

ISMB 2003 Tutorial:

Molecular Evolution: Evolutionary Dynamics and Molecular Biophysics

David Pollock and Richard Goldstein

Increasingly, biocomputing is taking advantage of the methods and approaches of evolutionary biology. This is due to the intersection of a number of different developments: the availability of whole genomes from a growing number of organisms, the availability of high-speed computational facilities that allow sophisticated computational and statistical models, and the growing realization of the power of comparative sequence analysis. Such approaches require an understanding of the ways that the corresponding organisms evolved and changed. There are, unfortunately, numerous misconceptions about the way that evolution occurs, misunderstandings about current evolutionary theory, and a lack of awareness of available methods and software.

This tutorial will focus on giving participants a broad overview of the nature of molecular evolution, techniques that have been developed for modeling this evolution, tools to interpret biological information in an evolutionary context, and software that has and is being developed to analyze evolutionary processes. The tutorial is intended to complement a molecular evolution tutorial given at this conference by G. Pesole that focuses on molecular mechanisms, evolutionary models and inferring molecular phylogeny. It will be useful for anyone working in the bioinformatics and computational biology areas who would like to know more about evolutionary theory and the opportunities this provides for comparative sequence analysis, as well as for molecular biologists who wish to know about some of the standard software tools. Only relatively basic understanding of biology is assumed.

We will discuss the following topics:

I. Modern uses for Evolutionary Analysis: Relationship

Evolutionary analysis and comparative genetics / comparative genomics.

II. The underlying process of evolutionary change

The manner in which evolution proceeds (Mutation, fixation, and substitution). The difference between genetic change and genomic change. Brief overview of various models of the substitution process at both the nucleic acid and protein level, as developed by Jukes and Cantor, Kimura, and others.

III. Recent theories of evolution

Eigen and the idea of pseudospecies; the neutral theory and near-neutral theory, neutral networks and their role in evolutionary dynamics. Selection vs. neutrality. Fitnesses and

fixation rates. Effect of population size and population structure on evolutionary dynamics. Robustness, redundancy, and evolvability.

III. Structure of biomolecular evolution and the evolution of biomolecular structure

What evolutionary record can tell you about the evolving molecules. Adaptation, coevolution, and ancestral reconstruction. Varieties of selective pressure, and its relationship to protein structure and function. Variable and changing selective pressure. Origin of the genetic code. Synonymous / non-synonymous substitution ratios, covarion models. Gene duplication and the rise of novelty. Exon shuffling. Role of non-genic DNA.

Biographical Sketches:

David Pollock is Assistant Professor in the Department of Biological Sciences and the Biological Computation and Visualization Center at Louisiana State University. His research focus is on the relationship between protein structure and function and sequence variation, particularly the effect of structural context on coevolution between residues. This focus has led to analysis of evolutionary dynamics in a variety of molecular systems, and recent interests include the effect of structural components of the mitochondrial genomic replication system on gradients of mutation, and the effects of high-density taxonomic sampling on bioinformatic analyses. Dr. Pollock teaches courses in Genomics and Bioinformatics, Protein Evolution, and Evolution.

Richard Goldstein is currently Head of Bioinformatics at Siena Biotech, a drug discovery start-up in Siena, Italy. Prior to this, he was Associative Professor in the Department of Chemistry and Biophysics Research Division at the University of Michigan. His research focuses on how we can understand the properties of biomolecules in their evolutionary context, how we can use the evolutionary record to understand specific proteins, and how we can use the properties of proteins to understand the evolutionary record.