# On the mechanism(s) of atrioventricular nodal transmission in atrial fibrillation

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## Introduction

In a letter, dated February 7, 1823, published by Kruta in 1968[1], Jan Evangelista Purkinje writes to Johann Wolfgang Goethe:
*"Sollte mich durch eine Reihe Jahren noch ferner eine ungetrübte Gesundheit beglücken, so hoffe ich die Empirie des Subjektiven noch dahin zu fördern, dasz eine hinreichende Anzahl Teilnehmer ihr zu einen tätigen Organe im Leben der Wissenschaft erwachse".*

Kruta has translated this sentence as follows:
*"Should I have the blessing of still some years of undisturbed health, I hope to further the subjective empiricism so that a sufficient number of participants promote it to an active organ in the life of science".*

Purkinje must have realized that in his days much of scientific thinking was based on "subjective empiricism" and he above all has contributed to science by his discovery and first description of the intramural conduction system of the mammalian heart[2]. It was not until more than half a century later that His[3] and Tawara[4] completed the knowledge of the morphology of the atrioventricular (AV) conduction system of the heart.

Understanding the function of the AV conduction system in general, and of the AV node in particular, in health and disease, depends to a large extent on clinical empiricism. In the footsteps of Purkinje[1], in this paper we will under take to analyze mechanisms of AV node transmission in atrial fibrillation (AF) trying to explain empirical clinical data using basic electrophysiological principles.

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After the occurrence of extrasystoles[5], AF is the most common arrhythmia in humans, especially in the elderly[6-8]. Fibrillation of the ventricles was first observed in an animal experiment by Hoffa and Ludwig in 1850[5,9] and later AF by Vulpian in 1874[5,10]. Although it was not yet recognized as such, AF was brought to the attention of clinicians by Hering in 1903 and Mackenzie in 1904[11,12] as a continuous irregularity of the heart beat. The link between AF and the irregularity of the heart was discovered by Lewis in 1912[13]. Lewis also suggested that a circus movement of electrical activity, as described by Garrey in 1914[14], could be the cause of fibrillating atria and ventricles.

Garrey[14] was probably the first to relate the nature of "fibrillatory contractions" of the heart to tissue mass and form. However, we owe much of our understanding of AF to the work of Moe and his associates[15,16]. Using computer simulation they analyzed the factors that may cause the transition of normal atrial excitation into a self-sustaining, irregular electrical behavior of the atrial myocardium[17]. Moe et al[17] discovered that fibrillation depends on the total number of cells involved and the electrical properties of those cells. It follows that large atria with a sufficient degree of electrical inhomogeneity may easily shift from organized excitation into fibrillatory action. AF is therefore seldom if ever observed in small hearts but is quite common in dogs weighing more than 20 Kg[18], in horses[19] and of course in humans. Recently it has been shown that the complex three dimensional structure of the atria plays a major role in the activation sequences during AF and its initiation[20].

Despite the fact that AF has been the subject of study for close to one and a half century there is still debate about a number of fundamental aspects of the arrhythmia, about the role of the AV node and about its treatment[21,22].

## Definition and diagnosis of atrial fibrillation

AF has been defined by a WHO/ISFC Task Force as "an irregular, disorganized electrical activity of the atria. P-waves are absent and the baseline consists of irregular wave forms which continuously change in shape, duration, amplitude and direction. In the absence of advanced or complete AV block, the resulting ventricular response is totally irregular (random)"[23]. This definition implies that the electrocardiographic diagnosis of AF is based on atrial electrical behavior, AV nodal function and the ventricular response.

The differential diagnosis between atrial flutter and AF may be quite difficult[24]. In AF the ventricular rhythm is random while during atrial flutter the ventricular response may also be irregular but then usually shows periodicity, due to a varying AV block. The establishment of randomness of the ventricular rhythm requires the recording of a sufficient number of QRS complexes and a computer program to analyze the RR intervals[25-27]. In daily practice the diagnosis of AF is based on the absence of P-waves and the irregularity of the ventricular rhythm.

## The functions of the atrioventricular node

The AV node has three functions: 1) it warrants an appropriate delay between atrial and ventricular contraction[28,29], 2) it protects the ventricles against high rate atrial arrhythmias[30,31], and 3) it serves as a back-up pacemaker in case of a sinoatrial node arrest or exit block without an atrial escape[32]. Form and function of the AV node are interlinked[33,34] but the exact site of its specific functions is difficult to establish, especially in vivo. Experimental conditions usually change the integrity of the node but at the same time have been essential for our current understanding of most of its basic electrophysiological properties. The question that concerns us is what mechanism(s) is (are) most likely involved in slowing the atrial rate during AF[35,36]. In this aspect we may consider the Wolff-Parkinson-White syndrome as an experiment of nature because when the AV node has been short circuited by an accessory AV pathway with a short refractory period, significant slowing of the ventricular rate during AF does not occur and the high ventricular rate may well endanger a patient's life[37,38].

## The atrial rhythm during atrial fibrillation

To analyze the mechanism(s) of AV nodal transmission during AF in human patients and animals it is mandatory to study the atrial rhythm and the ventricular response in a quantitative fashion and to look into the effects of drugs, exercise and electrical interventions on the resulting ventricular rate and rhythm[36,39].

It seems evident that during AF a random ventricular rhythm can only result from an irregular electrical behavior of the atria. Puech et al[40,41] and others[42-44] have studied the electrical activity of the atria in patients with AF. They recorded uni- and bipolar electrograms from different sites in the fibrillating atria and determined from the shape of the atrial electrograms whether or not AF was present. Meijler et al[42] performed signal analysis of the atrial electrograms obtained in patients with AF. This was done by measuring the intervals between the zero-crossings of the recorded electrical atrial signals and plotting serial autocorrelograms (SAC) and histograms of the intervals obtained in this fashion. Assuming that the zero-crossing method provides data that reliably represents the rate and rhythm of the fibrillating atria, we found that indeed the interval series showed a random pattern with a rate between 300 and 600 episodes per minute. However not only the sequence of the recorded atrial signals displays an erratic behavior also the shape, the amplitude and the direction of the spikes do not seem to show a repetitive pattern either. This finding offered support for our earlier hypothesis that the AV node is showered by atrial impulses of random strength coming from random directions with random intervals[39,44,45].

## The ventricular rhythm during atrial fibrillation

In order to make sure that AF is indeed AF, in any clinical or epidemiological study, one must analyze the ventricular rhythm in a quantitative fashion. This can be done by measuring the successive RR intervals and then computing the SAC and the histogram of those intervals. To obtain a SAC each RR interval is correlated with itself, then with the next RR interval, and so on[36,39]. With the exception of correlation coefficient 0, which of necessity equals 1, in case of true uncomplicated AF the values of the following correlation coefficients do not differ from 0. This proves that during AF the ventricular rhythm is random. Histograms are constructed by counting the number of RR intervals falling within one duration class; for instance 50 ms. In general the histograms show a typical unimodal skewed form.

Figure 1[39] shows the SAC and the histogram of the ventricular rhythm of a patient with AF, before (A) and after (B) treatment with digoxin. This figure al-

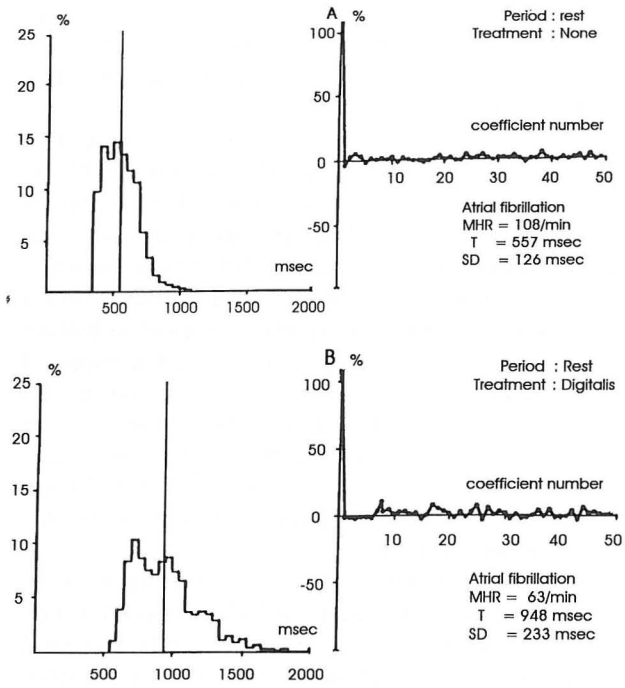


**Figure 1.** - Histogram and serial autocorrelogram of a patient with atrial fibrillation before (*A*) and after (*B*) digitalis treatment. The serial autocorrelogram remains unchanged during digitalis treatment despite a change in form and shift to the right of the histogram. From Bootsma et al[39] by permission of the American Heart Association.

lows for a number of important conclusions. Firstly the time between the left side of the histogram and the Y-axis represents the functional refractory period of the AV conduction system. Next, interestingly enough, when we compare A with B, following digitalis, we notice that the histogram shifts to the right, the mean RR interval increases from 557 ms to 948 ms by the longer functional refractory period and by an increase in number and duration of intervals longer than 1100 ms. The standard deviation (SD) increases from 126 to 233. The so called coefficient of variation (CV) defined by the SD divided by the mean RR interval remains constant; in this case 126/557 = 0.23 vs 233/948 = 0.25; a significant finding which implies that slowing of the ventricular rate in AF is not caused by simple selection or scaling of the atrial impulses. If scaling would have occurred the CV would have decreased. We observed that, in patients with AF under a variety of circumstances or interventions, the ventricular rhythm remains random and irrespective of the rate, the CV remains constant[36,46].

In experimentally induced (artificial) AF, often used for the study of atrial and ventricular electrophysiological behavior and for analyzing AV node function, the SAC of the RR intervals may not show the typical pattern of a random rhythm and thus artificial AF may not be representative of true AF[47]. Induced AF should thus be considered with caution when used as the basis for the interpretation of clinical electrocardiographic symptoms in patients with AF.

In summary, the ventricular rhythm during AF is random, the histogram of the RR intervals is skewed and usually has a unimodal shape. Slowing of the ventricular rate by digitalis is caused by an increase of the functional refractory period and by the occurrence of more RR intervals of longer duration. The CV is constant which implies that simple scaling (selection) of the atrial impulses by the AV node does not take place.

## Right ventricular pacing

Another important phenomenon in patients with AF is that anterograde conduction can be blocked by (right) ventricular pacing of appropriate rate while atrial captures are usually not observed[48]. This is demonstrated in figure 2. The ventricular rate and rhythm are given in the form of an interval scatter diagram. The first 500 RR intervals were obtained before ventricular pacing started. It can be seen that the longest RR intervals last about 1500 ms and the shortest less than 350 ms. In the second group of 500 RR intervals, N goes from 500-1000; at a pacing interval of 1000 ms all RR intervals over 1000 ms are abolished but the number of short RR intervals also decreases. The latter becomes even more evident in the third group of 500 RR intervals. At a pacing interval of 850 ms, there is further reduction in the number of short

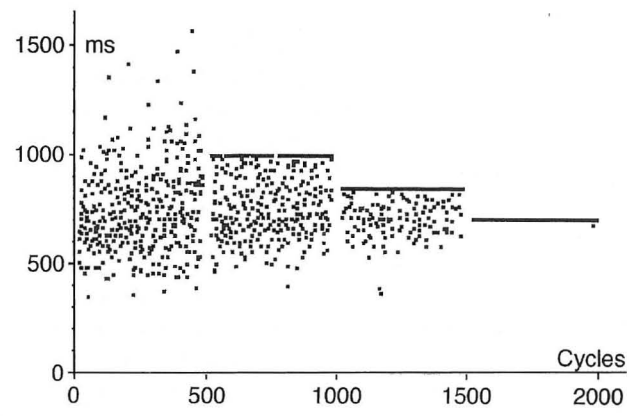


**Figure 2.** - Successive RR intervals in a patient with atrial fibrillation before (first 500 cycles) and during right ventricular pacing with a pacing interval of 1000, 850, and 700 ms (cycles 500-2000). At a pacing interval of 700 ms (last 500 cycles), all anterograde conduction has ceased. From Wittkampf et al[48] by permission of the American College of Cardiology.

RR intervals and at a pacing interval of 700 ms (fourth group of 500 cycles from 1500-2000), all anterograde conduction has disappeared despite the fact that the pacing interval is over twice as long as the shortest RR interval before pacing.

Related to the effect of ventricular pacing is the so called compensatory pause during AF. Langendorf and Pick[49] and Pritchett et al[50] have shown that the ventricular cycle is lengthened, like in sinus rhythm after a ventricular extrasystole, even in the presence of AF. Langendorf and Pick[49] termed this phenomenon the "compensatory pause in atrial fibrillation" and believed that it was caused by lengthening of the AV nodal refractory period due to retrograde concealed conduction into the AV node of the spontaneous or artificially induced ventricular extrasystole. Wittkampf et al[51] demonstrated that the histogram of the postextrasystolic RR intervals was insignificantly different from the spontaneous RR intervals, except for a shift to the right. As suggested by our recent modelling study[52], the rightward shift was probably caused by electrotonic inhibition, with lengthening of the AV nodal refractory period, caused by the (concealed) retrogradely propagating extrasystole. The compensatory pause in AF may be an important clinical tool because it can differentiate between a wide QRS complex due to aberration and a ventricular extrasystole. The former is usually not followed by a longer than average pause, while the latter is.

Thus right ventricular pacing can block all anterograde conduction and ventricular extrasystoles are usually followed by a pause longer than the average RR interval.

## Concealed conduction

At the center of the slowing (protection) capacity of the AV node is the concept of concealed conduction[53-55]. Using isolated perfused frog hearts Engelmann in 1894[56] observed that a conducted atrial extrasystole (A) was occasionally followed by a longer AV interval. He described his observation as follows: *"Dagegen wird durch jede wirksame A-Reizung, auch wenn sie keine Vs auslöste, das nächste Intervall A s-V s vergrössert, wennschon nicht so stark als wenn dem ersten A-Reiz auch eine Vs gefolgt wäre. Sowohl eine vorausgegangene Vorkammercontraction als eine vorhergegangene, von A aus veranlasste Kammercontraction wirken demnach verzögernd auf die Reizübertragung von A nach V".*

There are a number of satisfactory definitions of concealed conduction but we prefer the definition by Fisch[54]: "the presence of incomplete conduction coupled with an unexpected behavior of the subsequent impulse". In 1948 Langendorf[53] introduced the term "concealed conduction" for this phenomenon which he observed on the ECG.

In 1965 Langendorf et al[55] postulated that repetitive concealed conduction in the AV junction could explain ventricular rate and rhythm in AF. This implies that the repetitive arrival of more atrial impulses than the AV node can handle, causes incomplete penetration and conduction of single atrial impulses and a continuously varying electrophysiological substrate for the impulses coming thereafter. Each conducted atrial impulse has its own history caused by its strength, shape, direction, timing and by the effect of incomplete conduction of previous and abortive atrial impulses. What happens to impulses that do not make it and how is the electrophysiology of the AV node affected by them?

At this moment in time, three possible mechanisms that may explain concealed conduction and AV transmission during AF may be considered: 1) decremental conduction[57,58], 2) electrotonic modulation of automaticity[48,59-61], and 3) electrotonic modulation of propagation[52,62,63].

**Decremental conduction.** In their paper on "Impulse formation and conduction of excitation in the atrioventricular node" Watanabe and Watanabe[64] attempt to make a strong case for decremental conduction to explain concealment of atrial impulses in the AV node during AF. They challenge the postulate of Meijler et al[36,60] of electrotonic modulation of AV nodal automaticity during AF. Indeed concealed decremental conduction has been widely accepted as the most likely explanation for the characteristic slowing and block associated with repetitive premature excitation of the AV node by atrial impulses. However, as we will see below, this explanation is problematic.

The concept of decremental conduction derives from the original studies of Hoffman[57]. Together with Cranefield, Hoffman[65] described decremental conduction as "a type of conduction in which the properties of the fiber change along its length in such a manner that the action potential becomes progressively less effective as a stimulus to the unexcited portion of the fiber ahead". According to this view the impulses travel across the center of the AV node but a progressively increasing threshold, a decreasing space constant and a decreasing amplitude and rate of rise of the action potential will lead to a gradual loss of the effectiveness of the active regions to depolarize more distal fibers. If this reasoning is correct, it follows that block can occur if the area of decremental conduction

is sufficiently long and also that decremental conduction can occur only in a homogeneous and continuous medium. However the AV node is not such a medium; on the contrary, it is highly heterogeneous and discontinuous[33].

The Watanabes[64] postulated that in AF "... AV block occurs because of decremental conduction rather than by a refractory barrier, although the resultant concealed conduction would prolong the refractory period of distant nodal fibers and further modify the conduction pattern". Subsequently they proposed that decreases in the upstroke velocity of the AV nodal action potential, could possibly explain the occurrence of repetitive concealment in the N region "even after the expiration of its effective refractory period".

There are two problems with these speculations. The first one relates to the idea that decremental conduction and block can occur, irrespective of the timing of the atrial impulse. Indeed a close look at the ladder diagram in Watanabes' figure 3B shows that the third atrial impulse is blocked high in the AV node, despite the fact that it arrives later than the second atrial impulse. It is difficult to account for blockade high in the AV node under such conditions, even if the mechanism of blockade were a gradual decrease in upstroke velocity as the Watanabes propose. The second and even more pertinent problem is that they do not consider any after-effects (electrotonic or otherwise) of the concealed impulse on subsequent impulses. Again, analysis of their figure 3B shows that the fifth impulse, which is supposedly concealed, does not seem to have any effect on the sixth impulse, which conducts normally. Thus there is no evidence in the relevant electrophysiological literature to support the idea that conduction through the AV node during AF may in fact be decremental.

It is also not possible to explain an anterograde block by right ventricular stimulation[48] and the "compensatory" pause following ventricular extrasystole during AF[51] by decremental conduction of the atrial impulses. As stated above, the concept of decremental conduction does not consider the possible after-effects that impulses concealed within the AV node may have on subsequent impulses. Therefore it is difficult to reconcile the idea of decremental conduction with the postulate of Langendorf[53] for the mechanism of the compensatory pause in AF, as being the result of retrograde concealed conduction with resetting of AV nodal refractory period for subsequent incoming atrial impulses. Finally the absence of scaling in AF[36,46] is impossible to bring in line with decremental conduction, as this mechanism would result in a change of selection of atrial impulses and thus change the CV for instance during exercise or after the administration of digitalis.

**Automaticity in the atrioventricular node.** The role of the AV node as a subsidiary pacemaker in case of sinoatrial block or atrial arrest is well known. This proves that the AV node can indeed act as a pacemaker. In fact, the concept of the AV node as an oscillator or an unprotected pacemaker was already proposed by Lewis in 1925[66] because of the similarity in structure with the sinoatrial node. In 1929 Van der Pol and Van der Mark[67] concluded that the heart beat could be viewed as a relaxation oscillator. A relaxation oscillator can be described as a condenser that is periodically discharged by the ignition of a neon tube. The frequency of such an oscillator can be modulated by external periodic electrical phenomena like a sine wave current of a certain strength and periodicity[68]. It was therefore postulated that during AF, the AV node could be considered to function as an electrotonically modulated pacemaker[48,60]. Cohen et al[61] developed a hypothetical model of an AV nodal pacemaker during AF. The model could easily explain the mathematical characteristics of the ventricular rhythm during AF. It also agrees quite well with the effect of right ventricular pacing or of a ventricular extrasystole during AF. However some objections can be put forward against this model. For instance the AV node as a pacemaker cannot explain the absence of scaling of the atrial rhythm during AF. Also AV nodal pacemaker activity might be overdrive suppressed by rapidly incoming atrial impulses. This has led us to the conclusion that neither decremental conduction nor automaticity in the AV node may be involved as a mechanism responsible for the ventricular rate and rhythm during AF.

**Electrotonic modulation of propagation.** An attractive alternative, based on experimental and clinical observations[69-73], is that repetitive electrotonic modulation of AV nodal propagation may be used to understand most, if not all, of the phenomena described in relation with the ventricular response during AF. We believe that it is appropriate to think of the AV node as an area of electrical discontinuities whose safety factor for propagation is relatively small. Therefore frequency dependent AV nodal propagation during supraventricular tachyarrhythmias may be explained in terms of electrotonically mediated inhibition and/or facilitation[52].

It has been shown that electrotonic depolarizations can have profound effects on the electrophysiological properties of the tissue distal to the block[63,70]. Antzelevitch and Moe[63] used two different models of isolated cardiac Purkinje fibers to demonstrate that

electrotonic depolarizations can produce delay or even blockade in the transmission of subsequent impulses, depending on time relations. They used the term "electrotonic inhibition" to describe this phenomenon and suggested that many published clinical examples of concealed conduction may be explained in terms of electrotonic inhibition of excitability. Inhibition of excitability by subthreshold stimulation has been demonstrated in human hearts[72]. In addition, Oreto et al[73] interpreted a clinical electrocardiographic case of exit block from an idioventricular pacemaker as being the result of electrotonic inhibition by conducted impulses of supraventricular origin. It has been proposed that electrotonic inhibition may prevent ventricular fibrillation during AF[74], and the concept has been used also to explain functional inexcitability in the center of vortices of reentrant activity[75].

Recently, Davidenko et al[62] demonstrated electrotonic inhibition of excitability in single ventricular myocytes under current clamp conditions. Application of repetitive depolarizing pulses of threshold amplitude elicited action potentials in a one-to-one manner. Interpolation of single brief subthreshold pulses during individual diastolic intervals led to transient decays of excitability and even complete failure of subsequent excitation. Such results are in full agreement with the data obtained previously by Antzelevitch and Moe[63] in multicellular preparations.

More recently, Liu et al[76] carried out current and voltage clamp experiments in single, enzymatically dispersed, myocytes from the rabbit AV node, as well as computer simulations, to study the ionic mechanisms of electrotonic inhibition, and to determine the cellular basis of concealed AV nodal conduction. Voltage clamp analysis in both experiments and simulations demonstrated that electrotonic inhibition was the result of partial inactivation of the transient calcium current ($I_{Ca,T}$). In addition, Liu et al[76] demonstrated that the ability of the subthreshold response to prevent subsequent excitation of an AV nodal cell was increased when the interval between the conditioning subthreshold pulse and the succeeding pulse was shortened, or when the amplitude of the subthreshold pulse was increased. Moreover, they simulated AV nodal propagation using a linear array of "AV nodal" cells and demonstrated that when a premature impulse failed to traverse the AV node, the subthreshold depolarization elicited downstream of the site of block led to a transient reduction of excitability, with consequent delay or block of the following impulse. Such results have provided the strongest evidence to date in support of the idea that at least some of the manifestations of concealed AV nodal conduction can be the result of electrotonic inhibition secondary to a transient decrease in $I_{Ca,T}$.

When an impulse initiated in the atria or ventricles is blocked within the AV node, it is clear that the depolarization induced by that impulse may be subthreshold for cells just distal to the site of block. This subthreshold event is the result of electrotonic current flow from depolarized to non-depolarized cells, which may be manifest at appreciable distances ahead of the site of block. This can be demonstrated using microelectrode recordings of AV nodal action potentials during the application of premature stimuli[70].

**Computer simulation of electrotonic modulation**

In an effort to understand AV nodal function during AF we used a black-box approach and developed a computer model based on electrotonic modulation of AV nodal propagation by extra-atrial impulses[52]. The basic properties of the model were the temporary downward (left) or upward (right) shift of the AV nodal propagation curve dependent on the timing of an atrial extra impulse during a regular atrial rhythm. A sudden increase or decrease of the atrial rate will have a longer lasting and more profound electrotonically mediated effect on AV nodal propagation. Another feature of the model is that an atrial impulse that does not traverse the AV node has an "after-effect" on the conduction of the next atrial impulse. This is the classical example of concealed conduction as first described by Engelmann in 1894[56]. A series of atrial impulses at a faster rate may result in partial transmission and concealment of many impulses in the AV node. When atrial impulses at random intervals are applied the duration of the RR interval is unpredictable and a slower but random ventricular rhythm results. Each blocked and/or conducted atrial impulse has its electrotonic effect on the propagation properties of the AV node.

In figure 3[52], produced by our model, the upper histogram in panel A represents the distribution of random A-A intervals while the histogram in the lower panel shows the distribution of the V-V intervals (equivalent to RR intervals) that resulted from the random atrial rhythm. In panel B the AV conduction time of every successfully conducted atrial impulse is plotted against its A-A interval. ERP represents the effective refractory period. Note the complex (random) pattern and the smearing of the AV node propagation curve. We assume that, during AF these electrotonically mediated effects act in concert with the frequency dependence of AV propagation.

Conduction or block of an atrial impulse depends on the electrotonic effects of previous impulses on AV

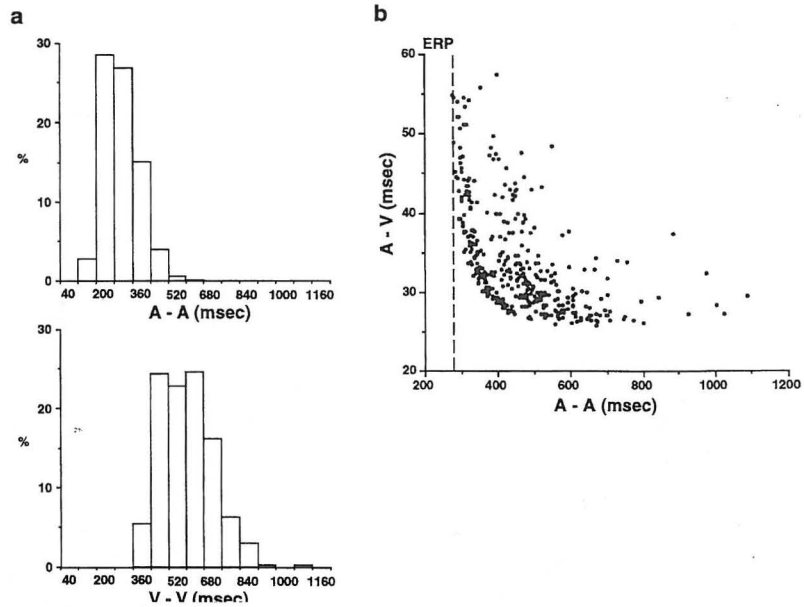


**Figure 3.** - *Panel a:* the upper histogram represents the distribution of A-A intervals randomly supplied to the system, while the lower histogram shows the distribution of V-V intervals obtained. *Panel b:* the conduction time of every successfully conducted impulse is plotted against its A-A interval. Note smearing and the complex pattern of the conduction delay curve, described in the text. ERP: effective refractory period. From Meijler et al[52] by permission of Futura Publishing Company, Inc.

nodal propagation and on the rate of the atrial rhythm. It follows that a higher atrial rate as may be caused by digitalis in a dose that does not effect AV conduction directly, results in more blocked atrial impulses and thus in a lower ventricular rate. Vice versa a lower atrial rate for instance due to quinidine would result in less blocked atrial impulses and a higher ventricular rate[36,52,77,78].

As shown in figure 3 electrotonic modulation of propagation[52] is in agreement with the randomly irregular ventricular rhythm, the landmark sign of AF in a clinical setting[39]. The CV is constant as it should be at varying ventricular rates[36,46]. Anterograde block during (right) ventricular pacing[48] and the "compensatory" pause following ventricular extrasystoles[51] is caused by retrograde excitation of the AV node, which resets the AV nodal propagation curve to the right[52]. This sets the stage for concealed block of anterograde impulses and electrotonic modulation of subsequent events.

It is important to realize that this model is a gross oversimplification of the complexity of the real AV node. For instance it does not take into account the (possible) presence of "dual pathways"[79], recently also demonstrated during sinus rhythm[80]. The result of AV node conduction modification with ablation procedures during AF[81-83] has to the best of our knowledge not yet been expressed in mathematical terms and therefore cannot yet be tested in the model. The lower ventricular rate following slow pathway ablation may not only be due to a longer functional refractory period but also to the possibility that more atrial impulses reach the AV node, caused by a loss of the inhibitory effect of atrial impulses that would otherwise have reached the AV node via the slow pathway.

## Testing the model

We tested this model by simulating a number of true life situations:

- the ventricular rhythm was random as could be expected from the random atrial input;
- the histogram of the ventricular rhythm resembles the histogram shown in figure 1;
- the ventricular rate decreases when atrial rate is increased as seen during digitalis therapy;
- the CV of the ventricular rhythm remains constant at different ventricular rates. In other words the SD of the V-V intervals varies linearly with the mean. That is, the AV node does not scale the atrial rhythm and conveys the atrial irregularity unchanged to the ventricles, as a result of the nonlinear effects of electrotonic modulation;
- during right ventricular pacing at an appropriate rate all anterograde conduction is blocked. This demonstrates that resetting of AV node automaticity

is not a prerequisite for anterograde blocking during ventricular pacing as was previously assumed;
- the model provides the so called compensatory pause following ventricular extrasystole which is based on the same electrotonic effect as anterograde block during ventricular pacing;
- digitalis and quinidine which, respectively increase and decrease atrial rate during AF without effecting its irregularity, respectively decrease and increase the ventricular rate while the CV, as expected, remains constant.

## Conclusions

- Electrotonic modulation of AV nodal propagation is compatible with concealed conduction in the AV node;
- electrotonic modulation of AV node excitability by repetitive chaotic atrial impulses explains the ventricular rate and random rhythm during AF;
- neither decremental conduction nor permanent AV node automaticity can be operative during AF;
- electrotonic modulation of AV nodal propagation is in agreement with a number of clinical symptoms observed during AF.

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