screen. Another graphic program GRAIP (GRaphics of Atomic Information Picture) used to draw a pixel image of the space filling model with its cross section is linked to Mild, using colours to indicate information.
Conformational energy calculation: FEDER (Fast ECEPP and its DERivatives) is a program used to calculate the conformational energy of proteins with respect to dihedral angles based upon the ECEPP function. It finds correct energy minima by a rapid calculation of the first and the second derivatives of the energy function using a new algorithm[1]. Its modified version for an array processor (S-810, Hitachi, 630MFLOPS) is much more effective.
Standard format to describe information of proteins: FLEXS (FLexible, EXtensible and Structural) format is a new format, which can describe any information of proteins with any type and any length, structurally. The Protein Data Bank (PDB) format is widely used, but there are many limitations, especially in describing protein structures by dihedral angles only. The FLEXS format links many program tools, such as between Mild and FEDER. Even when a relational database is available, such a format is still necessary for group work. Examples of the performance of these tools are shown by photos and a film, in which a Monte Carlo simulation of thermal fluctuation[2] of the ovomucoid and the manipulation of Mild are introduced.

References

1 **Abe, H et al.** *Comput. & Chem.* Vol 8 (1984) p 239
2 **Noguchi, Y and Go, N** *Biopolymers* Vol 24 (1985) p 537

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Molecular dynamics simulations: techniques, experimental basis and determination of free energies

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The basic procedures and techniques of the computer simulation method of molecular dynamics (MD) will shortly be reviewed. Its predictive power will critically depend on the basic approximations that are made and the force fields that are applied. Therefore, results of MD simulations of various molecules will be compared to experimental data derived from X-ray, neutron diffraction of 2D NMR experiments. Second, the derivation of the thermodynamic properties, entropy and free energy for systems of interacting particles from simulations will be discussed. This is by no means a trivial task, but recently progress has been made. Examples of the calculation of the free energy of hydration of methanol will be given. Possible application of these techniques to calculate binding constants of inhibitors or substrates to enzymes will be evaluated. As an example the calculation of the relative binding constant of two different inhibitors of dihydrofolate reductase (DHFR) will be discussed.

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Crystallographic approaches to nucleic acid structure and dynamics

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Our knowledge of the tertiary structure of nucleic acids is derived from X-ray diffraction studies of crystalline fibres and single crystals. However, the fact that X-ray crystallography yields well-defined structures characterized by a set of coordinates fosters a rather rigid and static view of nucleic acids. Only recently was it shown that X-ray diffraction can contribute to our knowledge of the dynamic properties of macromolecules. This advance was made possible by the development of refinement methods, which allow the precise determination of atomic coordinates and of the atomic Debye–Waller factors, together with the impetus given by molecular dynamics simulations of macromolecules. Further, the availability of X-ray structures of DNA oligomers and t-RNA molecules at various resolutions has opened up a new era in the study of the structure and biological functions of nucleic acids and of their interactions with other ligands and proteins. The correct interpretation of crystallographic data, especially of low to medium resolution, depends on a thorough understanding of the effects of the refinement model upon the derived quantities, such as coordinates, thermal parameters, and positions of solvent molecules. Several examples of nucleic acid structures refined with molecular graphics, molecular mechanics, or molecular dynamics will be presented and discussed: at high resolution, a Z-DNA hexamer and its solvation; at medium resolution, a comparison between two refinement methods of a B-DNA dodecamer as well as a comparison between two tRNA molecules; at low resolution, a study of heavy metal and drug binding to Z-DNA oligomers.

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MaxTwist: energy minimization of macromolecules in intelligent degrees of freedom

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'Babysitting' irrelevant degrees of freedom is an unnecessary and very time-consuming activity of energy minimization programs. For example, bond stretching requires an energy several times kT, at room temperature, for a single quantum excitation. So there is usually no biological interest in variations in bond length. Yet the most widely used intramolecular minimizers vary all $3*N$ atomic position coordinates, i.e. more than a thousand degrees of freedom for a 58-residue protein. A lot of time is spent changing variables that physically do not change. MaxTwist differs in two respects. 1) The basic description of molecular conformation is in terms of internal coordinates, not atomic position coordinates.