

The onset of selection

Natural selection started to drive evolution as soon as molecular replication became possible.

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Divined by the genius of Alfred Russell Wallace and Charles Darwin, the basic principles of evolution by natural selection are well known. First, there is genetic continuity, based on replication. Then, inevitably, comes variation. Finally, there is competition, leading to selection of the variants most apt to survive and proliferate under the prevailing conditions. The findings of modern biology have fully validated those principles, adding the fundamental fact that the causes of variation are strictly accidental and unintentional.

The key notion in this theory is replication. The rest follows obligatorily. Thus, in the origin of life, darwinian evolution must have started as soon as the first replicable molecules appeared. Here, I intend to draw attention to certain implications of this fact that are sometimes ignored or underestimated in discussions of the origin of life. I shall assume, in agreement with most workers in the field, that the first replicable molecules consisted of RNA.

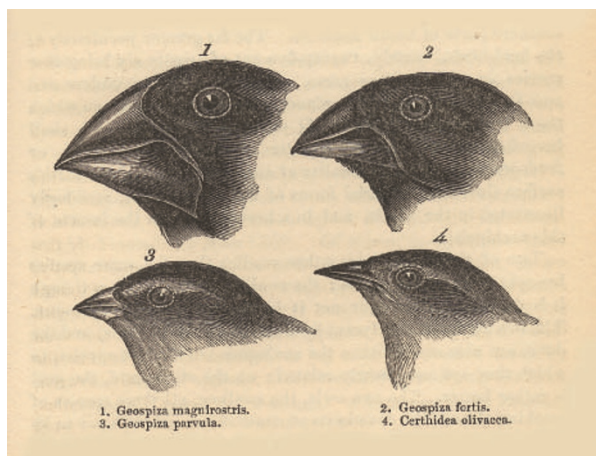
Direct versus indirect selection

The simplest manifestation of natural selection is the direct, molecular form — the object of many studies since it was first made to occur in the test tube by Sol Spiegelman in the 1960s. If RNA molecules are allowed to replicate *in vitro*, selection automatically screens out those mutant molecules that best combine stability and replicability — the molecular equivalent of darwinian survival and proliferation — under the adopted conditions.

By necessity, this kind of selection must have started with replication. In fact, the first product of molecular selection may well have been RNA itself. The mechanism whereby this substance arose is still unknown, but cannot possibly, unless guided by some prescient agency, have produced only authentic RNA molecules with the bases A, U, G and C as sole constituents. It is much more likely that such molecules were accompanied by other analogous assemblages and that they were selected out of this mixture and amplified, thanks to their ability to induce, by base pairing, the formation of complementary molecules that could in turn act similarly to reproduce the first ones.

Once initiated, such a process would have evolved naturally toward the production of what Manfred Eigen has called the Ur-Gen, the ancestor of all RNA molecules. This product would have arisen by molecular selection to form a 'quasi-species', consisting of a 'master sequence', optimized with respect to the prevailing environment, and of an ever-changing cohort of mutants arising through replication errors and other accidents.

The RNA molecules that initiated protein synthesis probably belonged to this early



The Galapagos finches inspired Darwin's theory of natural selection.

crop. It is widely believed that protein synthesis was launched by interactions between RNA and amino acid molecules, prefiguring the present role of transfer RNAs as carriers of the amino acids that are incorporated into proteins. Whereas the amino acids were present beforehand, the RNA partners of the primeval associations most likely arose as mutants of the Ur-Gen and were subsequently selected. This could have happened by a molecular mechanism. An RNA molecule bearing an amino acid could have adopted a more stable conformation. More importantly, for a long-lasting effect, it could have interacted more efficiently with the replication catalyst, thus furthering its own replication.

Other RNA molecules presumably also participated in the development of protein synthesis, for example by favouring the proper alignment of RNAs bearing amino acids, or by catalysing peptide bond formation, functions fulfilled today by messenger RNAs and ribosomal RNAs, respectively. Selection of such RNAs by a molecular mechanism cannot be ruled out, but is not readily visualized. In any case, a stage in the development of protein synthesis must have

been reached where direct selection ceased to be the sole operating process and a new, indirect form of selection was initiated because of the growing complexity of the system.

In this form of selection — which dominates darwinian evolution — genes are selected not because of what they are, but because of what they or their products do, which in the beginning must have been mainly to catalyse a chemical reaction useful to the gene's replication. Barring rare exceptions (such as self-replication), the criterion of usefulness requires the reproduction of the gene to be linked to that of an entity that derives an advantage from the new reaction allowed by the gene. This condition almost mandates the existence of primitive cells, or 'protocells', able to grow, multiply and compete with other protocells for available resources.

It follows that cellularization must have occurred very early in the development of life, probably no later than the inception of protein synthesis. Most of the catalytic RNAs (ribozymes) involved in the so-called 'RNA world' and all the first protein enzymes must have been 'invented' by protocells capable of participating in darwinian competition and of deriving a selective advantage from the catalyst. An important implication of this conclusion is that the early protocells must have been sufficiently individualized to be able to engage in competition and benefit from selection. This point is relevant to the proposal, advocated by Carl Woese, W. Ford Doolittle and others, that the first cells, up to the last universal common ancestor (LUCA) of all known living beings, formed a collective of ill-defined entities that freely exchanged and shared genes by horizontal transfer. This phenomenon may, indeed, have been more important in the early days of the development of life than it is today — which is not inconsiderable — but it cannot have been so extensive and frequent as to blur the distinctions between individual lineages, suppress competition and impede selection.

Mutual selection

Selection is usually visualized as a one-way process, in which a shifting collection of evolving entities is subject to screening by the environment. But the process is often mutual, with the environment being itself screened by the evolving entities. This reciprocity is asymmetric, involving an active and a passive

