Book Reviews

Methylation Reactions

Transmethylation. Proceedings of a conference, Bethesda, Md., Oct. 1978. EARL USDIN, RONALD T. BORCHARDT, and CYRUS R. CREVELING, Eds. Elsevier/North-Holland, New York, 1979. xxiv, 632 pp., illus. $55. Developments in Neuroscience, vol. 5.

An extraordinary range of biological molecules are covalently modified by addition of a methyl group donated by *S*-adenosyl-L-methionine. The reaction is involved in the synthesis or metabolism of a number of small molecules, notably some hormones and neuroactive compounds, as well as polyamines. In addition, a variety of nucleic acids and proteins are methylated at specific sites, though with two exceptions the effect of such modifications on the function of the macromolecules involved is not at all clear. In recent years many instances of modulation of the activity of macromolecules by covalent modification have been documented (for example protein phosphorylation). It appears that covalent alterations may be as prevalent as allosteric interactions in regulating the activity of nucleic acids and proteins, and the numerous examples of methylations to which no biological function can be assigned pose the tantalizing possibility that there are whole classes of methylation-related control mechanisms that have not yet been discovered.

Thus the present volume should be of interest to anyone studying regulation and control of activity at the molecular or cellular level, as well as to those already engaged in investigations of transmethylation. My own interest in the subject arose only recently, and as a new student of methylation I can recommend the volume as a good introduction to the field.

The book begins with sections about the chemistry and biochemistry of *S*-adenosylmethionine and *S*-adenosylhomocysteine, a product of the transmethylation reaction, and continues with considerations of specific methylations of small molecules, nucleic acids, and proteins, respectively. In general, the order of the subjects corresponds to the amount and sophistication of knowledge about them.

Perhaps the most exciting reports are descriptions by Cantoni and others of enzyme inhibitors that indirectly block methyltransferase activity and the effects of those compounds on cellular activities that are suspected to involve methylation reactions. The inhibitors appear to provide a simple way to investigate whether a cellular function is perturbed by the absence of methylation activity. They should be of great utility in initial survey work aimed at relating a particular function to a methylation.

Only in the case of methylation of bacterial DNA by restriction/modification systems is the purpose of a specific methylation of a nucleic acid understood. The situation is not any better for *N*-methylation of proteins. For example, some histones and ribosomal proteins contain methylated lysines or arginines, but the functional difference between the modified and unmodified proteins is unclear. It is only in the case of protein-carboxyl methylation that some functional correlations are available. Direct genetic and biochemical evidence, summarized in this volume by Adler and by Stock and Koshland, demonstrates that carboxyl methylation of certain cytoplasmic membrane proteins is intimately involved in bacterial chemotaxis. Protein-carboxyl methyltransferases are present in many mammalian tissues, with high activities in endocrine organs and certain areas of the brain. There is a growing body of evidence, some of it reported in this volume, suggesting that protein-carboxyl methylation is related to receptor-mediated responses in a number of cell types known to contain the relevant enzyme.

Another type of activity-modulating methylation is reported by Axelrod's group. They find that a methylated intermediate in phospholipid synthesis and transport affects membrane fluidity and that the level of the compound is hormonally influenced. Fluidity changes in turn can alter receptor-effector coupling.

The examples cited here indicate the variety of methylation reactions now being studied. For those who are interested in more detail as well as those who think there might be a methylation in their future, I suggest *Transmethylation* as a useful guide and reference.

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Recently Discovered Pathogens

Viroids and Viroid Diseases. T. O. DIENER. Wiley-Interscience, New York, 1979. xviii, 252 pp., illus. $19.95.

Viroids must certainly be close to the minimal size for a replicating infectious agent. These small RNA molecules, composed of only about 350 nucleotides, are less than one-tenth the size of the smallest known virus, yet they can induce severe diseases of economic significance in a number of plant species. Seven apparently distinct viroids have been described to date, and several other plant diseases have possible viroid etiologies. Suggestions have been made elsewhere and in this book that certain subacute spongiform "virus" encephalopathies of mammals (scrapie, kuru, transmissible mink encephalopathy, Creutzfeldt-Jakob disease) may be caused by small etiologic agents similar to viroids, although no firm proof exists for such a postulate. There is some evidence that the scrapie agent is a small piece of DNA.

This topical book is the first comprehensive review of the subject. Diener, who co-discovered viroids and coined the name of this class of agents, presents a compilation of the viroid literature, starting from studies of viroid diseases during the period when they were presumed to be caused by viruses, leading up to the realization in 1971 that the infectious agents were distinct from viruses, and going on to studies of the viroids themselves. The discovery that viroid diseases had unique etiologic agents came about during attempts by Diener and his colleagues to purify the "virus" of potato spindle tuber disease and, independently, during work with the exocortis disease of citrus by a group led by J. S. Semancik. In both cases no virus particles could be found, and the infectious principles in tissue extracts exhibited properties that were unlike those of conventional viruses but that might have been expected for small unencapsidated nucleic acids.

Acceptance of the concept of viroids did not come readily, particularly among animal virologists. Were these small agents really split genome viruses composed of a mixture of RNA molecules of different composition but of the same size? Were they defective or satellite viruses that required a helper virus already present in the plant? These and other notions have been shown to be untenable, and the concept of viroids has become established. The complete nucleotide sequence of infectious potato

spindle tuber viroid, published recently by West German scientists, has given credence to the idea of the small infectious RNA molecule. Interest in viroids is now directed toward unraveling the mechanism of their replication and determining how they cause disease. They apparently do not code for proteins, and thus their synthesis must be completely dependent upon host enzymes. The only proven viroid-coded product is a complementary RNA, suggesting that viroids have an RNA-directed replication, although there is some evidence that indicates possible DNA involvement.

In this book, the descriptions of the techniques used in viroid studies, the investigations concerning the nature of the agent, and so on are drawn from studies in Diener's laboratory, with work in other laboratories used largely as confirmation. The literature coverage is therefore not altogether evenhanded, but the book does collate useful information on the host ranges of several viroids, and it gives detailed procedures for the experimental transmission, bioassay, isolation, and purification of viroids.

In the final chapter, "Nature of viroids," Diener presents the interesting speculation that "viroid diseases of cultivated plants are of recent origin." He stresses that the diseases have only come to notice over the last 60 years, with one recognized as recently as 1974. It is probable that the spread of viroids is a consequence of human cultural practices; viroids, unlike conventional plant viruses, have no known insect vectors. Humans are the vectors. Thus viroid RNA's, which conceivably could derive from normal host-cell RNA, probably exist in many plant species without causing disease, but when they are inadvertently transferred by humans to particular cultivated plants a disease may develop.

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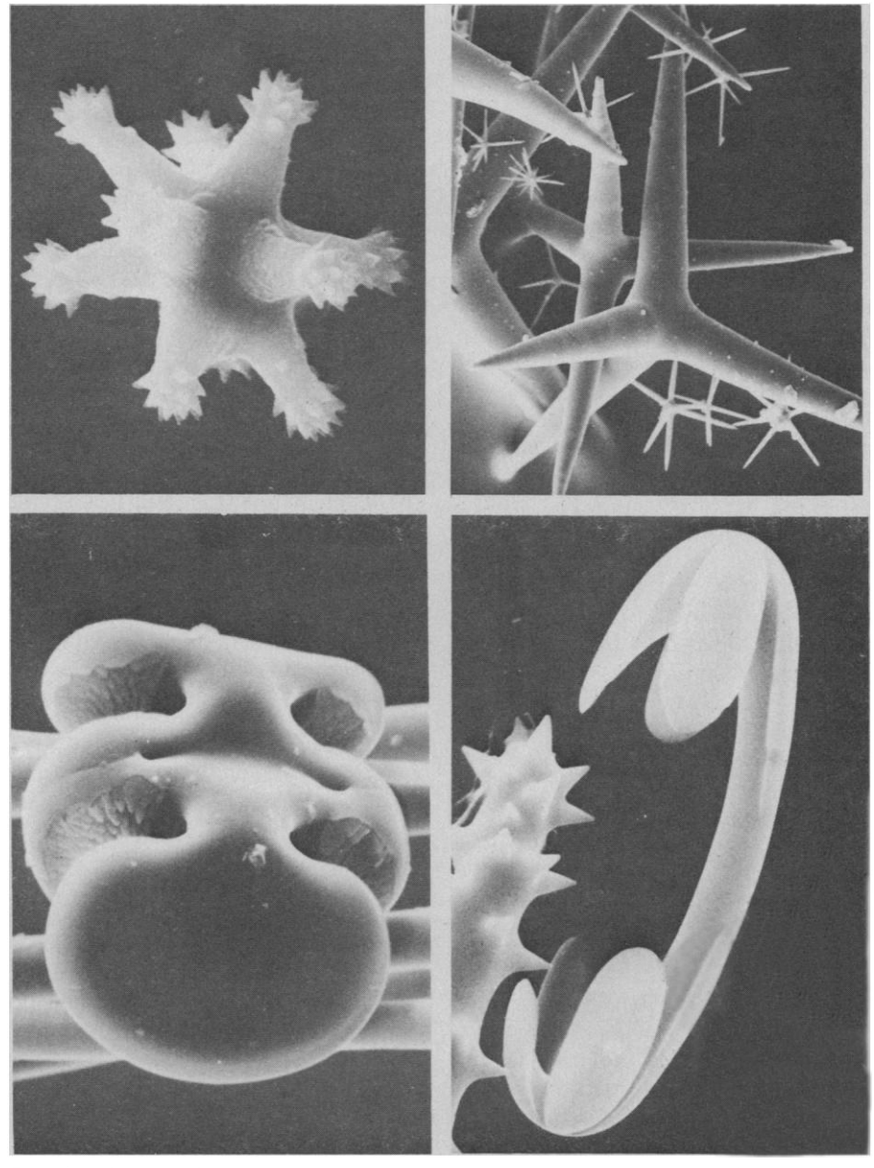
Porifera

Sponges. PATRICIA R. BERGQUIST. University of California Press, Berkeley, 1978. 268 pp., illus. + plates. $25.

Research interest in the Porifera has been growing steadily in both depth and breadth in the last two decades. Basic new information of many sorts has been brought to light by several active groups of workers in Europe, North America, and the Antipodes: findings concerning basic physiology and cellular recognition systems, identification of unique bioactive products, paleontological discoveries, and recognition of new major taxa. Bergquist has successfully integrated most of these advances in this first comprehensive review of sponge biology to appear in English since Hyman's now-outdated 1940 classic in volume 1 of *The Invertebrates*.

Bergquist develops two important themes. The first is the unique organizational characteristics of sponges, their morphological plasticity as individuals, and the persistence of cellular mobility and differentiation potential through adult stages. She maintains appreciation of this dynamism in outlining the special problems encountered in attempting to use research approaches that have been successful with other metazoans in research on sponges. Lack of understanding of the special features of the group on the part of many early workers has been the single most important cause of erroneous or worthless research results, and Bergquist's cautions for prospective research workers cannot be overemphasized.

Bergquist's second theme is the importance of taxonomists in studies of sponges—both in planning of comparative research projects and in developing



Scanning electron micrographs of some representative sponge spicules. (Top left) An asterose microsclere from a species of *Tethya*. This spicule has a pronounced core or centrum and many short rays each with a terminal cap of spines. (Top right) Tetraxon megascleres (calthrops) and asterose microscleres of an undescribed genus of the Choristida (Calthropellidae). The calthrops megasclere is typical of this order. (Bottom left) A bizzare type of cheloid microsclere as seen in *Tetrapocillon*. (Bottom right) A typical arcuate isochela as seen in *Ectyomyxilla*. Portion of a spiny (acanthose) megasclere, an acanthostyle is also shown. [From *Sponges*]