Hybrid sterility is often merely a consequence of mispairing of chromosomes: this aspect of speciation, then, will surely require merely an understanding of the molecular basis of chromosome pairing. Chromosome pairing may or may not be affected by repeated sequences, but it will almost certainly prove susceptible to a reductionist, rather than holistic, interpretation of the genome. And it is certainly possible (see M. Nei, in *Population Genetics and Ecology*, S. Karlin and E. Nevo, Eds., Academic Press, 1976) to develop simple models of genetic divergence that account for inviability or failure of gametogenesis in hybrids. Often, as Templeton notes, only a few segregating units participate in postzygotic incompatibility. Thus, rather than search for the basis of incompatibility in the integration of the whole genome, we need to model, and especially to identify at the biochemical level, critical developmental pathways in which incompatibilities arise in consequence of simple genetic changes. Neither the reductionist models of population genetics nor those of biochemistry figure prominently in this volume, but it is in such models that progress in speciation theory undoubtedly lies.

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Biological Chemistry

Stereochemistry. CH. TAMM, Ed. Elsevier, New York, 1982. x, 342 pp., illus. $65. New Comprehensive Biochemistry, vol. 3.

This volume is a collection of seven chapters of nearly equal length devoted to aspects of stereochemistry especially relevant to biochemistry and molecular biology. Each chapter has an extensive list of references, generally to work published in the 1970's; some references to papers published in 1980 and 1981 are included. The book contains a large number of carefully prepared and informative figures.

In an introductory chapter B. Testa outlines the basic principles and defines the nomenclature that can be used to describe the geometry of biochemical substrates. In addition to the conventional classification of isomers with contrasting molecular geometries as enantiomeric and diastereomeric stereoisomers, Testa describes the isomeric classification proposed by Mislow that is based upon the nature of the interactions of all atoms in a molecule, bonded and nonbonded. This analysis emphasizes the correspondence that exists between atoms in diastereomeric stereoisomers and in constitutional isomers. Since isometric comparisons are an important feature in biological stereoselectivity, their introduction in a book directed to biological scientists should be valuable. The chapter also clearly defines such terms as "chiral," "prochiral," "asymmetric," "dissymmetric," "enantiotopic," and "diastereotopic" groups and faces, symmetry planes and rotation-reflection axes, and chiral planes and axes. In addition to the customary stereochemical descriptions of tetrahedral centers, Testa introduces the stereochemical implications of pentacoordinate and hexacoordinate centers. Basic stereochemical nomenclatures (R, S, pro-R, pro-S, and so on) used to describe stereoisomers and stereoheterotopic groups are defined and illustrated.

Testa emphasizes that conformational isomers and configurational isomers are defined by differences in the energy barriers that separate the differing molecular geometries, configurational isomers being separated by "high energy" barriers and conformational isomers by "low energy" barriers. Therefore, in contrast to the sharp intrinsic division between enantiomers and diastereomers, the division between conformational and configurational isomers must allow for overlapping designations. A significant portion of the chapter is devoted to conformational isomerism, in both acyclic and five- and six-membered cyclic systems. Testa analyzes differences in the barriers to rotation about differing bond types (carbon-carbon and heteroatom-heteroatom single bonds and so on) and considers the process of heteroatom inversion upon the interconversion of conformers.

In a second introductory chapter R. Bentley illustrates how the basic concepts and terminology described by Testa can be applied in analyses of biochemical systems. In a description of the historical development of this field, Bentley makes the interesting observation that a "three-point attachment" mechanism to account for the differentiation of enantiomers by drug receptors was proposed by Easson and Stedman in 1933, 15 years before Ogston used a three-point attachment to illustrate how enzymes could differentiate between the enantiotopic *a,a* groups of a C_{aabc} center. Bentley also emphasizes the important point that actual three-point attachments are not required for differentiation between enantiomeric molecules or enantiotopic groups. What is required is the possibility of creating diastereomeric relationships. Thus, three-point attachment should be considered part of a convenient diagram, not a stereochemical principle.

Bentley illustrates various chemical and biochemical procedures that have been used in investigations of stereoselectivity. For example, the interconnecting experiments and methodologies used to establish the stereoselectivities of citrate biosynthesis, the stereoselectivities of various dehydrogenases toward the diastereotopic 4′-hydrogens of NADH and NADPH, and the stereoselectivity of malate synthetase with respect to acetyl substrates with chiral methyl groups are all reviewed in detail.

Chapters by H. G. Floss and J. C. Vederas on reactions catalyzed by pyridoxal phosphate, by P. A. Frey on enzyme-catalyzed substitutions at the phosphorus atom of phosphates, and by J. Rétey on reactions involving vitamin B_{12} effectively build upon the foundation developed in the introductory chapters. The chapter by Floss and Vederas comprehensively reviews the experiments that have established stereoselectivities for each class of reaction mediated by pyridoxal phosphate. These data are analyzed in terms of the proposals of Dunathan, that the bond to be cleaved will be oriented perpendicular to the plane of the conjugated π system of the pyridoxal moiety and that the binding sites for the pyridoxal phosphate cofactor of all enzymes are derived from one primordial enzyme, thereby creating a common structure and resulting in reactions upon a single face of the bound cofactor. The extensive experimental evidence supporting these proposals and the limited results in apparent conflict with them are both critically evaluated. The chapter by Frey describes the methods that have been used in the stereospecific syntheses and stereochemical analyses of substrates with chiral phosphate groups. Representative studies are then described that establish the stereoselectivities of four different classes of enzymes, phosphohydrolases, phosphotransferases, nucleotidyltransferases, and ATP-dependent synthetases. The results are interpreted in terms of stereochemical evidence for single-displacement or for double-displacement, Ping-Pong, mechanisms. The chapter by Rétey consists of a review of the stereochemical course of coenzyme-B_{12}-catalyzed rearrangements and a summary of the stereoselectivities manifest in the biosynthesis of

vitamin B_{12}. The detailed discussion of the B_{12}-catalyzed rearrangements is especially significant to a comprehensive understanding of biological stereoselectivity. The analyses of reactions catalyzed by diol-dehydrase and ethanolamine ammonia lyase emphasize that a given enzyme is capable of catalyzing reactions with different substrates via pathways that produce differing stereochemical results. As Rétey concludes, "The stereospecificity of most enzymes is based on the ability to differentiate between enantiotopic (or diastereotopic) faces or groups in metastable intermediates." Though this statement could serve as a conclusion for the book, other features of Rétey's chapter demonstrate some deficiencies of the volume.

Although the authors apparently read each other's manuscripts, it seems that the contributions were not modified as a result. For example, even though the introductory chapter describes the prochiral, H_S, H_R nomenclature of Hanson, Rétey chooses to use the H_{Re}, H_{Si} nomenclature of Prelog without explanation or definition. Furthermore, Rétey does not refer to Testa's extensive treatment of rotational barriers during his discussion of how "metastable trigonal intermediates" can result in the loss of enzymatic stereospecificity. Similarly, in a chapter on the stereochemistry of vision V. Balogh-Nair and K. Nakanishi do not utilize Testa's introduction of conformational equilibria even though a significant portion of their discussion examines the possibility that a *cis-trans* isomerization of retinal can be the primary event in vision. In a chapter on the stereochemistry of dehydrogenases J. Jeffery refers to the "belief" that (*R*)-[2-^{2}H]succinic acid is levorotatory even though in the previous chapter Bentley describes the stereospecific reaction sequence that was used to establish this correlation. Jeffery also refers to an enzyme in which the "stereospecificity" may not be "complete," although Bentley's chapter contains an extensive discussion of the various uses of the terms "stereospecific" and "stereoselective" and ends by recommending that biological processes be referred to as stereoselective, with qualifiers added when appropriate.

Scientists with an interest in stereochemistry, especially in biological stereoselectivity, will certainly want a copy of this volume in their libraries. Each of the chapters is a current review containing important information. It is unfortunate, however, that the book was not edited to provide a more consistent treatment. Though some of the inconsistencies may be dismissed as trivial the value of carefully defining stereochemical nomenclature or terms such as stereoselective is questionable if even one's coauthors fail to incorporate these concepts into their presentations.

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Synaptic Vesicles

Neurotransmitter Vesicles. RICHARD L. KLEIN, HUGO LAGERCRANTZ, and HERBERT ZIMMERMANN, Eds. Academic Press, New York, 1982. xvi, 384 pp., illus. $61.50.

It is hard to imagine the study of oxidative phosphorylation had no one isolated the mitochondrion, or of signal peptide recognition without stripped microsomes, or of breakdown processes without purified lysosomes. For many biological phenomena a crucial subcellular organelle has had to be isolated to allow further advances. The synapse has such organelles, the characteristic synaptic vesicles that cluster inside the presynaptic nerve terminal. Many hope that isolating and characterizing the synaptic vesicle will guide them to the molecules involved in synaptic transmission and to their functions.

Synaptic vesicles are identified biochemically by their high concentrations of neurotransmitters. The properties of three types of vesicle, those containing catecholamines, acetylcholine, and the hormones oxytocin and vasopressin, are detailed in *Neurotransmitter Vesicles*. By collecting information from quite diverse systems in one source the seven authors have generated a volume of considerable value. One is struck by how universally the authors stress the pitfalls of identifying true but minor vesicle components in vesicle fractions that must be at best only about 90 to 95 percent pure. The need for care in such cases should be self-evident but is not, as the authors point out. The authors note that when vesicles are isolated and characterized with some rigor incredibly high concentrations of transmitter are found inside them. Estimates of 50 to 100,000 molecules of acetylcholine per electric organ synaptic vesicle translate into internal concentrations of 0.5 to 0.8 molar. The norepinephrine concentration in large dense-core vesicles is about 0.2*M*, and there are about 1.8×10^5 molecules of oxytocin and neurophysin per vesicle in the posterior pituitary. Also remarked upon in the book is the simplicity of the vesicle membrane itself, at least in cholinergic vesicles, where the lack of protein contents allows more ready characterization of membrane protein constituents. Having few proteins, the membrane has one of the highest lipid-to-protein ratios in a biological membrane. Such simplicity is perhaps expected in a membrane with only two major functions, packaging transmitter and fusing with the plasma membrane.

Perhaps the most unexpected generalization to come from this juxtaposition of biological systems is that nerve terminals are not restricted to one type of synaptic vesicle. Cholinergic terminals can contain a subpopulation of vesicles, smaller and denser than the average, into which transmitter is more readily packaged. In the adrenergic system there are two types, large and small dense-core vesicles. Only the large vesicles have the enzyme dopamine beta-hydroxylase associated with them. Consequently the large but not the small vesicles can fill with norepinephrine when incubated in dopamine. Finally, labeled oxytocin and vasopressin first appear in dense granules in the nerve terminal, but with time these granules become less dense and osmotically fragile. Since they move to a new nerve terminal region rich in lysosomes it is possible that these vesicles are targeted for destruction, the phenomenon of crinopathy. These findings help resolve old conflicts and offer important insights into mechanisms.

The reader might wonder why only three types of neurotransmitter are discussed. The fault does not lie with the authors. Synaptic vesicles containing gamma-aminobutyric acid or the amino acid transmitters, for example, have remained elusive. As the book emphasizes, even cholinergic synaptic vesicles have not yet been isolated from brain with sufficient purity to allow decent characterization. The need here is obvious, and the prospects for rapid improvement are good, now that antibodies are available that are directed at the cytoplasmic face of vesicles. Unfortunately, since the literature review for this volume appears to end in mid-1981, recent advances in vesicle isolation by immunoadsorption are not discussed.

Reading the volume reinforces the prejudice that the best in this field is still to come. The major questions remain. How do synaptic vesicles package? How do they migrate down the axon? How do they dock and fuse with the plasma