

Wilson, who later went on from Cornell to build the world's largest particle accelerator near Chicago.

Sometimes, characters in a book can wrest the initiative away from the author and shade it in different colour. Perhaps Schweber did not intend it that way, but the two people who emerge as the most heroic characters in the book turn out to be neither Bethe nor Oppenheimer, the former a far too well-centred realist and the latter, a victim of his own moral compromises. It seems to me that the true heroes are two secondary actors in this drama, Bernard Peters and Philip Morrison. I personally found the section of the book dealing with their stories during the McCarthy era the most touching. Peters, a remarkably courageous man who escaped from a Nazi prison camp and crossed the Alps on a bicycle, later worked as a longshoreman in San Francisco before being discovered by Oppenheimer for his physics talents. This very same mentor later described Peters to the House Un-American Activities Committee variously as an intemperate person, 'quite Red' and one who favours 'direct action' – a loaded phrase during the McCarthy period, implying an unconstitutional overthrow of the US government. All this resulted in Peters almost losing his job and eventually having to leave the US. America's loss turned out to be India's gain as Peters then spent several very productive years at our own TIFR.

Philip Morrison was another remarkable person of the times, a brilliant physicist, a scintillating lecturer and among other things, one of the first Americans to walk through the rubble of Hiroshima. I remember sitting riveted in my chair in his classes at Cornell, hanging on to his every word as Morrison, unfazed by a longstanding physical handicap, dominated the classroom with his completely original and inimitable exposition of Statistical Mechanics. He too faced problems with his job at Cornell because of his past links and sympathies with the communists. His letters in response to the President of Cornell during that crisis are models of ethical precision and among the truly inspirational portions of Schweber's book.

This book understandably limits itself to American and European nuclear physicists. But the 'moral responsibility of the scientist' is a far more universal concept. We have much to ponder in our

own country about the moral posture of our scientists. This is not just because we too have gone nuclear. The larger issue (of which the ethics of bomb-making is only one example) is whether our scientists guard sufficiently zealously the values of independent thought and intellectual honesty essential for any form of ethical introspection. In our traditional culture, high academics – the Acharyas and Gurus – are also expected to act as the conscience keepers of society by advising and guiding both their students and their rulers equally fearlessly. One hopes our scientists still view themselves more as such academics rather than as briefcase-toting, jet-setting executives who, for a few crore rupees of grant money, feel no qualms about abandoning their critical faculties.

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There is need, no doubt, to digest the flood of research but when they are too many, it makes it difficult to keep track of even reviews. This is particularly so with a proliferation of review journals, including proceedings of conferences, assorted edited volumes and reviews of limited scope. *Annual Reviews* have traditionally avoided being so and have covered areas comprehensively and with invariably outstanding authors. The effort that has gone into the production of *Annual Review of Neuroscience Volume 24* is underscored by the fact that the team responsible for the contents was set-up in 1998. The canvas is broad; molecular, cellular and systems neuroscience and when you have multiple models and modalities it makes the effort daunting. The editors have achieved a

great synthesis and produced a volume of incomparable value.

Not too long ago neuroscience meant behaviour studies, chemistry of the brain, physiology and anatomy. It is possibly still that, but at a vastly different level of detail and understanding. The literature on behaviour used to be replete with measurements of dubious value, the anecdotal and the birdwatcher's variety. It did not help much with the understanding of the making and working of the brain. When do you learn about the working of an instrument? When you completely design and make it or when it fails and you trouble shoot and over several failures and all possible such you have a fair idea, if you are analytical and arrived at solutions not the style of 'Thuppariyum Shambu'. Evolution has gone ahead and designed brains over a few billion years and so we are left with an option, equivalent of turning on and turning off switches one at a time and retracing connectivity. This is what the tools of behaviour genetics and pharmacology have done and that which now molecular and cell biology is extending with unprecedented analytical vigour. Behaviour is a reflection of the response of cells to the environment it finds itself in. Genetics has turned this around to a precise and analytical area with even complex behaviour like learning and memory now amenable to analysis at all levels. Tools of genetic analysis are the mainstay of about half of the reviews in this volume.

The concluding piece on 'Flies, genes and learning' by Waddell and Quinn in this volume highlights the successes of a quarter century of research with *Drosophila* learning mutants. Flies can learn, remember and forget. Interestingly, while genetics has confirmed some classical models on learning, it has produced some remarkable new insights. Two distinct forms of long-term memory were demonstrated in flies; an unexpected relationship between learning and addictive drug response was also shown. Recent work in Tim Tully's laboratory at Cold Spring Harbor using genetic and molecular tools unique to *Drosophila* has been able to dissociate centres of memory formation and recall. While I was reviewing this volume, there were reports that the molecular machinery controlling addiction has been unravelled in fly mutants at Mani Ramaswami's laboratory at University of Arizona. These reflect the trend in neuro-

sciences, reminiscent of what happened with development biology a couple of decades ago. In fact in the past few years, fly neurobiology has become the most exciting field to be in, basically due to the power of forward and reverse genetic methods.

Twenty years ago a field which had much observation and little insight was chronobiology. We heard with enthusiasm the descriptions of bats taking off 'day after day after day after day after . . .' and how a few microseconds of light exposure synchronized a run-away clock in flies. But every time after such experiments one felt no wiser than after watching an Attenborough (David) movie on animal behaviour; exciting information and no more. For those of us mechanistically minded, the clock seemed like a machinery one could tease apart better than any other. Many looked for oscillators in glycolysis or enzyme cascades. It was left to *Drosophila* and the power of its genetics and behaviour studies to determine the molecular nature of the clocks with mutants aptly named Timeless, Period, Clock and Cycle to obtain analytical insights. Now we have come to a stage when we easily talk of 'circadian rhythm genes'. Mouse genetics has closely followed developments in flies. One can now identify a likely rhythm gene as one that is often transcribed rhythmically, feeds back to regulate its own transcription, with delays (feedback and delays are what everyone looked for in an oscillatory network, but then they looked at a different place!). Ravi Allada *et al.* describe the excitement in the area of genetics of circadian clocks in a succinct fashion.

Quantitative mouse genetics has recently proven to be an ideal model for analysis at the molecular, cellular and systems level, really human attributes like learning and memory, anxiety, seizures, pain and drug abuse. Wehner and others describe the progress in elucidating the genes underlying regulation of quantitative behavioural and pharmacological traits.

It is easily appreciated that during brain development, decisions in one cell will influence decisions in another, much more so than any other organ. Neurotrophins had influenced biology in a rather dramatic manner. A member of this family, NGF, was the first factor shown to be a signal secreted from one cell internalized by another, long before endocytosis and trafficking became fashiona-

ble. Once internalized, it is transported long distances in the recipient to influence its survival. This has become a benchmark paradigm and almost all cells are believed to depend upon neighbours for survival. Now, one talks of cells influencing other cells by an alphabet soup of factors, receptors and mechanisms for trafficking and regulation of gene expression by such factors in several organismal contexts. Huang and Reichardt exhaustively cover this area in an illuminating review. The neurological mutant *reeler* has been with neurobiology for fifty years. Only recently has the central role of the reelin pathway in CNS development, particularly neuronal migration, axonal branching synaptogenesis and pathology begun to be appreciated. Rice and Curran's review is timely. Genetic basis of human brain malformation and insights from such analysis into neuronal migration reviewed by Ross and Walsh exemplifies the power of genetic analysis in neuroscience. Interrelationships among proteins governing migration and process extension represented in a figure in this review, demonstrate this perception clearly.

It is clear that the design of logical units and wiring needs basic understanding of switching properties of component elements, not just elemental composition and details of wiring techniques. The art of living is the adaptation of the cell to respond effectively to the environment and survive. Cell biology is thus the real ultimate quest we must go all-out on, using tools of molecular biology and genetics, chemistry of all sorts and assorted tools of physics. Molecular cell biology has thus substantially replaced neurochemistry. The review by Burns and Denis Baylor on signal transduction in photoreceptor cells is illustrative of the manner in which even an area where there has been a reasonable understanding of the basic processes could benefit from the depth of analysis provided by molecular genetic methods.

If I were asked to choose one sensation which more than anything else defines quality of living, I would go for chemo-sensation. I believe that this is different from any other modality as far as brain mechanisms are concerned, and that chemo-sensation represents, unlike other modalities, an externalization of the same principles that evolved life out of the primordial soup. Molecular interactions from then on preserved through eons for survival of the single cell have found

ways of being retained in this modality. Others when they evolved more at the system's level, the basic sensation here evolved at the cellular level and the system just hijacked the scheme. In some sense I consider chemo-sensation a learnt modality, not an inherent one. Thus attempts at analysis have to take into account that one may find each system, each animal unique in detail. The chemo-sensory receptor story has emerged as the most talked about in months after the review by Caterina and Julius on vanilloid receptors was written. If the theme of the review is 'hot for touch is hot for taste', research in recent months has shown that menthol feels cold because it turns out that its molecular receptor is the one that senses cold.

Analysis of signal processing at higher levels with greater resolution in animals and finally humans will be the goal of future neuroscience. Imaging in animals that are awake has developed into a fine art with new tools. The review by Kauer and White on imaging and coding in olfactory system highlights trends in this area which will have a far greater impact than ever in the years to come. The tools and technology that will get even better are bound to lead to breakthroughs in understanding the living brain in greater depth. One may wire-up a computer but we still need to put in operating systems and software in place for it to function effectively. The physiology of earlier days is being replaced by more integrated imaging techniques and analysis.

It is finally nice to see that even research into the conscious now is quantitative, measurable and recordable. The review by Zeki is illustrative of this; it is simply a marvellous piece, informative and inspiring. In some sense, he further develops original ideas propounded in his book *A Vision of the Brain*. Zeki convincingly portrays the visual brain as an epistemic system, truly ideal for consciousness studies. I have known retired physicists who talk of solitons and consciousness. It was always non-communicative verbiage and wordplay, re-hashing philosophers' well-known paradigms and paradoxes in abstruse of the current. Zeki's review is a pleasure to read and in more or less understandable language, he highlights the significant questions and prospects of elegant research in this area.

As we went from the decade of the brain to the century of the neuron, *Annual Review of Neuroscience* has become sim-

ply large. The publishers might start thinking of splitting it into two or three, say on behavioural and genetic studies, one on cellular neuroscience and yet another on cognitive and systems neuroscience which is perhaps the way it will soon be. But I do hope they do not do so because the charm of *Annual Review of Neuroscience* has been the very breadth of its coverage. I hope they keep up this spirit even when growing. It seems like it took three years in the making and so some reviews are perhaps outdated, but still very useful. It will however be nice to review outstanding research in the calendar year, in addition perhaps to a specific write-up, just to bring to notice a few most outstanding papers and techniques that appeared in neuroscience journals or are relevant to neuroscience in the year or an 'Editors' Choices of the Year' section.

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The era of genomics has brought with it an onslaught of information. It is now up to the biologist to make sense of the reams of computer-generated data that make up the 'Book of Life'. The fast-expanding tome has no chapters explaining how things work at the level of the intact cell or the whole organism. Unravelling these mysteries requires a solid foundation in the basic principles of cell and developmental biology. The 17th volume of the *Annual Review of Cell and Developmental Biology* (2001) with an impressive list of editors, has done a fair job of choosing a varied blend of topics in the field of cell and developmental biology, ranging from the classical problems of cytokinesis, somatogenesis and patterning, to the current trends in stem cell biology.

What has always escaped me when browsing through the *Annual Reviews*, is the reasoning behind the haphazard arrangement of topics and the unwillingness of the editors to group them into categories wherever possible. For example, it would be logical to place chapters on vertebrate limb development, eye development, somatogenesis, left-right asymmetry and patterning sequentially, rather than interspersed with unrelated topics. The same holds good for chapters highlighting the amalgamation of chemical and biological strategies to study a given system, or chapters related to plant biology. Having said that, the content of the individual chapters is generally well-organized and in a format which makes reading enjoyable.

Excellent reviews on some popular topics in cell biology such as 'Animal cell cytokinesis' (by Glotzer), 'How matrix metalloproteinases regulate cell behaviour' (by Sternlicht and Werb), 'Biological basket-weaving: Formation and function of clathrin-coated vesicles' (by Brodsky *et al.*) and 'Getting the message across: The intracellular localization of mRNAs in higher eukaryotes' (by Palacios and St. Johnston) remind one of the awe-inspiring processes within a cell that we understand little about, but take for granted. This feeling is renewed by the chapters on 'Peroxisome biogenesis' (by Purdue and Lazarow) and 'The molecular basis of sister-chromatid cohesion' (by Lee and Orr-Weaver). The account on thrombospondins (by Adams) leaves a lot to be desired as it gives an assimilation of facts and little insight, making it hard to sustain the reader's interest. The chapter on cellular functions of PI3 kinase by Katso *et al.* highlights the importance of studying molecules in the context of normal development as well as in diseased states. Two chapters are devoted to plant development. The review on polarized growth in plants, while adequate, could be made more interesting by a brief comparison to polarized growth in animals. The authors have made good use of illustrations to hold the reader's interest and explain basic concepts and experimental data on seed development.

The inclusion of five chapters on classical problems in developmental biology ('Patterning mechanisms controlling vertebrate limb development' by Capdevila and Izpisua-Belmonte; 'Boundaries in development: Formation and Function'

by Irvine and Rauskolb; 'Early eye development in vertebrates' by Chow and Lang; 'Vertebrate somatogenesis' by Pourquie and 'Left-right asymmetry determination in vertebrates' by Mercola and Levin) reveals how little we know of these basic developmental processes, in spite of decades of analysis. All the five chapters are excellently organized and edited and do justice to the current overload of information available in these areas of research. The limb bud has been a favourite model of developmental biologists for decades because of the ease of manipulating this structure in the chick and the informative assays one can devise to study it. The authors start with a detailed introduction of the model, assimilating a plethora of information available on patterning and finally put it in the context of evolution. This makes an understandably long chapter, which should be of use to the novice as well as the experienced researcher.

The account on early development in vertebrates by Chow and Lang generates interest because, in addition to the expected details on eye development, the authors address the issue of generating two eyes from a single eye field and discuss the conservation of genes specifying eye development between vertebrates and *Drosophila*. The chapter on 'Vertebrate somatogenesis', in addition to discussing more genes and pathways involved in segmentation, introduces the concept of the segmentation clock, which controls the intrinsic determination of the segmentation programme. The book also highlights this emerging concept in developmental biology by devoting a chapter to the 'Molecular bases of circadian rhythms' (Harmer *et al.*).

Cell and developmental biology is no longer the domain of the biologist alone and three chapters highlight the importance of having both chemical and biological approaches to understanding biomolecular function. The chapter on 'Recent advances in chemical approaches to the study of biological systems' by Shogren-Knaak *et al.*, is a good starting point for the reader seeking an introduction to this concept. With several examples of chemical approaches, the authors bring out the shortcomings of classical genetics methods and discuss how forward chemical genetics can be used to overcome these. For example, we learn how protein-protein interactions can be influenced in a controlled manner