BOOKS: DEVELOPMENT

Varied Fates from Similar States

Steven Austad

Sherlock Holmes famously pointed out that Watson merely saw things, whereas he (Holmes) observed them. The point being, of course, that realizing something exists is not the same as noticing its significance. In this sense, gerontologists Caleb Finch and Thomas Kirkwood believe that chance variation—that is, variation specified neither by the genome nor by the environment as it is commonly defined—has been seen for years, but never properly observed. They intend with *Chance, Development, and Aging* to begin such observation. The result is an incisive and stimulating analysis of what the causes and consequences of chance variation might be. In challenging the increasingly geno-centric zeitgeist, the book promises to arouse controversy and, one hopes, provoke innovative research programs.

The empirical basis of the book's main idea is presented early. In trait after trait and species after species, identical genes and environment do not result in identical phenotypes, particularly with respect to aging. For instance, the nematode *Caenorhabditis elegans* is virtually invariant in external phenotype and even somatic cell number is determinate (959 cells in adult hermaphrodites). Yet when grown in culture under conditions as constant and well-defined as possible, genetically identical worms die over a threefold range of ages. Astonishingly, the degree of variability they exhibit in longevity is not much less than that of a genetically mixed population of humans, who eat a variety of diets, attend to or abuse their health, and are subject to all the vagaries of circumstance—car crashes, tainted beef, enraged postal workers—of modern industrialized life. Similarly, highly inbred female mice, born from the same mother and reared in the same environment, exhibit a three-fold range in oocyte numbers at birth (about the same range as is seen among unrelated humans). They die over a proportionally wide age interval and of an array of causes, with certain organs massively diseased in some individuals, perfectly healthy in others.

Chance, Development, and Aging
by Caleb E. Finch and Thomas B. L. Kirkwood
Oxford University Press, New York, 2000. 288 pp. $35, £24.95. ISBN 0-19-513361-7.

The authors' central hypothesis is that chance events, particularly developmental events, contribute substantially to this observed variability in aging. For instance, the variation in oocyte number mentioned above could affect the timing of reproductive cessation, which, given the increasing evidence for the protective effect of estrogen on the central nervous system, might affect the development, timing, or progression of neurodegenerative disease.

"Chance events," as Finch and Caleb use the term, really means two widely different things. One meaning has to do with uncontrolled, uncontrollable, or generally overlooked environmental events such as the age of an individual's mother at the time of its birth, unpredictable exposure to various neonatal stresses, or the sex of intrauterine neighbors. There is a great deal of fascinating biology beneath these sorts of environmental events. For instance, the length of the reproductive cycle, levels of adult aggression, the sex ratio of offspring, and the age at reproductive cessation are all affected by the sex of a mouse's closest neighbors within the mother's uterus. However, because these sorts of events are comfortably covered, at least in principle, by the traditional definition of environmental effects, this incarnation of "chance events" will not be as paradigm-challenging as their other use of the term, which refers to intrinsic and inescapable stochastic processes. They envision such processes to be the outcome of small-scale atomic- and molecular-level events, including the inherent pseudorandom location of somatic mutations, the impact of the statistical nature of diffusion on receptor-ligand interactions, and variability in gene expression due to physical jostling of complex transcription factors for docking sites. Intrinsic variation could also result from larger-scale intercellular events. For example, cell numbers might vary because of the poorly understood details of proliferation dynamics or the exact orientation of the division plane in asymmetrically dividing cells.

The bulk of the book presents an impressively wide-ranging compendium of case studies supporting the authors' main point, that this sort of variability persists in the face of the most extreme genetic and environmental uniformity. Interspersed among these studies are hypotheses that address how intrinsic random processes can lead to specific medical outcomes later in life.

Like most books with a radically new interpretation of commonly observed phenomena, *Chance, Development, and Aging* will likely provoke extreme responses. The key to its impact, however, will be how it affects future research. Turning random variation from bothersome experimental noise to the object of study is a formidable conceptual and empirical challenge. Finch and Kirkwood have convinced me that it is a challenge worth accepting.

BROWSINGS

The Coiled Spring. How Life Begins. *Ethan Bier.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 2000. 269 pp. $59. ISBN 0-87969-562-5. Paper, $39. ISBN 0-87969-563-3.

Bier offers the general science reader a well-illustrated and accessible account of our current understanding of how fertilized eggs are transformed into complex organisms (flies, worms, vertebrates, and plants). He discusses classic experiments in developmental biology, recent research that offers mechanistic explanations for these observations, and the scientific and ethical implications of current embryological research. He also highlights the stories of 17 individuals responsible for many of the key discoveries he covers.

Environmental Physiology of Animals. *Pat Willmer, Graham Stone, Ian Johnston.* Blackwell Science, Oxford, 2000. 654 pp. Paper, $59.95, £27.50. ISBN 0-632-03517-X.

This text combines comparative and environmental perspectives on animal adaptations. The authors first cover the key mechanisms of water balance, metabolism, respiration, and thermal regulation. They then discuss how vertebrates and invertebrates cope with the problems posed by particular aquatic, terrestrial, and parasitic habitats.

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