artefact. The best estimate of their real rate of recovery can be taken from the experiment on adsorption and adaptation described in chapter 3. The differences in percentage of positive response found in that experiment have been included here in brackets. The results of citral and m-xylene obtained in experiment 20 have not been used in calculating the average. They were also contaminated by

an artefact. For some of the substances that are not affected by any of these artefacts the differences found vary considerably from one experiment to another, but for other substances (dioxan, iso-propanol, etc.) the differences found in the three experiments are very similar.

Although both sets of data in table 5.23 are relatively uncertain, one is tempted to compare them in order to see how the state of recovery at 90 seconds after self-adaptation for a substance is related to the rate of recovery for that substance. If completion of the recovery is solely dependent upon the rate of recovery, i. e. if adaptation is just as deep for all substances, but some recover faster than others, a negative correlation between the two sets of data should be found. If, on the other hand, differences in rate of recovery may be compensated by differences in depth of adaptation the correlations found may be very low. The actual rank correlations found are $Rho = +.36$ for experiments 20 - 26 (including the results of the experiment of chapter 3 for these substances that suffered from the adsorption artefact) and $Rho = -.12$ for experiments 27 - 33.

Therefore, it is very likely that the completion of the recovery at 90 seconds after self-adaptation is not dependent upon the rate of recovery alone, but that there are also considerable differences in the initial amounts of response reduction caused by self-adaptation.

11. The shape of the recovery curve after cross-adaptation varies from adapting stimulus to adapting stimulus, but remains relatively constant with different test stimuli.

In general, it seems that the shape of the recovery curve after cross-adaptation is determined to a large extent by the adapting stimulus and not by the test stimulus used. This is illustrated in figure 5.3. and 5.4, where the recovery curves are shown which were obtained with different test stimuli after adaptation to the two odorous substances that were used in both groups of seven, m-xylene and cyclopentanone.

From these figures it becomes evident that recovery from cross-adaptation to m-xylene is relatively fast in the period between 30 and 60 seconds but levels off in the period between 60 and 90 seconds, whereas the recovery from cross-adaptation to cyclopentanone takes place mainly in the latter period after a very slow start. These findings are in accordance with the results of the recovery experiments in chapter 4 (experiments 6 - 9 and experiment 18), especially because it can be seen from the points indicating the highest percentages of

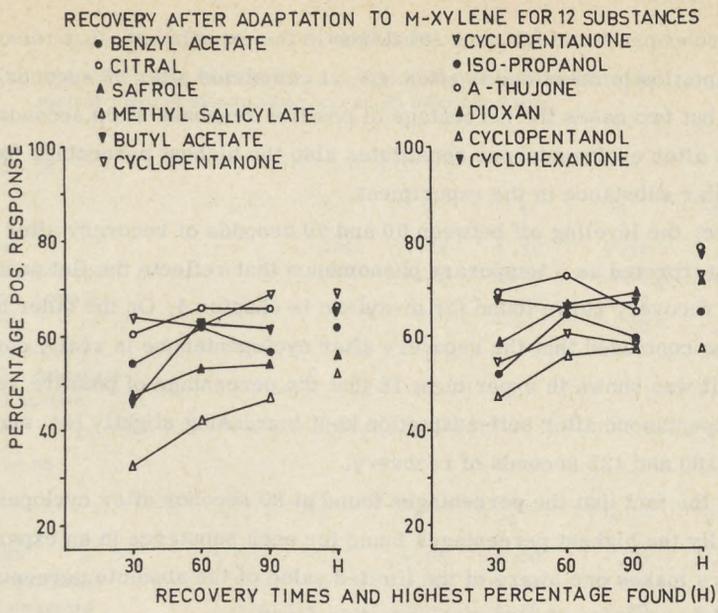


Fig. 5. 3. Recovery after adaptation to m-xylene for 12 substances and the highest percentage of positive response found for each of these substances in the same experiment.

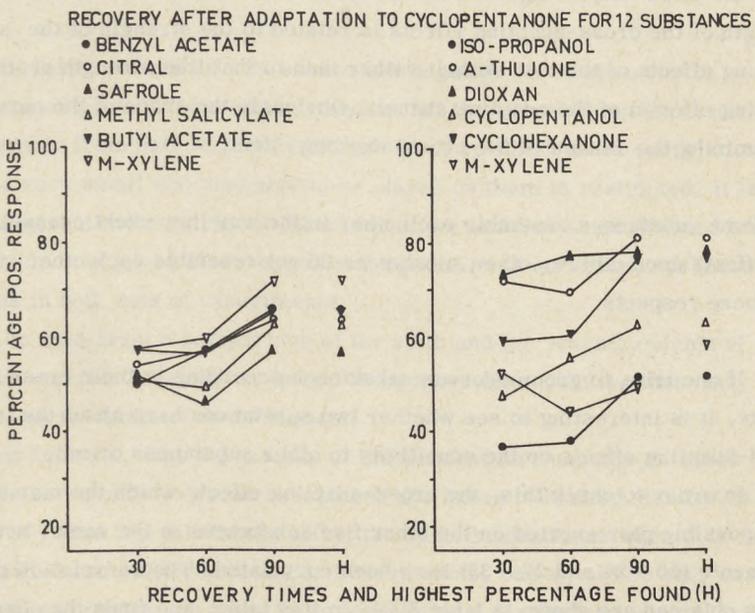


Fig. 5. 4. Recovery after adaptation to cyclopentanone for 12 substances and the highest percentage of positive response found for each of these substances in the same experiment.

positive response found for each substance in the experiment, that recovery after adaptation to m-xylene is often not yet completed after 90 seconds, whereas in all but two cases the percentage of positive response at 90 seconds of recovery after cyclopentanone constitutes also the highest percentage found for a particular substance in the experiment.

Therefore, the leveling off between 60 and 90 seconds of recovery after m-xylene can be interpreted as a temporary phenomenon that reflects the flat part of the biphasic recovery curve found for m-xylene in chapter 4. On the other hand, it can not be concluded that the recovery after cyclopentanone is really completed, because it was shown in experiment 18 that the percentage of positive response to cyclopentanone after self-adaptation kept increasing slightly but significantly between 100 and 125 seconds of recovery.

This and the fact that the percentages found at 90 seconds after cyclopentanone are usually the highest percentages found for each substance in an experiment, once more makes one aware of the limited value of the absolute percentages and the absolute amounts of response reduction found.

Nevertheless, the fact that the nature of the test stimulus is almost of no consequence in determining the shape of the recovery curve after cross-adaptation is all the more surprising since it was shown earlier (see rule 6) that the strength of the cross-adapting effects is related to the strength of the self-adapting effects of the test stimuli rather than to that (the strength of the self-adapting effects) of the adapting stimuli. Obviously the shape of the curve is not determining the amount of the cross-adapting effect.

12. Some substances resemble each other in the way they exert cross-adapting effects upon others, other substances do not resemble each other at all in these respects.

If one tries to group odorous substances according to their cross-adapting effects, it is interesting to see whether two substances have about the same cross-adapting effects on the sensitivity to other substances or not.

In order to check this, the cross-adapting effects which the members of each possible pair exerted on the other five substances in the same set of experiments (20 - 26 and 27 - 33) have been correlated. The correlation coefficients obtained are shown in table 5.24. In this table, one finds the correlations between the influences exerted by the particular pair members on the others. Thus, the influence exerted by citral and cyclopentanone on the other five sub-

TABLE 5.24.

Rank-correlations between the cross-adaptational influences exerted by each of a pair of odorous substances on all other substances.

Exp. 20 - 26

	1	2	3	4	5	6	7
1 Citral	---	- .30	+ .70	+ .60	+ .20	+ .20	- .30
2 Cyclopentanone		---	+ .70	- .30	0.00	- .10	+ .90
3 Benzyl Acetate			---	- .10	+ .70	+ .60	+ .60
4 Safrole				---	- .10	- .60	- .30
5 m-Xylene					---	+ .40	+ .50
6 Methyl Salicylate						---	+ .90
7 Butyl Acetate							---

Exp. 27 - 33

	1	2	3	4	5	6	7
1 Dioxan	---	- .50	+ .50	+ .90	+ .60	+ .30	+ .20
2 Cyclopentanone		---	+ .90	- .10	- .60	+ .30	+ .10
3 Cyclohexanone			---	+ .80	- .10	+ .40	+ .30
4 a-Thujone				---	+ .10	+ .80	+ .20
5 m-Xylene					---	- .20	+ .60
6 iso-Propanol						---	-1.00
7 Cyclopentanol							---

stances in experiments 20 - 26 show a low negative correlation (-.30).

Inspection of the table immediately shows that the correlations found vary considerably from pair to pair. Although the N on which these correlations are based is very small and the value to be placed on them is restricted, it is interesting that the majority of them is positive and that some of them are quite high. Table 5.25 gives a survey of the frequencies of occurrence of these correlations in both sets of experiments.

As can be seen from a comparison of the sixth and the seventh column of this table, the correlations appear indeed to be more often positive than may be expected on the basis of mere chance.

This may indicate, that the number of independent mechanisms on which the relations between the odorous substances are based is limited and that in a number of cases two substances affect the same mechanisms when they reduce the sensitivity to a third substance. Nevertheless, one should be very careful with drawing conclusions from these correlations, for the frequencies in the seventh column of table 5.25 show at the same time that quite a number of them

TABLE 5. 25. Frequencies of occurrence of the rank correlations in table 5. 24.
(frequencies = F; cumulative frequencies = CF)

Correlation Coefficient	Experiment						Expected by chance CF
	20 - 26		27 - 33		20 - 33		
	F	CF	F	CF	F	CF	
+ 1.00	0	0	0	0	0	0	0.35
+ .90	2	2	2	2	4	4	1.75
+ .80	0	2	2	4	2	6	2.80
+ .70	3	5	0	4	3	9	4.90
+ .60	3	8	2	6	5	14	7.35
+ .50	1	9	1	7	2	16	9.45
+ .40	1	10	1	8	2	18	10.85
+ .30	0	10	3	11	3	21	14.35
+ .20	2	12	2	13	4	25	16.45
+ .10	0	12	2	15	2	27	19.95
.00	1	13	0	15	1	28	22.05
- .10	3	16	2	17	5	33	25.55
- .20	0	16	1	18	1	34	27.65
- .30	4	20	0	18	4	38	31.15
- .40	0	20	1	19	1	39	32.55
- .50	0	20	1	20	1	40	34.65
- .60	1	21	0	20	1	41	37.10
- .70	0	21	0	20	0	41	39.20
- .80	0	21	0	20	0	41	40.25
- .90	0	21	0	20	0	41	41.65
- 1.00	0	21	1	21	1	42	42.00

may be purely accidental. In fact it remains possible that two substances correlate +.1.00 in their effects on others and that nevertheless the mechanisms by which they influence the other substances are entirely different. But if all the mechanisms of interaction were completely independent in this way, the number of positive correlations would not be higher than expected by chance. Therefore, the fact that more positive correlations are found may be considered as an indication of some dependency in the interactive mechanisms.

5.4. DISCUSSION

Before discussing the meaning of the rules mentioned in the last section, it should be pointed out once more that some of these rules have only restricted validity, because the data on which they are based are limited both quantitatively and (in some cases) qualitatively (see the artefacts mentioned and the remark on the absolute values of the reductions made in the discussion of rule 11). If the rules have interest, it is mainly because they show general tendencies and trends and may lead to some verifiable hypotheses.

The discussion will center around three main questions.

a. What do the results obtained contribute to the knowledge of adaptation and cross-adaptation phenomena?

Some of the rules mentioned in the preceding sections are in direct agreement with the findings of other investigators. Thus, all authors seem to agree that no other substance can reduce the sensitivity to a given odorous substance to a larger degree than that substance itself (under matched subjective intensity conditions). Rule 2 confirms their conclusions. In the same way, it is generally accepted that some pairs of substances have larger influence on each other than other pairs (rule 5) and most authors agree that there need not be reciprocity in the cross-adapting effects which the two members of a pair of stimuli exert on each other (rule 4). In general there is also agreement on the fact that adapting substances never enhance the sensitivity to another substance (rule 1). Although Engen and Bosack (1969) on the basis of experiments on cross-adaptation with neonates, have found some rare cases in which facilitation of the response to an odour after cross-adaptation could be demonstrated, no other authors have ever reported such phenomena and it appears necessary to verify them by different methods with ordinary subjects. Some of the rules found are not so much expected from the literature, but are in agreement with the results of the experiments discussed in chapter 4. Thus, it became clear again in the cross-adaptation experiments that recovery is not yet completed after 90 seconds (rule 9) and that the shape of the recovery curve may differ from adapting stimulus to adapting stimulus (rule 11). The implication that the shape of the curve is rather independent from the nature of the test stimulus is of course a new result which can not be checked with the experiments of chapter 4 since they were concerned with self-adaptation only.

The relatively small importance of the perceived intensity of a stimulus with regard to its cross-adapting strength (rule 8) is not really in contradiction with the conclusion reached in chapter 4, that the adapting effect increases with increasing concentration of the adapting stimulus. It simply means that the differences in adapting effects due to the relatively slight differences in adapting intensity are almost completely overruled by the differences in the adapting effects of the qualitatively different stimuli. The complexity of the cross-adapting relationships, illustrated by the fact that no clearcut divisions can be made between the adapting effects of groups of substances (see table 5.15) and the fact that all substances exert effects on all other substances to some extent (rule 1), is an indication of the multidimensional character of the interaction mechanism

and shows that simple models involving for instance only overlapping adsorption properties will not suffice to explain the psychophysical phenomena.

In itself this complexity is not an entirely new phenomenon. LeMagnen (1947) has shown that cross-adapting relations can be complicated, but he did not investigate all possible reciprocal relationships between pair members in his group of substances. The fact, that there is no one to one relationship between the direct cross-adapting influences which two substances exert on each other and the similarity in the influences which these two substances exert upon other substances (see below under 2), is just another demonstration of the complexity of these relationships.

Really new is the finding that substances may have a larger adapting effect on another substance than they have on themselves (rule 2) and the fact that the substances can be arranged in a "pecking order", in which the substance which is higher on the list has always more influence on the one that is lower on the list than this last one has on the first one (see under rule 4).

Both findings point in the direction of the existence of "strong and weak adaptors".

b. Can odorous substances be classified on the basis of the psychophysical cross-adaptation data obtained?

At the end of the first chapter it was indicated that investigating the possibility of a classification of odorous substances on the basis of the cross-adaptational relationships between them was one of the aims of these experiments. Now, at the end of this series of experiments, one is faced with the perplexing fact that the odorous substances can be classified in a number of different ways on the basis of the results obtained, but that these classifications differ and may be quite unrelated to each other.

The first type of classification that suggests itself is based on the direct cross-adapting effects which the odorous substances exert upon each other (see table 5.15). Classifying on this basis is by no means easy, for although it is true that some pairs of substances exert more influence on each other than others, (rule 5) they all reduce the sensitivity to each other to some extent (rule 1) and the decision which influences are to be considered big enough to group two substances together and which influences are small enough to set them apart remains an arbitrary one.

An even more serious handicap to a simple classification is the apparent

lack of reciprocity in the adapting effects (rule 4). This non-reciprocity makes it very difficult to use statistical procedures like multi-dimensional analysis. The models on which such statistical procedures are based usually translate similarities into distances in a multidimensional space, implicating that the distance between two points in the space is the same in both directions. Therefore, since non-reciprocity is excluded in principle by these procedures and any occurring non-reciprocity is ascribed to error, two different estimates of the same similarity are just averaged in these methods.

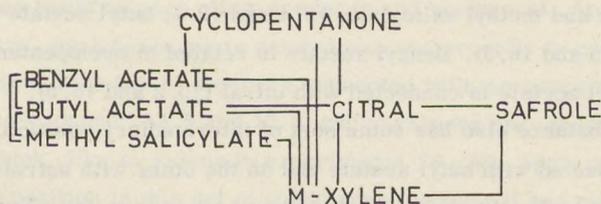
Although about fifty percent of the differences between the cross-adapting effects are smaller than five percent response reduction (see table 5.19) many of them are statistically significant and some are even very large. Moreover, the fact that the substances can be arranged in a "pecking order" on the basis of the differences in their cross-adapting effects makes it unlikely that ascribing the differences to pure experimental error would be justified.

With all these complications in mind, the best one can do is to indicate on the basis of ordinary inspection of the data which are the most striking relationships between the substances.

If one does so for experiments 20 - 26, one can group the substances in the way shown in figure 5.5 A.

MOST IMPORTANT CROSS-ADAPTATIONAL RELATIONSHIPS

A. EXPERIMENTS 20 - 26



B. EXPERIMENTS 27 - 33

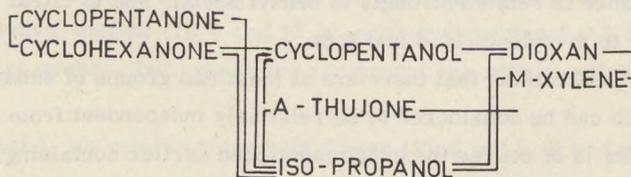


Fig. 5.5. The most important cross-adaptational relationships in the two groups of seven odorous substances.

There is one substance, m-xylene, which has strong relationships (i. e. the sum of the cross-adapting effects is at least 20%) with all six other substances.

Therefore, this substance occupies an intermediary position between the other groups that can be formed. It is very striking that this substance is at the same time the one that has the most non-reciprocal relationships with the other substances. Thus, the differences between the influences of citral, cyclopentanone, benzyl acetate and safrole on m-xylene and the influences of m-xylene on these substances are 13.4%, 8.8%, 10.2% and 9.9% respectively.

These are the four highest differences found in the whole group of experiments. This means, as can be seen also directly from inspection of the fifth column of table 5.15, that the strong relationships between m-xylene and the other substances are mainly due to the influence exerted by these other substances on m-xylene and not to the influences of m-xylene on these other substances.

Nevertheless, it should be mentioned that the one reciprocal relationship between m-xylene and butyl acetate (the influences of m-xylene on butyl acetate and vice versa are: 19.1 and 17.7) is at the same time the strongest relation of the whole set.

By far the most striking aspect of figure 5.5 A is the closely interrelated group formed by benzyl acetate, butyl acetate and methyl salicylate. Apart from their relationships with m-xylene these substances have only few connections with other substances, but the relations among themselves are strong (the influences of benzyl acetate on butyl acetate and vice versa are: 12.1 and 19.1; benzyl acetate and methyl salicylate: 15.4 and 12.4; butyl acetate and methyl salicylate 12.5 and 18.5). Benzyl acetate is related to cyclopentanone (11.0 and 15.7) and butyl acetate is connected with citral (10.2 and 16.0).

This latter substance also has some sort of intermediary position, since on the hand it is connected with butyl acetate and on the other with safrole (10.3 and 13.3), which is really the odd one out, because apart from its relation to m-xylene it has no other strong connections. Citral is also connected with cyclopentanone (12.0 and 9.5).

This substance is related strongly to benzyl acetate and to citral and only marginally to m-xylene (14.4 and 5.6).

One is inclined to think that there are at least two groups of substances in figure 5.5 A which can be considered to be relatively independent from each other.

The first one is of course the group mentioned earlier containing benzyl acetate, butyl acetate and methyl salicylate. The second one is formed by safrole alone or by the combination of safrole and citral. That this latter substance must be

seen as independent from the first group notwithstanding its relation to butyl acetate can be illustrated by the fact that it has no strong relation with methyl salicylate (11.4 and 5.5) and that its relation with benzyl acetate (4.1 and 2.4) is the weakest one of the whole set. Therefore, it seems likely that the property of butyl acetate which binds it to benzyl acetate and methyl salicylate differs from the one which is responsible for its relation to citral. Perhaps cyclopentanone constitutes a third group all by itself. It has relations with benzyl acetate and citral, but since these two substances are exactly the ones which appear to resemble each other least, the relation which cyclopentanone has with each of them is likely to be of a different nature.

The case of *m*-xylene is a peculiar one. Since the sensitivity to this substance is reduced substantially by all other substances, it appears to belong to all groups, but the lack of reciprocity of the effects mentioned earlier casts some doubt on this conclusion. Perhaps, some general factor like volatility or water solubility is involved in this case. It would also be possible that trigeminal effects play a role. This would be in line with the hypothesis of chapter 4 in which it was supposed that trigeminal effects influence the course of recovery of *m*-xylene and other substances.

Inspection of the results of experiments 27 - 33 results in a set of relations which are illustrated in figure 5.5 B. This figure immediately shows one group of substances which are clearly distinct from the other substances. It is the group of cyclopentanone and cyclohexanone (17.9 and 17.7). The effects these two substances exert on each other are large and reciprocal. Apart from this mutual relation, cyclohexanone is related non-reciprocally to cyclopentanol (19.7 and 8.2) and the two of them are connected with iso-propanol (cyclopentanone and iso-propanol: 14.6 and 12.5; cyclohexanone and iso-propanol (22.3 and 10.1), which, like *m*-xylene in experiments 20 - 26, appears to hold an intermediary position in this set of substances, because it has relatively strong relations with all others. However, the position of iso-propanol differs from the one of *m*-xylene in the previous set, because its relationships with other substances are more often reciprocal. It has a strong and almost reciprocal relationship with *a*-thujone (15.6 and 13.9), with cyclopentanol (13.8 and 11.9) and a somewhat weaker, but even more reciprocal one with *m*-xylene (11.4 and 11.6).

On the other hand, its relationships with dioxan (17.5 and 3.5) and with cyclohexanone (22.3 and 10.1) are highly non-reciprocal.

Apart from its relations to cyclohexanone and iso-propanol, cyclopentanol is

related in an extremely non-reciprocal way to dioxan (28.6 and 8.5) and to *a*-thujone (20.4 and 0.5), which two substances are not interrelated directly, but have both a relation with *m*-xylene (dioxan and *m*-xylene: 23.7 and 13.1; *a*-thujone and *m*-xylene 13.7 and 9.3).

Apart from the group mentioned, it is very hard to classify the substances in this set of seven. Perhaps the relationship between *a*-thujone and iso-propanol deserves some special attention, because it is the strongest reciprocal relationship of both these substances. Furthermore, dioxan and *m*-xylene have a very strong although non-reciprocal relationship which appears to justify classification of these two substances in one (rather loose) group.

Before discussing classification on the basis of other data than the direct cross-adapting influences, it should once more be pointed out that the groupings made are tentative and have only relative value, since all substances appear to reduce the sensitivity for each other to some extent (see under rule 1) and since the criterion used here to decide whether a relationship is a strong one or not (sum of the reductions equal to or larger than 20%) is an arbitrary one. Nevertheless, the groupings are based on the most evident relationships.

A second type of classification one might think of, would be based on the rank correlations found in tabel 5.24. The rank correlations in the two parts of that table are indications of similarities in the effects which the members of the different pairs of substances exert on the sensitivity to the five other substances in the set of seven. As was pointed out already in the discussion of table 5.25, the correlations have to be considered with much caution because quite a number of them may be just accidental. Therefore, it appears that these correlations do not provide a solid basis for classification. However, they can be used as illustrative evidence for the validity of other classifications. Thus, it could be argued that substances which were grouped together in fig. 5.5 A and fig. 5.5 B on the basis of their mutual effects (table 5.15) might also show relatively high positive correlations in the effects exerted by them on other substances. (It will of course be understood that this need not be so, but that it just seems more likely). The results of table 5.24 are in fact in agreement with these expectations. Of the substances that are grouped together in experiments 20 - 26 (see fig. 5.5 A) butyl acetate and methyl salicylate show a correlation coefficient of +.90, whereas both these substances show a correlation of +.60 with benzyl acetate, which is the third member of the group. Furthermore, it is quite striking that safrole, which was supposed to form the second group all by itself or in conjunction with citral, correlates negatively with all substances but citral (+.60).

Thus, the major groups of fig. 5.5 A appear to be reflected well in the correlations of table 5.24. The same is true for the main groups of fig. 5.5 B. Here, the most prominent relationship is the one between cyclopentanone and cyclohexanone and the correlation between the influences exerted by these two substances on the others is +.90.

The second combination of substances that appeared to be of some importance, the one between α -thujone and iso-propanol is correlated +.80 in their effects on other substances and the very strong, but non-reciprocal relationship between dioxan and m-xylene is reflected in a correlation of +.60 between their effects on others.

In both sets of experiments relatively high correlations have been found in table 5.24 which do not follow in such a direct way from the results of fig. 5.5 A and fig. 5.5 B. This was only to be expected in view of the fact that in these figures only the strongest relations of table 5.15 were used and because it was shown elsewhere that some positive correlations would already be found on the basis of pure chance.

A third type of classification of odorous substances could be made on the basis of the shape of the recovery curves obtained after adaptation to them. As was pointed out in rule 11, the shape of the recovery curve after cross-adaptation appears to vary with the adapting stimulus, but remains relatively constant with different test stimuli. Although no attempt will be made here to classify all substances in the two sets on the basis of shape differences - the results are scanty and three points do not provide enough information about the shape of their recovery curves - it seems worthwhile to consider the shape differences between the two substances which were present in both sets of substances: m-xylene and cyclopentanone. The recovery curves after self-adaptation of these substances have already been discussed in the previous chapter.

It can be shown, that recovery for almost all substances is much faster in the period between 30 and 60 seconds than in the period between 60 and 90 seconds after adaptation with m-xylene, but that the reverse is true when cyclopentanone has been the adapting stimulus. It is also striking that the percentage of positive response found for a stimulus at 90 seconds after cyclopentanone is nearly always the highest percentage found for that stimulus in the same experiment, whereas the percentage found at 90 seconds after m-xylene is hardly ever the highest one obtained. This means that whereas the recovery from cross-adaptation to cyclopentanone appears to be almost completed after 90 seconds, the sensitivity is still considerably reduced at 90 seconds after cross-adaptation

with m-xylene.

Therefore, it seems that different mechanisms with different recovery characteristics are involved in the perception of these two substances. The idea of such a difference is further corroborated by the fact that the relationship between m-xylene and cyclopentanone is only a marginal one in the data of experiments 20 - 26 (table 5.15) and a rather small one in the data of experiments 27 - 33.

Finally, the correlations between the effects of the two substances on others (table 5.24) are 0.00 and -.60 respectively, indicating that the effects are quite independent if not slightly opposite. Therefore, it appears right to classify cyclopentanone and m-xylene separately.

A fourth and last way of classifying the odorous substances may perhaps be found in the so-called "pecking order" which was discussed under rule 4. The idea of the existence of strong and weak adaptors may be a valid one. It appears that the arrangement of the pecking order is quite independent of the groups obtained by the previous classifications. Perhaps there is a general factor involved, which affects the sensitivity to different substances to a different degree rather than in a different way.

c. What is the meaning of the results obtained in the cross-adaptation experiments for an understanding of the mechanisms of olfaction?

The straightforward answer to this question is: little.

Even if it has been possible to make some tentative groupings among the odorous substances, hypotheses on the nature of the underlying mechanisms remain speculative and direct information can not be obtained. Nevertheless, it may be worthwhile to formulate some of these hypotheses and to see to what extent they are confirmed or contradicted by the results.

The first of these hypotheses might be that there are a number of receptor sites of different shapes and that molecules have to fit into these sites in order to be able to stimulate the receptor. This hypothesis has been proposed in an extreme form by Amoore (1962, 1963), who claimed at one time that there are only seven different types of receptor sites and that the shapes of five of them can be described roughly, whereas two of them should be characterized by electrical rather than by steric properties, one of them being a site for electrophilic molecules and the other one a site for nucleophilic molecules.

The shape of the steric receptor sites was deduced by Amoore from the shapes

of the molecules they seemed to accommodate. Thus, the so-called camphoraceous site was supposed to admit only small, rather sphere-like substances of approximately 7.5 to 9 Ångstrom in diameter. The selection of the molecules that were classified as belonging to one group was made on the basis of the qualitative similarity of their odours, established by mere descriptive means. Later Amoore and Venstrom (1966) provided also more quantitative data on the relationship between odour similarity and molecular shape. Experiments on cross-adaptation may of course be used to test the hypothesis, because only molecules that can enter the same site can cross-adapt for each other at the peripheral level. A problem which arises if one tries to test Amoore's hypothesis, is the flexibility of the shape of many molecules. Long chainlike molecules like for instance citral may assume a large number of shapes and may thus be accommodated by a number of different receptor sites in Amoore's system. A true test of the hypothesis can only be made by experiments with molecules of rigid structure and of great purity.

Unfortunately, the substances used in the experiments described here are not rigid and, in the case of citral which always contains some neral, not pure enough to decide whether the hypothesis is correct or false. However, a number of facts do fit in well with the shape hypothesis:

1. Flexible molecules like citral and perhaps also butyl acetate appear to take an intermediary position, which may indicate that the varying shapes which they present are indeed accommodated more easily by a number of different receptor sites.
2. The rather rigid and similar molecules of benzyl acetate and methyl salicylate, which both contain a benzene ring appear to block the sensitivity to each other to a large extent. The fact that butyl acetate also affects the sensitivity to these two substances can be explained by the flexibility of the aliphatic molecule, but it is more difficult to understand the considerable reduction of the sensitivity to butyl acetate caused by benzyl acetate and methyl salicylate. For if butyl acetate is flexible enough to fit in a number of different sites, it might be expected that only a limited number of these sites would be blocked by the larger and more rigid molecules.
3. The relationship between citral and butyl acetate is of course not surprising if one accepts the shape hypothesis because the molecules of both these substances are flexible enough to block a number of different sites. The fact, that citral has a much larger influence on the sensitivity to butyl acetate than butyl acetate has on the sensitivity to citral may also be understood, because

citral is by far the more flexible of the two. Furthermore, citral is less pure and it seems unlikely that butyl acetate could block all the stimulating possibilities of it.

4. Safrole, the other relatively rigid molecule in the group of substances used in experiments 20 - 26, forms really a group in itself. The only two molecules that show strong cross-adaptational relationships with it are the flexible citral and m-xylene, which is related to all substances.
5. The fact, that cyclopentanone and cyclopentanol show less cross-adaptational relationship than cyclopentanol and cyclohexanone, which may at first appear somewhat surprising, can also be explained by the shape hypothesis. As was pointed out by Beets (1970) cyclopentanone has a flat ringlike shape whereas cyclopentanol and cyclohexanone are more bulky and spherical. However, this means that the very strong and reciprocal relationship between cyclopentanone and cyclohexanone can not be explained entirely on the basis of shape resemblance. This fact leads to the discussion of other hypotheses on the mechanism of olfactory transduction.

A second hypothesis on the nature of the olfactory mechanism might be that there are specific groups in the molecules which are responsible for the stimulation. This hypothesis need not exclude the former one, since the shape of the molecules may still influence the possibilities of a functional group to get in contact with the receptive sites.

Ideally, this second hypothesis can only be tested with large molecules of almost the same rigid shape in which relatively small functional groups have been substituted for each other. Good examples of such molecules in which minor changes have caused large quantitative and qualitative olfactory effects can be found in the literature (Beets 1970).

Unfortunately, in the experiments described here, all the molecules used were rather small and in the one case in which a change of functional group was made (cyclopentanone and cyclopentanol) the general shape of the molecules was influenced to such an extent that the shape difference alone might be used to explain the lack of cross-adaptational relationship between the two substances (see above). Although there is therefore no direct evidence in favour of the second hypothesis, it should be pointed out that acceptance of the hypothesis would help to explain the very strong and reciprocal relationship between the two cycloketones. The fact, that the third ketone, α -thujone, is only weakly related to the two others may be due to the different shape of the molecule as well as to the presence of an isopropyl group.

A third hypothesis on the nature of the mechanisms underlying the tentative groupings made in the previous section might be that the receptive site is sensitive to some physical property of the molecules. In order to check this possibility a large number of physical properties of the molecules have been looked up or calculated.

Among these were molecular weight (M), relative density at 20°C with regard to water at 4°C (d), refraction index in the liquid state at 20°C for the D-ray of sodium ($n_{\text{liq}_D}^{20}$), boiling point in °Kelvin (B.P. °K), saturating vapour pressure at 37°C in atmospheres (P_{37}^0 in Atm.), molecular volume ($V = M/d$), molecular refraction proportional to the polarizability ($R_m = (n^2 - 1)M / (n^2 + 2)d$), average diamagnetic susceptibility (Chi), the negative logarithm of the thermodynamic activity at threshold and at 37°C (-log A), and water solubility (Aq. Sol.).

None of the physical constants appears to be related in any systematic way to the groupings made in the previous part of this section.

In order to see whether the "pecking order" in the cross-adaptational relationships which was established earlier (see rule 4) was related to any of these physical properties, rank correlations between these properties and the "pecking order" were calculated.

The highest rank correlation coefficient found was the one between molecular volume and the "pecking order" of the substances in experiments 20 - 26. ($Rho = +.39$). However, no such relation could be found in the second set of experiments ($Rho = -.07$).

Although these negative results do not exclude the possibility that the physical properties of the molecule mentioned play some role in the transduction of the olfactory message, none of them appears to be a dominant factor in the process. Apart from these comments on the relevance of the groupings described in the previous part of this section for the acceptability of specific hypotheses on the mechanisms involved in olfaction, two general statements can be made on the basis of the rules established in the previous section of this chapter.

1. The fact that some substances have more influence on the sensitivity to other substances than on the sensitivity to themselves (rule 3) may mean that there are large differences in the number of receptive sites available for different substances. For only if this is true a substance may occupy a relatively larger part of the sites available to another substance than of its own sites. If one assumes, that for any given substance stimulation of a certain number of sites is sufficient to lead to a certain level of perceived intensity (70% of positive response in the experiments described here) this means that some substances

have a large surplus of unoccupied sites at that level of perceived intensity, whereas others have only few sites left unoccupied.

If a new stimulus arrives the chances that it finds unoccupied sites are better for the first group of substances than for the last one. This idea is further corroborated by the finding that the cross-adapting effects are related to the self-adapting effects of the test stimuli, but not to those of the adapting stimuli (rule 6). This means that substances which show a strong adaptation for themselves are also the ones which are more strongly influenced by others. This may be due to the fact that the sites available to them are just occupied more completely by the number of molecules necessary to reach the criterion level (70% of positive response). Substances for which this is true would be the "weak adaptors" described above. They are easily put out of business by other substances, whereas the so-called "strong adaptors" are not easily affected by other substances because they always have enough unoccupied sites left over to reach a reasonably high level of perceived intensity. It should be noted that the reductions caused by self-adaptation are indeed lower for those substances which have a higher position in the "pecking order".

This is of course not an independent argument for the truth of the "site number" hypothesis forwarded here, because the self-adaptation data obtained for the different substance were used to calculate the values on which rule 3 (the first argument used here) was based, but it provides a different view on the same argument. So-called "strong adaptors" show little self-adaptation. Therefore, the terms "strong" and "weak" should not be taken too literally.

2. The fact that the number of positive correlations between the cross-adapting influences which the members of pairs of substances exert on the other five substances in the same experiment (rule 12) does exceed the number of positive correlations which could be expected on the basis of pure chance only to a limited extent, appears to indicate that the number of independent mechanisms involved in olfactory transduction is rather large. It should be possible to calculate the limitation in the number of independent variables that should be assumed to obtain a similar discrepancy between the number of positive correlations expected on the basis of mere chance. However, the sample of substances used in the experiments described here is far too small to do so effectively.

5.5. CONCLUSION

In concluding this chapter on olfactory cross-adaptation, one can say that

as a means for classifying odorous substances on the basis of the olfactory mechanisms involved in their perception, cross-adaptation has not stood up to the expectations formulated in the first chapter. The relationships between the cross-adapting effects are complex and they do not provide a clear and uniform classification of the substances.

Furthermore, it remains very difficult to formulate the molecular properties which the substances have to have in common in order to belong to the same (tentative) groupings or in which they have to differ in order to be grouped apart from each other. As long as such properties can not be described unequivocally, hypotheses on the nature of the olfactory mechanisms underlying the classifications such as the ones formulated in the last part of the previous section remain very speculative.

Finally, the fact that there seem to be a large number of independent receptive mechanisms in the system makes it necessary to use much larger samples of substances than the two groups of seven used in this study. This certainly makes this line of attack on the problem of odour classification a lot less attractive from an economical point of view. When cross-adaptation is to be used effectively, it should be used to solve limited problems such as the effects of functional group changes in large rigid molecules or the influences of specific molecular shape differences. Attempts to classify a wide variation of different substances with it should not be made.

If these are the largely negative conclusions to which the experiments on cross-adaptation have led, some positive points that resulted from them can also be mentioned. Thus, they have revealed a number of new cross-adapting phenomena, such as the fact that a substance may have a larger effect on the sensitivity to other substances than it has on the sensitivity to itself and the fact that cross-adapting relationships are very often non-reciprocal. As was pointed out, these phenomena may give us some insight in the relative numbers of receptive sites by which the molecules of different substances can be accommodated.

Perhaps the most important conclusion that can be drawn from the results of these experiments is that there are quite a large number of independent receptive mechanisms involved in the olfactory sense.

CHAPTER 6

SUMMARY

6.1. SUMMARY (in English)

Ignorance of the nature of the olfactory stimulus is by far the most important problem which the research worker in the field of olfaction has to face. It is still impossible to predict with any precision whether a chemical compound will have an odour and if so, what qualitative properties this odour will have. The only thing known, is that the perceived intensity of the odour impression increases with the concentration of the odorous substances in the air which reaches the olfactory epithelium in the nose.

In many ways investigators have tried to solve this problem and to understand the critical variables which govern the perceived quality of the odorous molecule. The experimental study described here, is one of the efforts to gain such insight.

In this investigation, a method has been used which is based on the specificity of the adaptation phenomena which occur when the olfactory sense is exposed to stimulation.

Adaptation, i. e. reduction of the sensitivity of a sense organ as a result of stimulation, is a common phenomenon. It is the result of a reduced reactivity, from which the sensory system recovers gradually after cessation of the stimulation. As long as this recovery has not been completed, the transmission of the stimulation to the central parts of the nervous system remains hampered. In this way adaptation protects the central parts of the nervous system from being flooded with monotonous stimulation and plays a role in the selection of stimuli from the environment of the organism.

Adaptation can take place in the peripheral receptors themselves as well as in more central parts of the receptive system.

To fulfill its selective function, the adaptive process has to have certain specificity, which assures that adaptation to one type of stimulus does not exclude the transmission of all other stimuli at the same time.

In order to explain this specificity, one has to assume that there exist a number of different and relatively independent receptor mechanisms, whose sensitivity can be influenced separately (or at least to a different degree) by adaptation to different stimuli.

The method, which is used in the investigation described here, the cross-adaptation method, presupposes that the influence which two odorous substances have on each others perceptibility and which is reflected in a reduction of the sensitivity to one of them after adaptation to the other, results from the fact that both substances stimulate the same receptor mechanisms.

If this supposition is right, the extent of the cross-adaptation, i. e. of the influence on sensitivity exerted reciprocally by odorous substances, can be used to group these substances on the basis of their common influence on the same receptor mechanisms.

In that case, searching for the molecular structures and properties which are shared by the odorous substances in a group and which are not shared or shared to a much lesser degree by odorous substances belonging to different groups, may lead to hypotheses about the critical variables involved in the stimulation of certain receptor mechanisms. These hypotheses may then in turn lead to hypotheses on the functioning of the receptor mechanism.

Apart from this general aim of the investigation, attention is given to the study of the adaptation and cross-adaptation phenomena themselves.

In the first chapter the problem mentioned above, ignorance about the nature of the critical features of the olfactory stimulus is discussed. This discussion is followed by a survey of the anatomy and histology of the peripheral parts of the olfactory system from the receptors to the connections in the olfactory bulb. The remaining part of the chapter is devoted to a discussion of three different ways of classifying odours:

1. Classification of odorous substances on the basis of similarity and dissimilarity in the perceptual quality of their odours.

This method has been used by a great many authors from Linne (1764) to Woskow (1968). The objections that can be raised against this method of

classification are based mainly on the fact that the qualitative appreciation of odours is determined to a large extent by cultural influences.

This means that the resulting classifications have a restricted relevance to problems related with the nature of the receptor mechanisms involved in olfactory perception.

2. Classification of odorous substances on the basis of the "common fate" of their odorous properties under abnormal perceptual conditions.

A number of studies on partial anosmia (a strong reduction of the sensitivity to certain odour qualities, which is ascribed to a loss of one or more receptor mechanisms) are discussed. In contrast to the disadvantages of this kind of research, in which the experimenter has to look for accidental phenomena of loss of sensitivity, the advantages are pointed out of cross-adaptation studies, in which the experimenter can introduce functional changes in olfactory sensitivity in a systematic way.

3. Classification of odorous substances on the basis of the differential nervous activity, evoked by their odours in parts of the receptive system.

Electrophysiological investigations of the olfactory epithelium and of the olfactory bulb provide information on the specificity of the receptor cells and secondary cells in the olfactory system. There is considerable specificity as is illustrated by the fact that it is possible, given any arbitrarily chosen pair of odorous compounds, to find a fiber of the olfactory nerve which responds differently to stimulation with one of the pair members than to stimulation with the other. In principle odours can be classified on the basis of this kind of electrophysiological data. However, the number of receptor cells and of secondary cells investigated so far is too small to provide a solid basis for classification. Nevertheless, this very direct approach to the problem of classification is very promising. Furthermore, it would be advisable to use electrophysiological methods to verify statements on odour classification from other sources.

Towards the end of the first chapter it is decided to use the cross-adaptation method in this study. Finally, a general outline of this thesis is given.

The second chapter is mainly devoted to a historical survey of research on adaptation and cross-adaptation phenomena in the sense of smell.

Four important phenomena are treated successively:

1. The adaptation time necessary for cessation of the smell sensation.

Many investigators have become intrigued by the fact that, upon prolonged

stimulation, the sense of smell loses its sensitivity rapidly to such an extent that the adapting stimulus is no longer perceived. The time necessary to reach this point at which the odorous sensation is lost, differs from odorous substance to odorous substance and increases with the intensity of the adapting stimulus.

2. The raising of the threshold during adaptation.

Although the time necessary for cessation of the smell sensation gives some indication of the speed of the adaptation processes, it does not provide any information on the course of the sensitivity reduction during the period between the onset of the adapting stimulus and its perceptual disappearance. Many authors have studied this course by determining olfactory thresholds after adaptation to stimuli of different duration. It could be shown that the increase of the olfactory threshold caused by continuous adaptation follows a negatively accelerated course. The level of sensitivity at a given moment during adaptation is dependent upon the intensity of adapting stimulus. The higher this intensity is, the greater is the loss in sensitivity. The claim of some authors, that reduction of olfactory sensitivity can only be brought about by relatively strong adapting stimuli, is not supported by evidence.

3. Recovery of olfactory sensitivity after previous adaptation.

Both the absolute duration and the course of recovery have been investigated by a number of authors. It could be shown that the duration of recovery depends upon the duration and the intensity of the preceding adapting stimulus. The duration of recovery varies from one odorous substance to another. In the course of recovery two phases can be distinguished. After a period of very rapid recovery which starts right after cessation of the adapting stimulus, a second phase sets in, in which recovery is extremely slow.

4. Cross-adaptation.

A number of authors have studied the influence of previous stimulation with one odorous substance on the sensitivity to another. It has been shown that odorous substances may reduce the sensitivity to one another and that they may do so reciprocally to the same extent or to a different degree. Some substances do not reduce the sensitivity to one another at all. There exists no clear relationship between the extent of the cross-adaptation which two substances exert on each other and the similarity of their odorous qualities.

The last part of chapter two is devoted to a discussion of the possible nature of the processes underlying adaptation phenomena. The phenomenon that has been

described here as adaptation, and which is reflected in a reduced responsivity of the organism, may be the result of a number of processes. The following possibilities are discussed:

1. Reflex mechanisms reducing admission of odorous molecules to the olfactory epithelium.
2. Physico-chemical processes in the olfactory mucus.
3. Processes at the receptor sites themselves.
4. Processes in the receptor cells.
5. Processes at the bulbar level.
6. Processes in higher olfactory centres.
7. Processes in other parts of the brain.

The experimental results obtained so far are not sufficient to make an unequivocal choice among these possible processes and mechanisms. However, some of the evidence collected is related to the question whether the adaptation processes are located in the peripheral or in the central parts of the receptive system or in both. On the basis of data on recovery of the contralateral olfactory sensitivity after monorhinal adaptation it is concluded that there appear to be adaptation processes both at the level of the receptors and in the more central parts of the receptive system. It seems that these two types of olfactory adaptation can be investigated rather independently, because recovery is much faster in the central parts than at the receptor level. Furthermore, it is shown that if strong adapting stimuli are used, the central component of the adaptation processes plays a much more important role than if the adapting stimulus is a weak one.

The results described in the historical survey are reviewed in the light of these conclusions. Nearly all authors have used very strong and long lasting adapting stimuli and have determined the sensitivity almost immediately after cessation of the adapting stimulus. The question arises whether they have not been measuring mainly adaptation in the more central parts of the receptive system and it is doubted whether results obtained in this way have a direct relevance with regard to the nature of the actual transducing mechanisms in the receptors. In view of these considerations, it is decided to use only weak stimuli in the cross-adaptation experiments described in this thesis and to let some time elapse between the cessation of the adapting stimulus and the sensitivity measurement, in order to allow for a good deal of central recovery before the measurements are made.

The first section of the third chapter is devoted to a detailed description of the modified Stuiver olfactometer used for presenting the odorous stimuli. Other topics, like the choice of the odorous substances, their concentrations, the selection of experimental subjects, the presentation series used and the methodological presuppositions of the experiments are also discussed in separate sections of the first part of this chapter.

In the second part attention is given to a number of technical and methodological difficulties, such as the influence of adsorption of odorous molecules on the glass walls of the olfactometer, the effects of air pollution and the possible influence of expectancy effects. Some of these difficulties are illustrated with the results of a special experiment.

In the fourth chapter the results of the experiments on adaptation are discussed. In each of these experiments only self-adaptation, i. e. the influence of stimulation with a given odorous substance on the sensitivity to that same substance, has been investigated.

It becomes clear that, contrary to the opinion of some authors, adaptation does occur also when very short adapting stimuli of low (near threshold) intensity are used. After such weak stimuli it may even take 60 seconds until complete recovery is reached.

It is shown also that, notwithstanding the fact that low intensity stimuli are employed, the possibility of adaptation in the central parts of the receptive system can not be ruled out. Nevertheless, it is clear that with these stimuli peripheral adaptation makes a larger contribution to the response reduction found than with the use of strong stimuli.

The chapter is concluded with a series of experiments on recovery of the olfactory sensitivity after adaptation to low intensity stimuli. The recovery curves found for various odorous substances differ considerably in shape. Some of them show a typical biphasic form.

An initial fast increase in sensitivity is followed by a period (between 60 and 90 seconds after cessation of the adapting stimulus), in which the sensitivity hardly rises at all. After this period the sensitivity rises again. There are even some indications, that there is a true negative phase in the recovery between 60 and 90 seconds.

Subsequently four hypotheses which might provide an explanation for the differences in the shapes of the recovery curves are presented.

1. The form of the curves is determined by the presence of specific receptors,

which each have their own characteristic recovery time. An objection to this hypothesis would be that it is difficult to explain a true negative phase in the recovery curve on the basis of it, unless one accepts the possibility that at least one of the receptor types involved acts as an inhibitor for the others. The gradual recovery of this receptor might cause the negative phase.

2. The form of the curves is determined by a combined action of the olfactory receptors and the free nerve endings of the trigeminal nerve which are stimulated by the odorous substance.

This hypothesis is discussed extensively. Some substances appear to stimulate the trigeminal nerve already at concentrations which are too low to lead to a real olfactory sensation. There is a possibility that the stimulation of the trigeminal nerve endings is accompanied secondarily by a reflex causing a dilatation of the blood vessels in the nose. Such a dilatation might lead to a lower accessibility of the olfactory epithelium and a reduced perceptibility of the next stimulus. Furthermore, the fact that the trigeminal nerve does not adapt rapidly under repeated stimulation, but gets rather more irritated by it, might provide an explanation for the negative phase in the recovery curve. This negative phase may mean that on a given point in the recovery (between 60 and 90 seconds) the interval between two successive stimuli becomes too long to result in a further irritation of the trigeminal nerve.

Notwithstanding the progressive recovery of the proper olfactory receptors, the perceived intensity of the stimulus might be reduced as a consequence of the reduction in the trigeminal irritation. An objection to this hypothesis might be that a similar negative phase was observed by other investigators (Perrin 1965) in the recovery of the electro-olfactogram (E.O.G.) of the rabbit for the same odorous substances. Since it is thought impossible that the non-directional free nerve endings contribute directly to the E.O.G., an explanation in terms of trigeminal influences is rendered less likely by these findings.

3. The form of the curves is determined by changes in the blood flow in the nose.

Without being aroused by trigeminal stimulations, changes in vaso-constriction and vaso-dilatation may perhaps also influence the accessibility of the olfactory epithelium. Some authors (Kottmeyer (1957), Schneider and Wolf (1960)) draw attention to the fact that olfactory stimuli may cause changes in the bloodflow in the nose. However, it seems improbable that the effects of the weak stimuli employed would be strong enough to provoke such changes

without mediation of the trigeminal nerve.

4. The form of the curves is determined by adsorption-, evaporation- or solubility properties of the odorous molecules.

Although there are clear indications that odorous substances differ considerably in the extent to which they are dissolved in the mucus, there is still far too little known about the composition of the mucus and of the odour-receptive parts of the receptors to verify this hypothesis.

It is concluded that none of the four hypotheses excludes the others and that only electrophysiological investigation can prove the validity of either one or more of them.

The fifth and last chapter contains a description of two series of experiments in which the mutual cross-adaptational relationships within two groups of seven odorous substances have been studied.

From the results of these experiments a number of general rules on cross-adaptational relationships could be deduced. The most important of these rules are:

1. No adapting substance enhances the sensitivity to another substance.
2. No other substance can reduce the sensitivity to a given odorous substance to a larger degree than that substance itself.
3. An odorous substance may have a larger adapting affect on the sensitivity to another substance than it has on the sensitivity to itself.
4. Most cross-adaptational relationships are non-reciprocal. One substance influences the sensitivity to another substance to a larger degree than the second one influences the sensitivity to the first one.
5. The sensitivity to an odorous substance which self-adapts rather strongly is usually also reduced strongly by other odorous substances.

It becomes evident in the discussion that it is difficult to classify odours reliably and unequivocally on the basis of the data obtained. Therefore, the results of these experiments can contribute relatively little to the formulation of specific hypotheses on the functioning of the olfactory transduction mechanism. Some existing hypotheses, like the "steric odor" theory of Amoore (1963) and the hypothesis that functional groups in the molecule determine the odorous properties, are discussed in the light of the data obtained. Both hypotheses appear to be in agreement with a number of aspects of the results.

On the basis of some of the general rules stated, it can be deduced that the number of receptor mechanisms that is stimulated appears to vary considerably from one odorous substance to another.

At the end of the chapter it is concluded that cross-adaptational relationships are too complex and that the number of independent receptor mechanisms is too large to make cross-adaptation a very fruitful method of odour classification. Nevertheless, it is pointed out that cross-adaptation may be a very useful tool in answering specific questions about the interaction of odorous substances. The formulation of the general rules pertaining to cross-adaptational relationships may lead the way to a multitude of such questions.

6.2. SAMENVATTING (Summary in Dutch)

Het grootste probleem waarvoor de onderzoeker op het gebied van de reukwaarneming zich geplaatst ziet, is zijn onbekendheid met de aard van de stimulus. Nog steeds is het onmogelijk met nauwkeurigheid te voorspellen of een chemische verbinding een geur zal hebben en, indien dit het geval is, welke kwalitatieve eigenschappen die geur zal hebben. Wel is bekend, dat de sterkte van de geurindruk toeneemt met de concentratie van de reukstof in de lucht die het reukgevoelige deel van de neus bereikt.

Langs vele wegen is gepoogd dit fundamentele probleem tot een oplossing te brengen en inzicht te krijgen in de kritische variabelen die de geurkwaliteit van het reukstofmolecuul beheersen. Het experimenteel onderzoek dat hier is beschreven vormt één van deze pogingen.

Bij dit onderzoek is gebruik gemaakt van een methode die zich baseert op de specificiteit van de adaptatieverschijnselen die optreden wanneer het reukzintuig aan prikkeling wordt blootgesteld. Adaptatie, dat wil zeggen vermindering van de gevoeligheid van een zintuig onder de invloed van prikkeling, is een algemeen verschijnsel. Het berust op een verminderde reactiviteit, waarvan het zintuig zich geleidelijk herstelt nadat de prikkeling is opgehouden. Zolang dit herstel niet is opgetreden blijft de transmissie van de prikkeling naar de centrale delen van het zenuwstelsel belemmerd. Op deze wijze beschermt adaptatie de centrale delen van het zenuwstelsel tegen een overmaat van monotone en oninteressante prikkeling en vervult het een functie bij de selectie van stimuli uit de omgeving van het organisme. Adaptatie kan zowel in de perifere receptororganen zelf, als in meer centrale delen van het zenuwstelsel optreden.

Om de selectieve functie goed te kunnen vervullen, dient het adaptatieve proces een zekere specificiteit te bezitten, die ervoor zorgt dat adaptatie aan een soort prikkel niet tegelijkertijd het doordringen van alle andere prikkels uitsluit. Om deze specificiteit in het geval van sensorische adaptatie te kunnen verklaren, moet men aannemen dat er een aantal verschillende relatief onafhankelijke receptormechanismen bestaan, die ieder afzonderlijk (of ieder in verschillende mate) door adaptatie aan verschillende reukstoffen beïnvloed kunnen worden.

De methode waarvan in het hier beschreven onderzoek gebruik wordt gemaakt, de kruis-adaptatieve methode, veronderstelt nu, dat de invloed die twee reukstoffen op elkaars waarneembaarheid hebben en die tot uitdrukking komt in een vermindering van de gevoeligheid voor een van deze stoffen na

adaptatie aan de andere, wordt veroorzaakt door het feit dat beide stoffen dezelfde receptormechanismen prikkelen.

Indien deze veronderstelling juist is, kan de mate van kruisadaptatie, dat wil zeggen van de wederzijdse beïnvloeding van de gevoeligheid, worden gebruikt om de geuren te groeperen op basis van hun gemeenschappelijke inwerking op dezelfde receptormechanismen. Het zoeken naar moleculaire structuren en eigenschappen die de reukstoffen binnen één op een dergelijke wijze gevormde groep gemeen hebben en die zij niet, of in veel mindere mate, delen met reukstoffen die tot een andere groep behoren, kan dan leiden tot hypothesen over de kritische variabelen die voor het stimuleren van bepaalde receptormechanismen verantwoordelijk zijn. Deze hypothesen kunnen op hun beurt leiden tot een hypothese over de werking van het receptormechanisme zelf.

Naast deze algemene doelstelling is in het onderzoek aandacht besteed aan de bestudering van de adaptatie- en kruis-adaptatieverschijnselen zelf.

In het eerste hoofdstuk is het probleem van de onbekendheid met de kritische variabelen van de stimulus uiteengezet. Verder wordt een kort overzicht gegeven van de anatomie en de histologie van het olfactorische systeem vanaf de receptoren tot en met de verbindingen in de bulbus olfactorius.

De rest van het hoofdstuk is gewijd aan een bespreking van drie verschillende methoden van geurklassifikatie:

1. Klassifikatie op basis van gelijkenis in de geurkwaliteit van de reukstoffen.

Deze methode is door tal van onderzoekers gebruikt van Linnaeus (1764) tot Woskow (1968). De bezwaren tegen deze methode van klassifikatie vloeien vooral voort uit het feit dat kwalitatieve waardering van geuren in hoge mate cultureel bepaald is. Dit betekent dat de resulterende klassifikaties vaak slechts een zeer beperkte relevantie bezitten voor de problemen die samenhangen met de aard van de receptormechanismen die bij de waarneming betrokken zijn.

2. Klassifikatie op basis van het gemeenschappelijk lot dat de geureigenschappen van reukstoffen ondergaan onder abnormale waarnemingscondities. Hier worden in de eerste plaats een aantal onderzoeken besproken over de gedeeltelijke geurblindheid (partiële anosmie), een sterke vermindering van de gevoeligheid voor bepaalde geurkwaliteiten, die wordt toegeschreven aan het uitvallen van een of meer receptormechanismen. Tegenover de nadelen van deze onderzoeken, waarin gezocht moet worden naar toevallige uitvalsverschijnselen, wordt gewezen op de voordelen van het kruis-adaptatieve onderzoek, waarin funktionele veranderingen in de geurwaarneming meer systema-

tisch kunnen worden aangebracht.

3. Klassifikatie op basis van de verschillende zenuwactiviteit die door prikkeling met verschillende reukstoffen in delen van het receptieve systeem te weeg wordt gebracht.

Het electrofysiologisch onderzoek van het reuk-epitheel en van de bulbus olfactorius verschaft informatie over de specificiteit in de reactiepatronen van de receptorcellen en de secundaire cellen in het olfactorische systeem. Deze specificiteit is vrij groot, zoals blijkt uit de mogelijkheid om voor ieder willekeurig gekozen stoffenpaar een fiber van de olfactorische zenuw (axon van de receptorcel) te vinden, die anders reageert op stimulatie met de ene stof dan op stimulatie met de andere stof.

In principe kunnen geuren geklassificeerd worden op basis van dergelijke electrofysiologische gegevens. Het aantal receptorcellen en cellen in de bulbus is echter zeer groot en het aantal tot nu toe onderzochte cellen is nog veel te klein om als basis voor een betrouwbare klassifikatie te kunnen dienen. Deze zeer directe aanpak van het klassifikatieprobleem houdt grote beloften in.

Het verdient ook aanbeveling uitspraken over geurindelingen die langs andere weg zijn verkregen te verifiëren met electrofysiologisch onderzoek.

Aan het eind van het eerste hoofdstuk wordt besloten de kruis-adaptatieve methode te gebruiken. Tot slot volgt dan nog een overzicht van de indeling van het proefschrift.

Het tweede hoofdstuk is voornamelijk gewijd aan een historisch overzicht van het onderzoek naar adaptatie- en kruis-adaptatieverschijnselen van het reukzintuig.

Vier belangrijke verschijnselen komen achtereenvolgens in dit overzicht aan de orde:

1. De adaptatietijd die nodig is voor een volledig verlies van de geurindruk. Het feit dat het reukzintuig bij voortdurende prikkeling met eenzelfde reukstof betrekkelijk snel zodanig aan gevoeligheid inboet dat de prikkel niet meer wordt waargenomen, heeft veel onderzoekers bezig gehouden. De tijd nodig voor het verlies van de geurindruk blijkt van stof tot stof te verschillen. Verder blijkt deze tijd toe te nemen met de intensiteit van de adapterende prikkel.
2. De verhoging van het drempelniveau tijdens adaptatie. Hoewel de tijd nodig voor het verdwijnen van de geurindruk een indicatie vormt van de snelheid van het adaptatie-proces, geeft de bestudering van dit

verschijnsel geen inzicht in het verloop van het gevoeligheidsverlies dat in de periode tussen het begin van de adapterende prikkel en het ophouden van de geurindruk plaatsvindt.

Veel onderzoekers hebben dit verloop bestudeerd door in een drempelonderzoek de gevoeligheid van het reukzintuig na een aantal adapterende prikkels van verschillende duur te bepalen.

De resultaten van dit onderzoek tonen aan dat de verhoging van de reukdrempel, die door voortdurende adaptatie veroorzaakt wordt, een negatief versneld verloop heeft.

Verder is het niveau van de reukgevoeligheid op een gegeven moment tijdens de adaptatieperiode afhankelijk van de intensiteit van de adapterende stimulus. Hoe sterker de stimulus, des te groter het gevoeligheidsverlies. De mening van sommige onderzoekers, dat vermindering van de reukgevoeligheid alleen door relatief sterke adapterende prikkels te weeg kan worden gebracht, blijkt ongegrond.

3. Herstel van de reukgevoeligheid na adaptatie.

Zowel de absolute duur als het verloop van het herstel van de reukgevoeligheid na adaptatie zijn onderzocht.

De resultaten van dit onderzoek tonen aan dat de duur van het herstel afhankelijk is van de duur en van de intensiteit van de voorafgaande adapterende prikkel en dat hij varieert van stof tot stof. Het verloop van het herstel bestaat uit twee fasen. Na een zeer snel herstel direkt na het stopzetten van de adapterende stimulus, treedt een tweede fase in, waarin het herstel uiterst langzaam verloopt.

4. Kruis-adaptatie.

De invloed van prikkeling met de ene stof op de gevoeligheid voor een andere stof is door een aantal onderzoekers onder de loupe genomen.

Het blijkt dat stoffen de gevoeligheid voor elkaar kunnen verminderen en dat zij dat wederzijds in gelijke mate of in ongelijke mate kunnen doen. Soms oefenen stoffen in het geheel geen effect uit op de gevoeligheid voor elkaar.

Verder blijkt er geen duidelijke relatie te bestaan tussen de mate van kruis-adaptatie die twee stoffen op elkaar uitoefenen en de subjectief ervaren gelijkenis van hun geurkwaliteiten.

Het laatste deel van het tweede hoofdstuk is gewijd aan een bespreking van de aard van de adaptatie processen.

Aan het verschijnsel dat hier beschreven is als adaptatie en dat tot uiting komt

in een verminderde responsiviteit van het organisme, kunnen een groot aantal verschillende processen ten grondslag liggen.

De volgende mogelijkheden worden kort aangeduid:

1. Reflex mechanismen die de toegang tot het reukepitheel voor de reukmoleculen belemmeren (zwellings, mucus afscheiding).
2. Physico-chemische processen in de mucus olfactorius.
3. Processen aan de reukgevoelige membranen van de receptorcel.
4. Processen in de receptorcel.
5. Processen op het niveau van de bulbus olfactorius.
6. Processen in hogere olfactorische centra.
7. Processen in andere delen van de hersenen.

Op grond van de experimentele gegevens die ter beschikking staan kan uit deze veelheid van mogelijke processen en mechanismen geen eenduidige keuze gemaakt worden. Wel is er enig onderzoek over de vraag of sensorische adaptatie plaats vindt in de receptorcellen, in hoger gelegen delen van het receptieve systeem of in beide.

Op grond van gegevens over het herstel van de contralaterale reukgevoeligheid na monorhinale adaptatie wordt geconcludeerd dat waarschijnlijk zowel adaptatie processen in de receptoren als in de hoger gelegen delen van het receptieve systeem tot de adaptatieve verschijnselen bijdragen, maar dat zij min of meer gescheiden kunnen worden onderzocht, omdat het herstel van de adaptatie in de hoger gelegen delen van het systeem aanmerkelijk sneller verloopt dan het herstel van de adaptatie die op receptor niveau plaats vindt. Bovendien blijkt de meer centrale component van het adaptatieve proces relatief een veel belangrijke rol te spelen wanneer sterke stimuli gebruikt worden, dan wanneer de adaptatieve stimulus zwak is.

Op grond van deze conclusies wordt het onderzoek dat in het historisch overzicht is beschreven opnieuw bezien. Het blijkt dat vrijwel alle onderzoekers hebben gewerkt met zeer krachtige en langdurige adapterende prikkels en dat zij de gevoeligheid van het zintuig vrijwel onmiddellijk na het stopzetten van de adapterende prikkel hebben bepaald. De vraag rijst in hoeverre zij daarmee niet in hoofdzaak de adaptatie in de meer centrale delen van het receptieve systeem hebben gemeten en het wordt betwijfeld of de resultaten, die op deze wijze zijn verkregen, wel relevant zijn voor het doen van uitspraken over de mechanismen die bij de prikkeling van de receptoren een rol spelen. Op grond van deze overwegingen wordt besloten in het onderzoek naar de kruis-adaptatieve relaties uitsluitend te werken met adapterende prikkels van lage intensi-

teit en de gevoeligheidsmeting niet direct na het ophouden van de adapterende stimulus te verrichten zodat het snelle herstel van de centrale component zich grotendeels kan hebben voltrokken voordat de gevoeligheidsmeting plaats vindt.

Het eerste deel van het derde hoofdstuk is gewijd aan een gedetailleerde beschrijving van de gewijzigde Stuiver-olfactometer waarmee de stimuli in het onderzoek zijn aangeboden. Verder is aandacht besteed aan de keuze van de reukstoffen, de selectie van de proefpersonen, de series waarin de geurprikkelers zijn aangeboden en de methodische vooronderstellingen van het onderzoek. In het tweede deel van het hoofdstuk wordt een aantal technische en methodische moeilijkheden besproken, zoals de invloed van adsorptie van de reukstoffen aan de glaswand van de olfactometer, effecten van luchtvervuiling en de mogelijke invloed van verwachtingspatronen bij de proefpersonen. Enkele van deze moeilijkheden worden met de resultaten van speciaal voor dit doel ingericht empirisch onderzoek geïllustreerd.

Het vierde hoofdstuk is gewijd aan het onderzoek van adaptatie-verschijnselen. Steeds is in de experimenten die in dit hoofdstuk aan de orde komen sprake van eigen-adaptatie, dat wil zeggen van de invloed van prikkeling met een bepaalde reukstof op de gevoeligheid voor diezelfde reukstof.

In dit onderzoek blijkt duidelijk, dat adaptatie ook optreedt wanneer kort durende prikkels van lage intensiteit als adapterende stimuli worden gebruikt en dat het na aanbieding van een dergelijke adapterende stimulus geruime tijd (minstens 60 seconden) duurt voordat de gevoeligheid volledig is hersteld.

Ook wordt aangetoond dat, ondanks het feit dat stimuli van lage intensiteit zijn gebruikt, de mogelijkheid van adaptatie in centrale delen van het receptieve systeem niet kan worden uitgesloten. Wel is het duidelijk dat de perifere adaptatie bij deze stimuli relatief meer bijdraagt in de gevonden gevoeligheidsvermindering dan wanneer sterke stimuli worden gebruikt.

Het hoofdstuk wordt besloten met een reeks experimenten over het herstel van de reukgevoeligheid na adaptatie. De herstelcurven die voor verschillende stoffen worden gevonden, wijken vaak sterk van elkaar af in vorm. Sommige vertonen een eigenaardige bifasische vorm, waarbij een aanvankelijke snelle stijging van de gevoeligheid wordt gevolgd door een periode (tussen 60 en 90 seconden na de beëindiging van de adapterende stimulus), waarin de gevoeligheid niet of nauwelijks toeneemt. Na deze periode treedt opnieuw een herstel van de gevoeligheid op. De indruk bestaat zelfs dat er sprake is van een echte negatieve tus-

senphase in het herstel.

Achtereenvolgens worden vier hypothesen besproken, waarmee het optreden van vorm verschillen in de curven verklaard zou kunnen worden.

1. De vorm van de curven wordt bepaald door de aanwezigheid van specifieke reukreceptoren die ieder een eigen hersteltijd hebben. Een bezwaar van deze hypothese is, dat het moeilijk valt een eventuele negatieve fase in het herstel te verklaren op basis van het herstel van specifieke receptoren, tenzij men de mogelijkheid aanvaardt dat een van de betrokken receptoren een inhiberende werking op de andere uitoefent. Het geleidelijk herstel van deze receptor zou dan tot de negatieve fase in de herstelcurve kunnen leiden.
2. De vorm van de curven wordt bepaald door een gecombineerde werking van reukreceptoren en vrije zenuweinden van de trigeminus die door de reukstof geprikkeld worden.

Deze hypothese wordt uitgebreid besproken. Sommige stoffen blijken de trigeminus reeds te prikkelen bij concentraties die te laag zijn voor een echte geur indruk. De mogelijkheid bestaat dat de inwerking op de trigeminus vezels als secundair effect een reflexmatige verhoging van de bloeddorstroming in de neus met zich meebrengt, die leidt tot een vernauwing van de toegangswegen tot het reukepitheel en die zodoende mede verantwoordelijk is voor de verminderde waarneembaarheid van de prikkel na adaptatie. Verder zou het feit, dat de trigeminus bij herhaalde prikkeling niet snel adapteert, maar integendeel eerder meer geïrriteerd raakt, een verklaring kunnen bieden voor de negatieve fase in het herstel. Deze negatieve fase zou kunnen betekenen dat op dat punt in het herstel (tussen 60 en 90 seconden) de tussentijd tussen de prikkels te lang is om tot verdere irritatie van de trigeminus te leiden. De waargenomen intensiteit van de prikkel zou door dit wegvallen van de irritatie kunnen afnemen, ondanks het voortschrijdend herstel van de eigenlijke reukreceptoren. Een bezwaar van deze hypothese is dat eenzelfde negatieve fase door andere onderzoekers (Perrin 1965) is geconstateerd in het herstel van het electro-olfactogram (EOG) van het konijn, terwijl het uitgesloten moet worden geacht dat de ongerichte vrije zenuweinden van de trigeminus direct tot het EOG bijdragen.

3. De vorm van de curven wordt bepaald door veranderingen in de bloeddorstroming van de neus.

Veranderingen in vaso-constrictie en vaso-dilatatie kunnen ook zonder dat zij door trigeminus veroorzaakt worden de bereikbaarheid van het reukepitheel beïnvloeden.

Sommige auteurs (Kottmeyer 1957; Schneider and Wolf 1960) wijzen erop dat reukstimuli veranderingen in de doorbloeding van de neus te weeg kunnen brengen. Het lijkt echter onwaarschijnlijk dat de effecten van de zwakke prikkels die in het onderzoek gebruikt worden, sterk genoeg zijn om zonder tussenkomst van de trigeminus dergelijke veranderingen tot stand te brengen.

4. De vorm van de curven wordt bepaald door adsorptieve en desorptieve eigenschappen van de moleculen of door hun mate van oplosbaarheid in het mucus van het reuk-epitheel.

Hoewel er duidelijke aanwijzingen zijn dat stoffen sterk verschillen in de mate waarin ze door het mucus worden opgenomen, is er nog te weinig van de samenstelling van het mucus en van de reukgevoelige delen van de receptoren bekend om deze hypothese te kunnen verifiëren.

Geconcludeerd wordt dat geen van de vier hypothesen elkaar uitsluiten en dat alleen electrofysiologisch onderzoek de juistheid van een of meer van hen kan aantonen.

Het vijfde en laatste hoofdstuk bevat de beschrijving van twee reeksen experimenten, waarin de onderlinge kruis-adaptatieve beïnvloeding binnen twee groepen van zeven reukstoffen is onderzocht.

- Op grond van dit onderzoek konden een aantal regels worden opgesteld, die voor kruis-adaptatieve relaties blijken te gelden. De belangrijkste regels zijn:
1. Geen enkele adapterende stof verhoogt de gevoeligheid voor een andere stof.
 2. Geen enkele andere stof kan de gevoeligheid voor een bepaalde stof in sterkere mate verminderen dan die stof zelf.
 3. Een stof kan een grotere invloed hebben op de gevoeligheid voor een andere stof dan op de gevoeligheid voor zichzelf.
 4. De meeste kruis-adaptatieve relaties tussen stoffen zijn niet reciprook. De ene stof beïnvloedt de gevoeligheid voor de andere stof in sterkere mate dan andersom.
 5. De gevoeligheid voor een stof die een sterke eigen-adaptatie vertoont, wordt doorgaans ook door adaptatie aan andere stoffen sterk beïnvloed.

Het blijkt moeilijk op grond van de gegevens tot een duidelijke en éénduidige indeling van de reukstoffen in groepen te komen. Over het algemeen kunnen de resultaten van het onderzoek daarom weinig bijdragen tot het formuleren van hypothesen over het reukmechanisme. Wel worden enkele van dergelijke hypo-

thesen besproken, zoals de "steric odor theory" van Amoore (1963) en de hypothese dat funktionele groepen in het molecuul een belangrijke rol spelen bij het bepalen van de geureigenschappen. Nagegaan wordt in hoeverre de gegevens uit dit hoofdstuk deze hypothesen bevestigen of tegenspreken. Beide genoemde hypothesen lijken goed met een aantal aspecten van de resultaten te verenigen. Op grond van enkele van de algemene regels die uit het onderzoek naar voren zijn gekomen wordt afgeleid dat het aantal receptormechanismen, dat gestimuleerd kan worden waarschijnlijk sterk varieert van stof tot stof.

Uit het hoofdstuk wordt tenslotte de conclusie getrokken dat de kruis-adaptatieve relaties te complex zijn en dat het aantal onafhankelijke receptor-mechanismen dat bij de reukwaarneming betrokken is te groot is, om kruis-adaptatie een erg vruchtbare methode van geurgroepering te doen zijn. Niettemin kan kruis-adaptatie-onderzoek een belangrijk hulpmiddel zijn bij het beantwoorden van specifieke vragen over de interactie van reukstoffen. De formulering van de algemene regels die voor kruis-adaptatieve relaties gelden kan de weg openen voor een groot aantal van dergelijke vragen.

LITERATURE

- ADRIAN, E. D., 1950. The electrical activity of the mammalian olfactory bulb. *Electroencephal. Clin. Neurophysiol.*, 1950, 2, 377-388.
- ADRIAN, E. D. 1951. Differential sensitivity of olfactory receptors. *J. Physiol.*, 1951, 115, 42P.
- ADRIAN, E. D., 1953. Sensory messages and sensation. The response of the olfactory organ to different smells. *Acta Physiol. Scand.*, 1953, 29, 5-14.
- ADRIAN, E. D., 1956. The action of the mammalian olfactory organ. *Journal of laryngology and otology*, 1956, 70, 1-14.
- ALLISON, A. C., 1953. The morphology of the olfactory system in the vertebrates. *Biol. Rev. Cambridge Philos. Soc.*, 1953, 28, 195-244.
- AMERINE, M. A., PANGBORN, R. M., ROESSLER, E. B., 1965. Principles of sensory evaluation of food. Academic Press, New York - London, 1965.
- AMOORE, J. E., 1962. The stereochemical theory of olfaction. 1. Identification of the seven primary odours. *Proc. of the scient. sect. of the toilet goods ass. no. 37 (suppl.)*, October 1962, 1-13.
- AMOORE, J. E., 1963. Stereochemical theory of olfaction. *Nature*, 1963, 198, 271-272.
- AMOORE, J. E., 1964. Current status of the steric theory of odor. *Ann. N. Y. Acad. Sci.*, 1964, 116, 457-476.
- AMOORE, J. E., VENSTROM, D., 1966. Sensory analysis of odor qualities in terms of the stereochemical theory. *J. of food science*, 1966, 31, 118-128.
- AMOORE, J. E., 1967. Specific anosmia: a clue to the olfactory code. *Nature*, 1967, 214, 1095-1098.
- AMOORE, J. E., VENSTROM, D., 1967. Correlations between stereochemical assessments and organoleptic analyses of odorous compounds. In: Hayashi. ed., *Olfaction and taste. II*. Pergamon Press, 1967.
- ARONSOHN, E., 1886. Experimentelle Untersuchungen zur Physiologie des Geruchs. *Archiv f. Anat. und Physiol.*, 1886, *Physiol. Abt.* 321-357.
- ASH, K. O., 1969. Ascorbic acid: cofactor in rabbit olfactory preparations. *Science*, 1969, 165, 901-902.
- BACKMANN, E. K., 1917. Experimentella undersökningar aft luktsinnets fysiologi. *Uppsala, Läk-Fören. Förh.*, 1917, 22, 319-464.
- BEETS, M. G. T., 1970. The Molecular parameters of olfactory response. *Pharmacological Reviews* 1970, 22, 1-34.
- BEIDLER, L. M., TUCKER, D., 1955. Response of nasal epithelium to odor stimulation. *Science*, 1955, 122, 76.
- BEIDLER, L. M., 1965. Comparison of gustatory receptors, olfactory receptors, and free nerve endings. In: Cold Spring Harbor Symposia on quantitative biology, *Sensory receptors*, 1965, 30, 191-200. Cold Spring Harbor L. I., New York, 1965.
- BOECKH, J., 1965. Inhibition and excitation of single insect olfactory receptors, and their role as a primary sensory code. In: Hayashi ed.: *Olfaction and taste. II*. Pergamon Press 1967.
- BOECKH, J., KAISLING, K. E., SCHNEIDER, D., 1965. Insect olfactory receptors. In: Cold Spring Harbor symposia on quantitative biology, *Sensory receptors*, 1965, 30, 263-280. Cold Spring Harbor L. I. New York, 1965.
- CAIN, W. S., ENGEN, T., 1969. Olfactory adaptation of odor intensity. In: C. Pfaffmann (ed.): *Olfaction and taste. III*. The Rockefeller University Press, 1969.

- CAIN, W. S., 1970. Odor intensity after self-adaptation and cross-adaptation. *Perception and Psychophysics*, 1970, 7, 271-275.
- CHEESMAN, G. H. MAYNE, S., 1953. The influence of adaptation on absolute threshold measurements for olfactory stimuli. *Quarterly J. of Exp. Psych.*, 1953, 5, 22-29.
- CHEESMAN, G. H. TOWNSEND, M. J., 1956. Further experiments on the olfactory thresholds of pure chemical substances, using the "sniff-bottle method". *Quarterly J. of Exp. Psych.*, 1956, 8, 8-14.
- CHEESMAN, G. H., 1965. Personal Communication.
- CROCKER, E. C., 1945. *Flavor*. McGraw-Hill, 1945.
- DAVIES, J. T., 1965. A theory of the quality of odours. *J. theoret. biol.*, 1965, 8, 1-7.
- DE LORENZO, A. J. D., 1963. Studies on the ultra structure and histophysiology of cell membranes, nerve fibers and synaptic junctions in chemoreceptors. In: Y. Zotterman, ed., *Olfaction and taste. I*. Pergamon Press, 1963, 5-18.
- DETHIER, V. G., LARSEN, J. R., ADAMS, J. R., 1963. The fine structure of the olfactory receptors of the blowfly. In: Y. Zotterman, ed., *Olfaction and taste. I*. Pergamon Press, 1963, 105-110.
- DÖVING, K. B., 1964. Studies of the relation between the frog's Electro-Olfactogram (E.O.G.) and single unit activity in the olfactory bulb. *Acta physiol. scand.*, 1964, 60, 150-163.
- DÖVING, K. B., 1965. Studies on the responses of bulbar neurons of frog to different odour stimuli. *Revue de Laryngol.*, Extrait du no Supplementum Octobre, 1965, 86, 845-854.
- DÖVING, K. B., 1966. An electrophysiological study of odour similarities of homologous substances. *J. Physiol.*, 1966, 186, 97-109.
- DÖVING, K. B., 1967. Analysis of odour similarities from electro-physiological data. *Acta physiol. scand.*, 1967. Preprint.
- DRAVNIKS, A., 1965. Theories of olfaction. Presented at the 4th Biennial Symposium on Foods: Chemistry and Physiology of Flavor. Oregon State University, September 8, 1965.
- EKMAN, G., BERGLUND, B., BERGLUND, U., LINDVALL, T., 1967. Perceived intensity of odor as a function of time of adaptation. *Rep. Psychol. Lab., Univ. Stockholm*, 1967, 225.
- ELSBERG, C. A., 1935. Olfactory fatigue. *Bull. Neurol. Inst. N.Y.*, 1935, 4, 479-495.
- ENGEN, T., 1962. The psychophysical similarity of the odors of aliphatic alcohols. *Reports from the Psychol. Lab., Univ. Stockholm*, 1962, 127.
- ENGEN, T., LINDSTRÖM, C., 1962. The effect of adaptation on odor mixtures. *Reports from the Psychol. Lab., Univ. Stockholm*, 1962, 138.
- ENGEN, T., LIPSITT, L. P., KAYE, H., 1963. Olfactory responses and adaptation in the human neonate. *J. of Comp. and Physiol. Psychol.*, 1963, 56, 73-77.
- ENGEN, T., LIPSITT, L. P., 1965. Decrement and recovery of responses to olfactory stimuli in the human neonate. *J. of Comp. and Physiol. Psychol.*, 1965, 59, 312-316.
- ENGEN, T., BOSACK, 1969. Facilitation in olfactory detection. *J. of Comp. and Physiol. Psychol.*, 1969, 68, 320-326.
- FINDLEY, A. E., 1924. Further studies of Henning's system of olfactory qualities. *Amer. J. of Psychol.*, 1924, 35, 436-445.
- FULLMAN, B., 1963. Stereochemical theory of olfaction. *Nature*, 1963, 199, 912.

- GESTELAND, R. C., LETTVIN, J. Y., PITTS, W. H., 1965. Chemical transmission in the nose of the frog. *J. Physiol.*, 1965, 181, 525-559.
- GESTELAND, R. C., 1970. Neural coding in olfactory receptor cells. In: Beidler (ed.): *Handbook of sensory physiology*. Vol. IV. Springer Verlag, Berlin.
- GUILLOT, M., 1948a. Physiologie des sensations. - Anosmies partielles et odeurs fondamentales. *C.R. Acad. Sc. Paris*, 1948, 226, 1307-1309.
- GUILLOT, M., 1948b. Sur quelques caractères des phénomènes d'anosmie partielle. *Comptes Rendus des Séances de la Société de Biologie*, 1948, 142, 161-162.
- HENNING, G., 1916. *Der Geruch*. Leipzig, 1916.
- HERMANIDES, J., 1909. Über die Konstanten der in der Olfaktologie gebräuchlichen neun Standardgerüche. Thesis, Utrecht, 1909.
- JOHNSTON, J. W. (jr.), SANDOVAL, A., 1962. The stereochemical theory of olfaction. 4. The validity of muskiness as a primary odor. *Proc. of the scient. sect. of the toilet goods ass. no. 37 (suppl.)*, 1962, 34-46.
- JOHNSTON, J. W., 1963. An application of the Steric Odor Theory. *The Georgetown Medical Bulletin*, 1963, 17, 40-42.
- KOMURO, K., 1922. L'Olfactométrie dans l'air parfumé. *Arch. Néerl. de Physiol.*, 1922, 6, 58-76.
- KÖSTER, E. P., 1960. Het probleem van de selectie van goede beoordelaars voor het organoleptisch onderzoek. Report Psychological Laboratory, Utrecht University, no. 6001.
- KÖSTER, E. P., 1965. Adaptation, recovery and specificity of olfactory receptors. *Rev. de Laryngologie, (Bordeaux)*, No. Supplémentum Octobre 1965, 86, 880-894.
- KÖSTER, E. P., 1968. Recovery of olfactory sensitivity after adaptation. In: N. Tanyolac. ed., *Odor theories and odor measurement*. Robert College, Bebek, Istanbul, 1968.
- KOTTMAYER, G., 1957-58. Über Durchblutungsänderungen nach Geruchsreizen. *Archiv für Ohren-, Nasen- und Kopfheilkunde*, 1957-58, 171, 291-294.
- LE GROS CLARK, W. E., 1951. The projection of the olfactory epithelium on the olfactory bulb of the rabbit. *J. Neurol. Neurosurg. Psychiat.*, 1951, 14, 1-10.
- LE GROS CLARK, W. E., 1957. Inquiries into the anatomical basis of olfactory discrimination. *Proc. Royal Soc. B*, 1957, 146, 299-319.
- LEMAGNEN, J., 1947. Étude d'une méthode d'analyse qualitative de l'olfaction. *Année Psychologique*, 1942/43 - 1947, 43 - 44, 249-264.
- LEMAGNEN, J., 1948. Physiologie des sensations.- Analyse d'odeurs complexes et homologues par fatigue. *C.R. Acad. Sc. Paris*, 1948, 226, 753-754.
- LEVETEAU, J., MACLEOD, P., 1969. La discrimination des odeurs par les glomérules olfactifs du lapin: influence de la concentration du stimulus. *J. de Physiol.*, 1969, 61, 5-16.
- LINNÉ, C. v., 1764. *Odores medicamentorum. Amoenitates academicae*, 1764, 3, 195.
- LOHMAN, A. H. M., LAMMERS, H. J., 1967. On the structure and fibre connections of the olfactory centres in mammals. In: Y. Zotterman, ed. *Sensory mechanisms*. *Progress in Brain Research*, 23, 65-82. Elsevier, Amsterdam, 1967.
- MARTIN, I., 1964. Adaptation. *Psychol. Bulletin*, 1964, 61, 35-44.
- MONCRIEFF, R. W., 1951. *The chemical senses*. Leonard Hill, London, 1951.
- MONCRIEFF, R. W., 1955. The sorptive properties of the olfactory membrane. *J. Physiol.*, 1955, 130, 543-558.
- MONCRIEFF, R. W., 1956. Olfactory adaptation and odour likeness. *J. Physiol.*, 1956, 133, 301-316.

- MONCRIEFF, R. W., 1957. Olfactory adaptation and odor-intensity. *Amer. J. Psychol.*, 1957, 70, 1-20.
- MONCRIEFF, R. W., 1966. *Odour Preferences*. Leonard Hill, London, 1966.
- MOULTON, D. G., TUCKER, D., 1964. Electrophysiology in the olfactory system. *Ann. of the N. Y. Acad. of Sci.*, 1964, 116, 380-428.
- MOULTON, D. G., 1965. Differential sensitivity to odors. *Cold Spring Harbor Symposia on Quantitative Biology*, 1965, 30, 201-206.
- MOULTON, D. G., 1967. Spatio-temporal patterning of response in the olfactory system. In: Hayashi, ed., *Olfaction and Taste II*. Pergamon Press, 1967.
- MOULTON, D. G., BEIDLER, L. M., 1967. Structure and function in the peripheral olfactory system. *Physiological Reviews*, 1967, 47.
- MOZELL, M. M., PFAFFMANN, C., 1954. The afferent neural process in odor perception. *Ann. N. Y. Acad. Sci.*, 1954, 58, 96-108.
- MOZELL, M. M., 1964a. Olfactory discrimination: Electrophysiological spatiotemporal basis. *Science*, 1964, 143, 1336-1337.
- MOZELL, M. M., 1964b. Evidence for sorption as a mechanism of the olfactory analysis of vapours. *Nature*, 1964, 203, 1181-1182.
- MÜLLER, A., 1955. *Quantitative Untersuchungen am Riechepithel des Hundes*. *Zeitschrift f. Zellforschung und Mikroskopische Anatomie*, 1955, 41, 335-350.
- MULLINS, L. J., 1955. Olfaction. *Ann. N. Y. Acad. Sci.*, 1955, 62, 247-276.
- NAGEL, W., 1903. *Handbuch der Physiologie des Menschen*. Braunschweig, 1903.
- NIEUWENHUYIS, R., 1967. Comparative anatomy of olfactory centres and tracts. In: Y. Zotterman, ed., *Sensory mechanisms. Progress in Brain Research*, 23, 1-64. Elsevier; Amsterdam, 1967.
- OHMA, S., 1922. La classification des odeurs aromatiques en sous-classes. *Arch. Néerl. de Physiol.*, 1922, 6, 567-590.
- OTTOSON, D., 1956. Analysis of the electrical activity of the olfactory epithelium. *Acta physiol. scand.*, 1956, 35, suppl. 122.
- OTTOSON, D., 1958. Studies on the relationship between olfactory stimulating effectiveness and physico-chemical properties of odorous compounds. *Acta physiol. scand.*, 1958, 43, 167-181.
- OTTOSON, D., 1959. Studies on slow potentials in the rabbit's olfactory bulb and nasal mucosa. *Acta physiol. scand.*, 1959, 47, 136-148.
- OTTOSON, D., SHEPHERD, G. M., 1967. Experiments and concepts in olfactory physiology. In: Y. Zotterman, ed., *Sensory mechanisms. Progress in Brain Research*, 23, Elsevier, Amsterdam, 1967.
- PANGBORN, R. M., BERG, H. W., ROESSLER, E. B., WEBB, A. D., 1964. Influence of methodology on olfactory response. *Perceptual and motor skills*, 1964, 18, 91-103.
- PANGBORN, R. M., 1965. see: Amerine, Pangborn and Roessler, 1965.
- PERRIN, C. M., 1965. *Etude de la discrimination olfactive sur animaux préparés pour l'observation permanente*. Thesis, Faculté des Sciences, Paris, 1965.
- PRYOR, G. T., STEINMETZ, G., STONE, H., 1970. Changes in absolute detection threshold and in subjective intensity of suprathreshold stimuli during olfactory adaptation and recovery. *Perception and Psychophysics*, 1970, 8, 331-335.

- RALL, W., SHEPHERD, G.M., REESE, T.S., BRIGHTMAN, M.W., 1966. Dendrodendritic synaptic pathway for inhibition in the olfactory bulb. *Exper. Neurol.*, 1966, 14, 44-56.
- REESE, T.S., 1965. Olfactory cilia in the frog. *The journal of cell biology*, 1965, 25, 209-230.
- ROSS, S., HARRIMAN, A.E., 1949. A preliminary study of the Crocker-Henderson Odor classification system. *Amer. J. Psychol.* 1949, 62, 399-404.
- RUBIN, M., APOTHEKER, D., LUTMER, R., 1962. Structure and odor: 1,4 cyclohexane lactones and related compounds. *Proc. Toilet Goods assoc.*, 1962, special supplement to 37, 24-33.
- SCHNEIDER, D., 1963. Electrophysiological investigation of insect olfaction. In: Y. Zotterman, ed., *Olfaction and taste*. Pergamon Press, 1963.
- SCHNEIDER, D., 1964. Insect antennae. *Ann. Rev. Entomol.* 1964, 9, 103-122.
- SCHNEIDER, D., LACHER, V., KAISSLING, K.E., 1964. Die Reaktionsweise und das Reaktionsspektrum von Riechzellen bei ANTHERAEEA PERNYL. (LEPIDOPTERA, SATURNIIDAE). *Zeitschr. für Vergleichende Physiol.* 1964, 48, 632-662.
- SCHNEIDER, R.A., WOLF, S., 1960. Relation of olfactory acuity to nasal membrane function. *J. Appl. Physiol.*, 1960, 15, 914-920.
- SCHUTZ, H.G., OVERBECK, R.C., LAYMAN, R.S. Relationship between flavor and physico-chemical properties of compounds. Final Report, Batelle Memorial Institute. Contract no. DA - 19 - 129 - QM 1141. Quartermaster Food and Container Institute for the Armed Forces.
- SHIBUYA, T., SHIBUYA, S., 1963. Olfactory epithelium: Unitary responses in the tortoise. *Science*, 1963, 140, 495-496.
- SIEGEL, S., 1956. Nonparametric statistics for the behavioral sciences. McGraw-Hill, New York, 1956.
- STEINMETZ, G., PRYOR, G.T., STONE, H., 1969. Effect of blank samples on absolute odor threshold determinations. *Perception and Psychophysics*, 1969, 6, 142-144.
- STEINMETZ, G., PRYOR, G.T., STONE, H., 1970. Olfactory adaptation and recovery in man as measured by two psychophysical techniques. *Perception and Psychophysics*, 1970, 8, 327-330.
- STONE, H., 1966. Factors influencing behavioral responses to odor discrimination - A review. *J. Food Sci.*, 1966, 31, 784-790.
- STUIVER, M., 1958. Biophysics of the sense of smell. Thesis, Groningen, The Netherlands, 1958.
- TONLOUSE, E., VASCHIDE, N., 1899. Mesure de la fatigue olfactive. *Comptes rend. de la soc. de biol.*, 1899, 913.
- TUCKER, D., 1962. Olfactory, vomeronasal and trigeminal receptor responses to odorants. In: Y. Zotterman, ed., *Olfaction and taste*. Pergamon Press, London, 1962.
- VASCHIDE, N., 1902. Recherches expérimentales sur la fatigue olfactive. *J. de l'Anatomie et de la Physiologie*, 1902, 38, 85-103.
- WENZEL, B.M., 1948. Techniques in olfactometry: A critical review of the last one hundred years. *Psychological Bulletin*, 1948, 45, 231.
- WENZEL, B.M., SIECK, M.H., 1966. Olfaction. *Ann. Rev. Physiol.*, 1966, 381-434.
- WOODROW, H., KARPMAN, B., 1917. A new olfactometric technique and some results. *J. of Exp. Psychol.*, 1917, 2, 431-447.
- WOSKOW, M.H., 1968. Multidimensional scaling of odors. In: N. Tanyolaç, ed., *Theories of odor and odor measurement*. Robert College, Bebek, Istanbul, 1968.
- WRIGHT, R., HUEY, MICHELS, K.M., 1964. Evaluation of far infrared relations to odor by a standards similarity method. *Ann. N.Y. Acad. Sci.*, 1964, 116, 535-551.

- YOSHIDA, M., 1962. Studies in psychometric classification of odors (2).
J. Japan Women's Univ., 1962, 12, 46-78.
- YOSHIDA, M., 1964a. Studies in psychometric classification of odors (3).
Jap. J. Psychol., 1964, 35, 1-17.
- YOSHIDA, M., 1964b. Studies in psychometric classification of odors (4).
The Jap. Psychol. Res., 1964, 6, 115-124.
- YOSHIDA, M., 1964c. Studies of psychometric classification of odors (5).
The Jap. Psychol. Res., 1964, 6, 145-154.
- ZWAARDEMAKER, H., 1895. Die Physiologie des Geruchs. Leipzig, 1895.
- ZWAARDEMAKER, H., 1925. l'Odorat. Librairie Octave Doin, Paris, 1925.

CURRICULUM VITAE

Egon Peter Köster werd op 28 september 1931 geboren te Utrecht. Na het eindexamen gymnasium in 1949 te Amsterdam, begon hij zijn studie in de chemie te Utrecht. In 1952 verwisselde hij deze studie voor de studie in de psychologie. Het kandidaatsexamen legde hij af in 1955. Na zijn doktoraalexamen in mei 1960 (hoofdrichting experimentele psychologie: Prof. Dr. J. Linschoten) trad hij in dienst als wetenschappelijk medewerker op het Psychologisch Laboratorium van de Rijksuniversiteit te Utrecht. In 1968 werd hij benoemd tot docent in de waarnemingspsychologie en in 1967 tot hoofd van de afdeling waarnemingspsychologie en ergonomie van het Laboratorium.

In 1961 werkte hij enige tijd in het laboratorium van Dr. J. LeMagen aan het Collège de France te Parijs en in 1968 verrichtte hij gedurende drie maanden onderzoek in het laboratorium van Prof. Dr. D.G. Moulton aan de Clark University te Worcester in de Verenigde Staten.

In de zomer van 1970 organiseerde hij te Utrecht een NUFFIC Summer School over "Odour perception: multidisciplinary research methods".

Naast zijn onderzoek op het gebied van de reukwaarneming besteedt hij een deel van zijn tijd aan onderzoek op het gebied van de ergonomie en de informatieverwerking.

STELLINGEN

I

Vermindering van de reukgevoeligheid ten gevolge van adaptatie treedt ook op wanneer korte geurprikkelers van lage (drempel-) intensiteit worden aangeboden.

Dit proefschrift: Hoofdstuk 4.

II

Reukstoffen kunnen worden gerangordend naar de grootte van de adaptatieve werking die zij op de gevoeligheid voor elkaars geuren uitoefenen.

Dit proefschrift: Hoofdstuk 5.

III

Bij het onderzoek van sensorische adaptatie leveren schaalmethoden, zoals magnitude estimation en category scaling, geen betrouwbare resultaten op.

W. S. Cain en T. Engen, Olfactory adaptation of odor intensity IN: C. Pfaffmann (ed.): Olfaction and taste III. The Rockefeller University Press 1969.

IV

De rangschikingsmethode die door Moncrieff is gebruikt bij de bepaling van geurpreferenties beperkt de waarde van zijn resultaten aanzienlijk.

R. W. Moncrieff, Odour preferences, Leonard Hill, London 1966.

V

De door LeMagnen aangetoonde variatie van de drempelgevoeligheid voor pentadecanolide (exaltolide), die bij vrouwen optreedt met het verloop van de menstruatiecyclus, berust niet op een specifieke werking van het exaltolide als sexuele attractiegeur.

J. LeMagnen: Les phénomènes olfacto-sexuels chez l'homme. Archives des Sciences Physiologiques, 1952, 6, 125-160.

VI

Het uitdrukken van de geurintensiteit van aroma componenten in veelvoud van hun drempelintensiteit, zoals dat bij aromabepalingen nog veelal gebruikelijk is, levert geen wetenschappelijk verantwoorde basis voor de onderlinge vergelijking van de intensiteiten.

VII

De positieve conclusie over de multidimensionaliteit van woord- en klankbetekenissen die Werner en Kaplan trekken uit het experiment van Iritani over de physiognomische kwaliteiten van een aantal klankpatronen, is aanvechtbaar.

H. Werner en B. Kaplan, *Symbol Formation* pag. 221-224, John Wiley, New York, 1963.

VIII

Het beeld van de "mensenhelpende" clinicus dat de Nederlandse psycholoog nog steeds omkleedt, gaat voorbij aan de toepassingsmogelijkheden van de experimentele psychologie en beperkt daardoor de bijdrage die de psychologie tot onze samenleving zou kunnen leveren aanzienlijk.

IX

Het verdient aanbeveling een elementair inzicht in de genetica als verplicht onderdeel bij de studie in de psychologie in te voeren.

X

Voor de opvatting dat men cliënten niet een psychotherapie mag onthouden om ze als controle groep te gebruiken, zijn, bij de huidige stand van de psychotherapie, geen redelijke gronden aan te voeren.

XI

Het feit dat de proefpersonen in het experiment van Weber en Bach, op de vraag waar zij voelden dat bepaalde gedachteprocessen in hun hoofd plaatsvonden, voornamelijk naar hun voorhoofd wezen, doet vermoeden dat zij op andere en meer adequate wijze van "implicit cultural stereotypes" gebruik hebben gemaakt dan de onderzoekers veronderstellen.

R. J. Weber en M. Bach, *Visual and speech Imagery*, *British Journal of Psychology* 1969, 60, 199-202.

