

Computational Biology: Quick reference

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November 16, 2011

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Part I

Themes

Use algorithms and computer simulation, to gain insight into biological processes.

0.1 Characterization of research effort

Highly experimental. Validation in wet-lab experiments essential.

There are a few very mathematical parts: such as understanding behaviour.

Part II

Computational biochemistry

0.2 Protein structure prediction

0.2.1 Protein structure

A chain of amino acids defines sequence. Structure preserved better than sequence. Some amino acids are hydrophobic, some are hydrophilic, some seek and form disulphide bonds with other amino acids. This results in protein folding. Hydrophobic interactions dominate, so try to minimize volume.

0.2.1.1 Nature of movement

Freedom in movement: rotation around 2 bonds in the backbone.

rAmachandran plot: a ϕ vs ψ contour map, showing low-energy regions of dihedral angles.

0.2.1.2 Folding in nature

Protein seeks the minimum energy conformation. Conformation space is huge. Searching in it is NP complete; Yet in nature, it is easily done: Levinthal paradox. Hypotheses: there is an energy funnel, falling into which leads to final conformation. So, some times not all initial conformations may lead to the final conformation.

0.2.2 Importance

Protein structure determines function; thence important in understanding function. Structure important in drug-design, protein design: make molecules to tack on to the right shapes.

X-Ray or NMR crystallography expensive. Want cheaper alternatives.

0.2.3 Approaches

Ab-initio. Homology modelling. Their combination.

In all, the objective is to minimize potential energy or its estimate.

0.3 Protein flexibility analysis

Part III

Genomics

1 Sequencing

1.1 Shotgun sequencing

The DNA is often too big to be sequenced, so one often breaks it up into tiny pieces, which are then sequenced. This is then 'stitched' together.

1.2 Social impact

1.2.1 Forensics

Paternity testing. Forensics: DNA testing has helped solve rape and murder cases.

1.2.2 Personalized medicine

1.2.2.1 Risk identification

There are variants of genes which are known to predispose one to cancer, polygamy etc.. So, at-risk individuals may take precautions, such as more frequent screening, dietary/ exercise alterations etc..

1.2.2.2 Better diagnosis

In many cases, ordinary diagnosis is unable to deduce the cause of a problem; worse: there can be misdiagnosis. In some of these cases, gene sequencing has helped provide marked, lasting relief.

1.2.3 History and legal issues

In late 1990's and early 2000's, the human genome was sequenced. Prior to that It was a race between the Venter corporation and freelancers, the latter won - so the human genome sequence was not patented.

2 Regulatory networks

Understand how proteins come together and function.

Microarray data analysis. Construction of biosensors, de-noising the data.

Part IV

Computational neuroscience

2.1 Sensory cortex: functioning and structure

Sensory cortices share a similar structure. V1 layer of visual cortex popular object of study. Different layers of neurons thought to abstract out different features.

Use models of wiring and functioning to understand how structure and function develop. Also, studying simpler models easier than studying the brain itself. Focus on important structural principles, thereby be not confounded by complexity in the brain.

Strategy: gather experimental data, make models, validate models, repeat.

Part V

Phylogenetics

Reconstruct the evolutionary tree or graph.

Part VI

Understanding animal behavior

2.2 Themes

Show how evolution has optimized a certain function, under certain constraints. Emergence of complex collective behavior from simple individual objectives. Eg: ducks flying in V shape.

Or show that the behavior is the equilibrium strategy in a game.