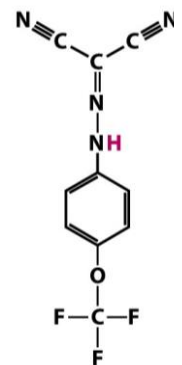


Problem Set 4**(Due February 11th)**

- We discussed how a single equivalent of ATP is produced by pumping 4 H⁺ from the matrix to the IMS.
 - Based on this observation, justify the P/O ratios for NADH, Succinate, and Ascorbate.
 - Consider the hypothetical situation in which it takes 2.8 H⁺ transferred across the IM to drive the synthesis of a single ATP.
 - Determine the P/O ratios for NADH, Succinate, and Ascorbate
 - How many ATP would completely oxidation of pyruvate to CO₂ generate?
- Starting with NADH, show all relevant enzyme catalyzed reduction/oxidation events that occur and result in the reduction of H₂O.
- Clearly describe the role of tyrosine in the catalytic cycle of Cytochrome C Oxidase (Complex IV).
- We will see next week that oxidation of a single glucose molecule to CO₂ should generate 32 ATP. However, in some tissue only 30 ATP equivalents are produced from the same oxidation process. How is this possible?
- Investigate the structure of the P₁-ATPase in pdbID1BMF. Examine the ADP site and ANP sites.
 - Is ANP a structural analogue of ADP or ATP? What is the difference and why is it a good analogue?
 - Compare and contrast these binding pockets. Please provide an image of the two sites and point out the most relevant similarities and differences.
- Addition of FCCP to respiring mitochondria will decouple electron transport and phosphorylation.
 - Given the structure of FCCP (red proton is acidic), describe how this molecule can function as a decoupling agent.
 - Using the graph on the adjacent page, plot the O₂ consumption and ATP synthesized as a function of time when each of the indicated molecules are added. Please justify your graph based on the function of each compound.
 - How would the graph differ if CN⁻ was added to the experiment prior to NADH?
- Using the affinities for ATP and ADP to the (F₁F₀) ATPase given in Lecture 8, determine if the stabilization of ATP relative to ADP is sufficient to drive the otherwise endergonic condensation of ADP and Pi.
- Please describe how the 3 conformations of the F₁F₀ ATPase are important for the synthesis of ATP. Make sure to include a discussion of relative energies for ATP and ADP in each conformation.
- IF₁ is a small protein that plays an important role in the F₁F₀ ATPase catalyzed hydrolysis of ATP under hypoxic (O₂ deprived) conditions. Please explore this regulatory mechanism and describe how it works. Make sure to consider the role of pH and discuss why there is a concern the ATP will be hydrolyzed.
- We have seen several examples of TCA Cycle enzymes (and will see many more in glycolysis) that respond to the concentration ratio of [NADH]/[NAD⁺] and [ATP]/[ADP]. Based on what you know about mitochondrial ATP synthesis, please justify this observation.

**FCCP**

11. Please familiarize yourself with the attached article and address the following questions:

- a.
- b.
- c.

