I. COURSE SUMMARY
A major purpose of this course is to provide an introduction to some aspects of physical chemistry through the subject of bioenergetics. After deriving the foundations of the thermodynamics of membrane energy transduction, the course will focus on biochemical and biophysical mechanisms of electron, proton, and light-energy transfer, utilizing the extensive array of information on mechanism that has emerged from high resolution structures of energy-transducing membrane proteins, also leading to a discussion of mitochondrial cell biology and myopathies. Relevant biophysical and spectroscopic techniques (flash kinetic, chemical difference, and low temperature, visible and electron paramagnetic resonance; fluorescence resonance energy transfer) will be discussed.

II. TOPICS
1. Thermodynamic background for biological energy transduction
   - Energy, Enthalpy, Entropy, Free energy; concentration dependence
   - Other kinds of work: electrical, chemical
   - Chemiosmotic formula for membrane energy transduction
   - $\Delta \tilde{\mu}_{H^+}$-linked active transport: symport, uniport, antiport
   - Structures of MFS transporters
   - $\Delta \tilde{\mu}_{H^+}$-coupled vectorial ATP synthesis
   - Oxidation-reduction reactions, direction of redox reactions; meaning of redox potentials ($E^\circ$, $E$); concentration dependence of $E$; pH dependence of $E$; coupled electron and proton transfer; measurement of potentials; protein determinants of redox potentials

2. Energy Storage-Membrane Structure
   - Fundamental aspects of membrane structure
   - Topography of mitochondrial, bacterial, and thylakoid membranes
   - Generation, utilization of $\Delta \tilde{\mu}_{H^+}$
   - Experimental basis for chemiosmotic energy transduction
   - Coupled and uncoupled reactions
   - Nature of ionophoric uncouplers
   - Uncoupling proteins and obesity.

3. Mitochondrial Diseases
   - Energy coupling; Luft’s disease
   - Permeability transition of the mitochondrial outer membrane in apoptosis
4. **Structure-function of energy-transducing membrane proteins, protein complexes:**
   A. Electron transfer proteins
   - Respiratory, photosynthetic electron transfer chains
   - Structures of heme proteins; cytochrome c, cytochrome f
   - Iron-sulfur proteins
   - Spectroscopic signatures of metalloproteins; optical, electron paramagnetic spectroscopy

5. **Integral membrane electron/H⁺ transfer proteins**
   Isolation and crystallization of integral membrane protein complexes: the detergent problem

6. **Structure-function of Integral Membrane Energy-Transducing Proteins**
   A. Respiratory electron transport; generation of the Δμ H⁺
      (i) Cytochrome bc complexes
      (ii) Cytochrome oxidase
      (iii) NADH dehydrogenase; genetic loci of mitochondrial myopathies
   B. Photosynthetic electron transport chain
      (i) Light-energy transfer (FRET)
          Structure of:
      (ii) Light-harvesting pigment proteins;
      (iii) Bacterial photosynthetic reaction center
      (iv) The Mr 1,000,000 Photosystem I complex of oxygenic photosynthesis
      (v) Photosystem II

7. **Primitive transmembrane proton transfer, mechanisms and pathways**
   A. Primitive H⁺ and sensory transducing proteins
   B. X-ray Structure-function of bacteriorhodopsin and rhodopsin

8. **ATPase/ATP synthase**
   Proton-and sodium motive ATPase
   - Nanomotor
   - X-ray structure of F₁ ATPase
   - ATPase as a rotational nanomotor; function of F₀ subunits
   - Coupling of electrochemical potential to ATP synthesis.
III. EXAMS, GRADES

1. MIDTERM (8th week of the semester; exact date to be announced)

2. REPORTS (13th week)

3. FINAL EXAM (Finals Week), 2 hrs.

   Grades will be based on the final exam (50%), midterm (25%), homework (15%),
   and written report (10%).
   Homework will be handed out most weeks on Thursday; to be returned on
   following Tuesday; homework solutions will be posted on a Web site on the day
   the homework is returned; therefore, late homework will not be accepted.

IV. TEXTS AND READINGS

D. S. Eisenberg and D. Crothers. 1979. *Physical Chemistry with Application to the Life
   Sciences*. Benjamin Cummings (on reserve).

   Website: www.biophysics.org/education/mechanisms.htm
   Readings in the literature, to be distributed.

V. Tutorial Sessions: Wednesdays, 4:00 p.m., B-420, Lilly.

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