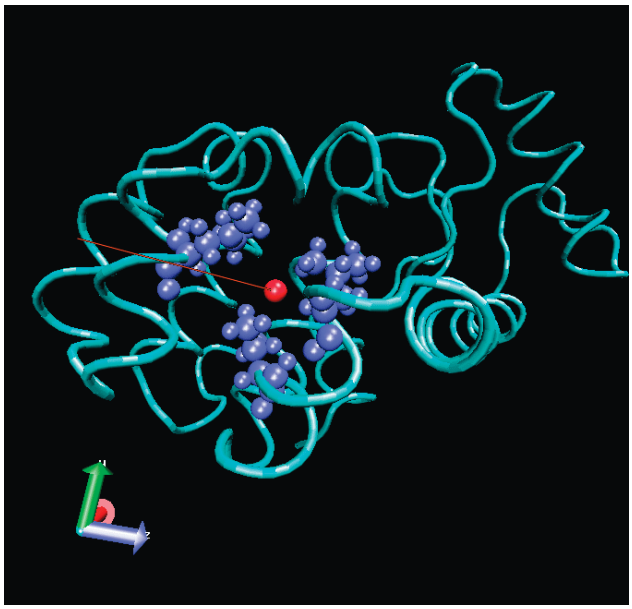
Computational Structural Biology Resource

Department of Computer Science University of North Carolina at Chapel Hill February 2004

The Challenge

Proteins play a central role in cellular function and are ultimately the mechanism through which many diseases have their effect. Increasingly the design of drugs to treat such diseases is based on a detailed understanding of protein structure and its interaction with small drug molecules. Computational structural biology is concerned with the modeling and computer simulation of structure, function, and dynamics of biological molecules. The Research Resource in Structural Biology, part of the National Institutes of Health, brings together a multidisciplinary group of researchers in biophysics, computer science, biochemistry, and mathematics to develop and apply new modeling and simulation techniques.

There are many challenges within the scope of the Research Resource, but computer simulation of molecular dynamics (behavior over time) is one in which computer science is most closely involved. Such simulations require a tremendous amount of computation because the basic simulation timestep is very small compared to the time-scale of the behaviors of interest. The challenge is to increase the simulation rate, and to provide the possibility of "steering" the simulations toward interesting phenomena.



Mutant T4-Lysozyme with xenon atom (red, with attached line) in non-native binding cavity. To minimize occlusion of the area of interest in the putative exit pathway of the xenon atom, only protein backbone and residues near the exit are shown. The line corresponds to the direction and magnitude of the steering forces injected into the simulation.

Highlights

- **Recently the Selected Molecular Dynamics (SMD) system was interfaced to the Protein Interactive Theater (PIT) to provide a virtual 3D environment for steering the simulation (see separate handout on the PIT).**
- **Analytical and experimental observations show that the performance of parallel algorithms using spatial decomposition for truncated interaction molecular dynamics simulations is more dependent on load balance than communication efficiency on modern parallel computers.**

The Approach

To accelerate molecular dynamics simulations, we are designing new parallel algorithms and are concentrating on their high-performance implementation on parallel computers with a potentially large number of processors.

To provide computational steering of molecular dynamics simulations, we are constructing the Selected Molecular Dynamics (SMD) system which provides a graphical interface to the dynamics simulation, through which we may introduce additional restraints into the simulation to effect, for example, a change of conformation in the molecule.

Project Leader

Jan Hermans (Principal Investigator), professor (Biochemistry and Biophysics)

Other Investigators

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Past Project Members

James Chen, Michael Lappe, Jonathan Leech, Martin Simons

Research Sponsors

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Selected Publications

Mann, G., R. Yun, L. Nyland, J. Prins, J. Board, and J. Hermans. "The Sigma MD Program and a Generic Interface Applicable to Multi-Functional Programs with Complex, Hierarchical Command Structure," in Macromolecular Modeling, T. Schlick, ed., Springer Verlag, 2001.

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Key Words

Molecular dynamics; computational steering; simulation; high-performance computing

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