vibrations occurring in a molecular system, are chosen. From molecular dynamics simulations, coordinates from equally spaced time steps along the trajectory are selected. These two approaches provide views of the changes that occur in electrostatic recognition as the system undergoes a number of concerted motions.

These computer graphics studies will be used to develop tools that provide insight into molecular recognition and interaction at a sufficiently detailed level to guide future site-directed mutagenesis experiments, which, in turn, will provide verification for these theoretical methods.

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Molecular Modeling of Silicon Compounds

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Zeolites, both naturally occurring and synthetic, have found widespread application owing to their capacity for selective absorption and catalysis.[1] In recent years considerable effort has been directed toward the elucidation of zeolite structures and the mechanisms of their catalytic processes. This has included extensive diffraction studies, together with the recent application of high-resolution magic angle spinning NMR techniques. An alternative approach is to apply computational methods. To date these have mainly been carried out on small Si, O and Al clusters using *ab initio* or semi-empirical methods, and have been restricted as to the number of atoms under consideration.

A molecular mechanics model has been developed that can handle high silica zeolites. The first stage in this development was the extension of an existing empirical scheme for partial charge calculation to include silicon-containing molecules. During the parameterization it was shown that it is necessary to include both σ and π interactions between silicon and electronegative atoms.[2] Force constants to describe the vibrations of the Si–O fragments have been calculated from an extensive theoretical study, at various levels, carried out on a number of model compounds, including disiloxane, dimethoxy-dimethylsilane and silanol; the conformation of the cyclic molecule cyclotrisiloxane has also been investigated. Our calculations show the importance of including polarization functions in order to reproduce unusual structural featues of Si-O compounds.[3] Finally, our molecular mechanics model has been tested against experimental geometries for silicon-oxygen containing molecules, and geometries and experimental energy differences for a number of alkyl silanes.[4] In each case good agreement was obtained, validating our modifications to the MM2 force filed, the application of our charges to molecular mechanics calculations and the ability of the calculated force constants to reproduce experimental features of silicon compounds.

To conclude, a discussion of applications of this model to zeolite structure will be presented. This includes optimization of substantial zeolite fragments with full relaxation.

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Spatial Density Distributions for Illustrating the Base Sequence Dependent Features of Double Helical DNA: Computer Graphic Visualization of Monte Carlo Chain Simulations

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Computer graphics is proving to be an essential tool in understanding the conformations and properties of biopolymers. The bulk of molecular applications to date have been static representations of crystallographically observed or energy minimized three-dimensional (3D) structures. A growing number of procedures, however, are being developed to study chain dynamics. Particularly popular is the animation of Newtonian molecular dynamics simulations, providing a visual description of the small-scale fluctuations of specific low-energy structures. Detailed study of large-scale molecular motions by such methods, however, is not yet computationally practical. Large-scale flexibility is generally described in terms of simplified artificial models or through computational short cuts that force the system over preselected energy barriers. Little, if any, attention has been given to visualization of the large-scale changes of macromolecular structure (involving the crossing of multiple torsional barriers) expected on the basis of local conformational flexibility.

Large-scale macromolecular motions are best deduced from direct Monte Carlo simulations. Such methods are particularly appropriate to studying polymers with properties determined by the chemical constitution of individual side groups. Specific chain conformations are generated from randomly chosen combinations of backbone structural parameters. Sequence-dependent features of structure are included in terms of the statistical

weights describing various combinations of residue orientations. Individual parameters can be varied in small fixed angular increments, generating smooth variations of structure that can be monitored graphically. The residues to be moved and the direction of angular change are chosen by random number techniques. The approach, unfortunately, is feasible only for small molecules in view of the time it takes to sample the range of low-energy states available to individual chain units. Other approaches that sample broader regions of torsion angle space must be employed in the study of long chains. Local conformations can be chosen, for example, on the basis of individual statistical weights with the crossing of high-energy barriers avoided. The smooth folding of the macromolecule is, unfortunately, lost in such an approach. The Monte Carlo sample is merely a collection of arbitrary, unrelated 3D structures. Sequential configurations of the Monte Carlo sample are random snapshots of overall chain movement, offering no clues to the transitional pathways that link them. Nevertheless, information concerning chain flexibility can be extracted from catalogs of conformational data accumulated during the sampling process. Structures can be organized on the basis of some criterion and distributions of the relevant parameters accumulated. The distributions can then be compared against ideal models or with those of related polymers.

One such probe of macromolecular flexibility is the spatial density distribution $\mathbf{W}_0(\mathbf{r})$. This quantity is a 3D function describing the probability of finding the terminus of a chain molecule at vectorial location $\mathbf{r}$ relative to a reference frame embedded at its origin (0). The location of the chain terminus in this manner is analogous to the use of distribution functions in describing the electron density of a molecular orbital. The characteristic shape of $\mathbf{W}_0(\mathbf{r})$ is tied to local chain properties, just as the shape of a molecular orbital is linked to the quantum states of its electrons. Because of the constraints of chemical bonding and the restrictions on local bending and twisting of chain residues, the distributions are skewed in short chains to shapes determined by the polymer architecture. The shapes can be correlated with observed measures of chain extension and flexibility, and the densities can be used to estimate the likelihood of polymer cyclization and looping as a function of chain length and sequence.

The conformation and properties of double-helical DNA are intimately tied to the linear sequence of its heterocyclic base side groups. A number of models have been offered to account for the subtle irregularities of local conformation in crystalline oligomers and the observed twisting and bending of the chain in solution. Computer programs have also been developed to translate the primary sequence of bases into 3D models on the basis of these rules. The flexible nature of the double helix is generally ignored in these representations with individual repeating residues of the chain described by fixed local geometries. Adjacent base pairs are found in experimental and theoretical studies, however, to adopt a broad range of accessible conformations rather than a single narrowly defined minimum energy state. The conformation of the DNA as a whole is more aptly described by a Monte Carlo computer monitored by the distribution of $\mathbf{W}_0(\mathbf{r})$.

We have taken advantage of color graphics techniques to study the conformation and mobility of selected DNA sequences. We have studied three short fragments of kinetoplast DNA from *Crithidia fasciculata* that exhibit dramatically different behavior on nondenaturing polyacrylamide gels. We find characteristic differences in the distributions of conformations between curved and rod-like sequences and in the overall flexibility of A·T and G·C rich regions. We employ a series of recent potential energy estimates of the local flexibility of adjacent nucleic acid base pairs to generate static representations and Monte Carlo samples of the double helix. We monitor the Monte Carlo chain flexibility with $\mathbf{W}_0(\mathbf{r})$, distinguishing regions of high and low probability density on the basis of color. These distributions incorporate a vast quantity of data that cannot be comprehended at the molecular level. We also color-code the DNA to examine effects of chain sequence on overall structure and flexibility. We additionally superimpose selected trajectories and various static representations of the double helix on the density distributions in an effort to understand the flexibility of the DNA as a whole.

Molecular Modeling of Two Regulatory Proteins, fix K and fn R, Homologous to CAP

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Two regulatory proteins — fix K of nitrogen fixation in the *Rhizobium* and Fn R of *E. coli* — are homologous to cAmp protein of *E. coli* or CAP. However, the homology is weak, about 25% of identical residues. In order to ascertain the alignment of the amino-acid sequences, secondary structure prediction was performed with the homolog program[1] with a specific weighting factor taking into account the homology. This procedure allows us to detect precisely the insertions or deletions to be made for further molecular modeling.

Subsequently, the conserved residues were assigned the corresponding coordinates of the CAP. These constitute the core of the two proteins, which have been energy minimized by quasi Newton or simplex methods. For the variable loops a specific method has been developed to avoid as much as possible the nearest minima. This is achieved essentially by simulated annealing, which takes care of the observed repartition of residue conformations in proteins of known structure. Tentative residues are proposed to interact with nucleotide bases of the putative recognition sequence.

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