Hands-on Workshop on Computational Biophysics

by

The Theoretical and Computational Biophysics Group (TCBG)

and

The National Center for Multiscale Modeling of Biological Systems (MMBioS)

June 6-10, 2016
TCBG Funded in 1989
NIH Biomedical "Bringing Physics to Life"

Software - Citations
NAMD 5,000+
VMD 10,000+

Klaus Schulten

Scientists solve chemical structure of HIV capsid

NIH-funded Biomedical Technology & Research Centers
TCBG Funded in 1989
NIH Biomedical “Bringing Physics to Life”

Professor Zaida (Zan) Luthey-Schulten

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Software - Citations
NAMD 7,000+
VMD 18,000+

Lattice microbes
Bacterial Colonies
Overarching biological theme:

- Spatial organization
- Temporal evolution

of (neuro)signaling systems/events
From small molecules, to multimeric assemblies, to cellular architecture, to neural circuits

from $6 \times 6 \times 5 \, \mu m^3$ sample of adult rat hippocampal stratum radiatum neuropil

From ssEM images, $400 \times 400 \times 50 \, \mu m^3$
Training and Dissemination

Co-Leaders

**Alex Ropelewski**
Senior Bioinformatics Specialist
Co-Director of MARC Initiative
Pittsburgh Supercomputing Center,
Carnegie Mellon University

**Joseph Ayoob**
Associate Professor, Computational and Systems Biology Department, Pitt Director, TecBio and DiscoBio Programs

MARC, training scientists/educators in minority-serving institutions
MMBioS Resources

Anisotropic Network Model Web Server 2.0 (2014)

What's new in this version? Having Java problems?
Enter the PDB id of your protein
- pdb coordinates
- biological unit

or
Submit your own protein

What is the GNM DB? Which questions can be answered?
Several studies in the last decade have drawn attention to the significance of intrinsic dynamics as a major determinant of the mechanism of action of proteins and their complexes. Intrinsic dynamics refer to conformational changes intrinsically favored by 3D structure, which often underlie the adaptation of biomolecules to functional interactions. As a consequence, an important question is to assess which structural elements (e.g. residues, secondary structures, domains, or entire subunits) undergo large fluctuations away from their mean positions (i.e. those experiencing high mobility), or which ones provide adequate flexibility to enable conformational changes (e.g. large binding sites) that may be relevant to function. Furthermore, it is of interest to determine which structural elements are subject to strongly correlated (or anticorrelated) motions toward gaining insight into allosterically coupled regions. The GNM (7,8) addresses these questions. It further allows to dissect these properties into the contributions of individual modes, thus elucidating the cooperative (global) couplings (cross-correlations) mediated by low frequency modes. For more information see Theory and Tutorial.

Note: Query the GNM DB (GNN 2.0) with a single PDB code (e.g., 101M and 4NH1, etc.); or, search the database with customized condition(s) using the "Advanced search".

PDB ID: [Enter]
Biological assembly: Yes / No
Molecular viewer: JisMol / Jmol (fast response for big structures)

Advanced search: Search conditions
Submit Query

Eyal et al., Bioinformatics 2015

Li et al., Nucleic Acids Res 2016
MMBioS Resources

ProDy
Protein Dynamics & Sequence Analysis

ProDy Project
ProDy is a free and open-source Python package for protein structural dynamics analysis. It is designed as a flexible and responsive API suitable for interactive usage and application development.

Structure analysis
ProDy has fast and flexible PDB and DCD file parsers, and powerful and customizable atom selections for contact identification, structure comparisons, and rapid implementation of new methods.

Dynamics analysis
- Principal component analysis can be performed for
  - heterogeneous X-ray structures (missing residues, mutations)
  - mixed structural datasets from Blast search
  - NMR models and MD snapshots (essential dynamics analysis)
- Normal mode analysis can be performed using
  - Anisotropic network model (ANM)
  - Gaussian network model (GNM)
- ANM/QUONN with distance and property dependent force constants

Dynamics from experimental datasets, theoretical models and simulations can be visualized using ANM/QUONN.

Reference:
Bakan et al., Bioinformatics 2011; 2014

WESTPA
(The Weighted Ensemble Simulation Toolkit with Parallelization and Analysis) is an open-source software package that provides a high-performance framework for carrying out extended-timescale simulations of rare events with rigorous kinetics using the weighted ensemble algorithm of Huber and Kim (1996). The software also includes (1) options for further enhancing the sampling efficiency through reassignment of weights according to either equilibrium or nonequilibrium steady state, and (2) a plugin for using a weighted ensemble-based string method.

Key features of the software:
- Highly scalable. Nearly perfect scaling up to thousands of cores.
- Interoperable. Designed to conveniently interoperate with any stochastic sampling engine (e.g., molecular dynamics, Brownian dynamics, and Monte Carlo engines).
- Portable. The software can be used with any Unix operating system (e.g., Linux or OS X), including typical clusters and supercomputers.
- Free and open source. All source code is available under the GNU GPL license.

Please cite the following for use of WESTPA:

WESTPA is used at more than 30 institutions around the world.

Funding
National Institutes of Health

Zwier et al., J Chem Theo Comp 2015

Bakan et al., Bioinformatics 2011; 2014
Workshop Program

Mon, June 6: Introduction to Protein Structure and Dynamics - Juan Perilla

Tue, June 7: Statistical Mechanics of Proteins; Force Field Parameterization - Juan Perilla

Wed, June 8: Introduction to Evolutionary Concepts, Network Analysis and Cell Simulations - Zaida Luthey-Schulten

Thu, June 9: Collective Dynamics of Proteins Using Elastic Network Models - Ivet Bahar

Fri, June 10: Statistical Mechanics of Trajectories, Weighted Ensemble method - Dan Zuckerman
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NIH National Institutes of Health
Turning Discovery Into Health
Tutorials

Days 1-3
http://www.ks.uiuc.edu/Training/Tutorials/

Day 4
http://www.csb.pitt.edu/prody/#tutorials