Electron Transport Chain

Cellular respiration is a series of reactions that:

-are oxidations – loss of electrons

-are also **dehydrogenations** lost electrons accompanied by hydrogen

= hydrogen atom = 1 electron + 1 proton).

H = H+ + e-

-electrons carry energy from one molecule to another.

-electrons shuttled through electron carriers to a final electron acceptor

aerobic respiration:

final electron receptor is oxygen (O_2)

NAD^+ is an electron carrier.

-NAD accepts electrons + 1 proton to become **NADH.**

-the reaction is reversible

Basics of Redox Chemistry

Term	Definition
Oxidation	Loss of hydrogen Loss of electrons
Reduction	Gain of hydrogen Gain of electrons
Oxidant	Oxidizes another chemical by taking electrons or hydrogen
Reductant	Reduces another chemical by supplying electrons or hydrogen

NADH + H + FAD $\longrightarrow$ NAD+FADH2

Reductant oxidant (= Redox couple)

e-donor e-acceptor

What is Electron Transport chain (respiratory chain)

- A chain of protein complexes embedded in inner mitochondrial membrane.

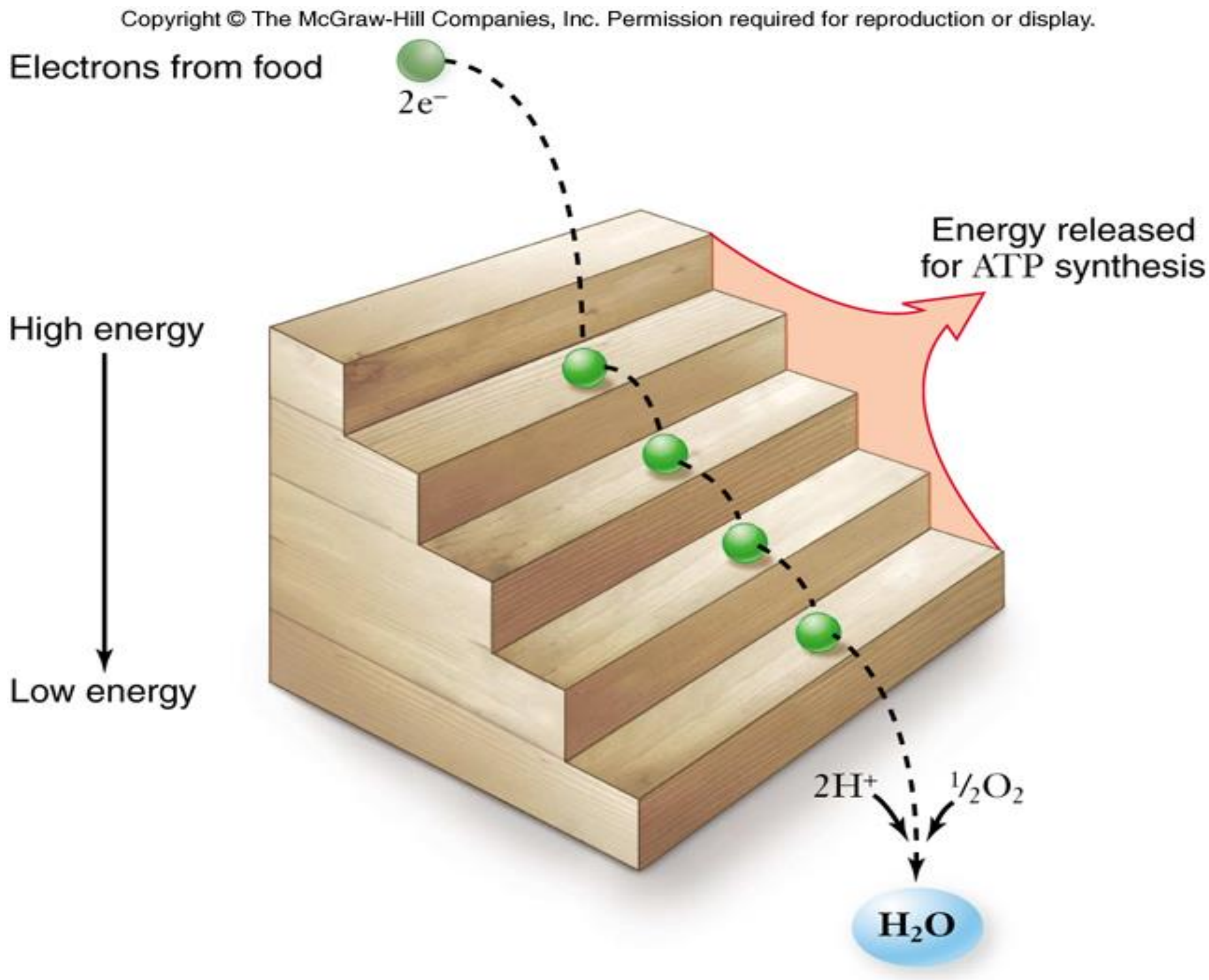
- Transports electrons & pumps hydrogen ions in intermembrane space to create a gradient.

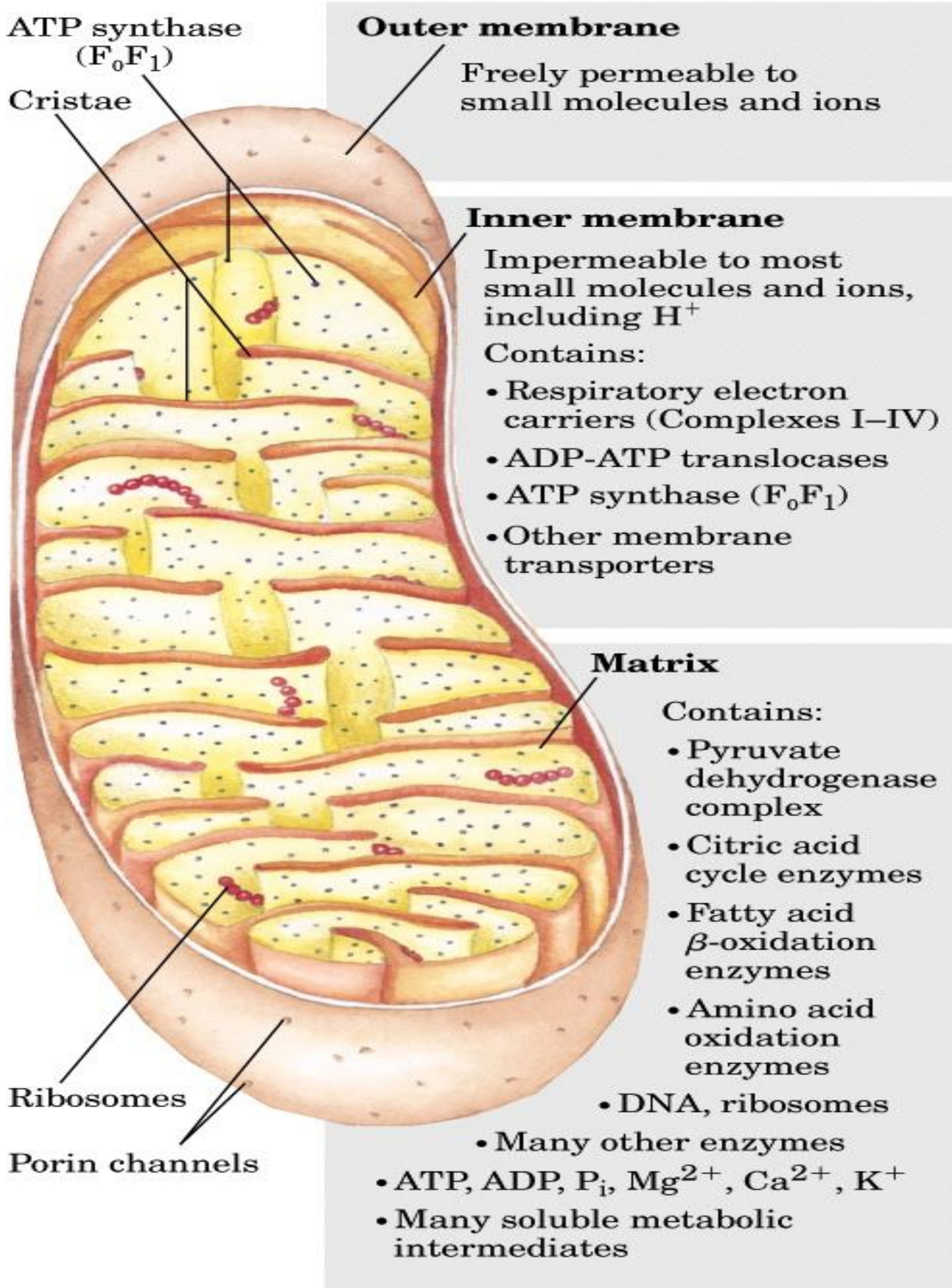
- The electron transport chain can be isolated in four proteins complexes(I, II, III, IV).
- Complex v: ATP synthase

- A lipid soluble coenzyme (Q) & a water soluble protein (cyt c) shuttle between protein complexes

The goal of respiration is to produce ATP.

- energy is released from oxidation reaction in the form of electrons
- electrons are shuttled by electron carriers (e.g. NAD+) to an **electron transport chain**
- electron energy is converted to ATP at the electron transport chain

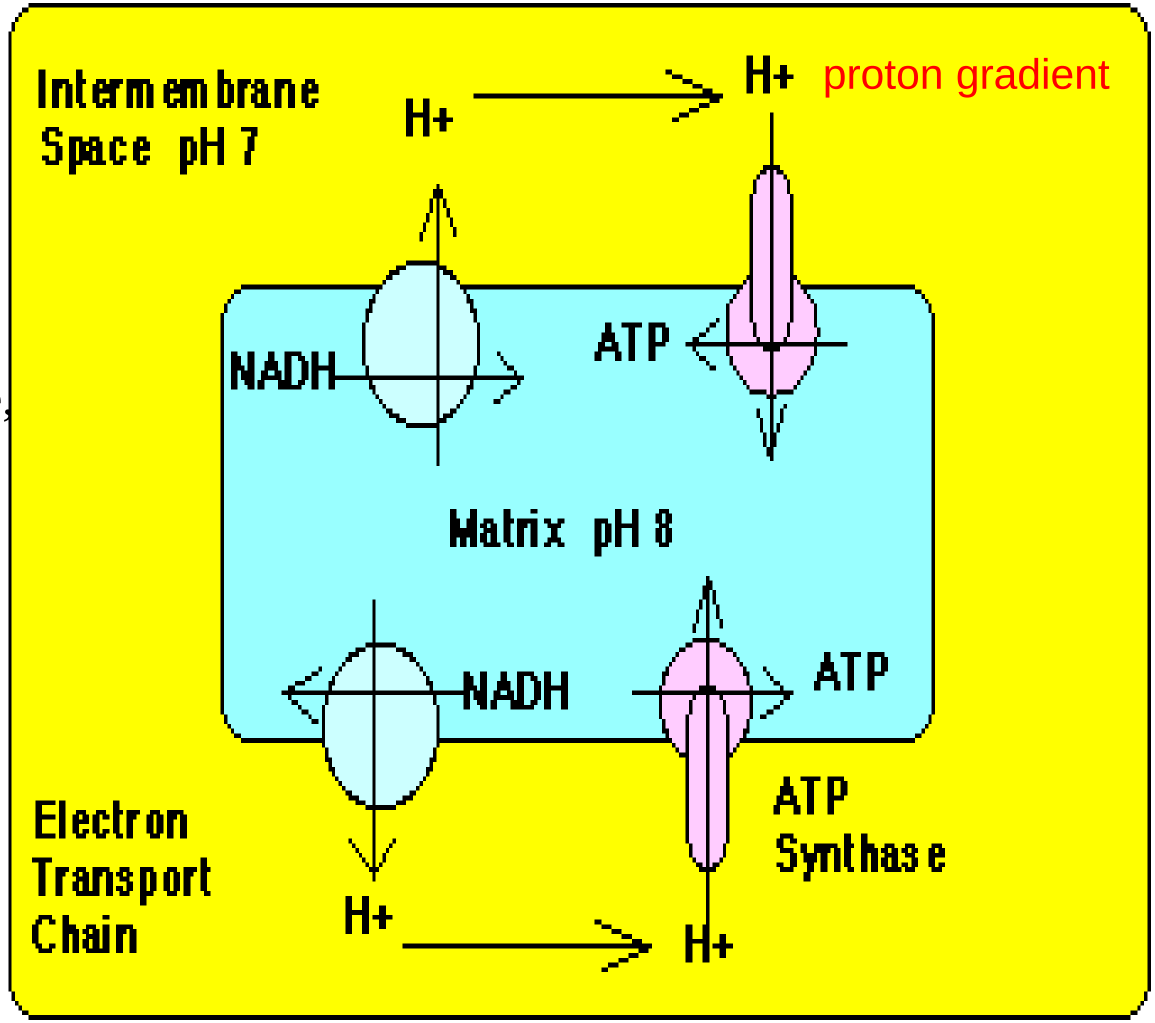




ATP synthase (F_oF_1)
Cristae
Outer membrane
Freely permeable to small molecules and ions
Inner membrane
Impermeable to most small molecules and ions, including H^+
Contains:
• Respiratory electron carriers (Complexes I–IV)
• ADP-ATP translocases
• ATP synthase (F_oF_1)
• Other membrane transporters
Matrix
Contains:
• Pyruvate dehydrogenase complex
• Citric acid cycle enzymes
• Fatty acid β-oxidation enzymes
• Amino acid oxidation enzymes
• DNA, ribosomes
• Many other enzymes
• ATP, ADP, P_i, Mg^{2+}, Ca^{2+}, K^+
• Many soluble metabolic intermediates
Ribosomes
Porin channels

An overview of electron transport chain operations

- hydrogen gradient: H+ concentration 10 X >>in intermembrane space than in the matrix
- H+ diffuses back into the matrix through a channel in ATP synthase, producing an electric current
- The shaft of the ATP synthase complex rotates (counter-clockwise)
- ATP formed in the inner matrix: transported across 2 membranes to get into the cytosol



The light blue circles (ETC complexes), the enzyme ATP synthase (pink)

Complexes have Fe, S, Cu reduced & oxidized as electrons & H+ move along.

table 19–3

Protein Components of the Mitochondrial Electron-Transfer Chain

Enzyme complex	Mass (kDa)	Number of subunits*	Prosthetic group(s)
I NADH dehydrogenase	850	42 (14)	FMN, Fe-S
II Succinate dehydrogenase	140	5	FAD, Fe-S
III Ubiquinone: cytochrome *c* oxidoreductase	250	11	Hemes, Fe-S
Cytochrome *c*[†]	13	1	Heme
IV Cytochrome oxidase	160	13 (3–4)	Hemes; Cu_A, Cu_B

*Numbers of subunits in the bacterial equivalents in parentheses.

[†]Cytochrome *c* is not part of an enzyme complex; it moves between Complexes III and IV as a freely soluble protein.

- Specific integral (intrinsic) membrane proteins accept electrons & H from NADH & FADH2 **in the presence of O2.**
- NADH → NAD+
  - NADH from rxn in Krebs & from the pyruvate dehydrogenase complex rxn.
  - **The name of the protein/enzyme that oxidizes NADH is <u>NADH reductase</u>.**
  - **This enzyme dumps H+ into the intermembrane space.**
- FADH2 → FAD
  - FADH2 from the succinate dehydrogenase rxn in Krebs.
  - **The protein/enzyme that oxidizes FADH2 is <u>succinate dehydrogenase</u>.**
  - **This enzyme dumps H+ into the intermembrane space.**

<u>Cytochrome oxidase</u> is the name of the protein/enzyme which interacts with oxygen.

- **This enzyme dumps H+ into the intermembrane space.**
- Any chemical interfering with the exchange of electrons & protons between cytochrome oxidase & oxygen will halt the electron transport chain function and will cause respiration to stop.

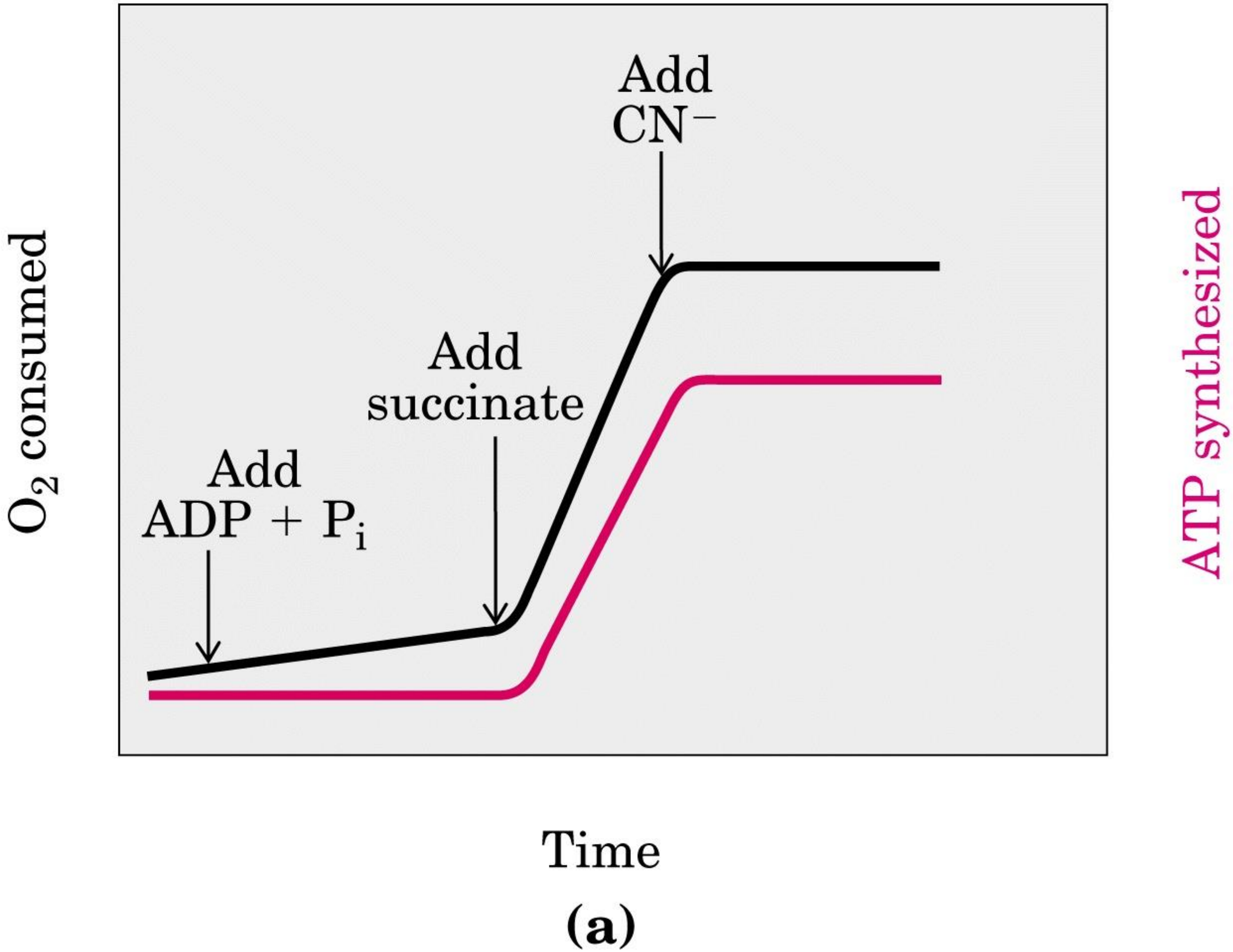
table 19–4

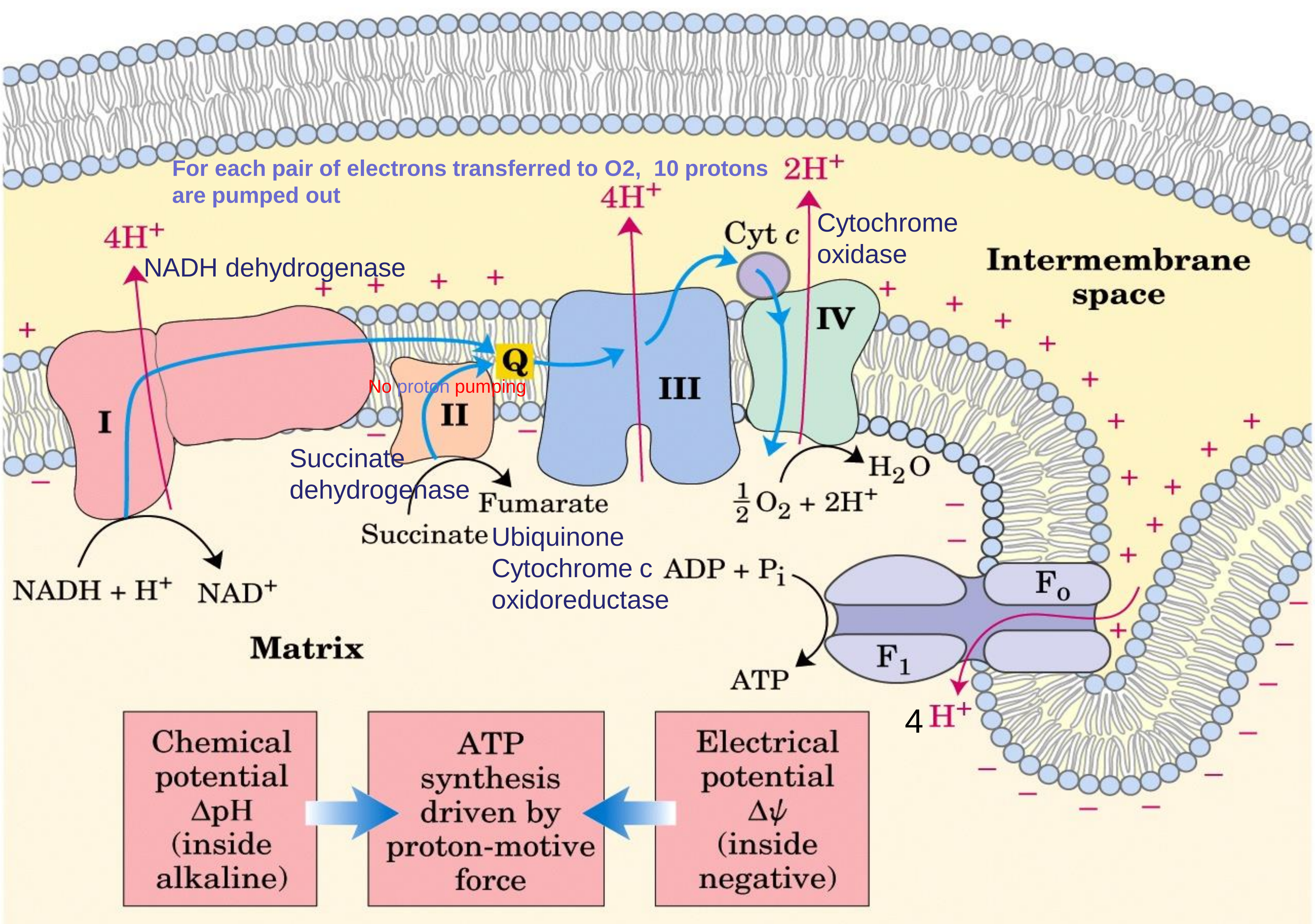
Some Agents That Interfere with Oxidative Phosphorylation or Photophosphorylation

Type of interference	Compound*	Target/mode of action
Inhibition of electron transfer	Cyanide Carbon monoxide	Inhibit cytochrome oxidase
	Antimycin A	Blocks electron transfer from cytochrome *b* to cytochrome c_1
	Myxothiazol Rotenone Amytal Piericidin A	Prevent electron transfer from Fe-S center to ubiquinone
	DCMU	Competes with Q_B for binding site in PSII
Inhibition of ATP synthase	Aurovertin	Inhibits F_1
	Oligomycin Venturicidin	Inhibit F_o and CF_o
	DCCD	Blocks proton flow through F_o and CF_o
Uncoupling of phosphorylation from electron transfer	FCCP DNP	Hydrophobic proton carriers
	Valinomycin	K^+ ionophore
	Thermogenin	Forms proton-conducting pores in inner membrane of brown fat mitochondria
Inhibition of ATP-ADP exchange	Atractyloside	Inhibits adenine nucleotide translocase

*DCMU is 3-(3,4-dichlorophenyl)-1,1-dimethylurea; DCCD, dicyclohexylcarbodiimide; FCCP, cyanide-*p*-trifluoromethoxyphenylhydrazone; DNP, 2,4-dinitrophenol.

Cyanide inhibits cytochrome oxidase





$$2\ H^+ + 2\ e^- + ½\ O_2 \dashrightarrow H_2O$$

The higher negative charge in the matrix attracts the protons (H^+) back from the intermembrane space to the matrix.

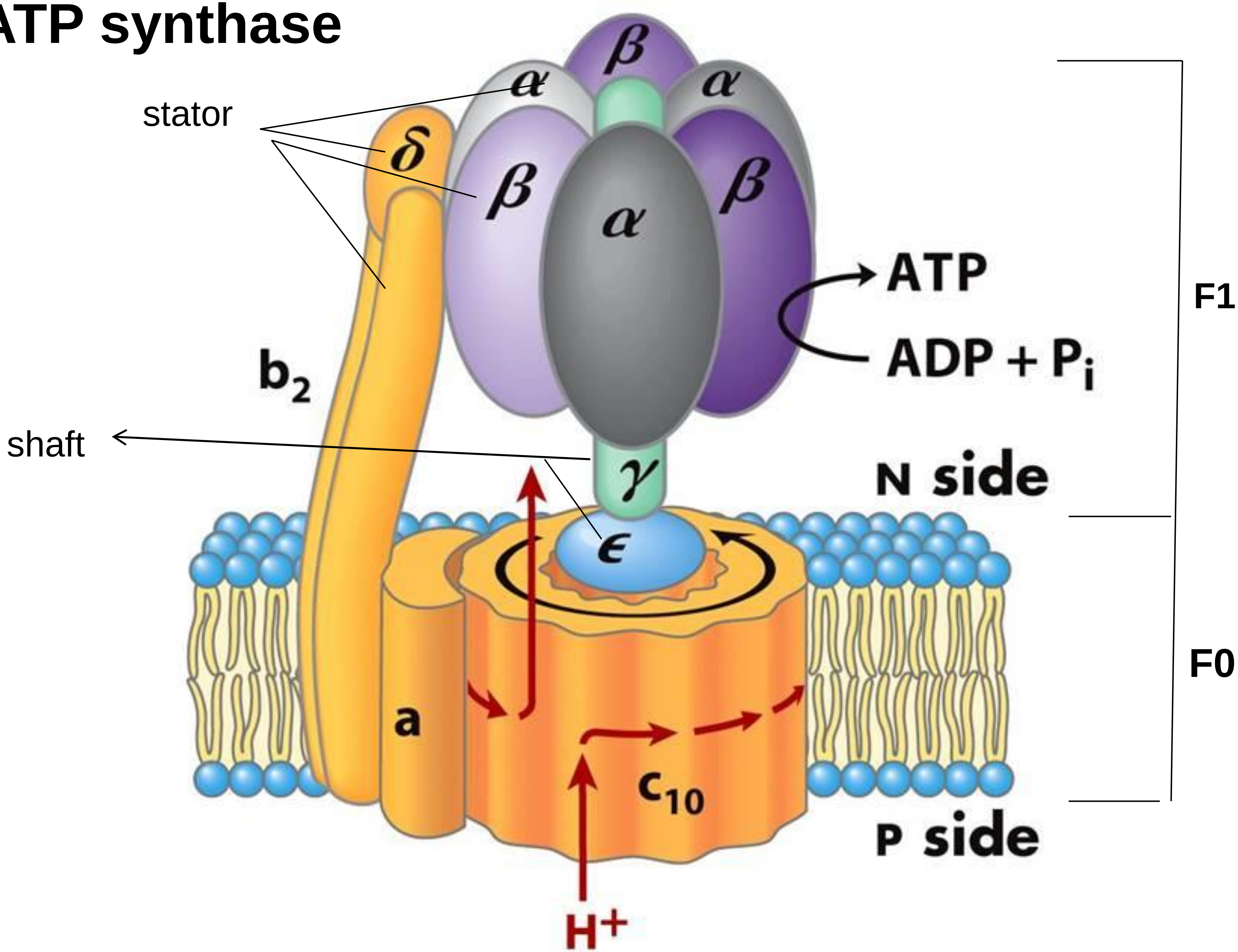
Most protons move back to the matrix through **ATP synthase**.

ATP synthase is a membrane-bound enzyme that uses the energy of the proton gradient to synthesize ATP from ADP + P_i.

Theoretical energy yields

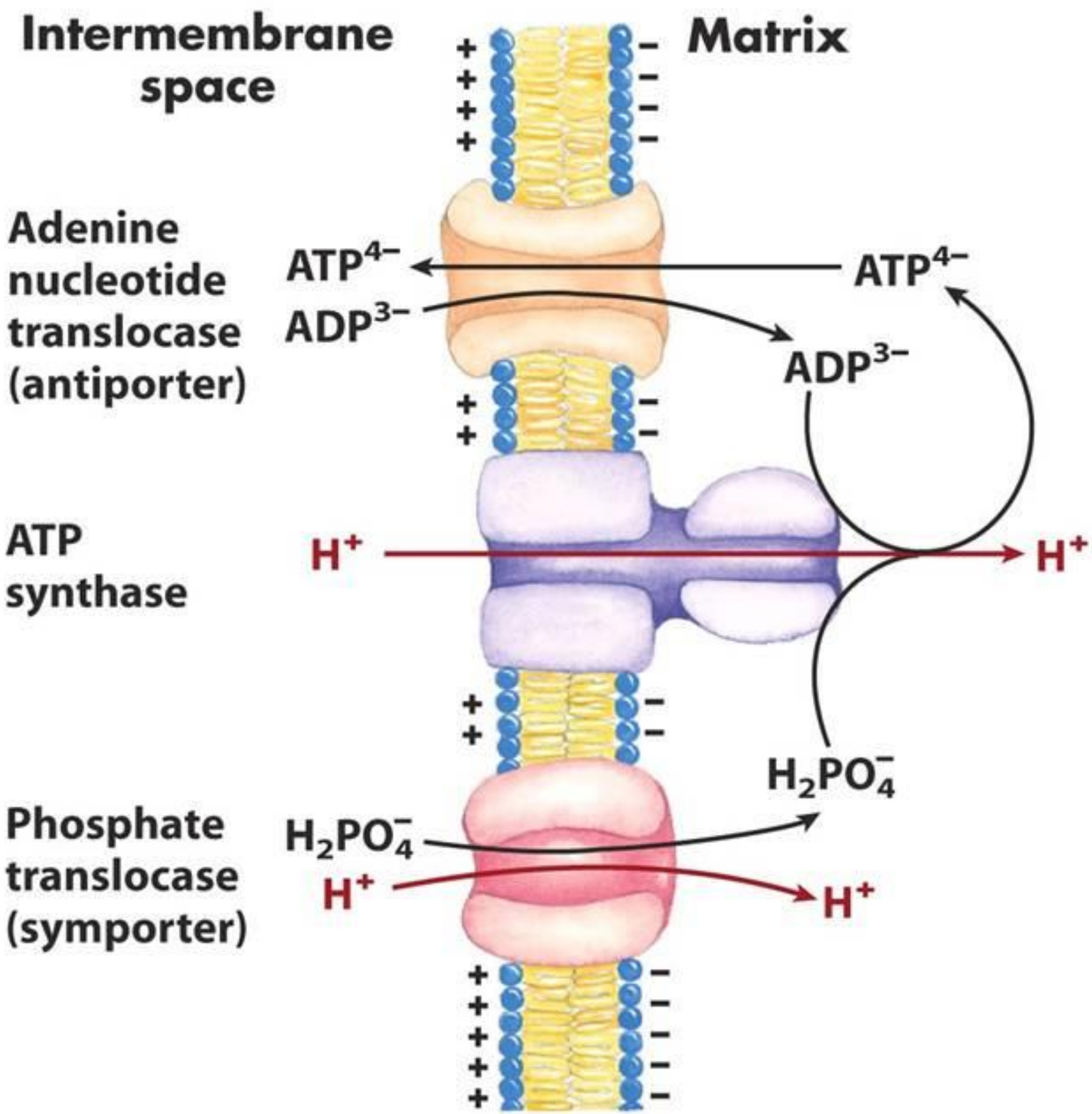
- 36 ATP per glucose

ATP synthase



ATP synthesis occurs on ß- subunit of F1. Fo contains a proton channel

Transport of Adenine nucleotide and phosphate



- The NADH dehydrogenase of the inner mitochondrial

membrane accept electrons only from NADH in the matrix.

Problem: the inner membrane is not permeable to NADH, how can the NADH generated by glycolysis in the cytosol be reoxidized to NAD by O2 via the respiratory chain?

Solution: Special shuttle systems carry reducing equivalents from cytosolic NADH into mitochondria by an indirect route.

The most active NADH shuttle, which functions in liver, kidney, and heart mitochondria, is the **malate-aspartate shuttle**

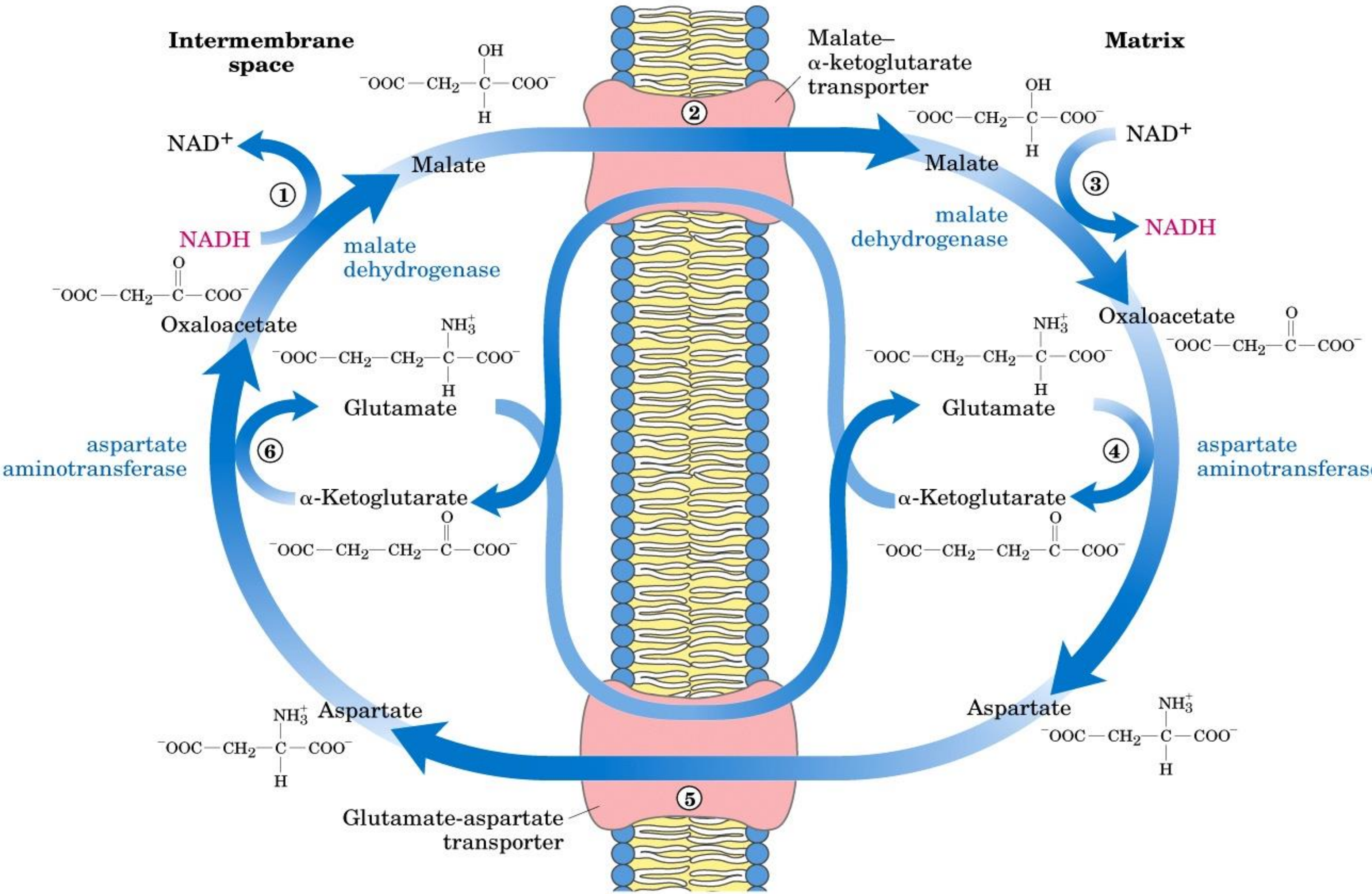
Malate Aspartate shuttle

- In contrast to oxidation of mitochondrial NADH, cytosolic NADH, when it is oxidized via the electron transport system

- if it proceeds via the malate aspartate shuttle gives rise to 2.5 ATPs

- if it is oxidized by the glycerol phosphate shuttle gives rise to 1.5 equivalents of ATP

Malate-Aspartate Shuttle Liver, kidney and heart.



Glycerol-3-phosphate shuttle :

In skeletal muscles & Brain:

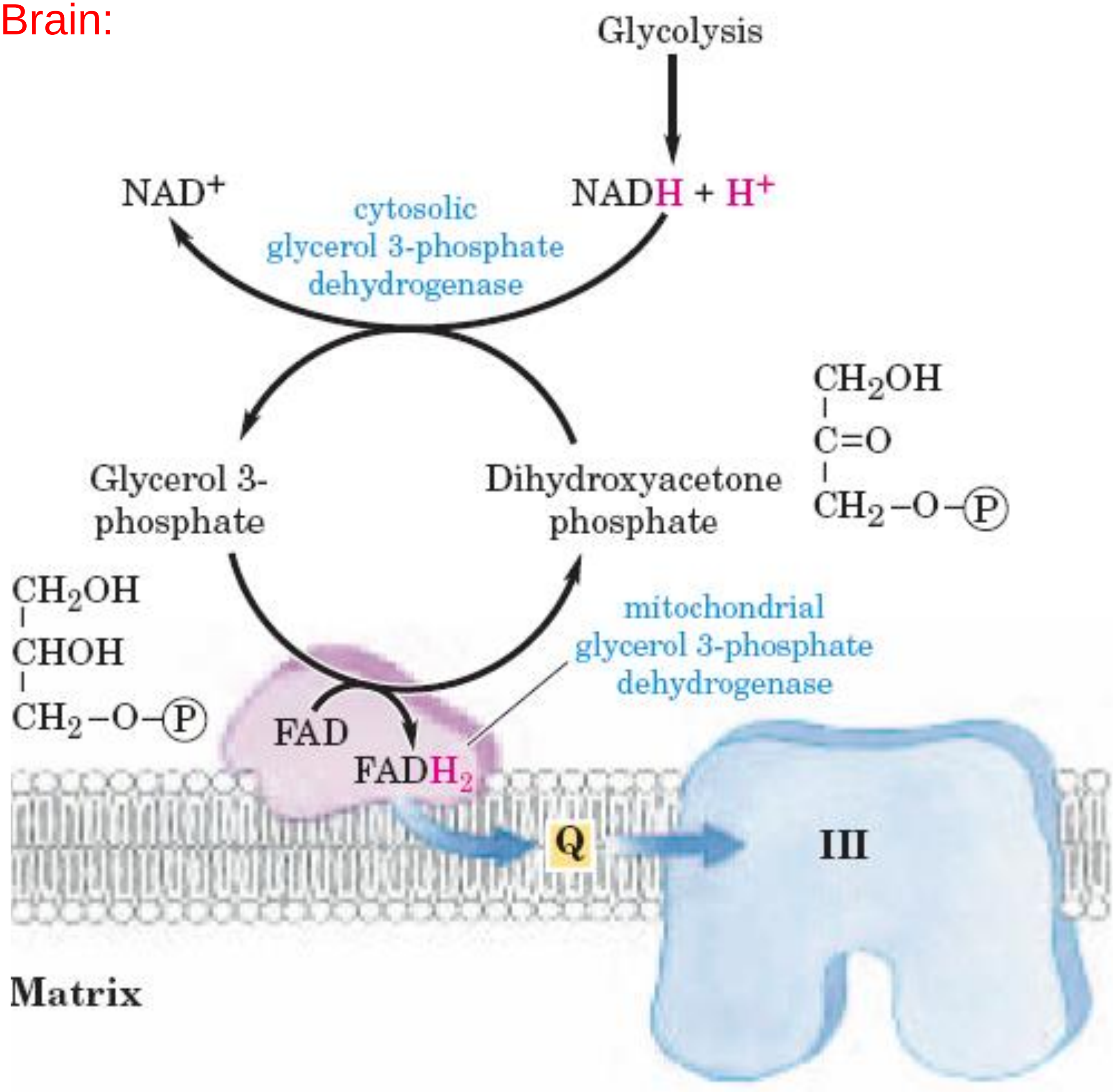


TABLE 19–5 **ATP Yield from Complete Oxidation of Glucose**

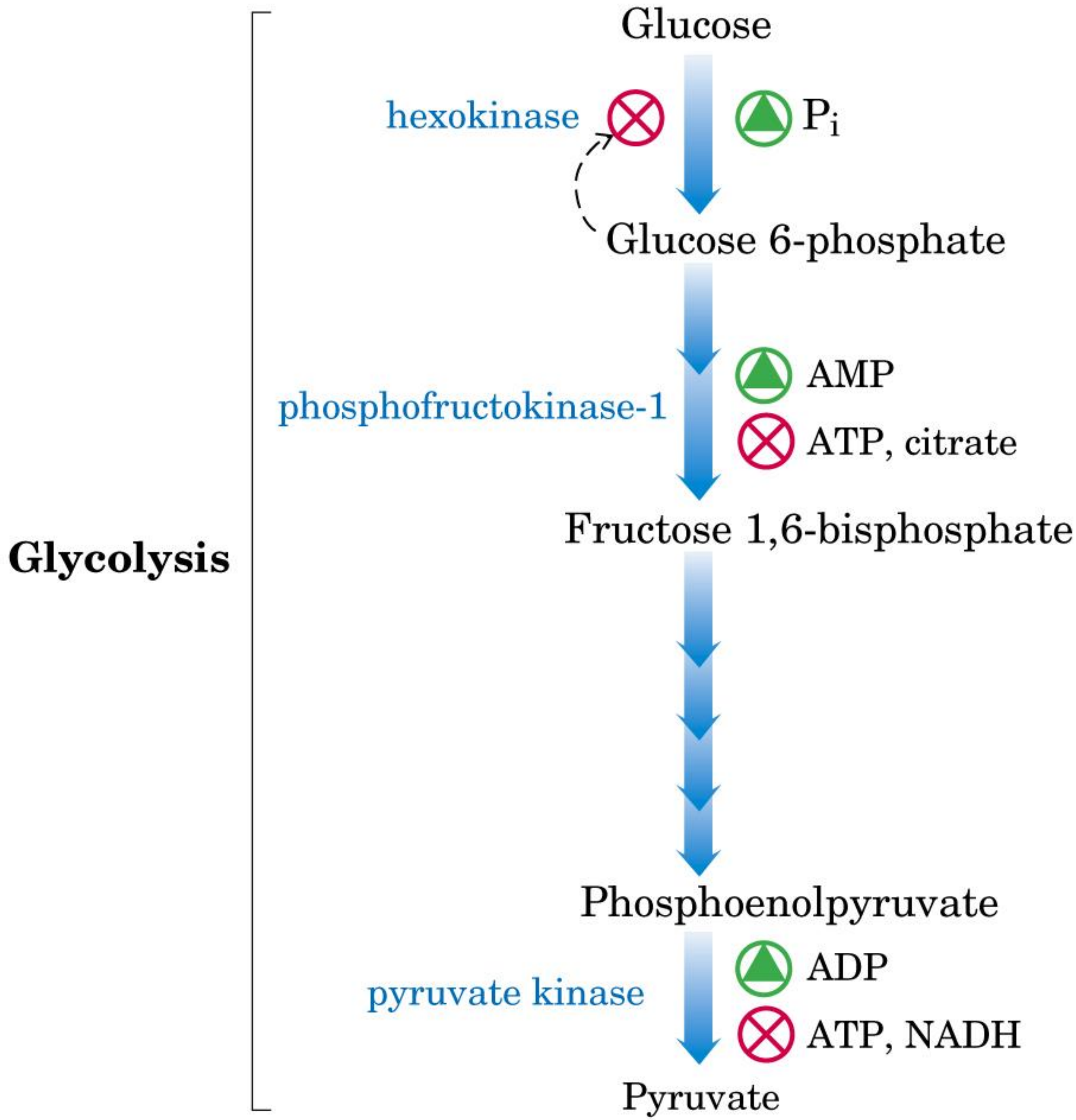
Process	*Direct product*	*Final ATP*
Glycolysis	2 NADH (cytosolic)	3 or 5*
	2 ATP	2
Pyruvate oxidation (two per glucose)	2 NADH (mitochondrial matrix)	5
Acetyl-CoA oxidation in citric acid cycle	6 NADH (mitochondrial matrix)	15
(two per glucose)	2 $FADH_2$	3
	2 ATP or 2 GTP	2
Total yield per glucose		30 or 32

*The number depends on which shuttle system transfers reducing equivalents into the mitochondrion.

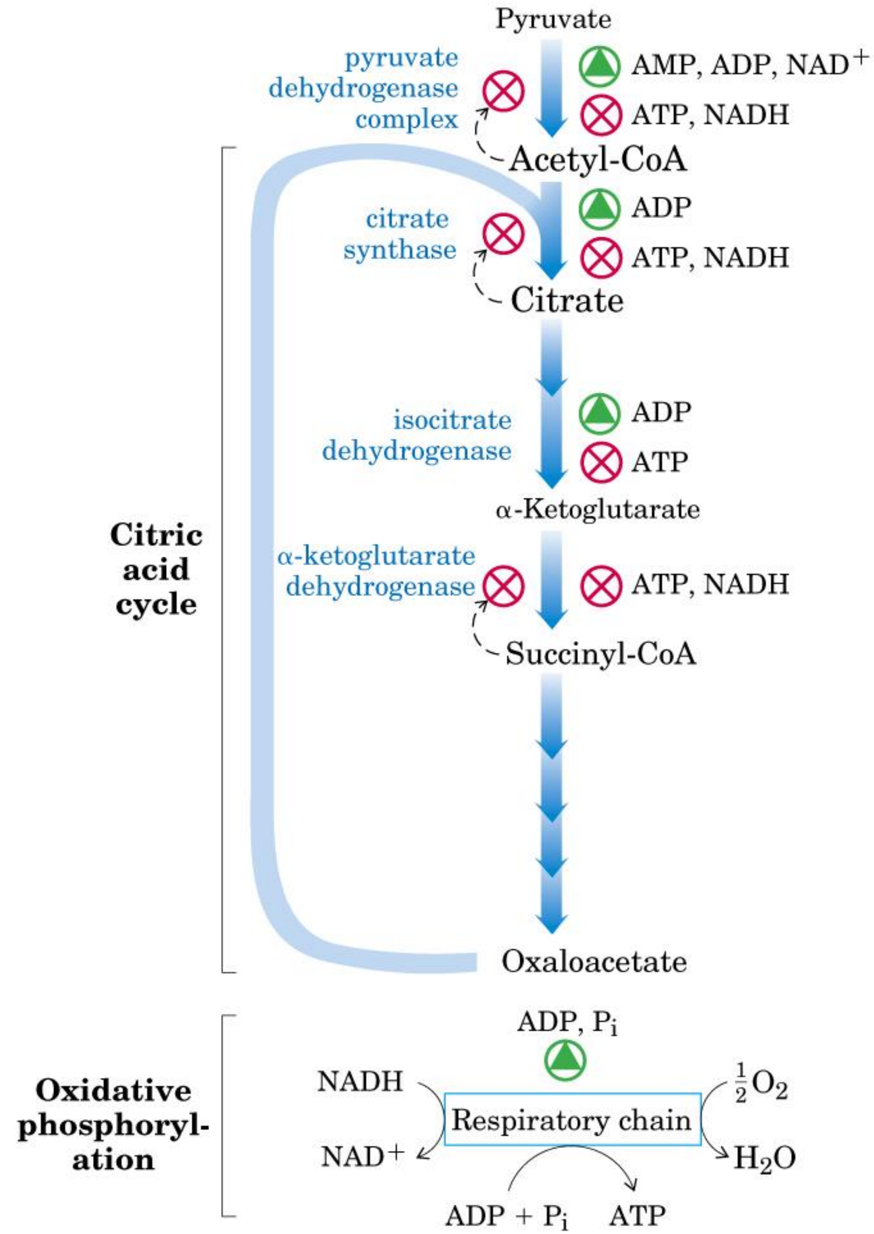
Oxidative Phosphorylation Is Regulated by Cellular Energy Needs

The rate of respiration (O_2 consumption) in mitochondria is tightly regulated;

it is generally limited by the **availability of ADP , Pi, O_2 consumption**



Glucose
hexokinase
P_i
Glucose 6-phosphate
phosphofructokinase-1
AMP
ATP, citrate
Fructose 1,6-bisphosphate
Glycolysis
Phosphoenolpyruvate
pyruvate kinase
ADP
ATP, NADH
Pyruvate



Pyruvate
pyruvate dehydrogenase complex
AMP, ADP, NAD+
ATP, NADH
Acetyl-CoA
citrate synthase
ADP
ATP, NADH
Citrate
isocitrate dehydrogenase
ADP
ATP
α-Ketoglutarate
α-ketoglutarate dehydrogenase
ATP, NADH
Succinyl-CoA
Oxaloacetate
Citric acid cycle
Oxidative phosphoryl-ation
ADP, Pi
NADH
NAD+
Respiratory chain
½O2
H2O
ADP + Pi
ATP