changing histidine 176 with Asn and Thr 179 with Asn. In both cases, the catalytic efficiency is strongly reduced. With glyceraldehyde-3-phosphate as substrate, the k_{cat} value is 1/50th that of the wild type. The fact that the activity is reduced but not entirely abolished when His 176 is changed to Asn, suggests that this residue is not essential for catalysis and so, does not act as an acid–base catalyst.

References

1 **Harris, J I and Walters, M** in **Boye, P (ed)** *The enzymes* Academic Press, New York Vol 8 (1976) pp 1–50
2 **Murthy, M R N et al.** *J. Mol. Biol.* Vol 138 (1980) pp 859–872
3 **Leslie, A G W and Wonacott, A J** *J. Mol. Biol.* Vol 178 (1984) pp 743–772
4 **Branlant, G et al.** *Gene* Vol 25 (1983) pp 1–7
5 **Branlant, G and Branlant, C** *Eur. J. Biochem.* Vol 150 (1985) pp 61–66
6 **Branlant, G** unpublished results

33

Molecular vibrations of Z-DNA

G Vergoten*, P Lagant*, Y Moschetto*, W L Peticolas†, I Morize‡, M C Vaney‡ and J P Mornon‡

*Faculté de Pharmacie, INSREMU, 3 rue Professeur Laguesse, 59045 Lille Cedex, France
†University of Oregon, Eugene, OR97403, USA
‡Mineralogie-Cristallographie, Tour 16, Université Paris VI, 4 Place Jussieu, 75230 Paris Cedex 05, France

A normal modes analysis has been performed on the hexanucleotide d(CpGpCpGpCpG) as a model for the Z conformation of the DNA left-hand double helix. The internal vibrations have to be separated into local vibrations (relatively small number of atoms involved, small amplitude, high frequency) and overall vibrations (all atoms of the molecule are concerned with the motion, large amplitude, low frequency). It is shown that the classical description of molecular vibrations in terms of internal coordinates is meaningless in the case of macromolecular systems, due to their great number for one mode. To overcome this difficulty, the Cartesian displacement coordinates are used for a direct visualization of the vibrational motion with the help of computer graphics. A 16 mm film will be presented in which the crystal structure, three high frequency modes (one of them being highly specific of the Z conformation) and three very low frequency modes are described. Emphasis is given to the later modes which are expected to be directly related to the biological functions and properties.

34

Comparative study of acid proteases active sites

Y Barrans, B Busetta, M Hospital and G Precigoux

Laboratoire de Cristallographie, UA144, Université de Bordeaux I, 33405 Talence, France

To dock a substrate or an inhibitor in the active site of an enzyme a program has been developed called 'Grapin'. It is written in FORTRAN for a Tektronix 4113 screen. Several steps are necessary:

- description of the accessible surface of the receptor site (geometry and anchoring points);
- description of the stereochemistry of the substrate or inhibitor (geometry and nature of chemical groups);
- docking itself by two different ways: interactive or automatic;
- in any case evaluation of the interaction energy.

To illustrate the possibilities of Grapin, examples are shown with 3 acid proteases (endothia, penicillo, rhizopus pepsine). Different points of the active site pockets were defined as suitable anchoring points for convenient chemical groups. Conformations of several peptidic substrates and inhibitors were generated and the docked solutions will be given. Comparisons of their stereochemistry in the site will be given to try to determine the reason of the specificity for every enzyme.

35

Molecular graphics at the City University

G W Pooler and E G Steward

Molecular Medicine Group, The City University, London EC1V 0HB, UK

Application of the MGC system (Molecular Graphics at City) is illustrated for a phospholipase–A2/substrate complex. Features of the system include:

- Docking of a substrate into an active site of an enzyme.
- Molecular superposition.
- Cleft searching (currently by employing a spherical probe).
- Energy calculations (molecular mechanics — plus Cartesian to internal coordinate conversion for interface to QM calculations with geometry optimization).
- Highlighting of key molecular features.
- Option for treating active-site residues in isolation. (All enzyme atoms within r Å of bound substrate).
- Atom/fragment addition/deletion (useful for building new molecules which can then be energy minimized).

The system is under continuing development, particularly with respect to energy minimization for enzyme–substrate complexes.

36

Aimm: 3D models from 2D Maccs connection tables — use of the Genie target language to specify rules for structure building

Y C Martin*, E B Dunaher*, A M Weininger† and D Weininger†

*Abbott Laboratories, Abbott Park, Ill 60064, USA
†Pomona College Medicinal Chemistry Project, Claremont, AC 91711, USA