Respiration in eukaryotic cells

Biochemistry; Garrett, Grisham
Alberts et al.; Molecular Biology of the Cell

Outline

1) Biological Definition

2) Generality and Ubiquity

3) Effects of Failure

4) Biological purpose

5) Chemical aspects

6) Cellular aspects

7) Source of atmospheric oxygen

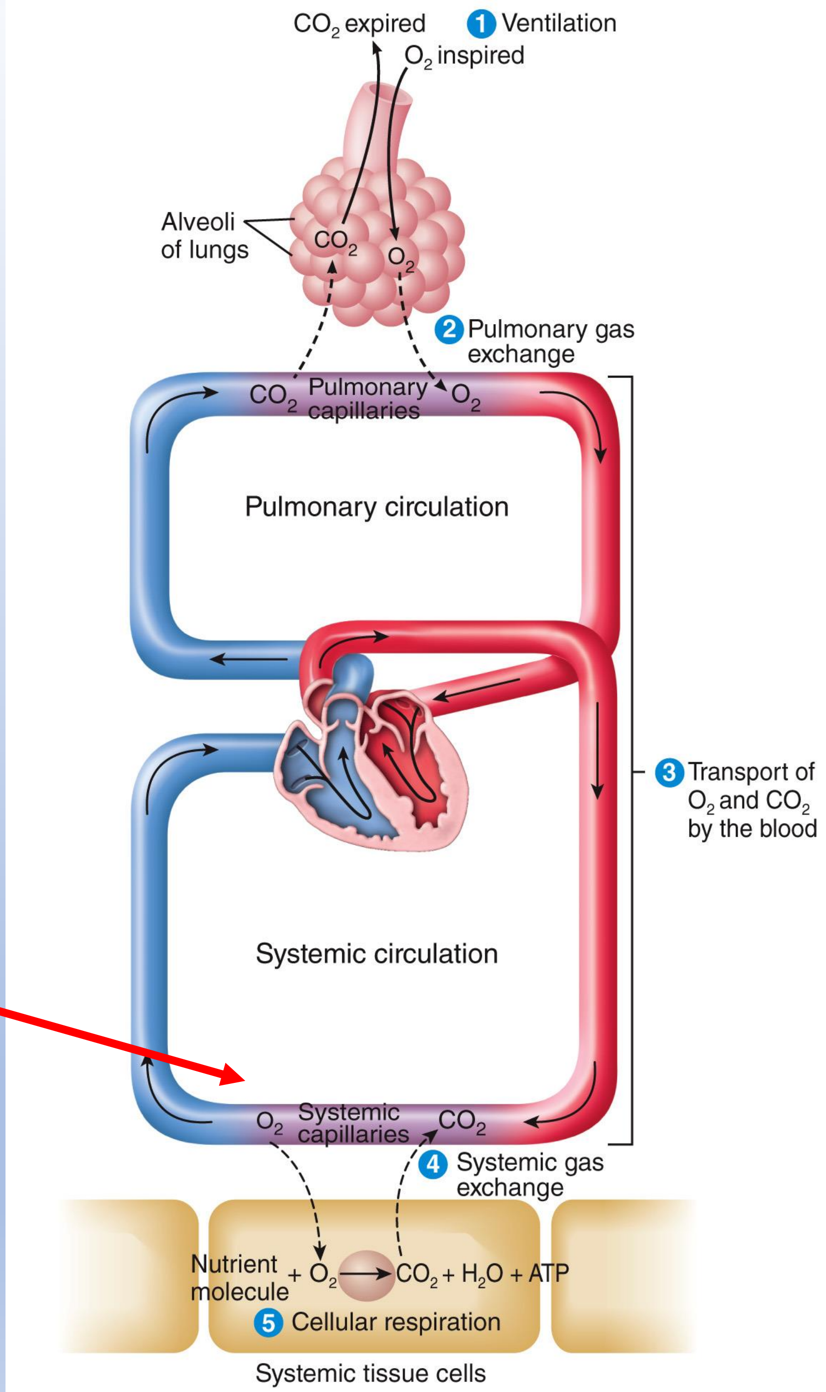
In humans: Respiration

External: lungs expansion/contraction

- Ventilation
- oxygen (O_2)/carbon dioxide (CO_2) exchange

Internal: **microscopic gas exchange**

- **Cellular respiration**



Ubiquity of Cellular respiration

Exchange of atmospheric oxygen O_2 for carbon dioxide CO_2

(almost) ALL ORGANISMS USE IT FOR PRODUCING METABOLIC ENERGY

- Humans
- Plants
- Animals
- Fungi
- Unicellular organisms
- Even most procaryotes (bacteria) use similar processes

How long can a cell survive without oxygen?

Tissue	**Survival time**
Brain	<3 min
Kidney and liver	15-20 min
Skeletal muscle	60-90 min
Vascular smooth muscle	24-72 h
Hair and nails	Several days

Tolerance to hypoxia of various tissues

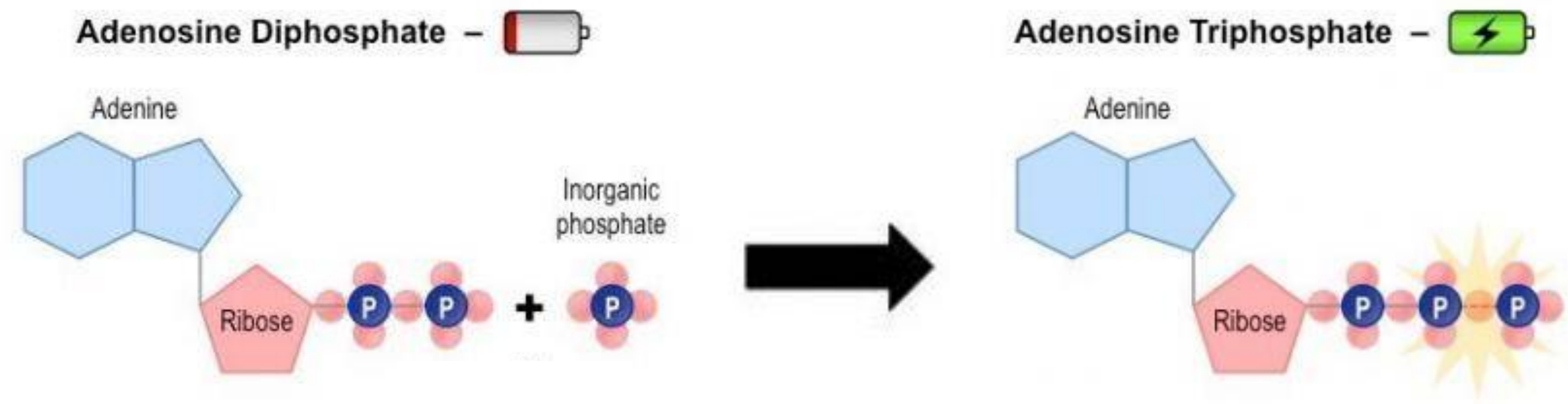
Effects of tissue hypoxia (low oxygen)

Ischaemia is a symptom of tissue hypoxia

Severe tissue hypoxia due to capillary microthrombosis in critically ill patient with *meningococcal septicaemia*

Lack of oxygen may lead to tissular death and organ amputation

Final result of cell respiration: synthesis of ATP from ADP



$$ADP + PO_4^{-2} + O_2 + energy = ATP + H_2O + CO_2$$

Where does the energy come from? Where does it go?

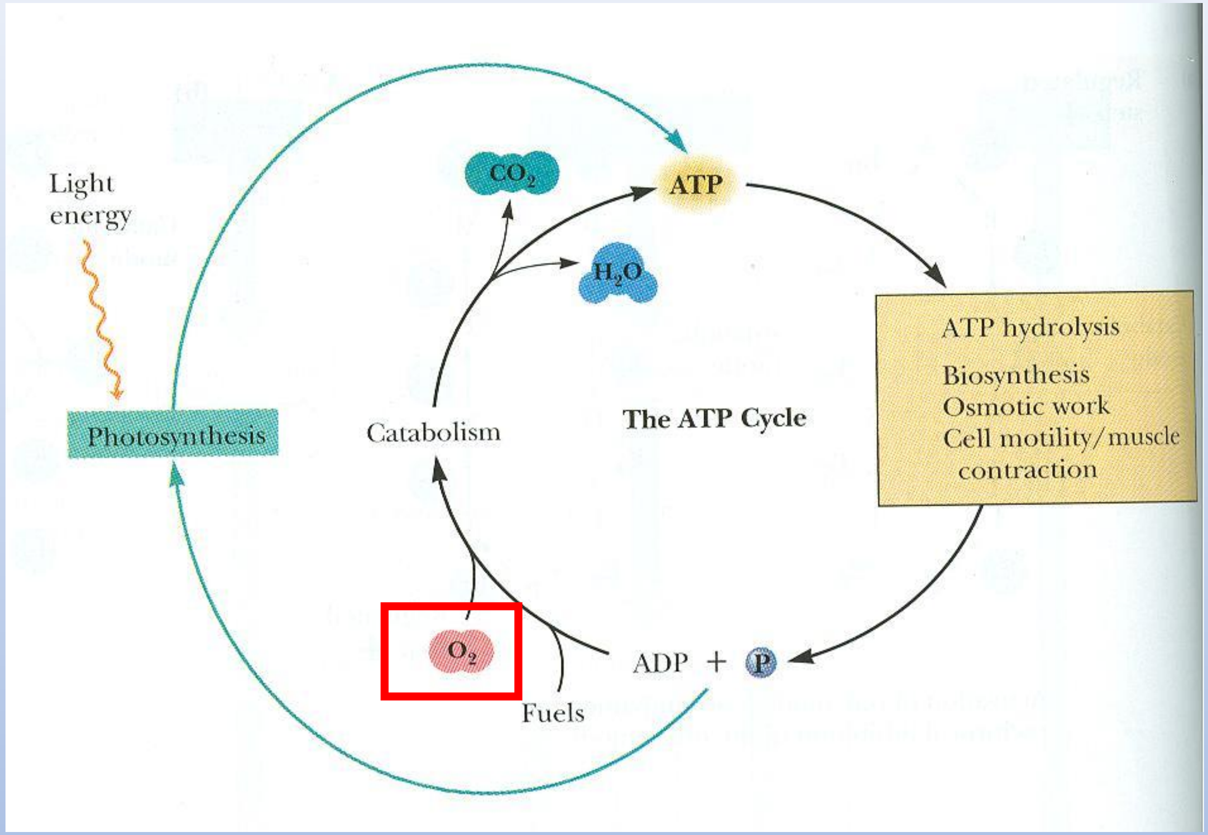
Source of energy

Proxy: food
Actual initial source: sunlight (photosynthesis)

- High energy electrons in food (fuels) supply the energy for ATP synthesis

Final destination of energy: metabolism

- Basal metabolism
- Biosynthesis
- Motility
- Many other biological processes



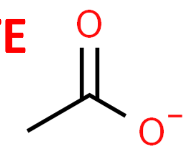
Example: carbohydrate synthesis

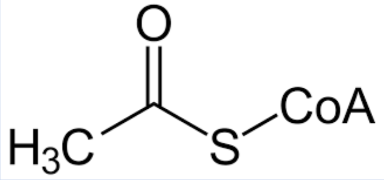
$$\text{Light} + 6\ CO_2 + 6\ H_2O \rightarrow C_6H_{12}O_6$$

Acetate (as **AcetylCoA**) **is the main source of energy**

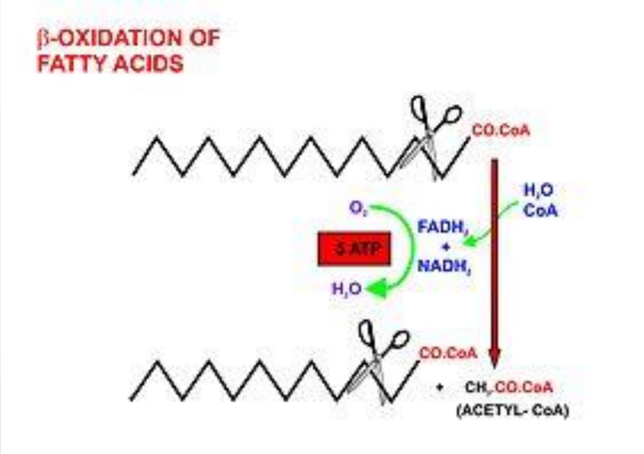
Acetyl-CoA (vitamin B_5, **acetate donor**) is the main source of energy

ACETATE

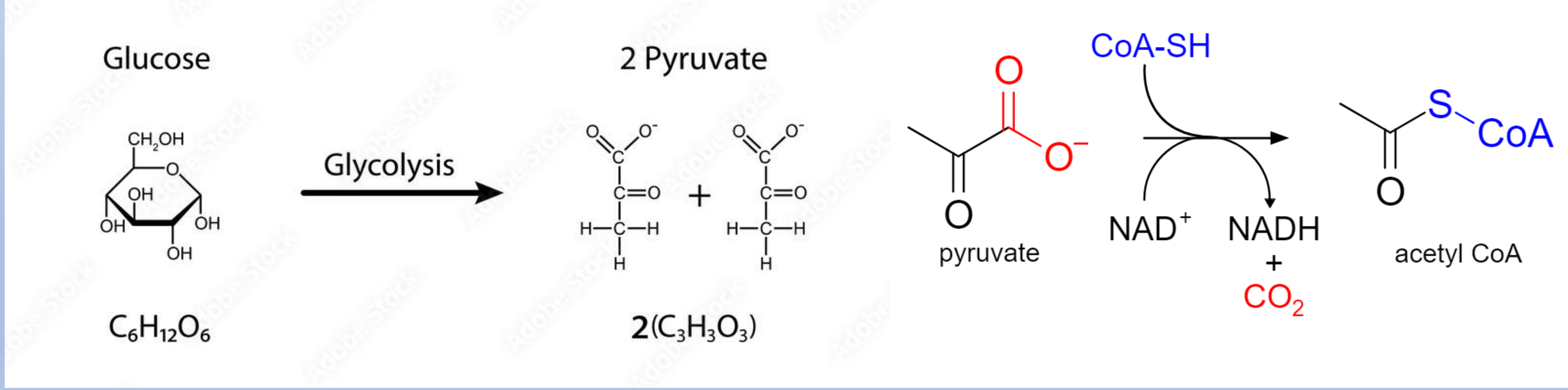




Source of energy: **fatty acids**
Process: β-oxidation
(mitochondrion)



Source of energy: **carbohydrates**
Process: Glycolysis
(cytoplasm)



Krebs cycle (mitochondrial matrix)

Acetate feeds the Krebs cycle *(complex biochemical process)* **allowing protonation** (H+ binding) **of two intermediate products:**

- **NADH: Nicotinamide (vitamin B_3), and**
- **$FADH_2$: Flavoprotein (vitamin B_2, or riboflavin)**

$NAD^- + H^+ \rightarrow NADH$

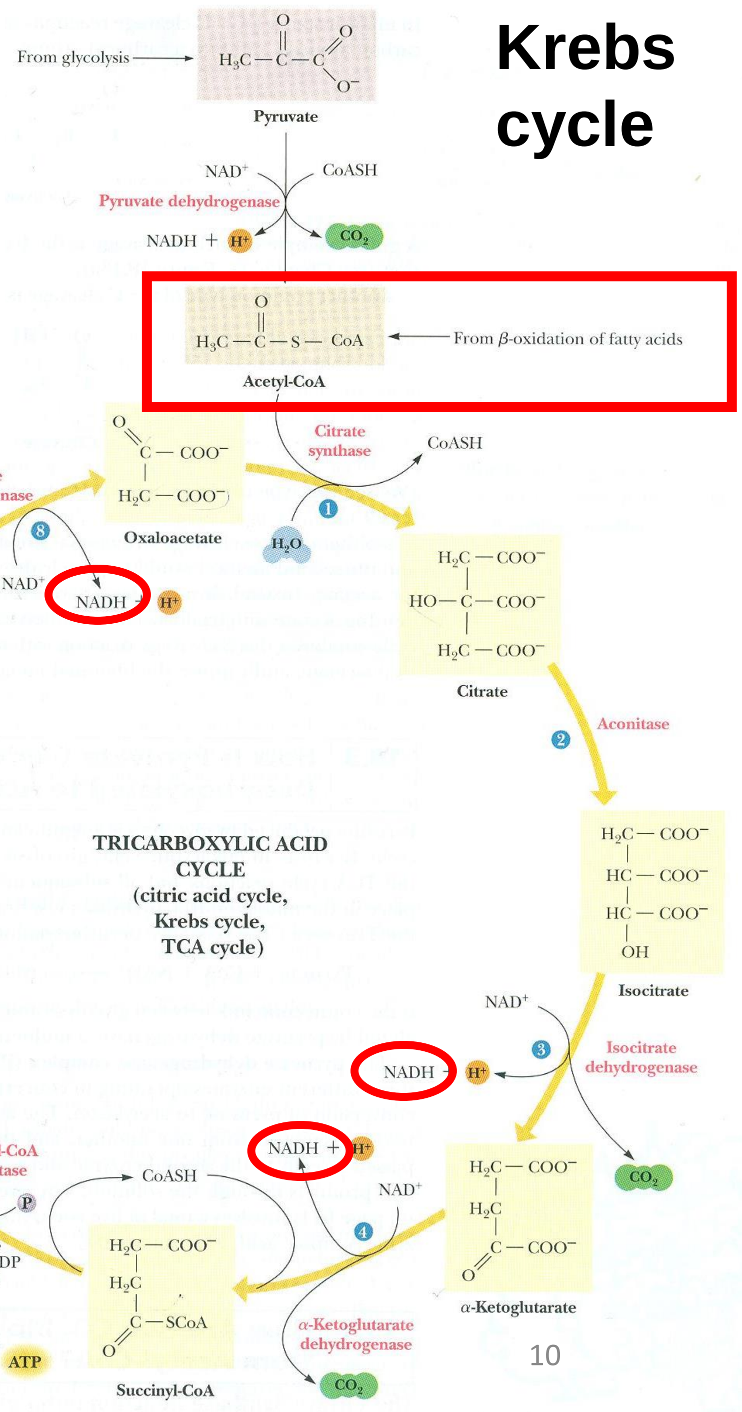
and

$FAD^- + 2H^+ \rightarrow FADH_2$

NADH and $FADH_2$ are proton donors in mitochondria

Production of NADH And $FADH_2$ from Acetate (AcetylCoA)

Krebs cycle



Oxidative Phosphorylation (mitochondria)

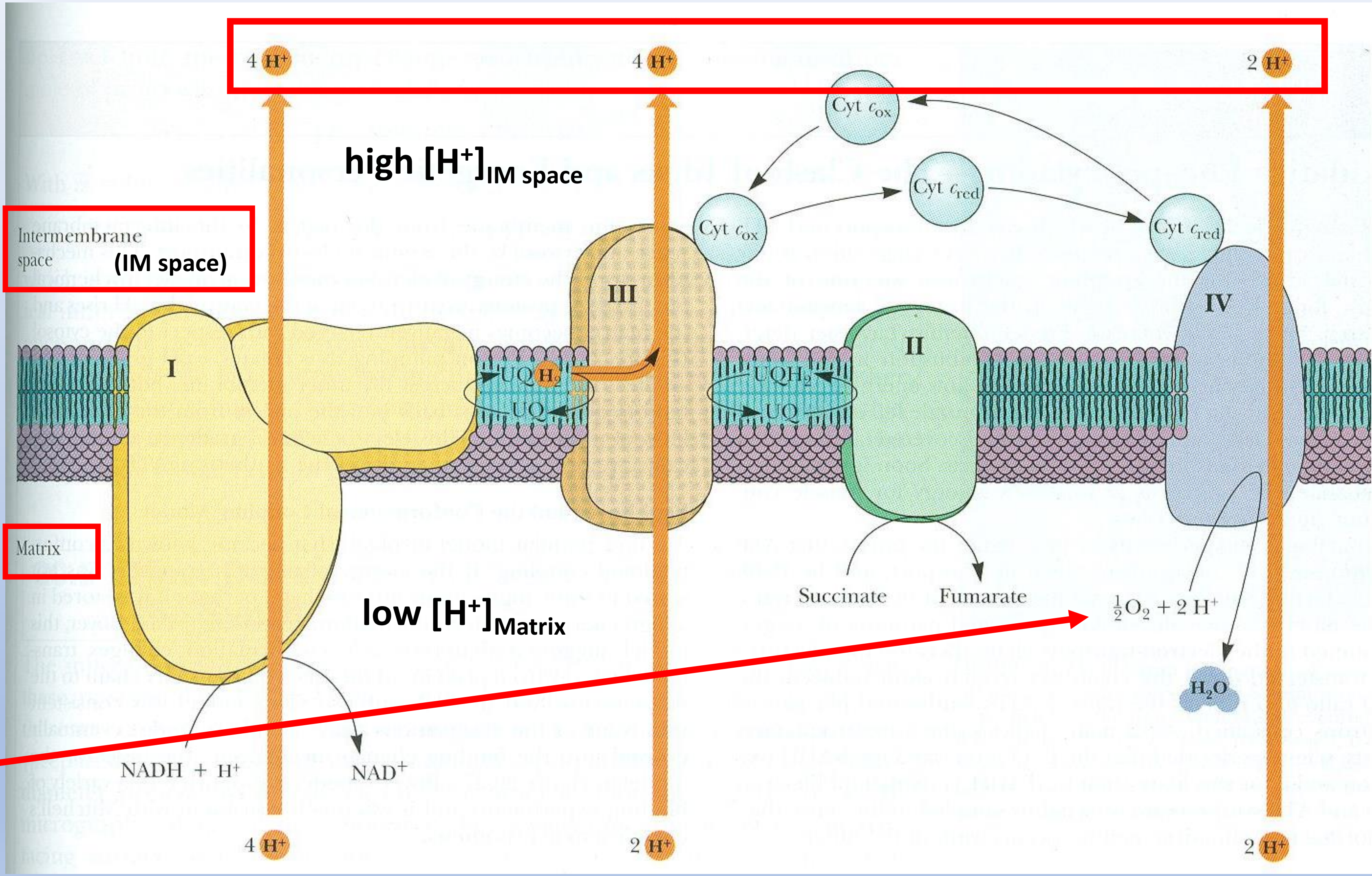
Creation of the proton gradient by a chain of cytochrome oxidoreductions

In the presence of O_2, a series of protein complexes use cytochrome, iron, and copper (complexes I-II-III-IV) to:

- take protons from NADH and $FADH_2$
- move them from the Matrix to the Intramembrane Mitochondrial (IM) membrane, and hence
- **create a H^+ gradient**

across the mitochondrial membrane

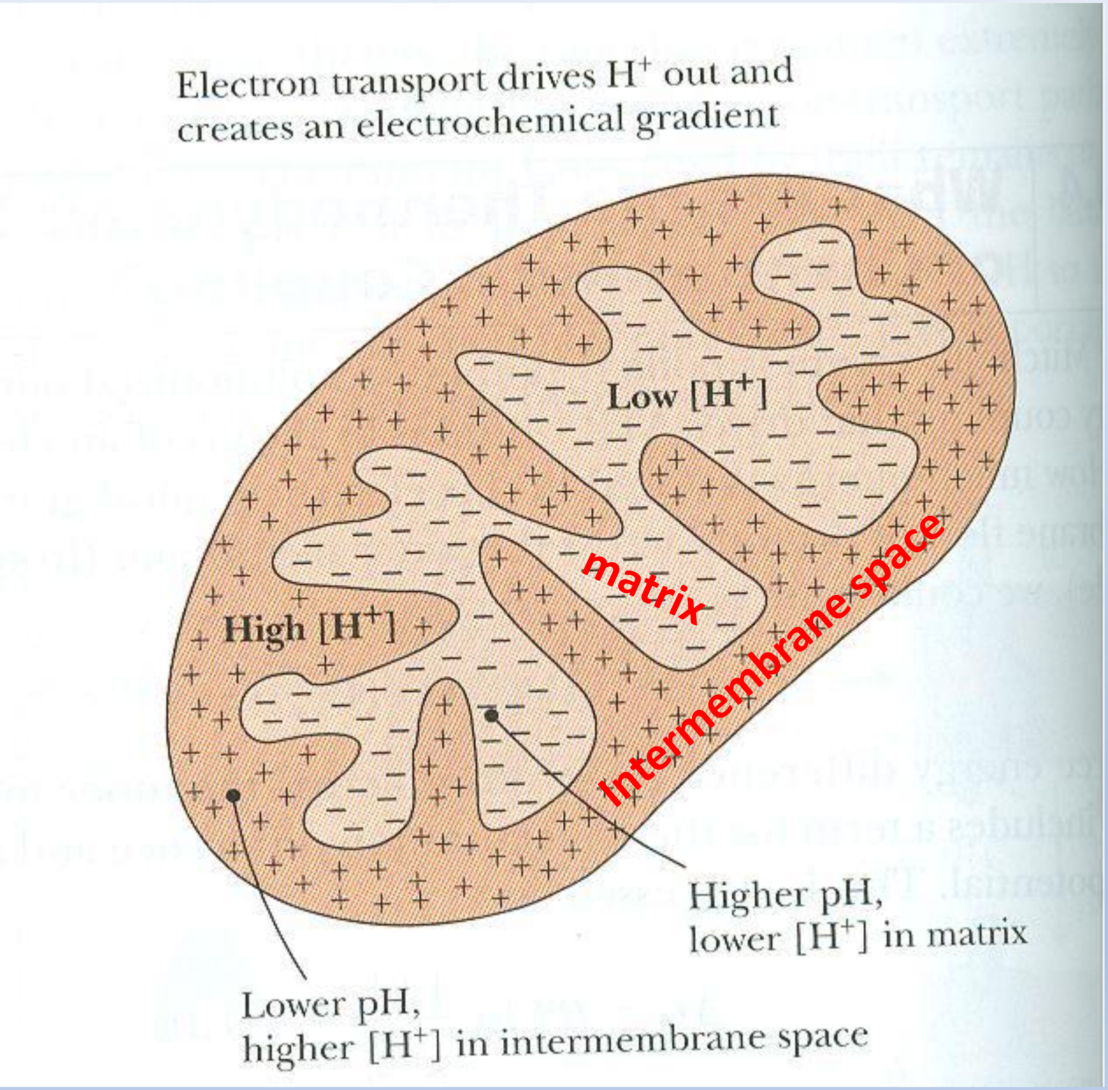
This process needs oxygen (O_2)



H^+ gradient = $[H^+]_{IM\ space}$ - $[H^+]_{Matrix}$

Where is mitochondrial energy stored?

Proton gradients temporarily store energy in mitochondria



A reverse proton pump synthetizes ATP

"Normally", a membrane pump (ATP-ase) uses energy from ATP to transport ions (in this case protons) against their gradient.

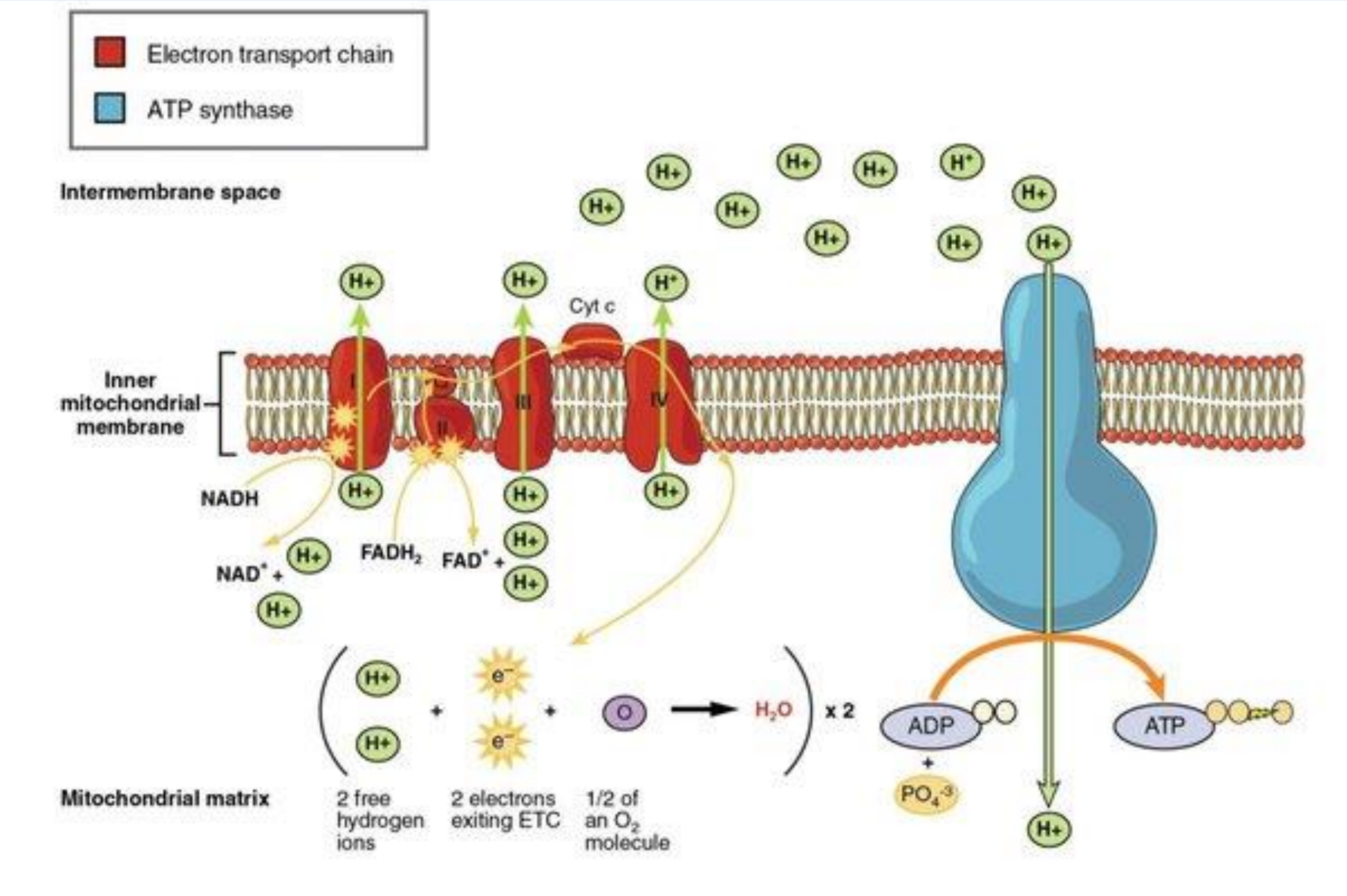
Conversely in conditions of ***low-ATP/high-ADP*** *concentrations and* ***strong H^+ gradient****, the H^+ pump works in reverse turning ADP into ATP*

In the matrix of mitochondria:

In the presence of a H^+ gradient, ATP is synthesized from ADP

How:

Using an ATP-ase hydrogen (H^+) pump working in reverse mode



Aerobic vs anaerobic energy production

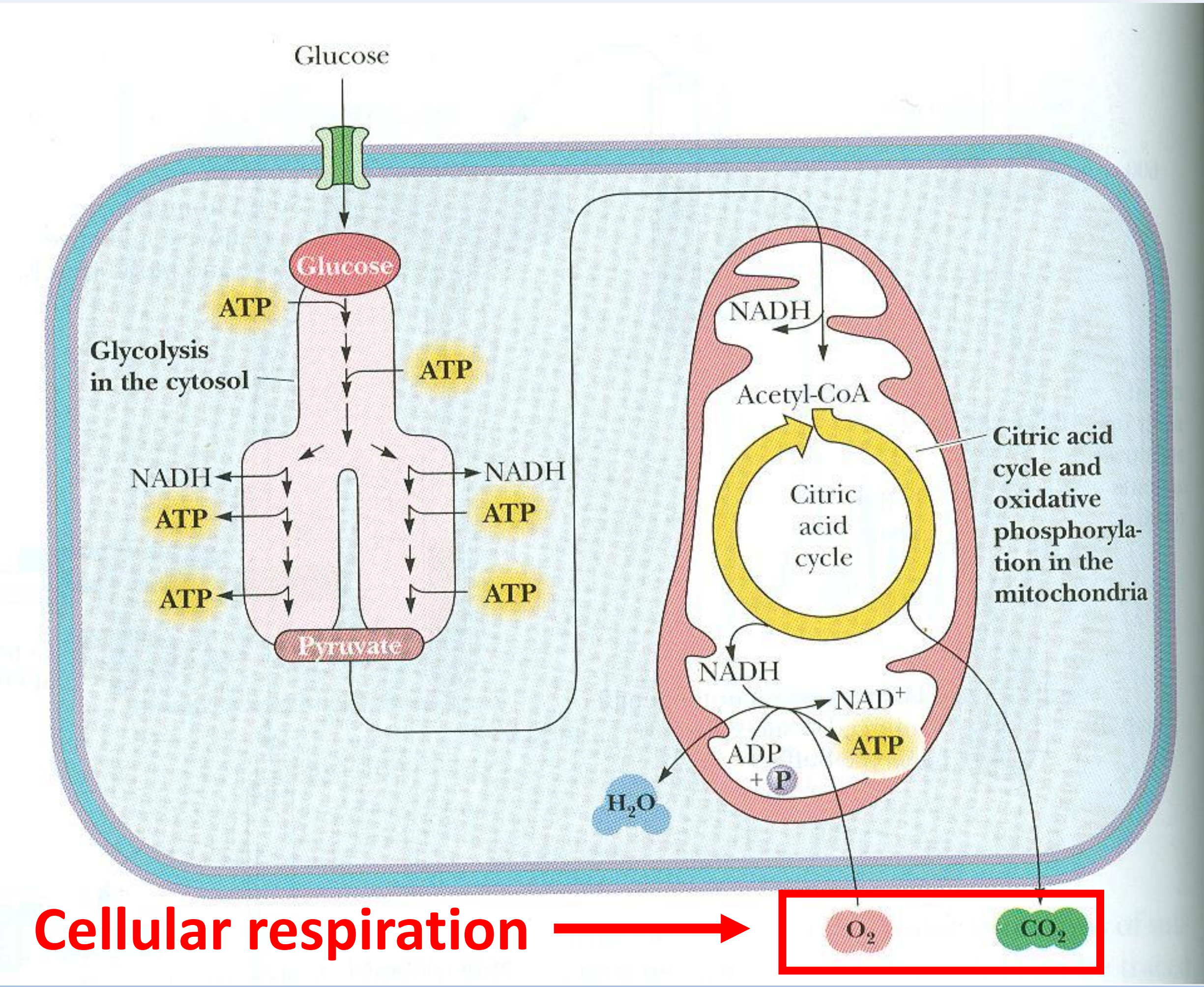
Small amounts of energy can be produced anaerobically for instance, from Krebs cycle (1 ATPs, O_2 not needed)

On the contrary

The production of larger amount of energy (≈ 5 ATPs per Krebs cycle), using any nutrients, including <u>fatty acids</u>, requires oxidative phosphorylation

(and O_2)

CO_2 is a waste product of cellular respiration



Cellular respiration

Where does atmospheric O_2 come from?

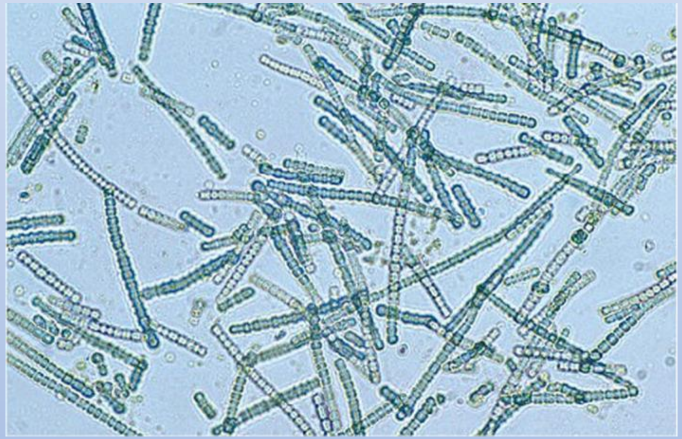
$6\ CO_2 + 6\ H_2O + \text{energy} = C_6H_{12}O_6 + \mathbf{6\ O_2}$

- **2B years ago**: from **CYANOBACTERIA**

cyanobacteria use(d) CO_2, and split H_2O into hydrogen and oxygen:

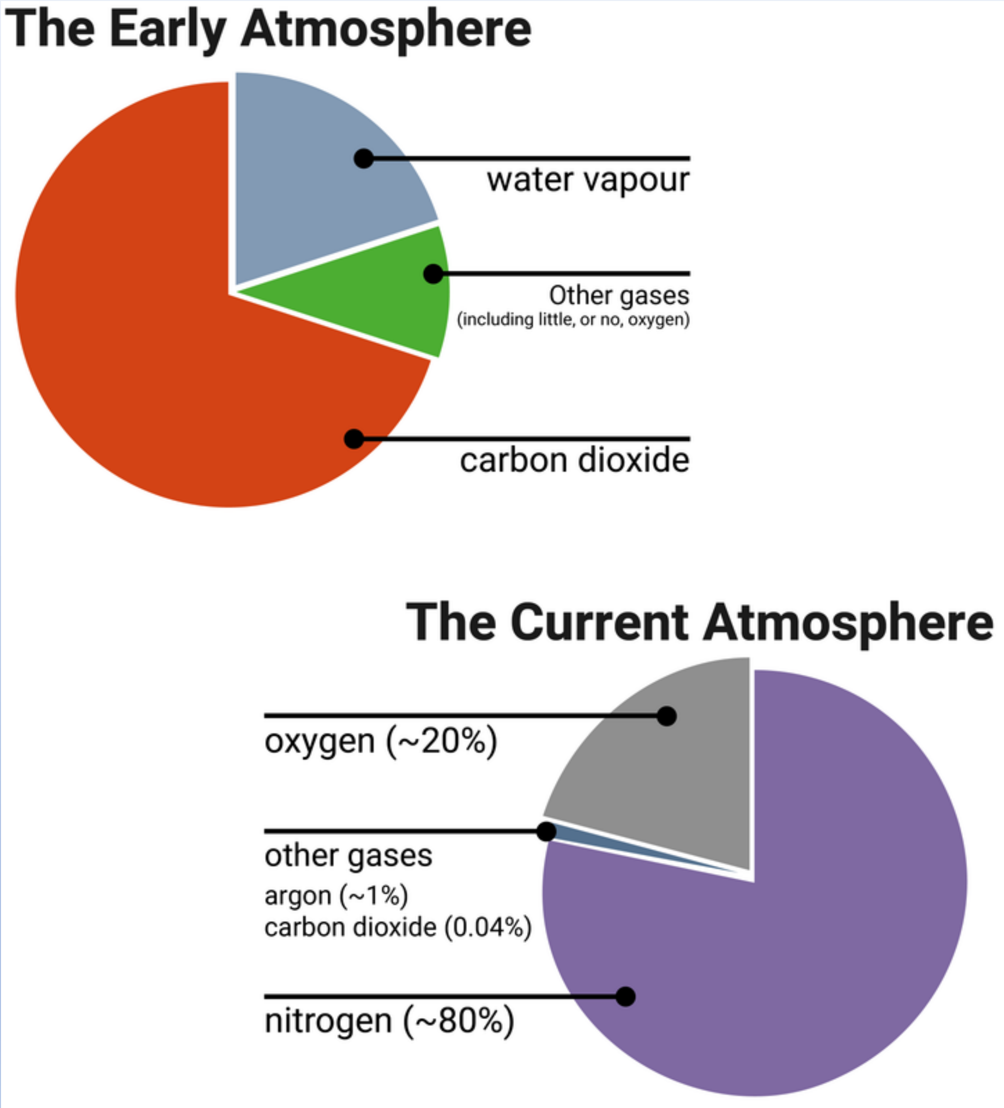
Cyanobacteria have blue-green color.

They first appeared about 2 billion years ago in the evolution of the Earth's atmosphere. Responsible for the **Great Oxidation**



- **Since then,** land plants and sea algae release:
- O_2 during day (with light), and
- CO_2 during the night (in darkness)

Overall, plants produce 10 times more O_2 than CO_2



summary

1) Nutrients are taken in by cells

2) They are broken down into pyruvate/acetate/acetyl-CoA

3) Krebs cycle uses acetate to protonate NAD^- and FAD^{-2}

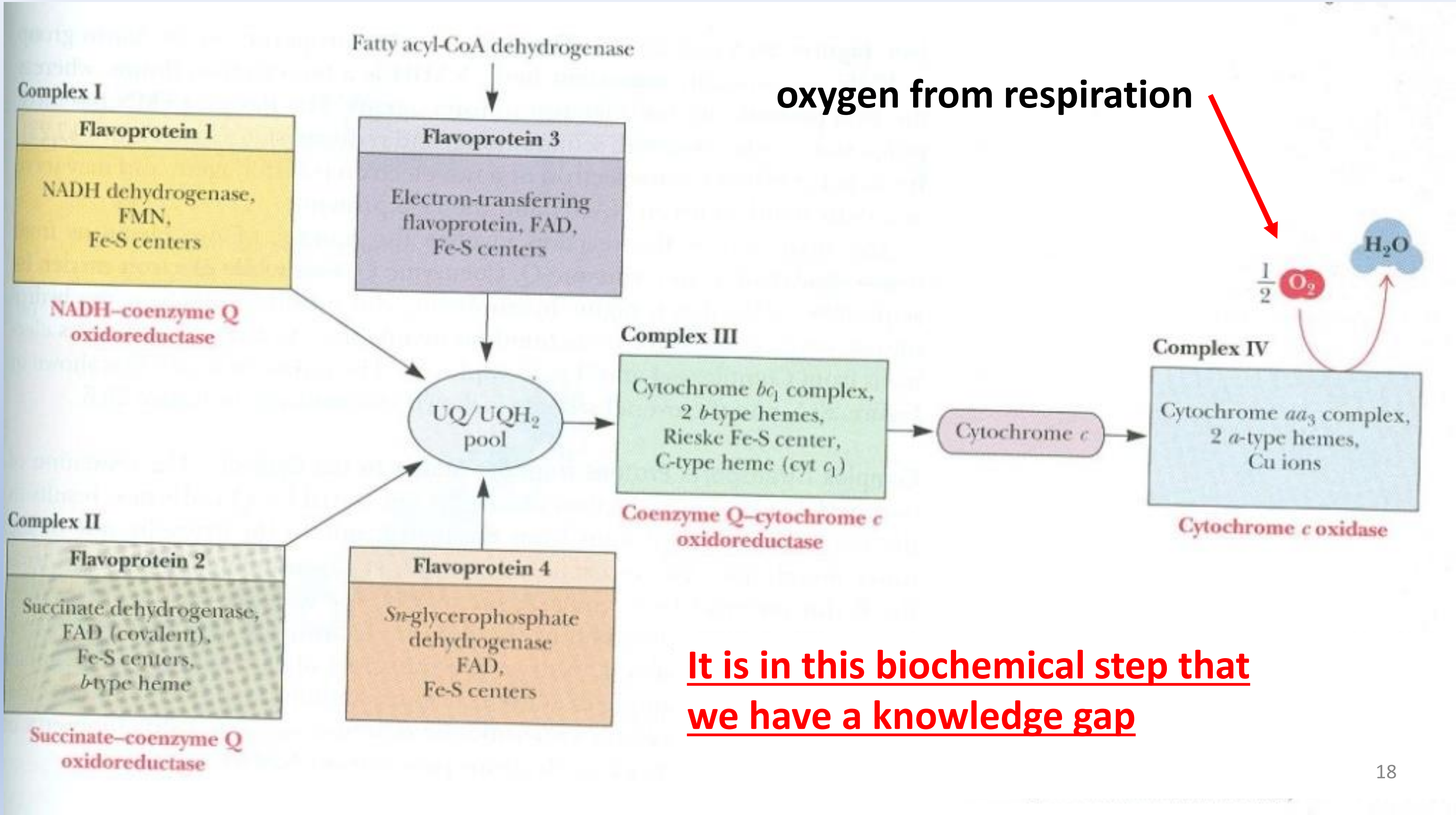
4) **NADH and $FADH_2$ create a proton gradient in mitochondria by oxidative phosphorylation (using oxygen)**

5) The proton gradient induces the synthesis of ATP from ADP

(in most animals the protein hemoglobin carries the poorly water-dissolvable O_2 inside the blood)

appendix

Role of the Ubiquinone complexes



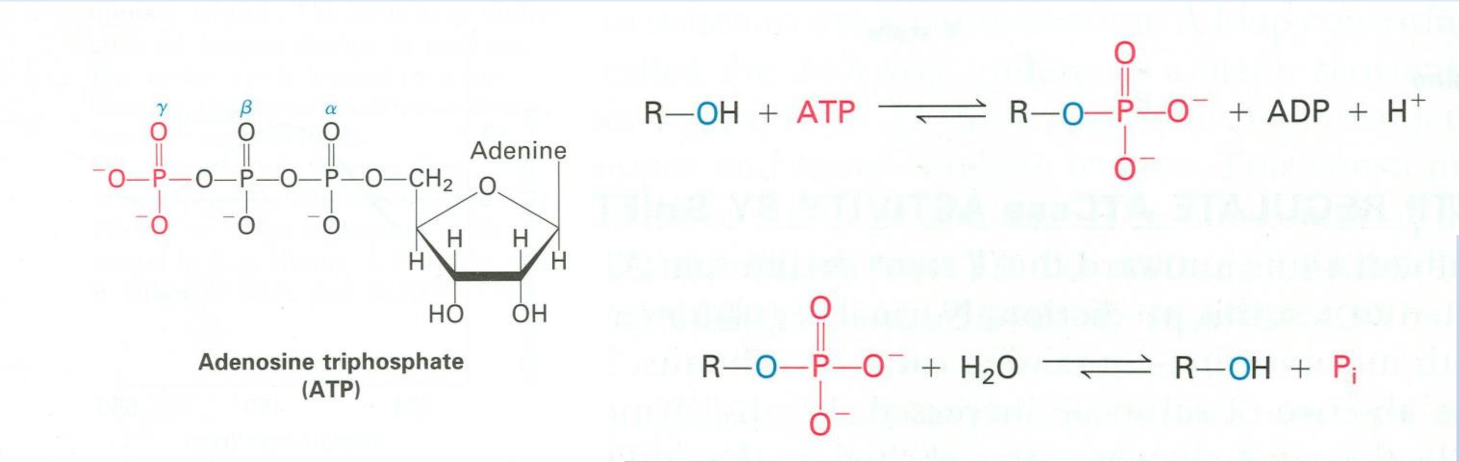
oxygen from respiration

It is in this biochemical step that we have a knowledge gap

Purpose of ATP: catalyze Phosphorylation

phosphorylation: reversible process

- protein **kinases** and
- protein **phosphatases**

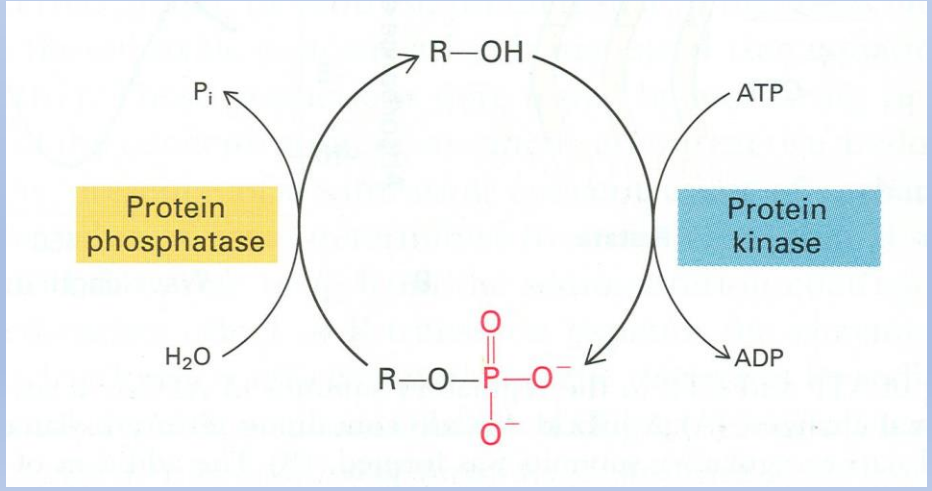


Kinases:

Enzymes (proteins) that induce phosphorylation (attachment of a PO4– group)

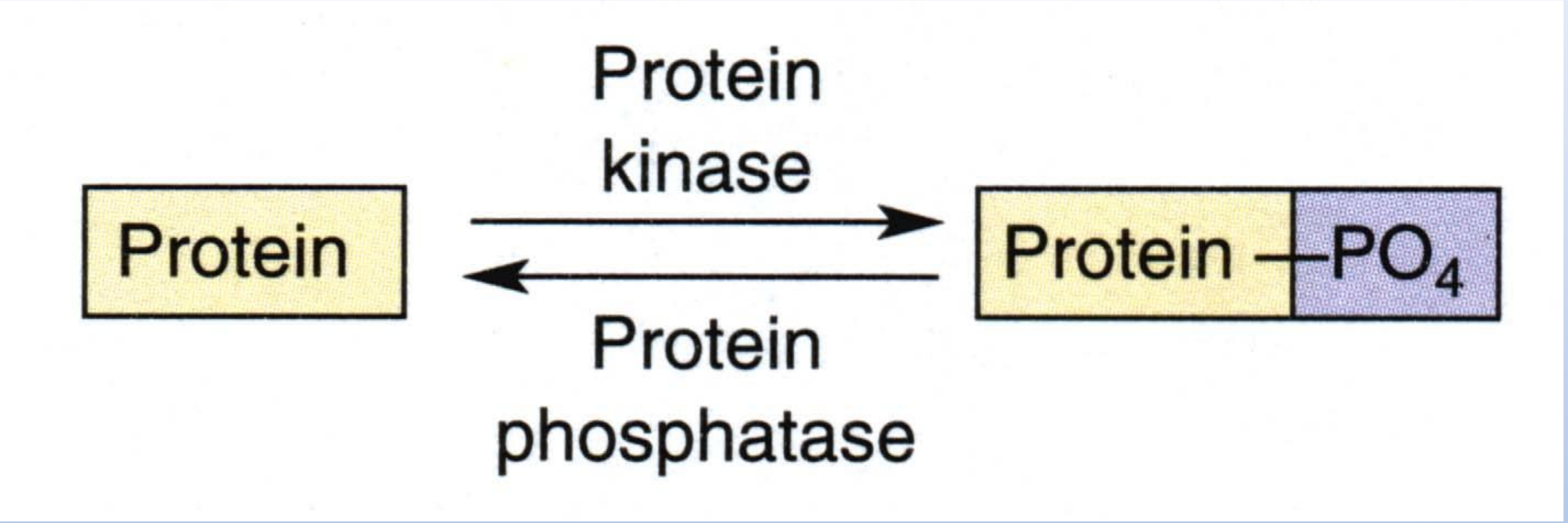
Phosphatases:

Enzymes that induce de-phosphorylation (removal of a PO4– group)



Behavior needs to be reversible

Example: Protein phosphorylation



Covalent and reversible binding of a phosphate group (PO_4^{2-})

Phosphorylation (typically) leads to temporary increase of function in the phosphorylated protein with corresponding behavioral change

Krebs cycle in the synthesis of biomolecules

Most biological important molecules (most aminoacids, nucleotide bases, steroids, neurotransmitters, fatty acids, etc.) can be synthetized from Krebs' cycle

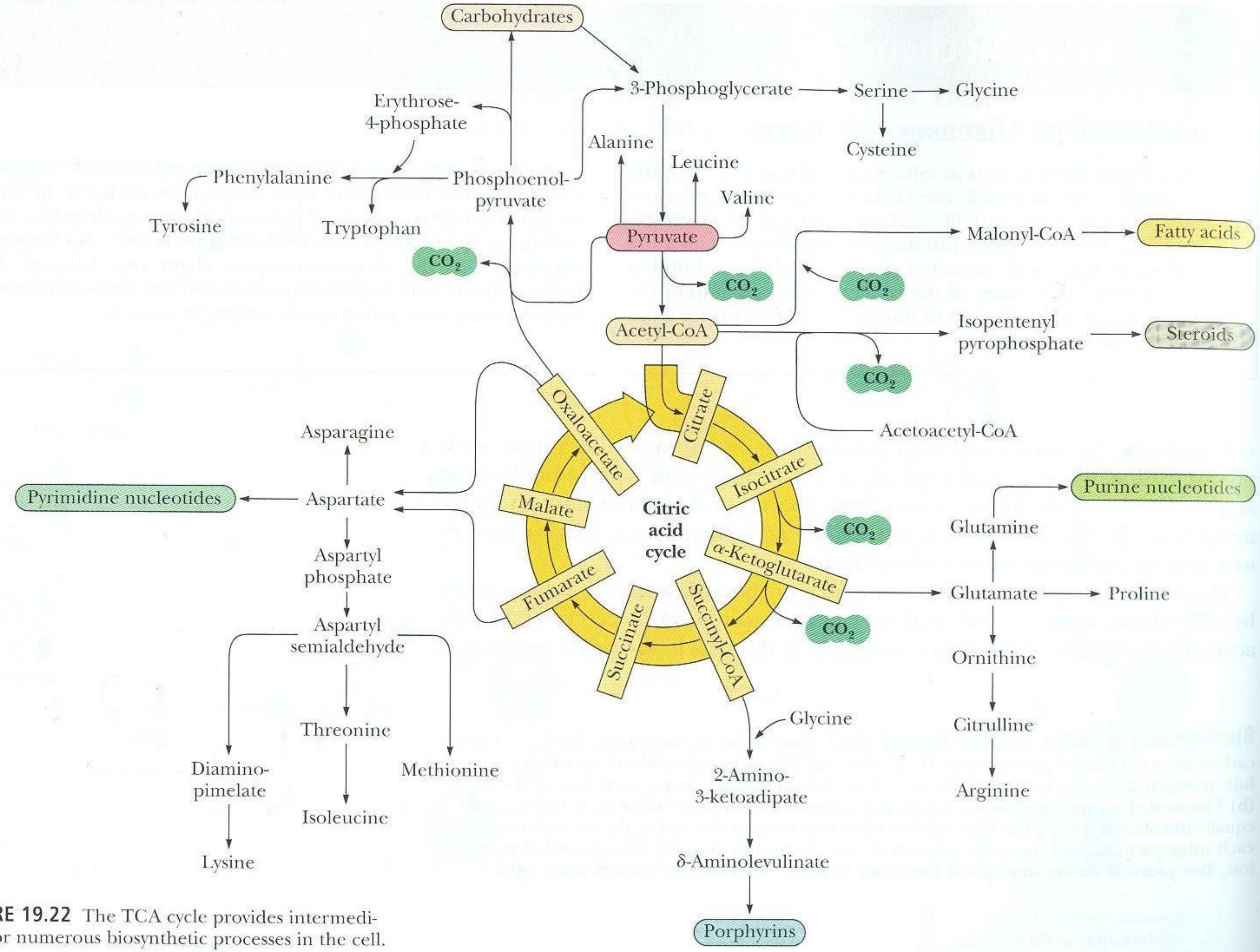
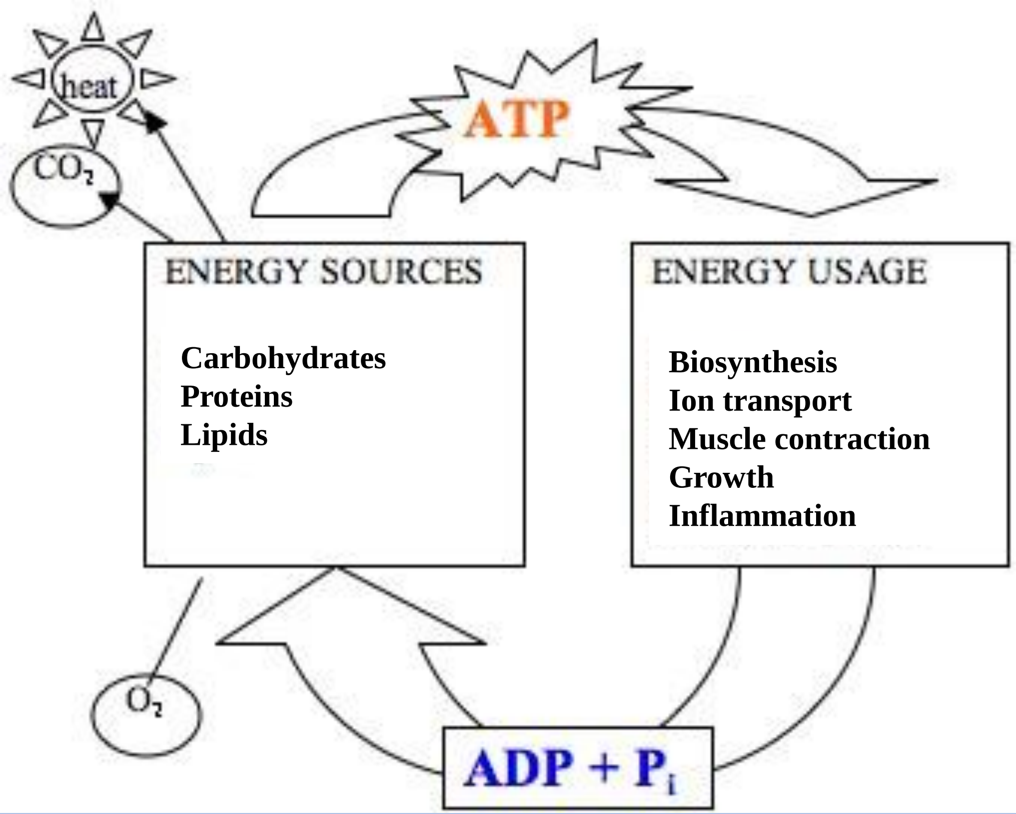


FIGURE 19.22 The TCA cycle provides intermediates for numerous biosynthetic processes in the cell.

Role of oxygen (O_2)



Eventually:

O_2 is necessary to convert ADP + phosphate (PO_4^{-2}) into ATP

Mitochondria at the Origin of life

Hypothesis for origin of life:

protobacteria (already using cellular respiration) were incorporated into protocells, and turned into mitochondria, allowing eukaryotic life