

## BOOK REVIEWS

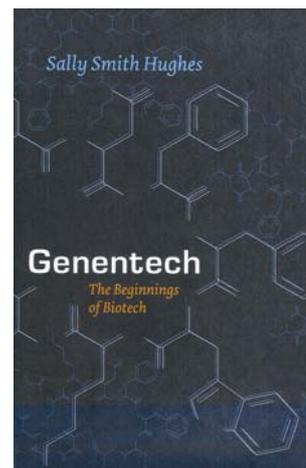
backbone assignment with known protein structure using RDCs. Dynein light chain and PDZ domain of PTP-Bas are two examples discussed in chapter 35 in which structures are incorrectly determined due to wrong assignment of NMR data. Details of Semidefinite programming and its applications in side-chain positioning problem and the sensor network localization problem are explained in chapter 36. Graph-embedding problem with local angle information is compared with the protein structure determination using RDCs in the same chapter. Graph cuts with broader applications in structural biology are discussed in chapters 37 and 38. Studying the structure of intrinsically disordered and unstructured proteins is an important and challenging area in structural biology. Using ensemble-averaged RDCs and small-angle X-ray scattering data to derive the structure of an unfolded protein is presented in chapter 39. Chapters 40 and 41 revisit the protein–ligand binding and present methods for flexible protein–ligand docking using continuum solvent model and metadynamics. The problem of comparing an ensemble of structures with a reference structure is addressed in chapter 42. Two different experimental approaches, mass spectroscopy and NMR, can complement each other when the systems are difficult to study. This is the major focus in chapter 43 in which mass spectroscopy-assisted NMR assignment is discussed. Another algorithm, Autolink, an automated method for NMR resonance assignment is presented in detail in chapter 44. A version of the Rosetta structure prediction program, called CS-Rosetta, for predicting the structure from experimentally determined NMR chemical shifts is described in chapter 45. Its accuracy in predicting 16 protein structures and its limitations are discussed in the same chapter. A new support vector machine-based approach for predicting substrate specificity of enzymes is discussed in chapter 46. CRANS (cross-rotation analysis), an algorithm to predict and analyse non-crystallographic symmetry in X-ray diffraction is dealt with in chapter 47. Phase problem, molecular replacement method in X-ray crystallography and application of normal mode analysis are some of the highlights in chapter 48. Another application of genetic algorithm in structural biology, namely optimizing the charge–charge interactions on the surface of protein

structures, is presented in chapter 49 and the example protein used is Fyn SH3 domain. The final chapter talks about computational topology, triangulation, alpha-shapes and applications in the contexts of protein structure.

It was almost 50 years ago, that G. N. Ramachandran and his colleagues made the fundamental contribution to structural biology in the form of the Ramachandran map. Today, it is not uncommon to encounter a student of biochemistry, biophysics or related discipline who cannot fully describe the significance of this map or the method used to calculate the  $\phi$ – $\psi$  plot. It is in this context that this book is an important step in introducing and familiarizing the algorithms used in the software tools for biomolecular structure determination. This book presents a nice collection of several popular algorithms used in structure determination and analysis of biomolecules. Perhaps, this is probably a first book of this kind, although several books describing the algorithms used in sequence analysis are available. With major emphasis on NMR data, the title *Algorithms in NMR Structural Biology* would have been more appropriate for the book. Computer science students with exposure to biochemistry and NMR would find the book helpful. However, the readers will have to go back to the original published papers to understand the algorithmic details in depth. As far as the biology/biochemistry students are concerned, they need a solid mathematics background to understand the different topics discussed in the book. The link between the chapters could have been better and the transition between one topic and another sometimes seems to be abrupt (for example, mass spectroscopy is suddenly introduced in chapter 19). More examples in detail to illustrate the application and significance of the algorithms would help the structural biologists with biology background to take an active interest in the book. Overall, this book will be a useful reference for advanced researchers working in the area of NMR structural biology.

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**Genentech – The Beginnings of Biotech.** Sally Smith Hughes. The University of Chicago Press, Chicago 60637, USA. 2011. xv + 213 pp. Price US\$ 25.00/£16.00.

The biotechnology company Genentech was co-founded by a researcher, Herbert Boyer and a venture capitalist, Robert A. Swanson about 36 years ago. While Swanson (who is no more) might be largely unheard of in the scientific community, Boyer happens to be a well-known figure, particularly in life sciences. The research Boyer carried out in collaboration with Stanley Cohen on recombinant DNA (rDNA) technology won them both the prestigious Lasker award in 1980 (with two other scientists).

The popularity of the duo and their work is apparent from the number of hits that Google returns when one types ‘Boyer and Cohen’. Following their collaboration on rDNA technology, both independently continued their scientific pursuits. Boyer went on to shape a new company (Genentech) with Swanson, whereas Cohen served as the scientific advisor to another company (Cetus). If one could compare, Cohen’s corporate involvement was much less than Boyer’s. A brief biographical account of the three key figures in Genentech’s history – Boyer, Cohen and Swanson – is provided in the book.

Boyer and Swanson were the ideal co-founders of the first-of-its-kind venture into the biotech industry, with Boyer at the forefront of rDNA technology and Swanson eager to market its applications. Even if the book is spun around the development of a business enterprise, what would interest a broad scientific

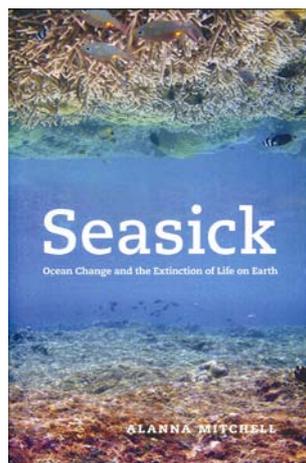
audience is the package – of scientific process, collaborations, authorship issues, politics, intellectual property rights and conflict of interest issues – that the book brings to light. These aspects were, by nature of the company, inherent to its functioning. The book points to the concerns (legal and others) that surrounded the ownership of research funded by a private company but conducted in university laboratories in the late 20th century.

The name ‘Genentech’ was coined by Boyer as an abbreviation for (Gen)etic (En)gineering (Tech)nology. Swanson had recommended a bizarre ‘HerBob’ (Herb from Herbert and Bob was Swanson’s nickname). Genentech survived the struggle that a company’s early years bring about. Not only that, it ventured into an area of science that established companies were hesitant to undertake, and in doing so left a trail for other biotech start-ups to follow. The genes for human insulin, human growth hormone and human interferon were cloned in three successive years. Genentech won the race for cloning these genes against leading academic research groups, and turned out to be a lucrative career option for young scientists. More so because Boyer emphasized that the company must encourage scientific publications, not just patents.

What stands out in the book is Swanson’s perseverance in establishing a start-up in the era of pharma giants. Nearly eight months after the company’s legal on-paper founding on 7 April 1976, when it laid a business plan, ‘It had no laboratories, no research equipment, no scientists of its own, no money for sustained development, no patents or licenses securely in hand, no certainty of the impact of the festering recombinant DNA debate.’ About two years down the line, ‘Genentech had made insulin, *human* insulin.... Two teams of unknowns [young postdocs and graduates] supported by an obscure company [Genentech]...managed to out-compete two elite academic teams [University of California–San Francisco and Harvard University] in making a form of a celebrated hormone.’

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**Seasick: Ocean Change and the Extinction of Life on Earth.** Alanna Mitchell. The University of Chicago Press, 1427 East 60th Street, Chicago, Illinois 60637-2954, USA. 2011. x + 161 pp. Price: US\$ 18.00.

That we are in the middle of a major environmental crisis is no longer in doubt. Governments, the public, the science community all largely agree that environmental conservation is one of the most significant challenges of the 21st century. However, much of this attention has been focused on terrestrial landscapes. Even climate change, now considered as one of the most pervasive threats, and recognized by even the most blinkered governments, is generally viewed through the lens of its impact on land. How, for example, will sea-level rise affect coasts and people living there? The fact that we live on a planet that is largely water does not enter the conservation consciousness of the public nearly enough. The book under review is an effort to bring to the forefront the human caused ills that are afflicting the world’s seas.

From the Great Barrier Reef in Australia to Panama and Puerto Rico and Zanzibar, Alanna Mitchell travels around the world, exploring a number of nearshore and oceanic habitats with scientific teams that are working on a variety of organisms and ecosystems. She follows their work on human-induced threats, ranging from coral bleaching to ocean acidification to the occurrence of dead zones. She writes with passion about the impacts that ocean change can have on ecosystems, such as the effect of warming on coral reefs which leads to the breakdown of the symbiotic association

between the coral and the algae, resulting in the death or expulsion of the algae, and consequently the death of the corals. Many severe bleaching episodes have now occurred in all major coral reefs across the world in the last few decades.

Mitchell travels with a group of scientists to study the dead zone, also called the blob, in the Gulf of Mexico. Dead zones are low-oxygen zones, that are probably caused by excessive nutrient pollution, from sources like, as in this case, fertilizers. An increase in nutrients causes an increase in cyanobacteria, which die and sink to the bottom and decompose, leading to a decrease in oxygen, and the near complete depletion of fish and other organisms. More than a 400 dead zones are known around the world today.

Ignoring iconic species such as whales and dolphins, sea turtles and sharks, Mitchell instead tells the more obscure stories, those that are in fact more important, more reflective of the health of the ocean, and with greater consequences for the future of the planet, and humanity. One of these is the study of plankton in Plymouth University, UK concerning the fate of coccolithophores, which have become less calcified with increased ocean acidity (though some studies have shown the opposite). Another concerns the rapidly declining trend in fish stocks, with dire predictions of the future of fisheries, made famous by studies from the University of Halifax, Canada.

In order to explore the past, Mitchell also visits the Pyrenees, formed when the Iberian peninsula pushed against Europe. Here, there are records of the Palaeocene–Eocene Thermal Maximum, a period when temperatures and carbon dioxide levels were much higher than they are now, which provides clues into how the earth’s biota responded.

Mitchell’s engagement with the scientists introduces us to their world, not just their passion about science or conservation, but also to their methods and instruments. Meet Scanfish, an instrument that moves through the water column collecting data. And Johnson-Sealink 1, the submersible that goes down to 3,000 ft. Mitchell attempts to make the technical seem fascinating and deconstruct the often arcane methods that we use to arrive at our inferences, and for the large part, succeeds.

Mitchell writes eloquently about her journey to the bottom of the sea, 900 m