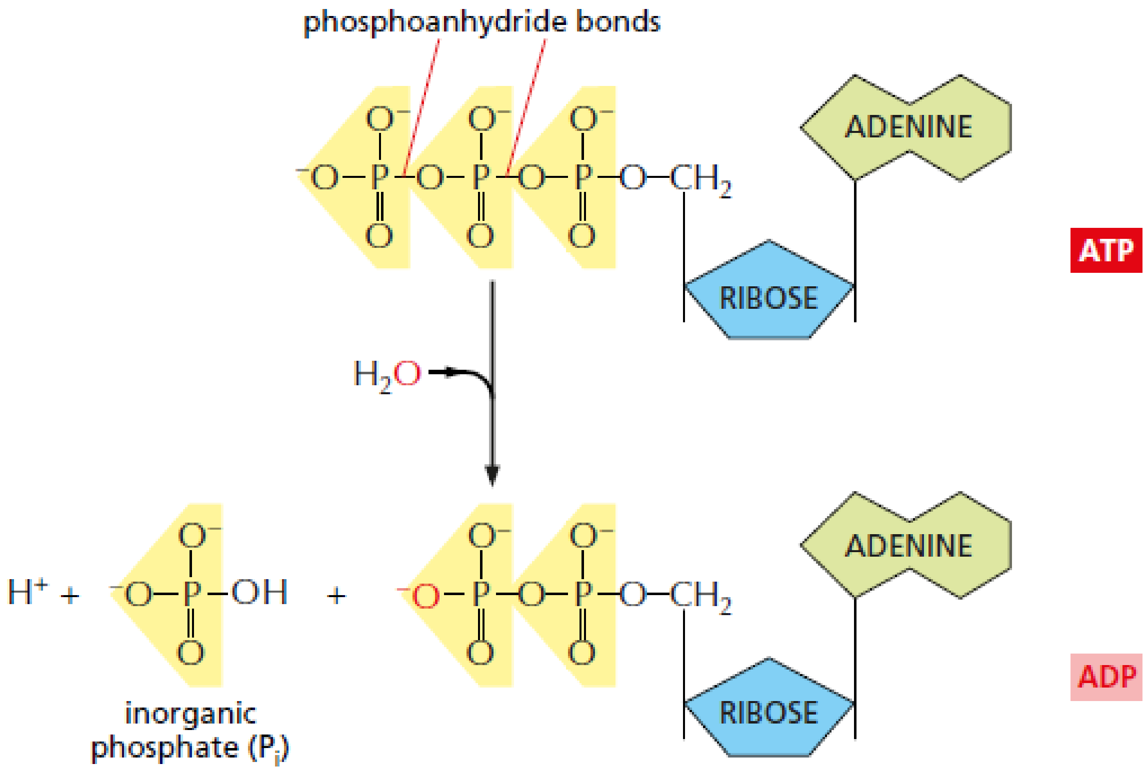
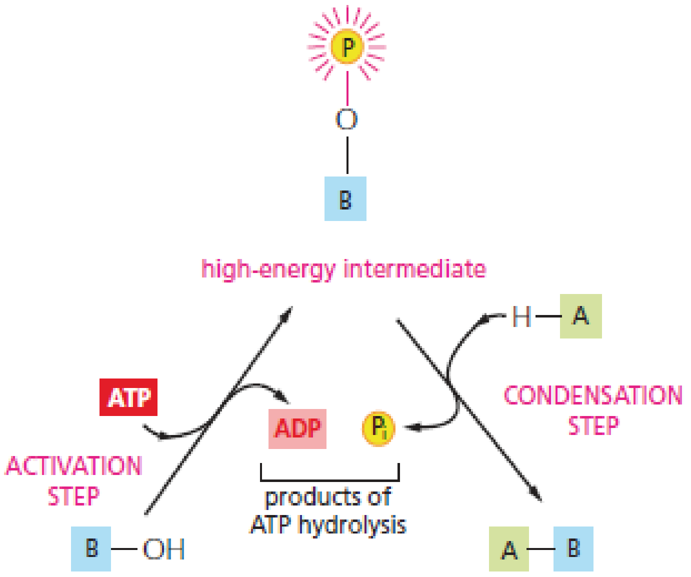
ATP Is the Most Widely Used Activated Carrier Molecule

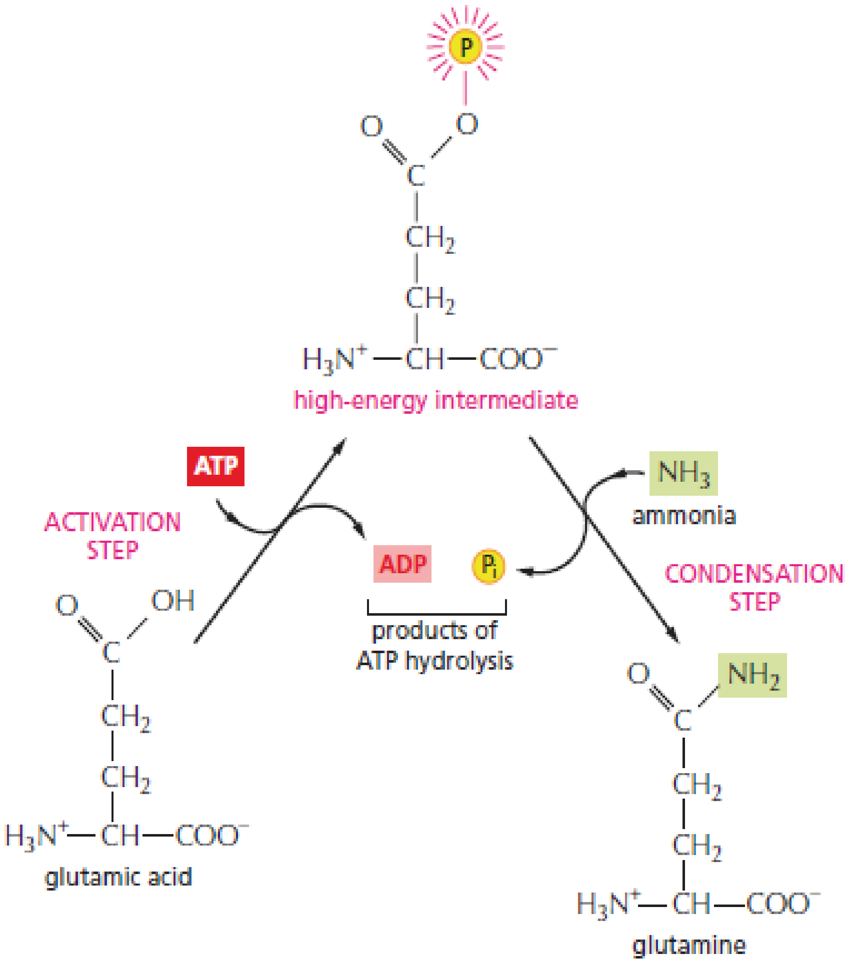


Hydrolysis of the terminal phosphate of ATP yields between 46 and 54 kJ/mole of usable energy

Biosynthetic reaction driven by ATP hydrolysis

$$A\text{–}H + B\text{–}OH \rightarrow A\text{–}B + H_2O$$

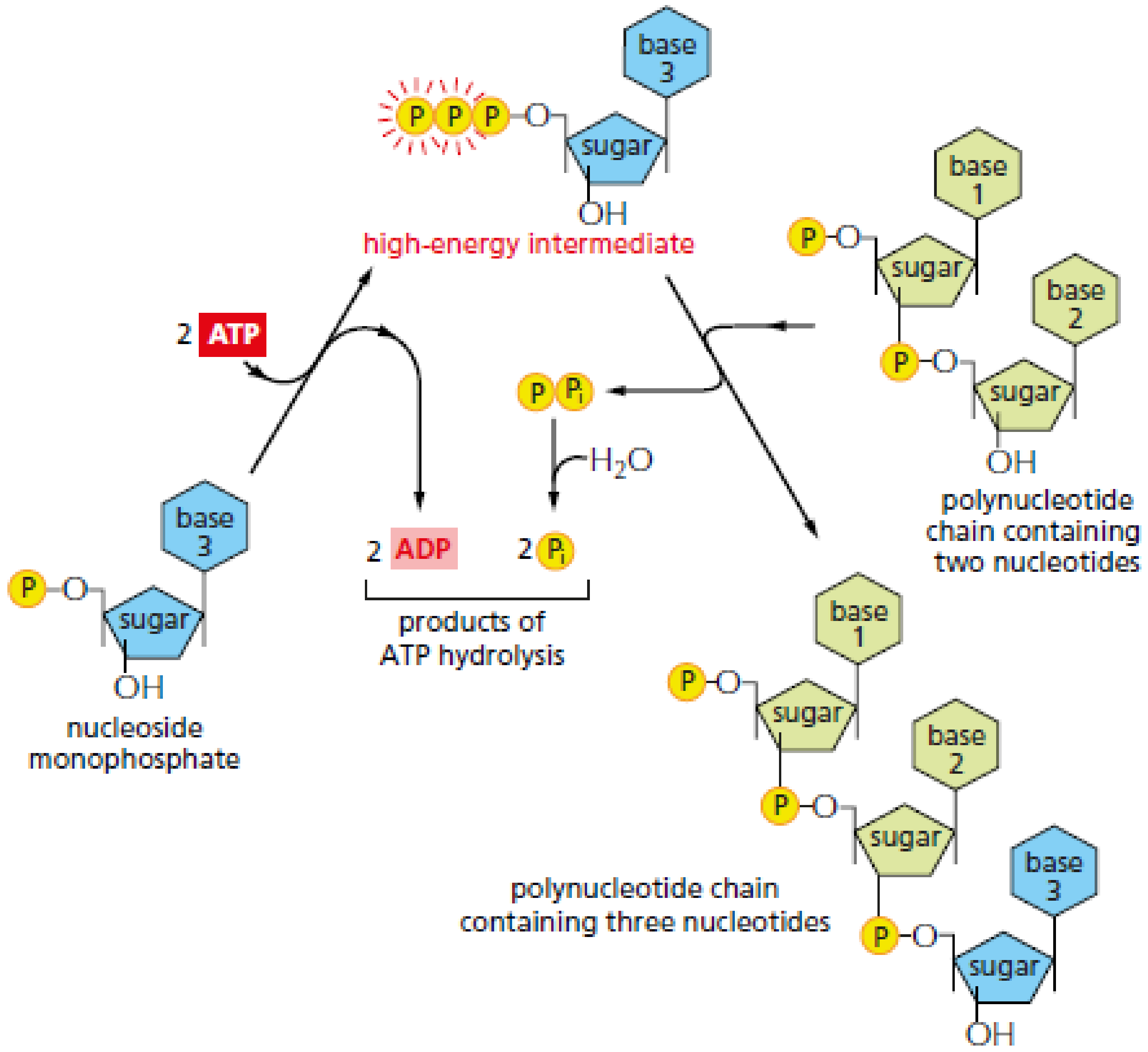




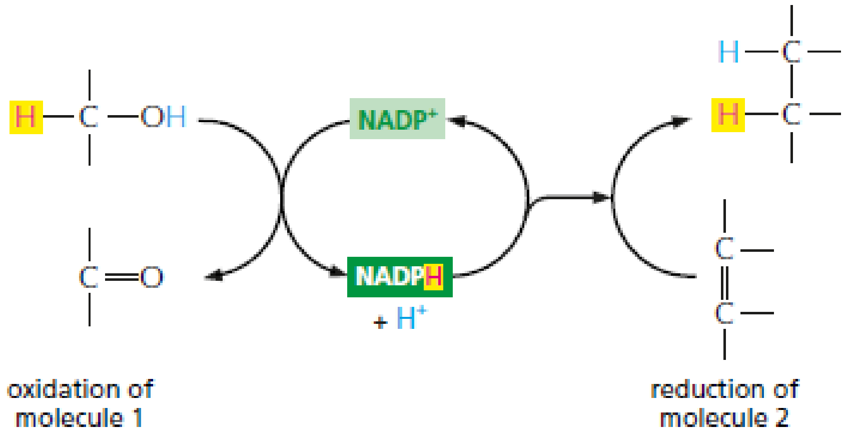
1. $B\text{–}OH + ATP \longrightarrow B\text{–}O\text{–}PO_3 + ADP$
2. $A\text{–}H + B\text{–}O\text{–}PO_3 \longrightarrow A\text{–}B + P_i$

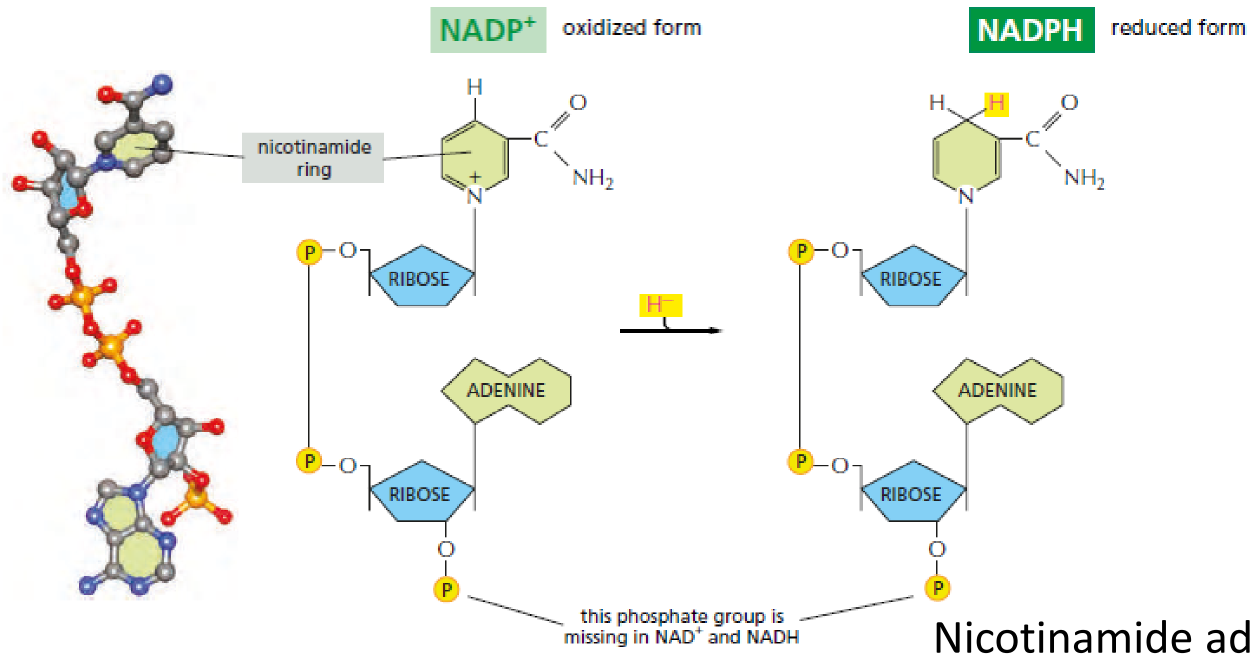
Net result: $B\text{–}OH + ATP + A\text{–}H \longrightarrow A\text{–}B + ADP + P_i$

Synthesis of a polynucleotide, RNA or DNA, is a multistep process driven by ATP hydrolysis



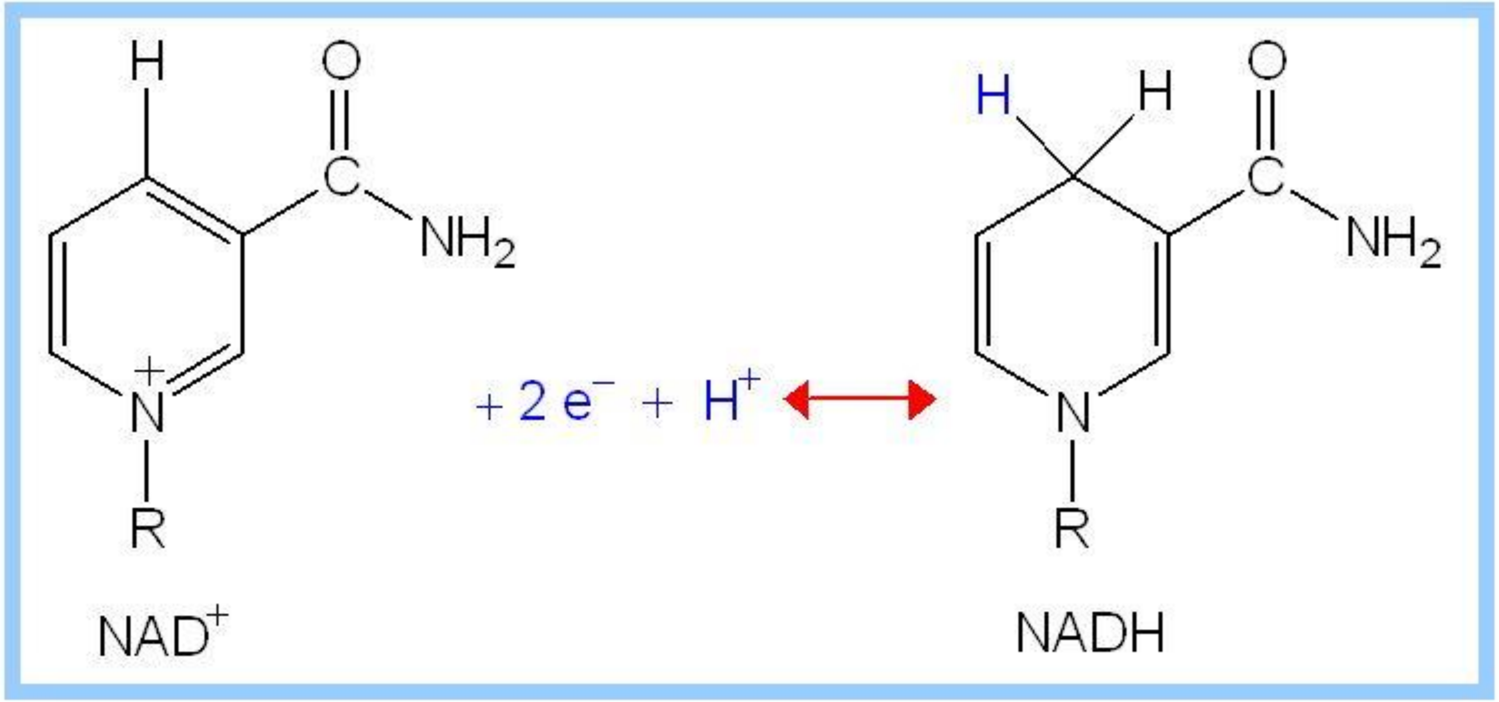
NADH and NADPH Are Important Electron Carriers





Nicotinamide adenine dinucleotide

NAD$^+$/NADH



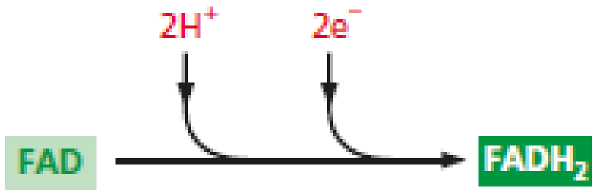
The electron transfer reaction may be summarized as :

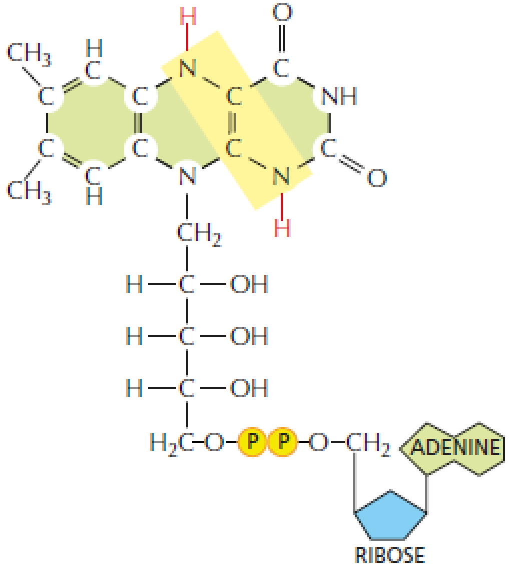
$NAD^+ + 2e^- + H^+ \leftrightarrow NADH.$

It may also be written as:

$NAD^+ + 2e^- + 2H^+ \leftrightarrow NADH + H^+$

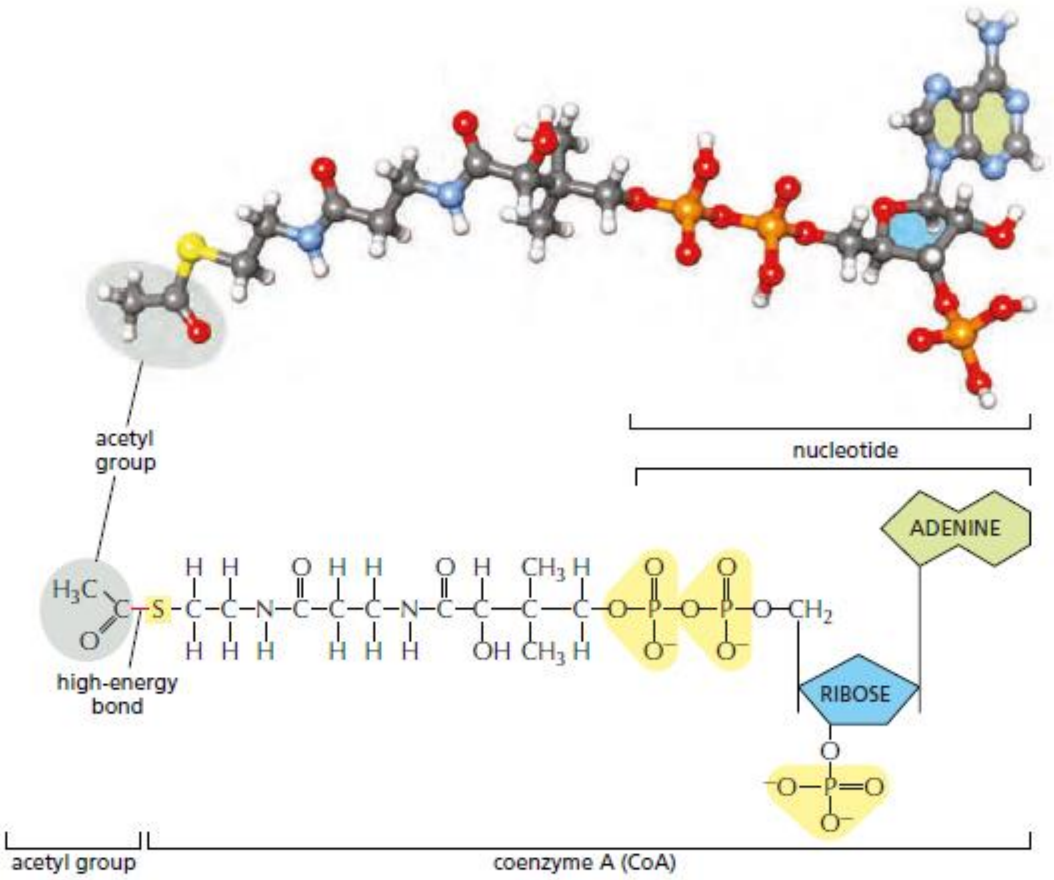
$FADH_2$





Flavin adenine dinucleotide

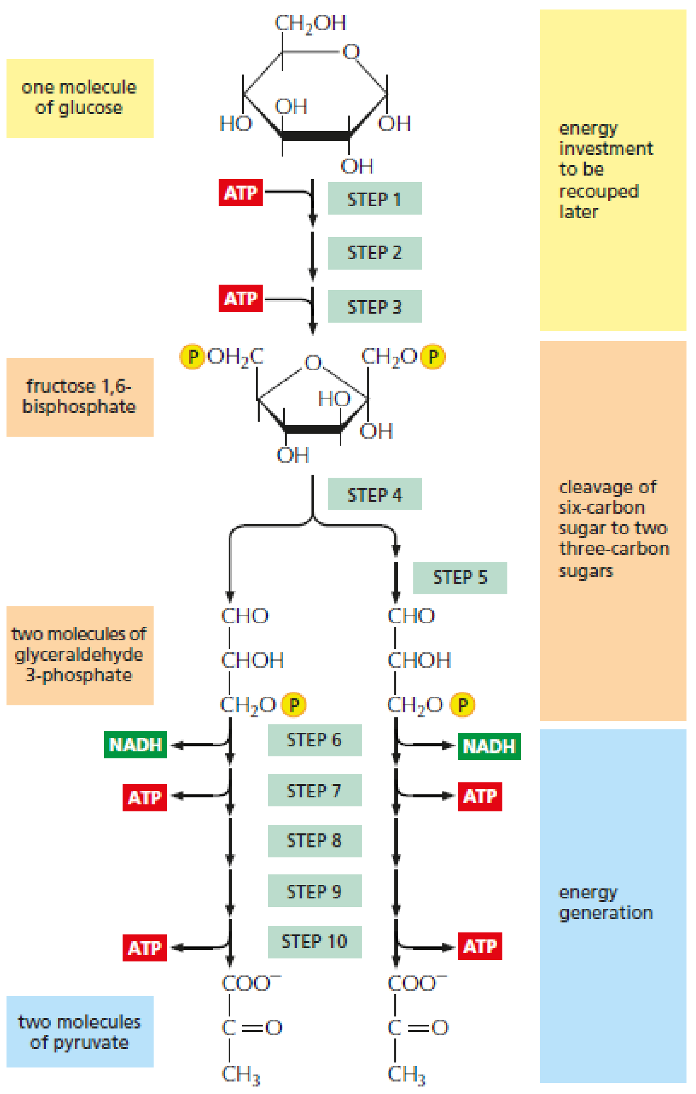
acetyl CoA



acetyl CoA transfers two-carbon acetyl groups

used to add two carbon units in the biosynthesis of larger molecules

Glycolysis is a Central ATP-Producing Pathway



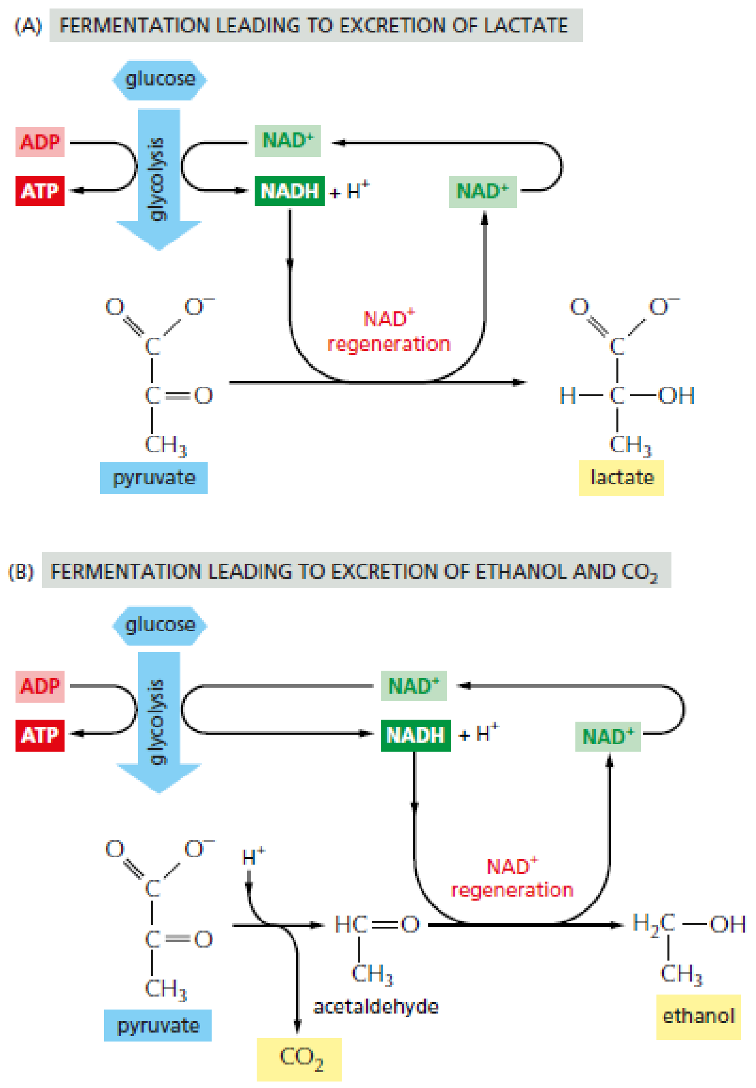
The overall equation for glycolysis

$$\text{Glucose} + 2NAD^+ + 2ADP + 2P_i \longrightarrow 2\ \text{pyruvate} + 2NADH + 2H^+ + 2ATP + 2H_2O$$

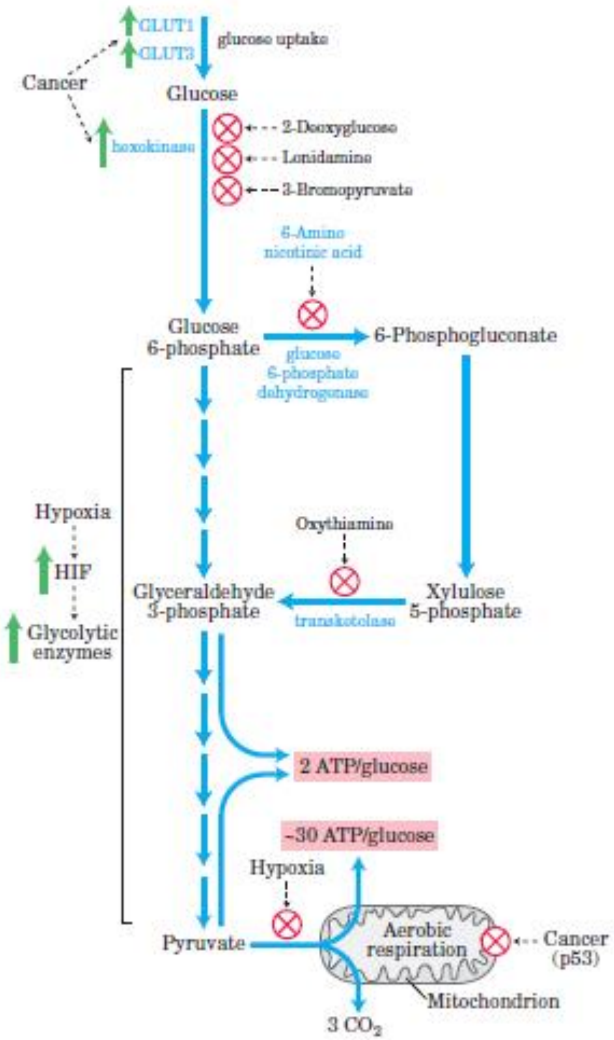
Some types of enzymes involved in glycolysis

Enzyme type	General function	Role in glycolysis
Kinase	catalyzes the addition of a phosphate group to molecules	a kinase transfers a phosphate group from ATP to a substrate in steps 1 and 3; other kinases transfer a phosphate to ADP to form ATP in steps 7 and 10
Isomerase	catalyzes the rearrangement of bonds within a single molecule	isomerases in steps 2 and 5 prepare molecules for the chemical alterations to come
Dehydrogenase	catalyzes the oxidation of a molecule by removing a hydrogen atom plus an electron (a hydride ion, H^-)	the enzyme glyceraldehyde 3-phosphate dehydrogenase generates NADH in step 6
Mutase	catalyzes the shifting of a chemical group from one position to another within a molecule	the movement of a phosphate by phosphoglycerate mutase in step 8 helps prepare the substrate to transfer this group to ADP to make ATP in step 10

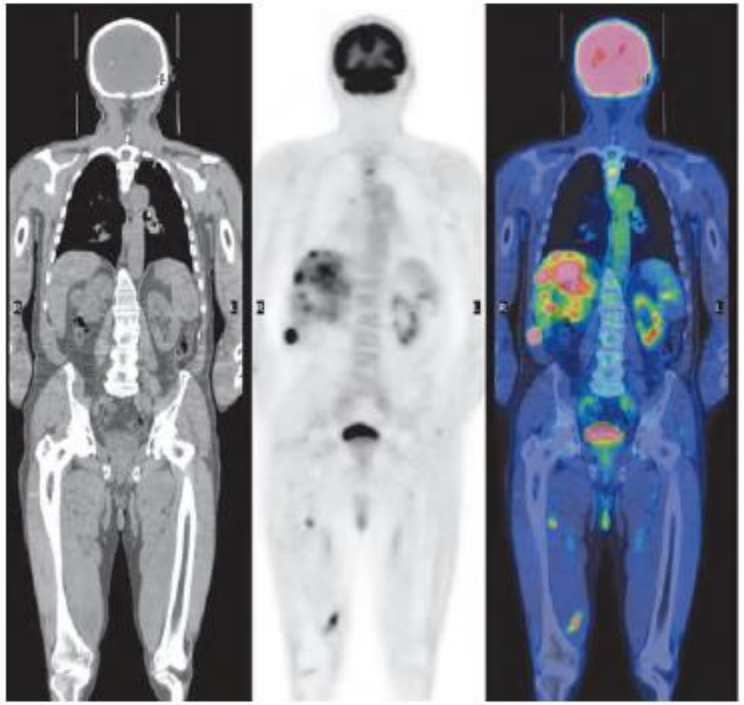
Anaerobic breakdown of pyruvate



The anaerobic metabolism of glucose in tumor cells

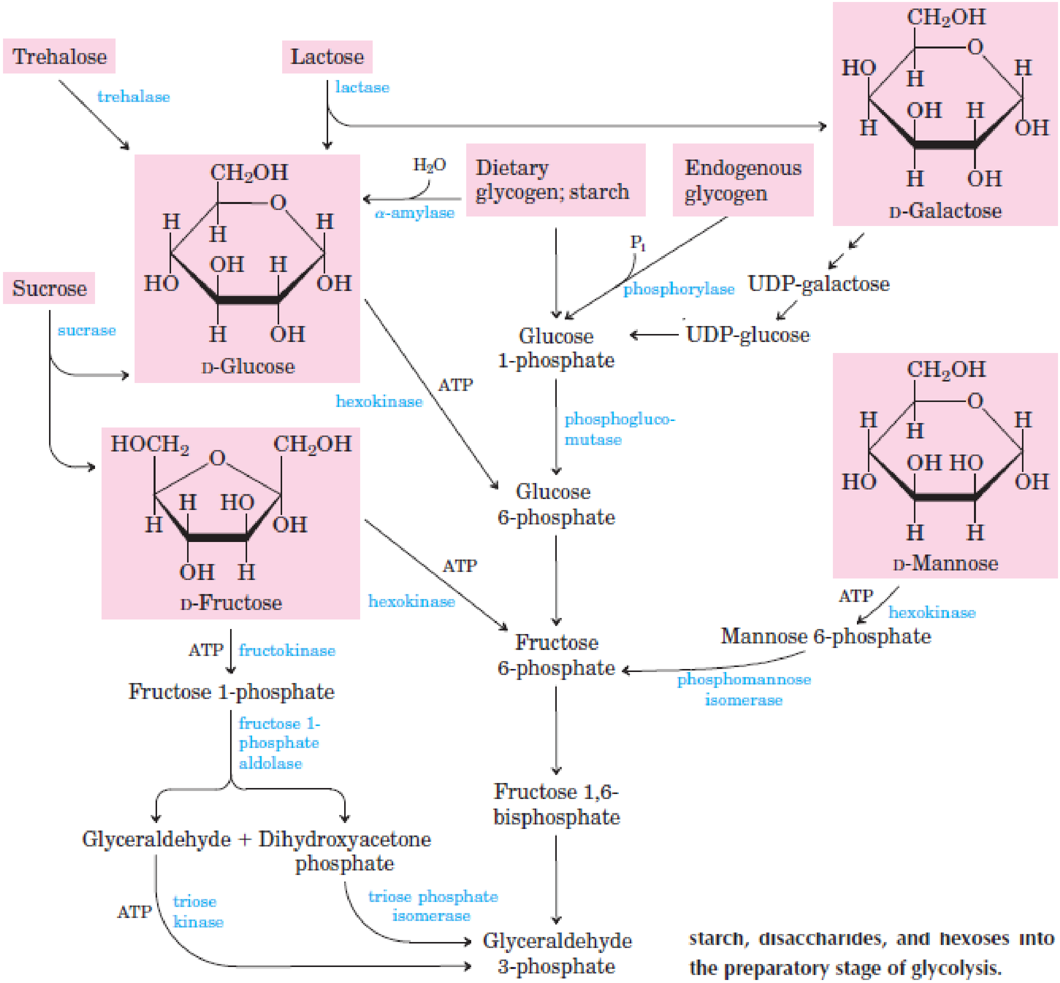


High glycolytic rate in tumor cells also has diagnostic usefulness.



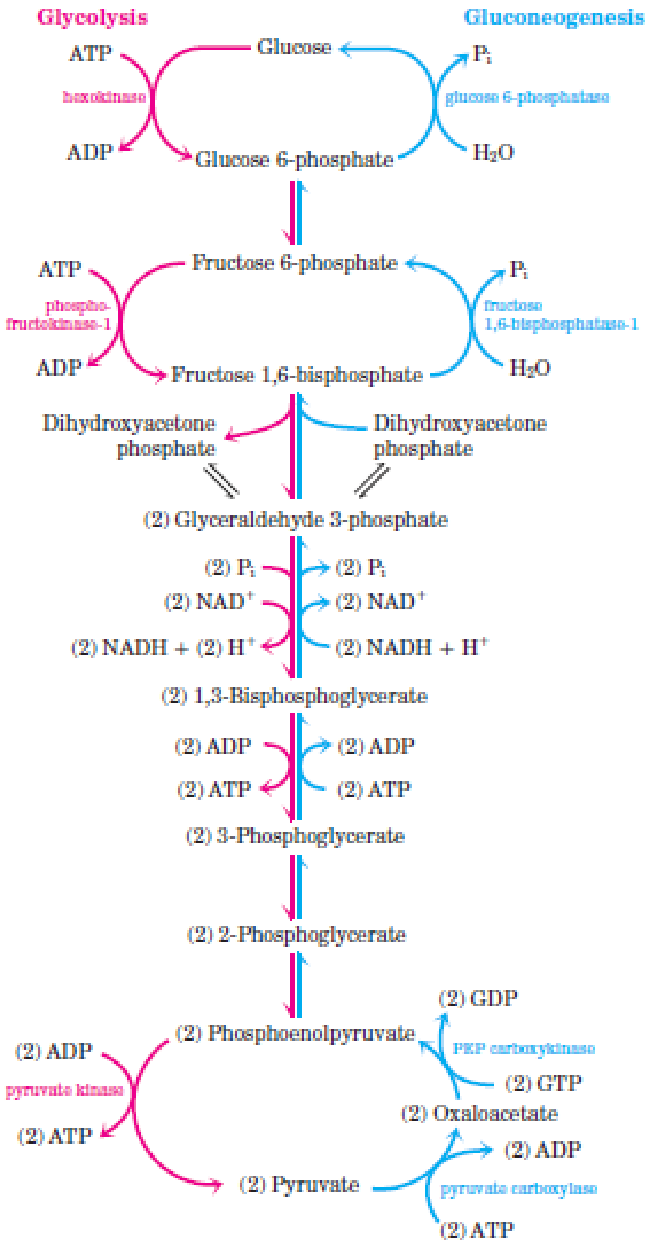
Positron emission tomography (PET) using isotopically
Labeled glucose analog

Entry of glycogen, starch, disaccharides, and hexoses into the preparatory stage of glycolysis



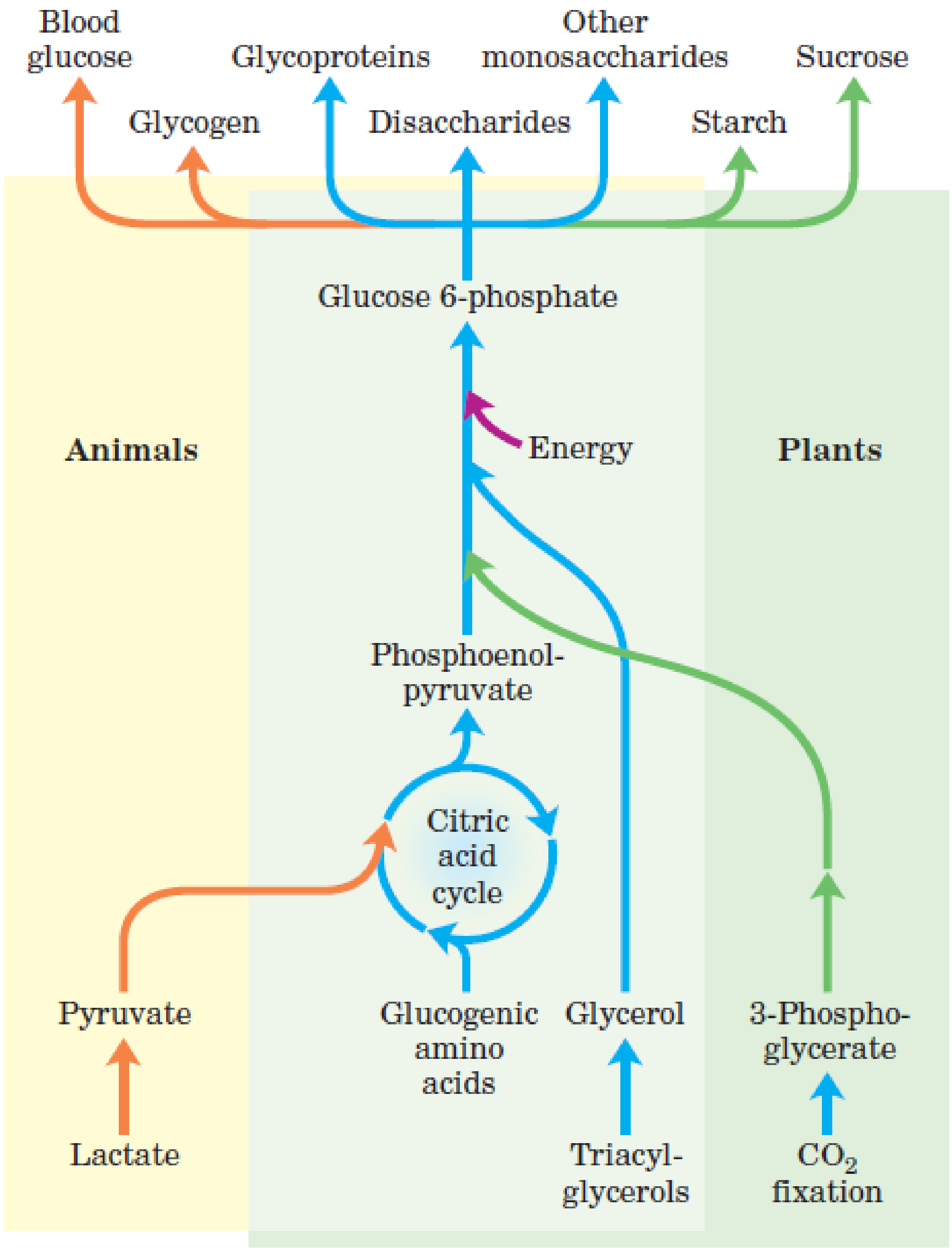
starch, disaccharides, and hexoses into the preparatory stage of glycolysis.

Opposing pathways of glycolysis and gluconeogenesis

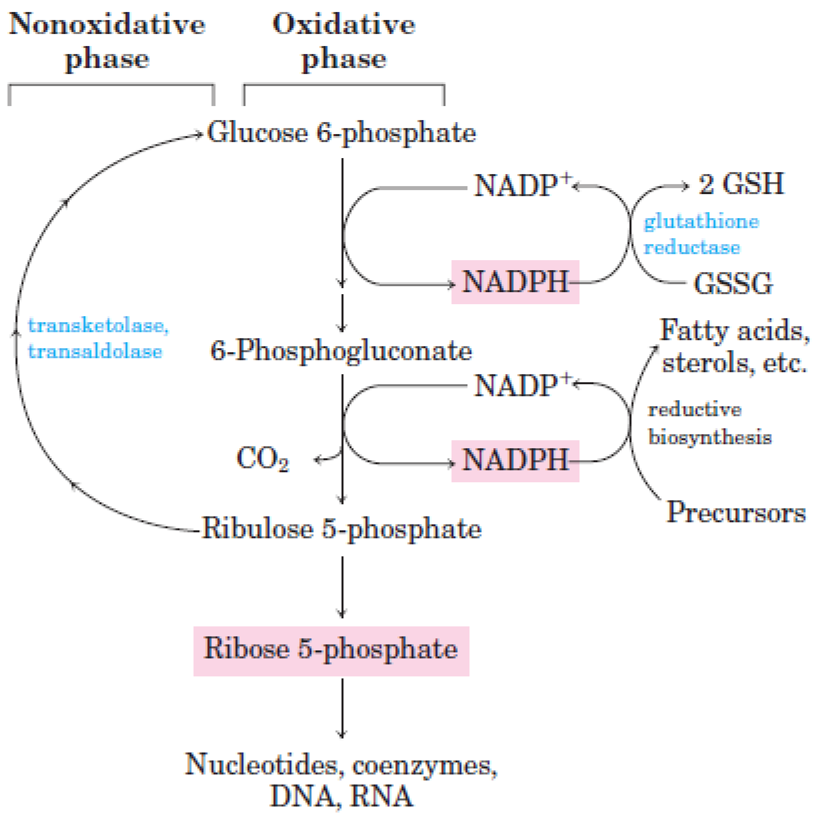


Gluconeogenesis is Energetically Expensive, but Essential

$$2\ \text{Pyruvate} + 4\text{ATP} + 2\text{GTP} + 2\text{NADH} + 2\text{H}^+ + 4\text{H}_2\text{O} \longrightarrow \text{glucose} + 4\text{ADP} + 2\text{GDP} + 6\text{P}_i + 2\text{NAD}^+$$


Blood glucose
Glycogen
Glycoproteins
Disaccharides
Other monosaccharides
Starch
Sucrose
Glucose 6-phosphate
Animals
Energy
Plants
Phosphoenol-pyruvate
Citric acid cycle
Pyruvate
Glucogenic amino acids
Glycerol
3-Phospho-glycerate
Lactate
Triacyl-glycerols
CO_2 fixation

Pentose Phosphate Pathway of Glucose Oxidation



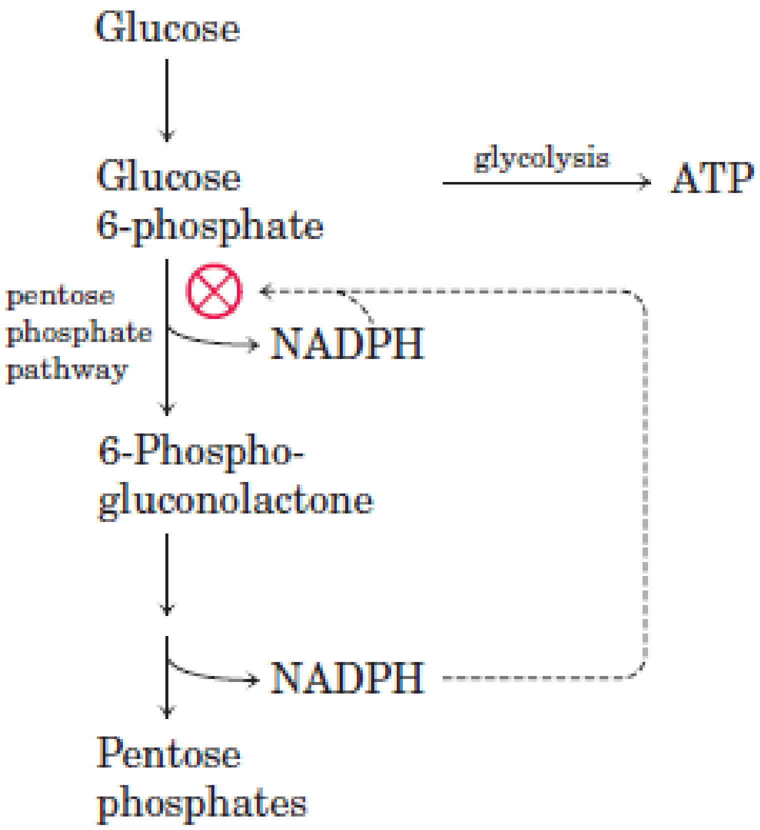
Rapidly dividing cells, such as those of bone marrow, skin, and intestinal mucosa, and those of tumors, use the pentose ribose 5-phosphate to make RNA, DNA, and such coenzymes as ATP, NADH, FADH2, and coenzyme A.

electron donor NADPH, needed for reductive biosynthesis or to counter the damaging effects of oxygen radicals

Tissues that carry out extensive fatty acid synthesis (liver, adipose, lactating mammary gland) or very active synthesis of cholesterol and steroid hormones (liver, adrenal glands, gonads) require the NADPH provided by this pathway.

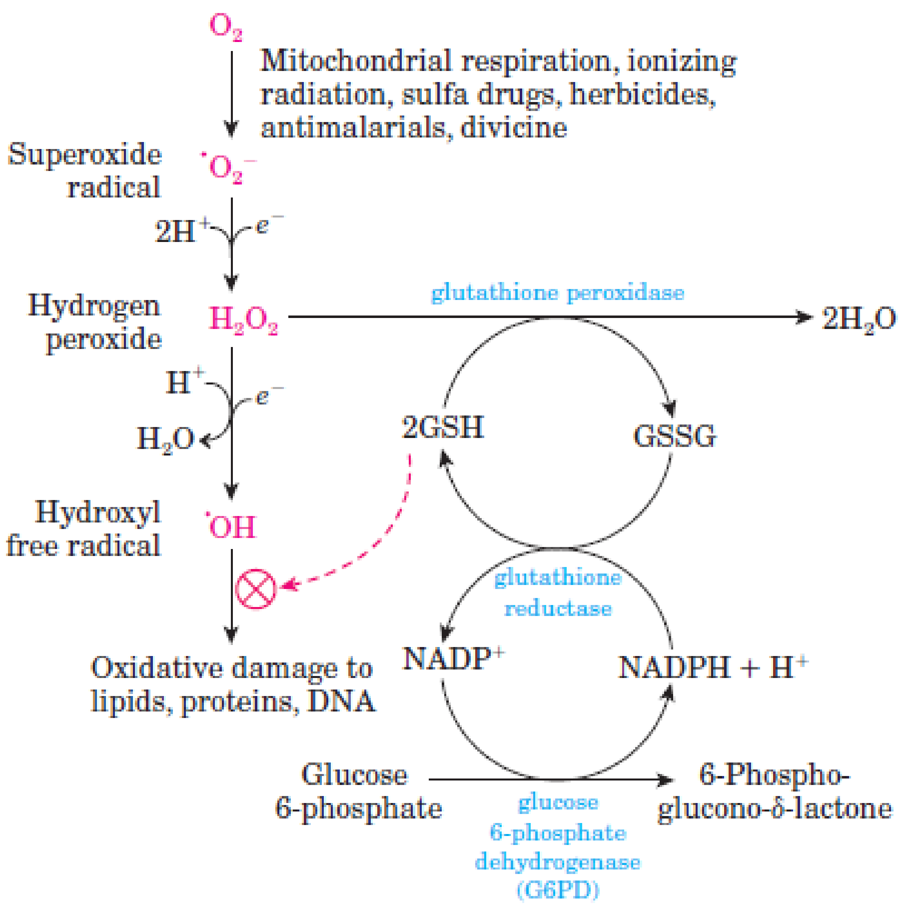
Also known as phosphogluconate pathway, or hexose monophosphate pathway

Glucose 6-Phosphate Is Partitioned between Glycolysis and the Pentose Phosphate Pathway



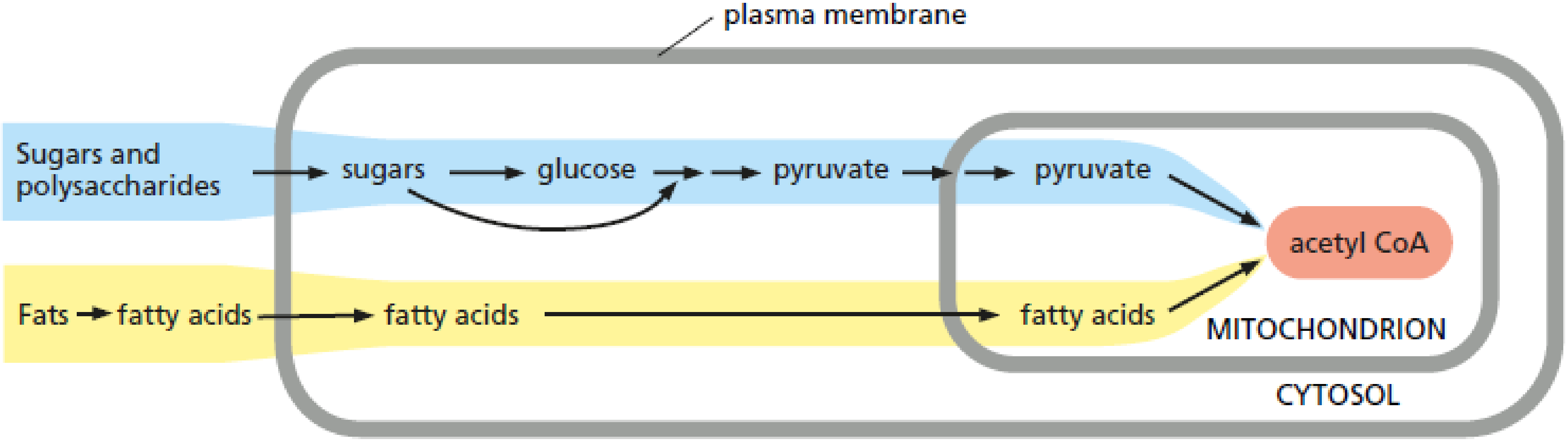
Whether glucose 6-phosphate enters glycolysis or the pentose phosphate pathway depends on the current needs of the cell and on the concentration of $NADP^+$ in the cytosol.

Role of NADPH and glutathione in protecting cells against highly reactive oxygen derivatives

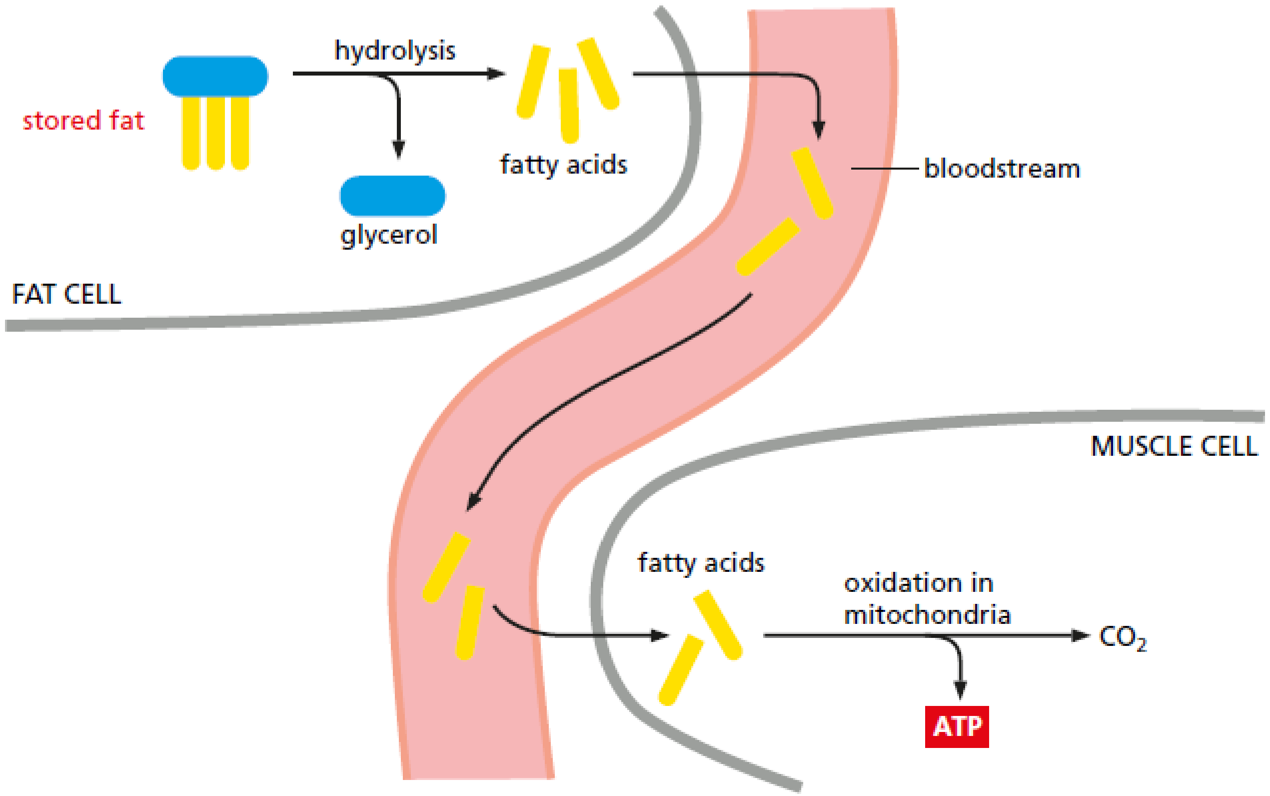


H_2O_2 is also broken down to H_2O and O_2 by catalase, which also requires NADPH

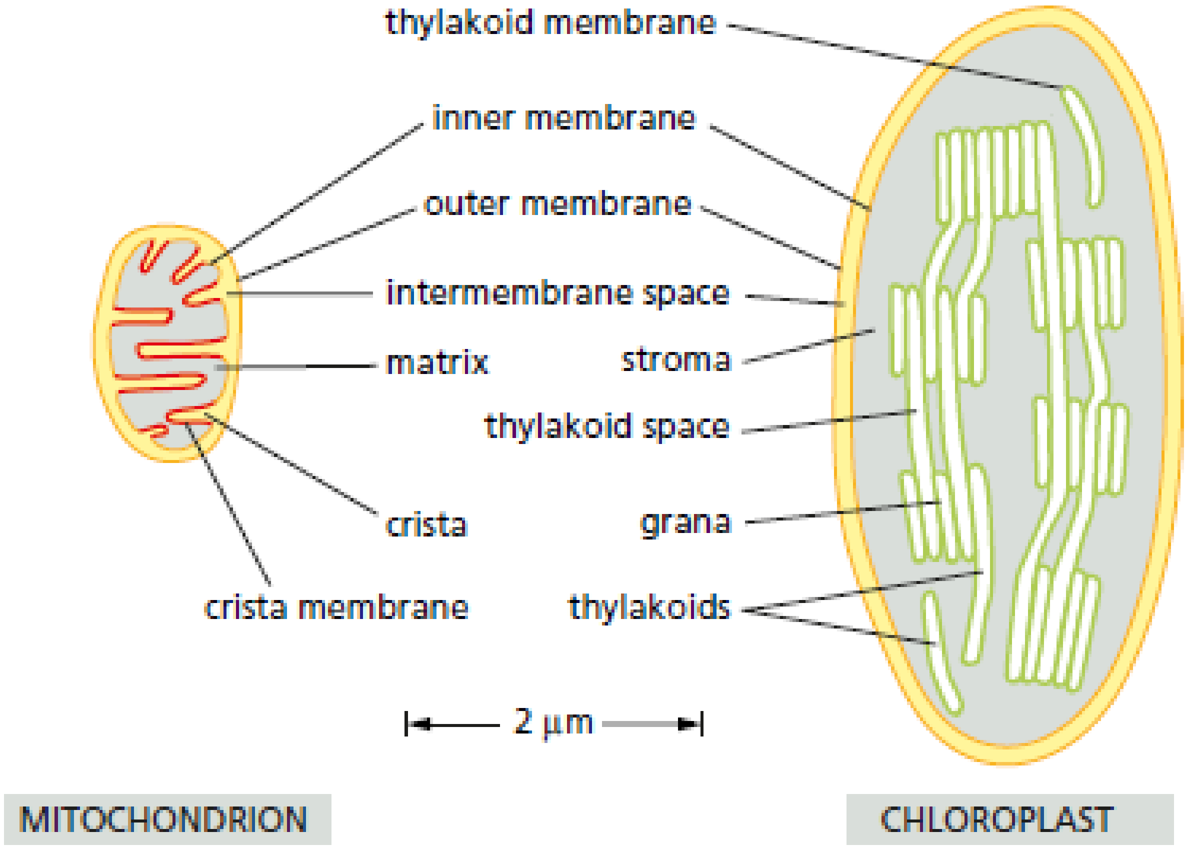
Sugars and Fats Are Both Degraded to Acetyl CoA in Mitochondria



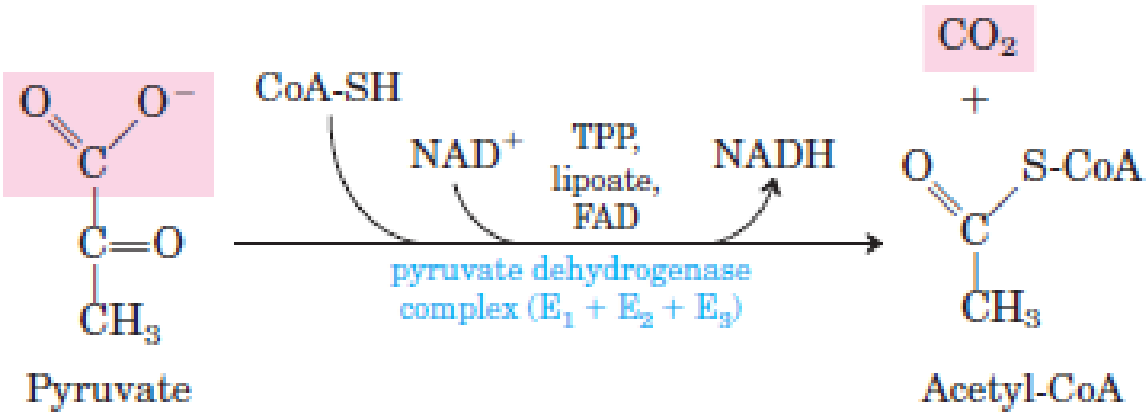
How stored fats are mobilized for energy production in animals



MITOCHONDRIA AND CHLOROPLASTS



Pyruvate is Oxidized to Acetyl-CoA and CO_2



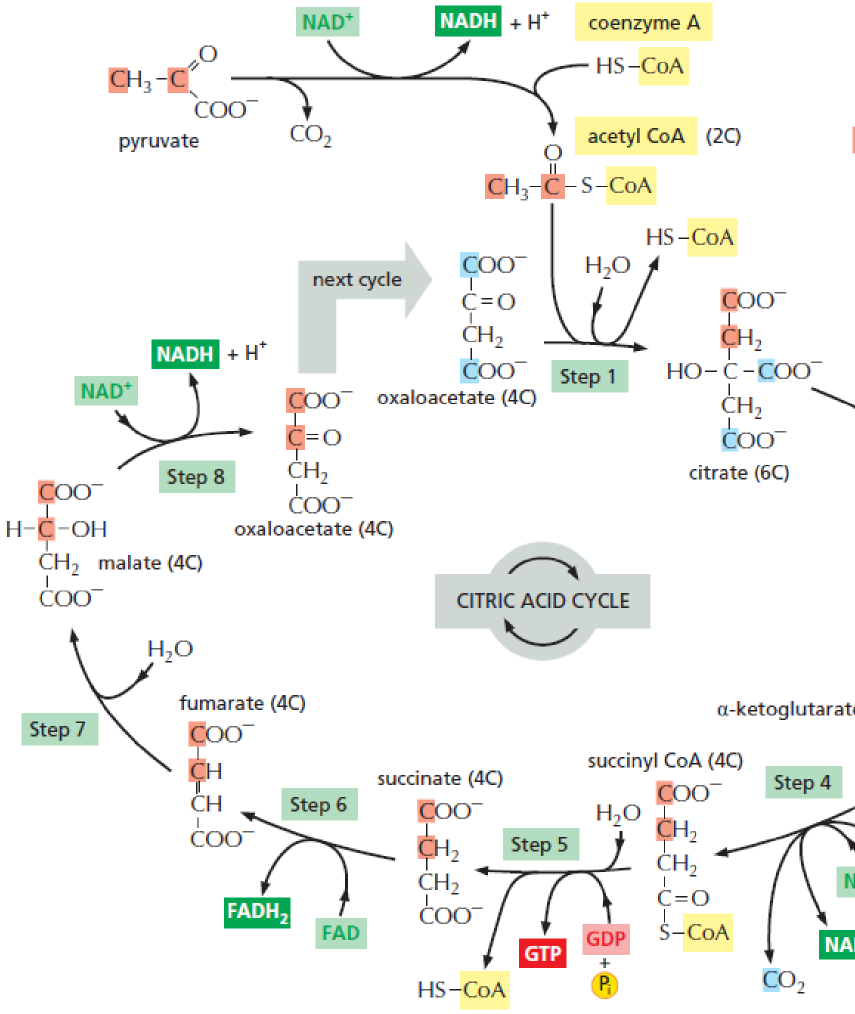
The PDH complex contains three enzymes—**pyruvate dehydrogenase** (E1), **dihydrolipoyl transacetylase** (E2), and **dihydrolipoyl dehydrogenase** (E3)—each present in multiple copies.

Thiamine pyrophosphate (TPP), flavin adenine dinucleotide (FAD), coenzyme A (CoA, sometimes denoted CoA-SH, to emphasize the role of the —SH group), nicotinamide adenine dinucleotide (NAD), and lipoate.

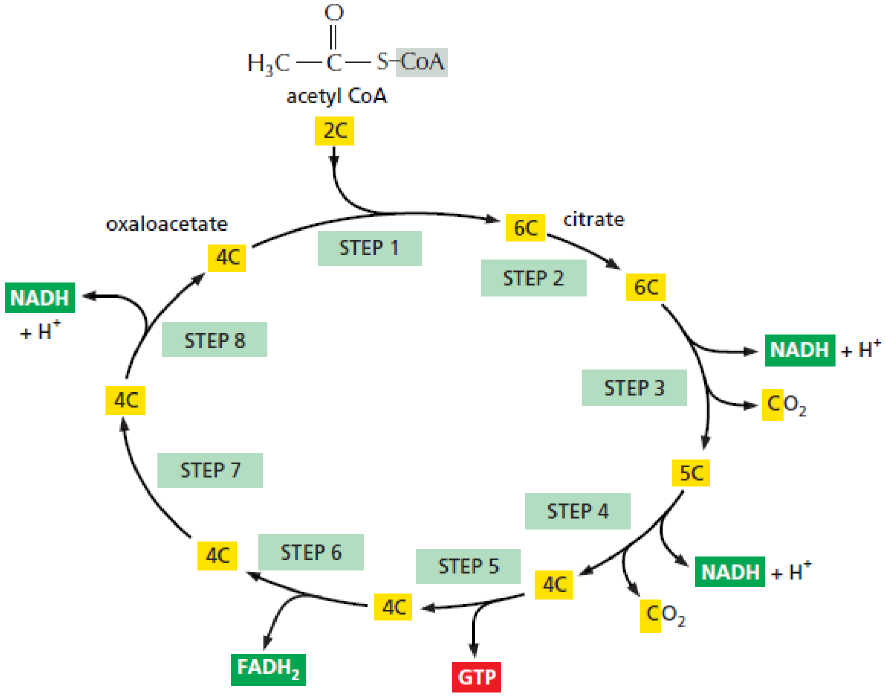
Four different vitamins required in human nutrition
are vital components of this system:

Thiamine (in TPP),
riboflavin (in FAD),
niacin (in NAD), and
pantothenate
(in CoA).

citric acid cycle

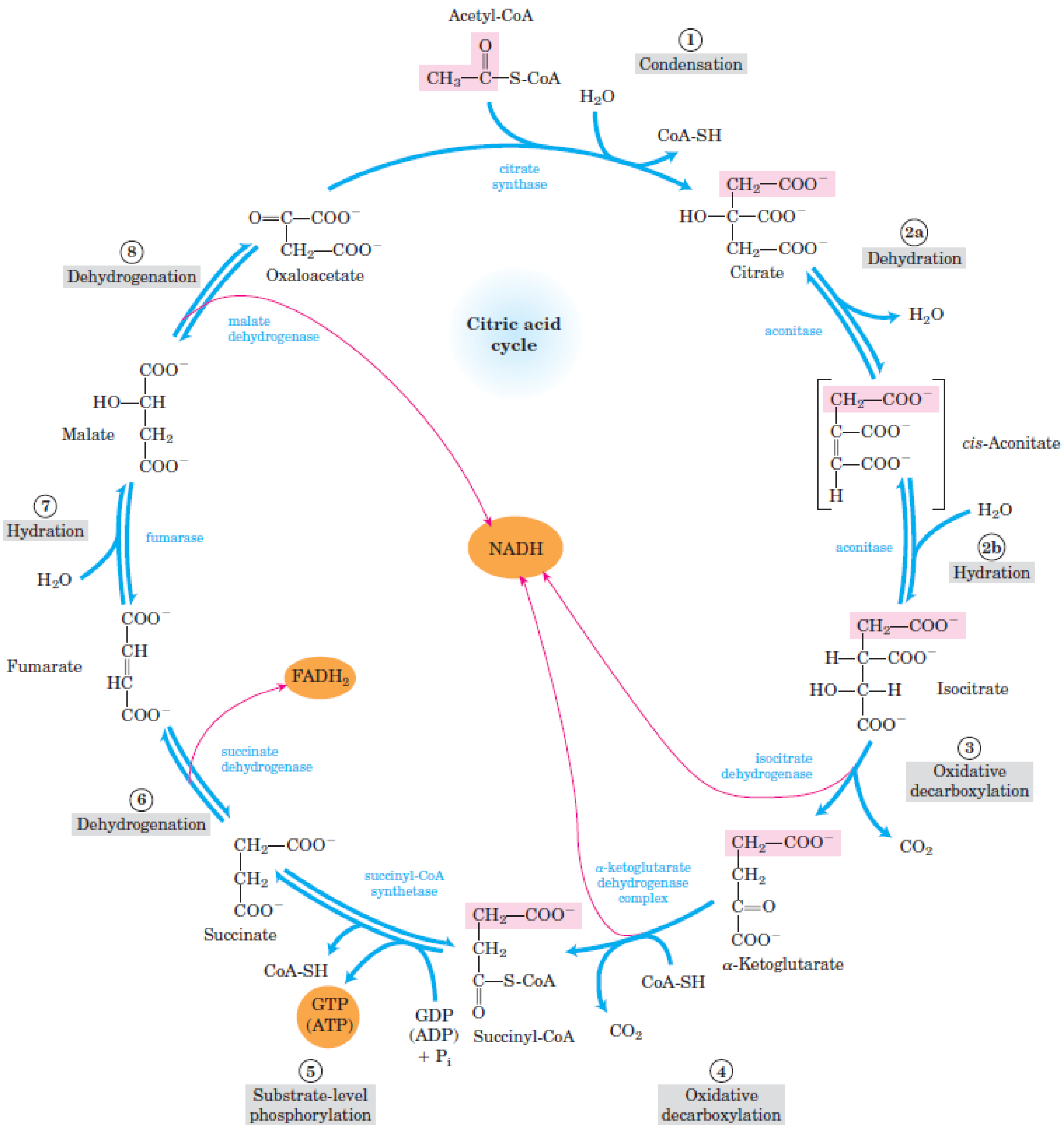


Overview of the complete citric acid cycle. The two carbons from acetyl CoA that enter this turn of the cycle (shadowed in red) will be converted to CO_2 in subsequent turns of the cycle: it is the two carbons shadowed in blue that are converted to CO_2 in this cycle.



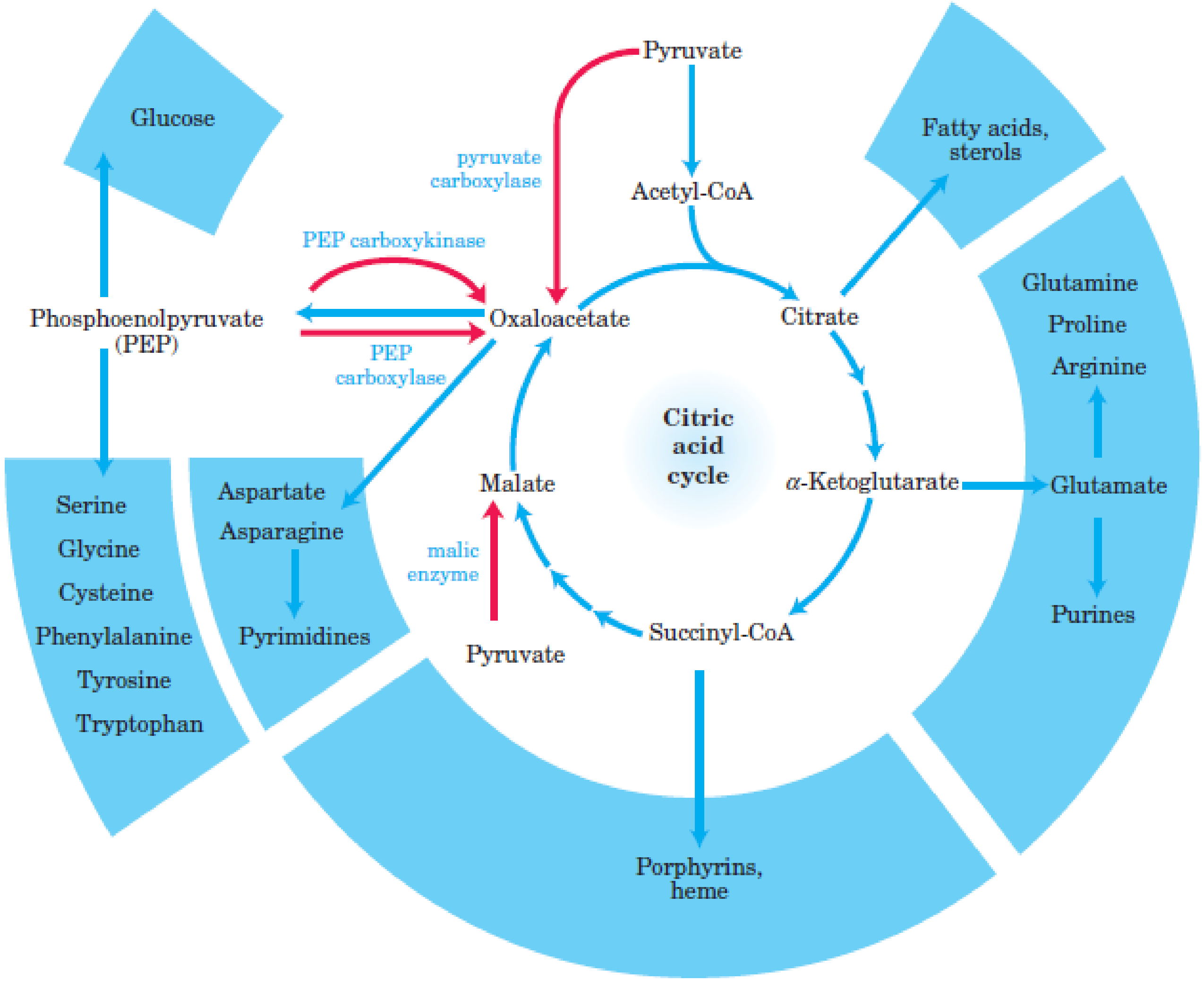
Hans Krebs, 1900–1981

NET RESULT: ONE TURN OF THE CYCLE PRODUCES THREE NADH, ONE GTP, AND ONE $FADH_2$ MOLECULE, AND RELEASES TWO MOLECULES OF CO_2



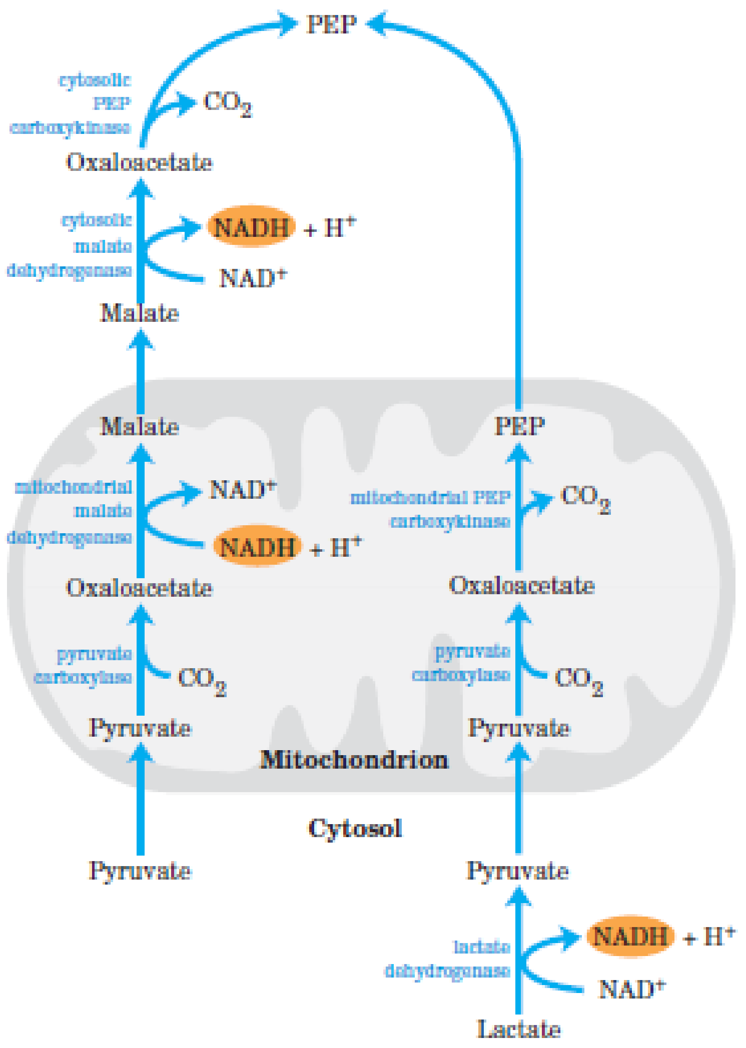
Acetyl-CoA
1 Condensation
H_2O
CoA-SH
citrate synthase
Citrate
2a Dehydration
H_2O
aconitase
cis-Aconitate
H_2O
aconitase
2b Hydration
Isocitrate
3 Oxidative decarboxylation
isocitrate dehydrogenase
CO_2
α-Ketoglutarate
α-ketoglutarate dehydrogenase complex
CoA-SH
CO_2
4 Oxidative decarboxylation
Succinyl-CoA
succinyl-CoA synthetase
GDP (ADP) + P_i
GTP (ATP)
CoA-SH
5 Substrate-level phosphorylation
Succinate
6 Dehydrogenation
succinate dehydrogenase
$FADH_2$
Fumarate
H_2O
7 Hydration
fumarase
Malate
malate dehydrogenase
8 Dehydrogenation
Oxaloacetate
NADH
Citric acid cycle

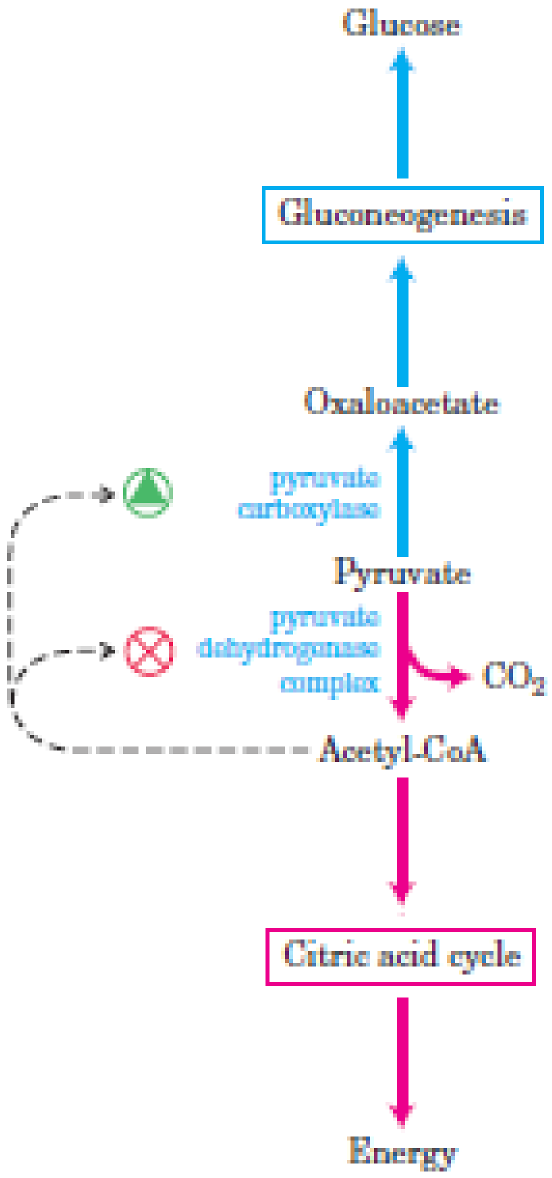
Role of the citric acid cycle in anabolism



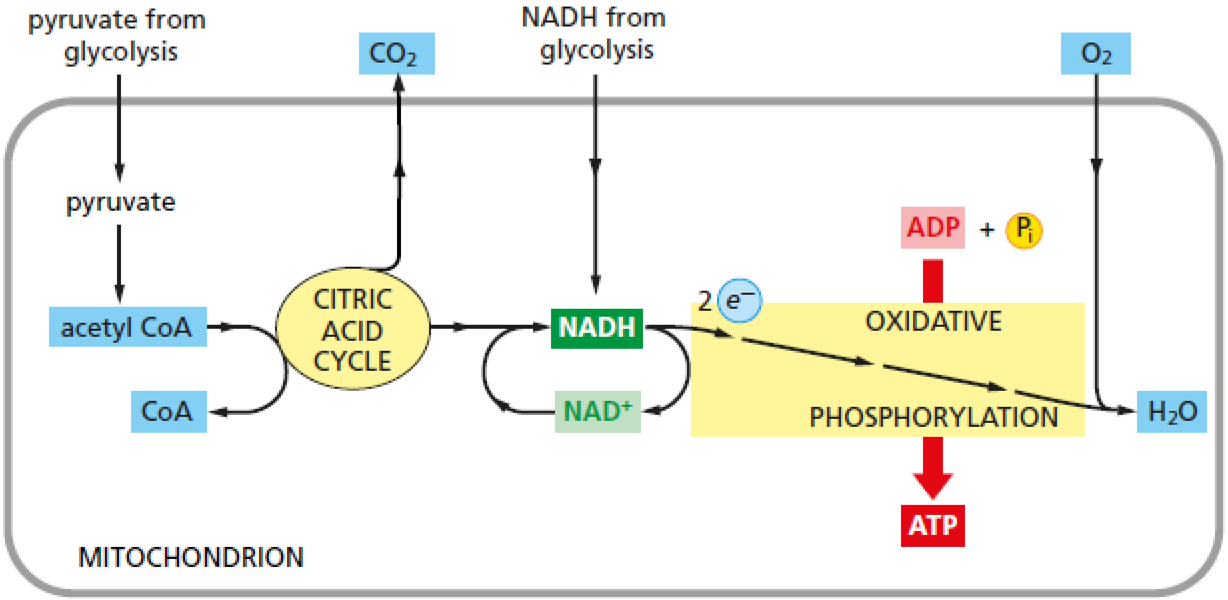
Anaplerotic Reactions Replenish Citric Acid

Alternative paths from pyruvate to phosphoenolpyruvate




Glucose
Gluconeogenesis
Oxaloacetate
pyruvate
carboxylase
Pyruvate
pyruvate
dehydrogenase
complex
CO_2
Acetyl-CoA
Citric acid cycle
Energy

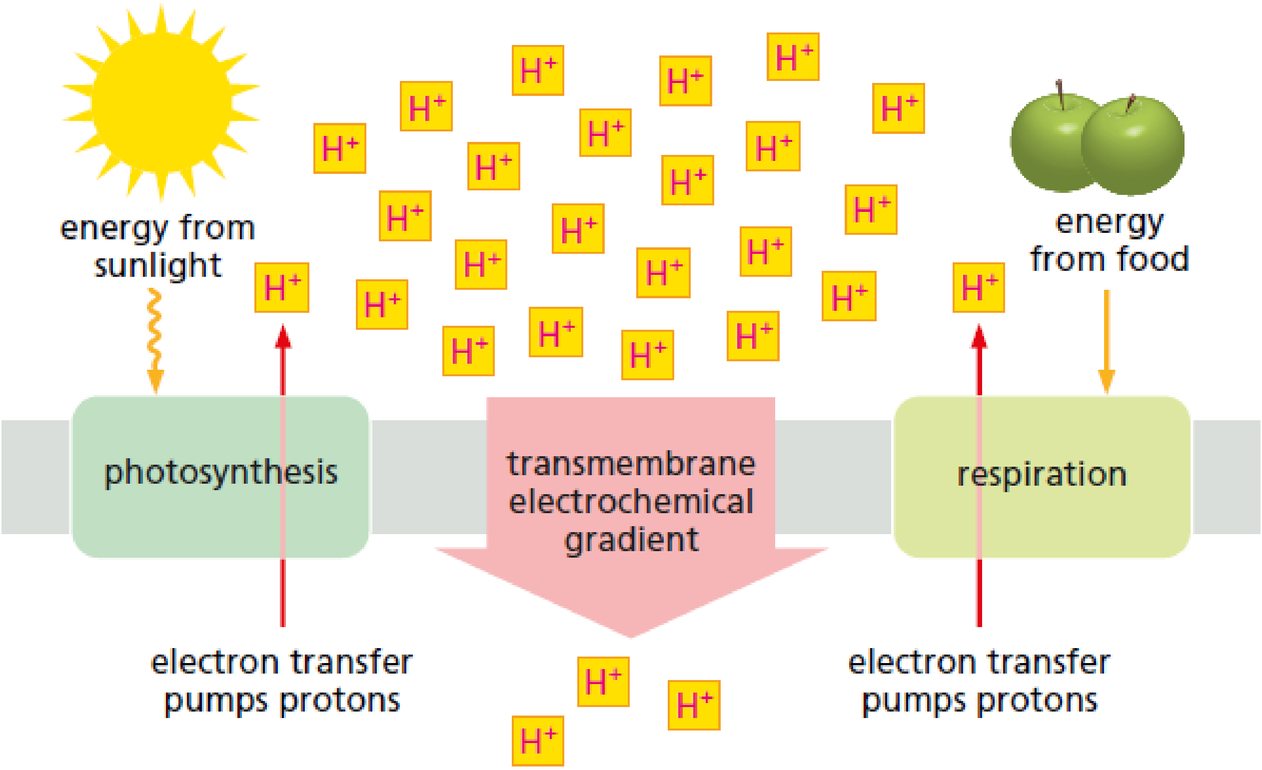
The final stages of oxidation of food molecules



Electron Transport Drives the Synthesis of the Majority of the ATP in Most Cells

High-energy electrons from NADH are passed to a membrane-bound electron-transport chain

Membrane-based mechanisms use the energy provided by food or sunlight to generate ATP

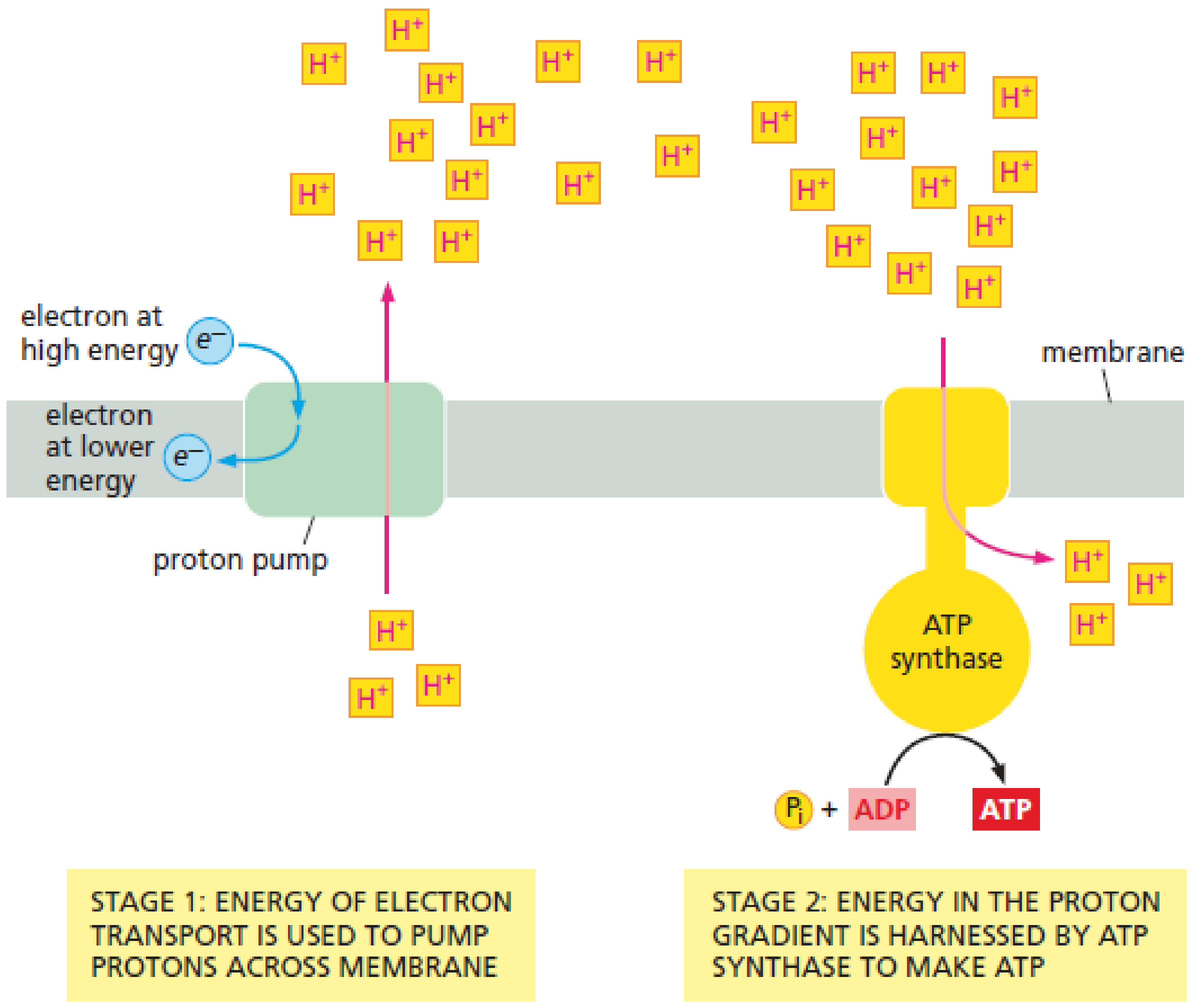


Electron transfers release energy that is used to pump protons

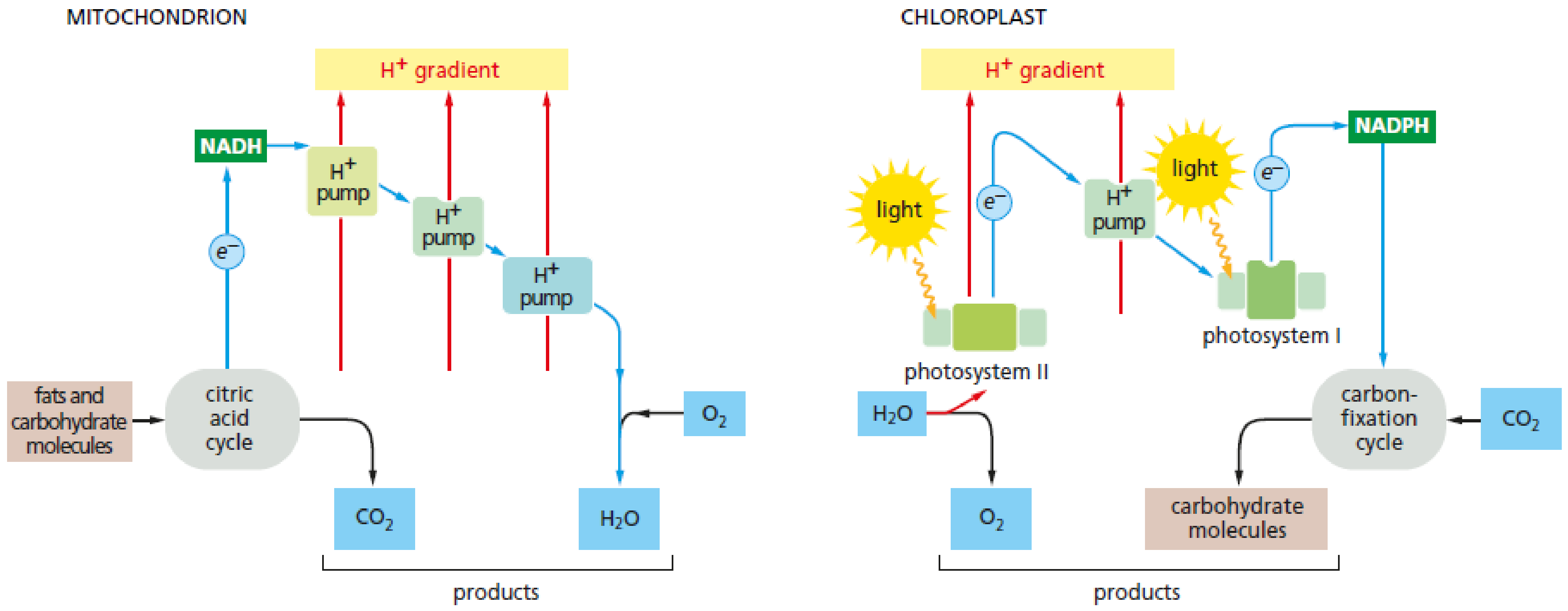
Generate an electrochemical proton gradient

An ion gradient across a membrane is a form of stored energy that can be harnessed to do useful work

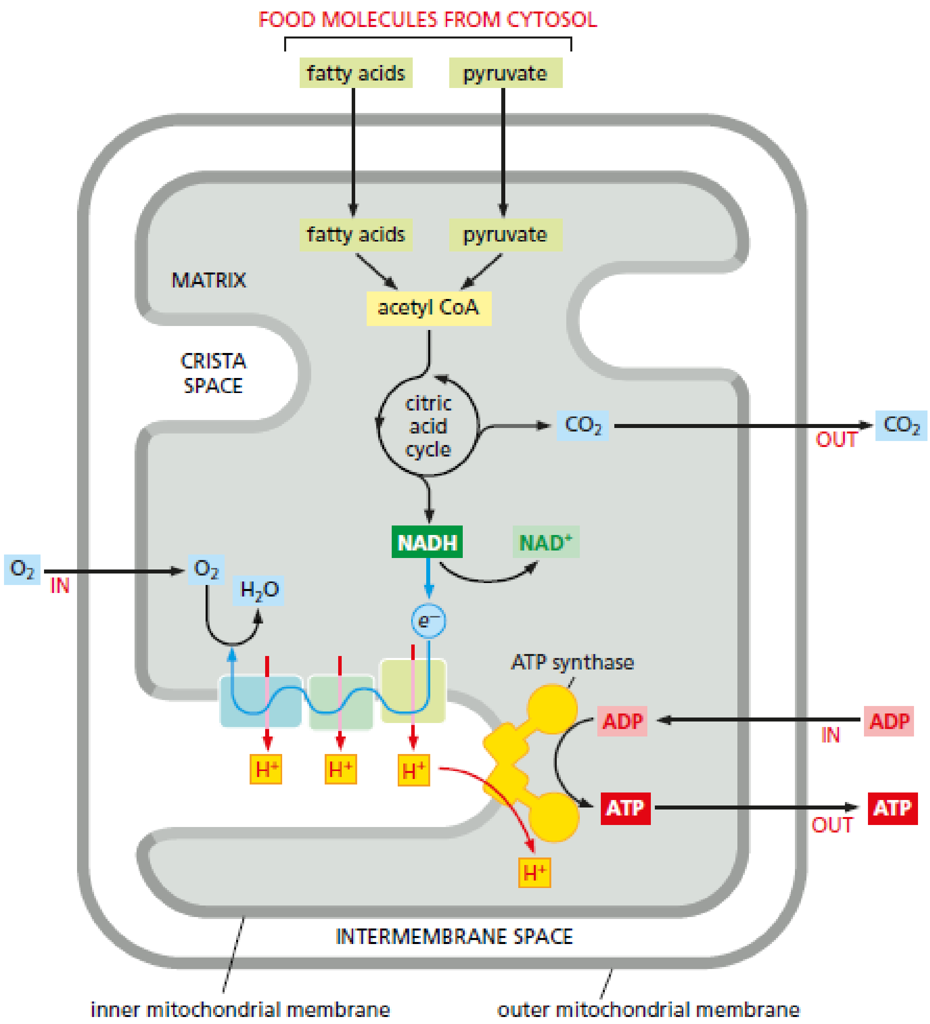
Membrane-based systems use the energy stored in an electrochemical proton gradient to synthesize ATP



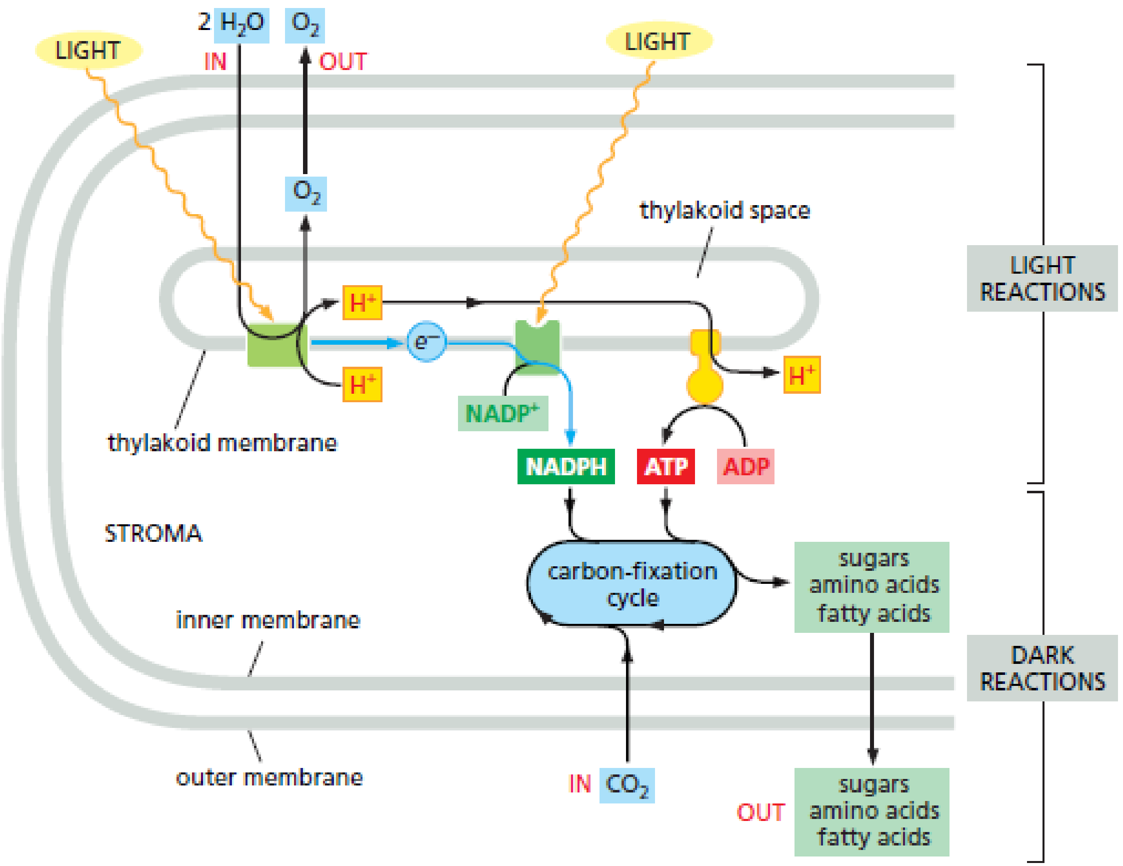
Electron-transport processes



The final stages of oxidation of food molecules

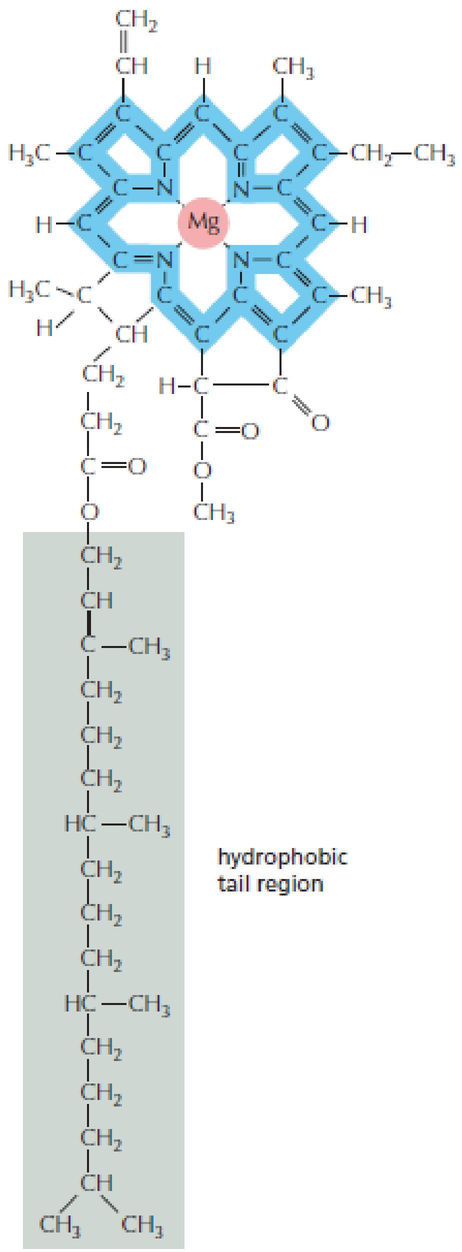


Both stages of photosynthesis depend on the chloroplast.

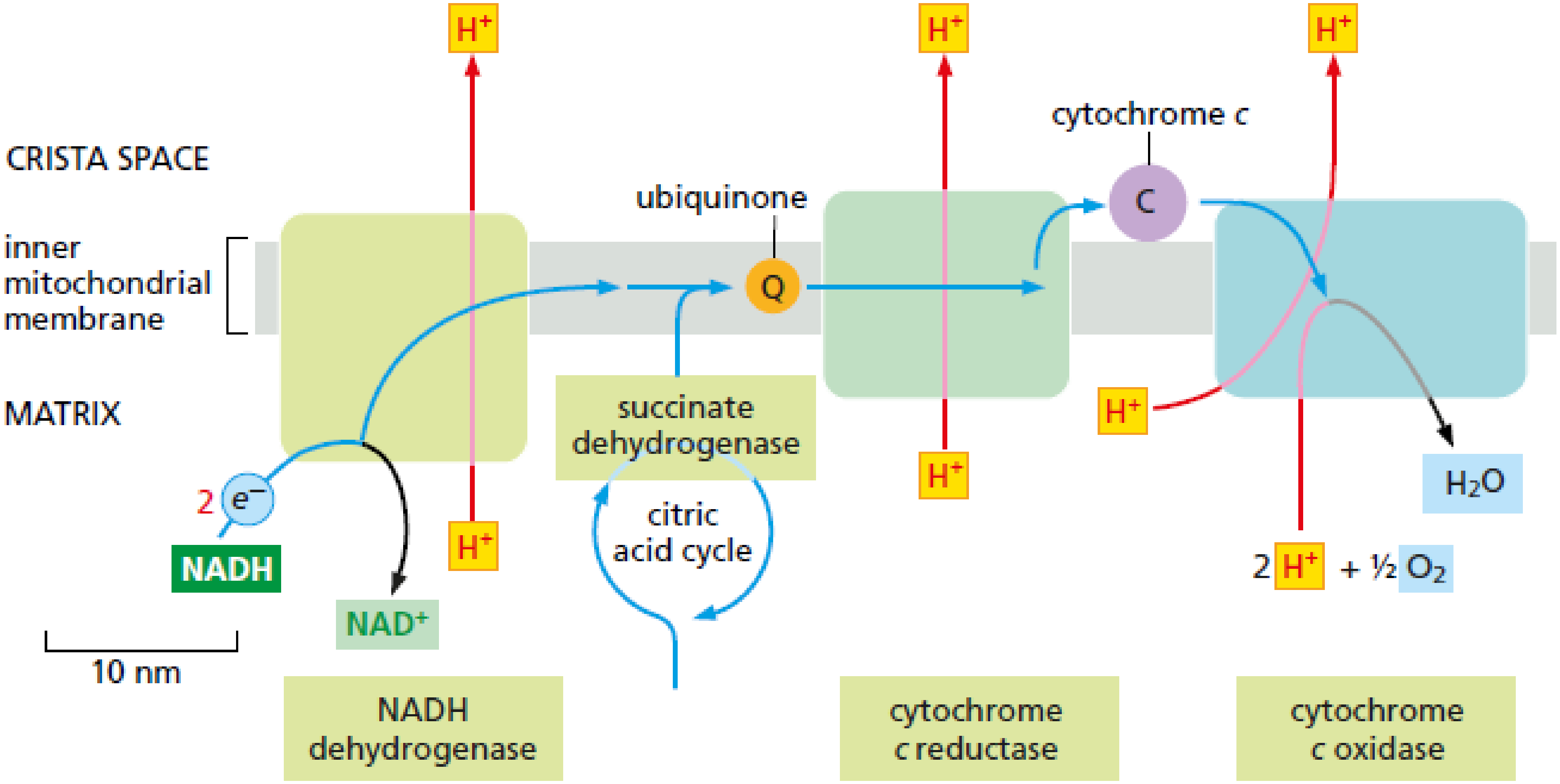


1. Chlorophyll's structure allows it to absorb energy from light. Each chlorophyll molecule contains a porphyrin ring with a magnesium atom (*pink*) at its center. This porphyrin ring is structurally similar to the one that binds iron in heme. Light is absorbed by electrons within the bond network shown in *blue*, while the long, hydrophobic tail (*gray*) helps hold the chlorophyll in the thylakoid membrane.

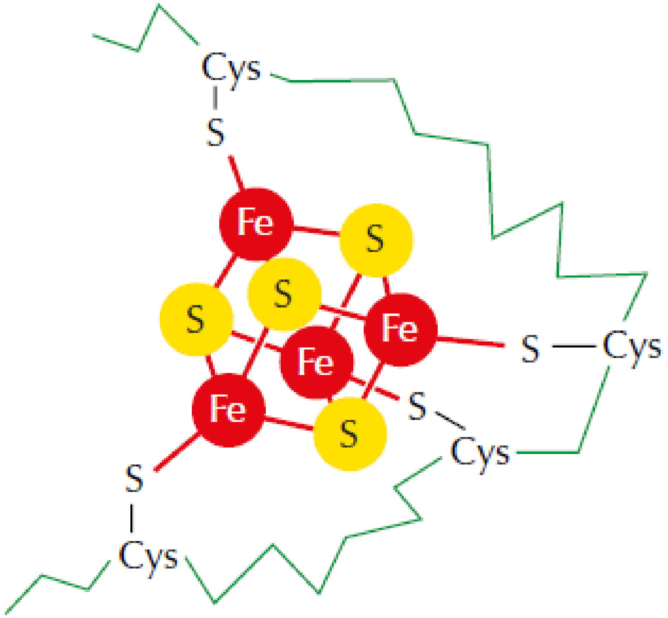
2. A photon (a quantum of light) knocks an electron out of the green pigment molecule *chlorophyll* in the first reaction center, creating a positively charged chlorophyll ion. This electron then moves along an electron-transport chain and through a second reaction center in much the same way that an electron moves along the respiratory chain in mitochondria.



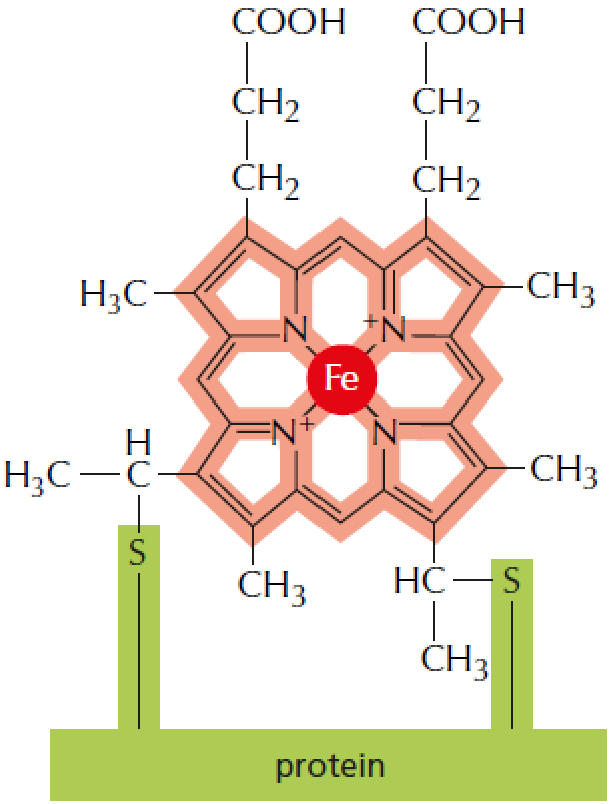
High-energy electrons are transferred through three respiratory enzyme complexes in the inner mitochondrial membrane



Transition Metal Ions and Quinones Accept and Release Electrons Readily

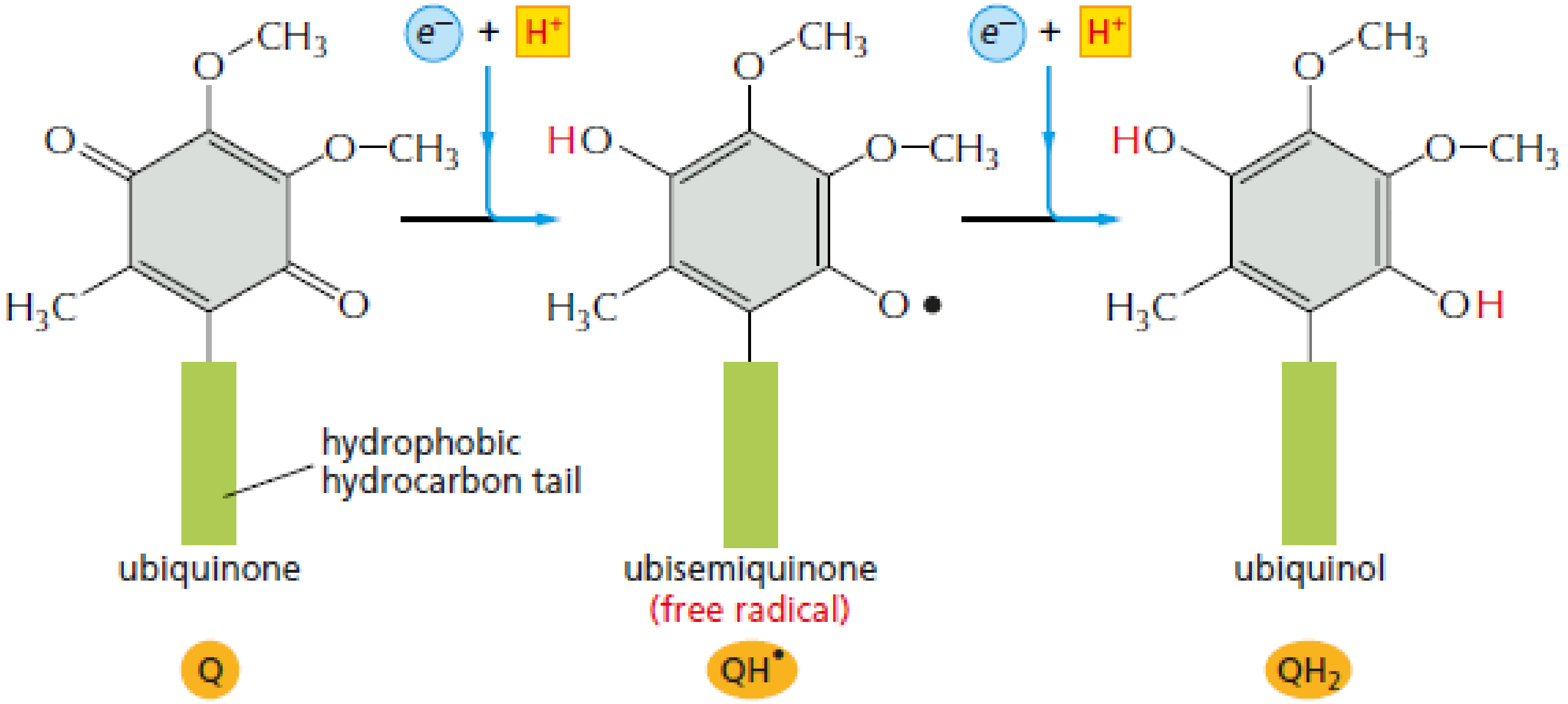


The structure of an iron–sulfur cluster

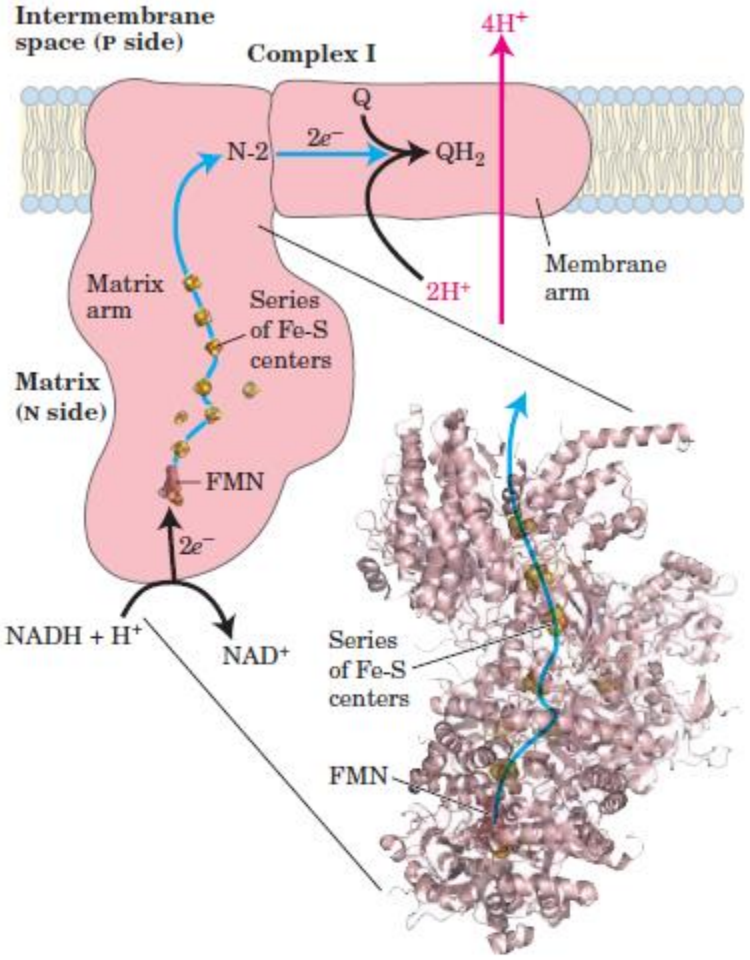


Heme group, in which an iron atom is tightly held by four nitrogen atoms at the corners of a square in a *porphyrin ring*

Quinone electron carriers



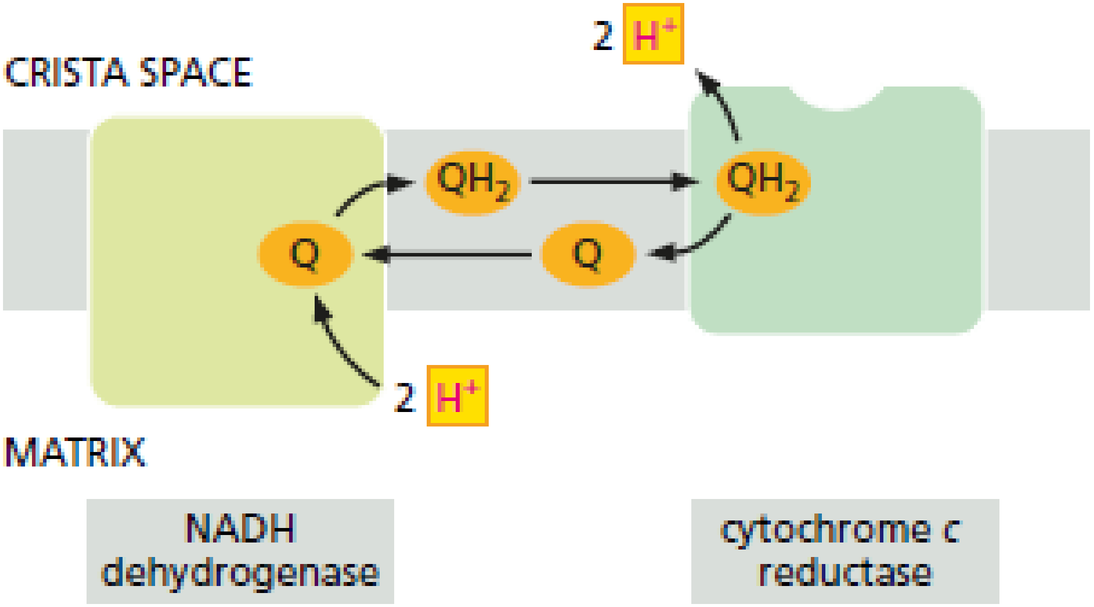
Electron-transport in NADH dehydrogenase (complex 1)



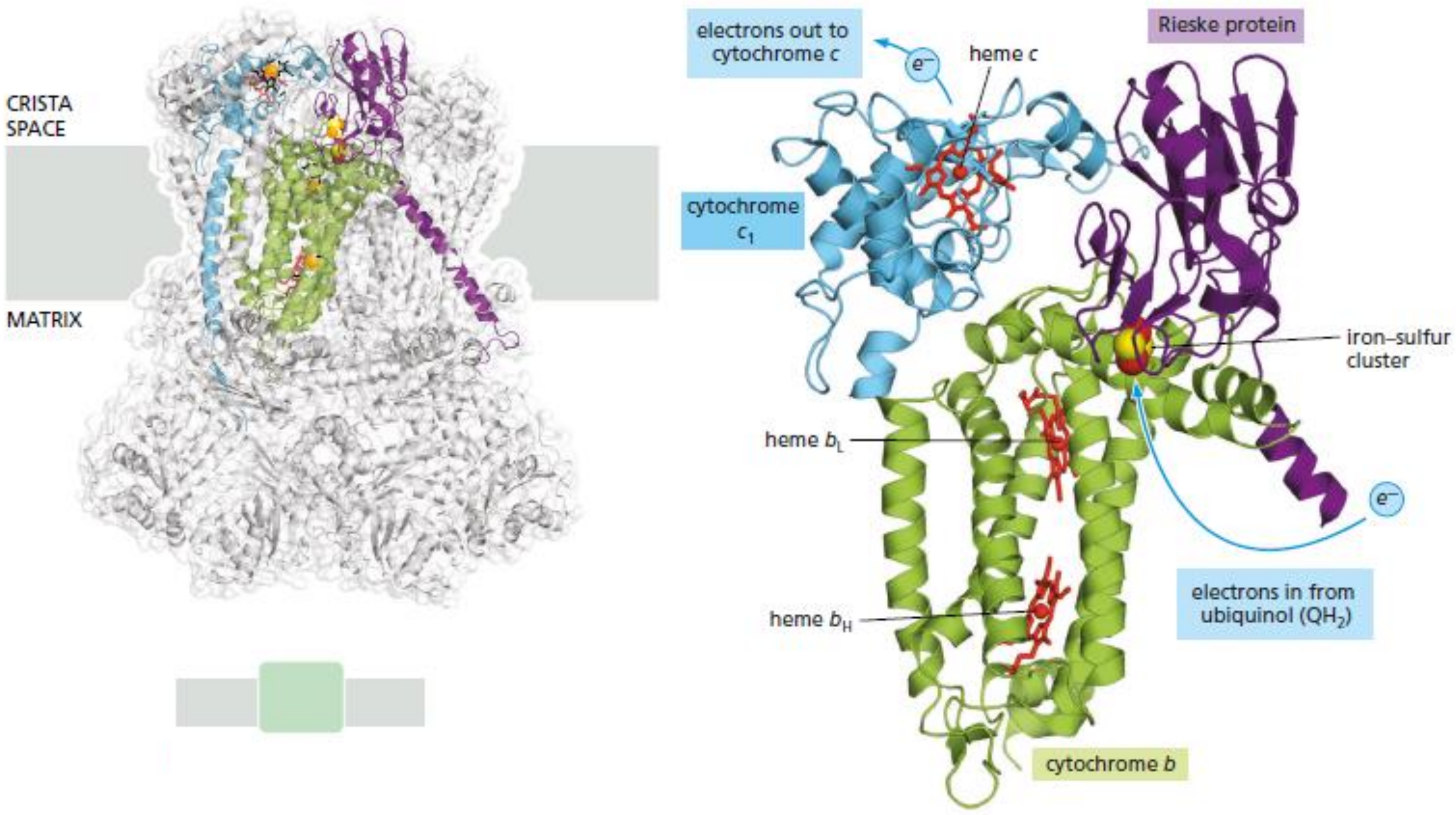
$$NADH + 5H^+_N + Q \longrightarrow NAD^+ + QH_2 + 4H^+_P$$

NADH donates two electrons, via a bound flavin mononucleotide (FMN)

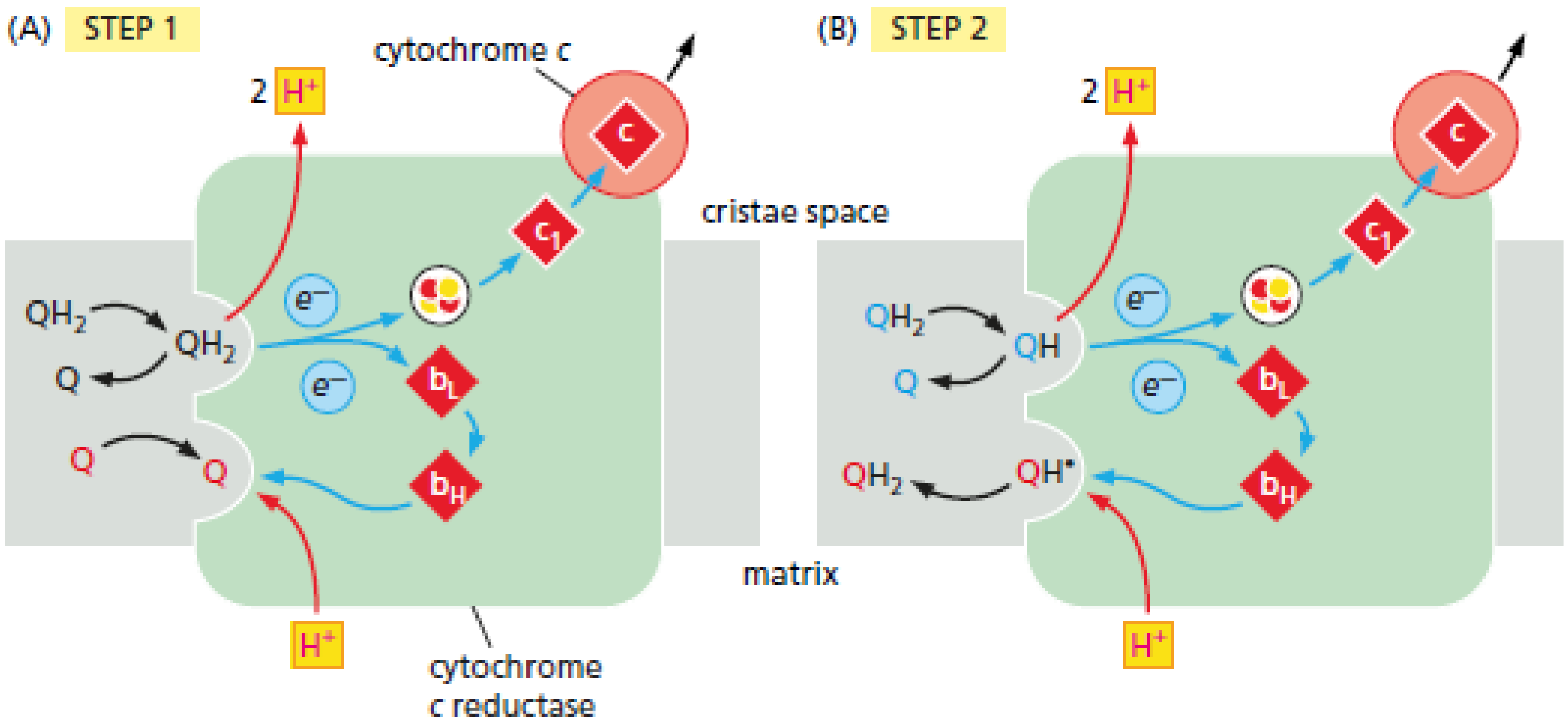
How a directional release and uptake of protons by a quinone pumps protons across a membrane



The structure of cytochrome c reductase



The two-step mechanism of the cytochrome c reductase Q-cycle

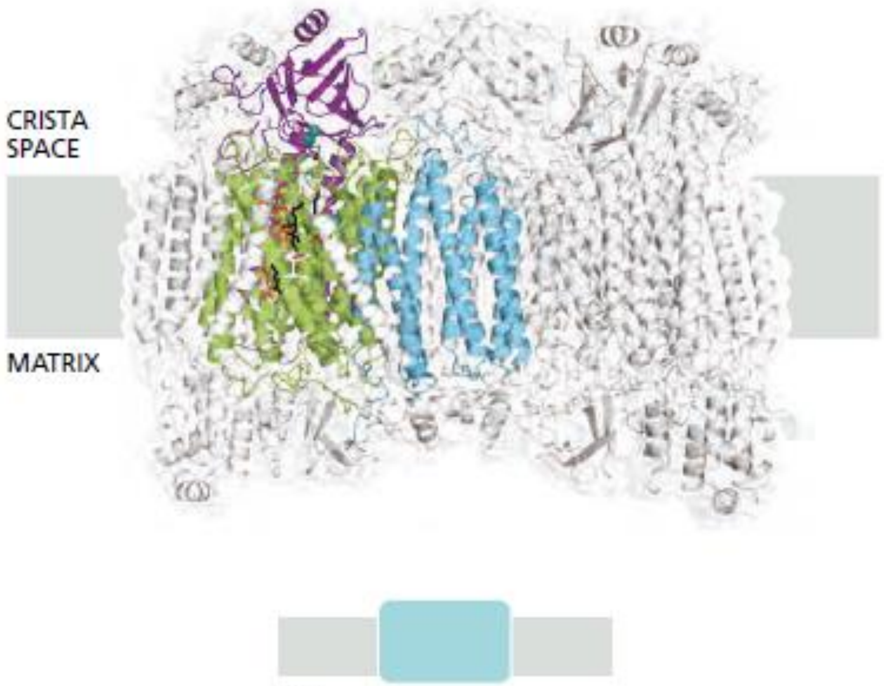


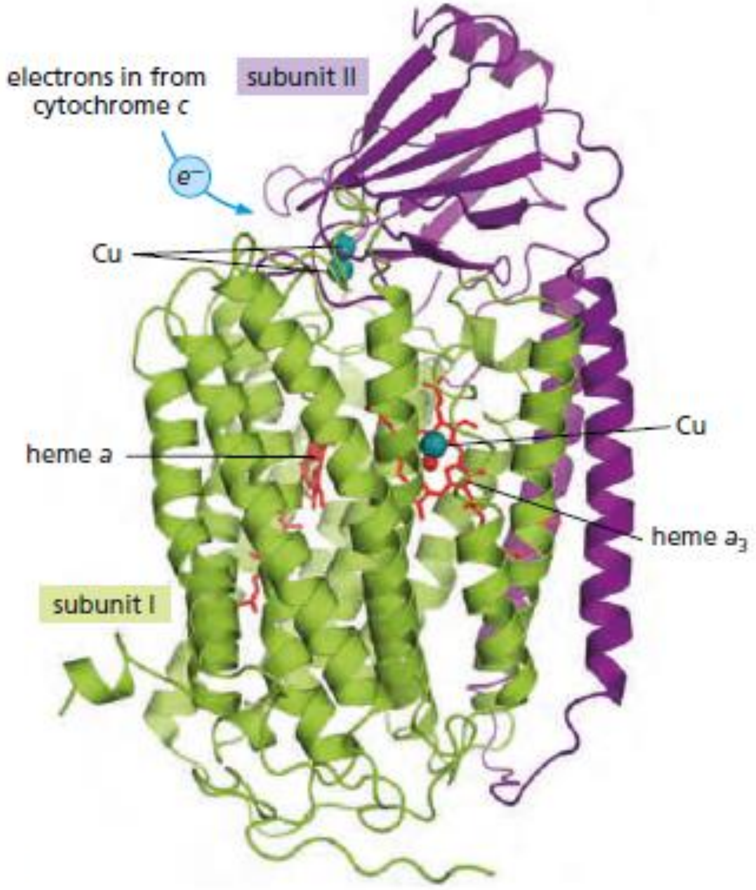
$$QH_2 + Q + \text{cyt } c_1 \text{ (oxidized)} \longrightarrow {}^{\bullet}Q^{-} + Q + 2H^+_P + \text{cyt } c_1 \text{ (reduced)}$$

$$QH_2 + {}^{\bullet}Q^{-} + 2H^+_N + \text{cyt } c_1 \text{ (oxidized)} \longrightarrow QH_2 + 2H^+_P + Q + \text{cyt } c_1 \text{ (reduced)}$$

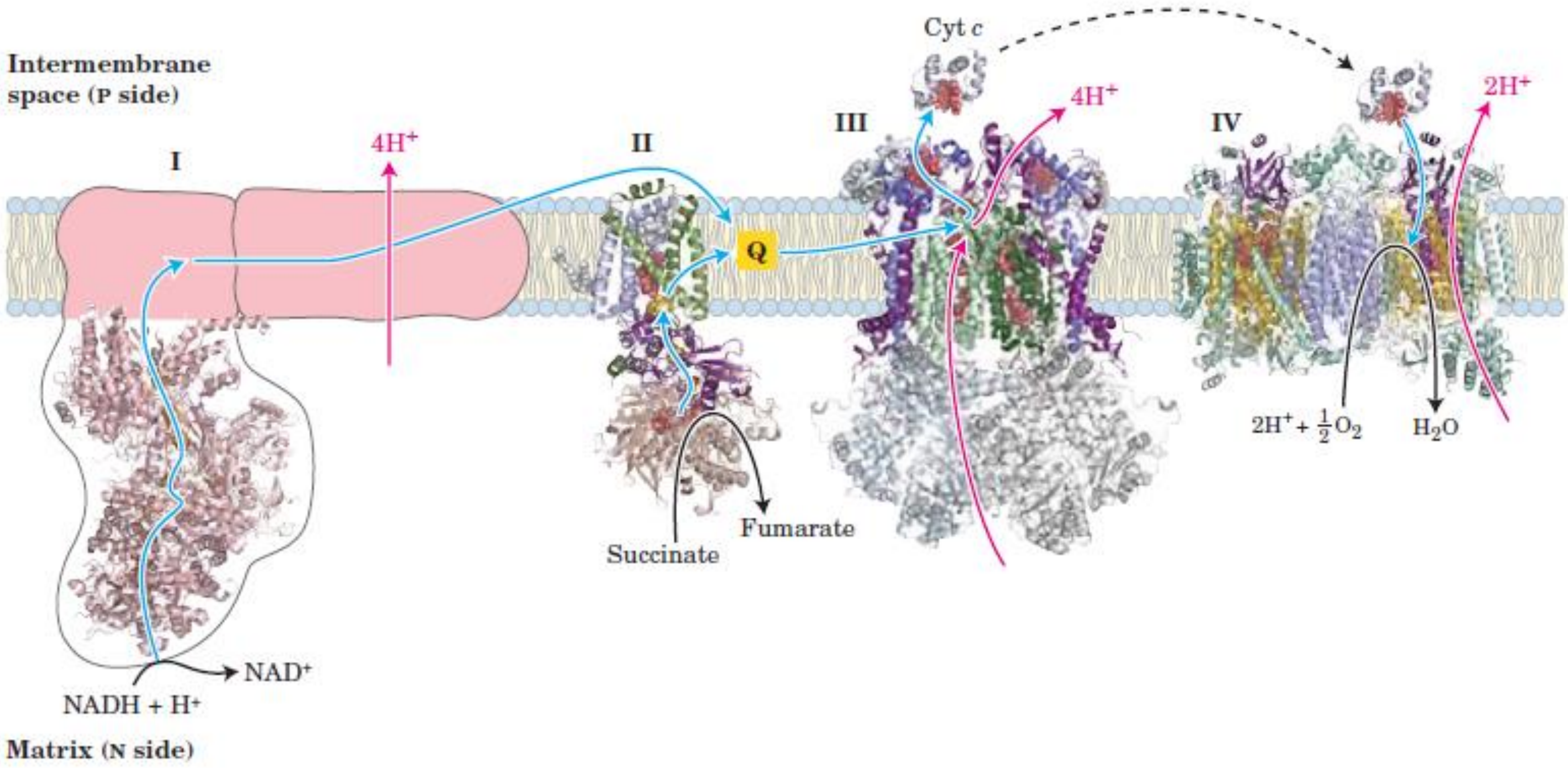
$$\text{Net equation: } QH_2 + 2 \text{ cyt } c_1 \text{ (oxidized)} + 2H^+_N \longrightarrow Q + 2 \text{ cyt } c_1 \text{ (reduced)} + 4H^+_P$$

The structure of cytochrome *c* oxidase



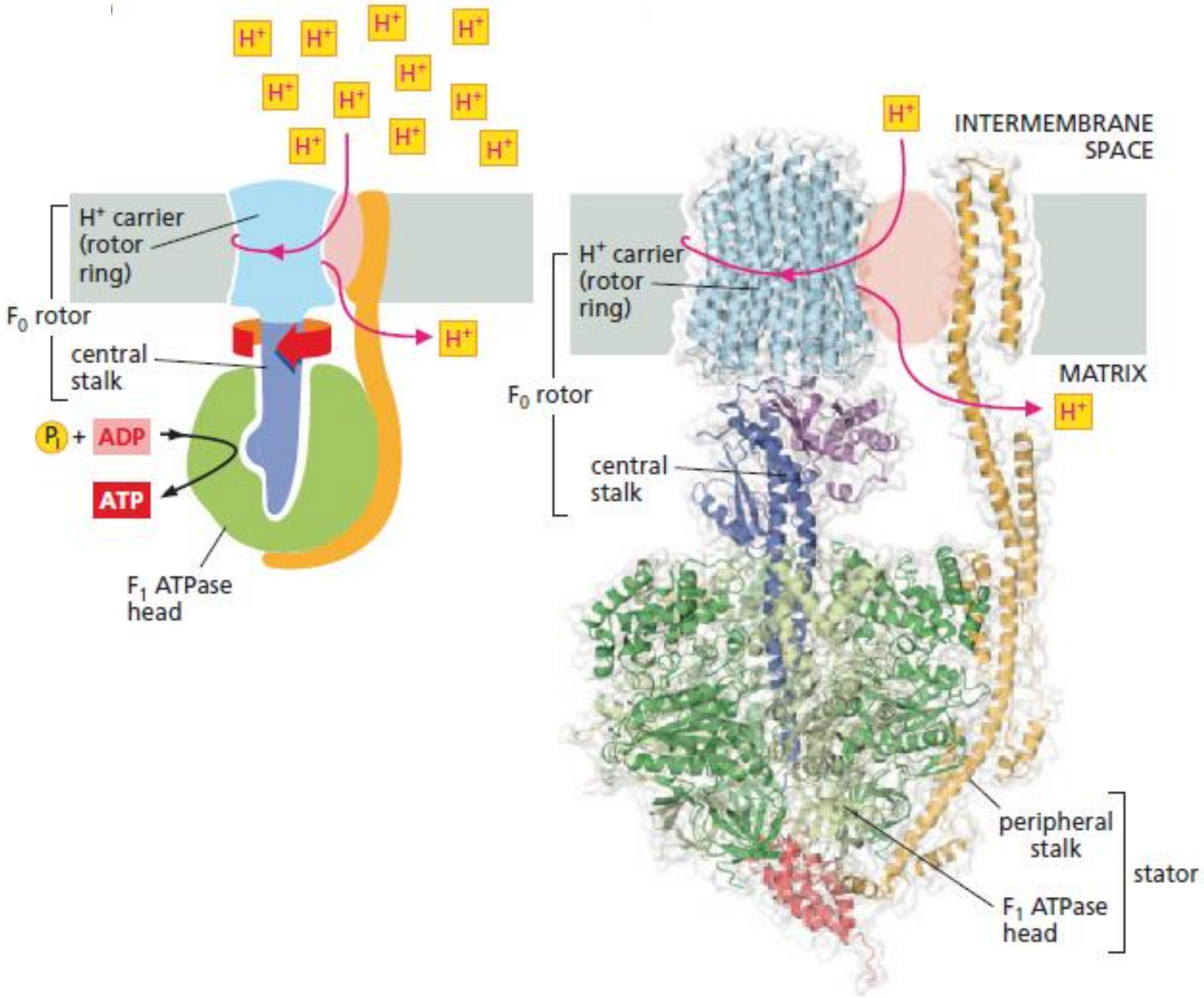


Summary of the flow of electrons and protons through the four complexes of the respiratory chain

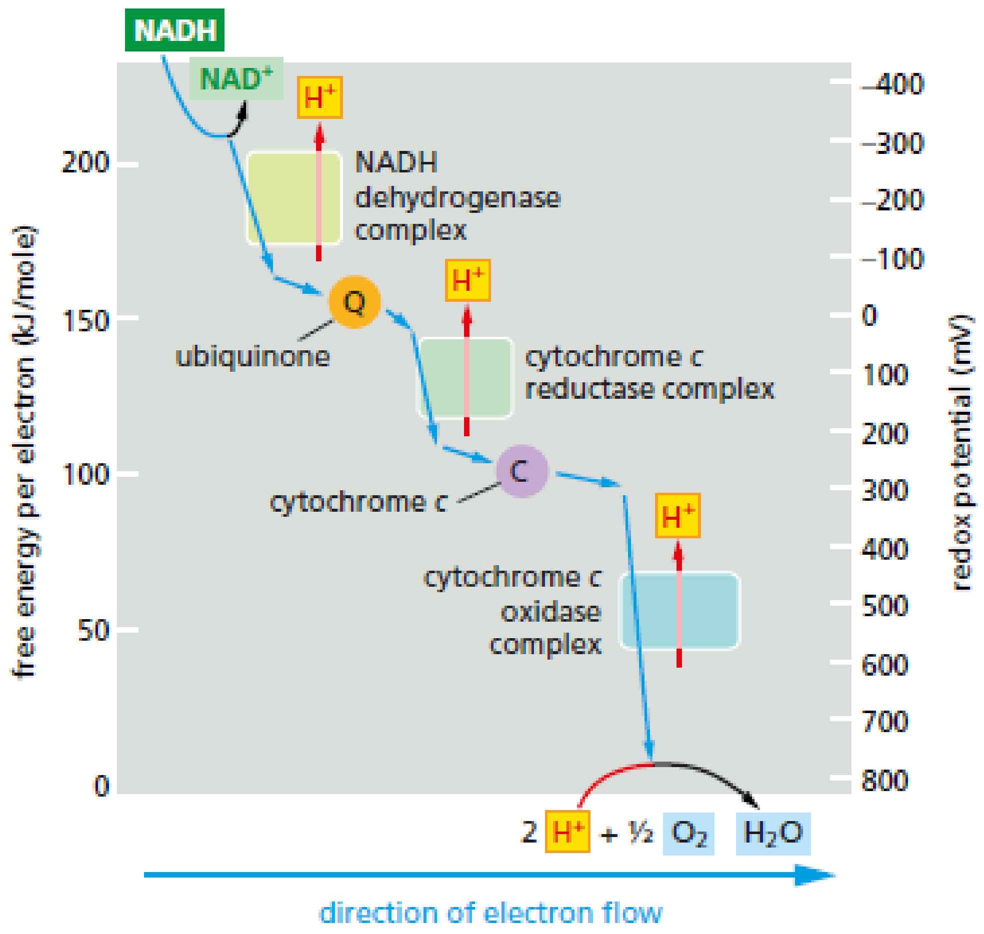


$$NADH + 11H_N^+ + \tfrac{1}{2}O_2 \longrightarrow NAD^+ + 10H_P^+ + H_2O$$

ATP synthase acts like a motor to convert the energy of protons flowing down their electrochemical gradient to chemical-bond energy in ATP



Redox potential changes along the mitochondrial electron transport chain



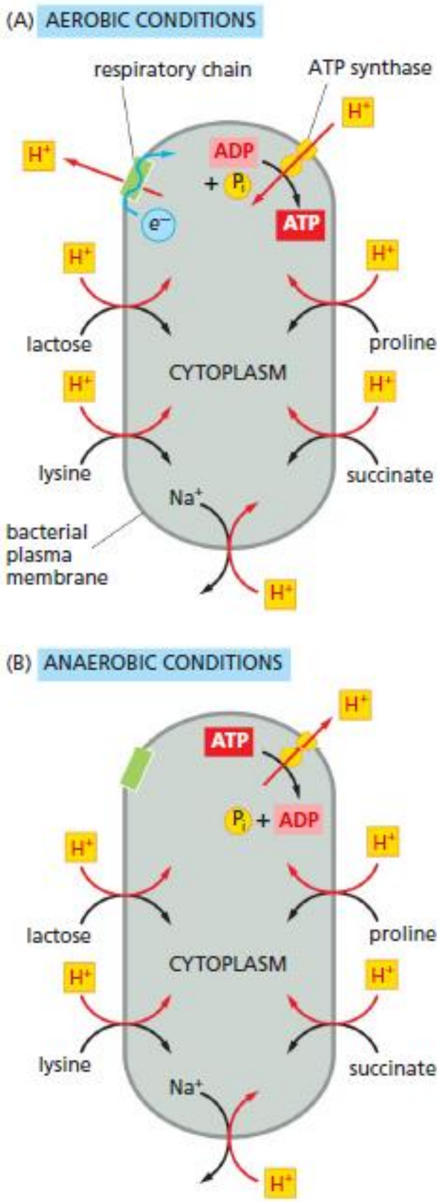
Product Yields from the Oxidation of Sugars and Fats

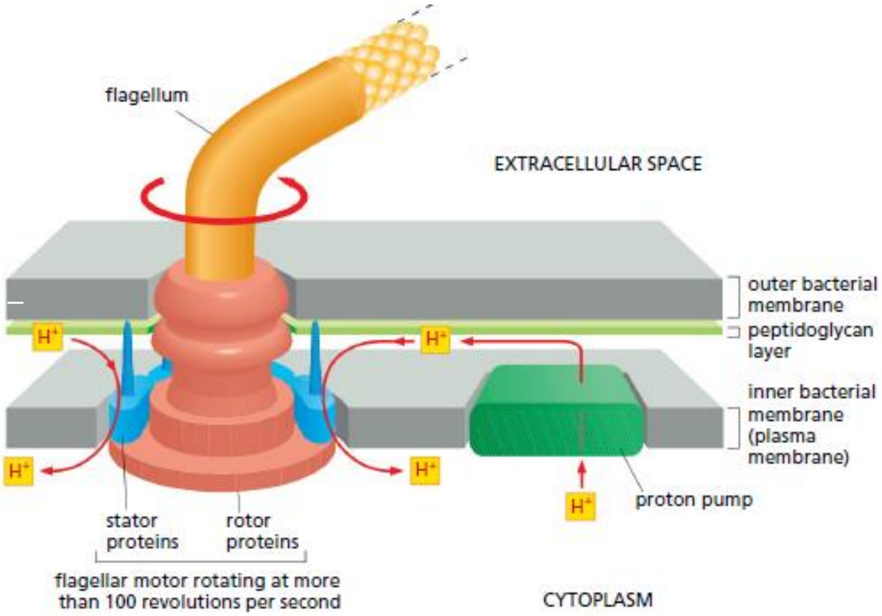
A. Net products from oxidation of one molecule of glucose
In cytosol (glycolysis) 1 glucose → 2 pyruvate + 2 NADH + 2 ATP In mitochondrion (pyruvate dehydrogenase and citric acid cycle) 2 pyruvate → 2 acetyl CoA + 2 NADH 2 acetyl CoA → 6 NADH + 2 $FADH_2$ + 2 GTP
Net result in mitochondrion 2 pyruvate → 8 NADH + 2 $FADH_2$ + 2 GTP
B. Net products from oxidation of one molecule of palmitoyl CoA (activated form of palmitate, a fatty acid)
In mitochondrion (fatty acid oxidation and citric acid cycle) 1 palmitoyl CoA → 8 acetyl CoA + 7 NADH + 7 $FADH_2$ 8 acetyl CoA → 24 NADH + 8 $FADH_2$ + 8 GTP
Net result in mitochondrion 1 palmitoyl CoA → 31 NADH + 15 $FADH_2$ + 8 GTP

NADH produced in mitochondria can provide energy for the formation of about 2.5 molecules of ATP

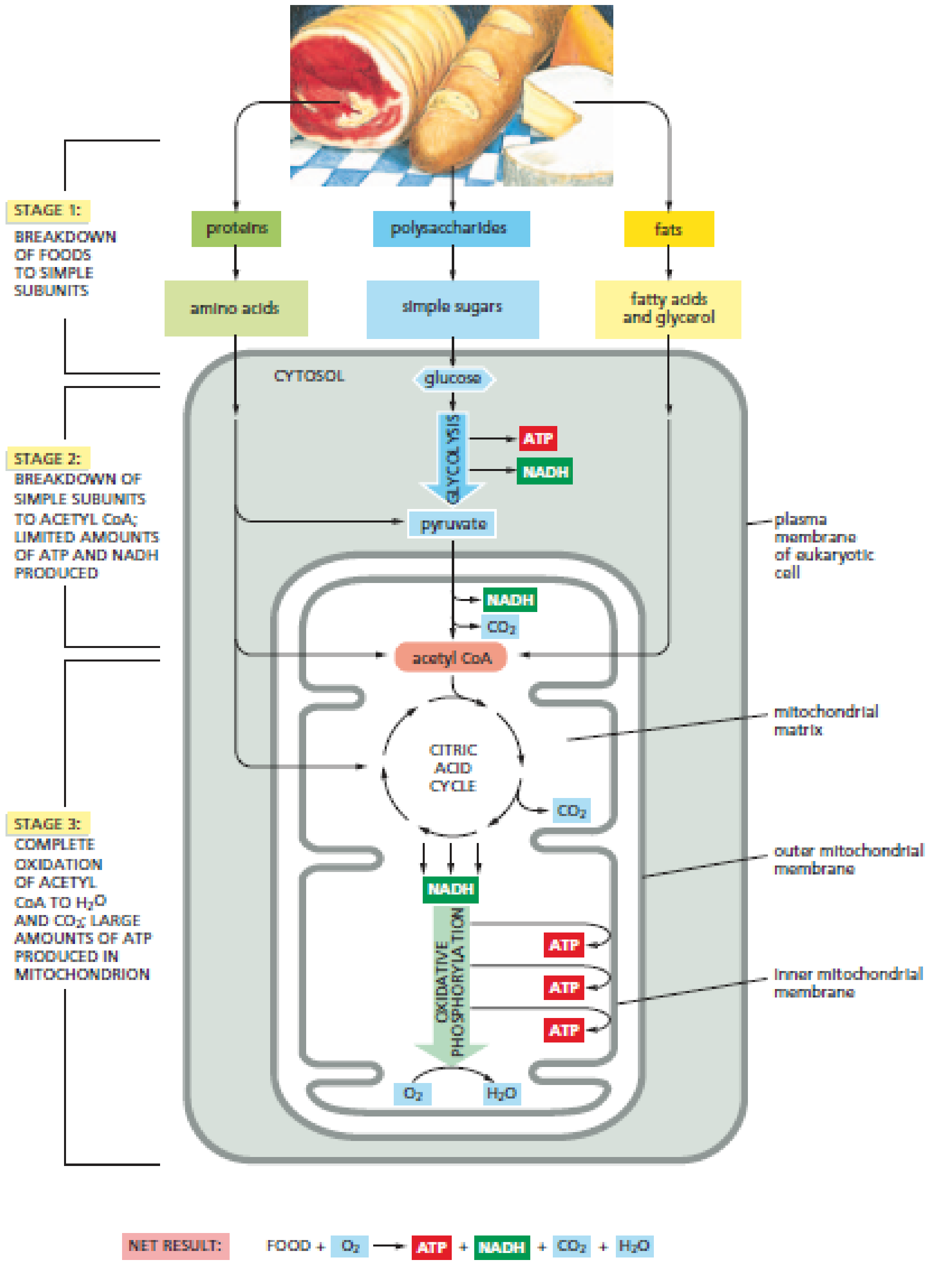
$FADH_2$ produced can provide 1.5 molecules of ATP

The importance of H^+-driven transport in bacteria

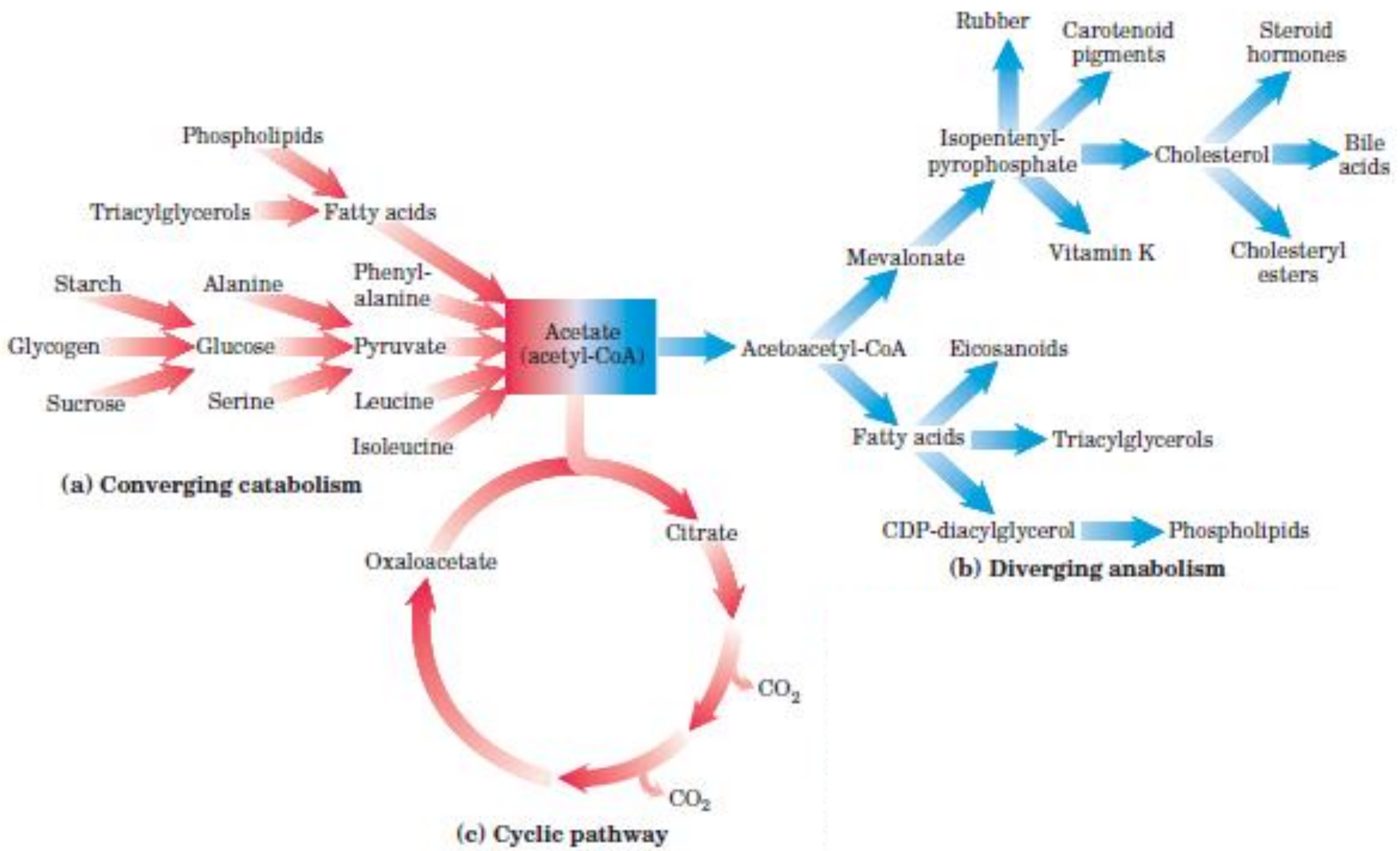




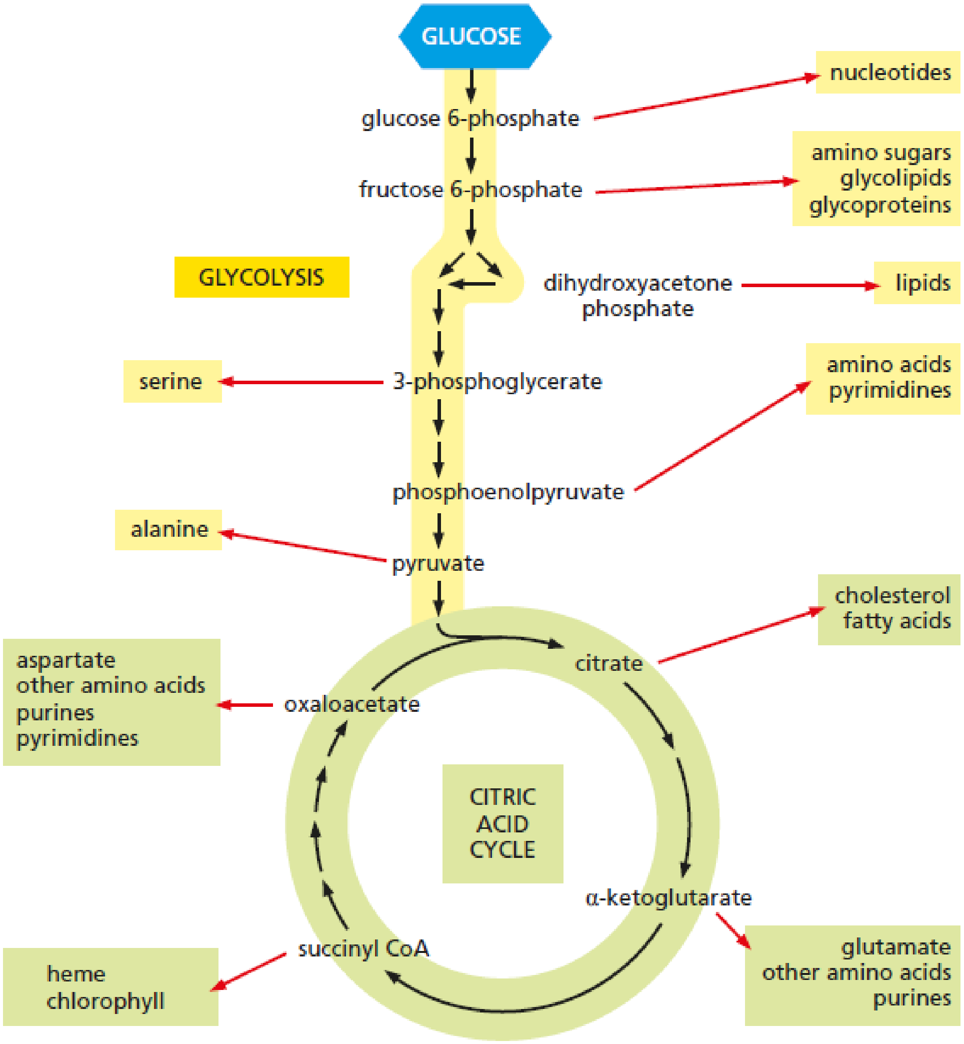
The breakdown of food molecules occurs in three stages



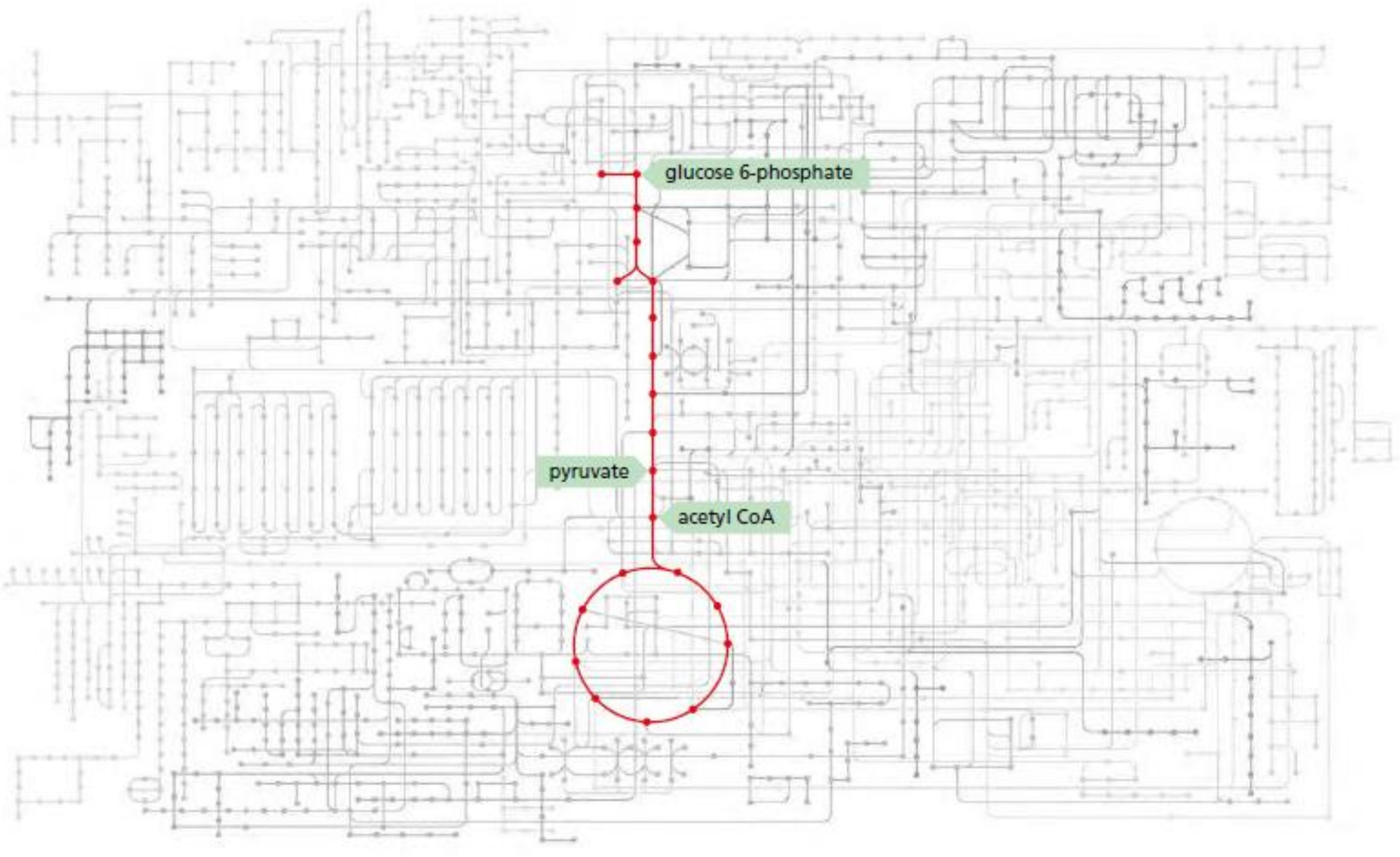
Three types of metabolic pathways



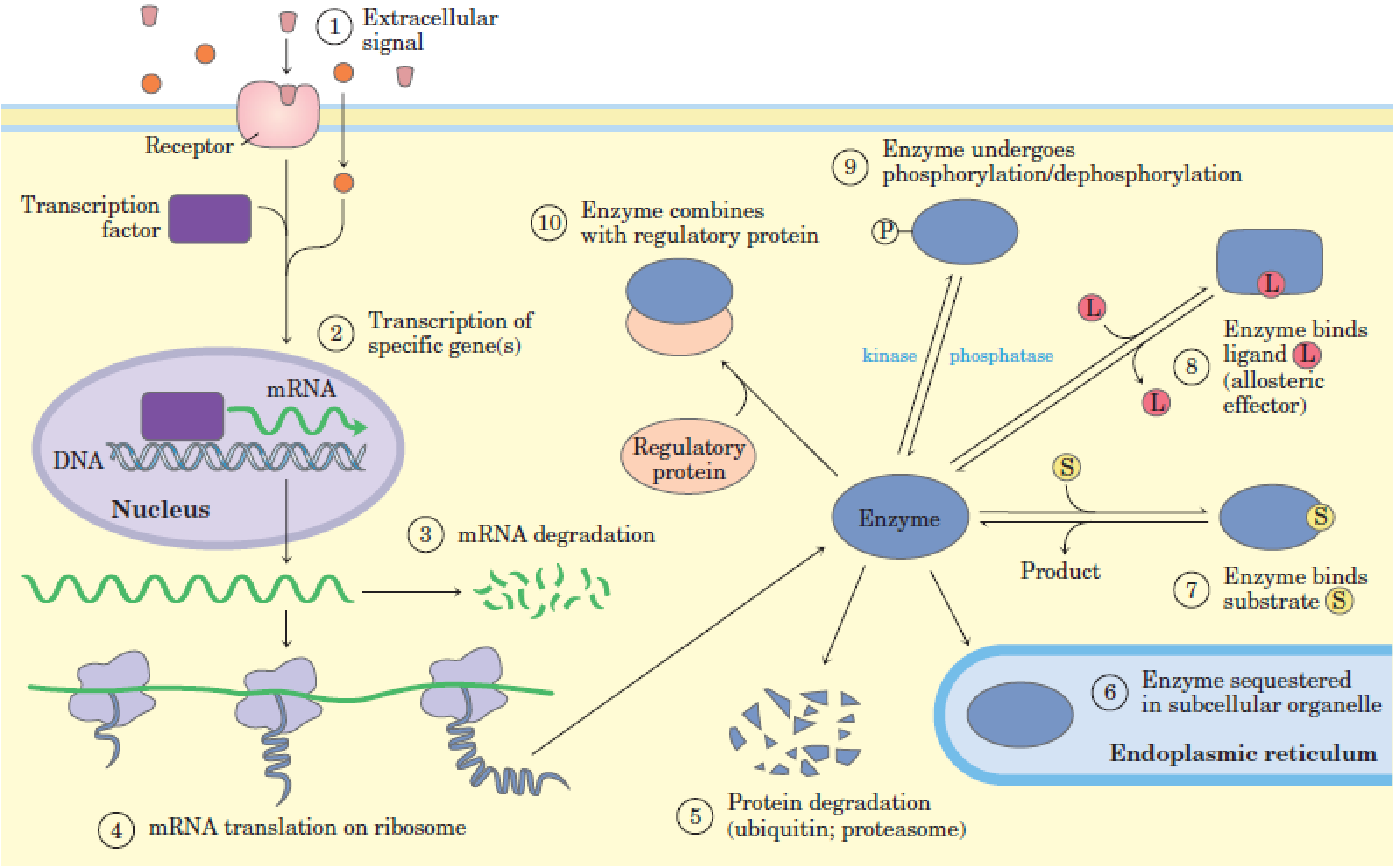
Glycolysis and the citric acid cycle provide the precursors needed to synthesize many important biological molecules



Glycolysis and the citric acid cycle are at the center of an elaborate set of metabolic pathways in human cells

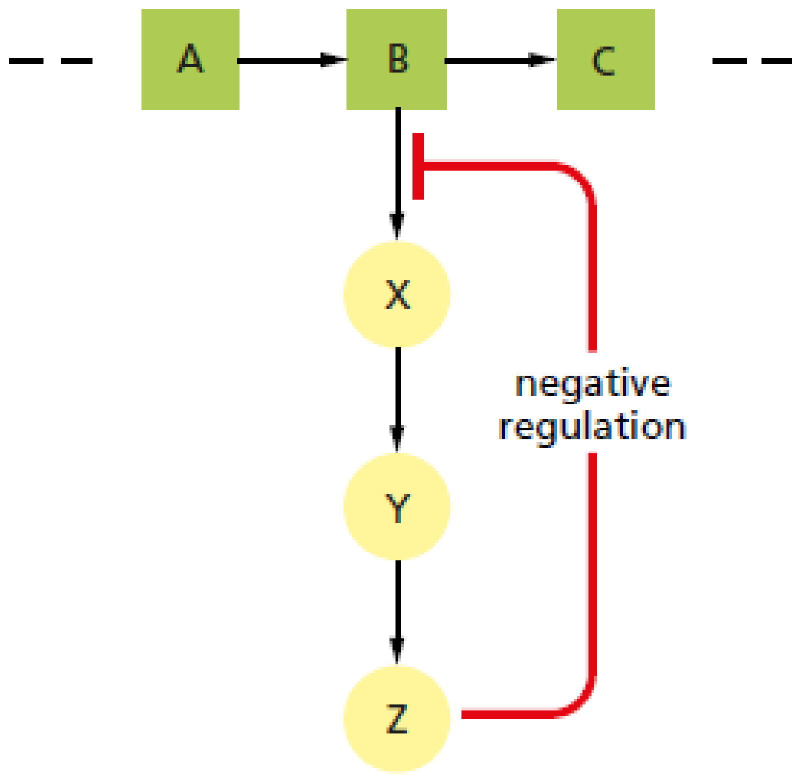


Factors affecting the activity of enzymes

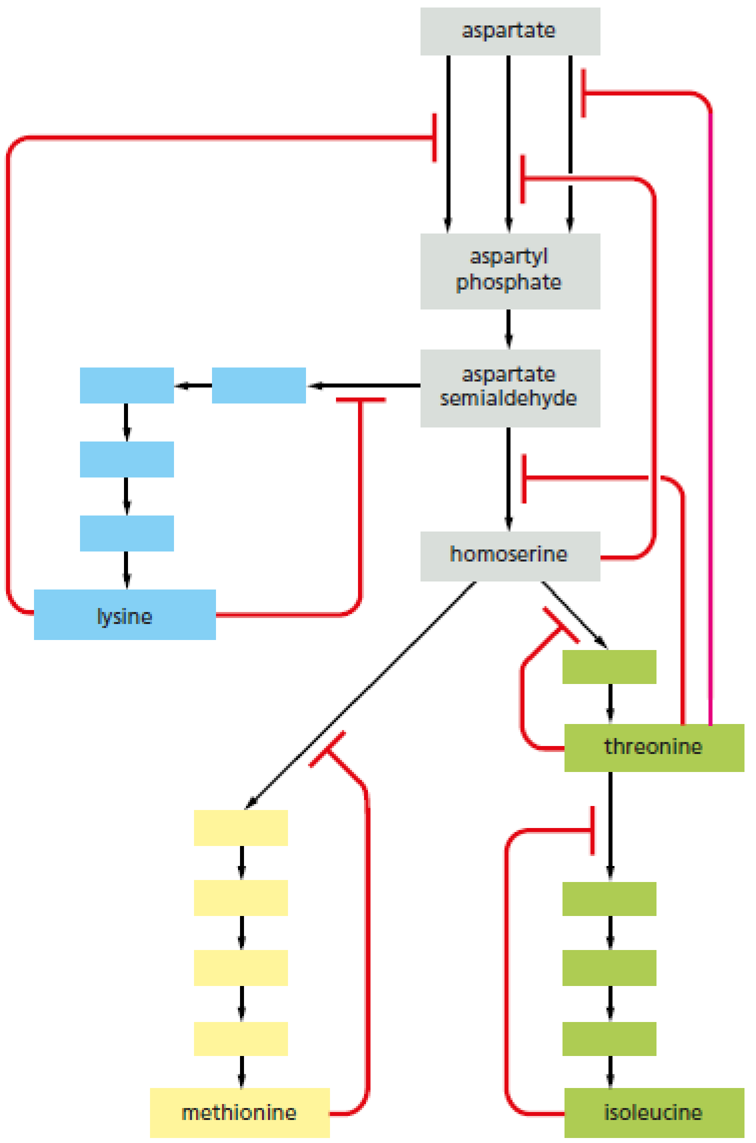


Feedback inhibition

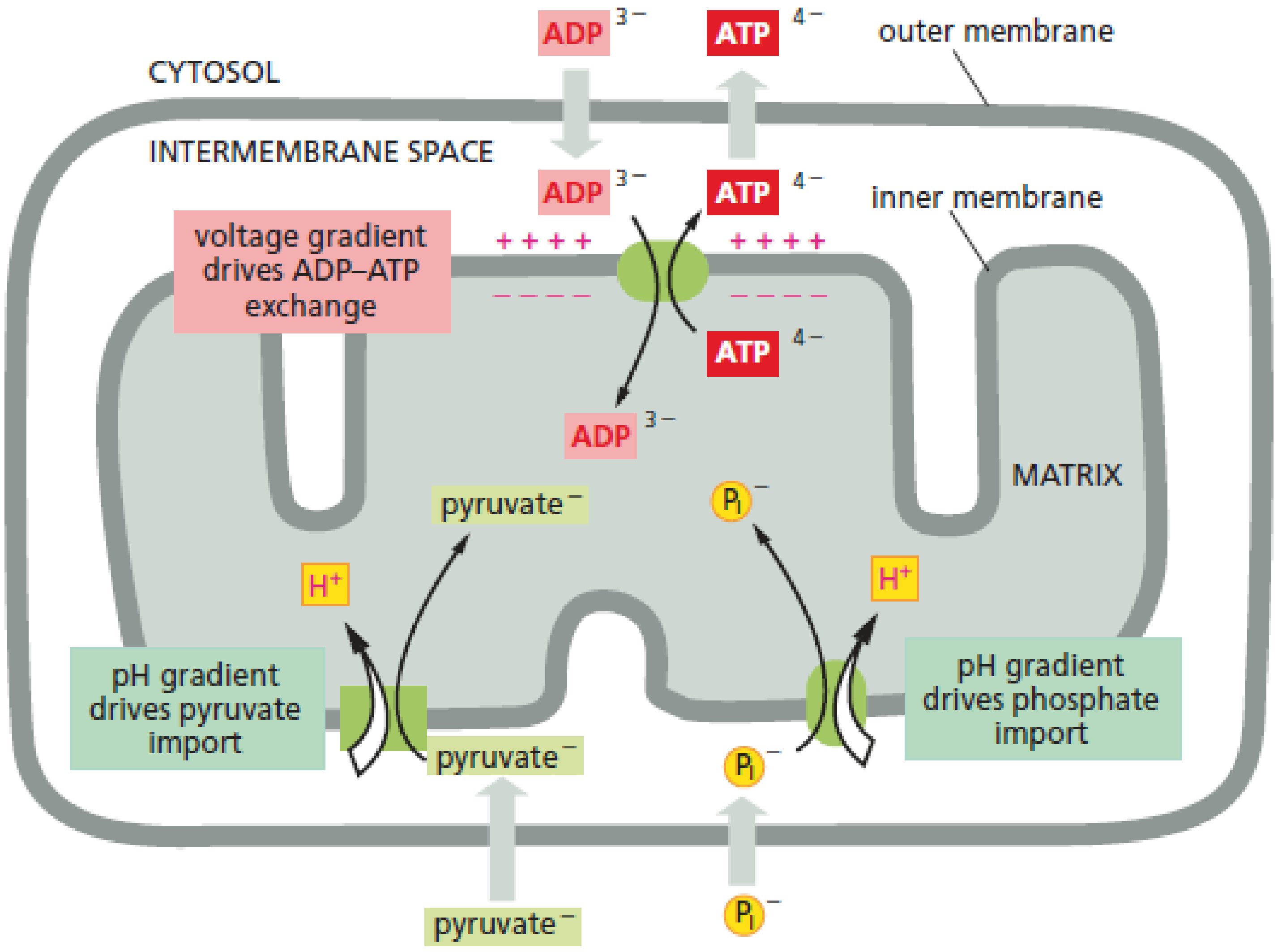
Feedback inhibition of a single biosynthetic pathway



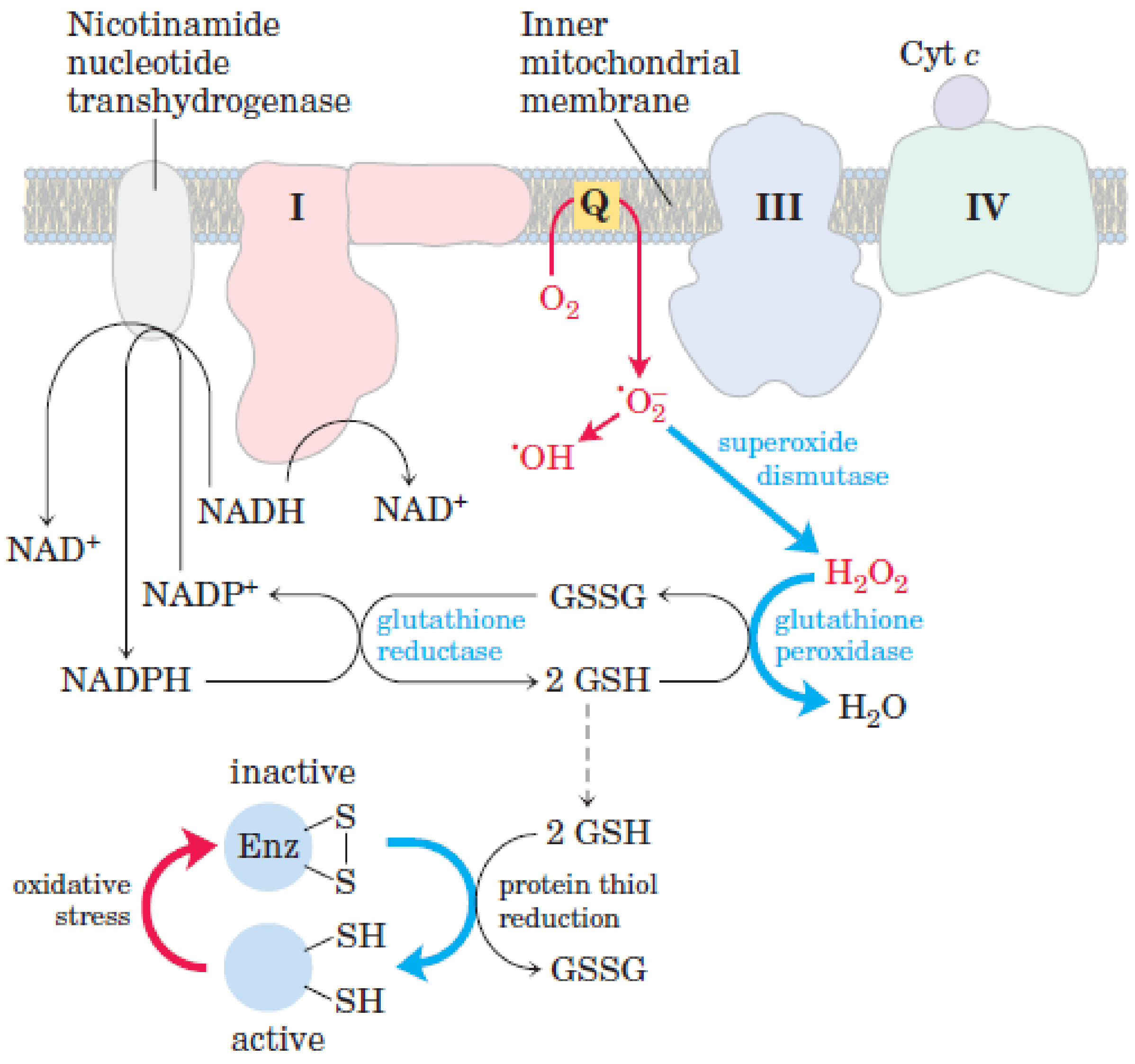
Multiple feedback inhibition



Coupled transport processes



ROS formation in mitochondria and mitochondrial defenses



Factors that slow the flow of electrons through the respiratory chain increase the formation of superoxide