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'The display of electrostatic fields on raster graphics devices' **Morffew, A J, Quarendon, P, Rogers, N K* and Sternberg, M J E†** IBM UK Scientific Centre, St Clement Street, Winchester, Hampshire. *Laboratory of Molecular Biophysics, South Parks Road, Oxford. †Department of Crystallography, Birkbeck College, Malet Street, London.

Electrostatic interactions in globular proteins play an important role in their folding and function. Charges of the side chains are distributed asymmetrically over the surface of the molecule giving a large molecular dipole. Secondary structure elements such as the alpha-helix also possess appreciable dipole moments[1]. Warwicker and Watson's[2] finite difference algorithm is used to calculate the potentials in and around enzymes. The power of the algorithm is that it models the markedly different dielectric responses of the protein ($\epsilon = 3.5$) and the solvent ($\epsilon = 80$) together with a detailed consideration of the shape and charge distribution of the protein. Potential values are calculated on the points of a 3D cartesian grid of 1A spacing in a box of side 60A. The examples here were calculated on the Cray IS at ULCC.

It is difficult to analyse the results of these calculations without a graphics device. The Winchester Graphics System is being used to explore various representations.

- WINSOM[3] is used to produce CPK and secondary structure raster pictures of the molecule, on which the potentials are mapped in colour.
- A half-plane may be passed through the centre of the molecule parallel to the screen, potentials surrounding the molecule may be displayed.
- The potentials around the molecule may also be displayed by drawing spheres of increasing radius and colour contouring the potential over the surface. The set of pictures may be animated giving the viewer the impression of a growing sphere sampling the potential field.
- Isopotential surfaces may be calculated and displayed in colour on the raster device.
- The most successful method investigated so far, is to calculate lines of force by plotting trajectories of 'inertialess' charged particles. These can be displayed on a vector refresh device allowing realtime interactive manipulation. Alternatively, they may be displayed as arrows surrounding the CPK or secondary structure representations on the raster device. The arrows may also be animated to aid clarity.

REFERENCES

1 **Rogers, N K and Sternberg, M J E** *J. Mol. Biol.* (in press)
2 **Warwicker, J and Watson, H C** *J. Mol. Biol.* (1982) Vol 157, pp 671–679
3 **Quarendon, P** (see abstract 18)

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'Computer-assisted modelling and examination of protein-molecule complexes' **Müller, K** Central Research Units, F Hoffmann-La Roche & Co Ltd, CH-4002 Basel, Switzerland

Some features and applications of the Roche Interactive Molecular Graphics (RIMG) system are discussed. This software package is being developed at Hoffmann-La Roche, Basel, on a DEC VAX-11/780 computer equipped with an Evans & Sutherland Color Multi-Picture System.

RIMG provides various facilities for interactive examination of protein structures and cavity analyses, for modelling, superposition and comparison of small molecules, and for design and evaluation of protein-molecule complexes. Efficient algorithms for complete topological analyses of complex molecular structures enhance many features of molecular modelling and structure matching. An extended module for interactive and computer-assisted superposition of partially or fully flexible molecular structures with various optional constraints is a major asset of RIMG. Several graphic techniques are available for the examination of intermolecular packing, such as body/surface-differentiated raster representations, dotted-surface, space-filling, or chickenwire representations of molecular volumes.

RIMG is illustrated by some recent applications in the field of anti-folate drug design.

Comparison of model complexes of *L casei* and *E coli* dihydrofolate reductases (DHFR) with selected diaminopyrimidine inhibitors gives a rationale for differences in their binding properties. Examination of the (hypothetical) binding of dihydrofolate and tetrahydrofolate to *L casei* DHFR points to a potential hydride-transfer activating mechanism involving the remote arginine 57. Modelling of ternary DHFR-inhibitor-NADPH complexes provides clues to questions of DHFR conformational changes upon inhibitor and/or cofactor binding.

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'A model for the graphical display of pseudorotation in small rings' **Murray-Rust, P and Tonge, A P** Chemical Research Department, Glaxo Group Research, Greenford, Middlesex UB6 0HE, UK

Five-membered rings, such as the furanose ring in nucleic acids and the cyclopentane ring in prostaglandins, are frequently found in biological molecules. The conformational flexibility of these rings can have a marked effect on the spatial relationship of substituent groups and hence influence the biological activity of these compounds.

We have developed algorithms for describing the motion of the ring atoms and their substituents during the pseudorotational cycle of both carbocyclic and heterocyclic rings. These routines have been incorporated into a molecular modelling system to permit interactive manipulation of molecules through the pseudorotational pathway. Realtime display of associated molecular properties have been implemented, such as conformational energies derived from torsional and nonbonded potential functions and proton coupling constants calculated from a modified Karplus equation.

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'Real time energy calculation and minimization in interactive three dimensional computer graphics'