



Boris Ephrussi and Herschel Roman, 13 rue Pierre Curie, 1953.
[From *The Early Days of Yeast Genetics*]

sons hinted at in Mortimer's essay became entangled by hopelessly complicated explanations for his discoveries and never received the credit for his work, which inspired Beadle and Tatum and forced a number of labs to consider gene conversion as a real process. Lindgren is the tragic figure in these pages.

It is difficult today to appreciate the skepticism that non-Mendelian patterns of inheritance faced in the not-so-distant past. Essays by Ephrussi (an early reprint) and by Gottfried Schatz, Alexander Tzagoloff, Brian Cox, and David Wilkie do justice to the climate of intellectual resistance to both mitochondrial genetics and the underlying unity in the biochemistry of mitochondria from yeast to beef heart. Under the influence of Austrian charm and wine (Schatz), yeast mitochondrial DNA was discovered, making its genetics legitimate if initially confusing.

The pair of essays on yeast mating present an interesting contrast in approaches to genetic research. One style is represented in the essay by Vivian Mackay, in which she describes her pioneering work on the isolation of mutants affecting mating that has led to so many subsequent discoveries. Because mating is essential to genetic analysis with yeast, the idea of purposely isolating mutants that block the process as a first

step in a genetic study must have seemed foolish to some, but the logic and luck that led to the success of this venture are described, if somewhat too briefly. The other style is revealed in the essay by Yasuji Oshima, whose lab's entire research program on mating-type switching was built on the study of natural variation between different strains. The fusion of these two approaches was most effective, and with molecular advances opening entire genomes to study we can hope that more labs will be inspired to explore the genetic basis of nat-

ural variation and benefit from, rather than be confused by, genetic differences between strains.

The introduction of molecular cloning was a watershed in yeast genetics. The essays by Benjamin Hall and John Carbon are unusually clear accounts of the early research achievements made through work with yeast, such as the proof that introns were in functional rather than in nonfunctional genes and the first description of eukaryotic centromeres and origins of replication. The essay by Botstein puts a more human face on the decision-making that led people from bacterial genetics to yeast, the trials and tribulations of the early molecular methods, and, remarkably, how the early aspirations were quickly outpaced by the reality.

Although yeast genetics has no Delbrück at its origin, the impact of Herschel Roman stands out in many of the essays. Roman had a strong influence on the origin of the yeast cell cycle studies as described by Leland Hartwell, on Rochelle Esposito's launching of her career on recombination and sporulation, and on Elizabeth Jones's studies on gene fine structure and the protease work to follow.

So what's missing from the book? It is a pity that the editors did not assemble a pedigree of who taught whom and when,

such as is found in Sturtevant's *History of Genetics*. Some obvious potential contributors, among them Piotr Slonimski, Ronald Davis, A. W. Linnane, Julius Marmur, and Ira Herskowitz, are conspicuously absent, but not everyone can be convinced to contribute to such a volume in any field. The dearth of information on *S. pombe* is noticeable, but most of the *pombe* advances have been more recent than the time period covered in the book. The book contains information and perspectives that are hard to find elsewhere and therefore should be available to all labs whose research involves yeast. Although few graduate students will need a copy, most will enjoy access to one.

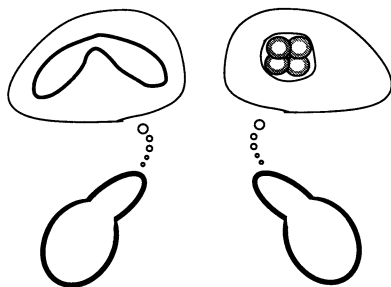
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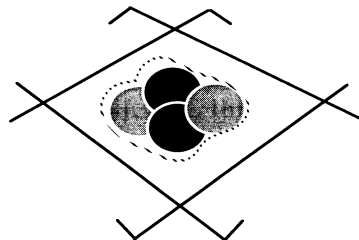
Evolution in the Fast Lane

The Evolutionary Biology of Viruses.
STEPHEN S. MORSE, Ed. Raven, New York,
1993. xiv, 353 pp., illus. \$69.

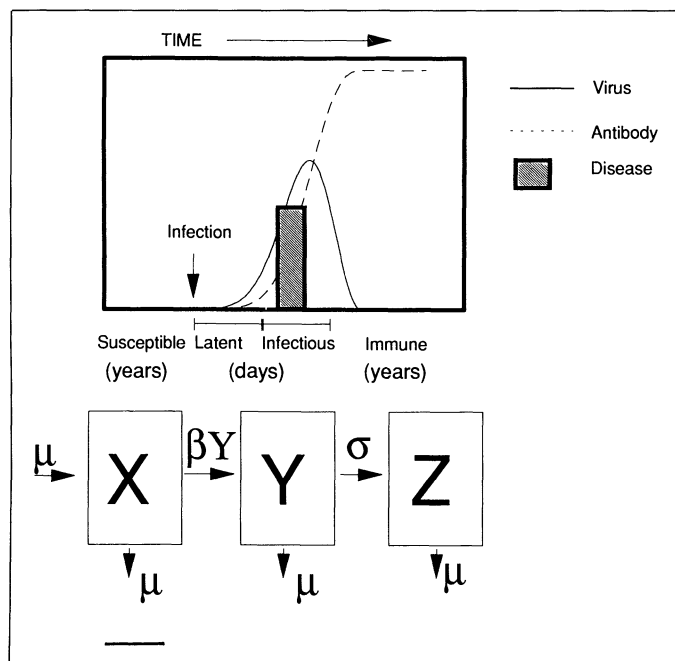
Nowhere in life are evolutionary processes as rapid, as easily observable, or as important for understanding short-term population dynamics as they are among the viruses. For instance, the current AIDS pandemic and the problems of combating its causes—the human immunodeficiency viruses (HIVs)—can only be understood in an evolutionary context. Not taking the evolution of HIVs into account would guarantee the failure of efforts to combat AIDS and in fact would likely lead to seriously counterproductive control measures. Understanding the biology of many other viruses critical to human welfare and basic research also requires a thorough knowledge of evolutionary processes, evolutionary theory, and evolutionary methods. At the same time, many viruses offer largely untapped experimental systems that are ideal for tests of evolutionary theory and methodology. It is both odd and unfortunate, then, that evolutionary biologists and virologists historically have had relatively little research overlap or scientific communication. Evolutionary biologists have been overwhelmingly eukaryocentric in their research programs, and only a few brave virologists have sought to apply or extend evolutionary principles to viral systems. The trend toward specialization and division of the biological sciences in academic environments has exacerbated the situation: evolutionary biologists and molecular



What is this?



T-shirt designs from the Cold Spring Harbor Yeast Course. [From *The Early Days of Yeast Genetics*]



"The progress of a simple viral infection, such as measles, through a host. The growth of the virus population, the immune response to the virus, and the timing of acute disease are illustrated. Below these curves a flow diagram of the transmission between infection categories represented in a simple model is illustrated. In a constant population the birth and death rate per capita are equal (μ). People are born susceptible X, are infected at a rate βY and recover from the infectious category Y, at a rate σ ." [From Garnett and Antia's paper in *The Evolutionary Biology of Viruses*]

biologists who study viruses are increasingly unlikely to be colleagues in the same department. This perpetuates the training of evolutionary biologists who are ignorant of viral biology and of virologists and molecular biologists who are ignorant of evolutionary biology. *The Evolutionary Biology of Viruses* attempts to bridge the gap between these research groups by introducing virologists to basic evolutionary principles and methods as well as tweaking the interest of evolutionary biologists in viruses.

The quality of the individual contributions to the book varies from highly informative to superficial. The material on viruses is, on the whole, much better than that dealing with evolutionary biology. Several authors discuss mutation rates, generation times, and population sizes of various viruses—useful information that highlights the underlying reasons why evolution occurs so quickly among viruses (especially RNA viruses, which receive much more attention in this book than DNA viruses). Domingo and Holland document that many RNA viruses accumulate substitutions at a rate of 10^{-3} to 10^{-2} per site per year, or roughly six orders of magnitude faster than the rates typical of eukaryotic genes. Thus a gene in an RNA virus infecting a human host may accumulate as many changes in one year as a host gene would

accumulate in a million years. Given the viral loads that may be present within a given host, the number of distinct genotypes present in an infected individual can be staggering. Wain-Hobson estimates that an HIV-infected individual harbors between 5×10^5 and 5×10^{10} genetically different variants of HIV, depending on the disease stage. Given that the entire genome of HIV comprises only 8×10^3 nucleotides, it is no surprise that drug-resistant strains of HIV are selected almost immediately after the onset of therapy, because most possible point mutations already exist in the population of viruses within an infected individual.

In his excellent review of the evolutionary relationships of retroelements Eickbush discusses the origins of

retroviruses, caulimoviruses, and hepadnaviruses and their complex relationships with retrotransposons. This chapter, along with others in the book, highlights the fact that viruses make up a class of organisms rather than a natural taxon: They have originated repeatedly from the cellular world, probably as escaped genetic elements. Neither viral taxonomists nor evolutionary biologists, however, seem to have grappled effectively with the obvious taxonomic implications of this fact. If the current hypotheses about viral origins are correct, retroviruses may all be more closely related to mammals than they are to most other viruses. It undoubtedly will upset traditionalists to think of retrovirologists as vertebrate biologists who study escaped portions of vertebrate genomes.

The book gives relatively little attention to the potential for experimental studies of evolution using viruses, although Chao does discuss experiments on the evolutionary effects of sex and the lack of sex in different viruses, and a few other natural or planned experiments are described and discussed elsewhere. Biologists are so accustomed to inferring evolutionary history and processes across millennia that many rarely consider the possibilities of directly observing large-scale evolutionary changes over months or years.

The appearance of *The Evolutionary Biology of Viruses* is especially timely, as virologists and evolutionary biologists are beginning to realize the importance and benefits of interdisciplinary interactions. The book succeeds in providing a forum for some of the work occurring at this interface, but it would have been even more successful had the chapters been planned and coordinated for better coverage of both disciplines. I suspect that some specialists will be frustrated by the relative superficiality of discussions of their own field but will find the material on other topics enlightening. The book should find a broad audience, particularly among evolutionary biologists, most of whom have much to gain from it.

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Getting into Shape

Kinetic Theory of Living Pattern. LIONEL G. HARRISON. Cambridge University Press, New York, 1993. xx, 354 pp., illus. \$69.95 or £40. Developmental and Cell Biology Series, 28.

*Like to a chaos, or an unlick'd bear-whelp
That carries no impression like the dam.*

[Shakespeare, *Henry VI, Part 3*, 3.2.161–62]

The origin of biological form has intrigued and puzzled us for a long time. One of the earliest written speculations appears in *Historia Animalium*, in which Aristotle writes, "After parturition [the vixen] warms her young and gets them into shape by licking them." By Shakespeare's time, the view that the shapeless newborn is given its proper shape by the mother's clever tongue had taken on the power of metaphor.

How indeed do the "formless young" get their proper shape? We owe the most influential modern speculation to Alan Turing, who published a remarkable analysis of the problem in 1952. In his paper we find the first detailed and explicit model of how reacting and diffusing chemicals might interact to form standing and traveling waves of chemical activity, the peaks of which could then be used to specify the location of body parts in the young embryo. He called these chemicals morphogens. Remarkably, the mechanism envisaged by Turing can break symmetries as well, so that periodic patterns can grow from what at first glance look like uniform morphogen concentrations.

During the past decade there has been an explosion of new experimental results that go a long way toward explaining the molecular and cellular basis of morphogen-