performance options. While it has been challenging to write software that conforms to the Macintosh standards, the result is a highly interactive, easy-to-use program.

Using these techniques and tools, we have created structures for, and analyzed the interactions of, a monolayer of DMPC, diacetylenic lipids, and the combination of the disaccharide trehalose and the polar surface of the DMPC monolayer.

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FUS: A Rule-Based System for the Rapid Evaluation of Folding and Unfolding Strategies

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In order to study the dynamics of protein and nucleic acid conformations, a molecular folding-unfolding system (FUS) has been implemented. Features of the secondary structure of these molecules, such as helices, β-strands and loops, are graphically represented by simple polygonal objects. Modeling of the unfolding (denaturation) and folding of their three-dimensional structure is made possible by the use of operators that allow displacement of these structural features in space. The system uses two primary operators that allow topological manipulation of the structure; these primary operators can be used in the implementation of higher-level operators. First-order logical rules are used to validate the action of these operators. Rules are stored in a database and can be modified by using a predicate calculus-like language. The user can implement his own algorithms using the default (furnished) rules, user-defined rules or a mixture of both combined with topological operators. For example, a user-defined rule could be constructed to infer the presence of complex structures like triplets in proteins (two parallel β-strands antiparallel to an adjacent helix). Due to this flexibility, FUS is a useful tool for the rapid evaluation of user-defined folding and unfolding strategies. Some of the advantages of such a system are: (1) topological validation based on logical rules is faster than validation based on energy calculations, and (2) logical structures are much closer to the reasoning process of biochemists. As an example, we use the yeast phenylalanine tRNA sequence as input to a secondary structure algorithm. The output is employed to deduce the secondary features that are the input of FUS. Then, a logical strategy can be designed based on a set of topological hypotheses, in order to obtain the final "L" structure of tRNA. Once accomplished, these same rules can be applied to other RNAs to test their generality.

Display and Interpretation of Protein Electrostatic Potential Maps

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A major class of heme containing proteins are the cytochromes c, which are crucial catalysts in electron transport chains. The exact function and position of the cytochromes c in electron transport chains is dependent on the redox potential of the heme protein. The redox potential has been found to vary from −290 mV to 400 mV, a large range for an enzyme with a remarkably conserved primary and tertiary structure.[1] A major objective in the study of cytochromes c is to determine how the protein's amino acid sequence and tertiary structure tunes its redox potential.

We have applied a continuum electrostatic model to describe the protein and surrounding solvent. Electrostatic potentials resulting from the protein's charge distribution and the high dielectric medium are calculated by the finite-difference solution to the Poisson-Boltzmann equation pioneered by Warwicker and Watson[2] and Honig and coworkers.[3,4] We have developed an interactive interface, within the framework provided by the HYDRA[5] molecular graphics package, to explore and interpret the information contained in the electrostatic potential map.

Our menu-driven routines read in calculated electrostatic maps in the format of a 65 × 65 × 65 lattice. From these maps isopotential surfaces, field-lines and solvent-accessible surface potentials can be generated and overlaid on molecular structures. These composite structures can be rotated and manipulated in real time. The field-line option can be used to examine the electrostatic gradient about selected atoms, residues or chain segments. This option is valuable in analyzing and comparing local perturbations to the electric field, resulting from point mutations, counterion binding, solvent interactions and protein conformational changes.

We have mapped the phosphate and carbonate binding sites of tuna cytochrome and shown the dependence of these binding sites on the counterion radius. Additionally, we have found the isopotential surface about the proposed contract region between tuna cytochrome c and its redox partners to be insensitive to changes in ionic strength, pH and iron oxidation state. In contrast, the isopotential surfaces on the "backside" (i.e., opposite the redox contact site) of tuna cytochrome c vary greatly with changes in solution conditions and the iron oxidation state.

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