New Course:

Computational Protein Folding

CSCI 2951G: TTh 1:00-2:20, CIT 345

No prerequisites.

This course investigates the challenges of protein folding from an algorithmic perspective. A mixture of lectures, discussions, and demonstrations is targeted at computer science graduate students (and advanced undergrads) with an interest in biology and physics but no prior experience necessary; students from other departments with expertise in the subject are welcome. This course is forward-looking, and aims to get students rapidly up to speed to conduct research projects.

Instructor: Paul Valiant

Format: Seminar-style lectures interspersed with discussions and introductions to software tools.

Student responsibilities: Do introductory and exploratory exercises with provided software tools; Bring new ideas to discussion; Do a final project in an area of your choice.

Topics:

- Kinetic energy, potential energy, forces, Hamiltonian dynamics, generalized coordinates, Liouville's theorem; temperature and degrees of freedom; thermodynamics theorems (equipartition, Boltzmann distribution); effects of coordinate changes on the above
- Fitting the parameters of a molecular dynamics "force field": the meaning of the different terms, fitting to experimental vibration mode data numerical integration/timestepping/stability ("symplectic" integrator), examples
- Standard analysis tools: RMSD with quaternions; backbone dihedral angles; hydrogen bonds
- Qualitative discussion of the energy landscape; different means of traversing it – simulation at temperature vs. momentumless minimization algorithms
- Modeling water: Fourier transforms; "implicit" water models (generalized Born, and approximations)
- Structural aspects of proteins: amino acid properties; alpha helices and beta sheets and intuitions; survey of folded proteins from data banks; important mechanisms typically not simulated: disulfide bonds, chaperones, metal ions
- Xray crystallography and NMR – data sources, and competition for the computational approach
- "Accelerated dynamics" via changing masses, changing degrees of freedom, modifying the energy landscape
- Alternate computational approaches to structure prediction – threading, machine learning approaches, practical examples.

Recommended textbook: *Introduction to Proteins: Structure, Function, and Motion* (2010)