Winter 2024

PHM1130Y/PHC421H Biomolecular Interactions and Thermodynamics

Outline and course information

Instructors
Prof. Tigran Chalikian t.chalikian@utoronto.ca
Prof. Rob Macgregor rob.macgregor@utoronto.ca (coordinator)

The final mark in this course will be made of the following four components:

1) 30% A 30-minute oral exam scheduled during the April exam period
2) 30% A 20-minute oral presentation to the entire class of a current topic in biothermodynamics. The students may choose among a list of relevant current papers that will be provided by the professors. Note: all students must attend these presentations unless the student provides a valid excuse for being absent. Students who do not attend will have 5% deducted from her/his mark on her/his oral presentation for each presentation that is missed without a valid excuse.
3) 30% A term paper covering a relevant topic in biothermodynamics. The students will choose among topics provided by the professors.
4) 10% An outline of the term paper, submitted by 5:00 pm, Monday 4 March 2024.

Additional details will be provided in class. Students who fail to submit the outline or term paper by the assigned date will have 3% taken from the score of the report for each day (or fraction of day) that the term paper or outline is late.

Outline of the lectures

The Physical and Structural Properties of DNA and DNA Ligand Complexes (R. Macgregor)

Structure of nucleic acids, canonical structures, non-canonical and other structures, state of DNA *in vivo*
Stability of the helical forms of DNA, the role sequence, chain length, solution conditions, nearest-neighbour interactions
Kinetics of helix formation: chain length, sequence effects
Non-covalent DNA-drug interactions: Intercalation, groove binding
Analysis of non-covalent interactions with nucleic acids: Binding site exclusion
Covalent DNA-drug Complexes
Methods of investigating the structure and stability of the complexes between nucleic acids and drugs.
Nucleic acids and nanotechnology

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Solution Thermodynamics and Protein Structure
(T. Chalikian)

Thermodynamic systems. Equilibrium. The first law of thermodynamics. Enthalpy. Heat capacity. Entropy. Free energy.

Calculation of changes in state functions. Chemical potential and other partial molar quantities. Standard thermodynamic functions of reactions. Le Chatelier's Principle.

Differential Scanning Calorimetry. Partition Function Analysis of the Heat capacity Curve. Isothermal Titration Calorimetry.

Volumetric Techniques. Equilibrium Perturbation Methods.

Ionic Interactions. Ion-Dipole and Dipole-Dipole Interactions. Ion-Induced Dipole and Dipole-Induced Dipole Interactions. Dispersion, or London, Interactions.

Hydrogen Bonding. Hydrophobic Effect.

Structure and Properties of Liquid Water. Water as a Solvent. Hydration.

Hydration of proteins and nucleic acids.

Native, Unfolded, and Intermediate States of Globular Proteins. The Protein Folding Problem. Primary, Secondary, Tertiary Structures.

Dominant Forces Stabilizing Native Protein Structure. Electrostatic Interactions. van der Waals Interactions. Hydrogen Bonding. Hydrophobic Forces. Configurational Entropy.

Thermodynamics of Conformational Transitions of Globular Proteins. Temperature-, Pressure-, Denaturant-, and pH-Induced Protein Denaturation.

Biopolymer-Ligand Interactions. Macroscopic and Microscopic Constants. Macromolecules with Identical Independent Binding Sites. Macromolecules with Multiple Classes of Independent Binding Sites. Interaction between sites.