A MODEL FOR THE DEVELOPMENT OF GENETIC TRANSLATION

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(Received August, 1982)

Abstract. Several models have been advanced, both in this journal and others, for the development of the genetic code and translation apparatus. Eigen in particular has put forward a detailed model based on the hypercycle. This paper uses some of these previous ideas to develop a new model of the code and translation in which the pairs AU and GC play complementary roles, and in which tRNAs develop from a molecule with two loops which stacks in repetitive patterns without the need for a messenger RNA. Thus a bridge is provided between random, (or autocatalytic) polymerization, and coded translation. In addition, alternative postulates to several of Eigen’s ideas are tested by computer simulation.

1. Complementary Polymerization and Translation

Two types of coded polymerization are essential for the development of living systems, complementary polymerization of polynucleotides (transcription, replication) and translation of RNA sequencing into proteins. Although both of these today depend on complex coded polymerases, ribosomes etc. for their functioning, it is logical to presume that at least one of them must have arisen spontaneously from a system not possessing these properties.

Of the two, complementary replication has a much more plausible basis for a spontaneous origin than translation. Firstly, unlike translation, it has a direct stereo-chemical basis in the polynucleotide double helix with inward pointing complementary bases. Secondly it is a homologous relation between polymers of the same type. By contrast the association between polynucleotides and amino acids is far less specific. Translation itself is mediated by tRNAs and hypotheses associating specific amino acids with nucleotide trimers remain inconclusive (Lacey, 1969; Melcher, 1974; Thomas, 1981). Furthermore the polymeric structures of amino acids and nucleotides, such as α-helix, β-pleated sheet, and double helix do not have a natural steric relationship (Dickerson and Geis, 1969; Marlborough, 1980). We thus develop a model based on spontaneous complementary polymerization.

An important factor favouring complementary replication would be the existence of a mixture of oligomers, which can bind competitively during periods of the kinetic ‘breathing’ or unzipping that periodically occur in polynucleotides, thus resulting in a jacking action accompanied by polymerization. Such zipping may travel as a soliton down the length of a double strand. This would apply particularly to hairpin forms of RNA, which have suitable initiation sites in the non self-complementary hairpin heads. I will call this process dynamic replication. It may have necessarily been accompanied by several other cooperative factors such as the presence of amine groups, metal ions etc.
Eigen et al. (1981) distinguish two types of evolution, which we will call quantum-phenotypic and quantum-genotypic. Quantum-genotypic RNA molecules evolve by mutations which after the character of their translated protein, whereas quantum-phenotypic alter the binding of RNA to other molecules directly, e.g. induction of transcription, or a direct catalytic effect of the RNA.

Since in this model translation arises after base-pairing processes, we expect evolution to be entirely phenotypic until translation is developed. In particular, RNA evolution will at first select for molecules having a direct catalytic influence in their own right.

Such a situation is highly plausible from an informational viewpoint. The bacterial ribosome is 65% RNA (Lehninger, 1975) and has a structure consistent with a primal origin consisting entirely of RNA (Lake, 1981). Only n nucleotides are required to code an n unit complementary RNA, but 3n are required for an n unit polypeptide with only 1/3 the molecular weight of an n unit RNA, thus the coding effectiveness by weight of RNA-RNA interactions is 9 times as high, as for translation (Lake 1981). This combined with the much higher spontaneous fidelity of complementary RNA polymerization supports a primordial role for direct RNA catalysis.

Although RNA bases form a much more restricted class than amino acid side chains, and would have limited effectiveness as enzymes, one function that stands out as suitable is interactions with other RNAs. A particularly important function is catalysis of RNA polymerization by RNA-based (bootstrap) polymerases. Although modern polymerases are protein based, the role of RNA in the ribosome is consistent with early RNA-based control, which is likely to have included polymerase activity. The model will use two polymerase functions, symmetric (bootstrap replicase) and asymmetric (bootstrap transcriptase).

2. Cell-Based Models and the Hypercycle Concept

A difficulty now has to be considered concerning such replicating RNAs in an open system, without compartmentalization. This is simply that the more rapidly replicating RNA types will out-reproduce the others leading to loss of essential members through structural instability of the system.

Eigen and Schuster, 1977, 1978a, b) have set out a model for the development of the genetic code based on open systems of molecules, rather than cellular compartmentalization. The key steps in this formulation are as follows:

(i) Study of the structural stability of uncompartmentalized systems of molecules with competitive growth rates leads to the deduction that hypercyclic organization is the only stable system with respect to mutational drift and molecular competition. Thus both first and second order growth rates under competitive growth lead to the multiplication of one molecular type to the exclusion of others in the system. By contrast, a cyclic catalytic interaction results in a stable equilibrium of the concentrations of the reacting system.