In this issue

Protein architecture

Proteins perform an exceedingly diverse range of functions in molecular biology. They are the principal actors in the biochemical drama that is enacted in living systems. The functional versatility of proteins is in large measure a consequence of the sophistication of their structural construction. The ability of specific protein sequences to fold into unique three-dimensional conformations, is a property that continues to fascinate structural biologists. Indeed, the 'protein folding problem' is one of the most active areas of research in molecular biology, today. Our understanding of protein structures relies almost entirely on a magnificent body of crystallographic work that has spanned over half a century, with the first successes appearing over three decades ago. Since the determination of the structures of myoglobin and haemoglobin, the wealth of structural detail provided by protein crystallography is astounding. Molecular graphics has made the aesthetic representation of protein structures a reality. It is difficult to imagine, that not too long ago protein models were hideously complicated, ungainly objects put together by painstaking use of molecular models. Today, the shapely curves of ribbon drawings of proteins adorn the covers of many biology journals.

In this issue (**page 85**), John Kuriyan reviews, in personalised fashion, the modular basis of the structures of several important enzymes, whose structures have been recently determined. The enzymes thioredoxin reductase and glutathione reductase share similarities in their functional properties—both are disulphide–dithiol redox enzymes, that require binding of nucleotide cofactors. Despite this similarity their amino-acid sequences are strikingly different. The recent determination of the crystal structure of thioredoxin reductase provides an opportunity to compare in detail the structures of the two enzymes. An analysis of the nucleotide binding domain suggests the possibility of a common evolutionary ancestor. The structural templates which are used for mediating the redox reactions are entirely different. The fact that mechanistic features can be inferred from crystal structures is amply illustrated by the structure of the β-subunit of the DNA polymerase, Pol III. Here, a large hole ($\sim$35 Å in diameter) unexpectedly, provides a clue to the manner of DNA-protein association leading to a 'sliding clamp' model. Despite a limited amount of symmetry in the amino-acid sequence, the structure reveals—high symmetry of super-secondary structure organization, suggesting a modular design theme, probably involving gene duplication events. The structure of the SH2 phosphotyrosine recognition domain provides an example of a eukaryotic 'mobile module' which functions even when isolated from the parent protein. The structure illustrates the precise nature of the phosphotyrosine binding site. However, a more detailed understanding of the molecular basis of signal transduction, must await the determination of the complete structure of the protein tyrosine kinase.

The flood of novel protein architectures is driving structural biology the way of 'pre-Darwinian biology and zoology', with the origins of these structures shrouded in the murky past of evolutionary history. The design principles on which these structures are based are, however, becoming clearer. It will still be a long time before an accurate prediction of three-dimensional structures from protein sequences becomes a reality. Until then studies of protein crystal structures will continue to yield wonderful surprises.

Cell-cycle regulation

Animals start their "life" as a fertilized egg. This single cell then undergoes division to produce two daughter cells that continue this process. This process of cell division goes through a series of steps called the cell-cycle. It is clear that cell division must be regulated to produce the correct numbers of cells in the correct place and time during development. The regulation of cell division is important for unicellular organisms too. The process of generating two daughters with the correct genetic material in each of them must be coordinated with the expression of specific genes that regulate the process of DNA replication and chromosome assortment. The study of cell-cycle has therefore had inputs from diverse fields. Defective regulation of cell-cycle can lead to a cancerous situation. Genes implicated in cancers (oncogenes) have normal functions that range from sensing the environment around specific cells to responding to the environment to finally control genes which have an effect on cell-cycle. Studies on the genetics of cell cycle in the baker's yeast *Saccharomyces cerevisiae* have proved crucial in unravelling the process. The conservation of many of the genes involved in the regulation of cell-cycle across species has been demonstrated by the ability of related genes from other species rescuing yeast mutant defects. In this issue Shanmugam (**page 95**) reviews the current literature in the field and relates the advances made to questions of regulating development.

Extra mural funding of research

Many university departments survive on money from major scientific agencies which fund research in academia under the broad rubric of 'Extra-Mural Research'. When M. G. K. Menon was Minister of State for Science and Technology he found that the major scientific agencies were funding research in the academic sector in a somewhat uncoordinated way with their own norms of funding and different 'admission policies' into their respective Junior and Senior Research Fellowship schemes. Thus, better coordination and coherence in the extra-mural funding schemes of the various agencies, became imperative. In early 1990, following Menon's initiative, an Inter-Agency Committee on Extra-Mural Funding was formed under the aegis of the Department of Science and Technology. The article on **page 76** describes the work of this committee and its recommendations to agencies funding research in the academic sector.