Randomness and Natural Selection in Genome Evolution

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1. Introduction

The evolution of living organisms is caused primarily by mutations that may subsequently be eliminated or become fixed in the genome. While it is generally agreed that elimination affects deleterious mutations and occurs by negative selection, fixation has been visualized as due either (i) to positive Darwinian selection acting on advantageous mutations or (ii) to random genetic drift acting on selectively neutral (i.e. selectively equivalent) mutations. Since both advantageous and neutral mutations definitely can be fixed in evolution, the issue is of a quantitative and not of a qualitative nature and concerns the predominance of deterministic or stochastic events in genome evolution. That the issue is a difficult one is proved by the fact that this debate has gone on, in the form just stated, for almost twenty years.

We will summarize here a new approach to the problem (see [1—3] for recent reports). The question we have asked basically concerns the degree of freedom in the fixation of mutations. According to the neutral theory [4—7], the fixation of mutations is free of constraints except for 'functional constraints', like the requirement of given aminoacids in certain positions of polypeptide chains. As a consequence, fixation of mutations in third codon positions and in non-coding sequences was considered to be essentially random. Our starting observation was that this certainly was not the case in the genome of warm-blooded vertebrates [8].

2. The Compositional Compartmentalization of Genomes

The genomes of warm-blooded vertebrates are highly compartmentalized, in that they mainly consist of a mosaic of very long ($\gg 300$ kilobases) DNA segments, the *isochores*, which (i) belong to a small number of classes characterized by different GC* levels and by fairly homogeneous base compositions (at least in the 3—300 kbase range); and (ii) seem to correspond to the DNA segments present in Giemsa and Reverse chromosomal bands. Since the families of DNA molecules derived from the isochore classes (or genome compartments) can be separated, it is possible to study the genome distribution of any sequence that can be detected with an appropriate probe. This approach revealed (i) that the distribution of

* GC = mole % of deoxyguanosine + deoxycytidine.

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