Evolution and Variation of Multigene Families. Lecture Notes in Biomathematics, Volume 37.


In the genomes of eukaryotes there are various classes of repeated DNAs or duplicate genes, located contiguously along a segment of chromosome. The number of repeats of these DNAs ranges from a few times to a million times. Well-known examples are ribosomal RNA genes, immunoglobulin genes, and globin genes. The nucleotide sequences of these multigene families are now being studied intensively, and many intriguing properties of the genes have already been uncovered. The mechanism of evolution of multigene families, however, is still unclear. The most appealing hypothesis for explaining the evolution is Smith's (1974) theory of unequal crossing-over. By using computer simulation, he has shown that if unequal crossing-over occurs occasionally among multigenes, a high homology of nucleotide sequences among them may be generated, despite the force of mutation pressure that makes the genes heterogeneous. After this hypothesis was put forward, a large number of workers investigated this problem experimentally and theoretically. There are now many observations that support this hypothesis. The major figure who studied the theoretical aspect of this problem is Tomoko Ohta, the author of this book. In the past five years she published many papers on mathematical problems related to the evolution of multigene families. In this book she summarizes her work and discusses the evolution of this group of genes.

Ohta first became interested in this problem immediately after Smith's work was published. She showed that the essential part of Smith's results can be obtained analytically by using the diffusion method. She then studied the expected variability of multigene families within and between populations (or species), considering interchromosomal crossing-over (equal or unequal), intrachromosomal unequal crossing-over, mutation, and random genetic drift. Because of the many factors involved, the mathematical treatment is necessarily complicated. Extracting the most essential elements, however, she manages to develop a neat mathematical theory. Actually, she examined various schemes of unequal crossing-over and developed several alternative mathematical models for the differentiation of multigenes on the same chromosomes as well as between different populations, as a function of evolutionary time. These models are expected to be useful in the future for analyzing experimental data and for understanding the real mechanism involved in the evolution of multigene families.

Her mathematical theory has already produced an interesting prediction about the generation of immunoglobulin diversity. The so-called variable region of immunoglobulins is known to consist of several hypervariable regions and framework regions. It has been controversial whether amino acid variation in hypervariable regions is caused by germ-line mutation, somatic mutation, or somatic recombination. Ohta's study of the relative magnitudes of variations in the hypervariable and framework regions of human, mouse, and rabbit immunoglobulins has suggested that germ-line mutation is the major source of variation.

In addition to the above problems, she has studied the effect of natural selection on gene diversity, linkage disequilibria among multigenes, and other problems. She has been a major innovator in this field, and has opened up a new area of mathematical population genetics.

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