Computational methods in bioinformatics

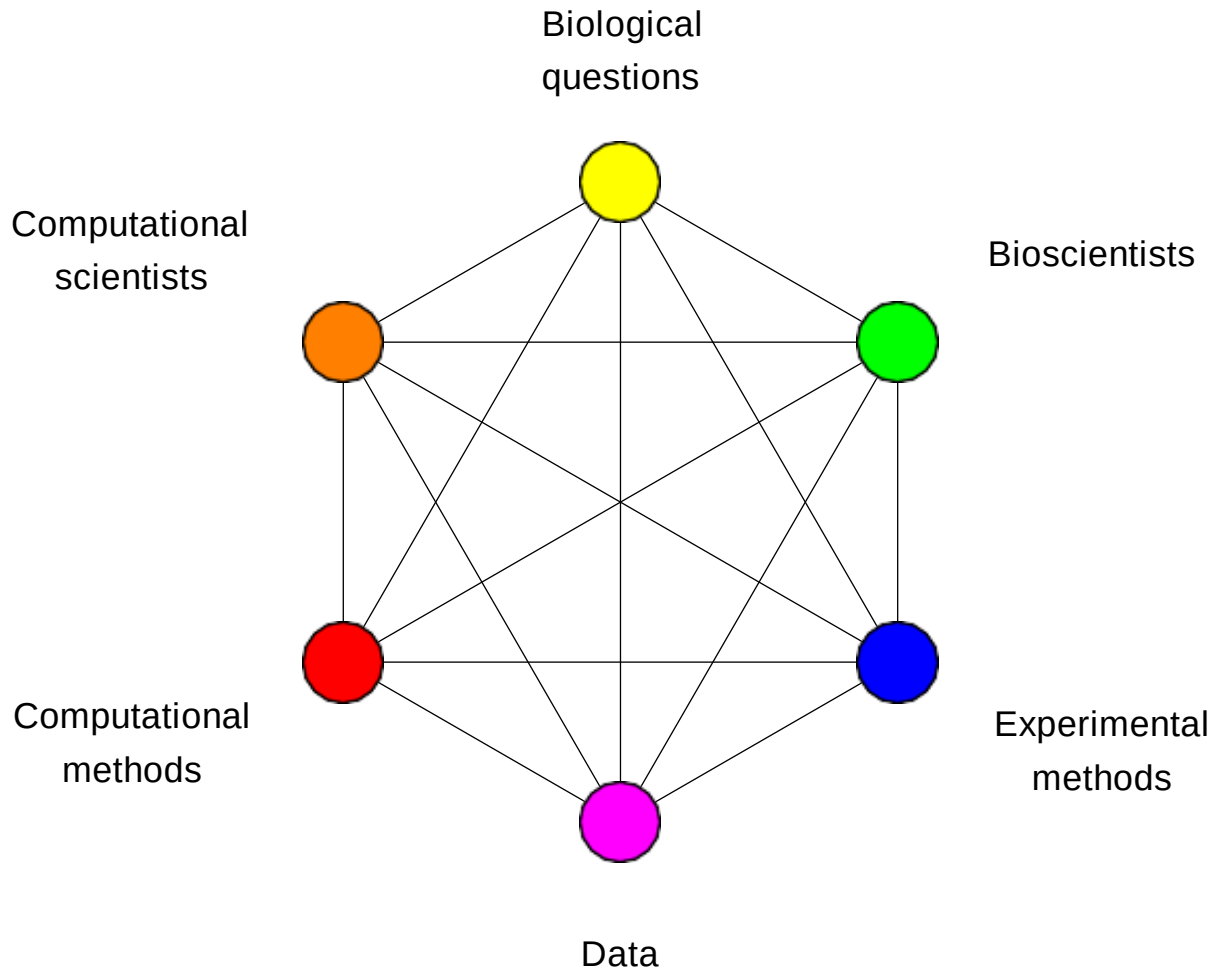
What is computational biology?

"The development and application of data-analytical and theoretical methods, mathematical modeling and computational simulation techniques to the study of biological, behavioral, and social systems.

"Computational biology uses mathematical and computational approaches to address theoretical and experimental questions in biology."

Working definition by the NIH Biomedical Information Science and Technology Initiative Consortium, 2000
http://www.bisti.nih.gov/docs/CompuBioDef.pdf

Addressing biological questions



What is a gene?

"Region of DNA that controls a discrete hereditary charactaristic, usually corresponding to a single protein or RNA."

Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P (2002). Molecular Biology of the Cell (Fourth ed.). New York: Garland Science.

Sequences, structures and systems

Sequences

- Nucleic acids (DNA and RNA) and proteins are (unbranched) polymers. Their composition can be described by the sequence of units (nucleotides or amino acid residues) in a chain.

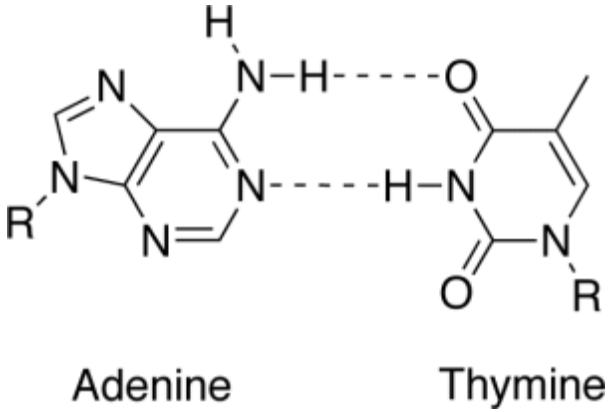
Structures

- Three-dimensional structures can give insights into the molecular basis of biological functions.

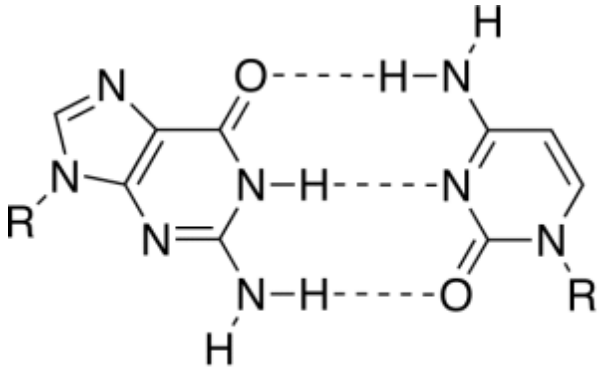
Systems

- Biological processes consist of the coordinated actions of molecules.

Base pairing in DNA



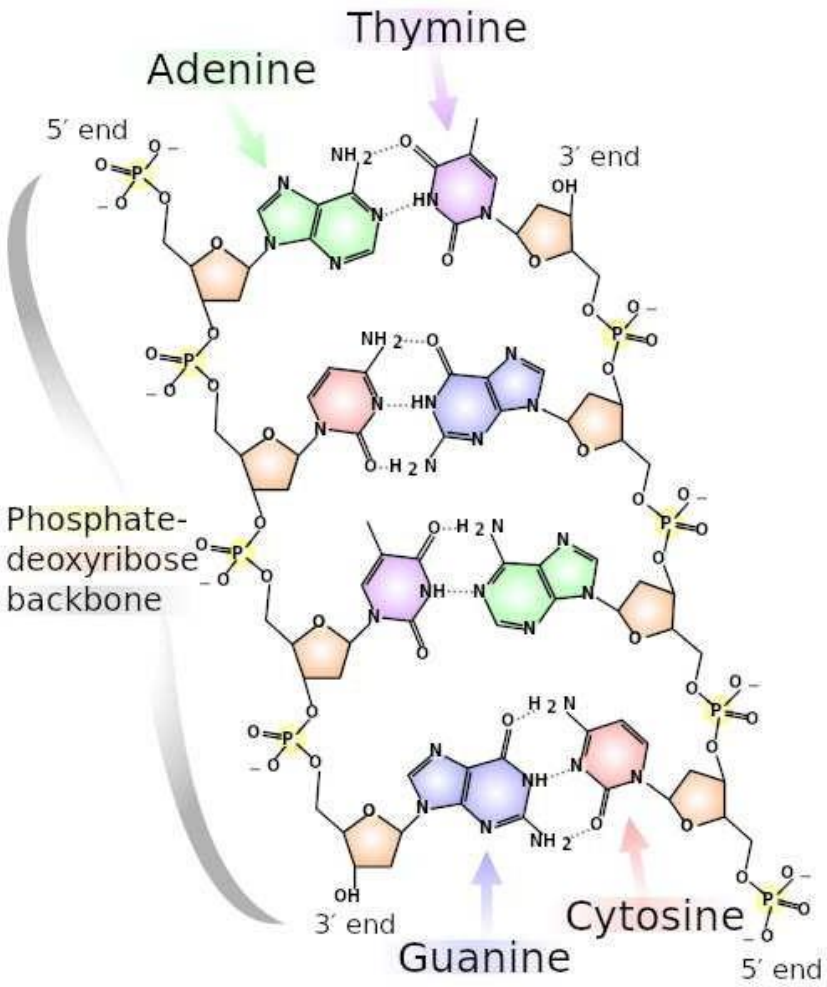
Adenine Thymine



Guanine Cytosine

http://en.wikipedia.org/wiki/File:AT_base_pair_jypx3.png
http://en.wikipedia.org/wiki/File:GC_base_pair_jypx3.png

Structure of DNA



http://en.wikipedia.org/wiki/File:DNA_chemical_structure.svg

Protein structure

Primary structure

- sequence of amino acid residues linked in a chain

Secondary structure

- locally, the main chain forms helices and strands

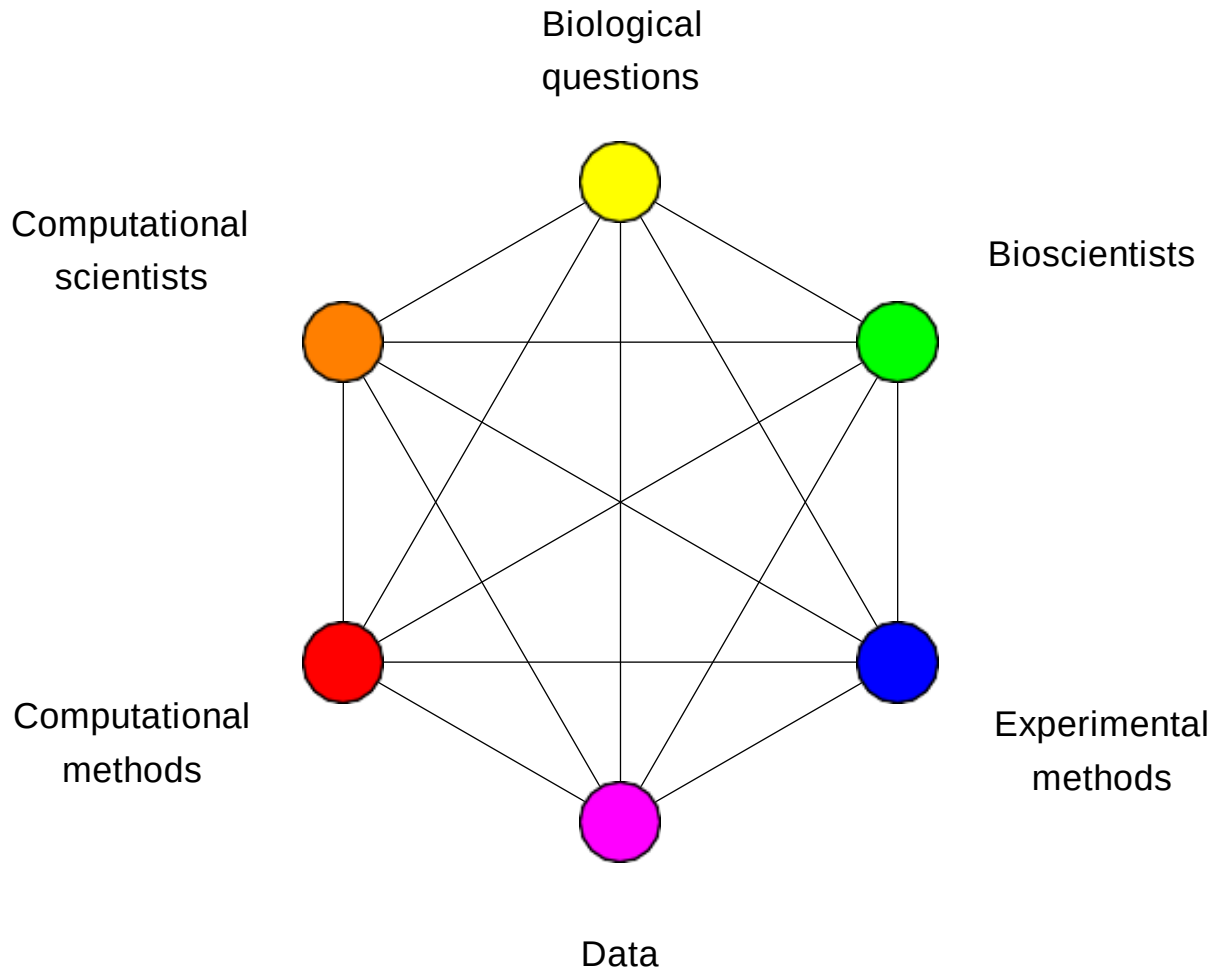
Tertiary structure

  - the 3-D structure
- assembly and interaction of helices and sheets

Quaternary structure

  - assembly of subunits

Addressing biological questions



Biological sequences: some experimental methods

- DNA sequencing
- Protein sequencing
- Next-generation sequencing (NGS)

Biological sequences: some questions

- How similar are a pair of sequences?
- Identify the corresponding units in a pair of homologous molecules that have undergone substitutions and insertions/deletions during their evolutionary history (*pairwise sequence alignment*).
- Given a new sequence, has anything similar (in whole or part) been seen before?
- Reconstruct a phylogenetic tree from the sequences of a set of homologous molecules.
- Given the sequences of many overlapping DNA fragments from a single organism, assemble them to reconstruct a full genome.
- Given the sequences of many DNA fragments from a mixture of organisms, identify the species present in the mixture.

Biological structures: some experimental methods

Find the atomic structure of a macromolecule or complex

- X-ray crystallography
- Nuclear magnetic resonance (NMR) spectroscopy

Identify a low-resolution "envelope" enclosing a large macromolecular complex

- Cryo-electron microscopy
- Small-angle x-ray scattering

Biological structures: some questions

- Can differences in the functions of two similar proteins be explained by differences in their structures?
- Can a drug be designed to fit into the active site of a target protein?
- Can the safety and efficacy of a potential therapeutic protein be predicted from its structure?
- Can the function of a protein be altered by changing its composition, and hence its structure?
- Can a protein's structure be predicted from its sequence?
  - the protein folding problem
- Given the structures of two proteins, will they associate with one another? If so, how will they fit together?
  - the protein docking problem

Biological systems: some experimental methods

Which mRNA molecules are being expressed?

- Microarray gene expression
- RNA-Seq

Which proteins are being expressed?

- (2-D) gel electrophoresis
- Mass spectrometry

In which tissue(s) are particular genes expressed?

- *in situ* hybridization

Biological systems: some questions

- Which genes/proteins are co-expressed (i.e. have similar expression profiles)?
- Which genes are expressed in tumour cells but not in healthy cells?
- If a gene is ”knocked out”, will an organism survive, and how will the expression of other genes be affected?
- Can protein expression profiles identify proteins that could be targets for drug development?
- Can an individual’s expression profile indicate whether they are likely to respond to a particular therapeutic treatment?
- How do biological networks respond to injury or to treatment with a therapeutic drug?

Sequences, structures and systems

Sequences

- MVE510 Introduction to bioinformatics
- BBT015 Advanced bioinformatics

Structures

- TDA507 Computational methods in bioinformatics

Systems

- KMG060 Systems biology

Computational methods and concepts featured

Computational methods and concepts featured in this course include: Graph theory and molecular networks, Dynamics and context-specificity in biological networks.