

## Poster III-48

### **Biomedical Initiative at the Pittsburgh Supercomputing Center**

***Roskies, Ralph, Stiles, Joel, Deerfield, David II***

***Pittsburgh Supercomputing Center, Pittsburgh, PA, USA***

The Biomedical Initiative at the Pittsburgh Supercomputing Center has been a leading program in high performance computing for over 15 years. Our group's mission is to develop and apply new computing and scientific solutions in important biomedical areas such as structural biology and bioinformatics, cellular microphysiology, neural modeling, the Visible Human Project, and pathology. The Education, Training and Outreach activities are especially vigorous, with the PSC team-teaching academic courses in bioinformatics at a number of institutions, leading workshops on structural biology, bioinformatics, and computational neuroscience in Pittsburgh, and involvement in the production of science museum shows.

Bioinformatics projects include investigating new algorithms for sensitive database searches, evaluating different representations of the information contained within a multiple sequence alignment, and the identification of residues that differentiate between different sequence subfamilies. We recently completed a detailed analysis of enzyme families that identified conserved motifs, key residues for specificity and catalytic activity and provided predictions used in laboratory research. PSC maintains a large suite of programs for database searching, multiple sequence alignment, pattern identification and searching, and phylogenetic analysis; all major sequence databases and a large number of the completed genomes.

A variety of computational chemistry approaches are used to obtain insights into structure, function and specificity, employing bioinformatics to help define questions, direct projects, and interpret results. The group works directly with other experimental groups to test the predictions derived from computations. The current projects include quantum chemical models for divalent metal ion binding sites, QM and QM/MM computations to investigate enzyme mechanisms, and MD simulations to study the dynamical behavior around active and binding sites. The service effort supports all major QM and MM programs plus some QM/MM programs.

Quantitative understanding of biological structure and function at the subcellular level requires predictive simulations of reaction pathways, variability, and switching, all in spatially realistic models. Thus, stochastic methods must be applied to complex 3-D reaction-diffusion problems, and incorporated into innovative "cells-as-machines" approaches. In collaboration with the Salk Institute, we are developing MCell, a general Monte Carlo simulator of microcellular physiology, and DReAMM, a companion model design, rendering, and analysis tool. To date we have simulated presynaptic calcium dynamics, neurotransmitter release, and postsynaptic signal generation.

NEOSIM, a next-generation simulation framework for modeling the electrical activity of large networks of nerve cells is being developed at PSC and Edinburgh. This framework employs discrete event simulation techniques to coordinate electrical signal (spike) delivery within a network model that is distributed across a large-scale parallel machine.

The PSC has developed a browser for viewing large 3D volumetric datasets that allows viewing of any arbitrary 2D slice with a second window providing the context of the slice in 3D space. The browser operates in a client-server mode and provides a number of tools for segmentation and image analysis. Current datasets include the Visible Human (optical data from cryo-section, both female and male, about 20 GB/dataset) and Visible Mouse (high resolution MRI data, about 2 GB/dataset). While existing datasets are 3-D (volumetric) for one point in time, we are expanding to 4-D data, with the fourth dimension being short-term time for viewing physiological processes such as breathing and heartbeats, or long-term time for viewing developmental processes, including multiple datasets obtained from animals generated in gene knockout studies.

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