mixture synthesis, emphasizing non-peptide approaches. Many of the methods discussed in this chapter have their roots at the beginning of combinatorial chemistry, such as Houghten's tea-bags, Geyson's pins, or Furka's split-mix method. Kiely maintains that deconvolution of mixtures "remains a robust and highly useful" method, and he provides three answers to the question, "Why mixtures?" First, current robotic synthesis of single compounds can not keep up with high-throughput screening. Second, the use of mixtures to find individual pure active compounds is well-precedented (cf. natural products). Finally, sometimes the biological target is in short supply, and it is desirable to minimize the number of assays. The second chapter, by Sarshar and Mjalli (Ontogen Corp.), reviews various techniques for synthesis of individual pure compounds—"singles." The next chapter, by Hall (Sphinx Pharmaceuticals), provides an overview of advances in solid-phase synthesis. He describes the state of the art and mentions the fact that most reactions are carried out on only two solid supports—cross-linked polystyrene (Merrifield resin) or Tentagel (a PEG-modified polystyrene). He discusses the use of linkers and describes solid-phase variants of many well-known name reactions. The chapter by Sucholeiki (Sphinx) details selection of commercially available solid supports and provides much useful data on physical properties of resin materials, including swelling and loading. Next, Coe and Storer (Glaxo) discuss solution-phase synthesis of compounds such as methods that employ soluble polymeric supports, dendrimeric solution-phase arrays, and other techniques. Mention is also made of the latest novel method—flourous-phase synthesis. The next chapter, by Fitch (Affymax), reports on analytical chemistry of combinatorial library synthesis. While product cleavage and off-bead analysis are widely used, measurement of yields by gravimetric methods is recommended by Fitch, based on experience at Affymax. The chapter also reports examples of on-bead spectroscopic methods such as IR, NMR, and ^{13}C NMR. A survey of the great advances in LC/MS techniques leads to a warning: "...there is no excuse for not fully characterizing compounds made by parallel synthesis". The assumption in this statement by Fitch is that mass spectrometry actually provides full compound characterization. It is widely known that this is not the case. In the next chapter, Dewitt (Diversomer Technologies) surveys the field of automated synthesis. Finally, the chapter by Patel (Versicor) discusses actual applications of combinatorial chemistry in drug discovery. Patel surveys both synthesis and screening and leaves the impression that diverse chemistry provides promising biological results.

The second major section is titled Combinatorial Biology and Evolution. The five chapters in this section provide an interesting collection of reviews on the more biological approaches to combinatorial chemistry. The first chapter, by Levitan (Santa Fe Institute), discusses both biological strategies for molecular diversity and information theory, as well as concepts underlying the application of such techniques to discovery. This is followed by a chapter by Schuster (Universitat Wien and Santa Fe Institute) that reviews the principles of evolutionary biotechnology. The following chapter by Ellington (Indiana University) continues with an excellent description of biological approaches to molecular evolution. The concept of "fitness landscape" for evolution and in vitro selection is very nicely described. The relationship of genetic diversity (random synthesis of DNA) and methods for the selection of compounds are examined; molecules that bind suitably to a receptor are allowed to "breed", for example, by PCR, which can amplify by a factor of 1 000 000 the desired molecule in a single generation. The next chapter, by Lam (Selectide), describes the solid-phase synthesis of peptide libraries by split-mix techniques. This topic examines a subject which truly is the roots of combinatorial chemistry. Lam makes a good case that the future for synthetic peptides is still bright, since many natural ligands are peptides. The final chapter in this section is an excellent review of phage display. Collins (Braunschweig) describes phage display in the context of the concepts of molecular diversity. He clearly presents the technique in comparison to organic chemistry methods. Collins describes the presentation of millions of ligands on the surface of a bacteriophage, the use of affinity selection techniques (called "panning") to concentrate the best specific binding clones, and finally sequencing of the consensus motifs and even model building to provide insights on the final structure. This chapter is long (52 pages with 255 references) and is quite comprehensive.

The final section, Informatics and Related Topics, is a collection of seven diverse topics: databases, high-throughput screening, deconvolution methods, combinatorial patent strategies, combinatorial business alliances, the promise of combinatorial chemistry, and a compendium of 643 solid-phase synthesis references. While these sections are not as detailed or comprehensive as those of parts I and II, they are filled with interesting tidbits. The penultimate chapter of the section is called Combinatorial Chemistry—Promise Fulfilled? This chapter is a teaser for the next volume of this series. The author claims: "The future versions of this section will provide the answer to this question."

In conclusion, this review volume is very worthwhile for all practitioners of molecular diversity: chemists, biologists, theoreticians, and even business types. One's first impression is that Volume 1 may be the best of the series. It will be interesting to see if the editors can continue to maintain such a meaty series. It may be largely determined by the efforts of scientists around the world who are discovering, developing, and publishing new advances in the fields of combinatorial chemistry and molecular diversity. In conclusion, I recommend this book to everyone with an interest in combinatorial chemistry and molecular diversity.

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Purinergic Approaches in Experimental Therapeutics. Edited by Kenneth A. Jacobson and Michael F. Jarvis. Wiley-Liss, New York. 1997. xiv + 581 pp. 16 × 24 cm. ISBN 0-47114071-6. $89.95.

Research in the area of purine and pyrimidine nucleosides and nucleotides in this decade has entered a new phase due to the increase in understanding of the adenosine (P1) receptors and several known and new nucleotide (P2) receptors, partially through cloning and expression. This book is a collection of articles summarizing the most recent understanding of various facets of purinergic research by some of the leading researchers in the field. A total of 28 articles are distributed into four parts in the book. Seven of these cover historical perspective, molecular pharmacology, and medicinal chemistry of nucleosides, nucleotides, and their receptors. The remaining articles cover a variety of physiological and therapeutic implications of activation or inhibition of the P1 and P2 receptors. Although the subject matter of a number of articles in the book is covered in review articles published in the literature, this book compiles these and several other important articles with up-to-date references on purinergic research and serves as a guidebook of the most recent understanding and bibliography in this field of research.

The article on historical perspective provides a brief overview of the research findings on P1 and P2 receptors and their ligands. An excellent summary of the receptor cloning and pharmacology of the P1 receptors and the role of adenosine as an inhibitor of excitotoxic neurotransmitters and in ischemia, inflammation, asthma, epilepsy, and nociception is provided with the most current literature references (Chapters 2, 8, 15−17, 19, and 25). Unlike the research on P1 receptors, that on P2 is relatively new, and therefore, fewer sources provide a collection of research articles on the topic. This book is one of a couple of sources available today on the topic of nucleotide receptors and their function. The structure and function of P2Y receptors is nicely summarized; however, that on P2X is missing (it has been described partially in the article on ATP in Brain Function). The potential role of P2 receptor modulating agents in the treatment of thrombosis, diabetes, and cancer is described clearly (Chapters 11, 13, and 28), while that on complications of the respiratory system (Chapter 18) is less-focused. The chapters on the medicinal chemistry of agents that modulate the P1 and P2 receptors and levels of adenosine are succinct, yet rich in bibliography.

The index has been written thoroughly and was found to be very useful in accessing subject matters quickly. Although the book is slightly expensive, it is a useful addition to one's collection of sources providing valuable information, summary, and bibliography.

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