CELLULAR RESPIRATION

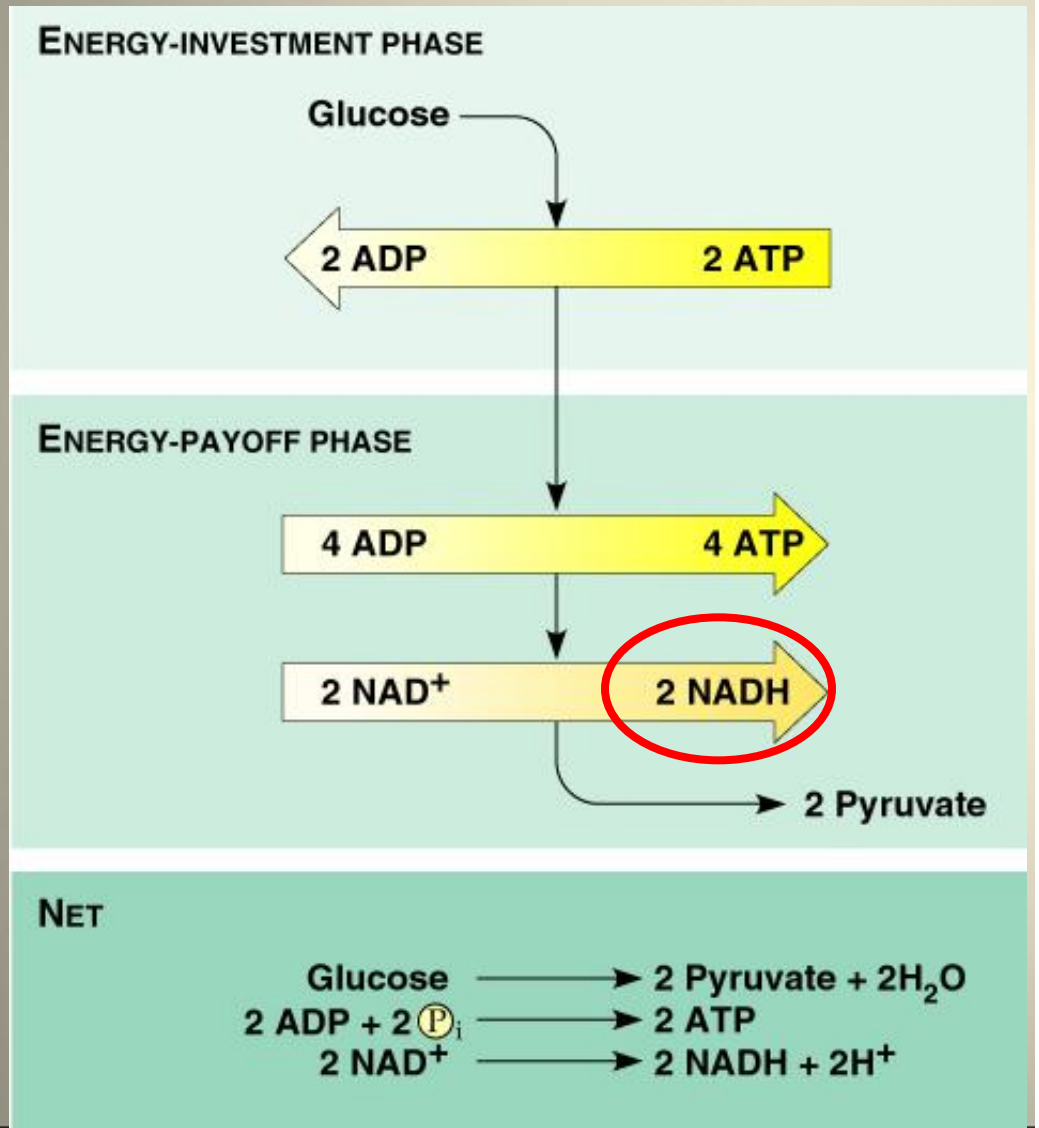
Part 3

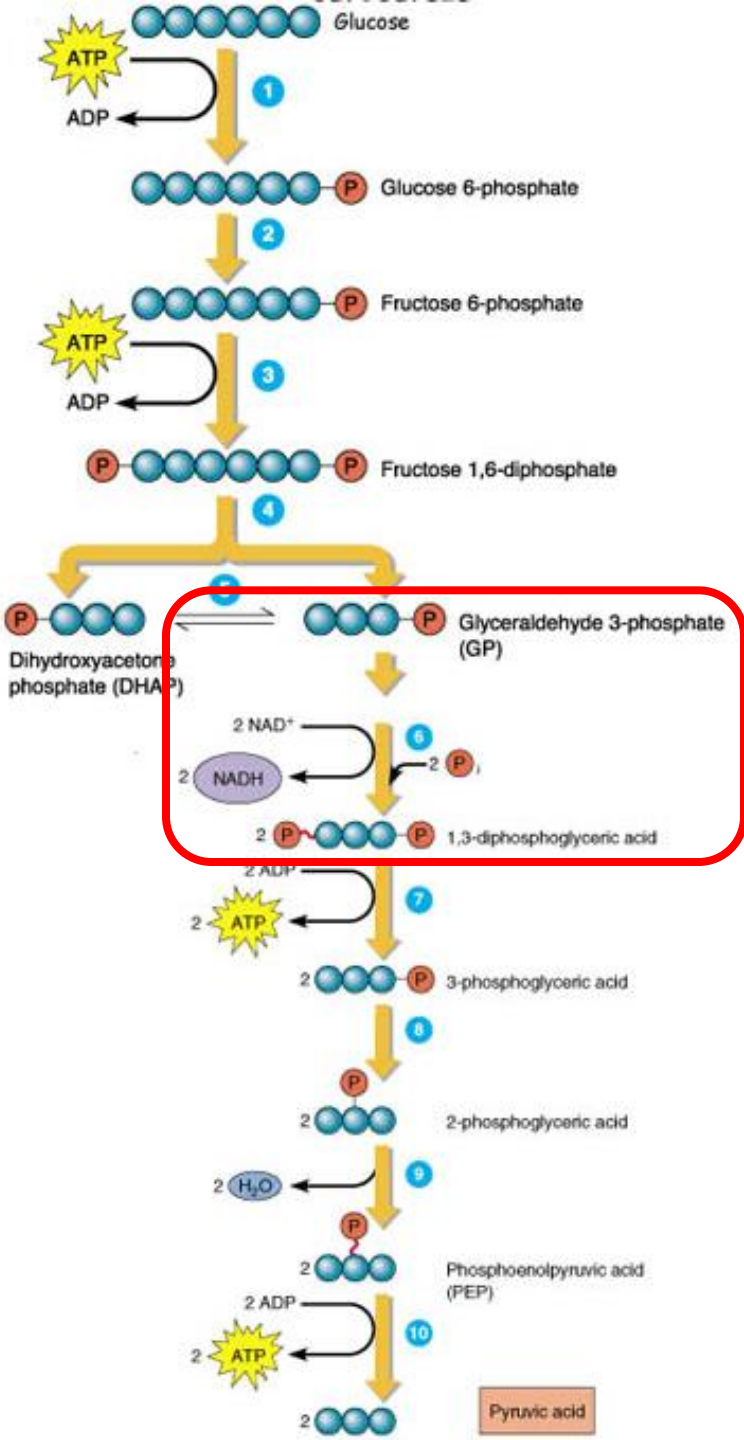
Electron Shuttle

Oxidative Phosphorylation

- Electron Transport Chain
- Chemiosmosis

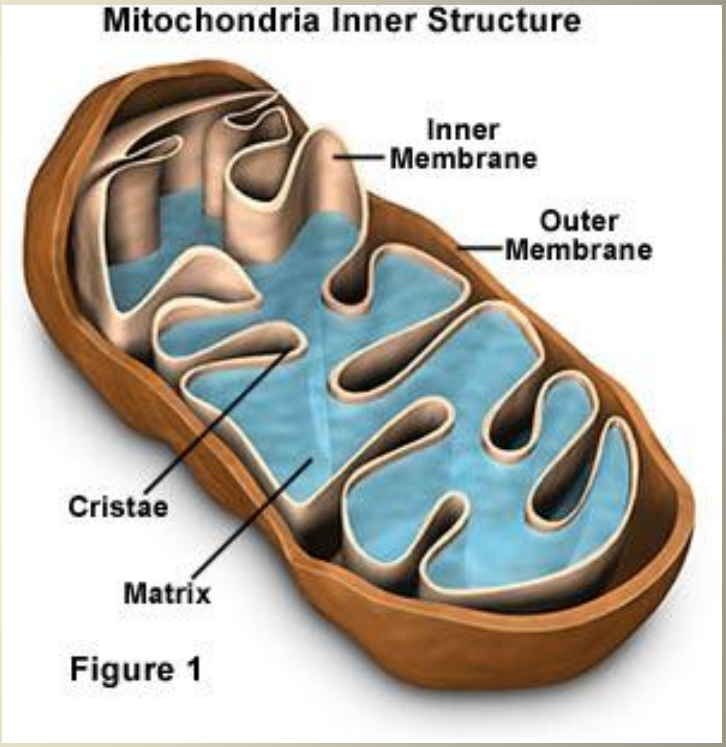
Recall: Glycolysis



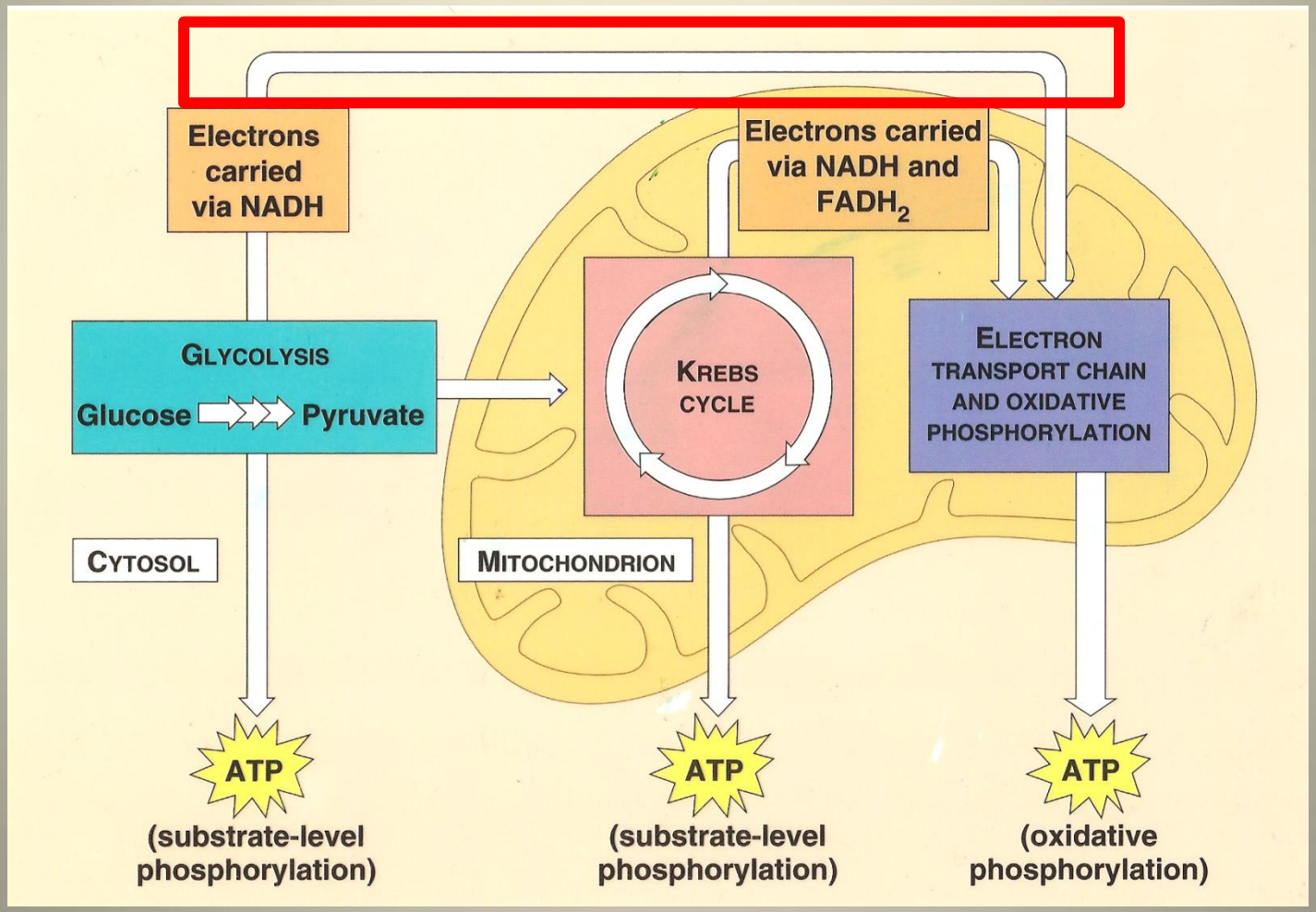


Recall: Location

- Glycolysis occurs in the cytoplasm
- Electron transport chain (ETC) starts in the mitochondrial matrix
- The NADH produced during glycolysis must make its way into the mitochondria



Electron Shuttle



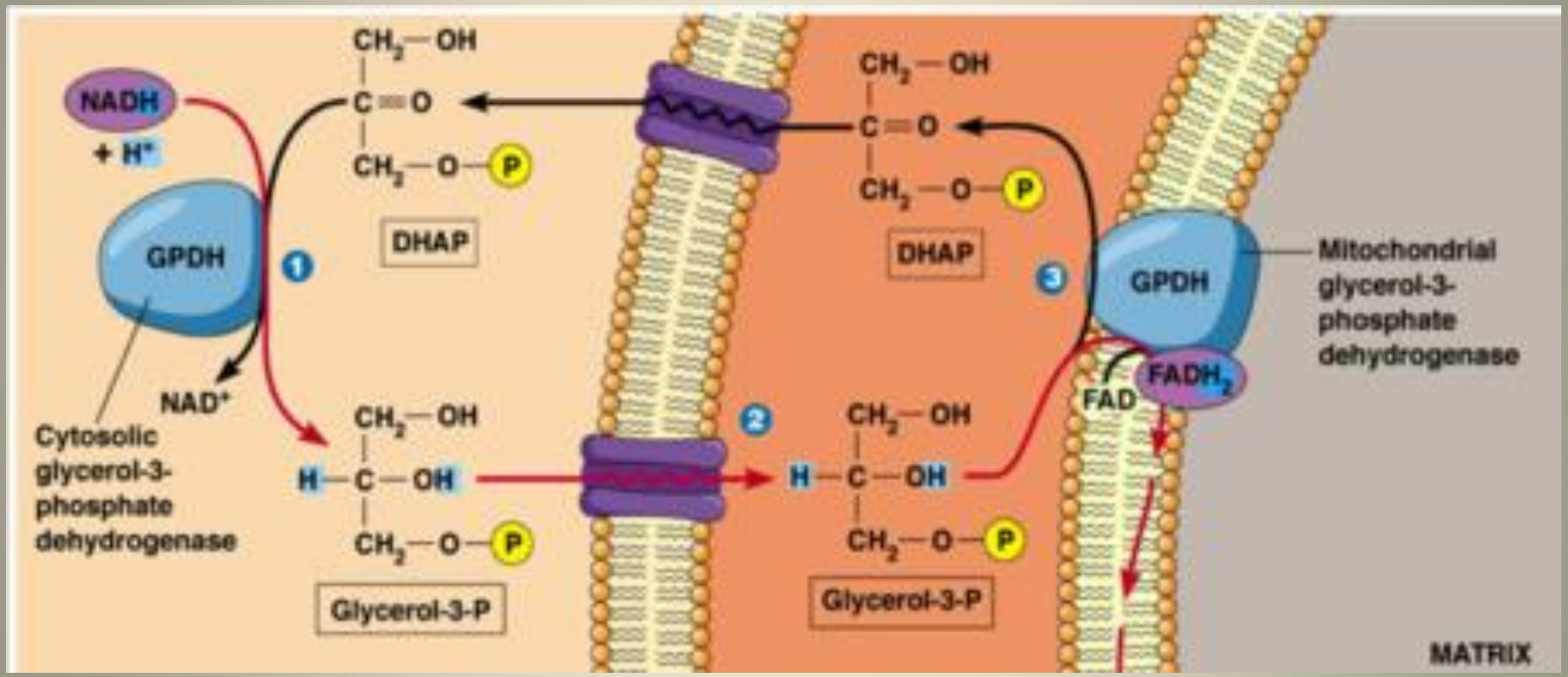
Electron Shuttle

- NADH produced in glycolysis must be transported from the cytoplasm into the mitochondria to enter the ETC
- Mitchondria is not permeable to NADH produced in the cytoplasm
- Shuttling of NADH is indirect

Two shuttle mechanisms:

- glycerol phosphate shuttle
- malate-aspartate shuttle

Glycerol Phosphate Shuttle



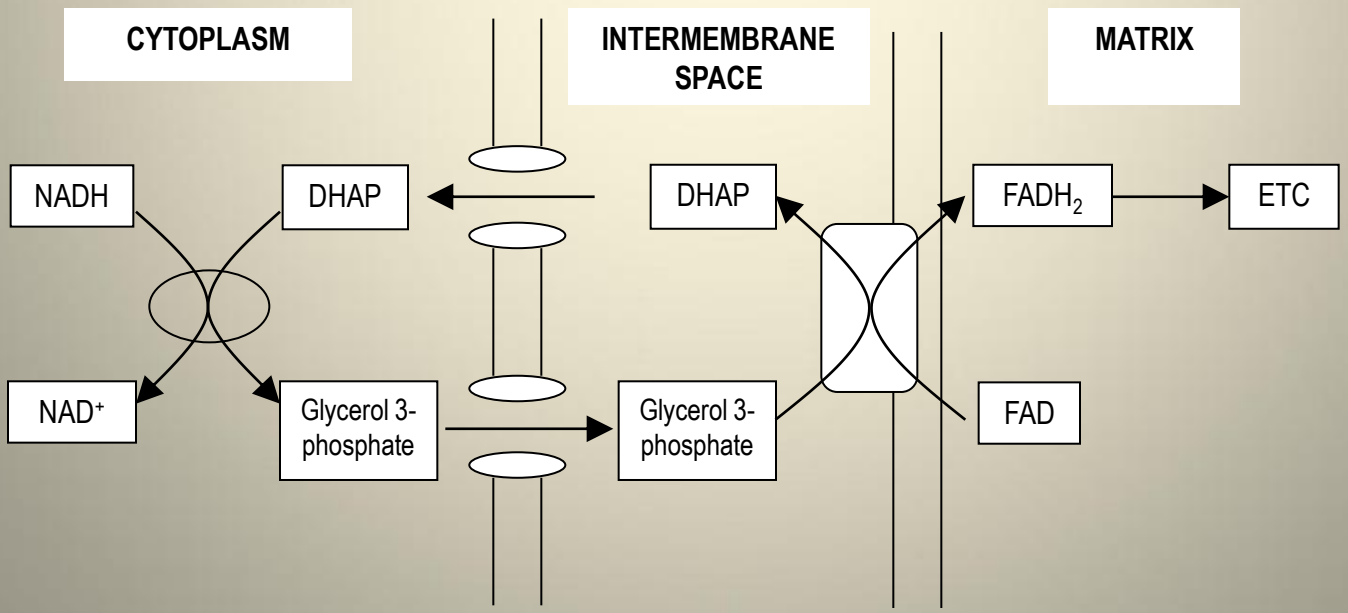
Glycerol Phosphate Shuttle

Steps:

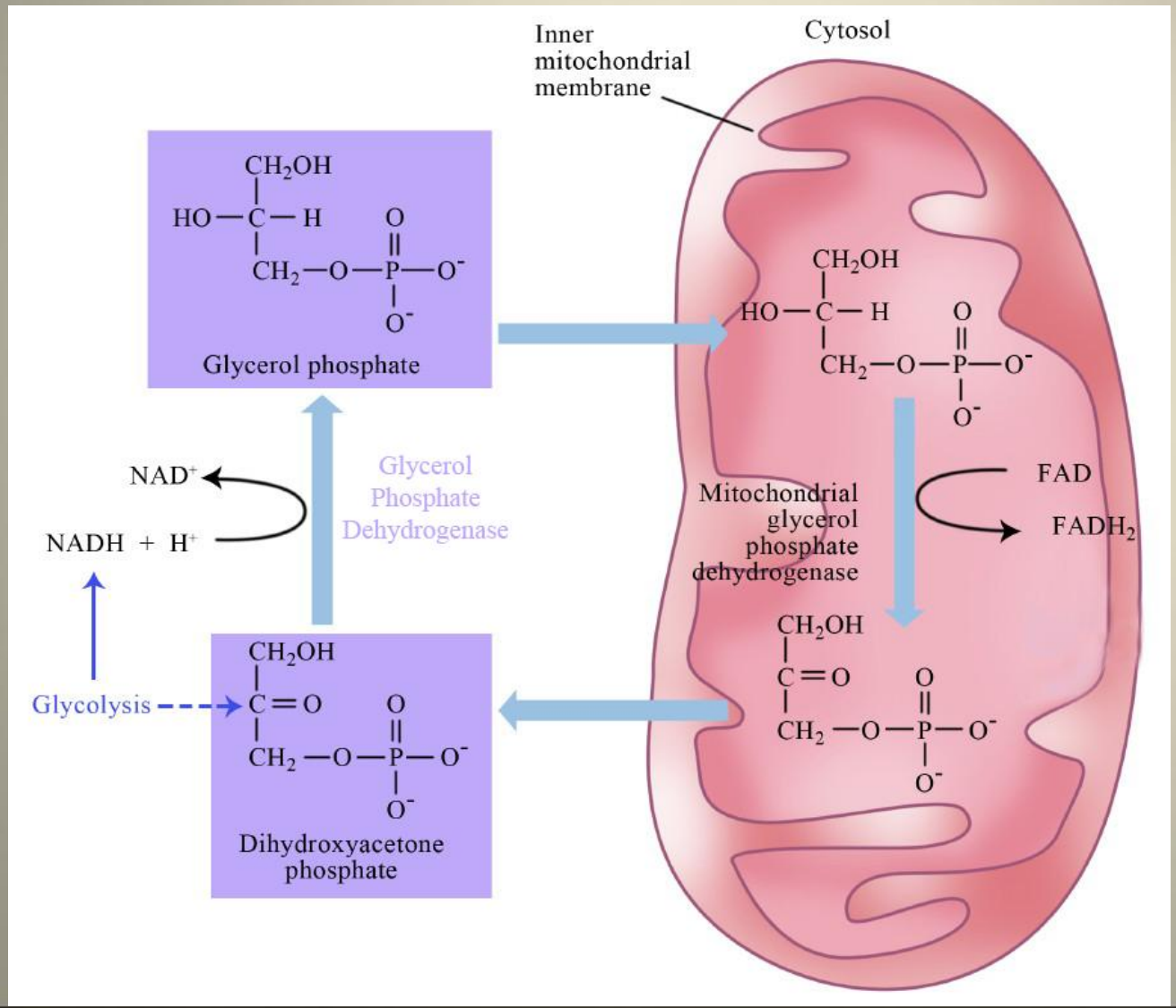
- Dehydrogenase in the cytoplasm transfers electrons from NADH to DHAP forming glycerol-3-P
- Porins on the outer mitochondrial membrane (OMM) allow glycerol3P to enter the intermembrane space
- Dehydrogenase on the inner mitochondrial membrane (IMM) removes electrons from glycerol3P and transfer it onto FAD forming FADH2

Glycerol Phosphate Shuttle

- Summary: electrons from NADH get shuttled into the mitochondria onto FAD resulting in FADH2 in the matrix
- Primarily in brain tissue and skeletal muscle tissue



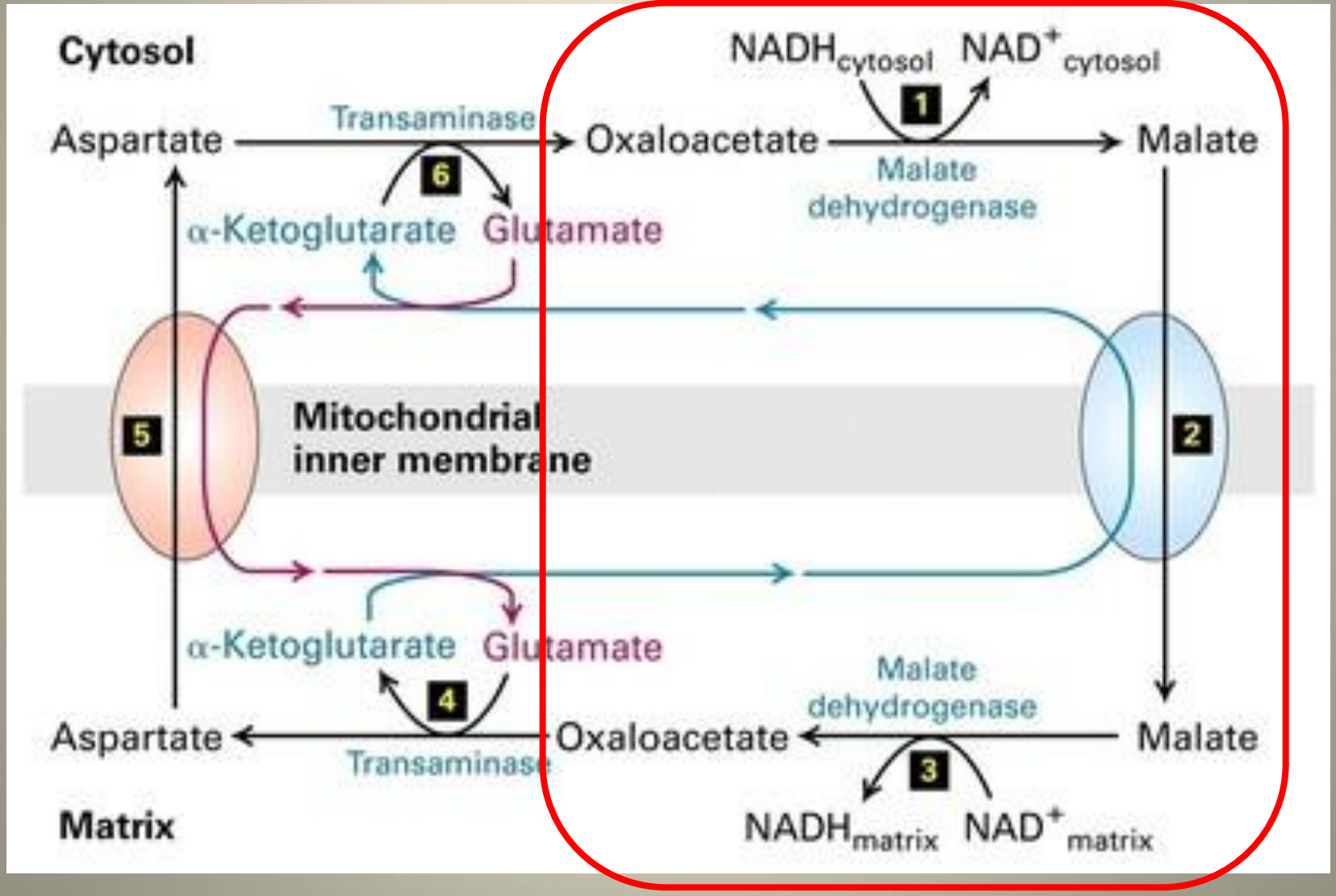
Glycerol Phosphate Shuttle



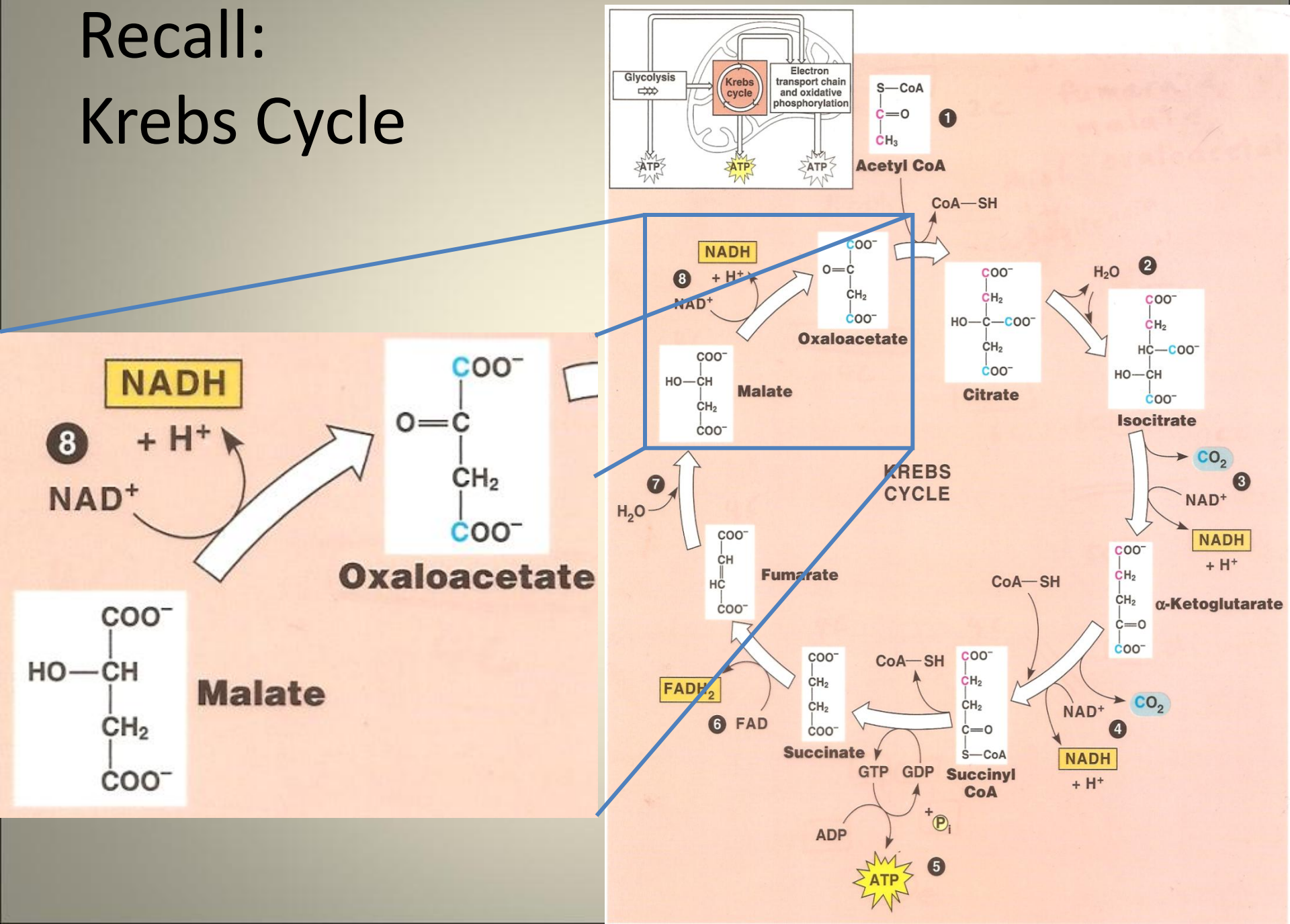
Molecule Count: Per Glucose

	ATP	NADH	$FADH_2$	
Glycolysis	2	2 →	0	
Pyruvate Oxidation	0	2	0	
Krebs	2	6	2	
Subtotal	4	8	4	
Conversion in ETC	4	24	8	36

Malate-Aspartate Shuttle



Recall:
Krebs Cycle

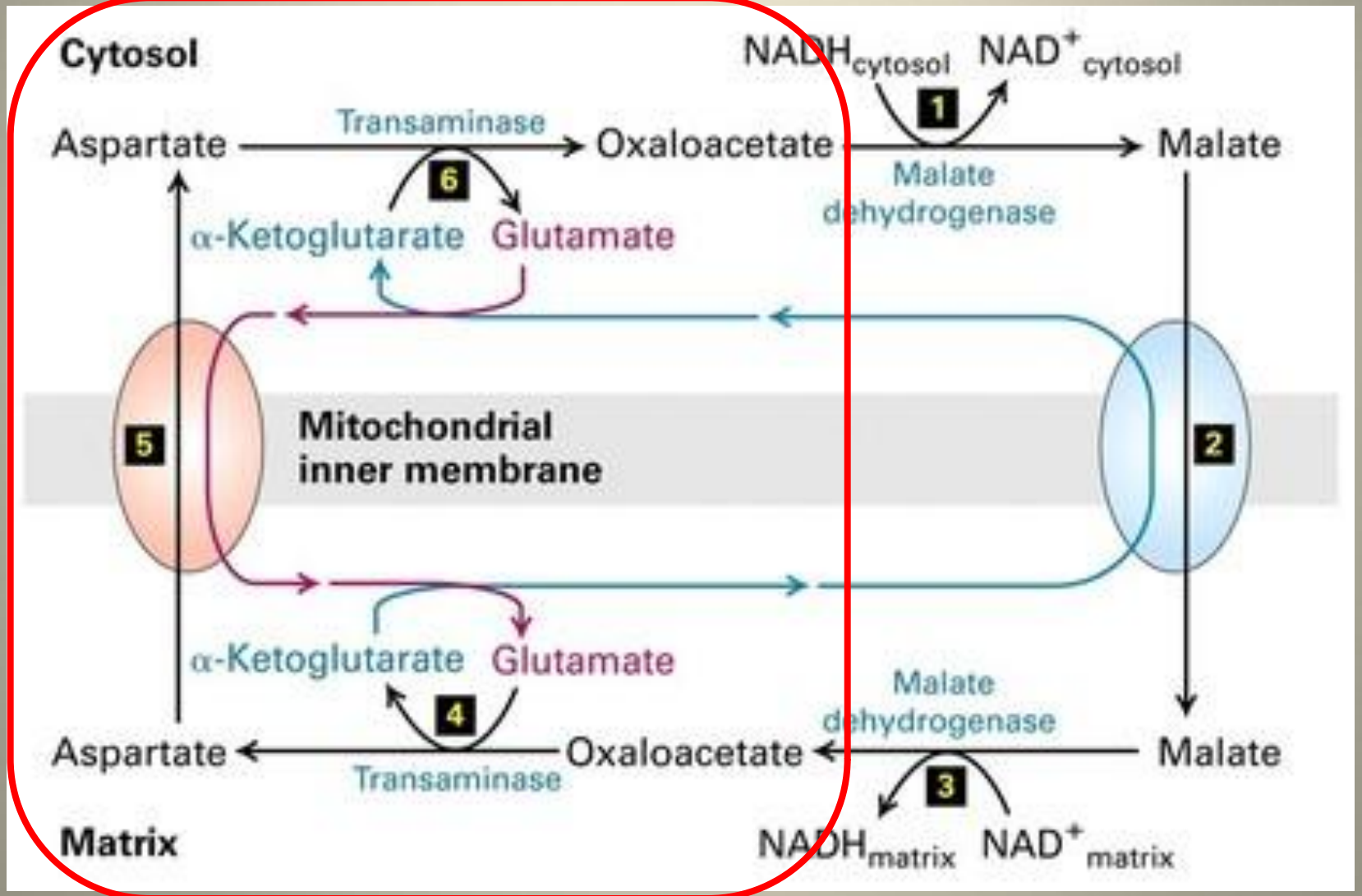


Malate-Aspartate Shuttle

Steps:

1. Dehydrogenase in the cytoplasm transfers electrons from NADH to OAA forming malate
2. Transporters on both the OMM and IMM allow malate to enter the matrix
3. Dehydrogenase in the matrix removes electrons from malate and transfer it onto NAD+ forming NADH

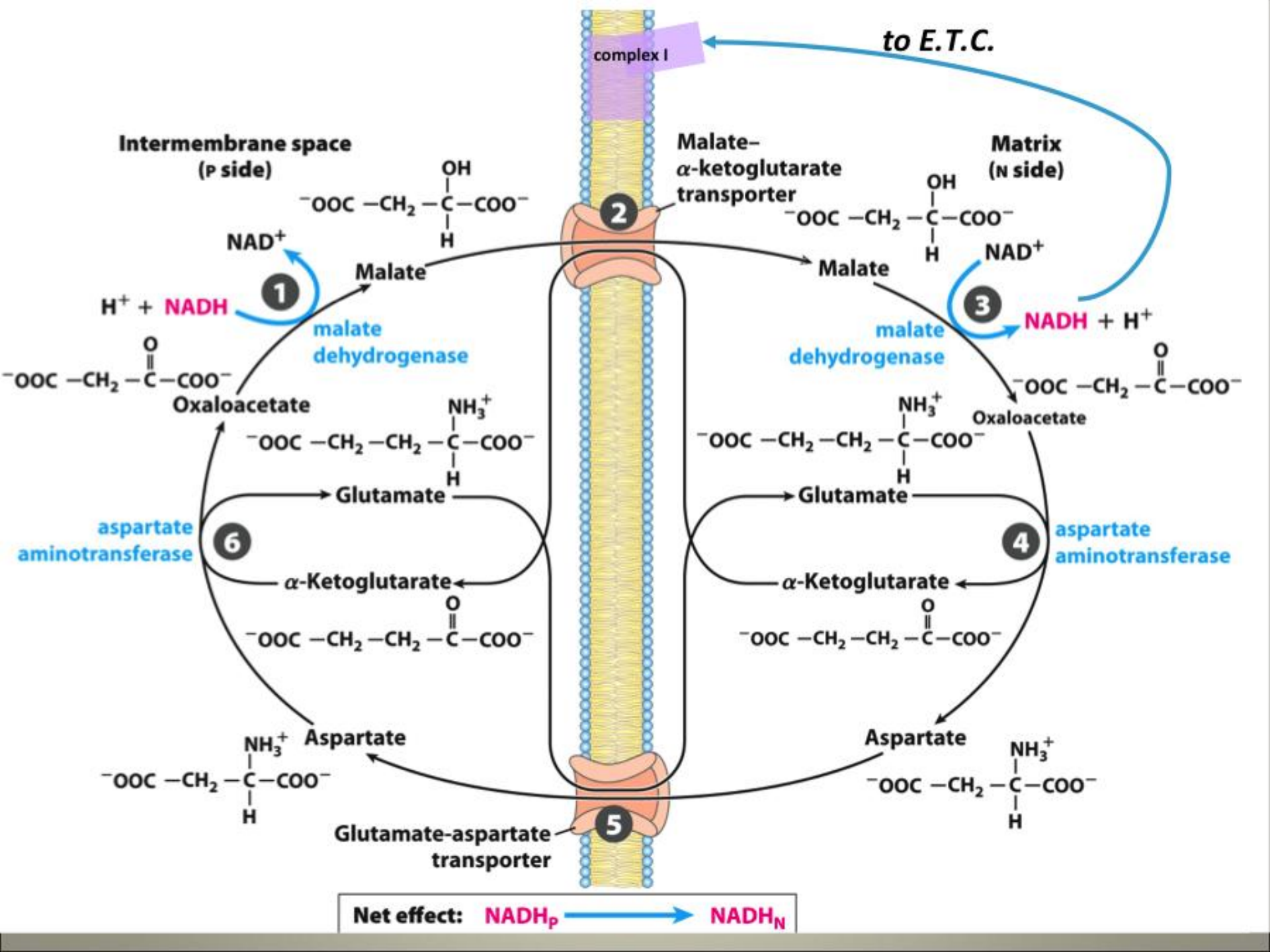
Malate-Aspartate Shuttle



Malate-Aspartate Shuttle

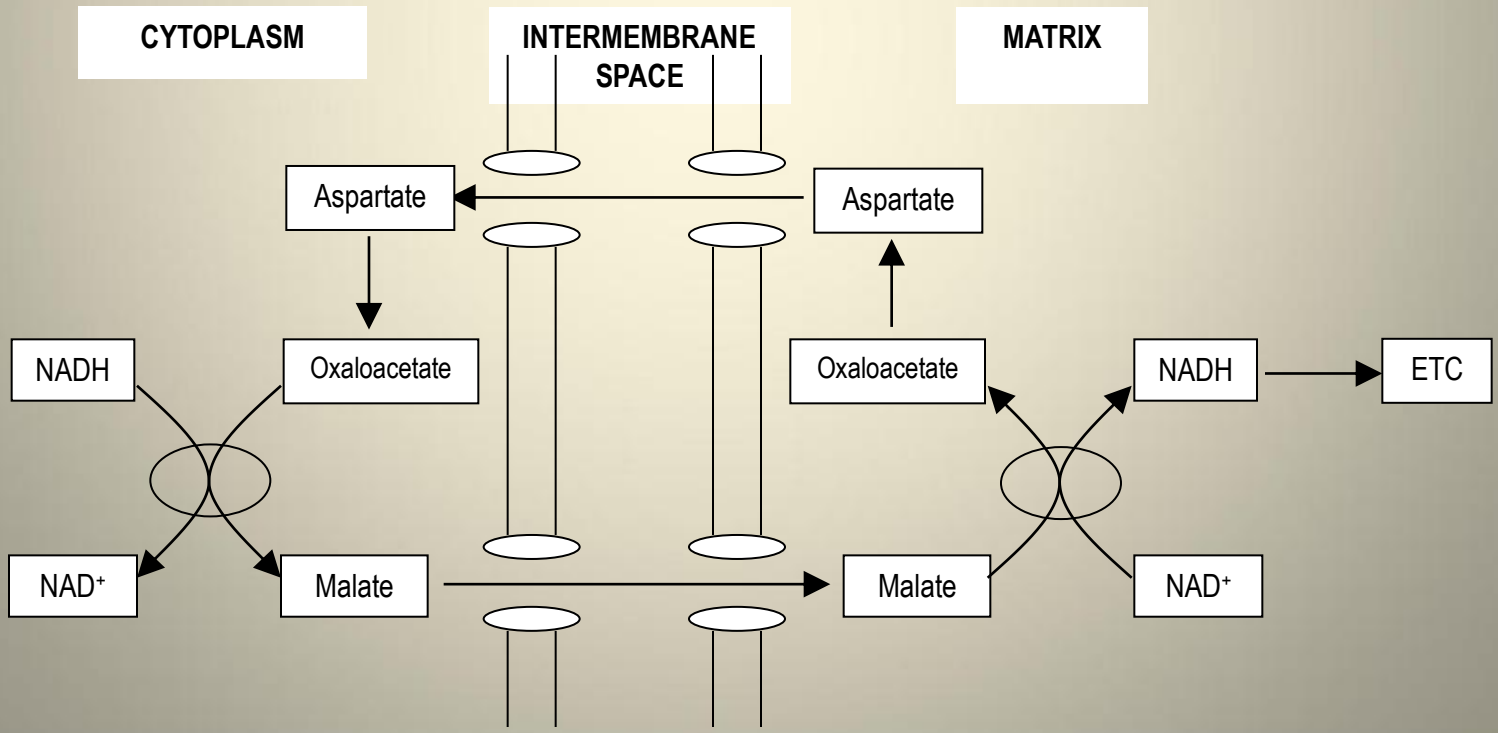
- Steps 4-6 is recycling of the molecules used in the shuttle regenerating OAA in the cytoplasm

4. OAA + glutamate → aspartate + aKG catalyzed by transaminase
   - Transaminase are also called aminotransferase
   - Aspartate and glutamate are amino acids
   - Enzyme switches a ketone group with an amino group
5. Transporters on both the OMM and IMM allow aspartate to exit the mitochondria
6. In the cytoplasm, the reverse transaminase reaction occurs: aspartate + aKG → OAA + glutamate

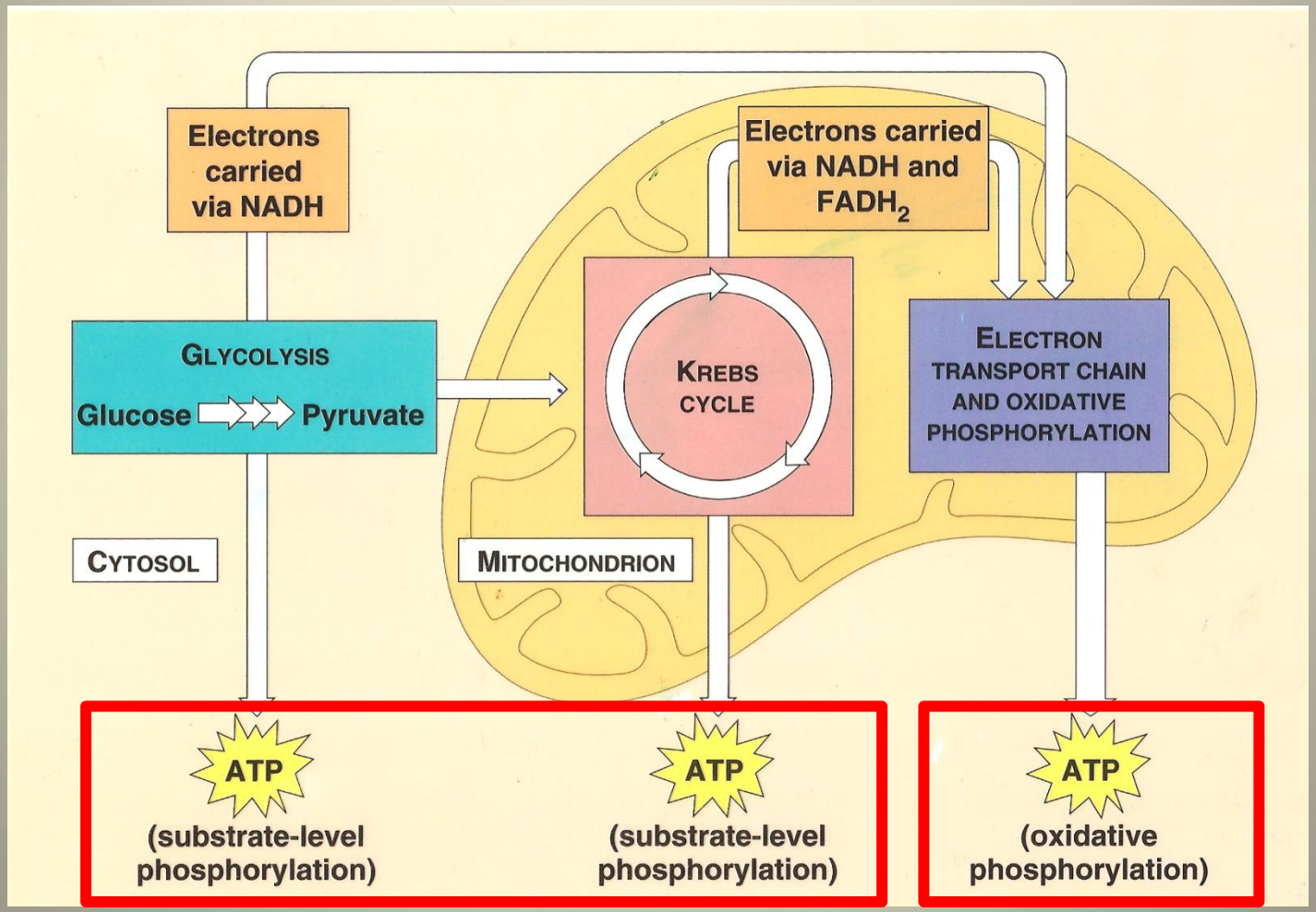

to E.T.C.
complex I
Intermembrane space
(P side)
Malate–
α-ketoglutarate
transporter
Matrix
(N side)
NAD+
Malate
H+ + NADH
malate
dehydrogenase
Malate
NADH + H+
malate
dehydrogenase
Oxaloacetate
Oxaloacetate
Glutamate
Glutamate
aspartate
aminotransferase
aspartate
aminotransferase
α-Ketoglutarate
α-Ketoglutarate
Aspartate
Aspartate
Glutamate-aspartate
transporter
1
2
3
4
5
6
Net effect: NADHP → NADHN

Malate-Aspartate Shuttle

- Summary: electrons from NADH get shuttled into the mitochondria onto NAD+ resulting in NADH in the matrix
- Primarily in the liver, kidney, heart



Two Methods of ATP Synthesis



Two Methods of ATP Synthesis

Substrate-level phosphorylation

- direct ATP formation through phosphate transfer from substrate to ADP
- Occurs in glycolysis & Kreb cycle

Oxidative phosphorylation

- indirect ATP formation through redox reactions involving O2 as a final electron acceptor
- Driven by the electron transport chain

Substrate-level Phosphorylation

- enzyme transfers a phosphate group from a substrate molecule to ADP
- rather than adding an inorganic phosphate to ADP as in oxidative phosphorylation

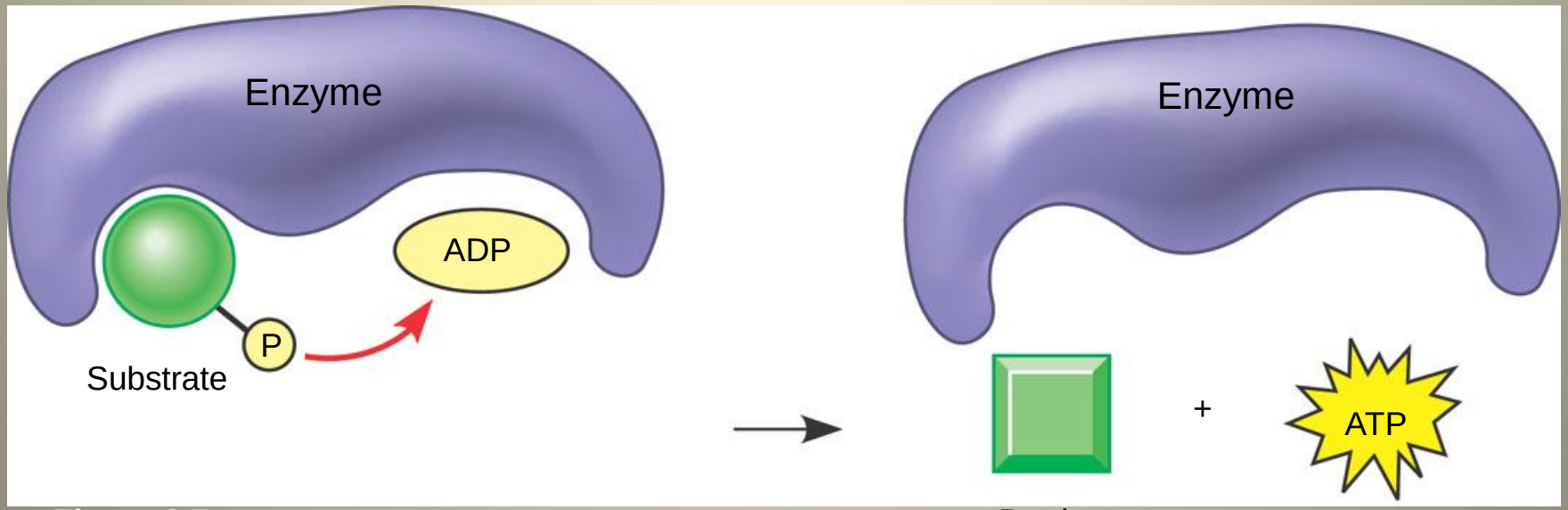


Figure 9.7

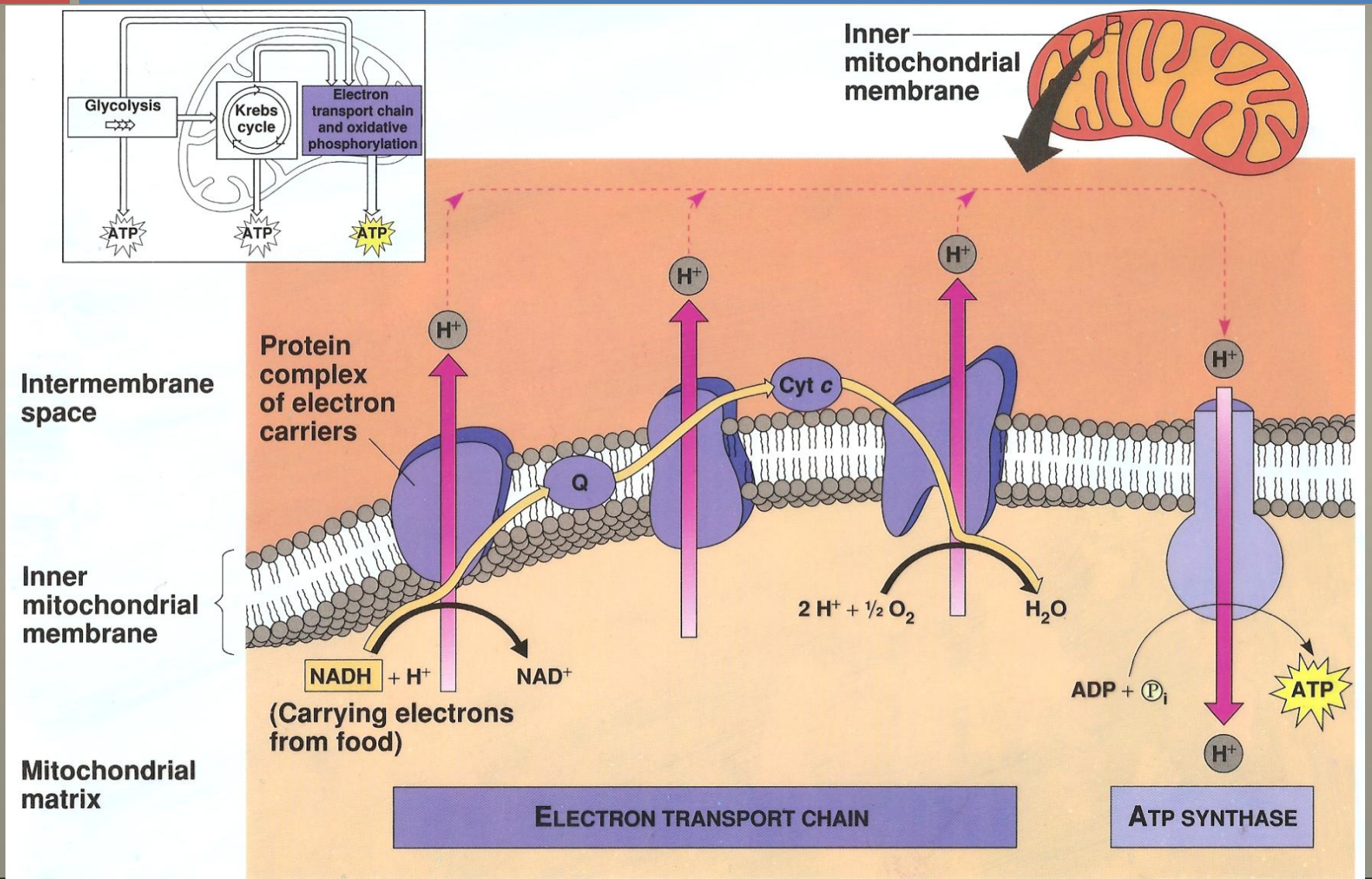
Oxidative Phosphorylation

- Coupling 2 processes that occur on the inner mitochondrial membrane (IMM)
  - Oxidation: Electron Transport Chain
    - Energy in electrons of NADH and FADH2 used to drive H+ against its concentration gradient
    - Electrons fall to oxygen (final electron acceptor)
  - Phosphorylation: Chemiosmosis
    - H+ to passive diffusion through IMM facilitated by ATP synthase
    - Drives the synthesis of ATP

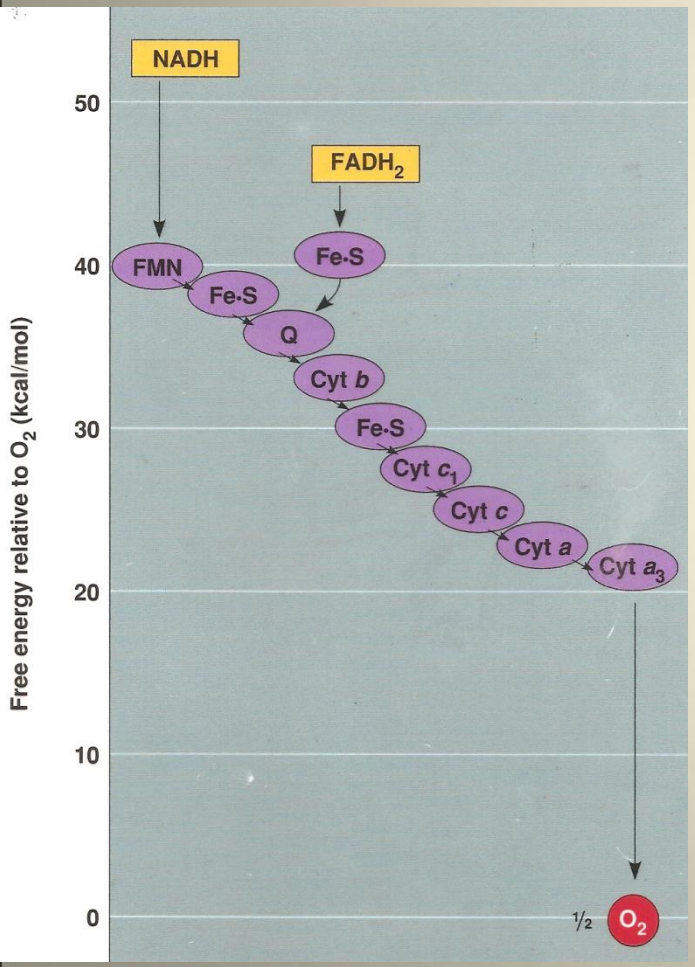
Electron Transport Chain Overview

- Removes energy stored in the NADH and FADH2
- Transfers it to electron carrier molecules embedded in inner mitochondrial membrane
- Energy use to move protons against its concentration gradient
- Final electron acceptor is oxygen which converts H_2O
- All reactions are redox reactions

Electron Transport Chain (ETC)



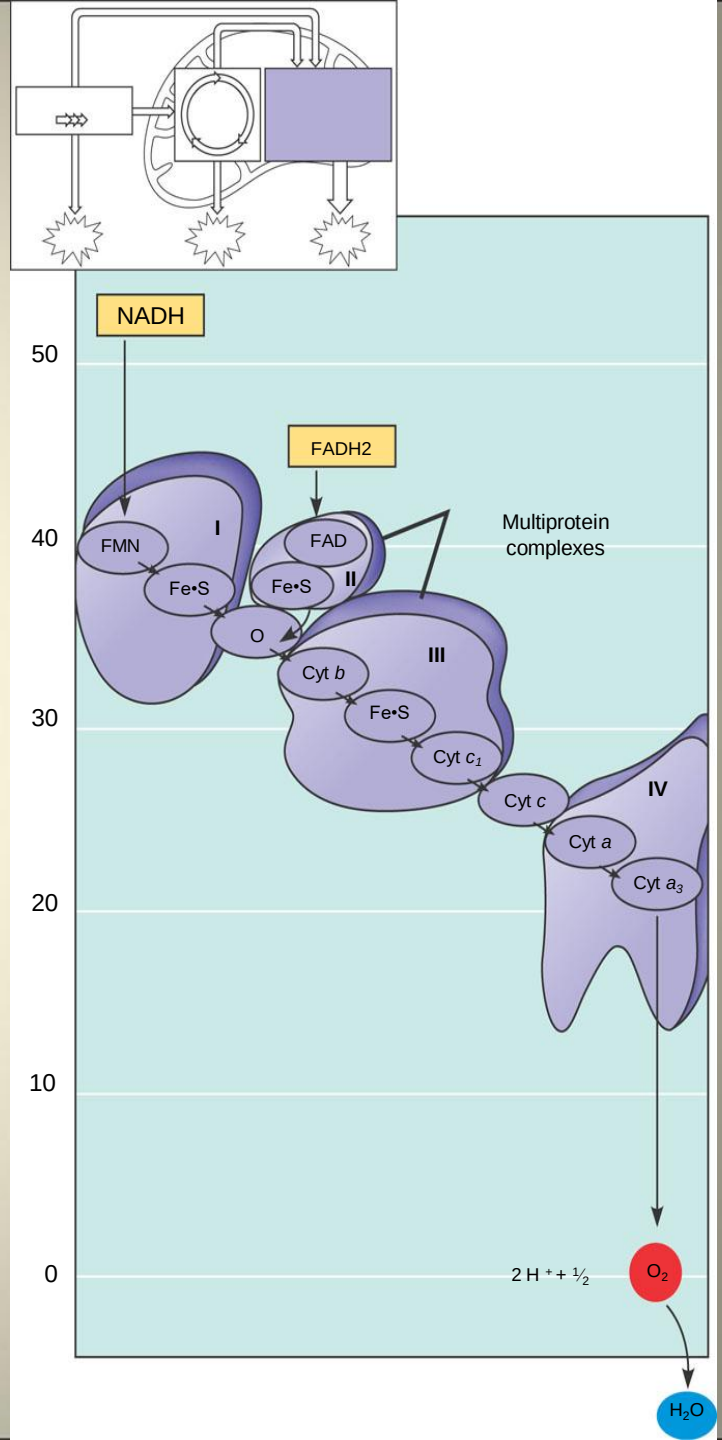
ETC Thermodynamics



- Each electron transfer step is energetically favourable
- Each carrier in the chain has a higher electronegativity than the carrier before it
- Electrons from NADH and FADH2 lose energy (pulled downhill) by each electron carrier

ETC & Oxygen

- Final electron acceptor is the very electronegative oxygen
- Oxygen drives the redox reactions
- Lack of oxygen prevents this whole process from occurring



ETC & Chemiosmosis Overview

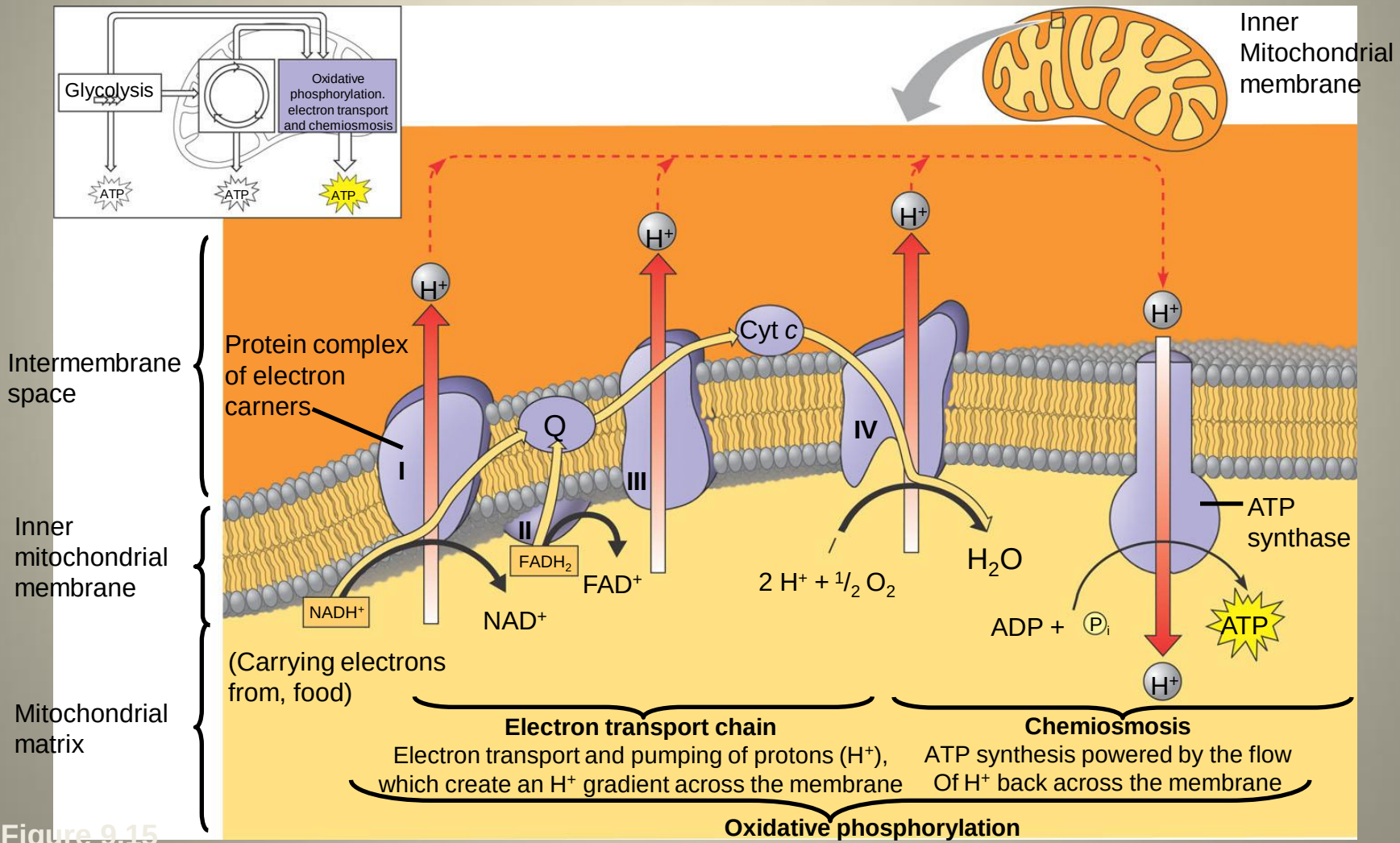
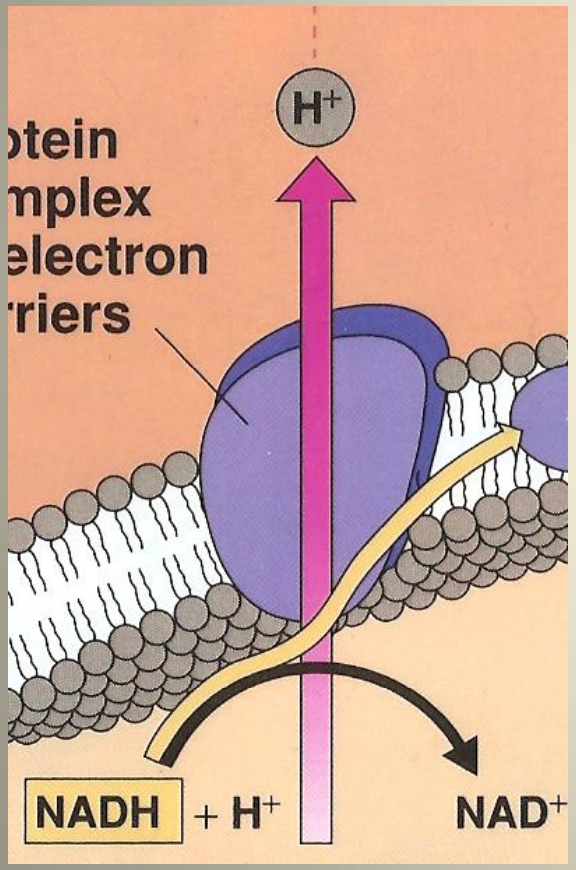


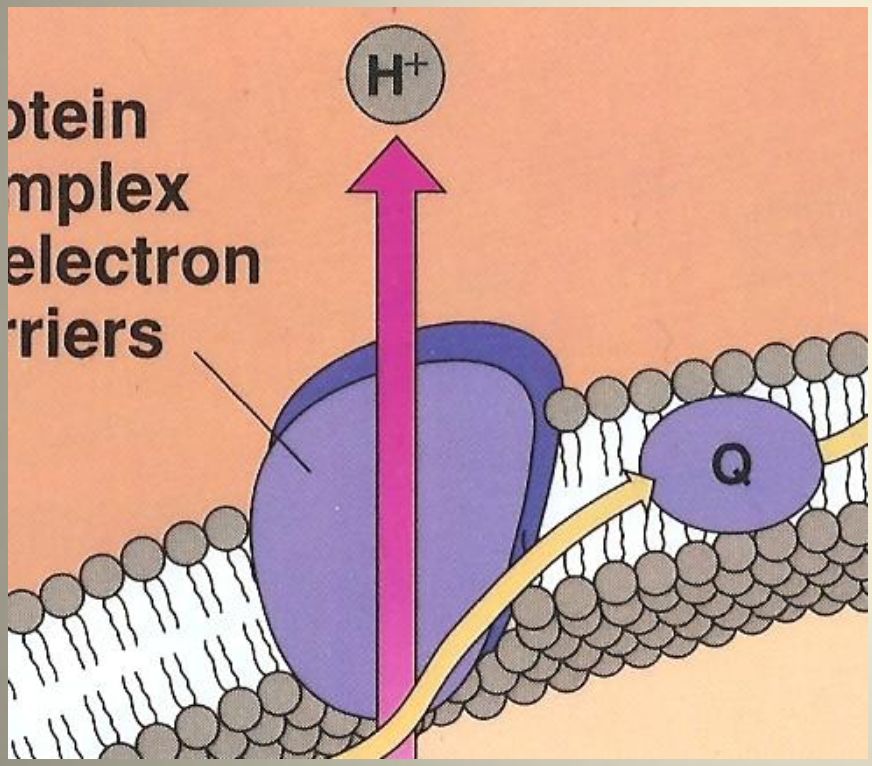
Figure 9.15

ETC Components: Complex I



- 2 e- from NADH are transferred to Complex I
- Protons are pumped across the inner mitochondrial membrane (IMM) by Complex I

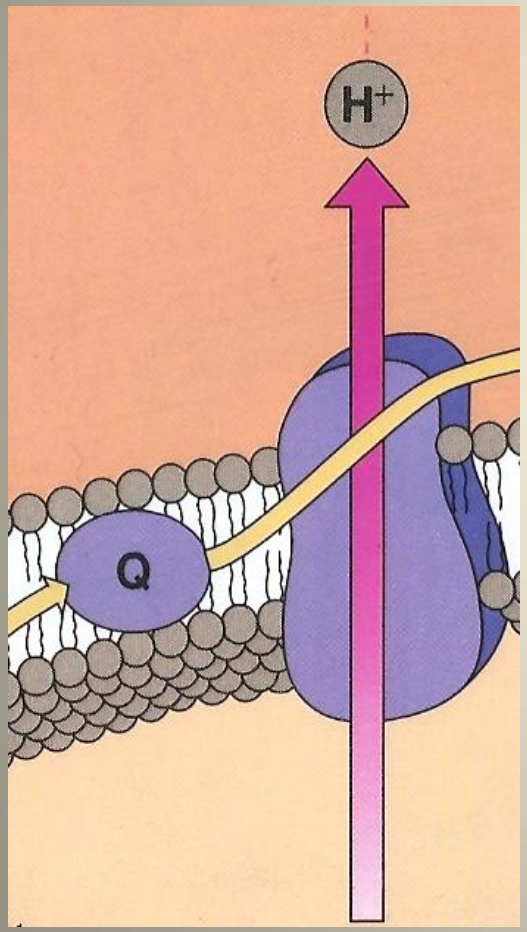
ETC Components: Q



- e- are transferred from Complex I to ubiquinone (Q)

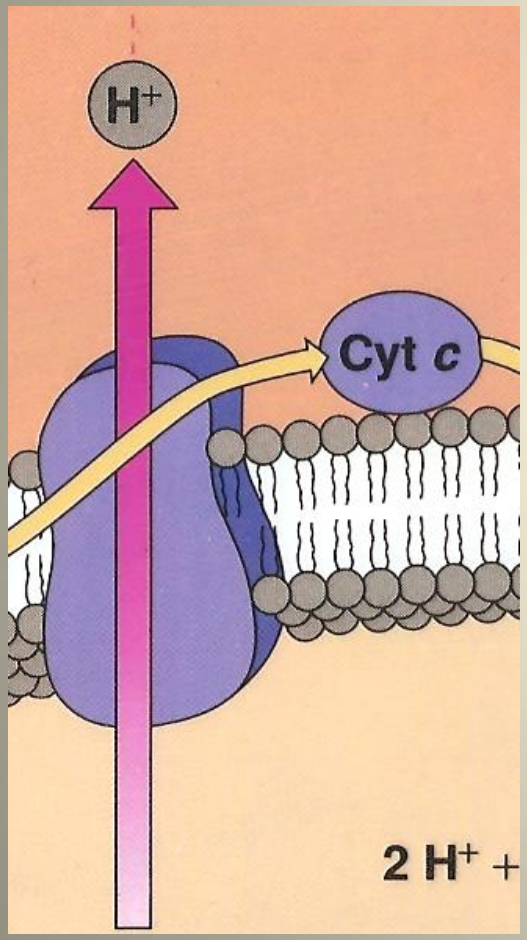
- Q is lipid soluble
- can move within the phospholipid bilayer
- mobile component within the IMM

ETC Components: Complex III



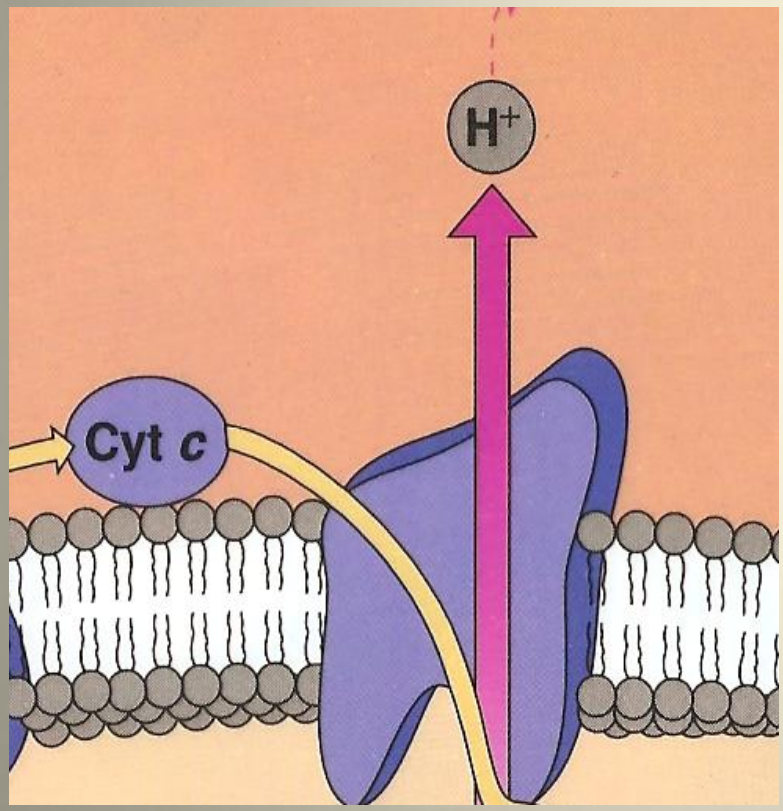
- e- are transferred from Q to Complex III
- Protons are pumped across the IMM by Complex III

ETC Components: Cyt C



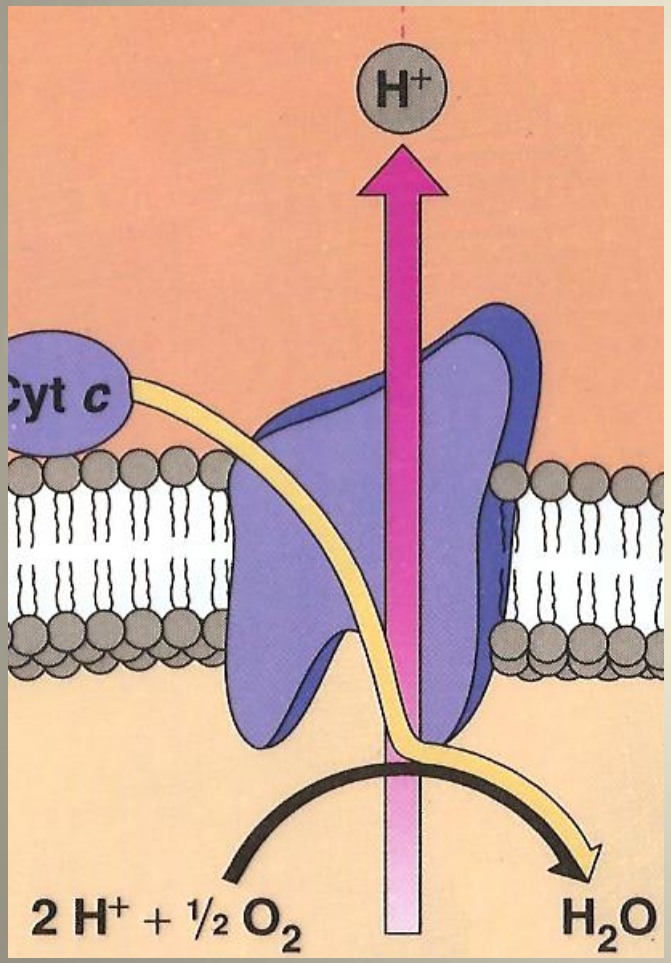
- e- are transferred from Complex III to cytochrome c (cyt c)
- cyt c is a mobile component on the surface of IMM (peripheral), in the intermembrane space

ETC Components: Complex IV



- e- are transferred from cyt c to Complex IV
- Protons are pumped across the IMM by Complex IV

ETC Components: O2



- O2 is the final electron acceptor of the ETC
- enough e- pass through the ETC to produce full H2O molecules

FADH2 Pathway

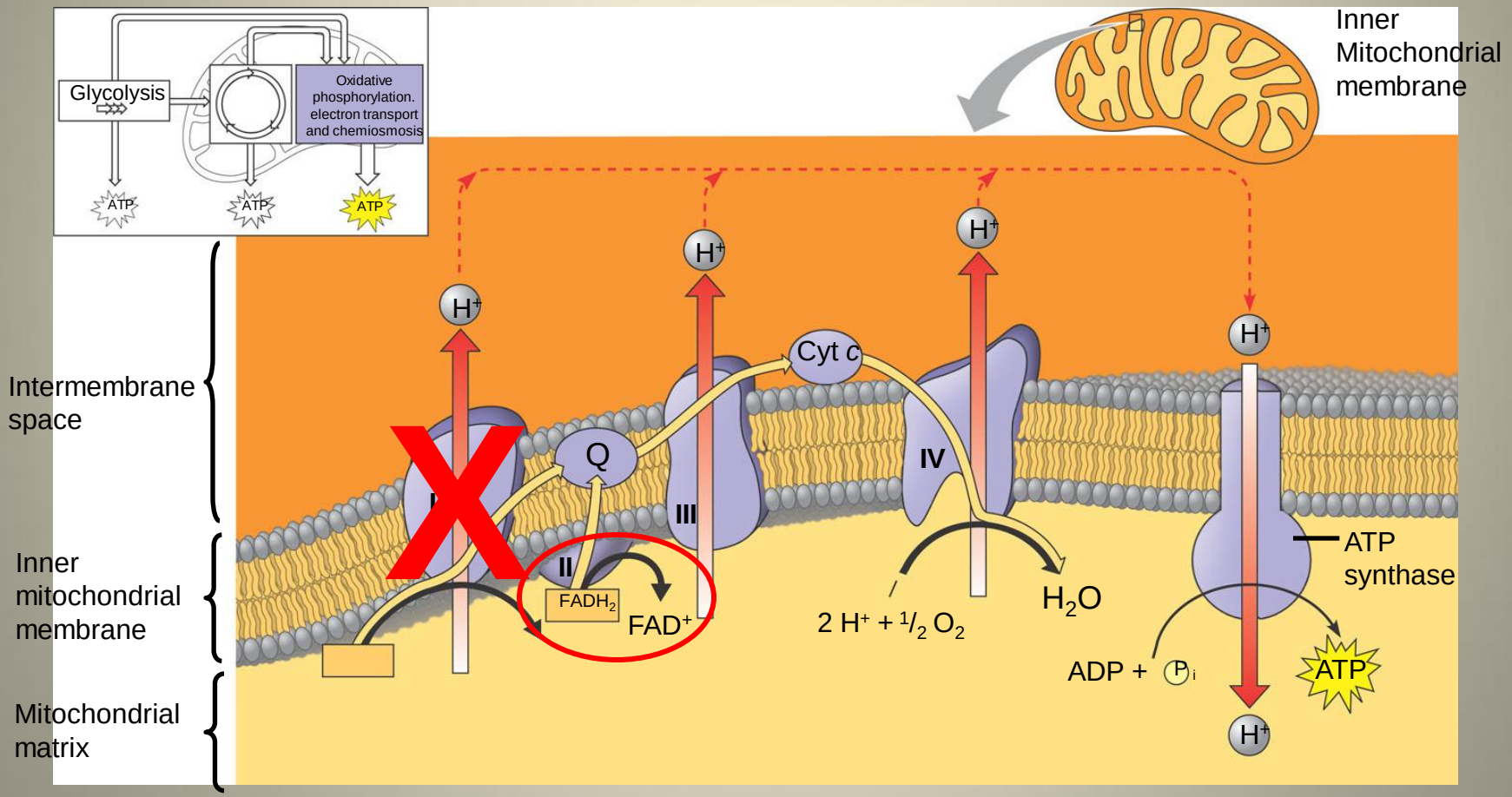
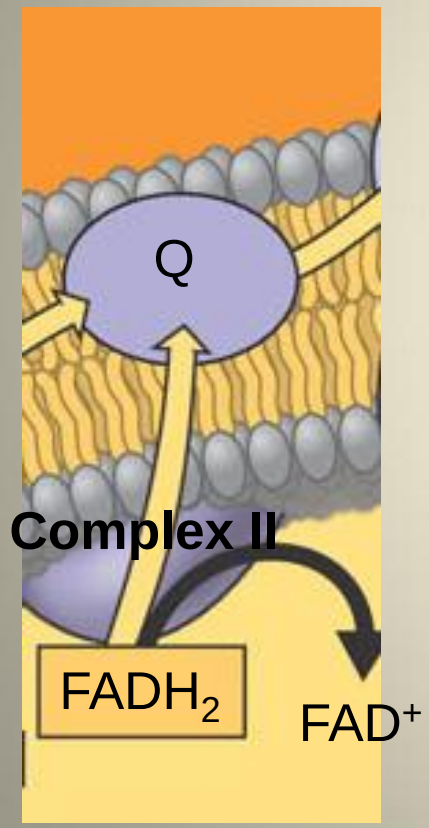


Figure 9.15

ETC Components: Complex II



- 2e- are transferred from FADH2 to Complex II
- no protons are pumped across the IMM
- e- are transferred from Complex II to Q and proceed through the rest of ETC

ETC Components: Complex II

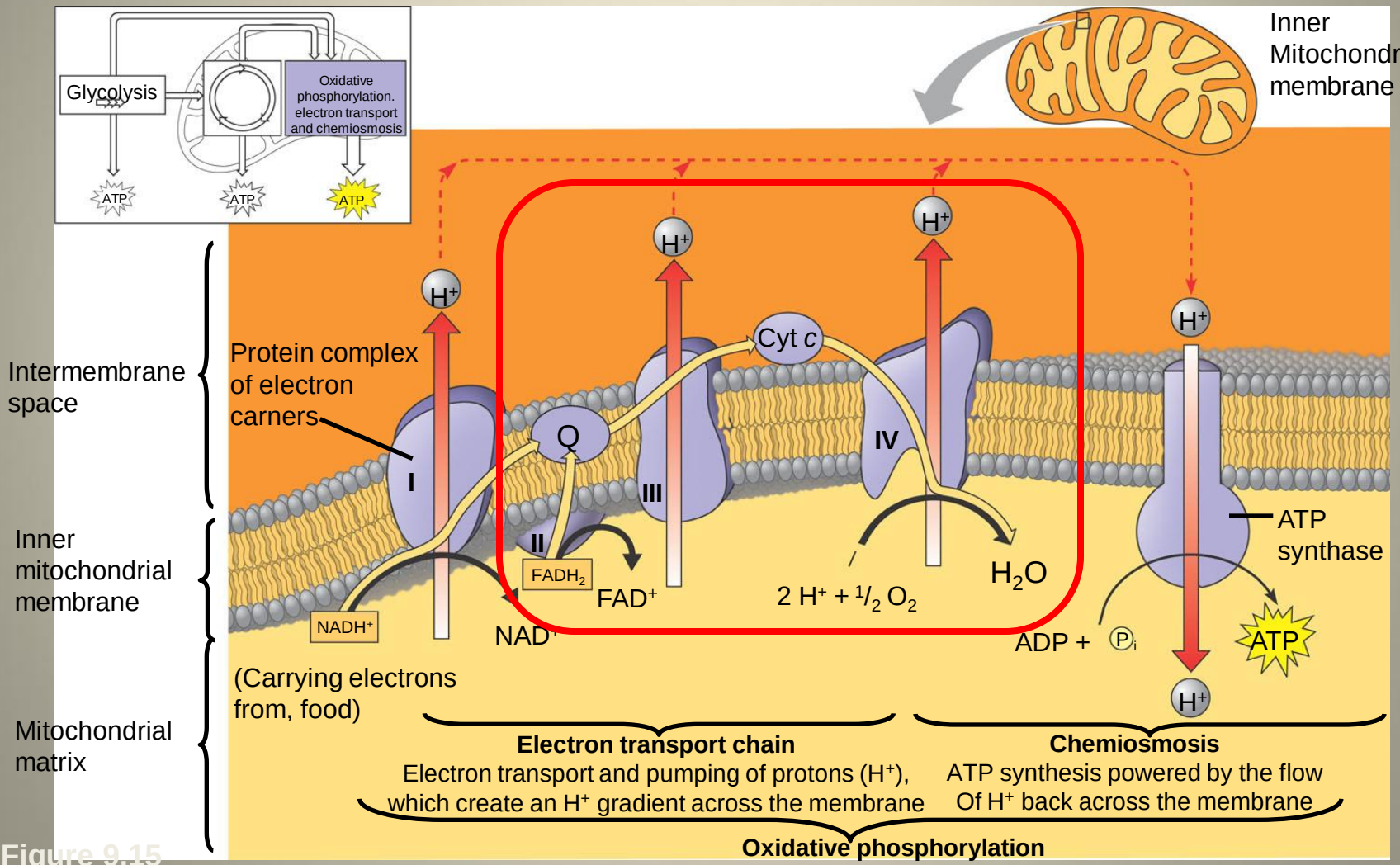
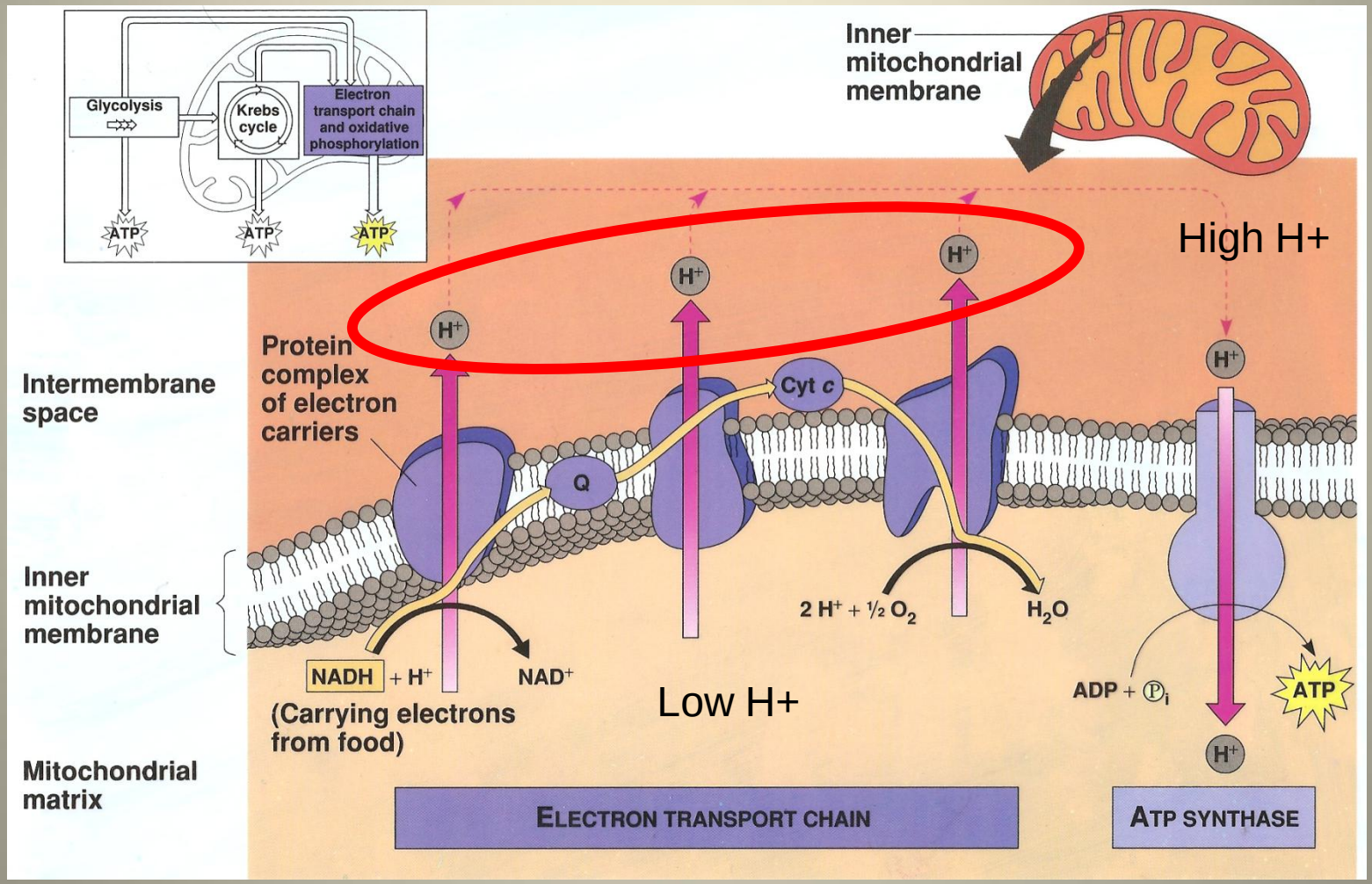


Figure 9.15

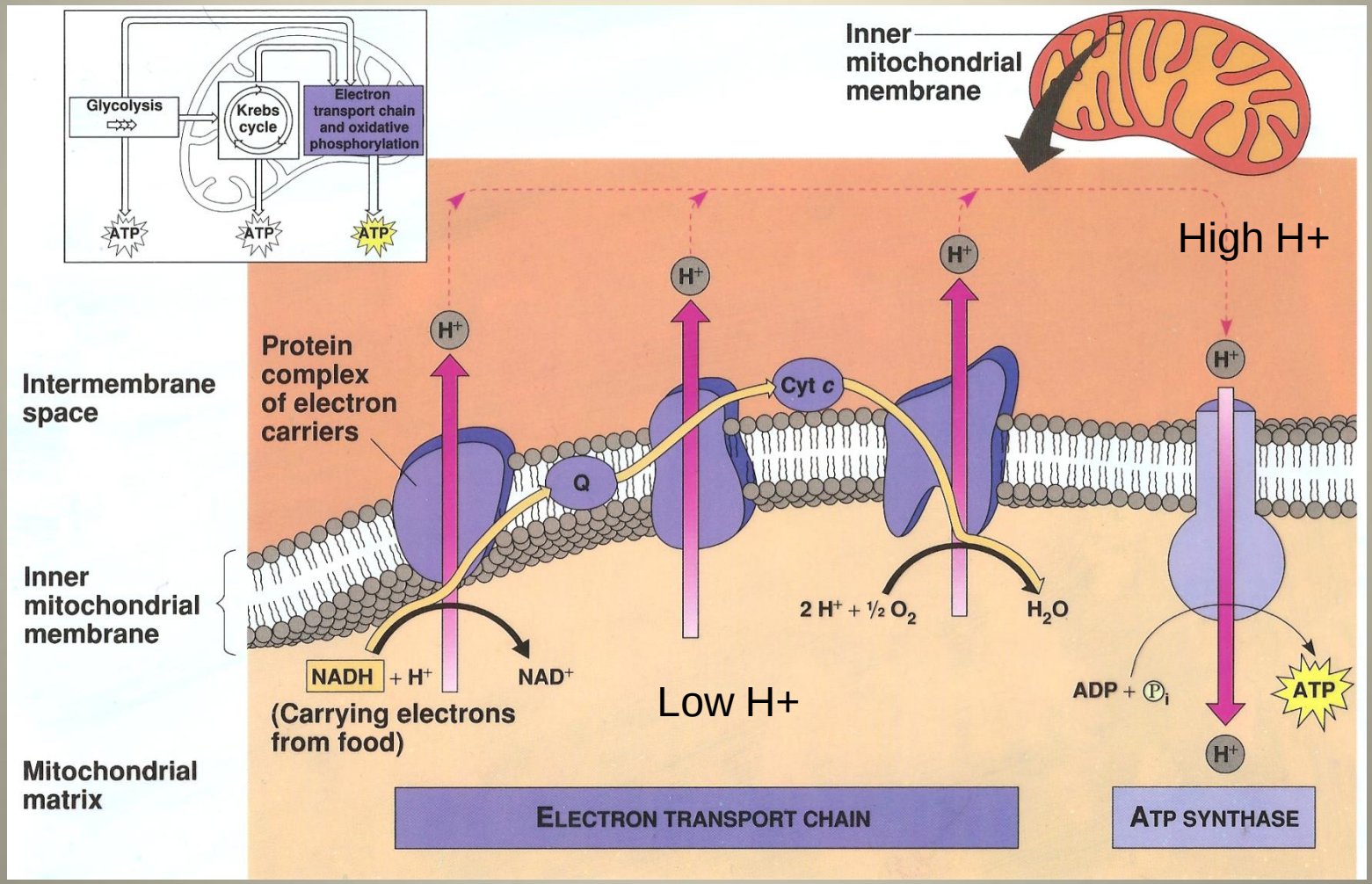
Electrochemical Proton Gradient



ETC Summary

- Electrochemical proton gradient formed across IMM
  - High proton concentration in the intermembrane space
- NADH e- transferred to O2
  - three proton pumps activated
- FADH2 e- transferred to O2
  - two proton pumps activated

Oxidative Phosphorylation



Proton Motive Force: Chemiosmosis

- ETC is coupled with ATP synthesis
  - 1 NADH → 3 ATP molecules
  - 1 FADH2 → 2 ATP molecules
- Chemiosmosis: facilitated diffusion of proton down the concentration gradient

ATP Synthase: Complex V

- Fo = rotor
  - Transmembrane
  - Proton channel
- F1 = knob, rod
  - Peripheral
  - catalytic sites that phosphorylate ADP to ATP

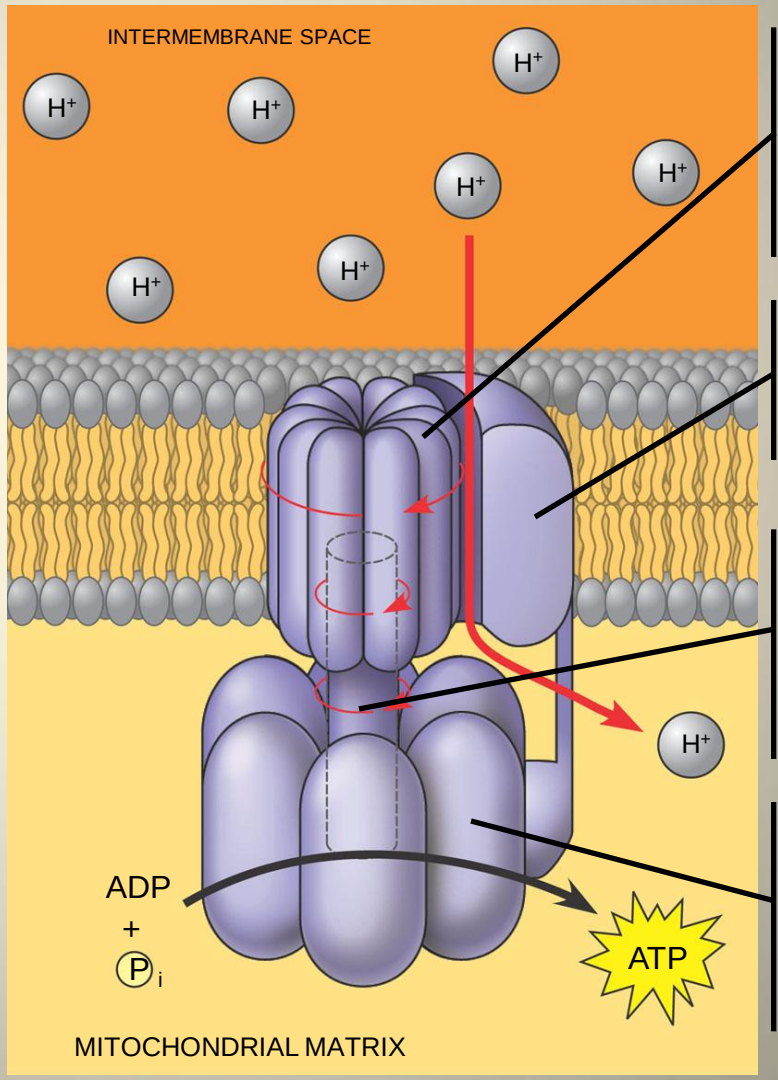
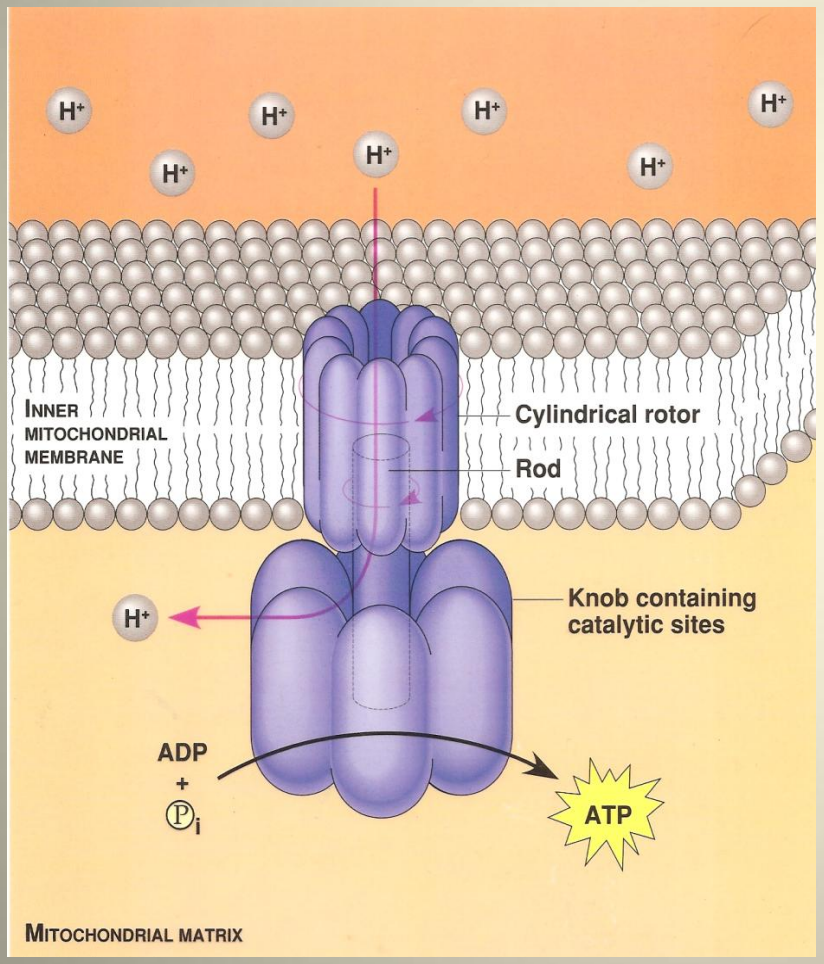
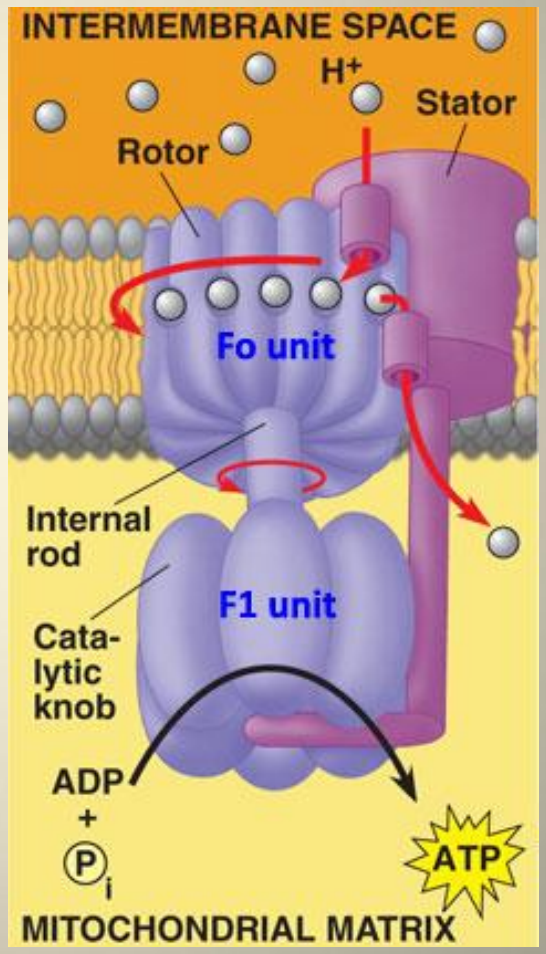


Figure 9.14

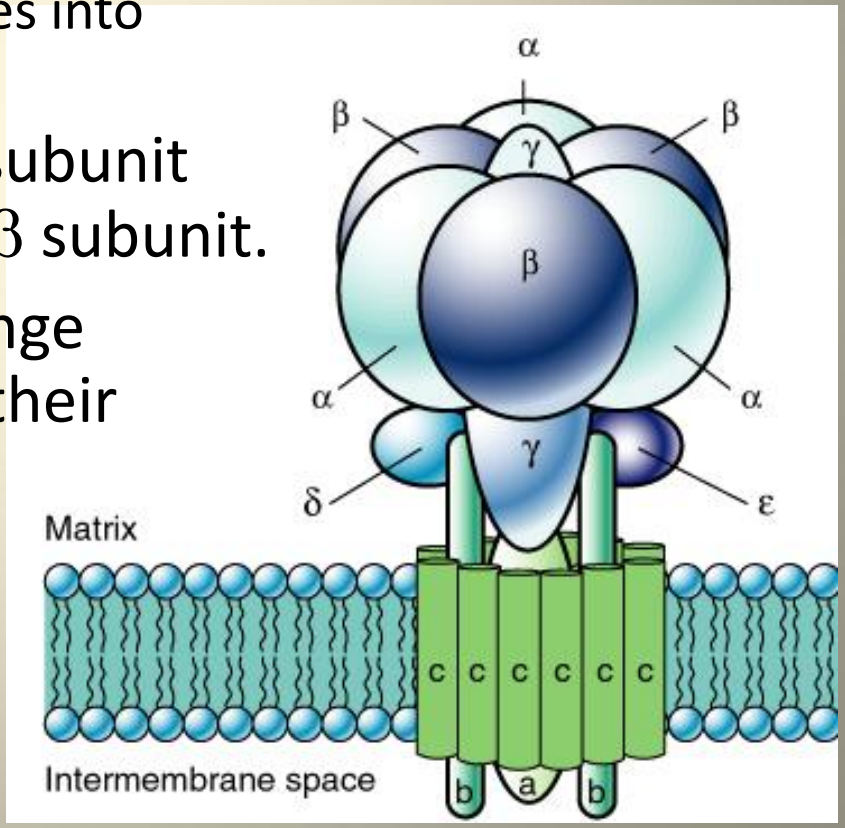
ATP Synthase: Complex V



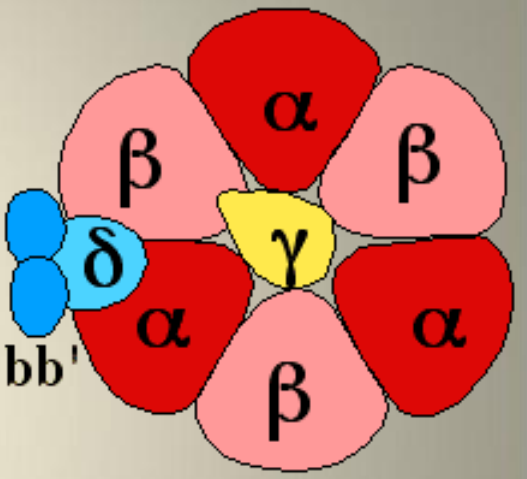


Rotational Catalysis

- Protons flowing through the F0 component cause the γ subunits in the rod to rotate.
  - electrochemical gradient translates into mechanical energy
- When an irregularly shaped γ subunit rotates, it contacts a different β subunit.
- As a result, the β subunits change conformation, which changes their affinity for ATP.



β subunit



- Catalytic subunit
- 3 conformation:
  - loosely binds ADP and P
  - tightly binds ADP and Pi to form ATP
  - releases ATP
- When the γ interacts closely with the β subunit, ATP is synthesized
- Each of the 3 β subunits in the F1 component take turn catalyzing the synthesis of ATP

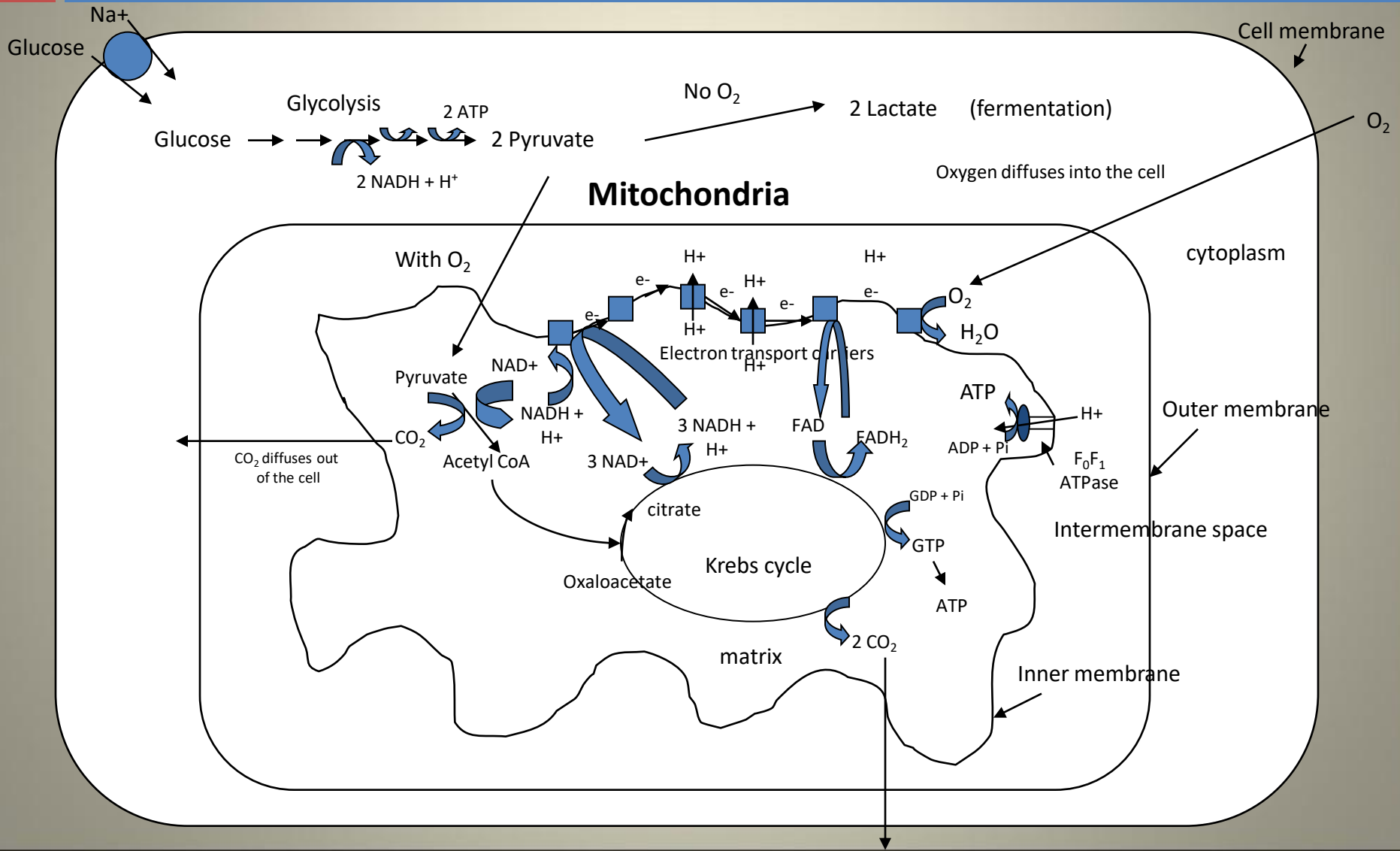
Animation

- ETC
  http://www.youtube.com/watch?v=lRlTBRPv6xM&feature=related
- Proton Gradient & ATP synthase
  http://www.youtube.com/watch?v=3y1dO4nNaKY&feature=related
- ATP synthase
  http://www.youtube.com/watch?v=PjdPTY1wHdQ&feature=related
- Cellular Respiration Lecture:
  http://www.youtube.com/watch?v=qviLDKDJNKM&feature=related

Molecule Count: Per Glucose

	ATP	NADH	$FADH_2$	
Glycolysis	2	2 ⟷	0	
Pyruvate Oxidation	0	2	0	
Krebs	2	6	2	
Subtotal	4	8-10	2-4	
Conversion in ETC	4	24-30	4-8	36-38

Cellular Respiration Review



Cellular Respiration Summary

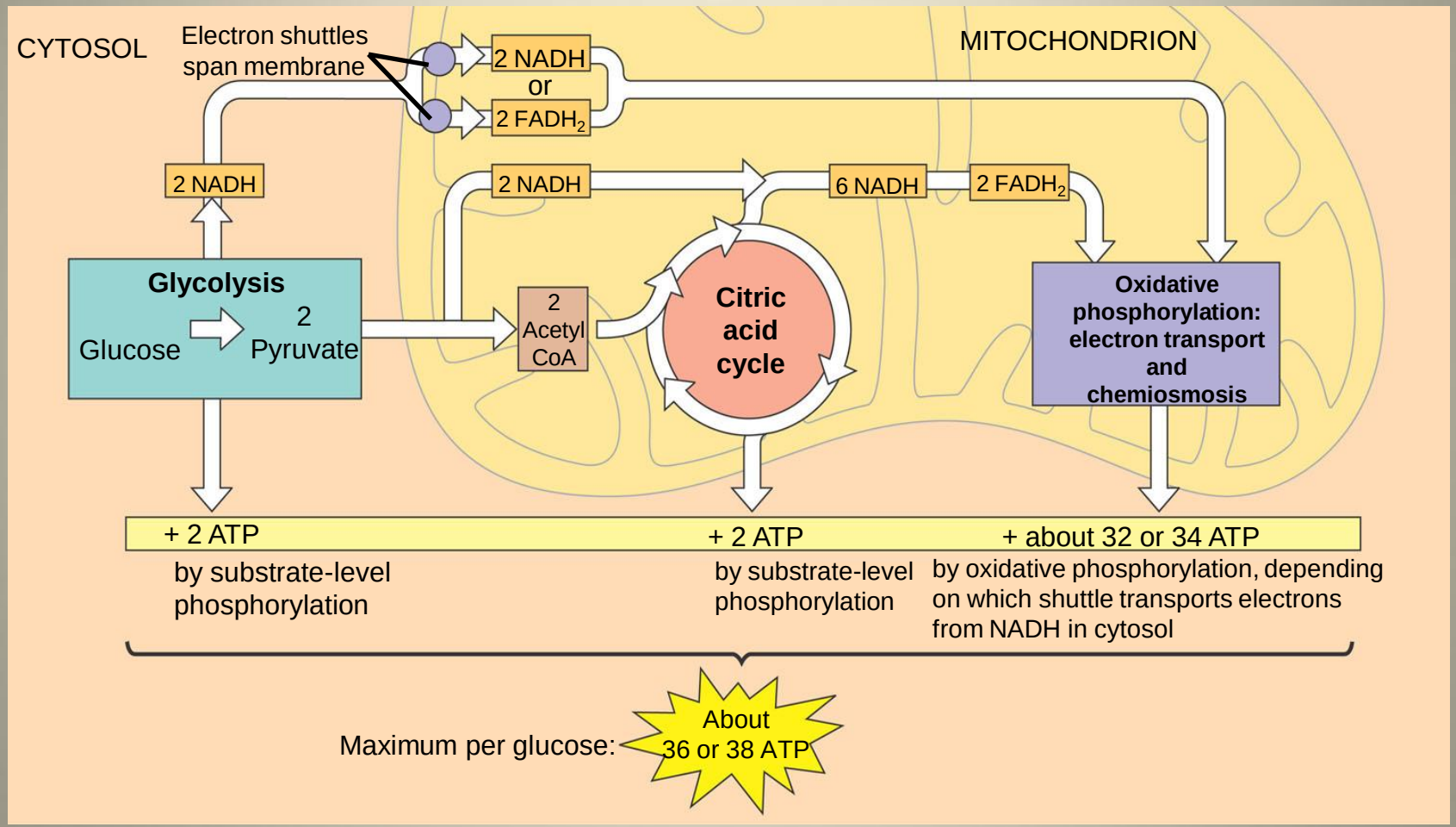


Figure 9.16

Catabolism of various molecules from food

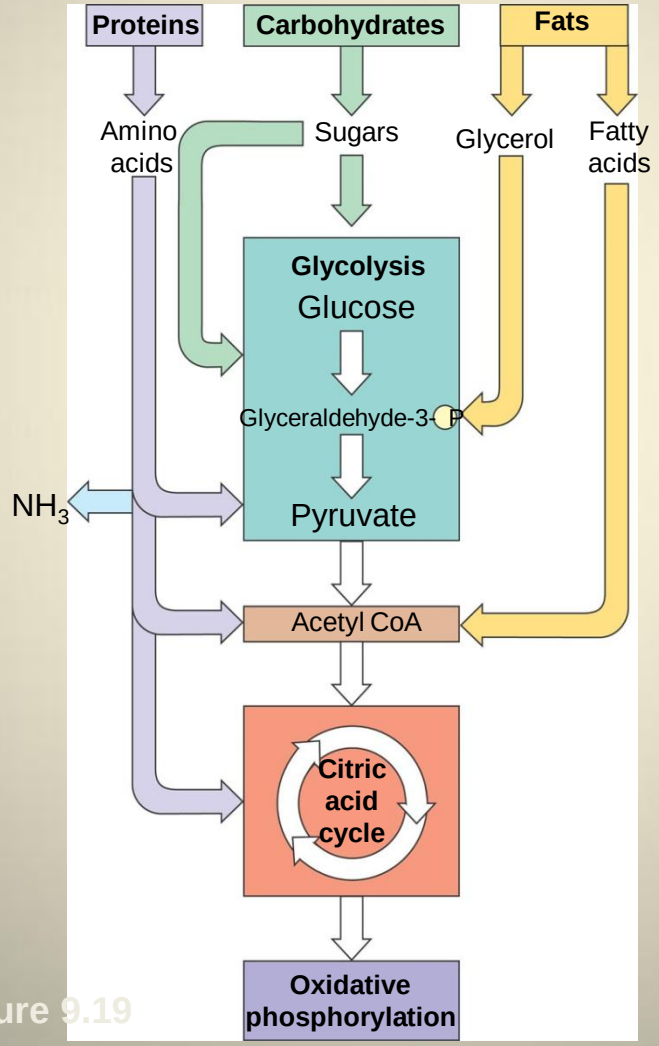
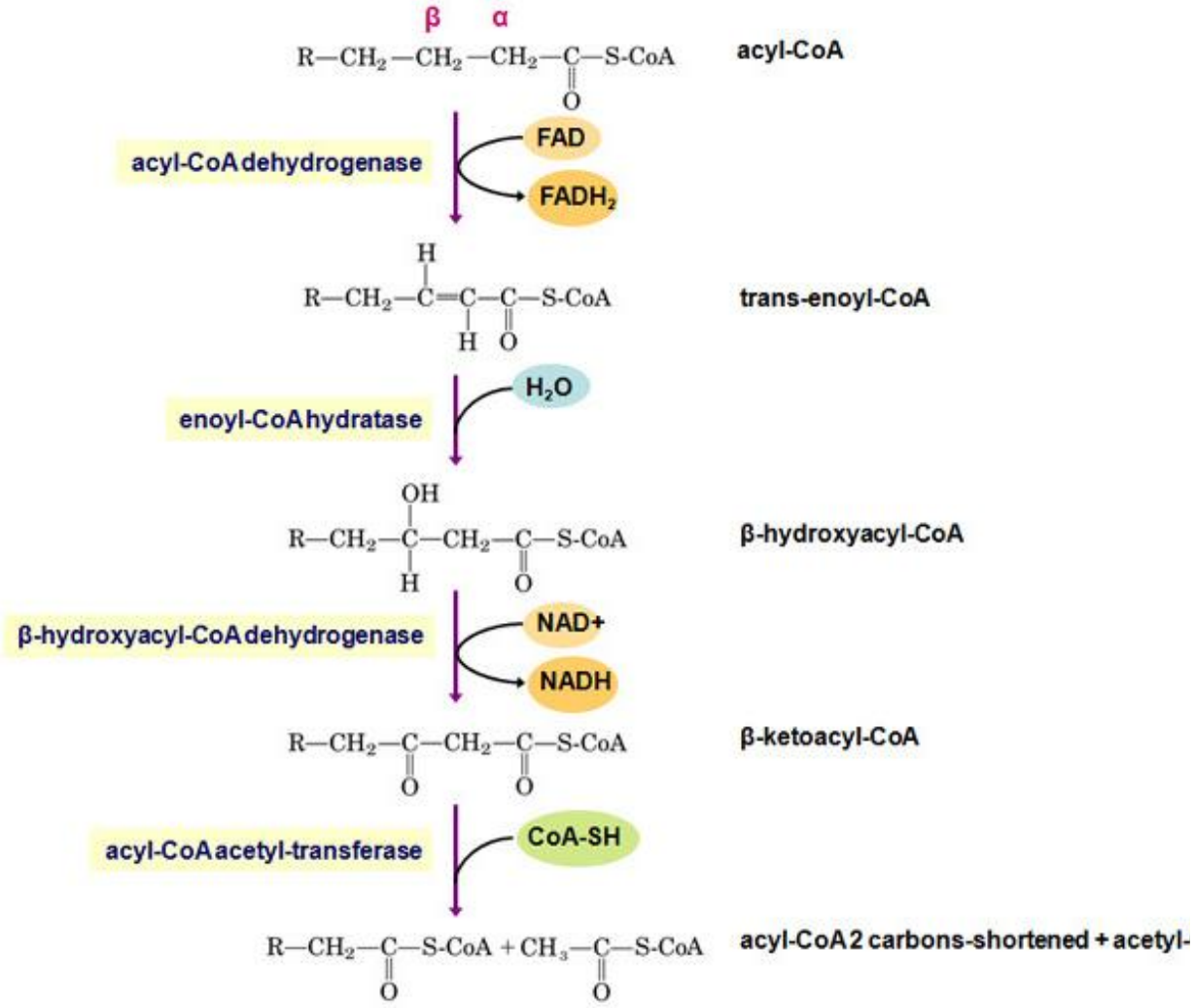


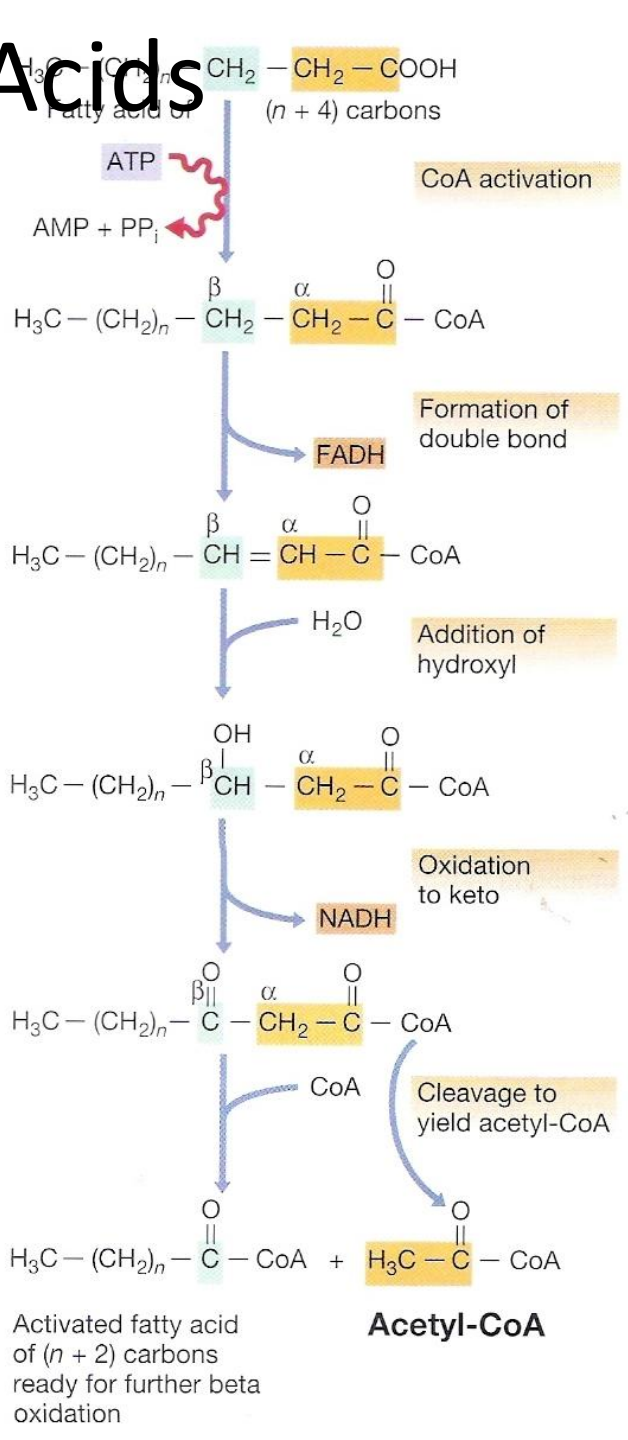
Figure 9.19

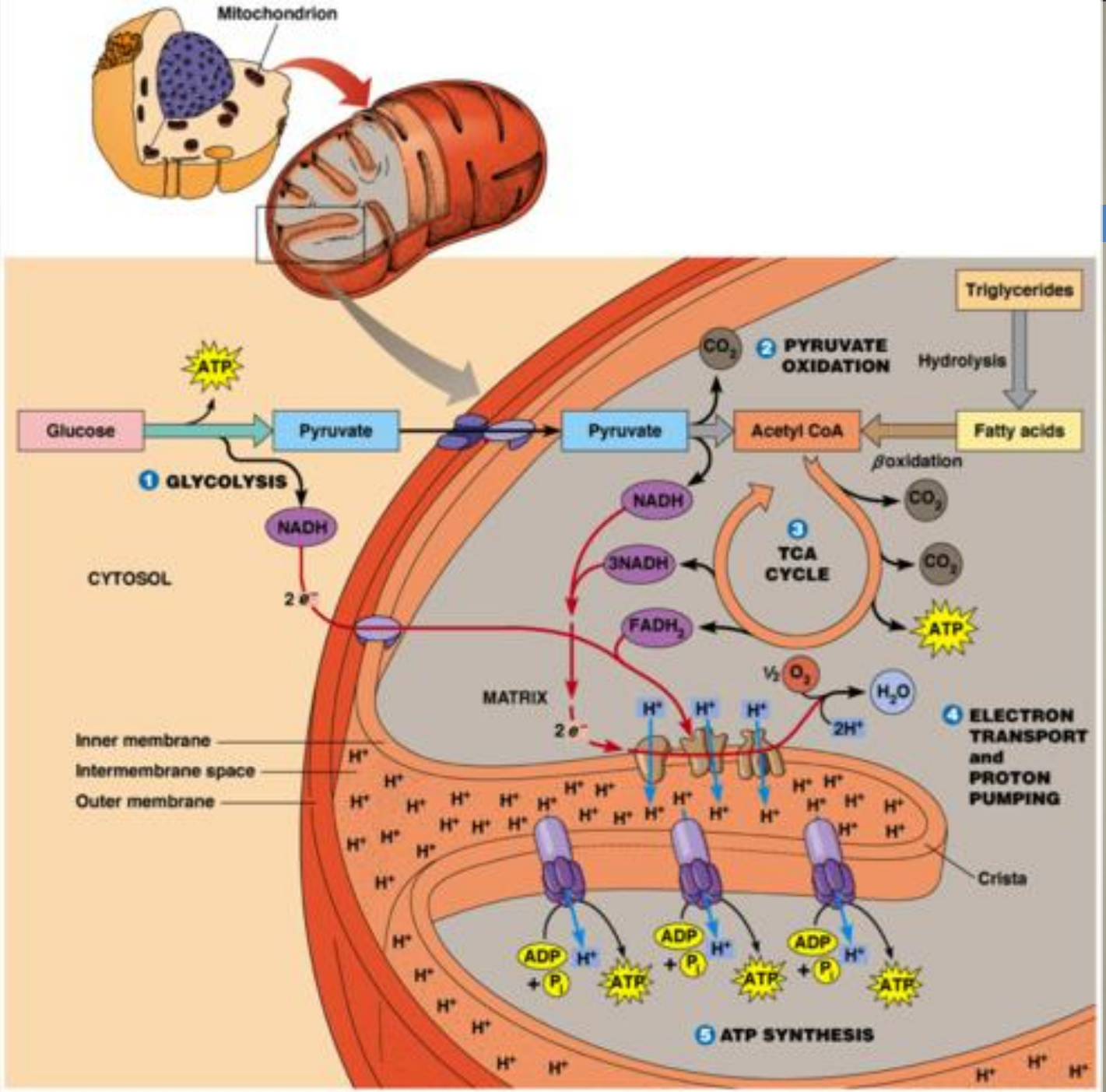
MaCS Only

- The following details on how lipids are involved in cellular respiration is only for the MaCS class

Metabolism of Fatty Acids (beta-oxidation)







Regulation of Cellular Respiration

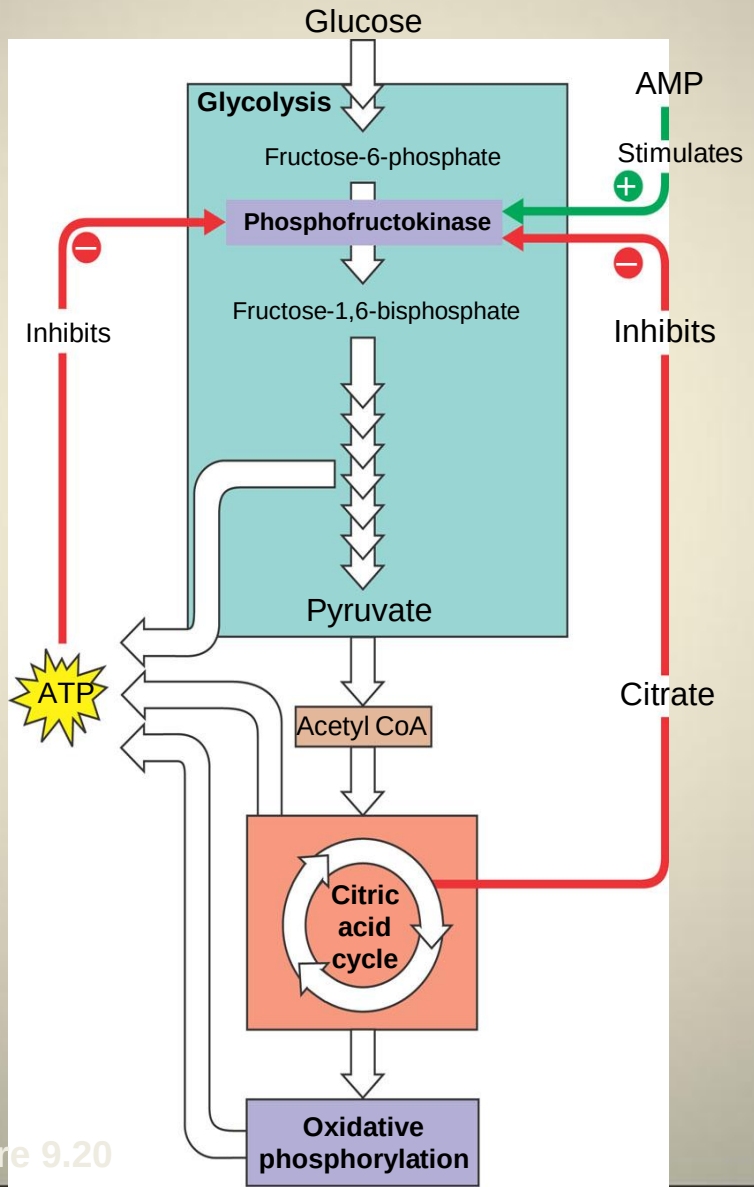


Figure 9.20