# GLOBEX Bioinformatics (Summer 2015)

**Review Session** 

# Basics of Molecular biology

#### Topics covered after midterm are highlighted in blue

- Central dogma
  - Transcription
  - Translation
    - Genetic code
- DNA
  - Double helix
  - Watson-Crick binding
- RNA
  - Secondary structures
- Genes
  - Compositional Structure
  - Reading frames
- Proteins
  - Secondary structure: alpha helices, beta sheets, and coils
  - 3-d structure
- Gene Regulations (Operons)
- DNA Microarray
- Cloning
- PCR
- Gel electrophoresis
- 2D gel + MS
- Yeast 2 hybrid system
- Gene orders

# Computational methods

Dynamic programming

- Problems can be dissect to sub-problems
- Recurrence equations
- DP Table
- Traceback

Maximum Likelihood (ML), and EM

Pairwise alignments Multiple alignments Hidden Markov models

- viterbi, forward, and viterbi training

Phylogenetic trees

- distance-based, character-based, and probability-based
- Bootstrap

Structural predictions

- secondary (RNA: Nussinov, Zuker; Proteins: ANN)
- lattice model for proteins.
- genetic algorithm

Clustering Profiles and inferring genetic networks

- K-means
- Boolean networks
- Bayesian (conditional independence, joint probability, factorization)
- Pearson correlation

# Computational methods

Dynamic programming

- Problems can be dissect to sub-problems
- Recurrence equations
- DP Table
- Traceback

# Maximum Likelihood (ML), and Expectation Maximization (EM)

Greedy Algorithms

Genetic Algorithms

#### Sequence alignments

- Motivations: evolution and homology
- Concepts and assumptions
  - Substitution scores: log-odds, PAM, BLOSUM, transition, transversion
  - gap penalties
  - Position independence
- Dynamic programming
  - Problems can be dissected to sub-problems
  - Recurrence equations
  - DP Table
  - Traceback
- Global v.s. local alignments
- Pairwise v.s. multiple alignments
  - Progressive approaches: guide tree, seq-profile, profile-profile
- Score statistics: E-value, p-value.

#### Hidden Markov models

- Motivations
- Concepts and assumptions
- Three tasks
  - Decoding (Viterbi algorithm)
    - Recurrence
    - Dynamic programming
  - Model likelihood (Forward algorithm, Backward algorithm)
    - Recurrence
    - Dynamic programming
  - Model building
    - Model architecture: profile HMM for sequence family
    - Model parameters
      - Labeled data
      - Unlabeled data (Viterbi training, Baum-Wunsch algorithm)

### Phylogenetic Trees

- Motivations
- Concepts and assumptions
  - Gene trees versus species trees
  - Rooted v.s. unrooted
- Mothods
  - Character-based
    - Maximum Parsimony: conventional and weighted
    - Traceback
  - Distance-based
    - UWPGA
    - Neighbor-joining
    - Metric distance, ultrametric distance, molecular clock, additive distance
  - Probability-based

#### RNA secondary structures

- Concepts
  - Single strand
  - Intra-molecular pairings
  - Structural categories
    - Hairpins, bulge loops, interior loops, and multi loops
    - Pseudo knots
  - Similarity in secondary structure plays a more important role than primary sequence in determining homology for RNAs
- Algorithms for predicting structures
  - Nussinov's
    - Maximum base pairing
  - Zuker's
    - Minimum energy

Protein structures

- Concepts
  - Anfinsen hypothesis
  - Primary, secondary, tertiary, and quaternary
- Algorithms for predicting structures
  - Secondary structure
    - encoding
    - Artificial neural networks
  - 3-dimensional
    - Lattice models
      - HP models: Genetic algorithm

### Systems Biology

- Concepts
  - Gene expression
  - Regulation, protein-protein interactions, ...
  - Operons, co-regulation
- Clustering and Modeling
  - Profiling, distance, hierarchical cluster, dendrograms.
  - K-mean
  - Genetic networks modeling
    - Boolean networks
    - Bayesian

## About the Final Exam

- Time and Place:
  - July 25, 8:00AM-11:00AM
  - 3<sup>Rd</sup> Teaching Building, Rm 106
- closed-book (One sheet of A4 size is allowed)
- Exam is cumulative.
- Four parts
  - Primary sequence analysis [~25 points]
  - Phylogenetic trees [~30 points]
  - Structural prediction [~25 points]
  - Systems biology [~20 points]: gene expression analysis, and regulation, genetic networks.