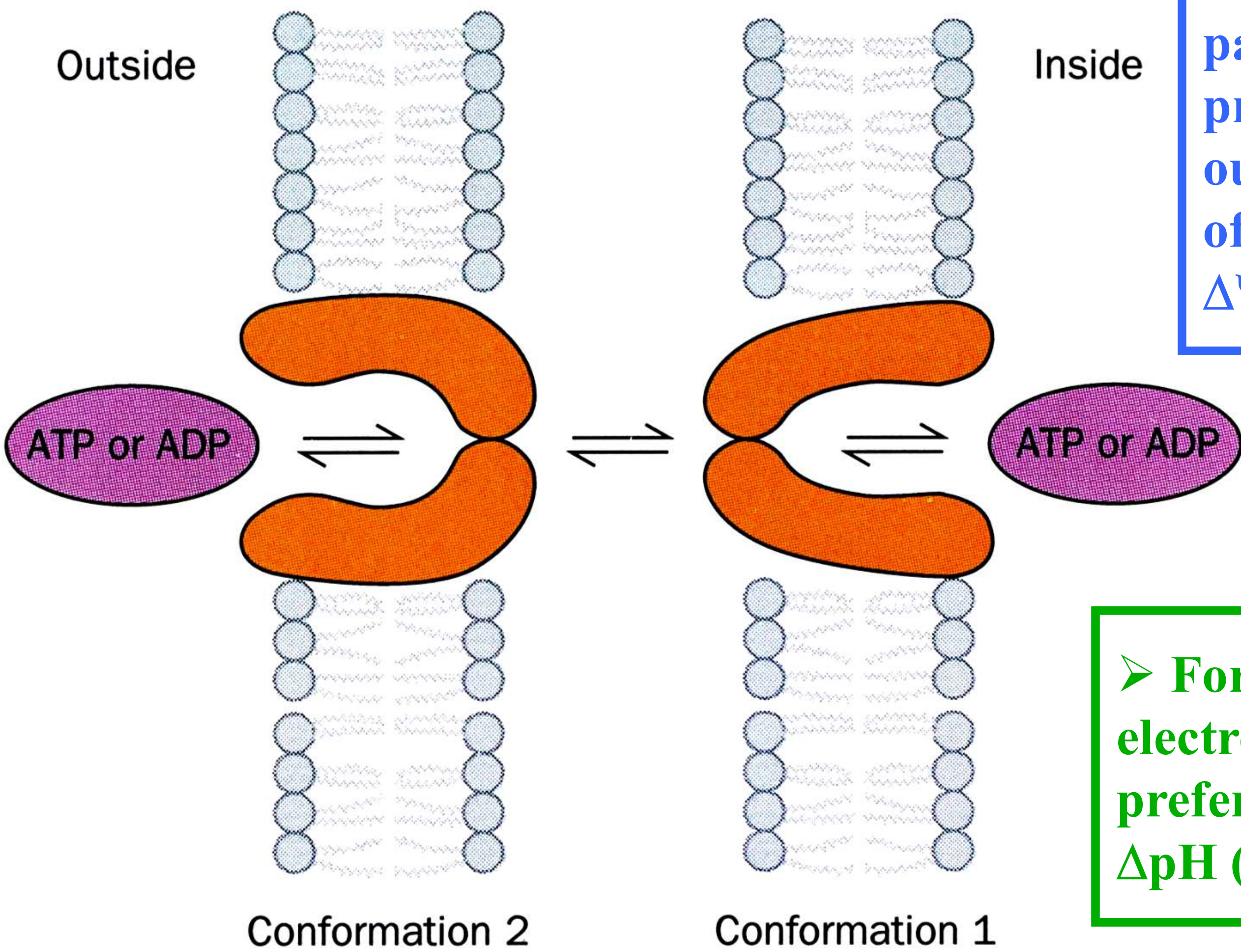
Mediated Transport Systems of the Mitochondrion



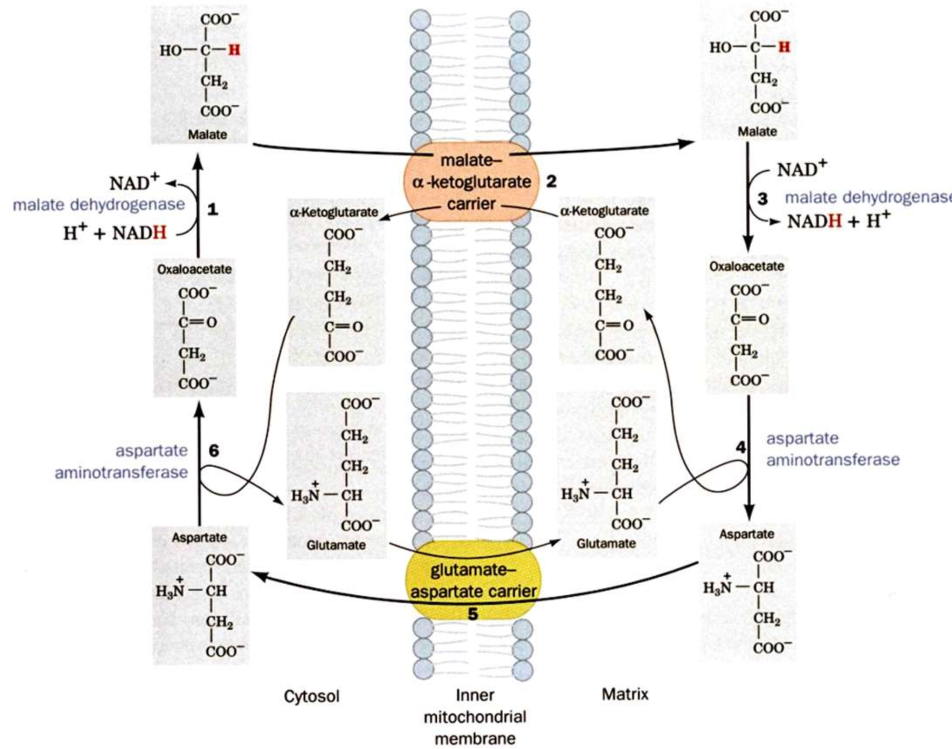
➢ **The ADP-ATP translocator:**
passive transport system; preferentially moves ATP^{4-} to outside and ADP^{3-} to inside because of membrane potential difference $\Delta\Psi < 0$ (negative inside)

➢ **For P_i:**
electroneutral P_i-H^+ symport, preferentially moves P_i inside because of ΔpH (pH higher, $[H^+]$ lower inside)!

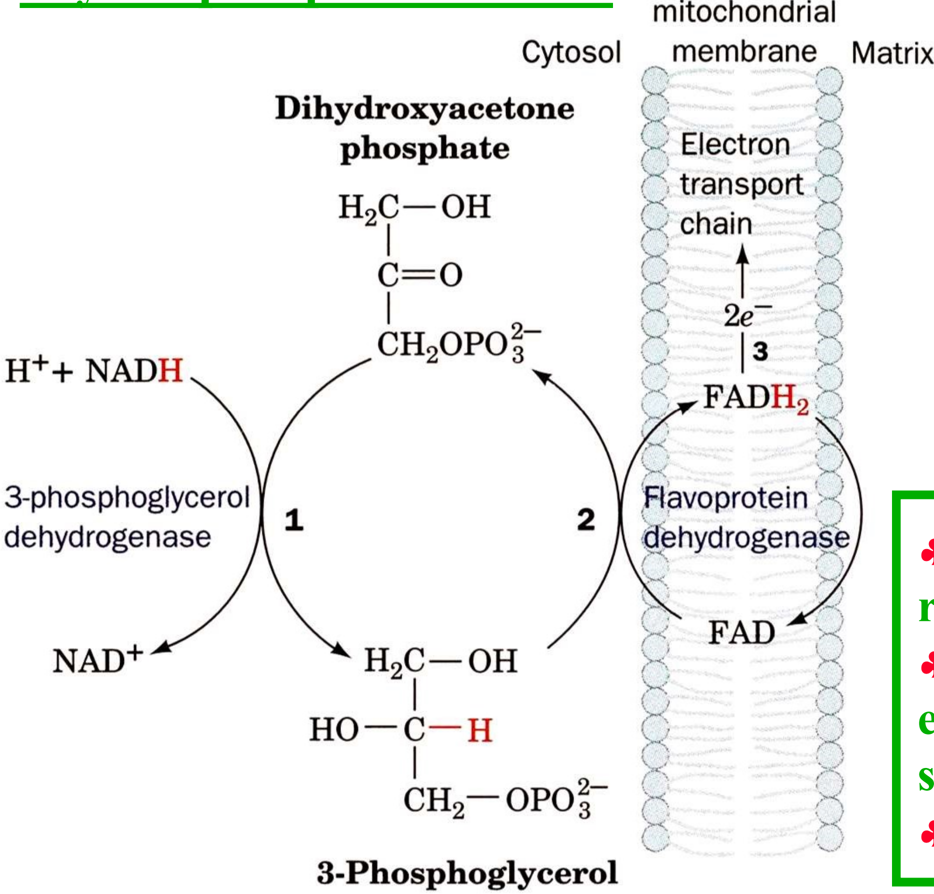
NADH Transport Across the Membrane

- Most NADH is produced during citric acid cycle in the mitochondrion; BUT glycolytic NADH has to be transported by one of two shuttle systems

Malate-aspartate shuttle (discussed in lecture on gluconeogenesis as oxaloacetate shuttle out of matrix):



Glycerophosphate shuttle:



- ♣ found in insect flight muscle (same power-to-weight ratio as car engine!)
- ♣ flavoprotein dehydrogenase is outer-surface bound enzyme that supplies e^- to electron-transport chain similar to succinate dehydrogenase
- ♣ synthesis of ONLY 2 ATP per NADH

The Thermodynamics of Electron Transport

Standard reduction potential difference for a redox reaction: $\Delta E^{o\prime} = E^{o\prime}_{e^- \, acceptor} - E^{o\prime}_{e^- \, donor}$

Reduced species

Oxidized species

$^1/_2O_2 + 2H^+ + 2e^- \rightleftharpoons H_2O \qquad E^{o\prime} = +0.815V$

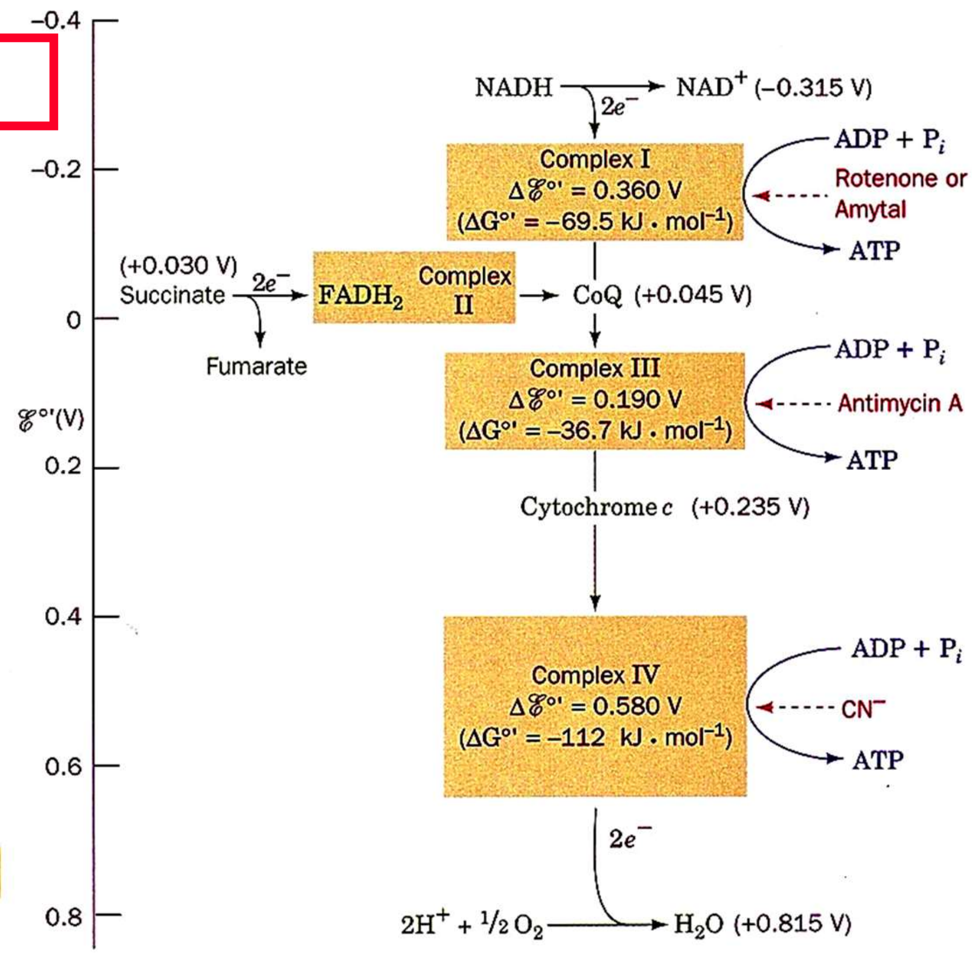
$NAD^+ + H^+ + 2e^- \rightleftharpoons NADH \qquad E^{o\prime} = -0.315V$

$^1/_2O_2 + NADH + H^+ \rightleftharpoons H_2O + NAD^+ \qquad \Rightarrow \Delta E^{o\prime} = 0.815 - (-0.315V) = 1.130V$

and $\Delta G^{o\prime} = -nF\Delta E^{o\prime}$ $\boxed{\Rightarrow \Delta G^{o\prime} = -218 \text{ kJ/mol}}$

# of e⁻ transferred

Faraday constant = 96,494 C/mol



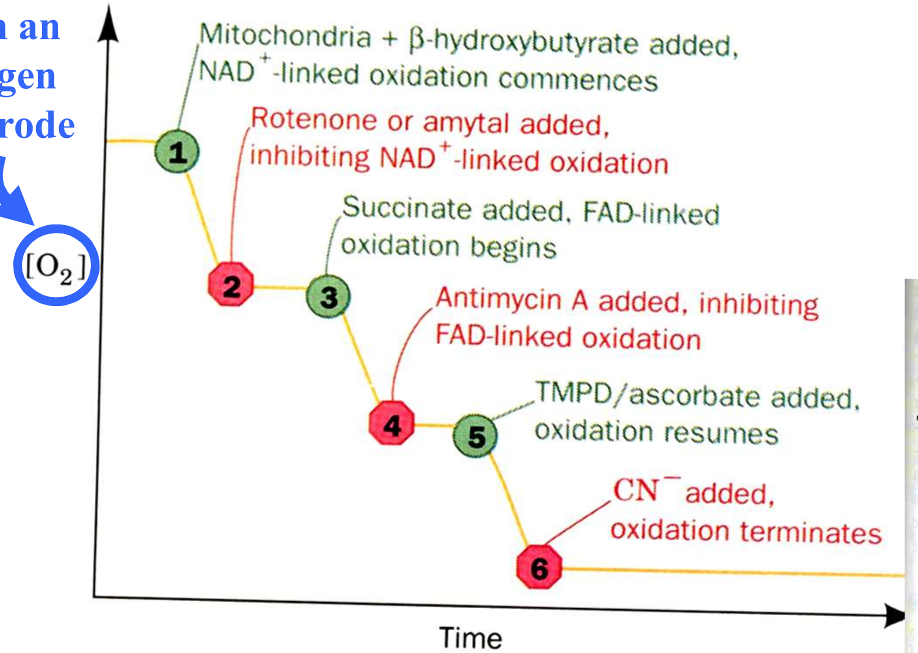
The electron transport chain breaks the overall free energy change into 3 smaller packets, each of which is coupled with ATP synthesis (worth 30.5 kJ/mol ATP) by harvesting a proton gradient

42% energy efficient under standard conditions, 70% under physiologic conditions (car engine: ONLY 30%!)

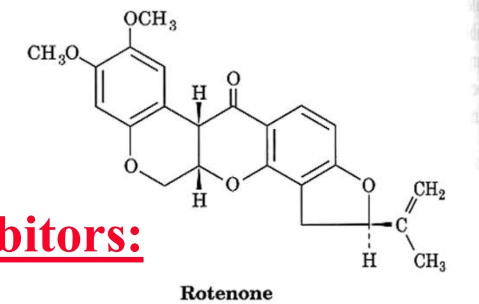
The Sequence of Electron Transport

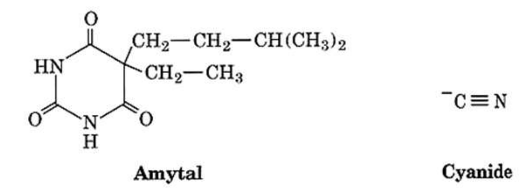
Experiment in a mitochondrion suspension:

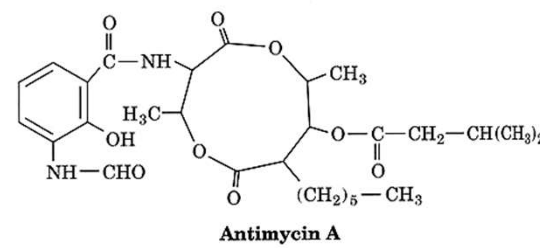
Measured with an oxygen electrode



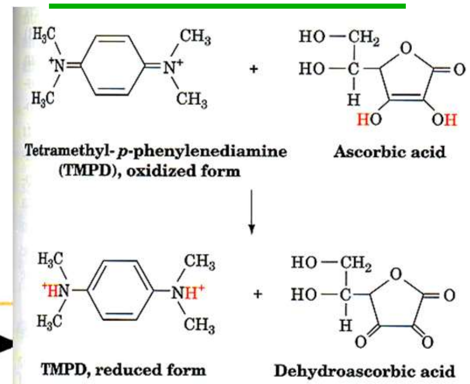
Using specific inhibitors:



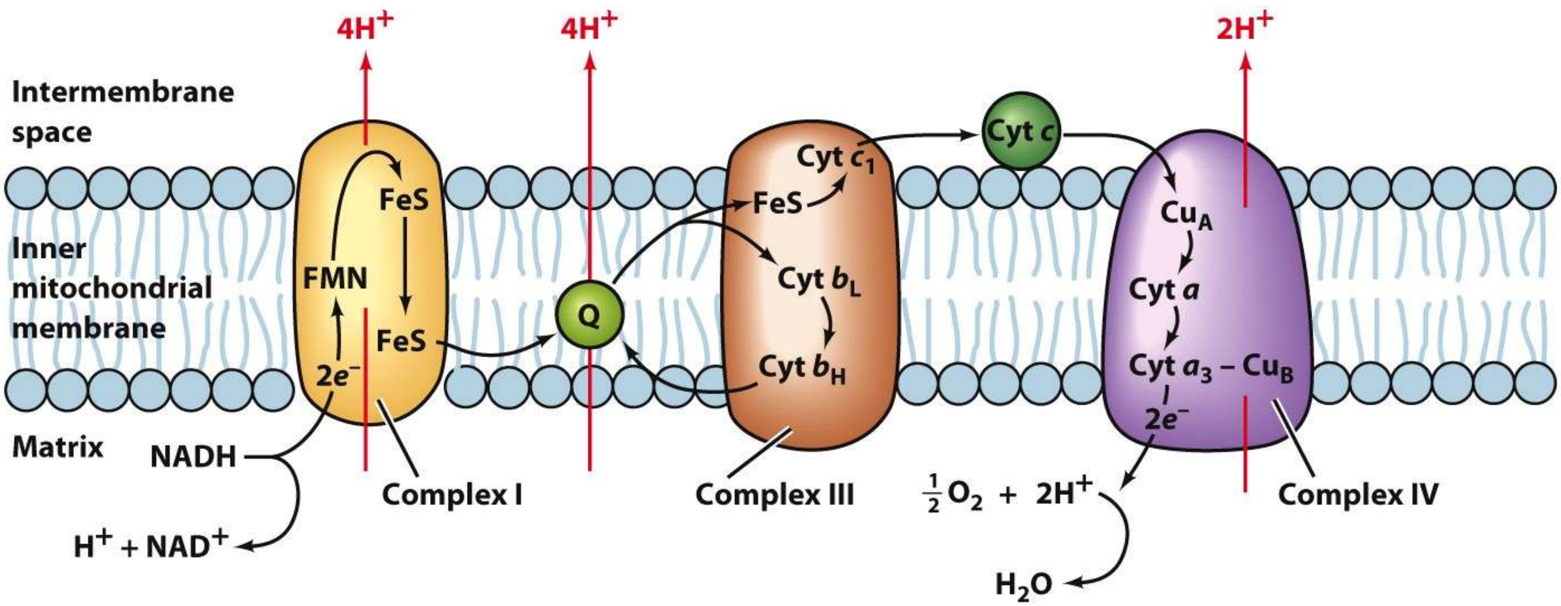




And substrates:

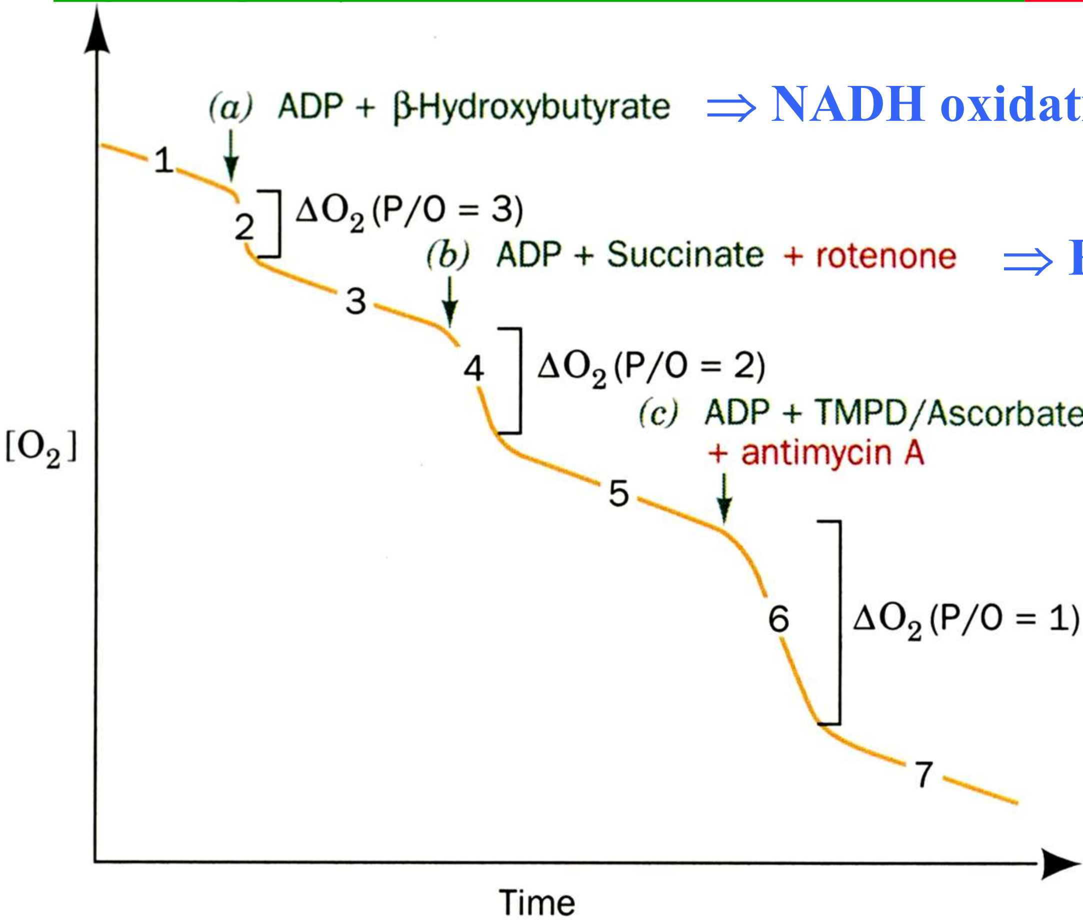


Leads to:



The P/O Ratio = Stoichiometry of ATP/O

Injecting 90 μmol ADP + excess metabolite (+inhibitor of previous step):



⇒ NADH oxidation leads to 3 ATPs per O (½ O_2 or $2e^-$ or 1 NADH)

⇒ $FADH_2$ oxidation leads to 2 ATPs per O (½ O_2 or $2e^-$ or 1 $FADH_2$)

⇒ Ascorbate oxidation leads to 1 ATP per O (½ O_2 or $2e^-$ or 1 ascorbate)

More recent measurements suggest P/O ratios of 2.5, 1.5, and 1 (instead of 3, 2, 1)
⇒ need not be integer!
⇒ only ~29-32 ATP/glucose (instead of 38, including each 2 from glycolysis & TCA);
Loss due to necessary ATP and P_i transport across mitochondrial membrane, using the H^+ gradient generated by electron transport!