astrophysics, gravitational lensing, Kerr–Newman black holes and black hole thermodynamics, cosmological models, the early universe, primordial nucleosynthesis and the formation of light nuclei, finally bringing the reader up-to-date on the theory of inflation, its experimental support and what is known about dark matter and dark energy. The wealth of up-to-date experimental and observational data places the book somewhere between a work of reference and the introductory text it claims to be. For further information, the reader is referred to Narlikar’s other Cambridge University Press volume An Introduction to Cosmology.

It would have been surprising if Narlikar made no reference to steady-state cosmology after delving into the mentioned subjects, but the discussion is limited to five pages; it is clear there is no underlying agenda of challenging the prevailing general Big Bang scenario. All in all, the book succeeds in being clear and concise, while simultaneously leaving out little of importance in the subject. As in the other books, there are many instructive exercises in this volume (the instructors’ job is made easier by password protected solutions to the problems), but a unique feature of Narlikar’s is the large number of solved examples; these will undoubtedly be appreciated especially by beginners. It is a very suitable introduction to the field for an advanced undergraduate or a first-year graduate student.

CHIJAŞ ŞACİLOĞLU
Sabancı University,
Orhanlı, Tuzla 34956,
Istanbul, Turkey
e-mail: sacliloglu@sabanciuniv.edu


The Annual Review of Biophysics has been at the forefront of presenting timely reviews and latest trends in biophysics over the years and the 2009 issue is no exception to this tradition. In recent years, this series has also been able to effectively capture the rapidly changing face of biophysics, and the 2009 issue strongly endorses this aspect. Whereas most of the reviews in this issue are scholarly compilations by leading researchers in the respective fields, some reviews also attempt to propose bold new hypotheses.

Every issue of Annual Review of Biophysics typically begins with an autobiographical sketch of an illustrious person which makes interesting reading. This year’s autobiographical sketch is by a distinguished biophysical chemist, Sumey I. Chan. He takes the readers through a fascinating journey of his growing up in the suburbs of San Francisco in very modest settings, being born to Chinese immigrant parents, having attempted to find Chinese roots of education in Hong Kong, and eventually ending up at the leading schools of UC Berkeley, Harvard and Caltech. This sketch also gives insights into the early evolution of spectroscopic methods, especially nuclear magnetic resonance (NMR), and their application to membrane proteins. There are some interesting anecdotes that a reader would not get to read in a typical research paper. For example, the crystal structure of the membrane bound monoxygenase is that of an inactive enzyme, and consequently the crystal structure does not reveal the trinuclear copper centre, which is an important component of this enzyme’s active site. It is activated by molecular oxygen, which then transfers a singlet oxene to methane at the active site. The author thus highlights a significant message, i.e. the importance of sample preparation, whether for spectroscopic, diffraction or any other experimental analyses, before the experimental measurements are actually undertaken.

Among the contemporary challenges that have arisen due to rapid advances in experimental techniques, is the storage, analysis and management of large data. It is anticipated that this challenge is going to get even more severe in the near future with rapid advances in instrumentation. The article on Bioimage informatics (pp. 327–346) lists some of the issues in management of large imaging data. The challenges are similar to the early days of management of sequence data gathering and storage (e.g. EMBL or GenBank), or the protein databank (PDB). Database managers usually have to deal with numerous file formats, uniformity among different experiments (or lack of it), dynamic and heterogeneous nature of the data, etc. The OME community (Open Microscopy Consortium) has been working towards meeting some of these challenges. In recent years, the consortium has expanded its scope to include data modelling, file format conversions, data management and image-based machine learning. This review nicely captures the efforts that are being made towards meeting the challenges in image informatics. Although the primary target of this consortium is biological microscopists, I wonder if the crystallographers might be interested in similar ideas in gathering and storing raw diffraction images. There has been an increasing uneasiness among crystallographers over the lack of information in the public domain on the early experimental steps before the actual structure determination, and an OME-like consortium might help addressing these questions.

For the practitioners of X-ray crystallography, there are three articles that are of interest. One of them highlights the advances in crystallizing membrane proteins using lipidic mesophas (pp. 29–52). The use of bicontinuous lipid mesophase for crystallizing membrane proteins has emerged only recently, and promises to be an exciting development in membrane protein crystallizations. However, many details about its mechanism are still not clear. The author, Martin Caffrey, attempts to provide a hypothesis on the mechanism of crystallization. Another review of interest to the crystallographers is by Fourme et al. (pp. 153–172), which details advances in high pressure crystallography, especially as applied to protein crystals. The applications of high pressure crystallography to inorganic and small molecule crystals have been in practice for several years. However, instrumentation aspects for similar applications in protein crystallography are not yet optimal. This article describes in detail various issues involved in instrumentation, diffraction data collection and potential applications of this technique to biological problems. This description is useful to those who would like to undertake similar research problems. The authors, however, make certain claims, for example, disassociation of oligomeric proteins, or the shortening of hydrogen bonds under high pressure, which might need better justification before being widely accepted.
The third review of interest to crystallographers is on Structural genomics (pp. 371–384), which provides insights into the methodological developments in recent years in attempting to make structure determinations a high-throughput exercise. Several structural genomics initiatives were undertaken almost 10 years ago, and therefore this article is introspective on the achievements of structural genomics. The article lists the success rate of each of the steps in structure determination, the details which were not available prior to the initiation of structural genomics programmes. However, in my opinion, many believe that these have not enhanced significantly. Despite the great progress made in generating recombinant proteins, faster and automated data collection, and automated electron density fitting, the major bottlenecks in structure determination remain the same as before. Moreover, when the structural genomics initiatives were undertaken 10 years ago, several benefits were envisaged: one of them was to make structures available for enhancing the rates of structure-guided drug discovery. This goal is admittedly nearer after 10 years, but disappointingly yet, there has been no spectacular increase in the evolution of new inhibitors of these proteins. Unfortunately, the authors do not allude to this point in the review. The only reference in this regard that the authors are able to cite is a personal communication from another laboratory. Thus, as the title of the review suggests, the real lessons of structural genomics will start becoming apparent only in the coming few years.

Tremendous advances have been made in understanding the transcription process in eukaryotic as well as prokaryotic cells in recent years. Apart from the high throughput methods which address genome-wide gene expression, the real time analyses have been possible because of the advances in new imaging techniques, emergence of methods to make single molecule and single cell measurements, and by an elegant combination of experimental data with mathematical modeling. The new concepts which have emerged suggest that transcription in a single cell is a stochastic process in general, and that promoter-proximal pausing is one of the rate limiting steps during the entire process. Two well-written articles in this issue highlight progress in understanding these processes (pp. 173–196 and 255–270). The first article introduces the readers to the latest imaging methods and their applications to study dynamics of transcription regulation in vivo, before describing the changes that take place in the organization of chromatin during transcription. There is an evidence in yeast that the genes which are transcribed are localized close to the nuclear periphery upon activation. Authors raise an important question if similar mechanisms might exist in higher eukaryotes. A conclusive proof for the same is awaited. Besides the chromatin reorganization during transcription, imaging experiments have yielded fascinating insights into single gene transcription, especially in bacteria. There appears to be a bimodal distribution of transcription arising out of frequent small bursts, which is equivalent to the resting or the uninduced state; and rarer large bursts of protein production, arising out of induction of the gene. The other fine review in this issue (pp. 255–270) begins where the first one ends, with a nice introduction to stochasticity in gene expression and bursts in transcription. The bursting in transcription has been documented by real time measurements, indicating that switching occurs between inactive and active states of gene transcription, leading to a Poisson distribution of mRNA per cell. The switching ‘ON’ may occur exponentially, justifying the transcriptional burst. The major real time detection techniques that are currently used are described in these articles, and interested readers are strongly encouraged to read both these articles. Indeed, as the authors of the second article state in their concluding paragraph, quantitative data on single gene expression makes the field poised for exciting developments in the coming years.

Another interesting review in this issue of Annual Review of Biophysics is on Amyloid diseases by Hlebda and Miranker (pp. 125–152). The review begins with simple concepts of protein folding and misfolding, the pharmacological consequences of misfolding and describes in detail the amyloid hypothesis. Examples of Type II diabetes, Alzheimer’s disease and Parkinson’s disease are presented to support the hypothesis. Having attempted to convince the readers of the detrimental consequences of protein misfolding and aggregation, the authors then pose a fundamental question – whether the misfolded aggregates themselves are toxic, or is the toxicity due to an hitherto unknown cause? Possible answer to this question is presented in the second half of the review, with a bold hypothesis that toxicity is caused by the amyloid intermediates and not by the aggregated plaques. The intermediates might possibly act in this manner by destabilizing and/or disruption of membranes. The review ends with a hypothetical roadmap towards designing strategies for novel therapeutics.

The expansion of biophysics in recent years has apparently made the task of the editors difficult to include all the contemporary topics. A few exciting topics are therefore left to other sister Annual Review series to be covered; the ones in biochemistry, physical chemistry and genetics also list interesting reviews that biophysicists might be interested in reading.

Shekhar C. Mande
Centre for DNA Fingerprinting and Diagnostics,
Building 7, Gruhalakpa,
5-4-399/B, Nampally,
Hyderabad 500 001, India
e-mail: shekhar@cdfd.org.in