Zeitschrift: Archives des sciences et compte rendu des séances de la Société
Herausgeber: Société de Physique et d'Histoire Naturelle de Genève
Band: 51 (1998)
Heft: 3

Artikel: Origin of life. I. Recurrent riddles about its genetic coding
Autor: Turian, Gilbert
DOI: https://doi.org/10.5169/seals-740159

Nutzungsbedingungen
Die ETH-Bibliothek ist die Anbieterin der digitalisierten Zeitschriften auf E-Periodica. Sie besitzt keine Urheberrechte an den Zeitschriften und ist nicht verantwortlich für deren Inhalte. Die Rechte liegen in der Regel bei den Herausgebern beziehungsweise den externen Rechteinhabern. Das Veröffentlichen von Bildern in Print- und Online-Publikationen sowie auf Social Media-Kanälen oder Webseiten ist nur mit vorheriger Genehmigung der Rechteinhaber erlaubt. Mehr erfahren

Conditions d'utilisation
L'ETH Library est le fournisseur des revues numérisées. Elle ne détient aucun droit d'auteur sur les revues et n'est pas responsable de leur contenu. En règle générale, les droits sont détenus par les éditeurs ou les détenteurs de droits externes. La reproduction d'images dans des publications imprimées ou en ligne ainsi que sur des canaux de médias sociaux ou des sites web n'est autorisée qu'avec l'accord préalable des détenteurs des droits. En savoir plus

Terms of use
The ETH Library is the provider of the digitised journals. It does not own any copyrights to the journals and is not responsible for their content. The rights usually lie with the publishers or the external rights holders. Publishing images in print and online publications, as well as on social media channels or websites, is only permitted with the prior consent of the rights holders. Find out more

Download PDF: 25.11.2025

ETH-Bibliothek Zürich, E-Periodica, https://www.e-periodica.ch

Archs Sci. Genève	Vol. 51	Fasc. 3	pp. 311-323	Décembre 1998

ORIGIN OF LIFE. I. RECURRENT RIDDLES ABOUT ITS GENETIC CODING

BY

Gilbert TURIAN*

(Ms. reçu le 5.12.1998, accepté le 23.12.1998)

ABSTRACT

Origin of Life. I. Recurrent riddles about its genetic coding. - Between the two extremes and exclusive views of a prebiotic world of peptidic "chicken-first" and a "RNA world" of ribozymic "egg-first", there was time for a pre-RNA world in which peptides-protoproteins and riboseless, prenucleic polybasephosphate infopolymers could have coevoluted as peptide-clothed protogenes or "chicken and egg". Thereby, amino acids of the poorly informational, primeval peptides would had been encoded by deterministic, stereochemically specific "frozen interactions" with the polybasephosphates visualized as primordial replicators.

Key-words: Primal genetic coding; anticodon doublets; peptides-protoproteins; prenucleic polybasephosphates; protogenes.

INTRODUCTION

The idea of some kind of genetic molecule at the origin of life has been a recurring one since the «naked gene» has been described in 1929 by the great geneticist H.J. MULLER. The same year, J.B.S. HALDANE endorsed this genetic view in his famous hypothesis about first life while his alter ego OPARIN (1938, 1957) rejected this idea of life originating from a fortuitously formed genetic molecule and rather took a more «metabolic» view of the nature and origin of life. It was not until 1944 that the physicist Erwin SCHRÖDINGER in his reknown question book «What is Life?» presciently materialized the original naked gene as an aperiodic crystal endowed with template-replicating properties. A decade later, these could be ascribed to the newly described helical structure of DNA (WATSON & CRICK, 1953) opening the question «Is the order assembled in a DNA aperiodic crystal, e.g. a «naked gene», sufficient for life's emergence?». More recently, with the discovery of ribozymes (CECH, 1986), the question moved to an RNA molecule which would function as a polymerase and therefore able to copy itself also as «naked gene». CAIRNS-SMITH (1982) still endorsed this expression but he safely and imagedly commented that «a naked gene would be mismatched on our Earth as a spaceman without his space suit would be mismatched on Mars». We will see in Part 1 that the suit could well be more or less random polypeptides inside which the gene would be confined to «clothe its nudity» and thereby become genotype plus phenotype. This

* Laboratoire de Microbiologie et de Bioénergétique, Pavillons des Isotopes, 20, boulevard d'Yvoy, CH-1211 Genève 4.

makes relevance to consider in Part 2 the other riddle of «protein or nucleic acid first»? Finally, concern about information storage will raise in Part 3 the fundamental riddle of «randomness or determinism» at the primal process of genetic coding, including the subsidiary questions of «codons or anticodons first»? and «nucleobase doublets or triplets»? from the start of amino acids encoding.

«NAKED» OR «CLOTHED» PRIMAL GENES ?

The simplest kinds of organisms could have been hardly more than pieces of unencumbered information-printing machinery or «naked genes». CAIRNS-SMITH (1982) who took this genetic view saw the origin of life from crystals of clay considered as geochemical genes secondarily taken over by organic «naked genes». However, he already conceded that this idea was somewhat out of favor because «a naked gene would not be – could not be – pure genotype».

There are chemical obstacles to the direct life emergence from «naked or nude» template-replicating RNA molecules - among which prebiotic synthesis and assembly of nucleotides. The problems which arise from theses difficulties have been carried out by the theory of hypercycles proposed in 1977-79 by EIGEN & SCHUSTER (1979). This concept designates an integrated set of autocatalytic cycles composed by a set of random polynucleotide information carriers, the genes, and by the polypeptide catalytic molecules, enzymes. The latter are encoded by polynucleotides which, in their turn, accelerate replication of polynucleotides as well as their own synthesis.

Recently, EIGEN (1995) reemphasized that "evolutionary optimization requires self-reproducing information storage and we only know nucleic acids to be capable of this role". So, RNA or precursors – such as prenucleic polymers (see below) – would have been necessary to set the merry-go-round of evolution in motion". However, the problem always arises when starting with nude replicating single-stranded RNA sequences (ORGEL, 1987; JOYCE, 1989). Such difficulties were already carried out by EIGEN & SCHUSTER (1979) when they argued that complex genetic information cannot be built up in single RNA replicating strands. However, KAUFFMAN (1993, 1995) tempered this theory when he stressed that evolution of a protein or ribozyme polymerase might well occur in an autocatalytic peptide-RNA system in which peptides serve as specific replicases for RNA sequences, while the latter serve as more or less specific catalysts for the peptides. He thus grafted a going metabolic concern to a coevolving set of template-replicating RNA polymers. Such a coevolution has recently been further endorsed by DELARUE (1995) who envisaged a possible molecular mechanism accounting for the evolution of a genetic code through the coupled synthesis of nucleic acids and genetically encoded proteins.

Another critical step in the evolution of the genetic code must have been the onset of colinearity, first proposed by BEDIAN (1982) in his astucious model asserting that «given a population of random peptides synthesized by fairly random and noncoded colinear polymerization via something like tRNA molecules, and given that these peptides

can charge amino acids to the tRNA molecules, selective coevolution of the peptides and underlying coding mRNA to a consistent coded state can occur» (KAUFFMAN, 1993). Consequently, origin and further evolution of natural life could only emerge from such ordered properties among the primeval complex systems of infopolymers.

In the «naked gene» hypothesis, any self-templating RNA such as CECH's (1986) ribozyme molecule could specify its base pair complement and thus might reproduce itself and, secondarily, these simplest replicating molecules would have built up around themselves the complex set of protein molecules constituting a self-reproducing system coordinating a metabolic flow and capable of evolving. However, this dominant view has been vigorously contradicted by KAUFFMAN (1993) who rather suggested «autocatalytic sets of polymers made of catalytic peptides and catalytic RNA sequences coupled with the subsequent evolution of peptide or ribozyme polymerases and hence template-replicating RNA or DNA». It is from this statement that he further imagined the dual existence – by coevolution and symbiosis (DYSON, 1985) – of those two collectively autocatalytic and template replicating systems. Remains the question of how did a proteinaceous metabolic web managed to evolve to «clothe the nudity» of primal genes? The answer would be that primeval peptidic clothes were available just *before* their complementary coding by the first lineaments of prenucleic polymers (see below) and that subsequent complexification of the protoprotein clothing was insured by energy-producing protometabolic processes. In these processes, cyclic redox reactions via iron-sulfur compounds (WÄCHTERSHÄUSER, 1988) could have been coupled to the synthesis of energy-rich pyrophosphates (FOX, 1988) and such coupling of exergonic and endergonic reactions would help drive the stochastic synthesis of peptides into an autocatalytic, polymer system.

In the above evolutive perspective, the prebiotic synthesis of the amino acid precursors of peptides was easier than that of the precursors of ribonucleic acid such as nucleobases (ÓRO, 1995) and, especially, ribose (SHAPIRO, 1988). In such a riboseless prenucleic phase of the pre-RNA world, autocatalytic sets of randomly produced primeval peptides could have been coupled to – and coded by – template-replicating prenucleic sequences (TURIAN, 1996b, 1997). Only such «clothed protogenes» associating protoproteins and prenucleic polymers could have insured a collective reflexive catalysis and a coordinated web of metabolism to achieve complexification of the first life forms.

PROTEIN OR NUCLEIC ACID FIRST ?

The search for compounds that could have initiated the origin of life elicited various hypotheses which fall roughly into two classes. According to LIFSON (1997), one class assumes the primacy of metabolism and cellular organization, the other class assumes the primacy of reproduction and genetic information. Therefore the question, "Which came first, metabolism (proteins) or reproduction (nucleic acids)?" is metaphorically the question «Which came first, the chicken or the egg?» or "l'œuf et la poule"? (DANCHIN, 1983).

Many authors favor the "chicken-first" hypothesis (OPARIN, 1938; CAIRNS-SMITH, 1982; KAUFFMAN, 1993; FOX, 1988; WÄCHTERSHÄUSER, 1992; DE DUVE, 1991) from polypeptides autocatalyzed either with clays (CAIRNS-SMITH, 1982), with thioesters (DE DUVE, 1991) or with pyrites (WÄCHTERSHÄUSER, 1992). Others favor the "egg-first" hypothesis (CRICK, 1968; EIGEN, 1971, 1992; ORGEL, 1992, 1995) with template-replicating polymers such as EIGEN (1995) who commented «From an historical perspective, proteins should have come first, but historical precedence is not necessarily identical with causal precedence. Evolutionary optimization requires self-reproducing information storage by nucleic acids only». KAUFFMAN (1993) rather stated that «Autocatalytic sets of peptides and catalytic RNA could coexist and then couple to arbitrary template replicating RNA sequences». In such «RNA world» (GESTELAND & ATKINS, 1993), it would thus no longer be necessary to solve the chicken-egg problem which would arise with the nude template-replicating RNA molecule or with selectively chosen, useful peptidic protoproteins. However, peptides could have first existed and possibly coded for themselves, as already shown in 1969 by CALVIN and, recently, by others with cyclic peptides (LEE *et al.*, 1996; TURIAN, 1996a). It could then be imagined such peptides gathering around themselves a connected protometabolism, their production thereby replacing the nude RNA (ribozymic or "egg") gene with a «naked protoprotein» (KAUFFMAN, 1993) and thus by the chicken. Nevertheless, it should be pointed out that peptides have the difficulty to specify their linear structure by a template-like mechanism because they lack the local point-point homology links of complementary positive and negative strands provided by nucleobase pair rules. Therefore, the loose sequential specificity of the first randomly formed peptides or protoproteins – the «chicken meat» – would soon have to be taken-over by "archaic" nucleobase doublets (before transition to triplets (HARTMAN, 1975; JIMÉNEZ-SÁNCHEZ, 1995), necessarily stabilized or «frozen» on polyphosphates (TURIAN, 1997; TURIAN & SCHÖNENBERGER-SOLÀ, 1997) like "eggs" for the evolutive conservation of the information first acquired by such prenucleic, riboseless infopolymers or primal "eggs". A 2nd take-over leading from the prenucleic polymers to ribonucleic acid would have further stabilized this self-replicating information by ribose insertion, possibly anticipated by glycolaldehyde (WÄCHTERSHÄUSER, 1988; ESCHENMOSER, 1994) or glycerol (SCHWARTZ & ORGEL, 1985). Such genetic take-overs open the next alternative riddle «were primal codings guided by a chemical reason or were they chemically arbitrary»?

«RANDOMNESS OR DETERMINISM» AT PRIMAL CODING ?

Modern knowledge of the genetic code tells us little about the reason this particular code, viewed as a correspondence between nucleotides and amino acids coding units, exists rather than some other. At one extreme of the speculations about its origin is the theory of randomness, namely that the assignment of amino acids to codons is a chance event. Such a stochastic theory (HOFFMANN, 1975) which envisages a code selected by circumstance and by virtue of its «workability» to be the best code corresponds to CRICK's (1968) proposal of the «frozen accident». At the other extreme, lies the

deterministic theory advocated by Woese since 1966 (WOESE *et al.*, 1966; WOESE, 1972) and others (PORSCHKE, 1985; etc.) that codons – or anticodons – select the corresponding amino acids through the specific stereochemical interactions of free amino acids with nucleotides. Since the 60ties, the search for a stereochemical affinity between the amino acids and their codons has been a recurrent theme in many reports on the genetic code as pioneered in 1966 by PELC & WELTON for codons and by DUNNILL (1966) for the specific interaction between the anticodon dinucleotides and their cognate amino acids. In 1968, RALPH concluded that there is still little convincing evidence for either the stochastic or the specific interaction hypothesized, and that «no sensible stereochemical or other interaction between amino acids and codons or polynucleotides have been discerned to date». However, he left open the possibility that an earlier imprecise code resulting from amino acid-polynucleotide interaction later developed greater specificity by purely stochastic processes. Later, in 1972 NELSESTUEN argued that the very nature of the «frozen accident» theory makes it untestable and presented a new concept about the origin of life in which he postulated that L-amino and ribonucleic acid structures were interwined from a time preceding even nucleotide formation and that copolymerization of these structures is the basis of code's origin. In 1975, WONG stated that since neither theory has given a systematic solution to the riddle of the «cracking of the code», he proposed as 3rd hypothesis a co-evolution theory from which he concluded that «the structure of the code begins to appear less haphazard in the light of the likely events of prebiotic evolution». Among other original proposals was that by DILLON in 1973 of a metabolic correspondence between certain amino acids – distributed in 4 groups – and mono-, di- and trinucleotides and, in 1979, by EGAMI who further considered this metabolic correspondence as a simultaneity of primitive synthesis of amino acids (from C2 to C6 subgroups) and nucleobases. In a different system, concerned with the distribution of doublets of the first two codon bases among amino acids, SUKHODOLETS in 1989 proposed that a definite order in the relative distribution of the 1st and the 2nd codon bases coincided with a definite order among the common amino acids and their distribution for the number of hydrogen atoms per molecule, an unexpected parameter.

According to HENDRY *et al.* (1981) there is a structural similarity in the amino acid radicals and the second bases of their codons, and almost all amino acids fit «cavities» formed by their second codon bases in the b-DNA helix. This concept of pairing amino acids and nucleotide bases proposed by many previous authors (45 references cited in 1981 by HENDRY *et al.*) and the relative importance attached to the role of the 2nd base position in the triplet code was supported by the established correlation of physicochemical properties of amino acids with nucleotide bases, in particular with the 2nd anticodon base.

In 1966, DUNHILL had already suggested a primordial role for anticodons, mediated by dinucleotide-doublets or by trinucleotide-triplets, a trend followed in 1978 by HOPFIELD. The same year, JUNGCK concluded experimentally that almost all properties of amino acids showed a greater correlation to anticodons than to codonic dinucleotides. He further demonstrated that the polarity and bulkiness of amino acid chains could be

used to predict the anticodon with considerable confidence, and concluded that the physical parameters of amino acids and nucleotides limit the stochastic possibilities for the genetic code. In 1981, DOUNCE also assumed that there are "fits" between the residues groups of the amino acids and specific nucleobase pairs which would have meaningful structural relationship to the JUKES (1965) dyads ascribed in a landmark paper (1983) to 16 anticodons – including stop doublet – to code for 15 amino acids.

This primal coupling base doublets-anticodons was further endorsed in 1983 by DAVYDOV in his proposal for a "reverse genetic code". More recently, and also drawing on Hendry's (HENDRY *et al.*, 1981) molecular models, OTROSHCHENKO & KRITSKY (1995) have hypothesized that the stereochemical constraints imposed by a specific proto-tRNA interaction with an amino acid may have come not from a modern version of anticodon triplet, but from a chemically degraded set of nucleotides composing the anticodon. According to these results, elimination of the 2nd base from a coding triplet also produces a «cavity» in the double helical molecule. The stereochemical properties of a side chain of the encoded amino acid would allow its specific entering into the cavity.

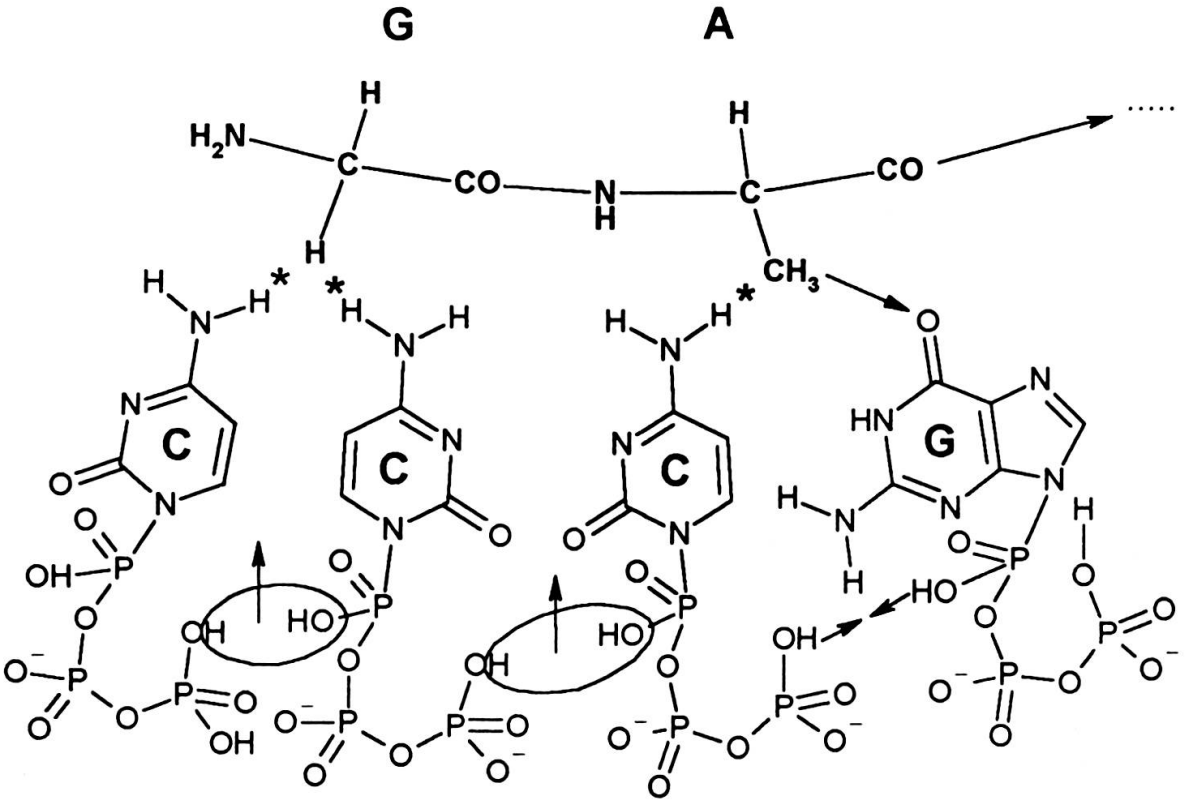
Concerning the deterministic approach, and as recently commented by ALBERTI (1997), there are still difficulties to accept the stereochemical theory in its original formulation, since there is little evidence for a selective binding of amino acids to isolated nucleotidic codons or anticodons (DILLON, 1978; SCHUSTER, 1981; SZATHMÁRY, 1993, CEDERGREN & MIRAMONTES, 1996) if only considering (ALBERTI, 1997) the sheer difference in size between the two structures. In our proposed model (see below), this difficulty has been largely overcome by the reduced bulkiness of free pyrimidine (especially) and purine nucleobases compared to their selectively "caged" amino acids thereby making easier the primary coding processes.

In his 1994 updating review of the onset of genetic coding, MADDOX commented «there is no obvious way in which the amino acid molecules that small tRNAs carry can interact with their signatures, the anticodons" and from that image, we have inferred (TURIAN, 1996b) that if, evolutionarily, anticodons moved far from their specifically assigned amino acids, originally they would have been in intimate contact. Because of steric hindrance at this molecular level, anticodons would still have been reduced to two free bases (JUKE's "archaic doublets") deprived of the d-ribose which, as widely admitted (JOYCE, 1989; SHAPIRO, 1988; TURIAN, 1997) could not yet have been abiotically synthesized. Such doublets of relatively lean, free nucleobases could have "caged" amino acids, presumably lined up on randomly formed peptides and weak bonded them by stereochemical specific affinities (TURIAN, 1998).

INTEGRATIVE MODELLING

The products of amino acids dehydrating condensations, linear or cyclic peptides (TURIAN, 1996*a*), were the easier and presumably the first made polymers but were still only endowed with a low degree of sequence specificity. Those spontaneously and randomly formed peptides which could have "survived" to the forces of natural selection would soon have been retrotranslated (reverse genetic coding) and thereby encoded by the

more sequentially-specific doublets of nucleobases of prenucleic infopolymers, by a primary genetic take-over, to what could be considered as "clothed" protogenes. However, to be endorsed as primal codings, the stereospecifically constituted couples of nucleobases should have to be "frozen" on polyphosphates into prenucleic polybasephosphates (Fig. 1).


G
A
H
H_2N
C
CO
N
H
H
C
CO
.....
H
CH_3
H
N
H
*
*
H
N
H
H
N
H
*
C
C
C
G
HN
N
N
N
N
N
N
O
O
O
O
O
O
OH
P
O
O
P
O
P
O
O
P
O
P
O
P

KEEFE & MILLER, 1995; LAZCANO & MILLER, 1996) and would merge with the "prenucleotide world", driven by the other energy-rich pyrophosphates as suggested by the BALTSCHEFFSKYS (1993).

After their presumed self-replication on complementary base pairs chains, the original nucleobase doublets would, in return, be anterotranslated into more of the selected, primeval peptidic sequences. These considerations thus provide an integrated answer to riddles 1 and 2 by envisaging the onset of genetic coding in a pre-RNA world of peptide-clothed protogenes. They are also a deterministic answer to the 3rd riddle because such onset could *not* result of a random or stochastic "frozen accident" but of a "frozen interaction", i.e. freezing on polyphosphate chains of the nucleobase doublets having first specifically recognized and stereochemically bonded amino acids of the primeval peptides.

The information of the protogenes would have been secondarily taken over by true nucleic genes according to the following sequential scheme:

Naked peptidic (proteinoid) polymers = "chicken"	Peptide-clothed prenucleic infopolymers or protogenes = "chicken-egg"	Naked ribonucleic (ribozymic) genes secondarily clothed = "egg-chicken"
	1st take-over	2nd take-over
Prebiotic - Prenucleic world		RNA world

The 2nd genetic take-over produced by some type of ribosylation of the prenucleic protogenes would have led to naked RNA genes which could have assumed, in their catalytic and replicative, self-sufficient ribozymic form, the primary functions of storing and passing on the evolutionarily cumulated information of the RNA world. However, it can be expected that such naked genes would soon have gathered around themselves protoprotein clothes in an "early RNA peptide world" (DI GIULIO, 1997) coupled with the energy producing protometabolism required for the structuro-functional complexification of the first life forms.

EPILOGUE

The facts presented as tentative answer to the 3rd riddle, endowed with a philosophical connotation, are mostly in favor of a shaping of the genetic code by basic chemical forces and not by chance. Interestingly, this opinion was parallely emphasized at the last meeting of the Society for the Study of Evolution (Gretchen VOGEL's report, 1998) by most scientists who also speculated about interactions of affinity forces between specific base sequences and amino acids rather than for a random accident "frozen" in time. This still theoretical scenario has been comforted by preliminary experimental evidence obtained by LANDWEBER-KNIGHT of a significant increase of arginine binding to its possible codons in randomly produced RNA strands which demonstrates that it is no accident that these codons specify arginine. As further commented by G. VOGEL, experi-

mental probings of specific interactions such as of alanine with GC(U), considered by TRIFONOV (1998) as the original codon (we rather favor GG → CC-glycine (see TURIAN, 1998), should convince deterministic doubters among which the evolutionist Nile LEHMAN.

Another dominant research theme today is the ability of infopolymers to self-replicate as primordial replicators. However, as commented by SZATHMÁRY (1997) the origin of non-enzymatic replication is still an unsolved problem, although artificial replicators have been grown without a replication enzyme in a test tube (VON KIEDROWSKI, 1986) and analogs of RNA molecules just two nucleotide long were able to act as template for their own replication (TJIVIKUA *et al.*, 1990). Other experimental models of RNA replication, considered as a key step in the emergence of life on Earth, have been developed by JOYCE & ORGEL (1986), SCHWARTZ *et al.* (1987), ORGEL (1995) and self-replicatory chemical systems further designed by SIEVERS & VON KIEDROWSKI (1994) and LI & NICOLAOU (1994). FERRIS *et al.* (1996) have then catalytically induced the formation of RNA molecules by surface-bond template polymerization on a clay, successful up to a length 55 nucleotides. More recently, an ingenious procedure described by LUTHER *et al.* (1998) combines the advantages of solid phase chemistry with chemical replication of DNA oligonucleotides and could be further developed for the non-enzymatic and enzymatic amplification of RNA, peptides and other templates.

The first replicators with limited heredity might have been much smaller molecules, with analogue rather than digital replication (WÄCHTERSCHÄUSER, 1997). However, how far the analogue replicators which proceed piecemeal could have evolved before the advent of digital replicators which act as a modular process remains an open problem (MAYNARD SMITH & SZATHMÁRY, 1995).

The power of selection conjuncted with the use of ribozymic aptamers has been exploited by several groups (WILSON & SZOSTAK, 1995; JIANG *et al.*, 1996; WILLIAMSON, 1996). However, the search with such short RNA sequences appears less relevant for a primordial role of RNA in the primal origin of life because of the "modernity" of their bonded ATP. We prefer to rejoin others (see in COHEN, 1996; HORGAN, 1996) with the opinion that a molecule as complex as RNA could not arise from scratch but evolved from simpler self-replicating molecules. These could have been peptide-nucleic acids (PNAs) which also have the ability to replicate themselves and catalyze reactions (BÖHLER *et al.*, 1995). However, with their unusual polyethylglycine backbone, these polymers might not have existed under plausible conditions on the early Earth. So, why rather not prenucleic polybasephosphate phosphoramide-bonded polymers, simpler than the phosphodiester-bonded polybaseribosephosphates of RNA-ribozymes, as primordial, prebiotic replicators?

ACKNOWLEDGEMENTS

We thank Dr. P.-Y. Morgantini (Lab. Chimie physique Prof. J. Weber) for the Graphics modelling and we are also grateful to Ariane Fehr for careful typing of the manuscript.

RÉSUMÉ

ORIGINE DE LA VIE. I. ENIGMES RÉCURRENTES CONCERNANT SON CODAGE GÉNÉTIQUE

L'alternative interrogative "l'œuf ou la poule?" à l'origine du monde prébiotique perd sa pertinence si on lui substitue la coévolution originelle de peptides-protoprotéines et d'infopolymères polybasephosphates prénucléiques en assurant le codage stéréochimique et la reproduction.

RÉFÉRENCES

ALBERTI, S. 1997. The origin of the genetic code and protein synthesis. *J. Mol. Evol.* 45: 352-358.

BALTSCHEFFSKY, H. & M. BALTSCHEFFSKY. 1993. Molecular origin and evolution of early biological energy conversion. *In: Early Life on Earth*, pp. 81-92, Bengtson, S. (ed.), Nobel Symposium 84, Columbia U.P., New York.

BEDIAN, V. 1982. The possible role of assignment catalysts in the origin of genetic code. *Origins of Life* 12: 181-190.

BÖHLER, C., P.E. NIELSEN & L.E. ORGEL. 1995. Template switching between PNA and RNA oligonucleotides. *Nature* 376: 578-581.

CAIRNS-SMITH, A.G. 1982. Genetic Takeover and the Mineral Origins of Life. Cambridge University Press, Cambridge.

CALVIN, M. 1969. Chemical Evolution. Molecular Evolution towards the Origin of Living Systems on the Earth and Elsewhere. Oxford Clarandon.

CECH, T.R. 1986. A model for the RNA-catalyzed replication of RNA. *Proc. Natl. Acad. Sci. U.S.A.* 83: 4360-4365.

CEDERGREN, R. & P. MIRAMONTES. 1996. The puzzling origin of the genetic code. *Trends Biochem. Sci.* 21: 199-200.

COHEN, P. 1996. Let there be life. *New Scientist* 151: 22-27.

CRICK, F.H.C. 1968. The origin of the genetic code. *J. Mol. Biol.* 38: 367-379.

DANCHIN, A. 1983. L'Oeuf et la Poule, Histoires du Code Génétique. Fayard. Paris.

DAVYDOV, O.V. 1983. Problem of the genetic code structure: new data and perspective. *In:* Poglazov, B.F., M.S. Kritsky & K.L. Gladilin. (1995). *Evolutionary Biochemistry and Related Areas of Physicochemical Biology*, pp. 283-295. Bach Institute of Biochemistry and ANKO. Moscow, 618 pp.

DE DUVE, C. 1991. Blueprint for a Cell: the Nature and Origin of Life. Patterson, N. (ed.), Burlington, N.C.

DELARUE, M. 1995. Partition of aminoacyl-tRNA synthetases in two different structural classes dating back to early metabolism: implications for the origin of the genetic code and the nature of protein sequences. *J. Mol. Evol.* 41: 703-711.

DI GIULIO, M. 1997. On the RNA world: evidence in favor of an early ribonucleopeptide world. *J. Mol. Evol.* 45: 571-578.

DILLON, L.S. 1973. The origins of the genetic code. *Bot. Rev.* 39: 301-345.

DILLON, L.S. 1978. The Genetic Mechanism and the Origin of Life. Plenum Press, New York and London.

DOUNCE, A.L. 1981. Origin of life-proposed mechanism for primeval polynucleotide and peptide chain synthesis. *J. Theor. Biol.* 90: 63-79.

DUNNILL, P. 1966. Triplet nucleotide-amino-acids pairing; a stereochemical basis for the division between protein and non-protein amino-acids. *Nature* 210: 1267-1268.

DYSON, F.J. 1985. Origins of Life. Cambridge University Press, London.

EGAMI, F. 1979. *J. Agricult. Chem. Soc. Jpn* 53: 173. *In:* Weigin, X. (1981) Origine du code génétique: les insuffisances du darwinisme. *La Recherche* 12: 1000-1003.

EIGEN, M. & P. SCHUSTER. 1979. The Hypercycle: a Principle of Natural Self-Organization. Springer Verlag, New York.

EIGEN, M. 1971. Self-organization of matter and the evolution of biological macromolecules. *Naturwissenschaften* 58: 465-523.

EIGEN, M. 1992. Steps toward Life: a Perspective on Evolution. Oxford University Press, Oxford.

EIGEN, M. 1995. What will endure of 20th century biology? *In: What is Life? The Next Fifty Years*, pp. 5-23, Murphy, M.P. & L.A.J. O'Neil (eds), Cambridge University Press, Cambridge.

ESCHENMOSER, A. 1994. Chemistry of potentially prebiological natural products. *Orig. Life Evol. Biosph.* 24: 389-423.

FERRIS, J.P., A.R. HILL, R. LIU & L.E. ORGEL. 1996. Synthesis of long prebiotic oligomers on mineral surfaces. *Nature* 381: 59-61.

FOX, R.F. 1988. Energy and the Evolution of Life. Freeman, New York.

GESTELAND, R.F. & J.F. ATKINS (eds) 1993. The RNA World. Cold Spring Harbor Laboratory Press.

HALDANE, J.B.S. 1929. The origin of life. Rationalist Annual 3. (Reprinted in BERNAL, J.D., 1967. The Origin of Life, pp. 242-249. Weidenfeld & Nicholson, London).

HARTMAN, H. 1975. Speculations on the evolution of the genetic code. *Origins of Life* 9: 133-136.

HENDRY, L.B., E.D. BRANSOME, M.S. HUTSON & L.K. CAMPBELL. 1981. First approximation of a stereochemical rationale for the genetic code based on the topography and physiochemical properties of "cavities" constructed from models of DNA. *Proc. Natl. Acad. Sci. U.S.A.* 78: 7440-7444.

HOFFMANN, G.W. 1975. The stochastic theory of the origin of the genetic code. *Annu. Rev. Phys. Chem.* 26: 123-144.

HOPFIELD, J.J. 1978. Origin of the genetic code: a testable hypothesis based on tRNA structure, sequence, and kinetic proofreading. *Proc. Natl. Acad. Sci. U.S.A.* 75: 4334-4338.

HORGAN, J. 1996. The world according to RNA. *Scientif. Amer.* 274: 16-17.

JIANG, F., R.A. KUMAR, R.A. JONES & D.J. PATEL. 1996. Structural basis of RNA folding and recognition in an AMP-RNA aptamer complex. *Nature* 382: 183-186.

JIMÉNEZ-SÁNCHEZ, A. 1995. On the origin and evolution of the genetic code. *J. Mol. Evol.* 41: 712-716.

JOYCE, G.F. 1989. RNA evolution and the origin of life. *Nature* 338: 217-224.

JOYCE, G.F. & L.E. ORGEL. 1986. None-enzymatic template-directed synthesis on RNA random copolymers: poly(C,U) templates. *J. Mol. Biol.* 188: 433-444.

JUKES, T.H. 1965. Coding triplets and their possible evolutionary implications. *Biochem. Biophys. Res. Comm.* 19: 361-365. + 1983. *J. Mol. Evol.* 19: 219-225.

JUNGCK, J.R. 1978. The genetic code as a periodic table. *J. Mol. Evol.* 11: 211-224.

KAUFFMAN, S.A. 1993. The Origins of Order. Self-organization and Selection in Evolution. Oxford University Press. 709 pp.

KAUFFMAN, S.A. 1995. "What is life": was Schrödinger right? *In: What is Life? The Next Fifty Years*, pp. 83-114, Murphy, M.P. and L.A.J. O'Neil (eds), Cambridge University Press, Cambridge.

KEEFE, A.D. & MILLER, S.L. 1995. Are polyphosphates or phosphate esters prebiotic reagents? *J. Mol. Evol.* 41: 693-702.

KNIGHT, L. 1998. *In:* Vogel, G. 1998.

KORNBERG, A. 1995. Inorganic polyphosphate: toward making a forgotten polymer unforgettable. *J. Bacteriol.* 177: 491-496.

KUHN, H. & J. WASER. 1981. Molecular self-organization and the origin of life. *Angew. Chem. Int. Ed. Engl.* 20: 500-520. ... (for II).

KULAEV, I.S. 1979. The Biochemistry of Inorganic Polyphosphates. John Wiley & Sons, Inc., New York.

LANDWEBER, R. 1998. *In:* Vogel, G. 1998.

LAZCANO, A. & S.T. MILLER. 1996. The origin and early evolution of life: prebiotic chemistry, the pre-RNA worlds, and time. *Cells* 85: 793-798.

LEE, D.H., J.R. GRANJA, J.E. MARTINEZ, K. SEVERIN & M.R. GHADIRI. 1996. A self-replicating peptide. *Nature* 382: 525-528.

LEHMAN, N. 1998. *In:* Vogel, G. 1998.

LI, T. & K.C. NICOLAOU. 1994. Chemical self-replication of palindromic duplex DNA. *Nature* 369: 218-221.

LIFSON, S. 1997. On the crucial stages in the origin of animate matter. *J. Mol. Evol.* 44: 1-8.

LUTHER, A., R. BRANDSCH & G. VON KIEDROWSKI. 1998. Surface-promoted replication and exponential amplification of DNA analogues. *Nature* 396: 245-248.

MADDOX, J. 1994. The genetic code by numbers. *Nature* 367: 111.

MAYNARD-SMITH, J. & E. SZATHMÁRY. 1995. The Major Transition in Evolution. Freeman, Oxford.

MULLER, H.J. 1929. The gene as the basis of life. *Proceedings International Congress of Plant Sciences* 1926, pp. 897-921, Dugger, B.M. (ed.), George Banta, Menasha, Wisconsin.

NELSESTUEN, G.L. 1978. Amino acid-directed nucleic acid synthesis. A possible mechanism in the origin of life. *J. Mol. Evol.* 11: 109-120.

OPARIN, A.I. 1938. Origin of Life. Reprinted 1953. Dauber, New York.

OPARIN, A.I. 1957. The Origin of Life on the Earth. Oliver and Boyd, Edinburgh.

ORGEL, L.E. 1987. Evolution of the genetic apparatus: A review. *Cold Spring Harbor Symp. Quant. Biol.* 52: 9-16.

ORGEL, L.E. 1992. Molecular replication. *Nature* 358: 203-209.

ORGEL, L.E. 1995. Unnatural selection in chemical systems. *Acc. Chem. Res.* 28: 109-118.

ÓRO, J. 1995. From cosmochemistry to life and man. *In:* Poglazov, B.F., M.S. Kritsky, and K.L. Gladilin (1995). *Evolutionary Biochemistry and Related Areas of Physicochemical Biology*, pp. 63-92. Bach Institute of Biochemistry and ANKO, Moscow, 618 pp.

OTROSHCHENKO, V.A. & M.S. KRITSKY. 1995. Search of evolutionary roots of informational coding systems. *In:* Poglazov, B.F., M.S. Kritsky, and K.L. Gladilin (1995). *Evolutionary Biochemistry and Related Areas of Physicochemical Biology*, pp. 251-259. Bach Institute of Biochemistry and ANKO, Moscow, 618 pp.

PELC, S.R. & M.G.E. WELTON. 1966. Stereochemical relationship between coding triplets amino acids. *Nature* 209: 868-872.

PORSCHKE, K.M. 1985. Differential effect of amino acid residues on the stability of double helices formed from polyribonucleotides and its possible relation to the evolution of the genetic code. *J. Mol. Evol.* 21: 192-198.

RALPH, R.K. 1968. A suggestion on the origin of the genetic code. *Biochem. Biophys. Res. Comm.* 33: 213-218.

SCHRÖDINGER, E. 1944. What is Life? The Physical Aspect of the Living Cell. University Press, Cambridge.

SCHUSTER, L.S. 1981. Prebiotic Evolution. *In: Biochemical Evolution*, pp. 15-20, Gutfreund, H. (ed.), Cambridge University Press, Cambridge.

SCHWARTZ, A.W. & L.E. ORGEL. 1985. Template-directed synthesis of novel, nucleic acid-like structures. *Science* 228: 585-588.

SCHWARTZ, A.W., J. VIESSCHER, R. VAN DER WOERD & C.G. BACKER. 1987. In search of RNA ancestors. *Cold Spring Harbor Symp. Quant. Biol.* 52: 37-39.

SHAPIRO, R. 1988. Prebiotic ribose synthesis: a critical analysis. *Origins of Life* 18: 71-85.

SIEVERS, D. & G. VON KIEDROWSKI. 1994. Self-replication of complementary nucleotide-base oligomers. *Nature* 369: 221-224.

SUKHODOLETS, V.V. 1989. The genetic code as a clue to understanding of molecular evolution. *J. Theor. Biol.* 141: 379-389.

SZATHMÁRY, E. 1993. Coding coenzyme handles: a hypothesis for the origin of the genetic code. *Proc. Natl. Acad. Sci. U.S.A.* 90: 9916-9920.

SZATHMÁRY. E. 1997. The first two billion years. Scientific Forum on the Origin of Life. Atken, Gothenburg, Sweden (7-9 April). *Nature* 387: 662-663.

TJIVIKUA, T., P. BALLESTER & J. REBEK, JR. 1990. A self-replicating system. *J. Amer. Chem. Soc.* 112: 1249-1250.

TRIFONOV, E. 1998. *In:* Vogel, G. 1998.

TURIAN, G. 1996*a*. Autocatalytic replication of the dipeptides bondings of a cyclo-tetrapeptide enforced by Mg^{2+}-saline anhydrization. *Archs Sci. Genève* 49: 45-50.

TURIAN, G. 1996*b*. Polarity at onset of genetic coding. I. Bipolar bondings in the two-step takeover of peptide templates by prenucleic-ribonucleic acids. *Archs Sci. Genève* 49: 213-227.

TURIAN, G. 1997. Polarity at onset of genetic coding. II. Primary recognition of amino acids by base doublets of prenucleic sugarless polymers secondarily taken over by ribonucleic acids. *Archs Sci. Genève* 50: 95-104.

TURIAN, G. 1998. Polarity at onset of genetic coding. III. Prenucleic stereochemical interactions between amino acids and nucleobases doublets. *Archs Sci. Genève* 51: 147-152.

TURIAN, G. & I. SCHÖNENBERGER-SOLÀ. 1997. Spectral evidence for phosphoramide bondings between nucleobases and tripolyphosphate possibly generative of prenucleic polybasephosphate chains. *Archs Sci. Genève* 50: 145-152.

TURIAN, G., E. RIVARA-MINTEN E. & A. CATTANEO. 1998. Similar ^{31}P-NMR signals emitted by imidazole and the nucleobases presumably phosphoramido-bonded to tri(meta)phosphates. *Archs Sci. Genève* 51: 187-193.

VOGEL, G. 1998. Tracking the history of the genetic code. *Annual meeting of the Society for the Study of Evolution, New York Acad. Sci.* On "Molecular Strategies in Biological Evolution". *Science* (New Focus) 281: 329-331.

VON KIEDROWSKI, G. 1986. A self-replicating hexadeoxynucleotide. *Angew. Chem. Int. Ed. Engl.* 25: 932-935.

WÄCHTERSHÄUSER, G. 1988. Before enzymes and templates: theory of surface metabolism. *Microbiol. Rev.* 52: 452-484.

WÄCHTERSHÄUSER, G. 1992. Groundworks for an evolutionary biochemistry: the iron-sulfur world. *Prog. Biophys. Mol. Biol.* 58: 85-201. + 1997 in SZATHMÁRY, 1997.

WATSON, J.D. & F.H.C. CRICK. 1953. Molecular structure of nucleic acid: a structure for deoxyribonucleic acid. *Nature* 171: 737-738.

WILLIAMSON, J.R. 1996. Aptly named aptamers display their attitude. *Nature* 382: 112-113.

WILSON, C. & W. SZOSTAK. 1995. *In vitro* evolution of a self-alkylating ribozyme. *Nature* 374: 777-782.

WOESE, C.R. 1972. The Genetic Code: the Molecular Basis for Genetic Expression. Harper & Row, New York.

WOESE, C.R., D.H. DUGRE, W.C. SAXINGER & S.A. DUGRE. 1966. The molecular basis for the genetic code. *Proc. Natl. Acad. Sci. U.S.A.* 55: 966-974.

WONG, J.T.-F. 1975. A co-evolution theory of the genetic code. *Proc. Natl. Acad. Sci. U.S.A.* 72: 1909-1912.