Computer-aided molecular design

The First European Seminar and Exhibition on Computer-Aided Molecular Design, organized by Oyez Scientific and Technical Services in association with the Molecular Graphics Society was held in the Connaught Rooms, London on 18 and 19 October 1984. It was attended by over 150 participants, the vast majority of whom were from outside Britain and non-members of the Society. The meeting was chaired by Professor Bob Langridge, U.C. San Francisco, and encouragement to join the Society and subscribe to this journal was provided by Dr P Murray-Rust of Glaxo.

The exhibition ran throughout the two days with some seven companies exhibiting: Advanced Processor Research Ltd, Beckman Instruments — SYNLIB; Chemical Design Ltd; Evans and Sutherland; Floating Point Systems; Molecular Design MDL AG ECS Ltd and Tripos Associates AG. Many of the participants were new to the field and clearly appreciated the chance of comparing the alternative approaches in terms of hardware and software as well as attending the lectures and discussions.

The formal proceedings started with an overview of drug design by Professor Garland Marshall, Washington University, St. Louis. Whilst providing a series of caveats he gave a powerfully documented case for designing drugs on the basis of an understanding of drug–receptor interactions.

Delegates working for major international companies were given much grist to take back to their own organizations in terms of the level and type of commitment of other rival firms. Dr R Glen of the Wellcome Foundation showed what could be achieved with 'a couple of Evans and Sutherland systems and a host of colour raster devices'. In particular he discussed the fitting of potential molecules into proposed active sites. In a similar way Dr R Pearlstein of G D Searle and Co showed what that company is capable of doing and also demonstrated with the aid of a film the dynamical behaviour of synthetic polymer chains; one of the few applications to non-biological chemistry during the meeting. Another non-organic application of molecular graphics was included by E K Davies of Chemical Design Ltd. He showed displays of zeolites in his presentation of the current state of the art in the CHEMGRAPH system.

Dr D N J White of Ciba-Geigy AG gave a new and completely general approach to molecular mechanics which does not suffer from the restriction of being applicable only to a limited range of functional groups. He also discussed the use of array processors. Quantum mechanical methods in molecular design were covered by W G Richards, Oxford University, who concentrated on the determination and display of electronic properties and described a way of making quantitative comparisons of electron distribution which could be used in the logical alignment of molecules, the investigation of novel bioisosteres and even perhaps patent avoidance.

The display of protein structure in its latest and most appealing form was presented by Dr R E Hubbard of York University. Dr P Quarendon of the IBM UK Scientific Centre showed and explained how to use solid constructive geometry in generating pictures of molecules on raster graphic terminals. Some of these representations are certainly the best and most beautiful displays ever seen, combining the best of protein crystallography, computer graphics and artistic flair.

Using protein crystal structures as the basis for the design of drugs was the theme of two papers from Dr P J Goodford, Molecular Biophysics Laboratory, Oxford University and Professor T L Blundell, Birkbeck College. The former described a novel approach using graphic displays of energy calculations involving a known protein with small molecular probes. In this way one can see the special sites on macromolecules at which the binding of particular ligand atoms or groups is favoured. Tom Blundell in a customary breath-taking multimedia presentation of the vast output of his own group gave descriptions of the work on the enzyme renin and demonstrated the prediction of protein structure from homologous sequences of aminoacids.

Whereas the protein structure databank has some 200 structures (requiring 40 Mbytes) the Cambridge Crystallography Data Centre has grown to some 40 000 structures (needing 80 000 Mbytes). Dr P Murray-Rust, Glaxo Group Research Ltd, discussed databases in general and demonstrated how they may be used to provide chemical information.

The meeting was brought to a close by Dr J Gasteiger, Technical University of Munich who extended the range of the meeting into the area of computer-aided synthesis design. The EROS system depends not on an extensive library of known reactions but on the logic of breaking and making chemical bonds. Logic provides all possible pathways and synthetic methods in either a forward or retrosynthetic sense: choice is then limited by evaluation of thermochemical criteria. Many examples were given.

The meeting included a number of round-table discussions where issues covered included the availability and restriction of software; the EEC patent arrangements; the future of computer simulation and how undergraduate chemists ought to be trained. The lasting impression was that computer-aided molecular design is still very much in a period of rapid growth with developments in both hardware and software well short of any plateau.