MBIO 4540 Biological Energy Transduction

Biological Energy Transduction is the subject of a specialized biochemical discipline – bioenergetics. In this course, the general topic is “Transformation of energy in biomembranes”. Specific topics include introduction into the chemiosmotic theory, relevant elements of thermodynamics, specific methods of membrane bioenergetics, molecular mechanisms of generation (e.g., respiration, photosynthesis, bacteriorhodopsin) and utilization of ion motive forces in ATP synthesis as well as in osmotic and mechanical work. Students are expected to be comfortable in elementary mathematics, physics and organic as well as inorganic chemistry. This course is based on a thermodynamic approach, and a certain amount of the relevant calculations will be included in both the mid-term and final examinations. Brief look into the Course Notes (UMLearn, the course site) will give a general idea about the expectations in math/physics/chemistry.

Marking: midterm (**30%**) and a final exam (**70%**).

Course outline:

Part I – GENERAL BIOENERGETICS

1. **Introduction**: cellular energy flow. ATP as the universal energy currency of all cells. Cellular energy metabolism. ATP–yielding pathways: substrate level phosphorylation, oxidative and photo-phosphorylation. ATP-consuming pathways: chemical, osmotic, and mechanical work in living systems.
2. **Chemiosmotic theory.** Definition of membrane bioenergetics. Scalar and vectorial biochemical reactions. Mitchell’s chemiosmotic principle – “quiet” scientific revolution. Energy-transducing membranes and coupling ions. The proton cycle. Introduction of the proton motive force (Δp) and its components ($\Delta\psi$ and ΔpH). Interconversion of Δp and ATP.

Part II – QUANTITATIVE BIOENERGETICS: THERMODYNAMICAL APPROACH

3. **Relevant elements of equilibrium thermodynamics.** The free energy change (ΔG). Gibbs energy and equilibrium. ΔG for the ATP hydrolysis and synthesis reactions. Oxidation-reduction (redox) potentials. Electron and hydrogen carriers. Redox potential (E_h) and pH.
4. **Thermodynamics of electron transfer and membrane transport.** Ion electrochemical potential differences. Relations between ΔG, ΔE_h, and Δp. Equilibrium distribution of ions, weak acids/bases. Diffusion potentials, Donnan potentials, and surface potentials.

Part III – SELECTED METHODS

5. **Specific methods of Membrane Bioenergetics.** Problems arising in the measurements of $\Delta\psi$ and ΔpH. Membrane potential measurements and penetrating ions. ΔpH measurements. Fluorescent amines. Penetrating weak bases/acids. Ionophores. Reconstitution of membrane proteins into proteoliposomes.

Part IV – KEY MOLECULAR MECHANISMS IN BIOENERGETICS

6. **Redox-coupled generation of the Δp in respiration: Complexes I and II.** Electron transport chain in mitochondria and some bacteria. Respiratory complexes of the inner mitochondrial membrane. Complex I: NADH-UQ oxidoreductase. Complex II: succinate dehydrogenase.

7. **Q-cycle and complexes III, IV.** The bc_1 complex and Q-cycle. Cytochrome c oxidase. Reduction of oxygen as a "thermodynamic sink".

8. **H^+ motive F_0F_1 ATPase: rotational catalysis.** The central enzyme of membrane bioenergetics. Molecular anatomy of the F_0F_1 ATPase. Unusual enzymology of the ATPase: binding change mechanism. Rotation in F_0F_1.

9. **Bacterial motility: membrane ion transport coupled to mechanical work.** The mechanics of bacterial motion. Structure of the basal body. Electrostatic model for the rotation. H^+ and Na^+ driven flagellar motors. Motility energized by artificial proton motive force.

10. **The sodium cycle.** Generalization of the proton cycle. Primary Na^+ transporters. Linkage between proton and sodium cycles: Na^+/H^+ antiporters.

Part V – DIVERSITY OF MOLECULAR MECHANISMS IN BIOENERGETICS

11. **Bacteriorhodopsin (BRh).** BRh as the simplest light-dependent proton pump. Structure and photochemical cycle of bacteriorhodopsin. Photoisomerization of retinal. Shiff base and its role in proton transfer. Halorhodopsin: a light-driven chloride pump. Sensory rhodopsin I and II.

12. **Photosynthesis (Introduction).** General introduction. Light and dark reactions of photosynthesis. Oxygenic *vs.* anoxygenic photosynthesis. Photosynthetic pigments. Excitation and different ways of de-excitation. Energy transfer between photosynthetic pigments. Photosynthetic membranes. Chloroplast. Photosynthetic unit. The reaction center and light-harvesting antenna pigments.

13. **Bacterial photosynthesis.** Cyclic photoredox chain in purple bacteria. Chromatophores. Composition of the purple bacterial photosynthetic apparatus. "Special pair" of bacteriochlorophyll *a*. Generation of a strong electron donor (P_{870}*). Cyclic electron flow. Q cycle. Cyclic photo-phosphorylation. Reduction of NAD^+ and reverse electron flow. Non-cyclic electron transport in green sulfur bacteria. Comparison of cyclic and non-cyclic photosynthetic electron transport.

14. **Photosynthesis in cyanobacteria and higher plants.** Photosystems I and II. Hill reaction. MnC cluster and redox-active tyrosyl of PS II. Water as primary electron donor. Cyclic and non-cyclic electron flow. Cyclic and non-cyclic photophosphorylation. Membrane topography of PS I and PS II. Generation of Δp in the course of electron transfer. Reduction of $NADP^+$. Interconversion of Δψ and ΔpH on the thylakoid membrane.

15. **Membrane bioenergetics of hydrogen-oxidizing bacteria.** Hydrogen as a primary electron donor. Membrane-bound and soluble hydrogenases. Major coupling sites of the redox chain: Q-cycle and terminal cytochrome oxidase. ATP synthesis coupled to the oxidation of H_2.

16. **Generation of the Δp in the course of fermentations.** "Energy recycling" based on electrogenic efflux of metabolic end-products. Precursor/product exchange. Systems based on the uniport of fermentable substrate. Separate generation of Δψ and ΔpH in the course of fermentations. Efficiency of Δp generation. Fermentation-driven generation of Δp possibly is an early evolutionary mechanism of energy conservation.

17. **The "sodium world".** Na^+-pumping oxaloacetate decarboxylase from *Klebsiella pneumonia*. Role of biotin. Catalytic mechanism. Reversibility and overall stoichiometry of Na^+ transport. Model for Na^+ transfer by oxaloacetate decarboxylase. Strict coupling between decarboxylation reaction and Na^+ transfer. Na^+ cycle in *Propionigenium modestum*. Na^+-motive ATPase of *P. modestum*. Na^+-motive NADH:quinone oxidoreductase (NQR). Major enterobacterial Na/H antiporter, NhaA: from structure to mechanism. Evolutionary relations between the proton and sodium cycles.

18. **The central dogma of membrane bioenergetics: a final look.** Three basic principles of cell energetics. Three convertible energy currencies of living systems.