The Acquisition of Sex

Molecular Genetics of Sex Determination. STEPHEN S. WACHTEL, Ed. Academic Press, San Diego, CA, 1993. xviii, 518 pp., illus. $89 or £68.

The most obvious—and, to many, the most fascinating—characteristic that distinguishes members of our own species from one another is gender. What is it that turns sexless human embryos into boys or girls in roughly equal proportions? And is "it" the same thing that determines sex in all other animals? Although questions of this type have been asked by many scientific thinkers since the days of Aristotle, it was only with the onset of 20th-century genetic analysis that they could begin to be answered. Surprisingly, unlike many other conserved biological features, sex is determined in a variety of ways in the animal world. In fact, in some unusual cases it is "nurture" (the environment) rather than "nature" (the genes) that does the job.

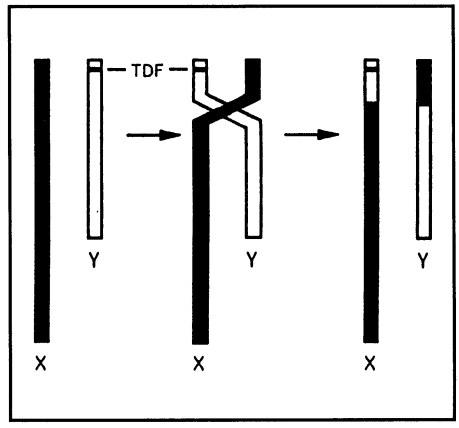
The first genetic system of sex determination to be understood at a basic level is the one that acts in *Drosophila melanogaster*. Male fruit flies have two sex chromosomes, X and Y, just like men. But the results of studies dating back to 1916 demonstrated that the Y chromosome itself does not play a role in sex determination. Rather, it is simply the number of X chromosomes (relative to a normal autosomal complement) that determines whether flies will develop as normal males or females. Could this be how gender is determined in humans as well?

It was not until 1959 that this question was answered: In humans (and, apparently, in all other mammals as well), the Y chromosome is required to direct embryos down the pathway of male development and away from the default pathway of female development. Further work pointed to the existence on the Y of a specific "testis-determining factor" (*TDF*) that induces the formation of testes in the undifferentiated fetal gonad; all other aspects of male sexual development follow from this initial event. Over the years, various molecular candidates for *TDF* have been put forward and shot down. These have included a cell-surface antigenic determinant (H-Y), a noncoding simple repeat sequence (Bkm), and a gene encoding a zinc finger protein (ZFY). Finally, as the climax of the final act in a long play, a gene that has demonstrable *TDF* activity, called *SRY*, was cloned and characterized by Goodfellow, Lovell-Badge, and their colleagues in 1990 and 1991.

Additional details from this scientific journey are recounted, often by the participants themselves, in *Molecular Genetics of Sex Determination*. The volume consists of 19 contributions by some of the most illustrious workers in the field, including early pioneers such as Anne McLaren, Mary Lyon, and Susumu Ohno. It should be pointed out that all the chapters but one focus on mammals, even though we have a much more advanced understanding of the details of sex determination in *Drosophila*, as described in the comprehensive overview of the topic by Cronmiller and Salz.

Many of the individual contributions to this book are excellent stand-alone reviews, and the book as a whole constitutes a valuable source of information on sex determination, the X and Y chromosomes, and sexual development—both normal and abnormal—in humans and mice. I found the rather personal chapter by Hampikian *et al.* on marsupials to be particularly useful in conjunction with the *Drosophila* chapter; together they provide a sense of the commonalities and differences that determine sexual dimorphism in each of these groups relative to each other and to the eutherian mouse-human group.

The book's only serious defect is its redundant coverage of the *SRY* gene, which is the focus of six different chapters, with many aspects of the work leading up to its discovery and characterization repeated over and over again. In addition, the book could have been made more accessible by better coordination of terminology in the final two contributions, which focus on the same protein—referred to as anti-Müllerian hormone (AMH) in one and as Müllerian-inhibiting substance (MIS) in the other.



"Translocation of the male-determining gene. Crossover of a portion of the Y chromosome to the X during meiosis. If the translocated portion contains the testis-determining gene, *TDF*, and if an egg is fertilized by the sperm carrying the X;Y translocation chromosome, the resulting embryo becomes an XX male. X–Y crossovers have been confirmed in most, but not all, 46,XX males." [From Wachtel and Tiersch's paper in *Molecular Genetics of Sex Determination*]

These problems notwithstanding, I suspect that anyone with even a peripheral interest in sex determination will enjoy this book and will be glad to have it handy for quick reference.

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Biological Patterns

Life History Invariants. Some Explorations of Symmetry in Evolutionary Biology. ERIC L. CHARNOV. Oxford University Press, New York, 1993. xvi, 167 pp., illus. $37.50 or £25; paper, $19.95 or £13.50.

Life-history theory seeks to explain patterns in demographic variables that are directly related to evolutionary fitness by simple quantitative expressions—for example, fecundity, mortality rate, development rate, age at maturity, allocation of resources between male and female sexual function, and senescence. Investigation of life histories has produced a substantial body of published work including, recently, several comprehensive syntheses. Not surprisingly, then, Charnov addresses many recurrent issues in this book, some of them developed in his earlier *The Theory of Sex Allocation* (Princeton University Press, 1982). What is new in *Life History Invariants* is the perspective of symmetry and invariance. Charnov's approach will be stimulating and provocative to those willing to consider his arguments carefully. This is not an easy book, but it is well worth the effort.

Life-history invariants are life-history variables that do not change through "transformations" as other aspects of the life history do with variation in body size or ecological relationships. Examples of such practically universal invariants are the 1:1 sex ratio of most populations of animals and the product of age at maturity (α) and adult mortality rate (M), both of which are elaborated in this book. Charnov points out that life-history invariants usually are dimensionless numbers and argues (p. 6) that "invariance at one level will almost always imply symmetry at a deeper level of causative factors." Thus, 1:1 sex ratios are seen as reflecting the "symmetry" that each individual has one mother and one father. Close inbreeding among siblings, which blurs the genetic distinction between "mother" and "father," and other gender-related ecological or social asymmetries

break down this symmetry and cause the optimal sex ratio to deviate from unity. The invariance of the product αM with respect to body size expresses the symmetrically opposing allometric relationships of α (0.25 power) and M (−0.25 power) to body mass, their product being related to the $0.25 - 0.25 = 0$ power of body mass, or 1 (constant).

One may ask whether the ideas of symmetry and invariance really add to understanding, especially of such an issue as sex ratio, of which evolutionary biologists including Charnov have developed a profound understanding without the benefit of the symmetry/invariance concept. Charnov would argue that his approach helps to reorient one's thinking about life histories and leads one to both recognize and inquire about patterns that have previously escaped notice. Compelling support for this rationale can be found in Charnov's own treatment of indeterminant growth. Charnov points out that life-history invariants described for fish more than 30 years ago by Beverton have not been pursued by theoreticians, who have been more preoccupied with the things about life histories that change. Beverton characterized three invariant, dimensionless numbers: the ratio of adult mortality to growth rate, the ratio of length at maturity to maximum length, and the negative exponential relating adult length to growth rate; Charnov adds to these another invariant related to the first two—the product αM. After characterizing these patterns empirically, Charnov proceeds to develop simple optimization models that predict the observed invariants, creating a plausible hypothesis for the causal relationships that control the evolutionary diversification of life-history patterns among fish.

Charnov's approach to understanding life-history evolution is distinctive and consistent. He consciously ignores (i) genetics, by confining his models to the fitness consequences of continuous phenotypic traits; (ii) historical effects, by assuming evolutionary equilibrium; (iii) phylogeny, by assuming that the traits of concern are responsive to selective forces; and (iv) internal physiological constraints, by assuming that optimization deals primarily with the allocation of time and resources among such competing demands as growth and reproduction.

The fundamental life-history relationships recognized by Charnov and his success in providing a theoretical rationale for them make *Life History Invariants* an important book. Charnov would, however, be the first to admit that much of what he has accomplished is only one hopeful step toward a goal still shrouded in the mists of ignorance. Even the impressive fit of Charnov's theory to data may, in some cases, be misleading or lack generality. For example, Charnov explains the 0.25 power relationship of age at maturity to adult body mass in mammals as a direct outcome of the 0.75 power scaling of net production to body mass, combined with optimizing the switch point between growth and reproduction. In this view, adult size is simply a consequence of the optimized age at maturity, after which net production is diverted from personal growth and allocated to offspring production. Thus, adult size is not targeted and has no particular ecological consequence. In contrast, birds grow to a targeted adult size long before achieving sexual maturity. Birds also exhibit an approximately 0.25 power relationship between age at sexual maturity and adult body mass. Thus Charnov's theoretical development either does not provide a generalizable explanation for a pattern common to several groups of organisms or has produced a fortuitous explanation for one of them.

In other cases, there is as yet no theory. Charnov himself suggests that "it would often be easier to find invariants than to explain them." Such a case is the ratio of annual fecundity to adult mortality rate in birds (about 5), further implying invariance in prereproductive survival (about 0.2), irrespective of the order-of-magnitude variation in mortality, fecundity, and age at maturity among species. In his final chapter, Charnov suggests directions for future inquiry into such questions, focusing on the insights of symmetry and invariance. After reading this book, it seemed to me that progress also will depend on developing a deeper understanding of the functional architecture of the organism and of its relationship to the environment. Only in this way will the empirical inspiration for theory adequately reflect the richness and complexity of life-history phenomena. And as Charnov rightly and thoughtfully points out, things that don't change are often as interesting as those that do.

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Vignettes: Genobiography

Sure, George Washington was tall, he did have long hands and feet, he had a prominent nasal bridge and bad teeth, and he was infertile, but that's not nearly enough to prove conclusively that the man had a 47,XYY chromosome complement.

—*Robert Marion*, in *Was George Washington Really the Father of Our Country? A Clinical Geneticist Looks at World History* (Addison-Wesley)

In writing the biography of great men and women, printing the DNA sequence of their genome would not be a good place to start.

—*Robert Cook-Degan*, in *The Gene Wars: Science, Politics, and the Human Genome* (Norton)

The Next Nets

The Neurobiology of Neural Networks. DANIEL GARDNER, Ed. MIT Press, Cambridge, MA, 1993. xiv, 227 pp., illus. $45 or £40.50. Computational Neuroscience.

Attempts to investigate the workings of the nervous system by computer simulation began with the pioneering work of Edwards and Minsky in the 1950s and now range from biologically detailed, conductance-based, *in silico* model neurons to abstract algorithmic approaches. Neural networks (distributed networks of simplified neuron-like elements) lie in the middle of this continuum. They have become popular owing to their remarkable ability, after training, to replicate many aspects of nervous system functioning.

The relevance of artificial neural networks to biology has nonetheless been questioned. This resistance may stem in part from the unfortunate naming of this modeling approach: co-opting a neurobiological term (and thus implying neurobiological verisimilitude) invites criticism. Three more substantive objections have been raised to the supposedly nonbiological properties of these networks. First, one widely used training method, back propagation, requires retrograde passing of an error signal from