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Conclusion

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Development of our understanding of population genetics, including the analysis of populations on the molecular and biochemical levels, and the rapid growth of molecular biology and biochemistry in recent years, allow a new and more accurate approach to evolution mechanisms, as is demonstrated by Ayala's and Stebbins' articles. The question is then whether the 'Modern Synthesis' theory of evolution, elaborated in the 1940s on a basis of Darwinism, has broken down under the enormous amount of information collected during the last 40 years.

The fundamental claim of Modern Synthesis is that, during geological history, higher taxa diverged gradually, and the mechanisms involved were the same as those we can observe every day in populations. Modern Synthesis, using advances in formal and population genetics, has based evolution on the mutation-selection-drift triptych. Selection, working on the variability of populations, progressively adapts genetic pools to environments. Since available environments on earth are discontinuous, a number of genetic pools are isolated from each other by speciation (microevolution), then diverge more and more in higher taxa (macroevolution), the mechanisms being the same in micro and macroevolution[1-4].

For Darwin, the main difficulty was the lack of knowledge about the nature of variability; for us, the main difficulty lies in the enormous amount of biochemical polymorphism demonstrated first by electrophoresis and, today, by the modern techniques of DNA analysis. While Lewontin[5] in 1966 wrote: 'We then have a dilemma', Ayala can write in this review (p.820): 'If the non-coding regions of genes are included, it seems likely that most, if not all genes are heterozygous in every outbred individual', which makes one feel dizzy, and raises the question of why such a high level of polymorphism has been maintained in spite of selection.

Two kinds of solutions have been proposed to solve the paradox; on the one hand the theoreticians propose with Kimura the 'neutralist theory', which erases the paradox itself[6,7], though they admit the existence of a number of deleterious alleles weeded out by selection, these authors consider enzymatic alleles as neutral; thus polymorphism is maintained by a balance between mutation pressure and the chance elimination of many alleles, very few of the enormous number of available gametes being used to make the following generation. On the other hand, almost all selectionists have based their work on an evaluation of the adaptive value of alloenzymes[8-12], on comparisons of neutralist's theoretical predictions with the results obtained in natural populations[13], and on studies of the mechanisms of polymorphism maintenance[8,14,15]. Recent work on the rate of evolution of proteins and of DNA does not fit the theory of neutralism, as Ayala demonstrates in his paper. This author's conclusions appear reasonable, even though the problem of the adaptive value of a single locus is often irrelevant, and in so far as the fitness of an organism often results from complex metabolic sequences among which there is rarely only one optimal path[16,17]. Thus, even if the problem cannot be regarded as completely solved, one cannot consider that molecular analysis of populations has weakened Modern Synthesis. On the contrary, it has strengthened it by being able to quantify the theory of balanced polymorphism.

Another level on which the theory has received support from molecular analysis is that of the increase in information quantity. In 1940, duplications had been described but their exact mechanisms were still unknown; chemical paleogenetics, with sequence analyses of proteins[18,19] and, today, of DNA[20], and the comparison of sequences in different groups, have answered the question by demonstrating precisely the structure of duplications[21]. Today, nobody denies that globins arise from each other by duplication[22], and the detailed structure of the gene, recently discovered[23,24], makes the proposed mechanisms easier to comprehend. In addition, transposons, of which some cases are now well known, even in eukaryotes[25,26], may well be involved in information increase.

The 'mutation' panel of Modern Synthesis is still solid and has even been enlarged, thanks to progress in molecular biology.

Is the role of selection considered as important as before, in spite of the caricatures of the theory produced by some sociobiologists[27]? Whatever the approach, organismic of molecular, the answer is 'yes'. Ayala and Stebbins give many examples. Even neutralists accept a stabilizing selection that eliminates the deleterious mutants.

But geneticists define more prudently the real 'targets' of selection: 1. the selected character may be determined by a pleiotropic gene, and the target of selection be not the visible character itself, but another gene manifestation which is completely invisible; 2. the selected character has no adaptive value but is selected because it is linked to another gene, whose adaptive value is unquestionable; today, those who speak of the adaptive value of a locus add 'or another locus, closely linke to it'. This is equally true for polygenic correlated characters[28].

Moreover, genotype fitness in a given environment has lost its absolute value, as it is now known often to be frequency dependent[15].

At the same time, the relative and progressive character of adaptation becomes more and more obvious: selection is made within a living genetic pool and the solution retained by selection is not always the simplest one, and results sometimes in changes in function. F. Jacob[29] does not hesitate to talk about 'tinkering', and provides examples to show that it is precisely that.

In spite of these reservations, the role of selection is not called into question. It is, on the contrary, confirmed on the molecular level; analysis of globin genes has shown that the rate of nucleotide substitutions for nucleotides in positions 1 and 2, where substitution leads to amino acid substitutions, is significantly different from the rate for nucleotides in redundant third positions; for those in the translated segments (exons) compared with those in the non-translated segments (introns) of genes; for those in genes compared with those in intergenic sequences (cf. Ayala, p. 813, and Stebbins).

The third 'panel' of the triptych, chance, has always been considered important in evolution on three levels: a) in mutations; b) in the large and random elimination noted among gametes and first life stages; c) in genetic drift, whose importance was strongly emphasized Sewall Wright[30,31]. The importance of genetic drift is fundamental into Mayr's theory of speciation, the 'Founder Principle'[2]; the founders of a new colony of a species inevitably contain only a small fraction of the total variation of the parental species. To survive, the population, passing through the bottleneck of reduced population size, has to reorganize its disrupted parental gene pool, to carry out a 'genetic revolution' that ensures adaptation of the new gene pool to the new environment. But when this population comes back into contact with the mother population, the gene pool modifications can make crosses with the old one impossible; a new species is born.

It is probably on this last point that Modern Synthesis has been most challenged; first neutralists, who considered that the theory under-estimates the importance of chance in evolution (a point that has already been discussed) and today by paleontologists. The punctualists have claimed that 'Modern Synthesis ... has broken down on both of its fundamental claims'[32-35]. From the existence of discontinuities in the distribution of some fossil trilobites, they conclude that species are stable entities whose evolution takes place quickly and only during speciation, a model they call quantum speciation. The inconsistencies between the punctualist model and Modern Synthesis do not seem to me very evident; the stability of a species is due, for the biologist, to its integrated genetic pool; quantum speciation looks like Mayr's Founder Principle, and the geologist's 'short' period represents, for the biologist, a great number of generations.

Thus, we have to examine a) whether microevolution patterns can be applied to taxonomic levels considered in macroevolution and can explain it; b) whether macroevolution patterns can be inferred from microevolution ones.

I shall answer 'yes' to the first question. While the positive answer of the founders of Modern Synthesis was essentially built on rational arguments, the present one is founded on molecular biology and chemical paleogenetics. Today, macromolecular sequences allow us to build molecular phylogenetic trees similar to the classical ones obtained by comparative anatomy and physiology. The molecular ones were built on the hypothesis that evolutionary changes are due either to successive mutations that changed different amino acids and the corresponding proteins, or to duplications that increased genetic information and, sometimes, changed gene functions. How can the agreement between molecular and classical trees be explained if the hypothesis used to build the molecular trees is wrong?

The very problem of the appearance of life on earth seems to be on the verge of being solved thanks to advances in chemistry[37]. And models of primitive genetic codes can be imagined, of which Kuhn and Waser give an example. This is a simplified model, a purely theoretical one that may well not emphasize enough some of the difficulties linked with the origin of symmetry. But it is coherent, and it can be hoped that current research will allow us, in a relatively short time, to confront models with experiments.

Thus, evolutionary theory and biochemical progress evolve simultaneously, the latter giving valuable information about the former. The integration of the theory with the laws of physics is, however, not possible yet, and Walker's attempt results in several conclusions which cannot be accepted by a biologist.

Does this mean that Modern Synthesis can explain everything? Of course not. Many important physiological functions, such as the transition from aquatic to terrestrial life, remain partially hypothetical in the absence of records, even if a number of cross-checks allow us to build an intellectually satisfying model (Stebbins, p. 823), and even if progress in the study of protein evolution allows us to specify fundamental points like the date of change from the hemoglobin monomeric chain to the tetrameric one, a change that allowed aerial respiration.

It is certain that a better knowledge of ontogenesis and developmental genetics is essential to explain speciation mechanisms. Nothing, or nearly nothing, is known about eukaryote regulation genes, although they probably play a major role in morphological differentiation. Wilson's demonstration[38], comparing morphologically homogeneous frogs with heterogeneous placental mammals, is convincing; the different abilities to hybridize in the two groups demonstrates that the rate of evolution of regulatory genes is slower in frogs than in mammals, although the rate of evolution of structural DNA is the same in both groups. Comparison between humans and chimpanzees, species which are morphologically different, although they are alike as to the structural DNA and their foetuses are quite similar, leads to the same conclusion. But the answer is unlikely to be found tomorrow.

Again concerning speciation, we need to know the influence of chromosomal mutations in speciation[40]. But this field is developing so quickly that we can hope for a rapid answer.

In the same field, we need to know the role of transposable DNA sequences. Two systems called I/R and P/M are now known in *Drosophila;* a cross between the two types of strains results in high mutability and more or less sterility depending on the incompatibility between paternal chromosomes, which present moderately repetitive DNA sequences of unknown origin, with the female cytotype[41,42]. Strong differences in the distribution of some of these elements in natural populations[43,44] lead us to think that they can play an important role in differentiation between populations and, eventually, in speciation[45]. Even if their dispersion mode is still conjectural, they result in interesting hypotheses like molecular drive[46].

However, in spite of our ignorance on many important points, it seems reasonable to admit that micro and macroevolution mechanisms are the same. This does not mean that the latter can be deduced from the former. The latter rests upon evidence that can be furnished only by paleontology. Thus, gradualism, Simpson's progressive evolution, or Gould's punctualism are not inconsistent with microevolution models. But a choice between the two can be made only by paleontologists looking at fossils, that is to say, within the limits of macroevolution. Having made this restriction, it seems possible to conclude that, even taking into account the progress of all the biological and biochemical sciences and in spite of gaps, some of which will be filled up although others never will be, Modern Synthesis[47] is still able to explain the main mechanisms of evolution and to support them by scientific demonstrations.

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