

particular interest are the papers in the relatively new areas of coalescent processes and measure valued diffusion processes. Overall, the technical quality of the book is good and most of the papers are fairly readable.

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Accuracy in Molecular Processes—Its Control and Relevance to Living Systems, T. B. L. Kirkwood, R. F. Rosenberger and D. J. Galas (Eds). Chapman and Hall, London, 1986. \$105.00 (cloth), 398 pp.

There has always been a tension in biology between constancy and change. The origins of this are usually traced back to the early Greeks: Democritus stressed an irreducible unchanging material basis, while Heraclitus championed the idea that everything is in flux. One or the other idea has often dominated thought at particular times and in different fields of biology, and the resolution of the apparent dichotomy has never been definitive.

As Darwin noted, evolution requires change (variants) as well as constancy (like begets like). There must be occasional errors to generate the diversity upon which natural selection operates, and these must be reproducibly passed on to descendants that accumulate in the population. This resolution raised additional issues for biologists ever since. Does the evolutionary process itself lead to stable structures with discoverable rules or is it an open-ended process, i.e. does it lead back to Democritus or Heraclitus? One group of biologists have sought to account for the stability of heritable traits by elucidating the underlying molecular mechanisms. Another group has sought to account for the flux of populations in space and time by elucidating their origins, relations to one another, rates of change, and extinctions—in short, determining their histories. Biology is still trying to integrate the findings of these very different approaches.

What is the accuracy of biological reproduction? It was difficult to measure accuracy when one examined rather complex morphological phenotypes. Nevertheless, it was the constancy of such a trait—the famous Habsburg lip—over a period of centuries that attracted the attention of the physicist Erwin Schrodinger. He reasoned that the only structure in nature known to

possess such stability was a crystal. However, to encode biological information this crystal could not be like the monotonous crystals of inorganic chemistry; it would have to be an "aperiodic crystal", which became identified with DNA following the discoveries of Watson and Crick. Even though it was quickly realized that tautomeric shifts could lead to mispairing of bases during replication of a DNA molecule, the dominant image, still popular in most text books, is that of bases pairing off lock-and-key fashion to produce flawless copies of the parent double-helix.

The lock-and-key image also has dominated thinking about protein interactions, antibody-antigen and enzyme-substrate interactions. Pauling pointed out the limitations of this sort of structural discrimination. He noted that it would be difficult to exclude valine from a binding site designed for isoleucine and calculated that this would occur with a frequency of a few percent. When Loftfield and his colleagues determined the frequency of valine substitutions for isoleucine in native proteins to be about 1 in 10^4 , the question was sharpened: how can relatively high accuracy be achieved in the overall process when the component processes themselves are relatively error prone? In the late 1960s and early 1970s an answer to this dilemma was found experimentally for the charging of tRNA (Baldwin and Berg, Yarus, Eldred and Schimmel) and the replication of DNA (Brutlag and Kornberg). In each case, it was envisioned that errors are detected and removed by editing mechanisms. The fundamental requirements for this process also were illuminated at this time by the theoretical work of Ninio and of Hopfield. Editing or proofreading mechanisms have subsequently been found for most processes involved in the maintenance and transmission of genetic information, and refinements of the theory have been provided by a number of laboratories.

Accuracy of Molecular Processes deals with the developments that have occurred in this field over the past 10 years. It begins with an introductory chapter by the editors that sets the problem of accuracy in perspective. Next is a chapter dealing with the overall integrity of genetic information transfer (Rosenberger and Kirkwood), which is followed by six chapters that cover the major processes: enzyme-substrate interactions (Page), charging of tRNA (Fersht), mRNA-tRNA recognition (Buckingham and Grosjean), ribosome function (Kurland and Gallant), RNA synthesis (Anderson and Menninger) and DNA replication (Goodman and Branscomb). The remaining chapters cover DNA repair (Sedgwick), kinetic and probabilistic methods of analysis (Ninio), kinetic costs (Ehrenberg, Kurland and Blomberg), optimization and ageing (Kirkwood and Holliday), and molecular evolution (Ninio). The principal themes are:

- “. . . (1) an ever more detailed analysis of the molecular structures and the kinetics involved in determining accuracy and (2) a convergence and cross-fertilization of ideas

found useful in the various realms of molecular accuracy in biology—transcription, translation, charging of tRNAs, DNA replication and repair, and the substrate specificity of various enzymes”.

Hence, the book is an account of a field in consolidation emphasizing the molecular bases of biological accuracy.

How well does it succeed? As with most multi-authored volumes, the result is somewhat uneven. In some cases this has to do with the nature of the subject matter. There are chapters that cover familiar territory but nevertheless have a good story to tell; others conclude that it is premature to make sense of the accuracy question for some processes and instead challenge investigators in the area to design appropriate experiments. In other cases the unevenness has to do with the style of presentation. Some chapters are carefully reasoned and well documented, while others are loosely written, speculative and given to overstatement. There also is the issue of redundancy and internal inconsistency. For example, the expression for the discrimination between alternative substrates by a Michaelis–Menten-like mechanism is derived repeatedly. “The cost” of proofreading is defined in nearly every chapter and the definitions often are different.

Given the limitations of the genre, I believe this book succeeds better than most. The individual chapters are understandable on their own and are generally well written. Readers will find many worth reading. There is good mix of experimental and theoretical approaches. The mathematical level is that of elementary algebra and probability. Taken together, the references provide a fairly complete bibliography of the field as of about 1985. However, at U.S. \$105.00, I find it difficult to recommend this book for individual purchase, especially since much of the material can be found in recent reviews published elsewhere.

Although the need for error as substrate for natural selection is noted, and the evolution of accurate systems from inaccurate ones is discussed, the emphasis in this book is on molecular mechanism, statics, optimization, and accuracy. There are no contributions from the evolutionary and population biologists who consider mutation, environment perturbation and selection with a view toward their emergent and *dynamic* consequences. Democritus and Heraclitus remain to be reconciled on the issue of accuracy.

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