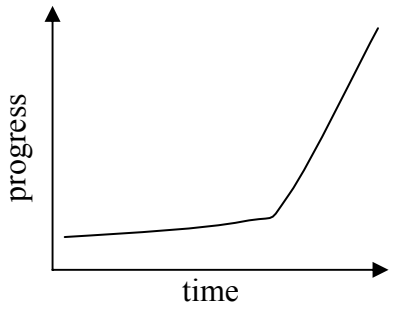
MIT 6.581/20.482J

FOUNDATIONS OF ALGORITHMS AND COMPUTATIONAL TECHNIQUES IN SYSTEMS BIOLOGY
Spring 2006

7 February 2006
Tuesday

MOTIVATION/OVERVIEW

There is a disconnect between biology and computer science.
The biologist will pose the problem statement, but it may not be amenable for the computer scientist to solve it.
There is a need for scientists who posses the breadth of knowledge to marry the two realms.



PROBLEM ⟶ FORMULATION ⟶ SOLUTION

- assumptions
- set up

- algorithms
- computer techniques
- numerical methods

ecologies

populations

individuals
↓↑
organ systems
↓↑
organs
↓↑
tissues
↓↑
cellular ⇆ experiment
↓↑
molecular ⇆ physics

focus of this course

MOLECULAR LEVEL (atoms)	CELLULAR LEVEL (concentration of biomolecules)	IMAGING	
✓		✓	Fast Fourier Transform
✓	✓		Combinatorial Search
	✓		Model Reduction
✓	✓	✓	Singular Value Decomposition
✓			Multipole Algorithm
✓	✓	✓	Numerical Differentiation
✓	✓	✓	Optimization
✓	✓		Newton Methods

PHYSICAL, CHEMICAL, & BIOLOGICAL MODELING OF PROTEINS

Proteins:

- biological polymers of about 20 amino acids
  polymers are any kind of large molecules made of repeating identical or similar subunits called monomers
- "perfect" homogeneous, pure synthesis
- around 10k copies in a cell
- linear, unbranched chains of a unique sequence
- generally fold to characteristic structure with no additional information

sequence (1D)	*folding* →	structure (3D)	→	chemical functions	→	biological functions	→	network functions ✱
protein ↑ mRNA ↑ genome (DNA)		x-ray crystallography NMR		binding catalysis		synthesis/ degradation energy storage/ utilization gene expression development immune surveillance		control points – decision "robustness" time keepers oscillators important area of growth

Why Model?

- Understanding : model facilitates development of understanding reason for properties
  - mechanistic basis for function
  - disease
- Prediction
  - experiment planning
  - validate a model or select among models
- Design
  - perturbation : improve properties
  - intervention : repair