

## A Spatial Depiction for the Systematically Degenerate Genetic Code

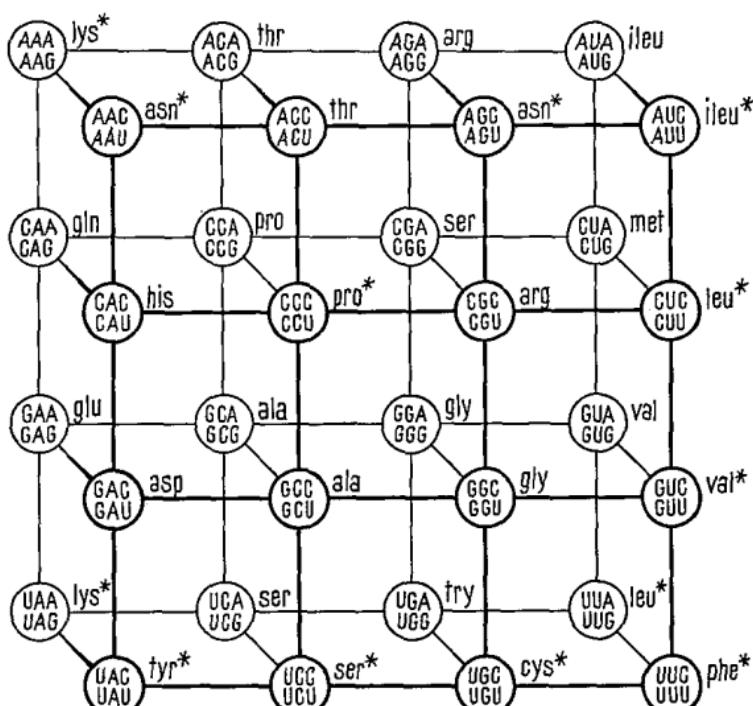
On the basis of their experiments with trinucleotides of defined base sequence, BERNFIELD and NIRENBERG<sup>1</sup>, LEDER et al.<sup>2</sup>, and TRUPIN et al.<sup>3</sup> proposed that the genetic code is degenerate according to a general pattern. In their view, the 64 possible code words are arranged in 32 pairs of triplets with identical bases in the first and second position of each pair. 16 of these pairs have either cytidine (C) or uridine (U) as 3' terminal nucleosides, and the 16 other pairs have either adenosine (A) or guanosine (G) as 3' terminal nucleosides. Both triplets of a codon-pair are coding for the same amino acid (compare the scheme of ECK<sup>4</sup>). We want to put forward a spatial depiction, in which the relations between these 32 triplet pairs are clearly visualized. The amino acids corresponding to the codes are included, so that the consequence of single base conversions in a codon, with respect to amino acid coding,

Amino acids	RNA codons	Literature
Asparagine	A <sub>p</sub> G <sub>p</sub> C; A <sub>p</sub> G <sub>p</sub> U	5
Asparagine	A <sub>p</sub> A <sub>p</sub> C; A <sub>p</sub> A <sub>p</sub> U	2, 3
Cysteine	U <sub>p</sub> G <sub>p</sub> U	1
Isoleucine	A <sub>p</sub> U <sub>p</sub> C; A <sub>p</sub> U <sub>p</sub> U	2, 3
Leucine	C <sub>p</sub> U <sub>p</sub> C; C <sub>p</sub> U <sub>p</sub> U	1, 7
Leucine	U <sub>p</sub> U <sub>p</sub> G	1, 6
Phenylalanine	U <sub>p</sub> U <sub>p</sub> C; U <sub>p</sub> U <sub>p</sub> U	1, 7
Proline	C <sub>p</sub> C <sub>p</sub> C; C <sub>p</sub> C <sub>p</sub> U	1, 7
Serine	U <sub>p</sub> C <sub>p</sub> C; U <sub>p</sub> C <sub>p</sub> U	1, 7
Tyrosine	U <sub>p</sub> A <sub>p</sub> C; U <sub>p</sub> A <sub>p</sub> U	2, 3
Valine	G <sub>p</sub> U <sub>p</sub> U	1
Lysine	A <sub>p</sub> A <sub>p</sub> A; A <sub>p</sub> A <sub>p</sub> G	2, 3
Lysine*	U <sub>p</sub> A <sub>p</sub> A	2

\* uncertain

can be read off on the three lines crossing the codon. Starting from the known data, which are summarized in the Table, we deduced the meaning in terms of amino acid of the 19 remaining codon-pairs. For this purpose we made use of the *in vitro* amino acid incorporation data of NIRENBERG and JONES<sup>8</sup>, and of OCHOA<sup>9</sup>; amino acid replacements in the A protein of tryptophan synthetase of *E. coli* mutants<sup>10,11</sup>; and of amino acid substitutions in abnormal hemoglobins<sup>12</sup>. We presumed the genetic code to be universal.

It is worth noting that our deductions have led to results which differ on several points from comparable predictions of YANOFSKI<sup>11</sup> and of TRUPIN et al.<sup>3</sup>. The scheme derived by OSGOOD<sup>13</sup> does not fit the present state of knowledge. The genetic code may be more complicated if 5' terminal, 3' terminal and internal codons are recognized in somewhat different ways<sup>3</sup>, and if the code is not as consistently degenerate as supposed here<sup>14</sup>.



Spatial depiction of the degenerate genetic code. \* Literature data.

*Zusammenfassung.* Auf Grund von Literaturangaben und durch Deduktion haben wir ein dreidimensionales Schema (oder Modell) des systematisch degenerierten genetischen Codes entworfen, aus dem man in einfacher Weise ablesen kann, welche Aminosäuresubstitutionen aus der Veränderung einer Base folgen.

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- <sup>2</sup> P. LEDER, F. M. ROTTMAN, R. L. C. BRIMACOMBE, J. S. TRUPIN, C. O'NEAL, and M. W. NIRENBERG, *Fed. Proc.* **24**, 408 (1965).
- <sup>3</sup> J. S. TRUPIN, F. M. ROTTMAN, R. L. C. BRIMACOMBE, P. LEDER, M. R. BERNFIELD, and M. W. NIRENBERG, *Proc. nat. Acad. Sci., US* **53**, 807 (1965).
- <sup>4</sup> R. V. ECK, *Science* **140**, 477 (1963).
- <sup>5</sup> J. H. MATTHAEI, H. KLEINKAUF, and G. SCHRAMM, *Angew. Chem.* **76**, 717 (1964).
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- <sup>7</sup> M. R. BERNFIELD, *Fed. Proc.* **24**, 409 (1965).
- <sup>8</sup> M. W. NIRENBERG and O. W. JONES, *Symposium on Informational Macromolecules* (Eds. H. J. VOGEL, V. BRYSON, and J. O. LAMPEN; Academic Press, New York 1963), p. 451.
- <sup>9</sup> S. OCHOA, *Symposium on Informational Macromolecules* (Eds. H. J. VOGEL, V. BRYSON, and J. O. LAMPEN; Academic Press, New York 1963), p. 437.
- <sup>10</sup> C. YANOFSKI, B. C. CARLTON, J. R. GUEST, D. R. HELINSKI, and U. HENNING, *Proc. nat. Acad. Sci., US* **51**, 266 (1964).
- <sup>11</sup> C. YANOFSKI, *Biochem. biophys. Res. Commun.* **18**, 898 (1965).
- <sup>12</sup> V. M. INGRAM, *Fed. Proc.* **21**, 1053 (1962).
- <sup>13</sup> E. E. OSGOOD, *Nature* **206**, 471 (1965).
- <sup>14</sup> Note added in proof: Compare the recent paper: M. NIRENBERG, P. LEDER, M. BERNFIELD, R. BRIMACOMBE, J. TRUPIN, F. ROTTMAN, and C. O'NEAL, *Proc. nat. Acad. Sci. US* **53**, 1161 (1965).
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