
BOOK REVIEW

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The 56th volume in this series has 29 articles covering a wide range of subjects in Biochemistry with indexes occupying about 10% of the pages.

The traditional first article of retrospection by a biochemist has been written by Konrad Bloch under the title "Summing up". These articles are always educative and tell us how these great, yet modest persons, looked at research. They make us feel that discoveries are simple and can be achieved by proper perspective of the problem, and perseverance. The anecdotes of success and failure are worth reading. Some examples are — the failure to appreciate the decrease in boiling point of acetone at altitudes, serving as an experimental animal in youthful enthusiasm and being left with 2 inch scars, having his Ph.D thesis rejected by the University of Basel for failing to cite references of the examiner, how knowledge to play music on a cello helped in becoming a graduate student. Some statements which are examples of messages with brevity are worth reproducing: "Avoid chemical reasoning for biological activity"; "We must not allow the biogenetic tail to wag the chemical dog"; having received his Ph.D degree 15 years ago, Bloch was told by Ruzicka "Then you no longer know how to do experiments"; "Happily, it was friendly, agreed-upon division of labor, not a race" describing his arrangement with Cornforth and Popjak in the study of cholesterol biogenesis for which he was awarded a Nobel Prize; and a final remark — "Science is indeed a glorious enterprise... and glorious entertainment."

The subjects of glycoproteins and glycosylation are covered in four articles. Recent advances in the application of immobilized lectin columns for the fractionation and structural studies of oligosaccharides and glycopeptides have been reviewed. The topography of N- and O-linked glycosylations in endoplasmic reticulum, much less understood than the Golgi apparatus with respect to movement of nucleotide sugar substrates, is now drawing attention. A whole chapter is devoted for information on inhibitors of biosynthesis and processing of N-linked

sugars, particularly the steps of lipid-linked sugar intermediates such as tunicamycin, of glycoprotein processing and of modifying protein structure and synthesis. The glycoproteins, interestingly compared to chimeras such as centaurs (man/horse) and mermaids (woman/fish), influence a number of biological processes such as cell-cell recognition, hormone-receptor binding, protein targeting, malignant transformation and phagocytosis. Yeast has gained an important status in the studies on expression of heterologous genes, being similar to eukaryotes in metabolic pathways and early stages of glycan processing and studies on the genes and mutants in glycosylation in yeast is given a full chapter.

Membrane studies occupy three chapters. Intracellular movement of lipids — spontaneous, protein facilitated and vascular transport — are the focus of a review on membrane lipid dynamics, distinct from the assembly of lipids into membranes, and concentrated on phospholipids, cholesterol and glycolipids. One omission noted was ubiquinone, which if included, would have brought in work done in India and from our laboratory — now made conspicuous by absence. The process of binding of a haemagglutinin membrane glycoprotein to a sialic acid containing receptor on a target cell to initiate virus-cell interaction followed by a membrane-fusion event that mediates the entry of the virus into the cytoplasm, and the antigenic variation that this glycoprotein, the major surface antigen, undergoes, are dealt with in another chapter. The plasma membranes of target cells provide high-affinity binding receptors for mitogenic peptide growth factors, to help transduce the external signal. Seven such receptors have been described, with epidermal growth factor (EGF) as the major focus. These studies also revealed that signalling mechanisms other than tyrosine kinase are used by these growth factors.

Metabolism and cellular regulation are covered in six articles. A very interesting perspective is brought out on specific interaction between many soluble sequential enzymes of metabolic pathways which underlines a new theme that "few, if any, free enzymes within cells" exist. It is now recognised that proteolytic processing of nascent polypeptide chains accompanies protein synthesis and a review described cellular proteinases, some with large subunit molecular weights of 50000 to 100000, which are varied in

their compositions (glycoproteins, lipoproteins) and requirements (divalent cations, ATP and other small ligands). The four classes of proteinases are localized differently in cells to suit the metabolic needs as given below: serine proteinases — secretory granules; cysteine proteinases — cytosol, lysosomes; aspartic proteinases — endosomes or lysosomes and secretory granules; metallo-proteinases — endomembranes or cytosol. Protein phosphorylation is a major process in regulating cellular functions and signal transduction. An excellent compilation of protein serine/threonine kinases is given which covers a wide variety of such kinases — cyclic AMP/GMP-dependent, phosphorylases, myosin light chain — calmodulin-dependent, calcium-dependent, heme-regulated, double-stranded RNA-dependent, pyruvate dehydrogenase, casein I and II, rhodopsin, beta-adrenergic receptor, HMGCoA reductase, histone H1, glycogen synthase and others. The reviewers found this a very balanced review and would have liked to see an expression of caution on the acceptability of HMGCoA reductase as a kinase, on which doubt exists. Inositol triphosphate and diacylglycerols have turned out to be "preeminent" intracellular secondary messengers, and have overtaken cyclic nucleotides in holding attention in this field. These act through release of calcium and activation of protein kinase C and constitute the two elements of the bifurcating signal pathway which is now well understood for the calcium-messenger system. For its operation, intracellular homeostasis is important, which is achieved through high-affinity binding proteins and transport of calcium by plasma membranes and across intracellular membranes. Receptor-generated signals are transduced through a family of membrane-bound guanine nucleotides-binding proteins, known as G-proteins, which are regulated by binding of GTP, its hydrolysis and release of GDP and also by ADP ribosylation of its alpha-subunit among the heterotrimer.

The structure, synthesis, gene regulation and cellular function of ferritin, with subcellular location in cytosol and lysosomes in vertebrates, vacuoles in insects or chloroplasts in green plants, has been explored. In another chapter the domination of cellular translational apparatus after infection by viruses, and recent work on identification of viral gene products that counter cellular defence normally induced by interferon treatment are discussed. One of the most intriguing and active fields of research is the transport of nascent proteins to the target compartments. The various aspects of this process

are summarized under sections of bulk flow to cell surface, signal-mediated diversion to organelles and reconstitution of transport machinery and studies on its genetics. A comprehensive account on aminoacyl tRNA synthetases, which coevolved with the genetic code and are responsible for fidelity in protein synthesis, is also given. A paradox exists that this class of enzymes with common catalytic features have widely diverse subunit sizes and quaternary structures that have been evolutionarily preserved. The highlight of the findings is the binding of the enzyme "along the inside of the three-dimensional L-shaped tRNA structure". Another chapter deals with the subject of modifications of tRNA and the regulatory roles they play.

Recombination enzymes which exchange DNA sequences between homologous chromosomes are receiving increasing attention. A review considers in detail the products of genes of *recA*, *recB*, *recC*, *recD* and *ssb* (single-stranded DNA binding protein). It is interesting to note that the *recBCD* enzyme uses ATP hydrolysis for the degradation of linear duplex and single-stranded DNA, and for helicase to unwind linear duplex DNA. The *recA* protein (mol.wt.40000) forms a nucleoprotein complex with ssDNA, the "active species in the subsequent phases of strand exchange" which also hydrolyses almost 100 molecules of ATP for each base pair of heteroduplex formed. In another chapter the correction of DNA mismatch arising out of genetic recombination and as a result of DNA biosynthetic errors on the deamination of 5-methylcytosine had been described. One new development to be underscored is the occurrence of alternative splicing of mRNA, as a part of excising the intervening sequences — introns, — from the primary transcript, a necessary process in eukaryotic gene expression, and this process generates protein diversity and in a way increases the coding power of the genome.

The increasing interest in studies on gene structure and activity is brought to focus in eight articles. *Drosophila*'s estimated 5000 genes and 15000 different transcripts are low to explain the complexities of the fly. Molecular studies of its complex loci have revealed three type of complexities: a large array of cis-acting regulatory elements, variable products, and altered gene function. The structure, function and dynamics of the nucleus, the specialized organelle for DNA enclosure in eukaryotes, with emphasis on nuclear transport, composition and regulation of nuclear lamina, chromatin organization and nuclear growth, assembly and disassembly,

have been covered. The hepatitis B virus (HBV), a member of the hepadna virus family, is the causative agent of the infectious hepatitis, whose replication proceeds via reverse transcription of an RNA intermediate, using protein and RNA primers for the generation of first and second DNA strands. One article reviews the recent progress on the genes encoding heavy, light and regulatory chains of myosin, and provides the first complete primary sequences, and also information on the diversity of protein isoforms generated by "alternative RNA splicing" the mapping of specific chromosomal loci for mutations that cause muscle dysfunctions. Large quantities of interferons are now available through recombinant DNA technology and a "scaffold" of the new information during the past five years is presented for the readers to build upon further, on the three classes of interferons (alpha, beta and gamma IFNs) present in all mammalian species which are induced by double-stranded RNA and viruses and exert antiviral activity. This is followed by another specialized article on the gene family "ras", an acronym for rat sarcoma, which gained importance when mutated alleles of these were identified as the transforming genes, or oncogenes, in human tumours induced by carcinogens and by retroviruses, and are now shown to code for proteins that bind guanine nucleotides, to have GTPase activity, and to be associated with plasma membranes, with indications of their participating in signal transduction, cellular proliferation and terminal differentiation. Studies on development and differentiation are directed towards understanding how cells switch from one state to another and how they diversify. Dictyostelium discoideum offers excellent oppor-

tunities for these studies because of its unique developmental cycle with the entire period running in the haploid state, making it easy to detect and to use mutations for analysis of development. A review on the signals including cyclic AMP that control these processes has been included. The final chapter gives a comprehensive account of "P450 genes: structure, evolution and regulation", a field that has "literally exploded". Gene structure and evolution of 10 known P450 gene families are now described and the protein sequences are deduced from cDNA nucleotide sequences. This ancient gene superfamily has expanded via divergent evolution with the ancestral gene (1.5 billion years old) having 22 exons. One of the intriguing questions in this field is whether the P450 enzymes play a physiological role in addition to detoxification, although synthesis and metabolism of cholesterol clearly depend on P450 systems. Product of the P1 450 gene is found to control its own expression as well as two other phase II enzymes. Some of these genes are also shown to be under control of the aromatic hydrocarbon (Ah) receptor, referred to as the Ah gene battery.

It has been a pleasure to read the Annual Review of Biochemistry series. The enormity of information it gives makes it a valuable reference for any biochemistry laboratory. No wonder it is ranked highest among all the scientific journals/volumes for the impact factor.

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ANNOUNCEMENT

NATIONAL SYMPOSIUM ON ANIMAL BEHAVIOUR AND 17TH ANNUAL MEETING OF THE ETHOLOGICAL SOCIETY OF INDIA

The National Symposium on Animal Behaviour and the 17th Annual Meeting of the Ethological Society of India will be held during 3rd, 4th and 5th November 1988 at Bhavnagar, Gujarat. For more

details write to Dr B. H. Patel, Organizing Secretary, Department of Zoology, Sir P.P. Institute of Science, Bhavnagar University, Bhavnagar 364 002.