BOOK REVIEWS

Annual Review of Genomics and Human Genetics, 2006. Aravinda Chakravarti and Eric Green (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, California 94303-0139, USA. Vol. 7, 486 pp. Price not mentioned.

The seventh volume of *Annual Review of Genomics and Human Genetics* is an interesting mix of reviews on genomics of human diseases, genome regulation and genome data mining. Victor McKusick recounts what he calls 'This is an account of 60 years' experience in the clinical delineation of genetic disorders, mapping genes on chromosomes, and cataloguing human disease-related genes and genetic disorders'. As a pioneer in human genome mapping and creator of the database 'Mendelian Inheritance in Man (MIM)', he describes his journey from being a premed student in the 1940s to his experience in cataloging human genes and genetic disorders. An ardent supporter of the human genome project, his efforts in cataloguing genetic disorders is unparalleled and forms an integral part of human genome data-mining efforts today.

Genomics of human diseases is an area which has got tremendous boost because of the human genome mapping. The last review in this issue 'Resources for genetic variation studies' by David Serre and Thomas Hudson discusses the implications of genome-wide diversity databases in the context of mapping disease genes. Staying with the theme of human diseases, the reviews on ciliopathies by Badano *et al.* (p. 125), genetic disorders of adipose tissue by Agarwal and Garg (p. 175), and laminopathies by Burke and Stewart (p. 369) have spelt out in detail the various aspects of these disorders. In addition, the review on laminopathies discusses the effect of mutations in *Lamin A* gene. It is interesting to note, especially with respect to genomics, that different mutations in the same gene (*Lamin A*) result in a multitude of seemingly different and unrelated diseases. The review provides an insight into how different tissue-specific diseases arise from unique *LMNA* mutations. In contrast, several different types of diseases such as phenylketonuria, Parkinson's, familial neurohypophyseal diabetes insipidus, and short-chain acyl-CoA dehydrogenase deficiency can have a common framework involving protein misfolding. This and other aspects of protein misfolding have been dealt by Gregersen *et al.* in their review 'Protein misfolding and human disease' (p. 103).

With the completion of the human genome map, the focus is slowly shifting from data-mining to studies on regulation of genetic information, which provides for a plethora of functions in different cells and tissues. The realization is slowly dawning that the environment along with genotype plays an important part in modulating the genotype-to-phenotype correlation. Mackay *et al.* (p. 339) argue for *Drosophila* as a model organism to study that effect of environmental factors in conjugation with genetic factors on human complex genetic diseases like Alzheimer's and Parkinson's and traits like sleep and alcoholism. The human genome project has also revealed the rich diversity in the genetic make-up of individual human beings. In addition to the review by Serre and Hudson on genetic variation (p. 443), genetic variation also forms the basis of two other reviews. One on pharmacogenetics and pharmacogenomics by Weinshilboum and Wang (p. 223), where the authors chart out the history of these disciplines in correlation with the need of developing drugs with therapeutic efficacy catering to individuals rather than the whole population. The second review by Sharp *et al.* (p. 407) catalogues structural rearrangements such as insertions, deletions, etc. present in the human genome.

The theme of genome data-mining continues in several other reviews in this issue. Maston *et al.* (p. 29) discuss the importance of various classes of transcriptional regulatory elements like promoters and enhancers and transcription factors in development and diseases. In 'Genome-wide analysis of protein–DNA interactions', Kim and Ren (p. 81) advocate the use of high throughput techniques like DNA microarray, and chromatin immunoprecipitation for genome data-mining. This review focuses on the technology and methodology underlining these techniques. The authors have also exhaustively discussed the applications of these approaches. Another interesting review of data-mining is on prediction of the effects of amino acid substitutions on protein function by Ng and Henikoff (p. 61), where they discuss not only the various prediction methods to this effect, but also the utility of their prediction for inherited diseases. Steven Jones in his review on 'Prediction of genomic functional elements' (p. 315) has put up a case for automated genome-wide annotation of functional elements in mammalian genomes.

Lastly and perhaps the most thought-provoking is the review on 'Preimplantation genetic diagnosis: An overview of socio-ethical and legal considerations' by Knoppers *et al.* (p. 201). The authors have raised several relevant questions on the selection of human embryos of a particular genotype prior to implantation. In addition, they have tried to familiarize the reader with the various regulatory mechanisms that are operative in this regard in different countries. The editors, Aravinda Chakravarti and Eric Green have collated an engaging mix of reviews that will not only be useful for those in the field of genomics and human genetics, but also a must read for researchers wanting to realize the true potential of the human genome project.

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Annual Review of Biophysics and Biomolecular Structure, 2007. Rees, Sheetz and Williamson (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, California 94303-0139, USA. Vol. 36, 501 pp. Price not mentioned.

One of the most fascinating aspects of the *Annual Review* series is that they have their own publishing house, AR, with a characteristic logo, which brings out timely and well compiled reviews. This volume, close to 500 pages is no exception. On the one hand, there are some long-standing questions in biophysics dealing with macromolecular recognition and specificity, while on the other hand, newer methods are being continuously developed to address these problems at the single-molecule level. Structure–function relationships in proteins have come a long way after the discovery of excellent analytical tools together with rapid development of existing techniques like X-ray diffraction. However, recognition between DNA and protein still generates various arguments, models, mathematical

formulations and an investigator needs to address all these issues in order to come to any meaningful conclusion. However, when one considers a network of interactions, the problem increases manifold. In the present volume, a large number of reviewers (five in all) have dealt with gene expression and network analysis, whereas an equal number of reviews are dedicated to protein structure and function. The other articles can be divided in three groups, namely spectroscopic analysis of protein interaction, membrane proteins and single-molecule analysis of protein and other macromolecules.

In recent years, there has been growing interest in the network analysis of gene expression, i.e. 'Systems biology'. However, a major problem is how to assay and control the switch. Mathematical models have been developed, yet complete description of the control is missing. Haseltine and Arnold claim in their review that modelling identifies mutation targets and limits the evolutationary search space, thus, attempting to integrate modelling with directed evolution. Description of any network has some inherent problems. First, only a part of the network is modelled ignoring long-range interactions. In most cases the control switch connected to the transcription machinery is taken into consideration. However, the continuous changes in environment resulting in discontinuous input flux make any model untenable.

de-Leon and Davidson, review the gene control network and development of an organism. They emphasize in their model the role of interconnected *cis*-regulatory elements, which may be an one-sided view. It is needless to mention that the development process is not merely the interplay among *cis*-regulatory elements. The pictures documented here are of the highest order. In my opinion, this review will go a long way to guide students for taking up active research in this area.

One of the most interesting articles in this series is that by Maheshri and O'Shea, where they recognize the importance to the fluctuations in gene expression and develop some formulations with the help of chemical kinetics. This article considers the expression of genes at a single-molecule level and statistical interpretation of noise. Currently, gene expression is measured with respect to a reporter gene, in this case green fluorescent protein (GFP) or its variants. Here again one wonders the level of changes in GFP fluorescence due to long-range interactions or second-order effects. Thus, interpretation of noise becomes significant and perhaps will lead the way to develop the field in future. There are many attempts now in various other fields to interpret correctly the influence of noise and attempts are being made to generate some patterns in noise analysis. The present article is one such effort. It was stimulating to read a section on protein distribution of single genes and the nature of extrinsic noise (p. 421).

Teachers of molecular biology and gene regulation are familiar with the name of Peter Von Hippel and the large number of papers that came out from his laboratory on operator–repressor interactions. He formulated several new concepts on search mechanism by a protein for its binding site on DNA and these include sliding or one-dimensional diffusion, hopping and interdomain transfer. The other person who has significantly contributed in this area is Tom Record, who applied polyelectrolyte theory to the study of DNA–protein interactions. The article by Von Hippel does not bring out any new concept, but provides good resource material for an overall view.

It is difficult to imagine any treatise on biophysics today without discussing single-molecule behaviour and function. Is the behaviour of an individual molecule significantly different from that when it is part of an ensemble or crowd? Single-molecule fluorescence studies of molecular interactions have been dealt with by some experts in the field; Steven Block's, review is almost entirely based on the work from his group. Toprak and Selvin present a comprehensive analysis of new fluorescence tools which should serve as an excellent introduction for students starting a research career in biophysics.

Other chapters on protein dynamics, protein–ligand affinities, and membrane proteins are well written and I am particularly amazed by one molecular dynamics stimulation of the lipid bilayer (p. 113), which is absolutely fascinating to look at. The printing errors are minimal, but I did find a couple.

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