

Book Reviews

Bioethics and the New Embryology: Springboards for Debate. Scott F. Gilbert, Anna L. Tyler, and Emily J. Zackin. Sunderland, Massachusetts: Sinauer; 2005, 261 pp. \$14.95. Paperback.

Stem cells have taken a place alongside gene therapy as the promised cures of the future, but the average voter, student, or politician seems to have a poor understanding of the science behind the cells. This book, written to be accessible to readers with little biological knowledge, seeks to provide non-scientists with comprehensible basic information on the fundamental processes behind stem cell research. It is divided into seven sections, each of which treats one major biological issue and its related ethical concerns. For example, one section has a chapter on stem cell organ regeneration, which includes the general schema of how pluripotent cells commit to a fate and summarizes research to date on this type of therapy, followed by a chapter briefly treating current policy and regulations, the ethics of oocyte harvest, and balancing the rights of patients vs. embryos. The first chapters include an excellent survey of how cell division works, how oocytes are fertilized, how embryos become fetuses, and the stages of fetal development.

The scientific, informative portions of the text are generally well-written, with abundant figures that help make the ideas seem more concrete and relevant. Some figures are unnecessary; in several instances, two figures on successive pages demonstrate the process of differentiation in nearly identical situations, and there is a somewhat gratuitous diagram of a child leaving the womb. However, all of the pictures, whether artist's renderings, micro-

graphs, or photographs, are colorful, attractive, and usually interesting. The text is nonetheless guilty of occasional oversimplification or omission. To say "the genotype does not predict the phenotype" is inaccurate, since some traits are entirely predicted by genotype, although genotype is not sufficient for complete specification of phenotype. The necessity of folic acid in pregnancy is cited, without any elaboration, while tedious detail is given on RNA processing. Similarly, in the discussion of gene therapy, the authors fail to cite the well-known leukemia-causing gene insertions in French trials. Nonetheless, the explanations and descriptions of fertilization and embryonic development are excellent, and, overall, the book succeeds in providing sufficient technical information for a reasonable understanding of the concepts and processes.

Historical ethics cases are well integrated into the text, with abundant examples of ethical (pre-implantation embryo diagnosis) and grossly unethical (Nazi eugenics) experiments. The current state of regulation is well summarized in each section, with attention to different policies across countries and states and the results these policies have had. Perspectives from major world religions are discussed, along with the official or consensus opinions from those religions' representatives; when these opinions are based on scientifically erroneous ideas, this difficulty is gently pointed out. The possible consequences of various regulatory choices, such as banning human cloning but allowing organ cloning, are treated briefly by bringing up possible questions and problems, such as access, cost, and misuses.

Since many of the ethical questions in embryology do not have clear or distinct

“right answers,” the sections on ethical difficulties are often vague. The authors focus on what might happen and what problems might occur, seemingly aiming to bring up topics rather than to propose any solution. They also attempt to include all the concerns that have been raised by a concerned public: chimeras, brains in vats, engineered children. Instead of giving any answers, they provide only the questions. By the end of the text, one is left with the feeling of a class outline rather than an ethics text per se; indeed, the authors have in part intended the book for a classroom text. Nonetheless, the book remains a useful reference for those interested in basic embryo biology or those seeking subjects for debate.

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Foundations of Image Science. H.H. Barrett and K.J. Myers. Hoboken, New Jersey: John Wiley and Sons, Inc.; Hoboken, New Jersey; 2004, 1,584 pp. \$140.00. Hardcover.

Foundations of Image Science by Barrett and Myers is a superb textbook describing the mathematics used for image analysis. The authors direct their text primarily toward graduate students, radiologists, and technicians working with imaging systems, and perhaps eager undergraduate students. At over 1,500 pages, *Foundations of Image Science* is a tome, but it delivers tremendous value as each of the equations and principles are thoroughly explained and documented for further study. For students in radiology or other math-intensive applications or studies, this book is a worthwhile investment for current study and future reference. This book has it all: the theoretical tools, the principles, the mathematics, and the statistics. A thorough treatment of the continuous-to-discrete model of digital imaging is presented, and numerous examples and appli-

cations are described. In complete agreement with the many other glowing reviews I've found about this book, there is little more I can add.

So I would like to contrast the weight and comprehensiveness of this text of Barrett and Myers with a succinct review: *Foundations of Image Science* is an impressive tour-de-force textbook of imaging systems that deserves a place on the bookshelves of many radiologists and graduate students.

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The War of the Soups and the Sparks: The Discovery of Neurotransmitters and the Dispute Over How Nerves Communicate. Elliot S. Valenstein. New York: Columbia University Press; 2005, 256 pp. \$31.00. Hardcover.

Controversy often surrounds scientific discoveries. *The War of the Soups and the Sparks* by Elliot S. Valenstein examines the discovery of neurotransmitters and the dispute between pharmacologists and neurophysiologists about their existence. Pharmacologists supported the seemingly novel concept of communicating chemicals between neurons, while experts in neurophysiology often committed themselves to an electrical explanation. Resolving this controversy required the work of 20th-century scientists Otto Loewi, Henry Dale, and Walter Cannon.

Beyond describing the 20th-century observations and experiments leading to the discovery of neurotransmitters, Valenstein provides insight into the personal lives of Otto Loewi and Henry Dale, who received Nobel Prizes in 1936 in physiology and medicine, and Walter Cannon, who would have shared the prize with them if he had not adopted a controversial theory. The story of the work and lives of these scientists occurred against

the backdrop of two world wars, and Valenstein weaves into the book the affect of these wars, such as Loewi's arrest by Nazis and how Dale helped scientists escape Germany.

People curious about fundamental scientific developments of the 20th century will find this book to be well-written and insightful. Those interested in neuroscience research and scientific history will find this book resourceful and appropriately detailed. However, for those people who do not fall into either of these categories, the book may not be captivating enough to transform them into neurotransmitter aficionados.

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Aglow in the Dark: The Revolutionary Science of Biofluorescence. Vincent Pieribone and David F. Gruber. New York: Columbia University Press; 2006, 256 pp. \$31.00. Hardcover.

Some biomedical researchers may take for granted Green Fluorescent Protein (GFP) because of its ubiquity. From labeling new proteins with unknown function to creating transgenic organisms that fluoresce in the dark, GFP has revolutionized the study of biology. However, the general public is not aware of GFP. Although GFP has not quite become a familiar mainstream acronym such as FDA, this reviewer feels that GFP is on the short list for the Nobel Prize. When Stockholm announces a Nobel for GFP's discoverers or those who brought its application to fruition, people will become curious to learn about GFP's story. It is only a matter of time before GFP has the spotlight shone on itself. So for the general public and specialists alike who are curious to learn more about GFP and its illustrious history, before its future heralded day, *Aglow in the Dark* tells the exciting story of how

GFP came to be discovered, its present day use, and its many future applications in fields such as neuroscience.

Pieribone and Gruber start their story by describing how the phenomenon of bioluminescence has captured the human imagination since antiquity. Aristotle wrote, "Some things which are neither fire nor forms of firm seem to produce light nature," pointing out that one of the qualities of bioluminescence is the generation of light with minimal heat. Although this feature of light without heat has been a peculiarity appreciated by inquisitive children, it was not until Raphael Dubois in 1887 purified and isolated two chemical components for bioluminescence, luciferin and luciferase, that a natural curiosity could become a tool. Interestingly, Dubois did have the idea of transforming his discovery into practical application. However, he was ahead of his time. He proposed a miner's safety lamp made of luminescent bacteria, but his idea never caught on.

Nearly 50 years later, the Japanese military during World War II planned to use Dubois' hunch of using bioluminescence as safe lighting to allow soldiers to navigate in the pitch of night without raising enemy suspicions. Fortunately for the Allies, U.S. submarines sank Japanese ships carrying dried powder of glowing Cypridina. Out of that period of devastation wrought by the Imperial Army of Japan came Osamu Shimomura, a Japanese Fulbright Scholar who has contributed the most to our understanding of bioluminescence since Dubois. Shimomura purified a photoprotein he called "Aequorin" and was the first to describe a novel form of bioluminescence that depended on calcium rather than ATP. Although GFP is a story of science, the reader can't help but notice the twists and turns that make discovery and progress unexpected, unpredictable, and human.

Apart from recapitulating the story of GFP told by the authors, I have to comment that Pieribone and Gruber's photos and illustrations are of first-rate quality.

Just flipping through the pages, I am left with a sense of awe at the beauty of glowing coral and other denizens of the deep such as clownfish nestled in a bubble-tip anemone. Returning to the application theme, the industrial and practical possibilities of GFP are apparent to the reader when a rainbow of fluorescent protein is beautifully and crisply presented in tandem like a box of Crayola crayons.

Nature's Crayola has been a boon for molecular medicine. Gruber and Pieribone explain the myriad applications: from tagging proteins, monitoring calcium levels, to creating transgenic organisms. It seems from their description that the application of biofluorescent proteins is only limited by imagination. One of the people heavily responsible for transforming GFP from the jellyfish protein into a molecular beacon is Roger Tsien. Pieribone and Gruber highlight the character of Dr. Tsien with much gusto. Dr. Tsien comes across as brilliant, financially minded, and competitive. He seems to be the first to successfully realize Dubois' dream to turn bioluminescence into a profitable tool. Aurora Biosciences, a company centered on new fluorescent proteins, founded by Dr. Tsien and Dr. Zuker, had a market capitalization of \$1.5 billion in 1999.

In the chapter titled, "Shimmering Reefs," we learn that the authors are not just academics but accomplished scuba divers who went to Lizard Island in the Great Barrier Reef, Australia, to photograph and collect samples from fluorescent anemone and coral. Within a month, they encountered and catalogued over a hundred different species of corals expressing yellow, green, orange, and red fluorescent proteins. Given the concentration of fluorescent proteins in coral, the authors speculate on its function. Perhaps fluorescent proteins aid in photosynthesis, act as sunscreen, or act as free-radical scavengers. Given that some of their functions remain a mystery, the authors point out that it behooves society to do its best to

preserve coral and their natural environment for future generations to gaze and ponder.

Whether nature intended fluorescent proteins to be used by scientists in the brain becomes a moot debate as the pictures presented in the book's penultimate chapter show that these fluorescent proteins are lighting the way toward a deeper fundamental understanding of the brain. Researchers are now using fluorescent proteins to visualize living neurons and witness them shriveling during Alzheimer's disease. The possibility of using fluorescent proteins to noninvasively label living neurons may allow scientists to one day unlock the secrets of cognition or at least the code by which neurons communicate.

In summary, whether you are a scientist peering down a fluorescent microscope to determine whether two proteins colocalize or a curious on-looker ready to go scuba diving in the Great Barrier Reef in Australia, I highly recommend *Aglow in the Dark* to read about biofluorescence's fascinating past, current uses, and potential applications.

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Patient Adherence to Medical Treatment Regimens: Bridging the Gap Between Behavioral Science and Biomedicine (Current Perspectives in Psychology). Alan J. Christensen. New Haven: Yale University Press; 2004, 192 pp. Hardcover.

It seems reasonable to assume that after having spent the time, effort, and money of going to a doctor to figure out why their health is deteriorating, most patients would be motivated to go through with their prescribed treatments. Unfortunately, this basic premise, which physicians tend to assume, is glaringly

naïve, as Alan Christensen attempts to show in this well-needed manifesto on patient adherence.

The reality is quite unlike what physicians would hope. Christensen cites that it is estimated that between 20 percent to a record 80 percent of patients actually are nonadherent to the treatment that their doctors suggest for them, resulting in unfavorable medical outcomes and large economic costs. He claims these staggering statistics of nonadherence occur because, during the course of treatment, patients resent losing control of their daily activities. This frustration and unwillingness to change leads to lack of compliance, termed the “Psychological Reactance Theory.” Some patients will feel more frustrated by their restrictions to normal life than others, based upon their individual differences, and hence will become more nonadherent.

This theory then supports the idea that treatments that interfere with patients’ normal lives the most are positively correlated with nonadherence, including more frequent dosing of medication and treatments having more adverse side effects. Positive correlations with patient adherence, on the other hand, include treatments that involve the patient through self-monitoring and provide good social supports flexible to a patients’ new needs. Christensen also notes that physicians can help patient adherence by using positive language with patients and staying involved with their progress by scheduling follow-up visits. He concludes that more research has to be conducted on patient adherence to better understand the phenomenon and attitudes need to change in the medical profession to regard nonadherence, not as a nuisance that can’t be helped but rather something they can affect.

Overall, Christensen’s work does a concise job of highlighting possible factors contributing to patients’ nonadherence, citing past behavioral studies and also suggestions for the health care

provider to facilitate adherence. Flow charts and graphs were present in key points throughout the book and were apt illustrations of pertinent concepts. In addition, his partiality to the theory of psychological reactance as a model of patient nonadherence is compelling, given the evidence. Nevertheless, it would be interesting to see, as research progresses, if other theories he mentions can be given further credence. In particular, he mentions the protection motivation theory, which attempts to describe the role of fear as a way to describe patient nonadherence. To date, few or no studies have been done to examine the usefulness of this theory. However, it may be possible that more support for this theory may emerge as more studies are done in this area. Only with further research in patient adherence, and its recognition as something to be changed, as Christensen states, will more progress be made.

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Present at the Flood: How Structural Molecular Biology Came About. Richard E. Dickerson. Sunderland, Massachusetts: Sinauer Associates, Inc.; 2005, 307 pp. \$34.95. Paperback.

A must for students of structural biology, *Present at the Flood* explores the conception and evolution of macromolecular structural analysis beginning in the late 19th century and culminating in the fundamental discoveries of the structures of B-form DNA and hemoglobin in the 1950s and 1960s. Dickerson masterfully describes the science behind structural analysis while simultaneously placing the works into historical context. Included with each chapter are the original papers, thankfully abbreviated at times, describing the findings of key players in their own words. Additionally, Dickerson presents

particularly clear explanations of both X-ray fiber diffraction and crystallography as an accompaniment to the text, which helps a first-time reader of the subject.

The first four chapters of the book discuss the prevailing theories of protein structure in the early 20th century, namely, the idea of proteins as colloids, the cyclol theory, and the eventual success of Pauling and Corey with the realization of the alpha-helix. Dickerson guides the reader through fiber diffraction and its role in the tumultuous early days of structure determination. He begins with the work of William Astbury at Leeds University on fiber diffraction of keratin and silk fibers and moves on to illustrate the work of Dorothy Wrinch and her ultimately incorrect model of proteins as composites of cyclol rings. Finally, he completes the first stretch of his exploration describing the competition between Caltech and Cambridge for the structure of the alpha helix and how Pauling's concept of partial bonding (resonance) helped lead him to it on one cold day in England.

Subsequently, Dickerson describes the events leading up to the discovery of the double helical structure of B-form DNA. It is here that Dickerson also provides a greatly simplified version of X-ray crystallography ("crystallography without mathematics") so that the reader might better understand the data presented in the accompanying papers. In general, Dickerson refrains from discussing the standard fare of the double helix story.

Instead, he presents reflections on wrong turns and side notes usually left out, including the triple helical structure proposed by Watson and Crick as well as the negative feelings of Chargaff coupled with the discussion of the role that Rosalind Franklin played in the solution of the double helix.

The final chapters of the book discuss how protein structures are solved using X-ray crystallography with emphasis on the structures of hemoglobin and myoglobin. This segment begins with a description of Fourier synthesis, multiple isomorphous replacement (MIR) phasing, and the need for phase information itself. Dickerson moves on to describe the initial solution structure of hemoglobin at 5.5 Å by Perutz and the higher resolution structure of myoglobin at 2 Å by Kendrew. Of particular note are a discussion of the "Faltentrommel" theory of protein structure, which was disproven by Kendrew and Perutz's globin structures, and the humorous globl-globin paper by Donohue. All told, *Present at the Flood* provides an excellent synthesis of the early years of structural biology that not only surveys the science behind the critical discoveries of the era, but also places them in a historical context. As such, the reader gains full perspective on the work of these key figures and the view of structural biology in the mid-20th century.

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