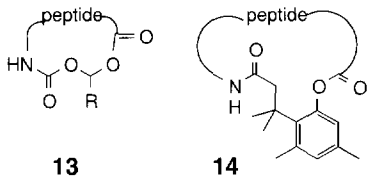
Prodrugs

Professor D. Crommelin (University of Utrecht, The Netherlands) reported on the use of liposomes as versatile colloidal carrier systems for the delivery of peptides and proteins. Liposomes are advantageous in having low toxicity and in their ability to provide an internal aqueous medium for the encapsulated drug. His group has found evidence for the accumulation of such liposome carriers at diseased sites such as tumour cells and inflammation. Therefore these compounds have potential use as homing devices that can be used to deliver drugs to a target site.

Dr Gangwar and coworkers (University of Kansas, KS, USA) have improved the metabolic stability of peptides by synthesizing esterase-sensitive prodrugs **13** and **14** (Figure 3). Both prodrugs can mask a peptide against metabolic degradation by peptidases and increase permeation through biological membranes. Degradation of these prodrugs is catalysed by esterases.



13 **14**

Figure 3. *Esterase-sensitive prodrugs for peptides.*

Dr R. Cecchelli and coworkers (Serlia, Lille, France) have developed an *in vitro* system for studying the blood–brain barrier. A model of the endothelial–glial interface has been set up *in vitro* by coculturing brain capillary endothelial cells on one side of a porous filter and astrocytes on the other. Permeability of a variety of drugs through the *in vitro* system showed good correlation with results determined *in vivo*.

Over 300 posters were presented, and awards were given to the following: Professor R. Ganellin and coworkers (University College, London, UK) *Rational Design of Butabindide, The First Inhibitor of the Newly Identified Cholecystokinin-Inactivating Peptidase*; Dr C. Sahlberg and coworkers (Medivir AB, Huddinge, Sweden) *Synthesis and Anti HIV-1 Activities of Urea-PETT Analogues Belonging to a New Series of Potent Non-Nucleoside HIV-1 Reverse Transcriptase Inhibitors*; Dr W. Tögel and coworkers (Freie Universität Berlin, Germany) *Guanidines and Related Compounds With Direct G Protein Stimulatory Activity.*

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Book reviews

Computer Modelling in Molecular Biology edited by Julia M. Goodfellow, VCH, 1995. DM 178 (300 pages) ISBN 3 527 30062 7

The preface of this book states that it is intended to provide 'a series of snap-shots of the use of molecular simulation techniques to study a wide range of biological problems.' As such, it should not be viewed as a textbook or a systematic treatment of molecular modelling. Rather, the editor has assembled seven chapters, each covering a different topic, in addition to a brief general introduction. The topics include: modelling protein structures, molecular dynamics simulations on small peptides, molecular dynamics and free-energy perturbation calculations applied to barnase, molecular dynamics simulations applied to nucleic acids, molecular dynamics simulations applied to ion channels, modelling of major histocompatibility complex (MHC) protein–peptide interactions, and modelling of conformational transitions in large molecules. Obviously the particular choice of topics reflects the bias of the editor and the other contributors, but it is representative of the kind of computer modelling that is prevalent in molecular biology, and it does indeed provide a 'snapshot' of the field.

Each chapter is systematically laid out, covers its material thoroughly, and is well supported by figures, graphs and tables. All chapters are also well-referenced. Unfortunately, the references stop in 1993, suggesting that this book has taken too long in production. Most of the chapters describe one particular application of a computational method; other important applications of that method are not discussed. For example, the chapter on free-energy perturbation simulations only describes the application of those simulations to the enzyme barnase. The final chapter, which describes a new method for simulating conformational transitions in large molecules, such as proteins, seems slightly out of place. While interesting to those with a serious interest in the development of novel computational methods, this chapter is likely to be of less interest to the general reader.

The book has a continental flavor, with all but one of the contributors coming from Europe. Indeed, eight of the sixteen authors come from the UK. None of the contributors comes from the pharmaceutical industry, which along with the selection of contributors suggests that the perspective of the book may be somewhat narrow.

Overall, this is a useful book to gain a quick appreciation for a variety of ways in which modelling may be useful in molecular biology.

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