mutation. Even though nuclear reactors are immensely beneficial to society at large for the amount of nuclear power they produce, there is an associated concern of safe disposal or storage of long-lived nuclear wastes consisting of plutonium, minor actinides, some of the long-lived fission fragments and their radioactive daughter products. In recent years there has been considerable interest in developing techniques for transmutation of the above-mentioned nuclear wastes. A promising route is the accelerator-driven subcritical system which consists of intense neutrons produced from a spallation reaction induced by high energy protons, followed by slowing down of these neutrons to initiate secondary fission and capture reactions to carry out the task of waste transmutation. It appears that the liquid fueled thermal neutron spectrum offers major advantages over the solid fueled fast spectrum system in accomplishing this task. As a bonus, electrical power can also be made available from the accelerator-driven subcritical assemblies.

S. K. GUPTA
S. KAILAS

Nuclear Physics Division,
Bhabha Atomic Research Centre,
Mumbai 400 085, India

Neural Networks and Analog Computation. H. T. Siegelmann. Birkhäuser Verlag AG, P.O. Box 133, CH-4010 Basel, Switzerland. 1998. 200 pp. Price: SFr 88/DM 98.

Numerous physical processes in nature are hard to simulate on a digital computer. This led to a paradigm shift in the field of computation, revising the Turing model of computation to encompass physical processes. For example, Feynman suggested using quantum mechanical systems to simulate quantum mechanics. Models of neurons also turned out to be powerful computing systems. Can these physical process models (quantum computers, neural networks, DNA computation) be viewed as general-purpose computers? How do these models fare with respect to the conventional digital computer and the Turing model? *Neural Networks and Analog Computation* by Hava T. Siegelman addresses this question.

One obvious difference is the continuous phase space of physical processes. The computational advantages of neural networks and quantum computers over classical computing are in part due to the fact that these systems can be in a state of superposition of different states. Unfortunately Siegelman overlooks this important issue. These physical computers are reaction–diffusion systems, for example, DNA computer can be viewed as a reaction–diffusion system where patterns formed are given computational interpretation. A diffusion process by virtue of its ability to fill the entire volume enumerates all possibilities. A reaction mechanism selects and amplifies those that satisfy a certain criterion (solution). In this book we have the interesting result that recurrent neural networks with real weights and sigmoid activation are more powerful than quantum and DNA computers. It would be interesting to see where reaction–diffusion, which is giving all the patterns we see in nature, fits in the computational hierarchy.

The thesis of the author is – no possible abstract analog device can have more computational capabilities than first-order recurrent network. In chapter 2, the author first identifies weights and activation functions as the two key determinants of its computational power and shows that neural networks with integer weights and threshold function can simulate finite automata. In chapter 3, we find that Turing machines can be simulated with neural networks having rational weights. In this book we find a detailed study of the activation function with respect to the Turing model. In chapter 7, the author shows the universality of sigmoidal networks; and gives the lower bound on the computational power of sigmoidal networks. Chapter 10 gives the upper bound. Chapter 8 proves that any function for which the left and right limits exist and are different gives networks that are at least as powerful as finite automaton.

Chaotic motion (Henon map) cannot be mimicked by the Turing machine, but can be simulated with recurrent neural networks with real weights and sigmoid activation function, which leads to the super-Turing model. We also find that randomness does not increase the computational power in the case of integer and real weights, but stochastic rational weight neural networks are more powerful than deterministic (rational) neural networks (chapter 9). In chapter 10, the author shows that higher-order neurons are not computationally superior to first-order neurons.

In summary, this book is a comprehensive study showing the universality of recurrent neural networks and measures the changes brought about by changing weights (integer, rational, real) and activation functions (threshold, sigmoid) against the benchmark of the Turing model.

L. M. PATNAIK

Computer Science and Automation,
Indian Institute of Science,
Bangalore 560 012, India

In Vivo Models of Inflammation. D. W. Morgan and L. A. Marshall (eds). Birkhäuser Verlag AG. P.O. Box 133, Basel, Switzerland. 1999. 360 pp. Price: Sfr 198/DM238 (Hardbound).

Inflammation is a response of the living tissue to injury. Injury could be physical, chemical, biological or immunological. 'Inflammation in itself is not to be considered as a disease, but as a salutary operation consequent either to some violence or some disease' wrote John Hunter three decades ago. It was in the 18th century that the precise well-timed process of inflammation was described step by step. Observations of Conheim in the frog mesentery, and Metchnikoff in the starfish, of the sequence of events and the cells taking part in this dynamic process were only the beginning of a number of explosive discoveries. Thenceforth, detailed microscopic descriptions of inflammation in various tissues, function of the different types of cells, the interplay of numerous cytokines these cells release and biochemical changes taking place have found place in all standard text books.

It is not the process of inflammation, which resolves in healing following removal of the injurious agent, that is of interest today. It is inflammation that persists as a chronic process resulting in disease that intrigues researchers. Features of this disease differ with respect to site and the causative agent. Study of this disease has not been easy. During the last century there has been directed research to unravel the mechanism of chronic inflammation and to find clinical means of early diagnosis and various therapeutic measures for relief of symptoms as well as cure. This has been possible mostly because of the availability of animal models.

Development of a perfect animal model, which mimics the disease in humans, is a science by itself today. What a young researcher needs for his investigations in a defined disease is an authoritative account of the different animal models for the particular disease, their uses, ways of producing them, their advantages and their disadvantages. This is what he or she will find in the book *In Vivo Models of Inflammation*. This volume is aptly included in the series on 'Progress in Inflammation Research' edited by Michael J. Parnham.

The animal models discussed in this book are for those common inflammatory conditions which affect locomotive, pulmonary, skin and gastrointestinal systems where there is a persistent inflammatory change leading to a pathological process. The diseases include rheumatoid arthritis (RA), asthma, chronic obstructive pulmonary disease, inflammatory bowel disease and a few inflammatory conditions of the skin. The book is complete with two instructive chapters on transplantation and transgenic animal models for inflammatory diseases. In the final chapter of the book, the reader is also informed about ethical matters one has to follow during animal experimentation.

RA is a chronic systemic inflammatory disease predominantly affecting diarthrodial joints. The pathological feature of RA is synovial membrane proliferation and outgrowth associated with erosion of articular cartilage and subchondral bone. Microvascular injury, proliferation of synovial cells and infiltration of mononuclear cells mainly T lymphocytes are observed resulting in joint swelling, pain, stiffness and impairment of joint function ultimately resulting in deformities.

Adequate anti-inflammatory therapy being critical, testing of any drug would need an ideal animal model with exactly similar pathological changes and clinical symptoms as in the human condition. Exhaustive accounts regarding various animal models available for this disease and therapeutic interventions are the contents of three chapters. Even a novice will find the methods described easy to follow. Richard P. Carlson and Peer B. Jacobson have clearly elucidated the chronology of events in the joint following injection of the streptococcal cell wall. The author's own work on magnetic resonance imaging for *in vivo* evaluation of disease progression in a rat model of adjuvant arthritis reveals the impact of new technology in investigative work.

Development of collagen-induced arthritis in a mouse model and elucidation of the role of cytokines with proof of their involvement are described at length by Whim B. van den Berg and Leo A. B. Joosten. They emphasize the advantage of this model to study immunoregulation in autoimmune arthritis. E. Jonathan Lewis and his colleagues focus on the nitty-gritty details of quantitative estimation of changes in the joint cartilage during inflammatory reactions in arthritis. They describe two rat models, one to evaluate the degeneration of collagen/cartilage implanted subcutaneously and the other on Propionibacterium acnes-induced monoarthritis. Their investigations are predominantly quantitative. Though these models have proved advantageous in testing drug efficacy, I do agree with the authors that extrapolating the data to clinical situations is not possible because of the absence of load bearing in these experiments.

Four chapters are devoted to animal models of pulmonary inflammatory conditions. Two chapters describe models to investigate molecular, immunological and pharmacological approaches to treat asthma. While giving a detailed account of the similarities and dissimilarities of the animal models with respect to the clinical situation in humans, the authors also mention recent techniques to evaluate the condition in animals. Use of primate models of asthma to evaluate newer therapies like leukotriene B4 and D4 receptor antagonists are mentioned.

Chronic obstructive pulmonary disorders include several specific disorders with varying clinical manifestations, pathological findings, therapy requirements and prognosis. David C. Underwood describes animal models for two specific disorders, namely chronic bronchitis and emphysema. The list of available models and types of inductive agents is exhaustive. Genetically-prone murine strains of emphysema are described. A pulmonary hypertension model is also described and seems to be out of place in a book on inflammation.

The need to therapeutically target molecular mediators or cytokines released during inflammation is nowhere so much applicable as in inflammation of the skin. Kenneth M. Tramposch relates animal models for psoriasis and delayed type hypersensitivity (DTH). Numerous bioassays have been investigated in both immune and nonimmune-mediated models to study the effect of anti-inflammatory drugs. The murine model has proved useful in unraveling the immune changes that take place in DTH responses and the effect of new drugs on these changes. Tramposch suggests the use of a combination of models in a tiered screening system, employing both gross pathological and biochemical end points. Models of skin inflammation are a boon to the pharmaceutical industry for the investigation of topically applied drugs for various diseases. A word of caution in the extrapolation of data in topical drug delivery studies in animal models to humans is that the permeability properties of the skin are different in animals and humans.

Crohn's disease and ulcerative colitis together are termed as Inflammatory Bowel Disorders (IBD). IBD is a genetically complex multifactorial disease. Genetic susceptibility may be driven by many environmental factors, which ultimately may aggravate the immune response, resulting in chronic disease pathology. Sreekanth Murthy and Anne Flanigan lay down specific criteria to be taken into account when developing an animal model for IBD. A substrain of C3H/HeJ murine model is extensively used in genetic mapping studies to identify genes that determine susceptibility for colitis. Overwhelming evidence that IBD is T cell and neutrophil-mediated disease has led to the development of transgenic and knock out models. These include T cell and bone marrow transplant models. The authors say that it is difficult to produce the T cell transplant

model in laboratories which are not equipped with a sophisticated FAC Star Plus flowcytometer, since very high purity T cells are required.

The T lymphocyte being a prominent cell in most of the inflammatory diseases, the editors have aptly included animal models solely of T cell-mediated diseases. The diseases are well chosen. Experimental allergic encephalomyelitis resembles multiple sclerosis and insulin-dependent diabetes mellitus (IDDM) is an autoimmune disease resulting from destruction of pancreatic islet cells by both cell-mediated and humoral mechanisms. Spontaneous systemic autoimmune disease models for systemic lupus erythematosus are also described.

Angiogenesis, defined as the growth of new blood vessels, is one of the components of chronic inflammation. James D. Winkler and his colleagues give a brief account of the various animal models that are available to study the effects of various angiogenic factors and also inhibitors of angiogenesis.

Though organ transplantation is common place today, rejection continues to be a stumbling block in many cases. The success of organ transplantation has relied on studies in animal models to understand the basic mechanism of rejection. Orosz *et al.* have given detailed methods for evaluation of transplantation rejection in skin, cardiac, renal and pancreatic tissues. They also propose a model for acute rejection produced with transfer of allogenic leukocytes into immunocompromised mice. This, they say is a simple and often overlooked model for studies on drugs that influence mechanisms of allosensitization, tissue inflammation and leukocyte migration. There is also an interesting section on allograft tissue remodelling.

Recent development of special technologies to alter or block gene functions in organisms has led to the development of animal models to define gene function and understand altered gene function in a disease. Creating an animal model in which a particular adhesion molecule, a cytokine, a receptor, a major histocompatible molecule or an enzyme is absent or overexpressed will provide valuable information regarding basic pathological process in inflammation. In addition to a lucid description of the principle and technical features of gene transfer, Anderson *et al.* and David S. Grass have brought us up to date on the various vectors in use today in gene transfer, their advantages and disadvantages, steps required to generate these vectors and transfer genes.

Kenneth N. Litwak and Howard C. Hughes pack the concluding short chapter with updated guidelines and regulations for animal experimentation. The reader is also referred to the relevant internet sites for more information.

The editors Douglas W. Morgan and Lisa A. Marshall have provided the state of the art on animal models in use for study of inflammatory diseases. A newcomer to this field would find the detailed descriptions of methods with explicit black and white as well as colour histological pictures and comparative descriptions of animal models and disease in humans extremely useful. An introductory chapter on inflammation *per se* is missing. Future models and suggestions for new directions are found in the book. The vast amount of work being done on animal models across the globe is reflected in the large number of references at the end of each chapter. Publications up to 1998 have been included in the reference sections.

The book is adequately indexed. It would be an asset to institutions indulging in any type of medical research. It is valuable to immunologists, pathologists, pharmacologists, clinicians and veterinary scientists interested in research on inflammatory diseases.

MIRA MOHANTY

Division of Pathophysiology,
Biomedical Technology Wing,
Sree Chitra Tirunal Institute for
Medical Sciences and Technology,
Thiruvananthapuram 695 012, India

A History of Molecular Biology. Michel Morange (Translated by Matthew Cobb). Oxford University Press, YMCA Library Building, Jai Singh Road, New Delhi 110 001. 1999. 336 pp. Price: Rs 495.00

The past 5–6 decades have been very exciting for biologists, thanks to the birth of a new synthetic approach to the study of life processes and an unprecedented rate of growth of this new subdiscipline. This synthetic approach, which resulted from a synergy between specialists in very different branches of science, has generally been designated as 'Molecular Biology'. Although without a clear and generally agreed upon definition, molecular biology has remained the most talked- and written-about subject which most students of biology desire to pursue. Thus, though very young, molecular biology already has a lengthy and complicated history. Several historical accounts have attempted to record the torrents of discoveries in biology that resulted from the molecular biological approaches. Michel Morange's book is one of the latest in such endeavours.

Histories are written post-facto and are essentially personalized interpretations of events in which the writer is generally not directly involved. However, in the case of molecular biology, the situation is different: this field was born and has grown in recent times and the historians of this relatively young but mature field have themselves often participated to varying extents in making the history. Morange is no exception.

The book is arranged into three major sections: the birth, development and expansion of molecular biology. As may be expected from the fact that very diverse areas of scientific enquiries contributed to the birth and development of molecular biology, its history cannot be a simple narration of temporal events where one event leads to the next. The historical narration, therefore, has to follow a criss-cross path. This may make it difficult to read and follow, but Morange has done a good job in tracing some of the more important events and discoveries that gave birth to molecular biology and fostered its rapid growth.

As Morange states 'Molecular biology is a result of the encounter between genetics and biochemistry, two branches of biology that developed at the beginning of the twentieth century'. This encounter was not only catalysed by non-biologists, especially physicists, but they actually actively participated in its subsequent growth. To acknowledge this, Morange has devoted one chapter exclusively to 'The role of the physicists' and another to 'The role of physics'. These 'aliens' to biology contributed substantially in shaping 'modern biology'.