Sunday, 14 October 12

Cell Biology and Developmental Genetics

Lectures by

John F. Allen

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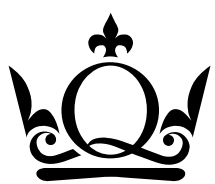
jfallen.org



Queen Mary
University of London

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Slides and supplementary information:

jfallen.org/lectures

Cell Biology and Developmental Genetics

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Endosymbiosis and the origin of bioenergetic organelles. Some history

Endosymbiosis and the origin of bioenergetic organelles.
A modern view

Mitochondria as we know them and don't know them

Why do chloroplasts and mitochondria have genomes?

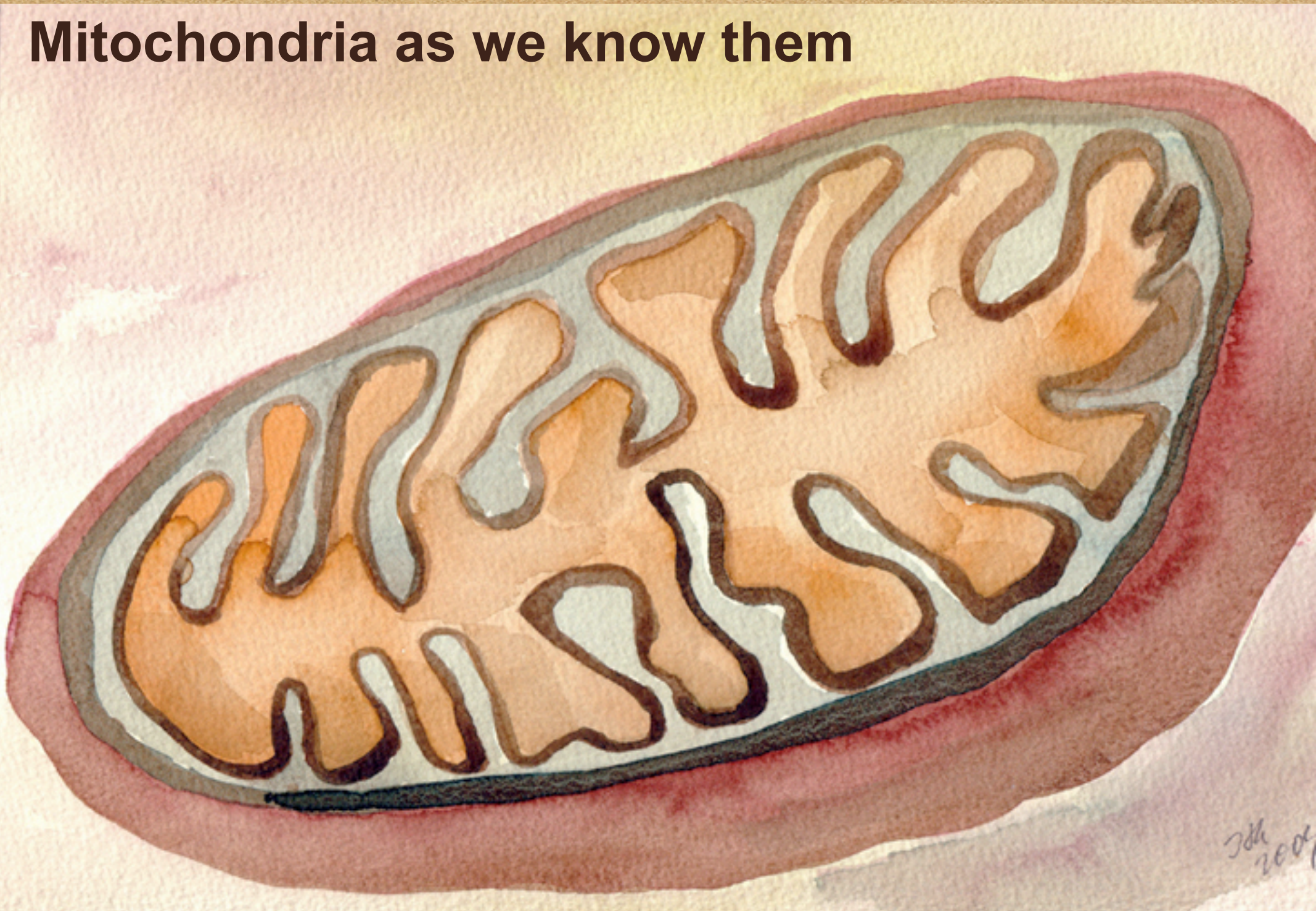
Co-location for Redox Regulation

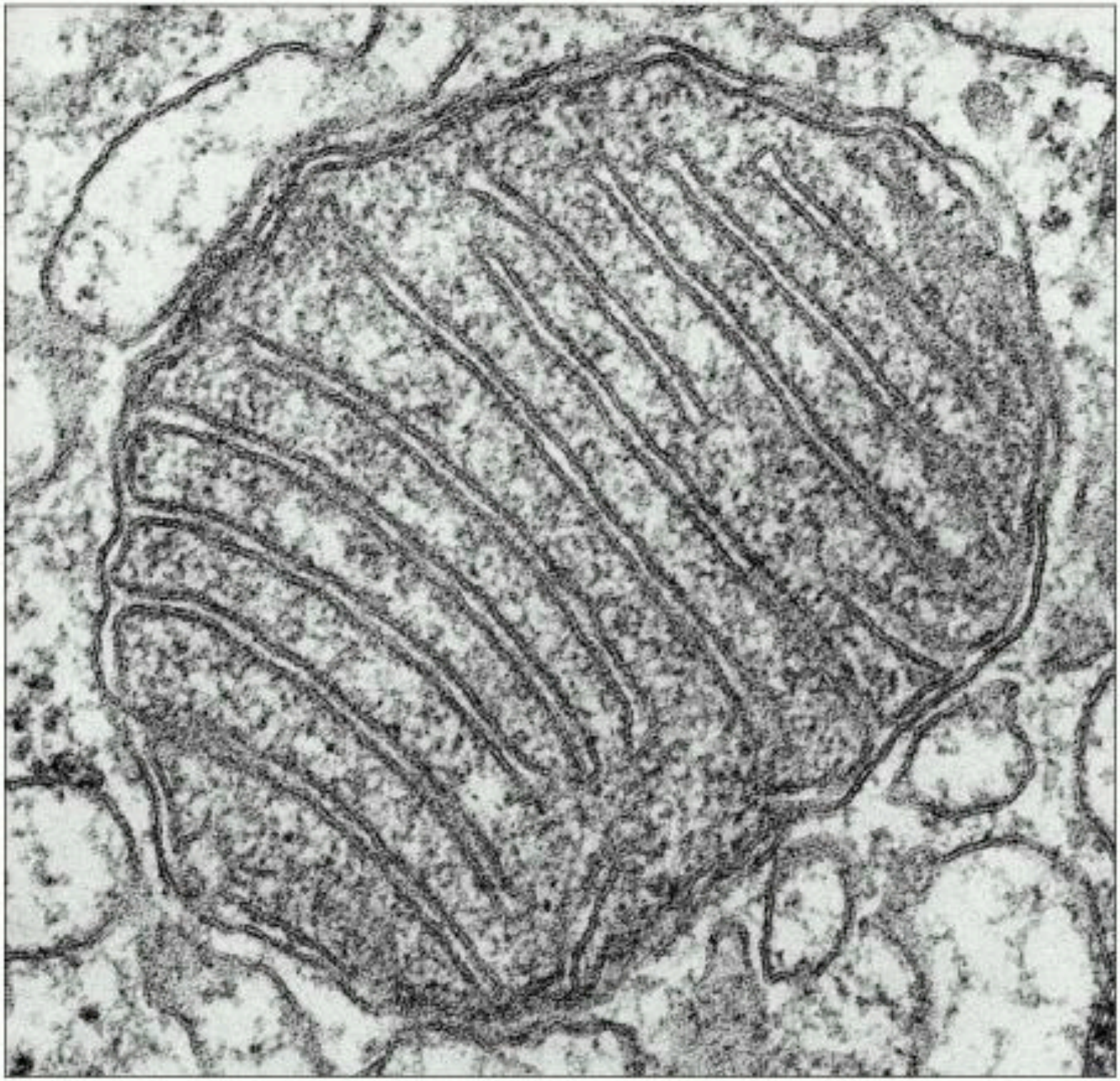
Mitochondria, ageing, and sex – energy versus fidelity

Lecture 3

Mitochondria as we know them and don't know them

Mitochondria as we know them



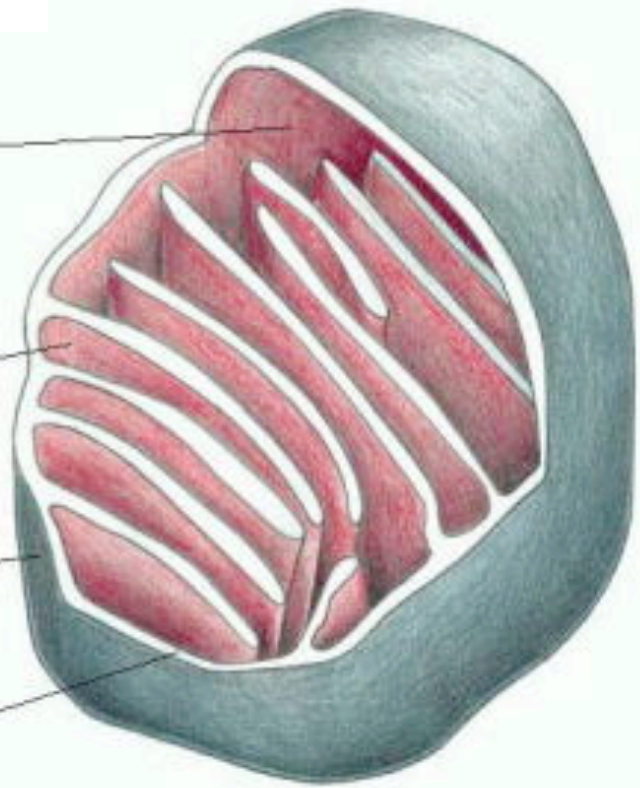

100 nm

Matrix. This large internal space contains a highly concentrated mixture of hundreds of enzymes, including those required for the oxidation of pyruvate and fatty acids and for the citric acid cycle. The matrix also contains several identical copies of the mitochondrial DNA genome, special mitochondrial ribosomes, tRNAs, and various enzymes required for expression of the mitochondrial genes.

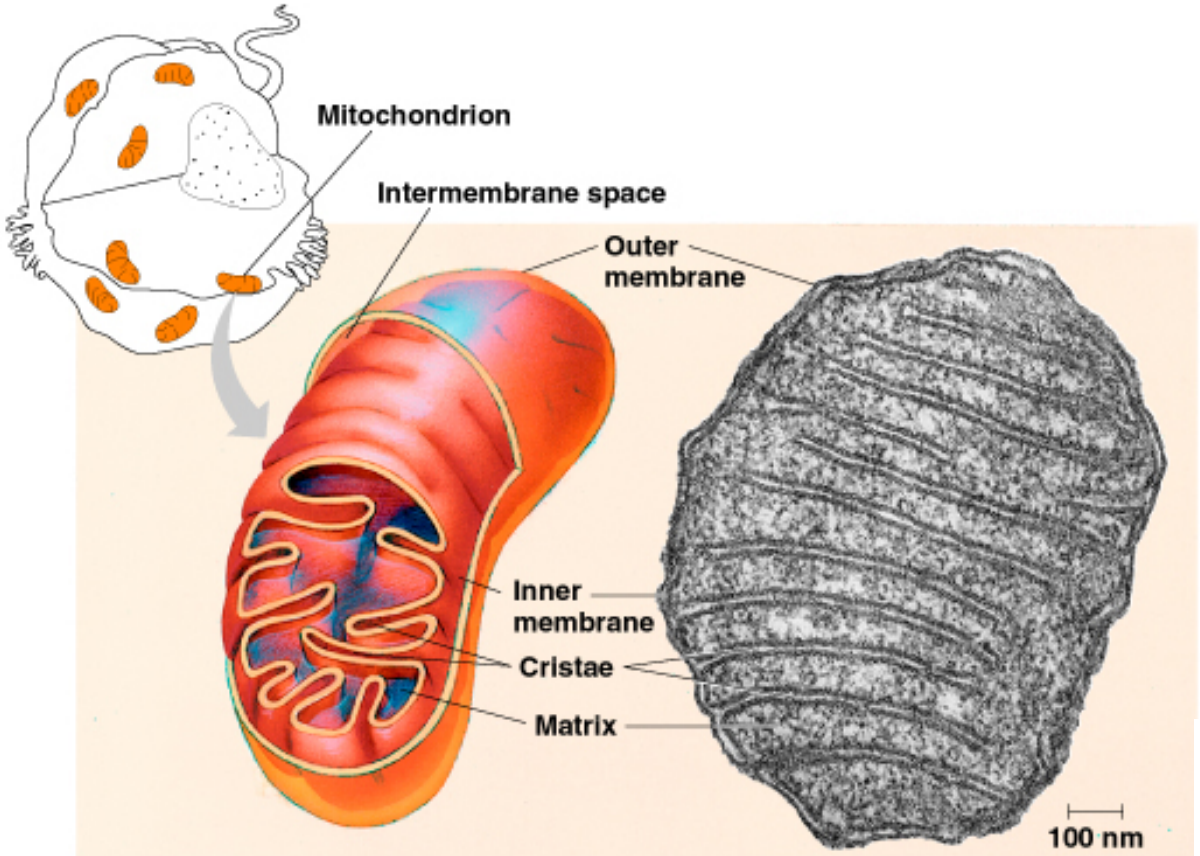
Inner membrane. The inner membrane *(red)* is folded into numerous cristae, greatly increasing its total surface area. It contains proteins with three types of functions: (1) those that carry out the oxidation reactions of the electron-transport chain, (2) the ATP synthase that makes ATP in the matrix, and (3) transport proteins that allow the passage of metabolites into and out of the matrix. An electrochemical gradient of H^+, which drives the ATP synthase, is established across this membrane, so the membrane must be impermeable to ions and most small charged molecules.

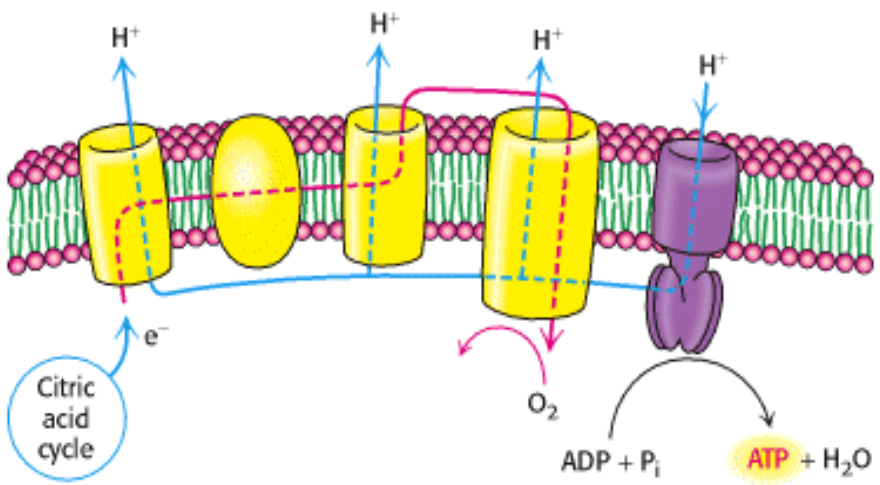
Outer membrane. Because it contains a large channel-forming protein (called porin), the outer membrane is permeable to all molecules of 5000 daltons or less. Other proteins in this membrane include enzymes involved in mitochondrial lipid synthesis and enzymes that convert lipid substrates into forms that are subsequently metabolized in the matrix.

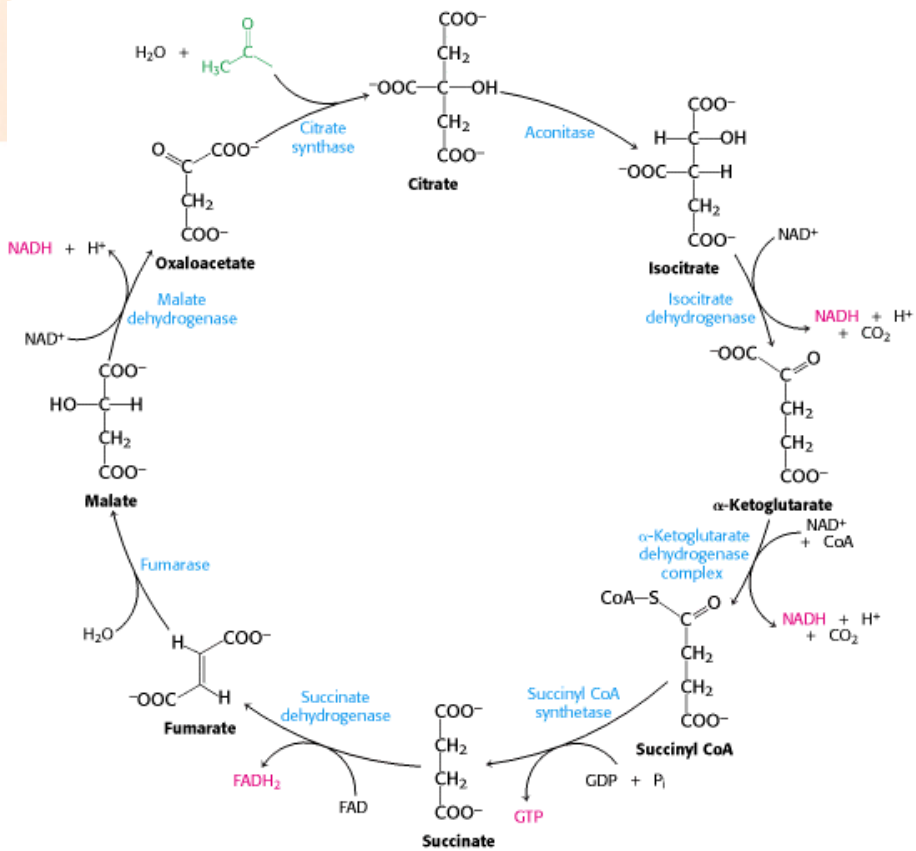
Intermembrane space. This space *(white)* contains several enzymes that use the ATP passing out of the matrix to phosphorylate other nucleotides.



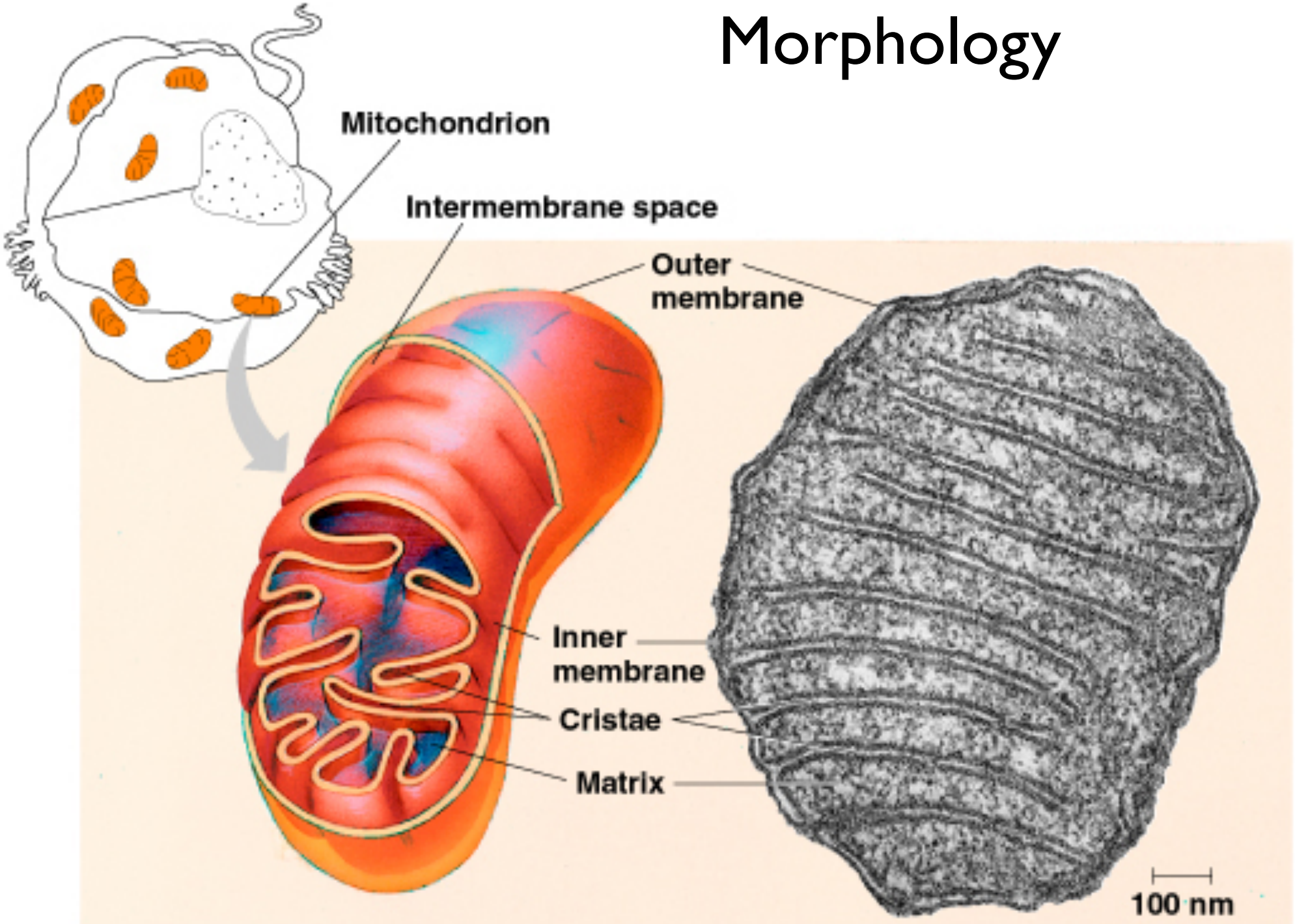
Mitochondria





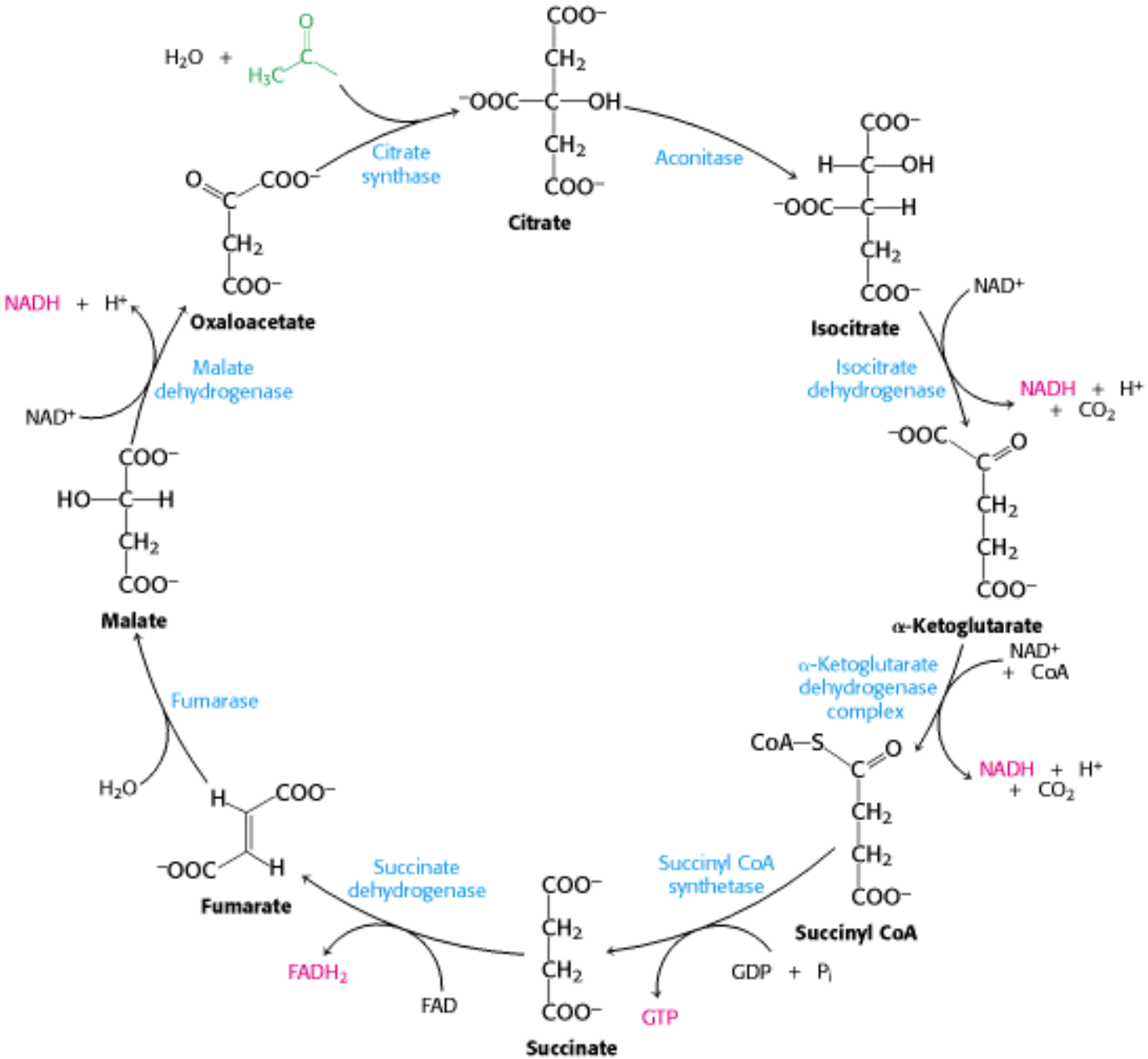


Morphology



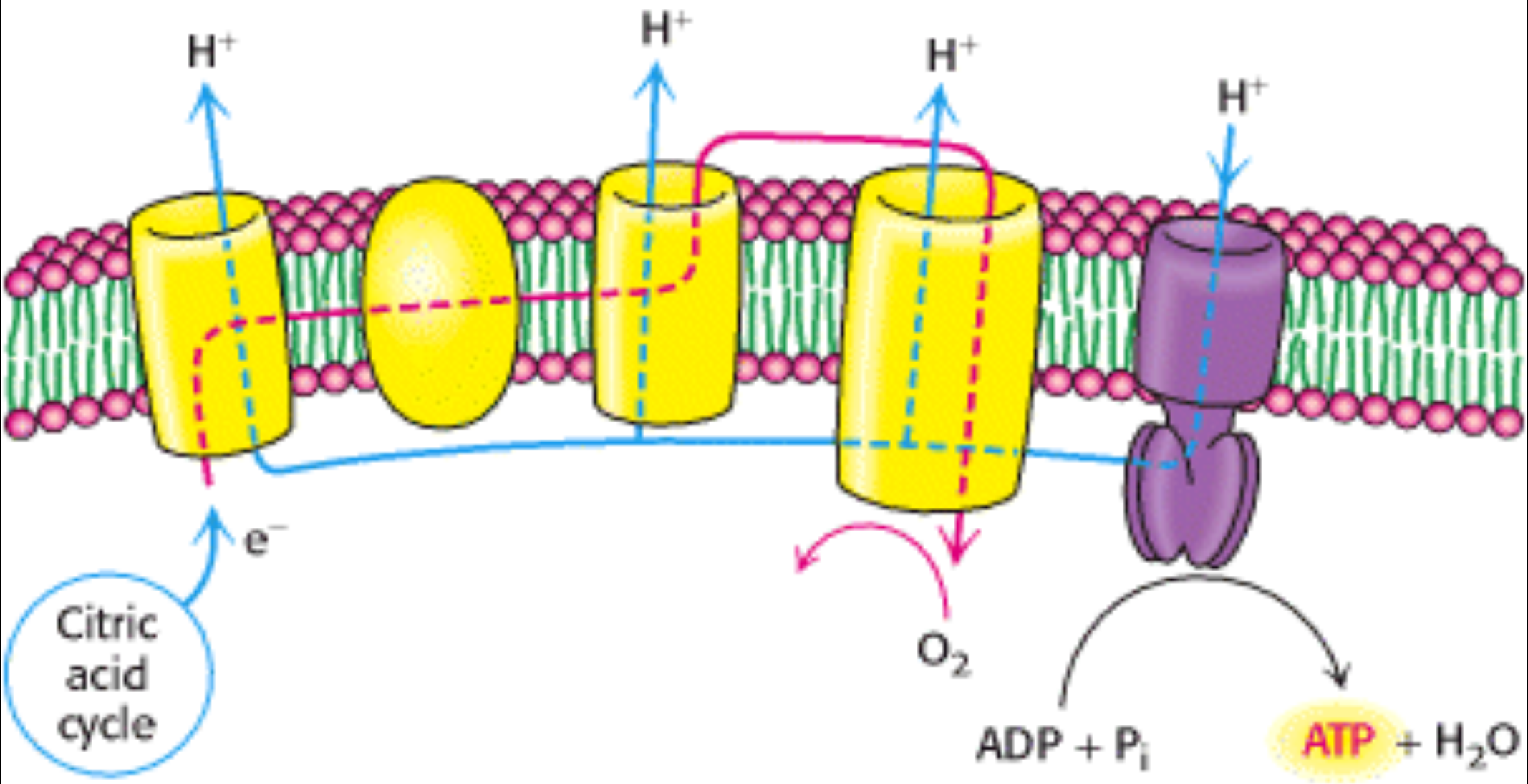
- Mitochondria have cristae and are sausage-shaped

Citric acid cycle



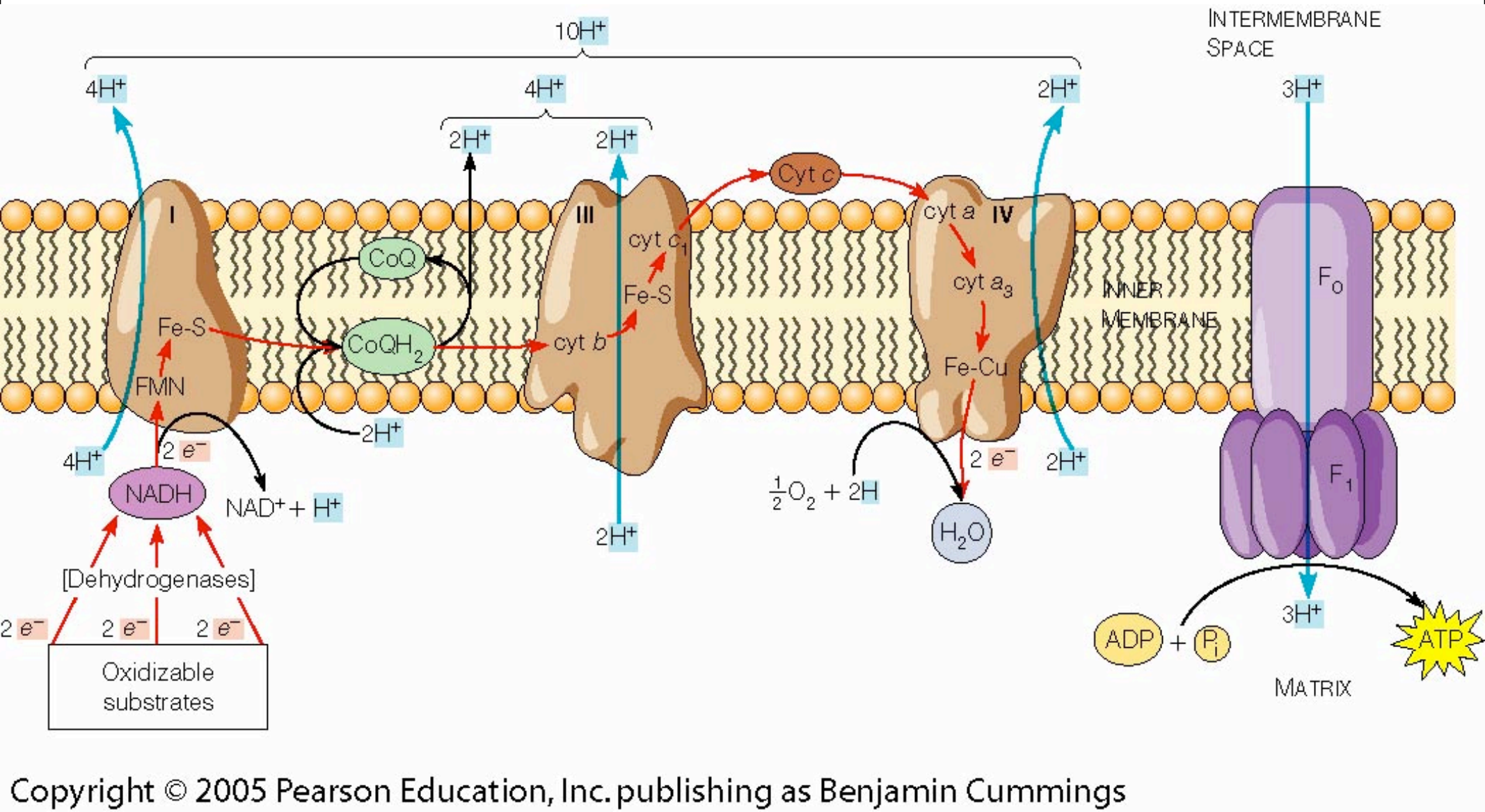
- Oxidises acetyl residues (CH_3-CO-) to carbon dioxide
- Two turns produce 8 NADH, 2 $FADH_2$, and 2 ATP
- Reducing equivalents transferred to NAD+/FAD and then to the respiratory chain

Electron transport chain



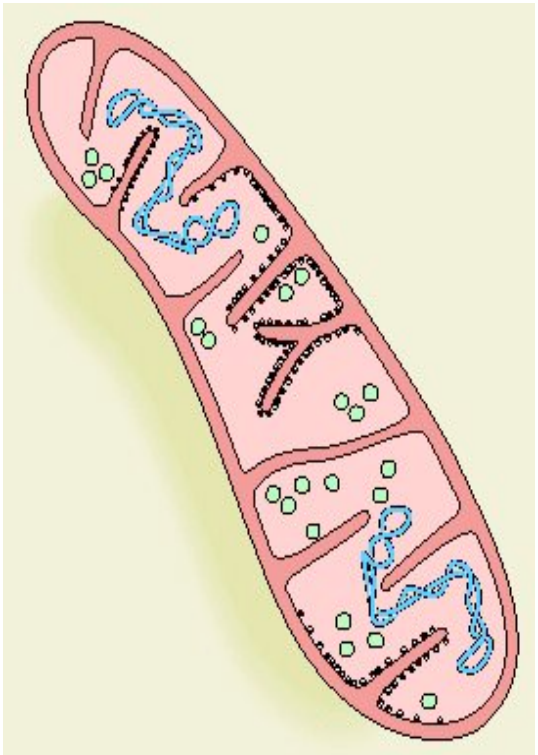
- Generates a proton motive force for ATP synthesis

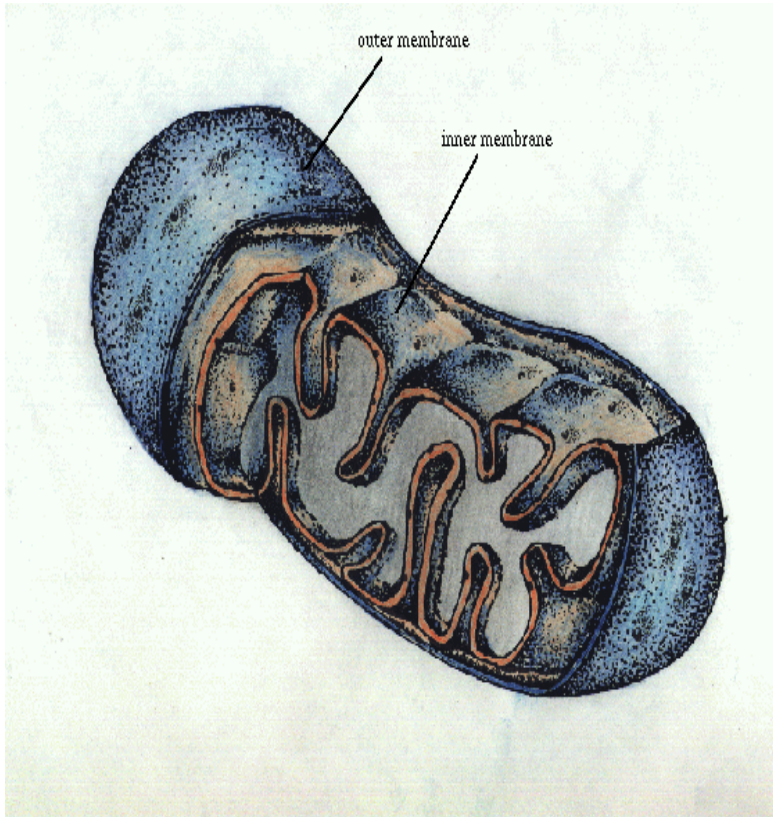
Electron transport chain

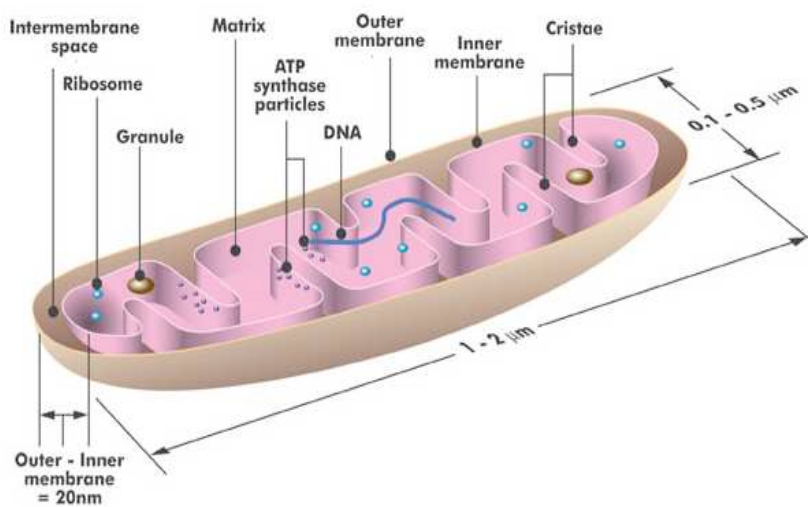


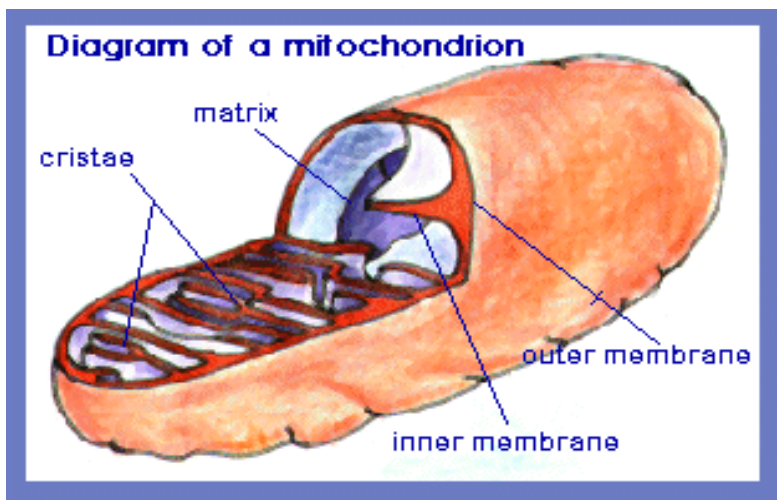
- Oxidation of reduced cofactors results in transfer of protons across membrane

Mitochondrial morphology







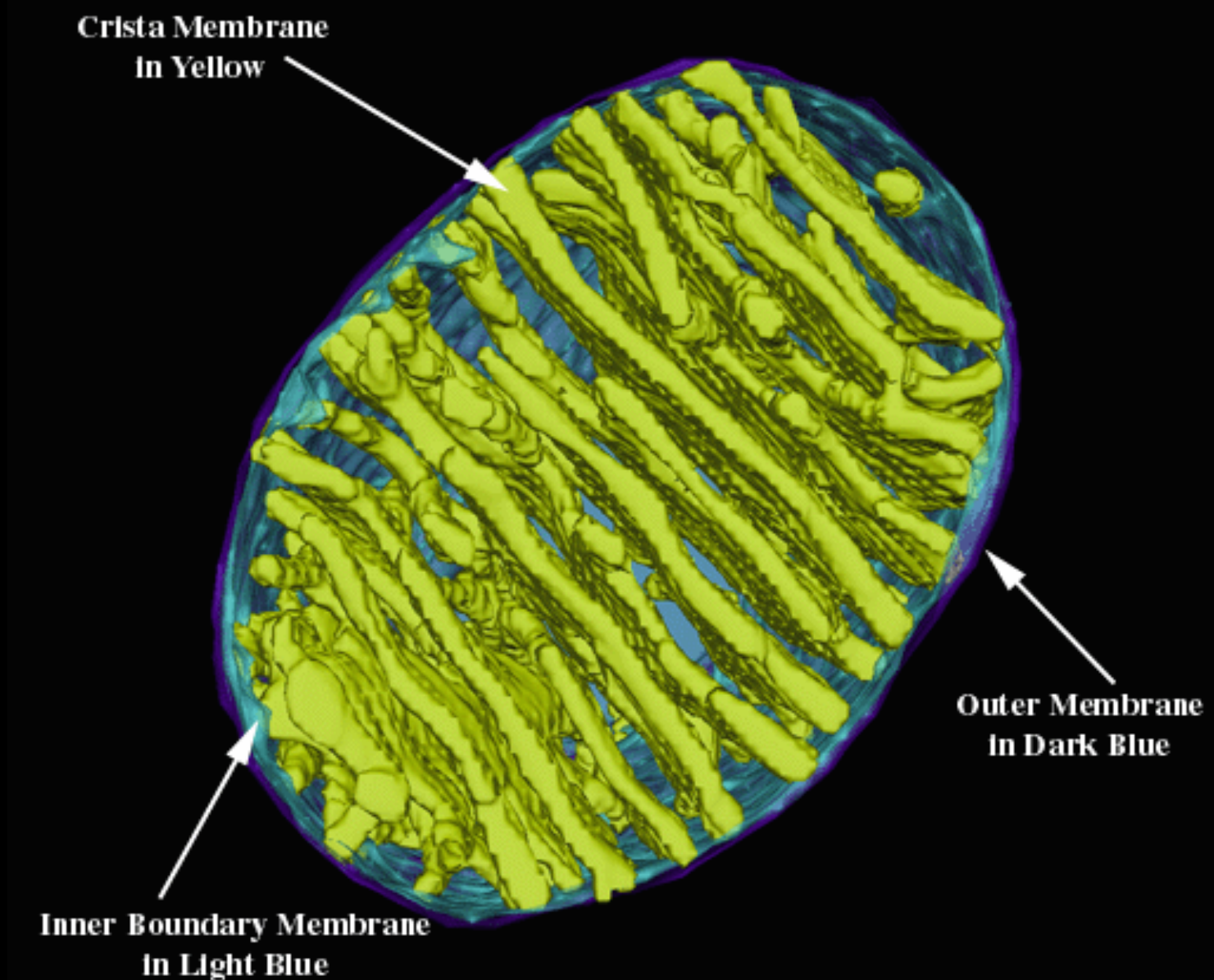


- Mitochondria are invariably sausage-shaped and have a baffles

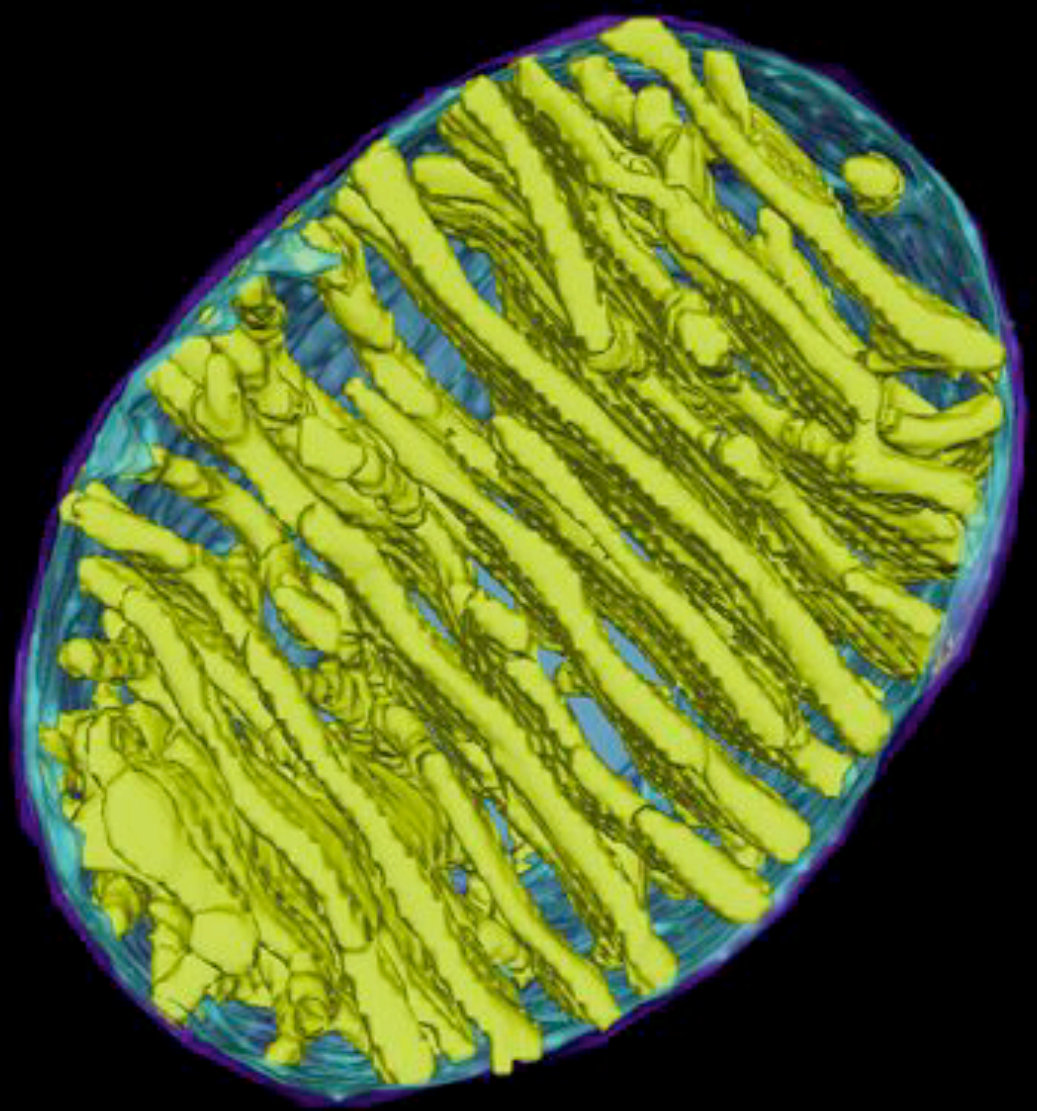
Mitochondria as we didn't know them

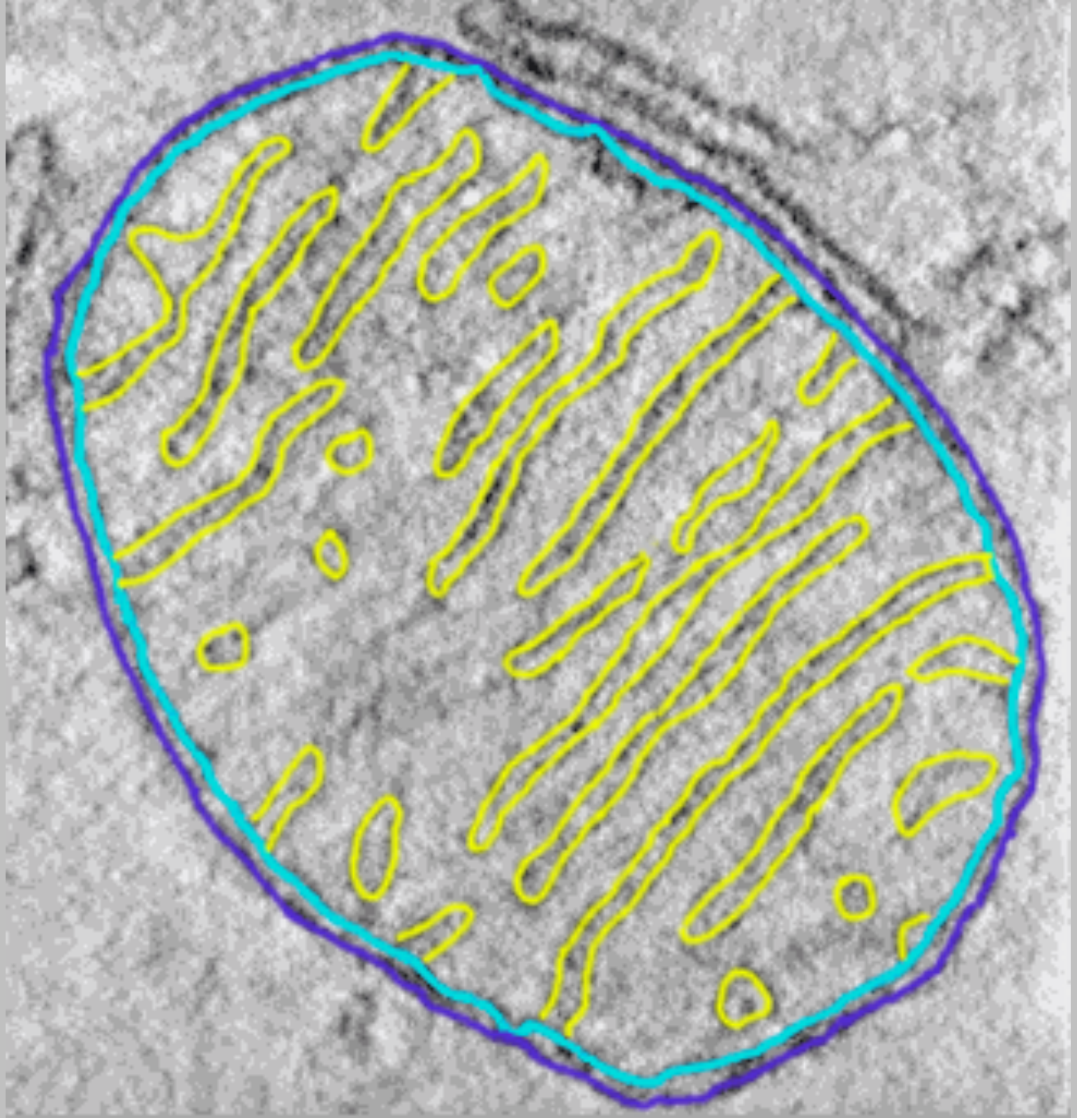
- Simple text-book depiction of cristate mitochondria is incorrect

Mitochondrial morphology

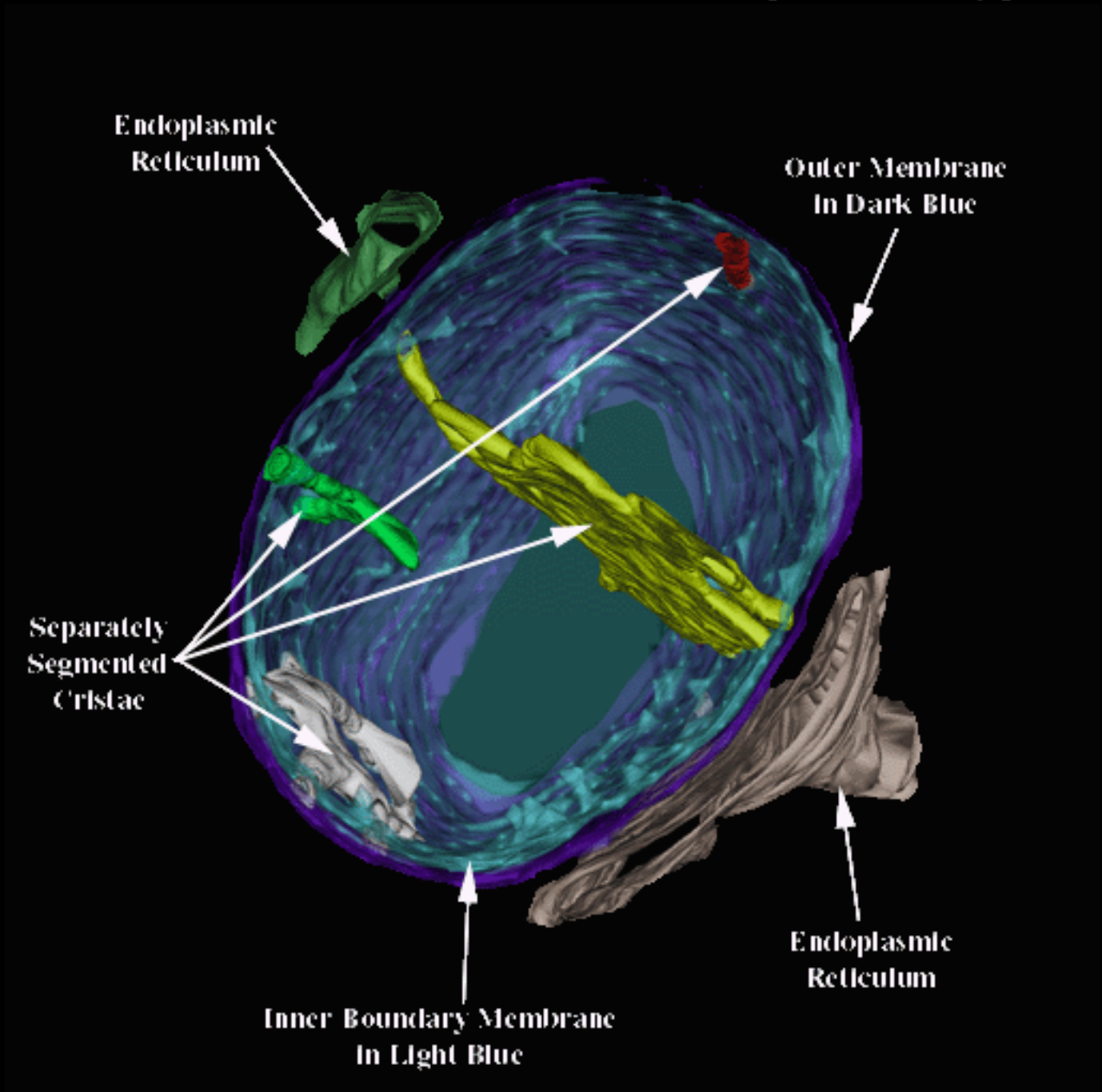


- Seems still ok

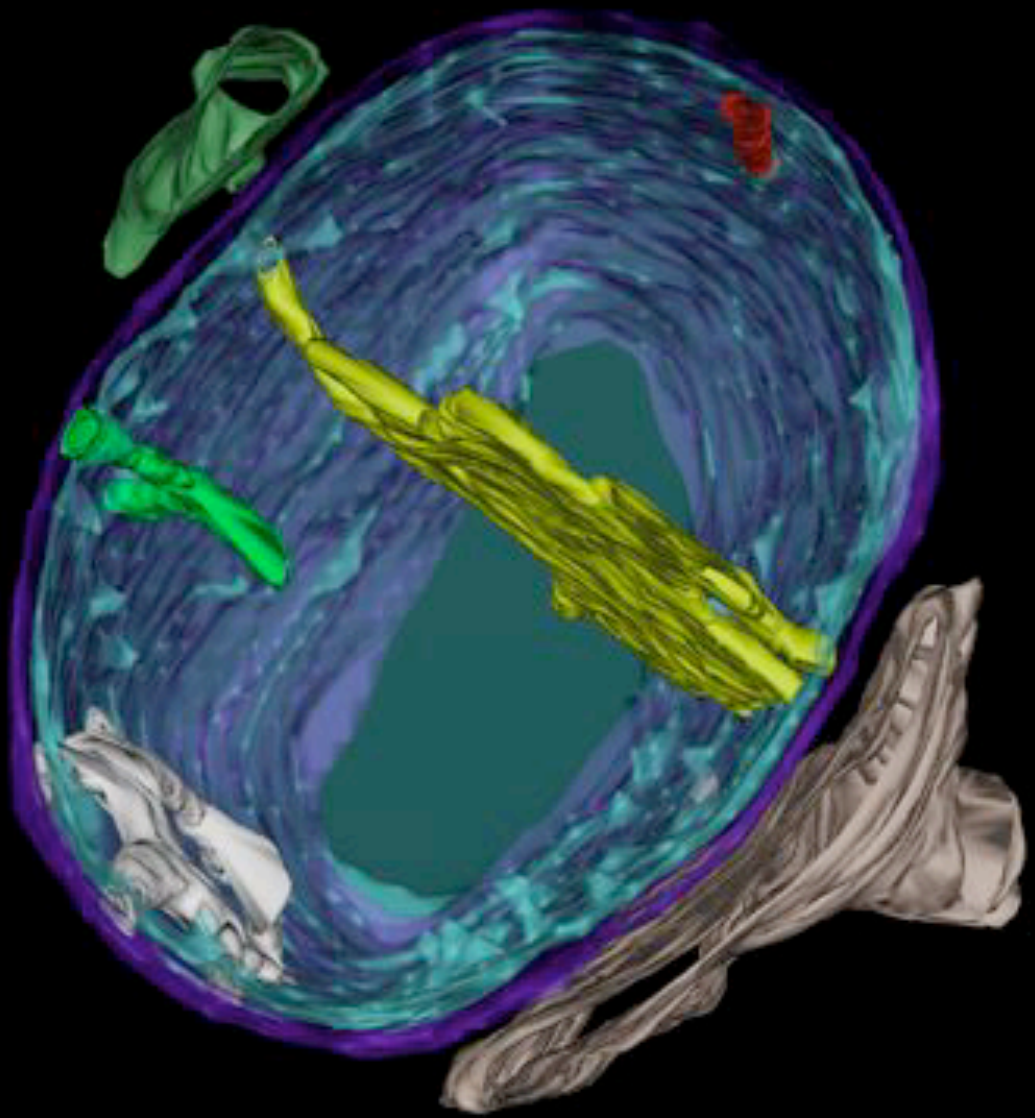




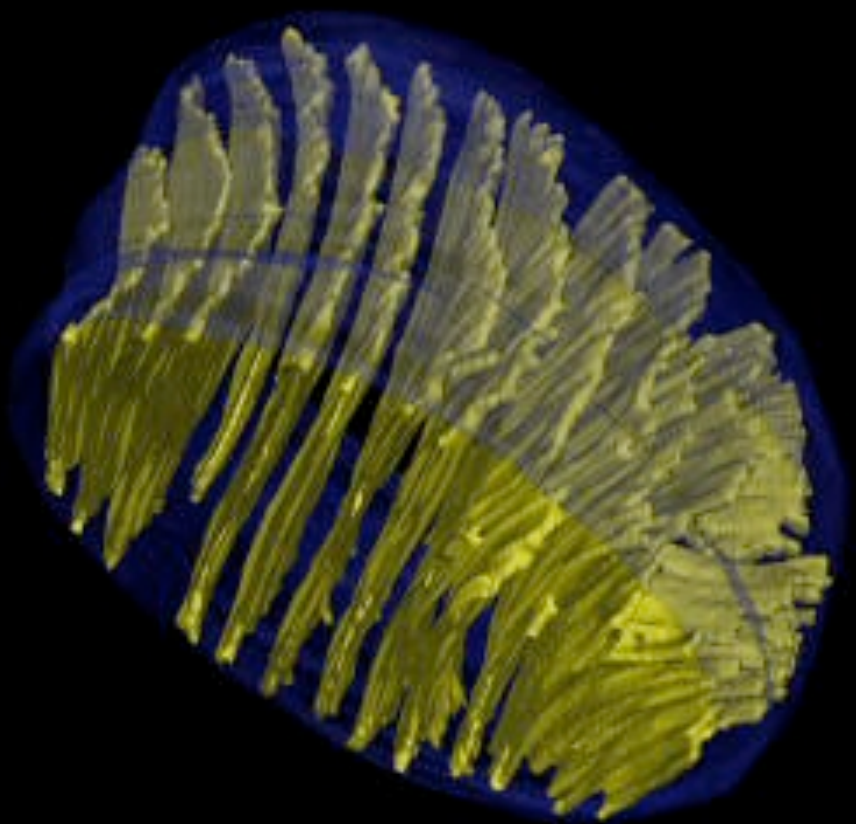
Mitochondrial morphology



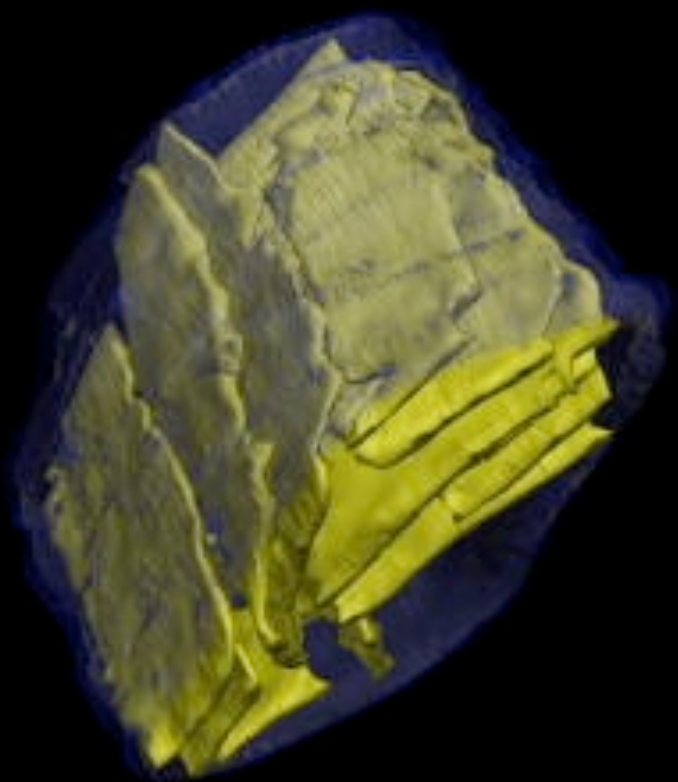
- Does not agree with text books!



Mitochondrial morphology



Brown fat adipose tissue



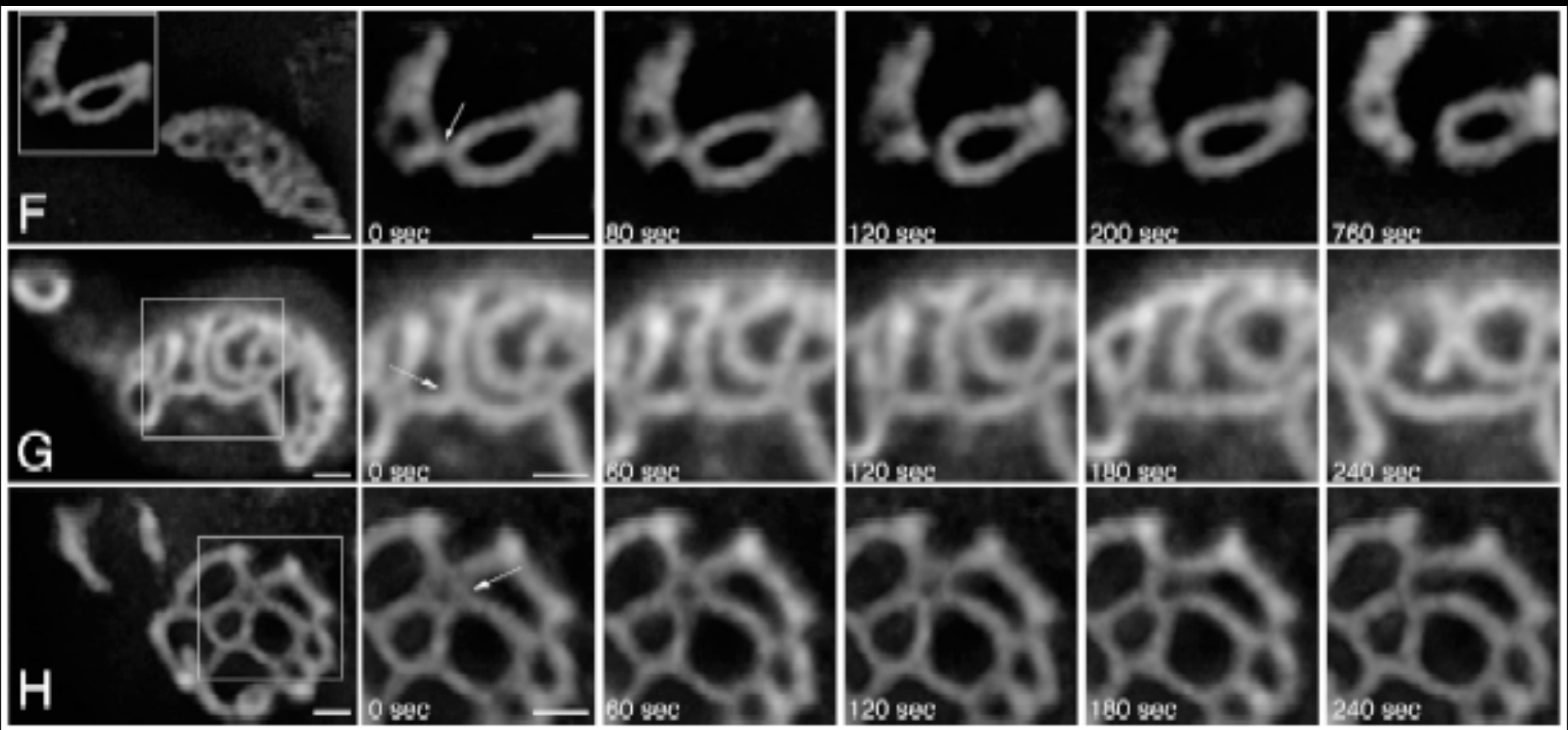
Neurospora

Terry Frey (San Diego State Univ.)
Guy Perkins (UCSD)

Mitochondrial morphology

- Mitochondria are NOT invariably sausage-shaped

Mitochondrial morphology



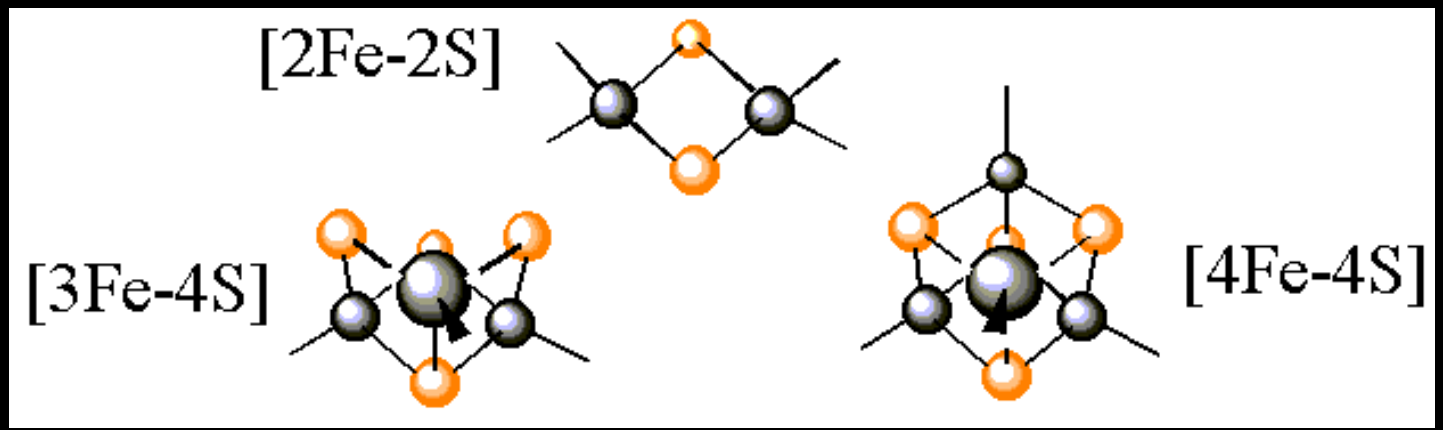
Griffin et al (2005)

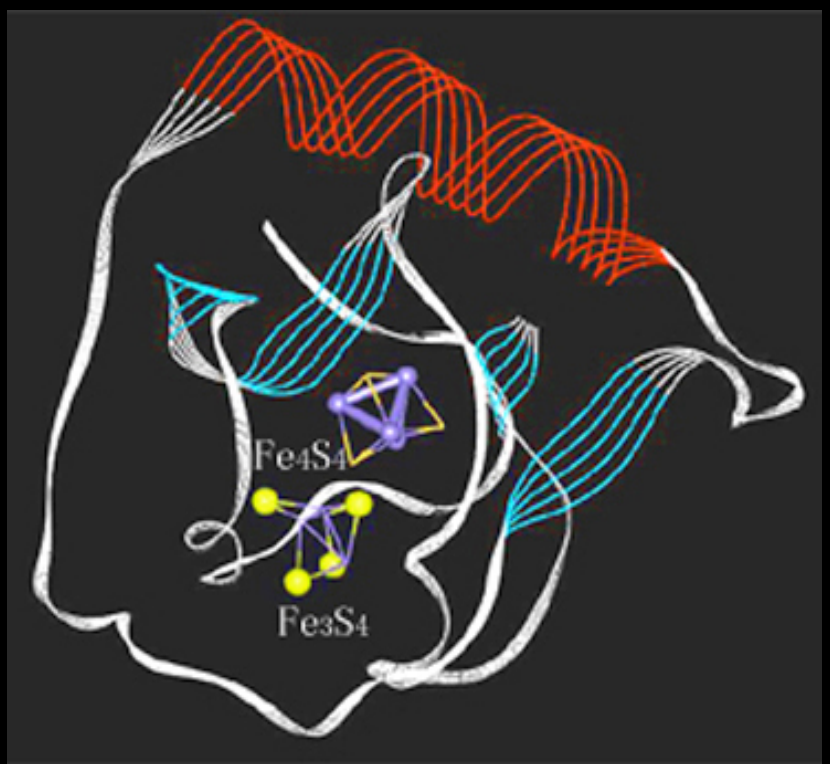
- Mitochondria form a highly dynamic network which divides and fuses continuously

Mitochondria as we didn't know them

- Mitochondria are the sites of iron-sulphur cluster assembly

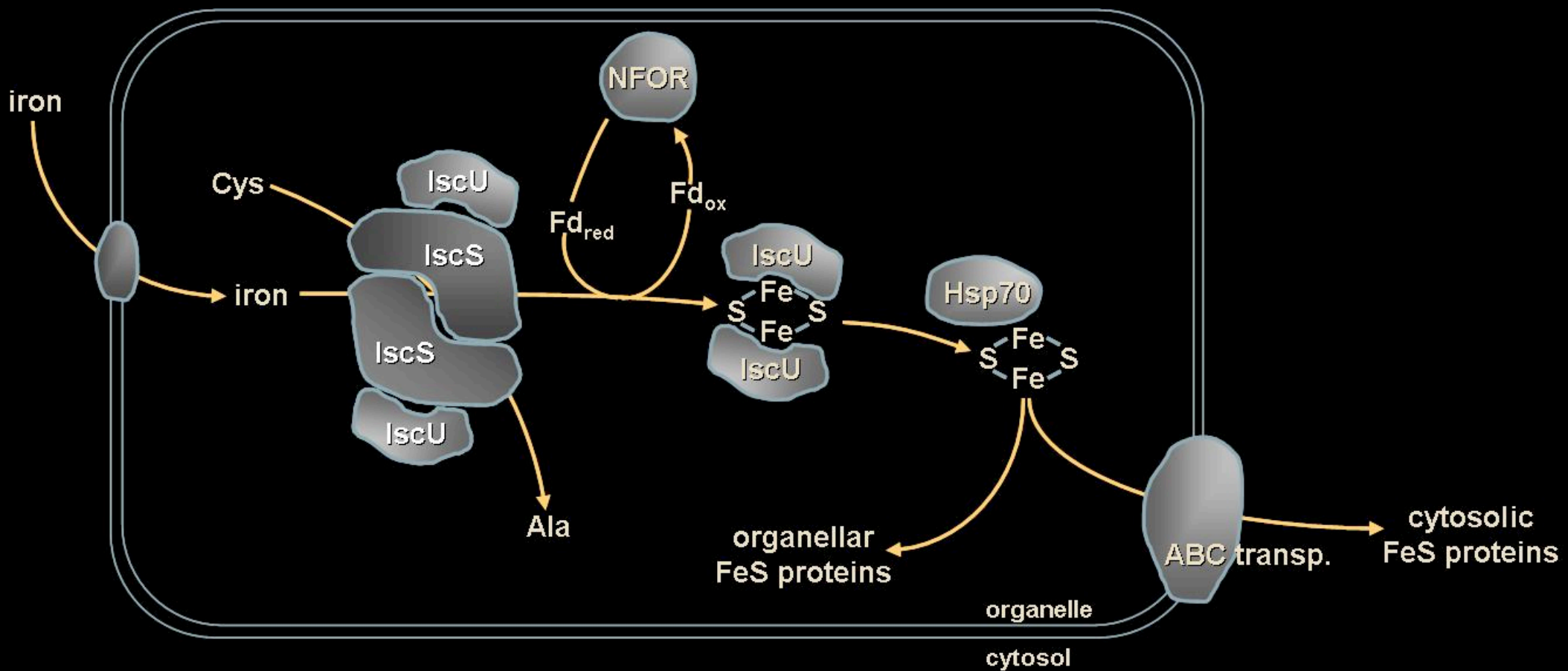
Iron sulphur clusters





- Co-factors of proteins that play an important role in metabolism, electron-transfer and regulation of gene expression

Iron sulphur clusters



- In eukaryotes mitochondria are the primary site of Fe-S cluster biogenesis

Respiration

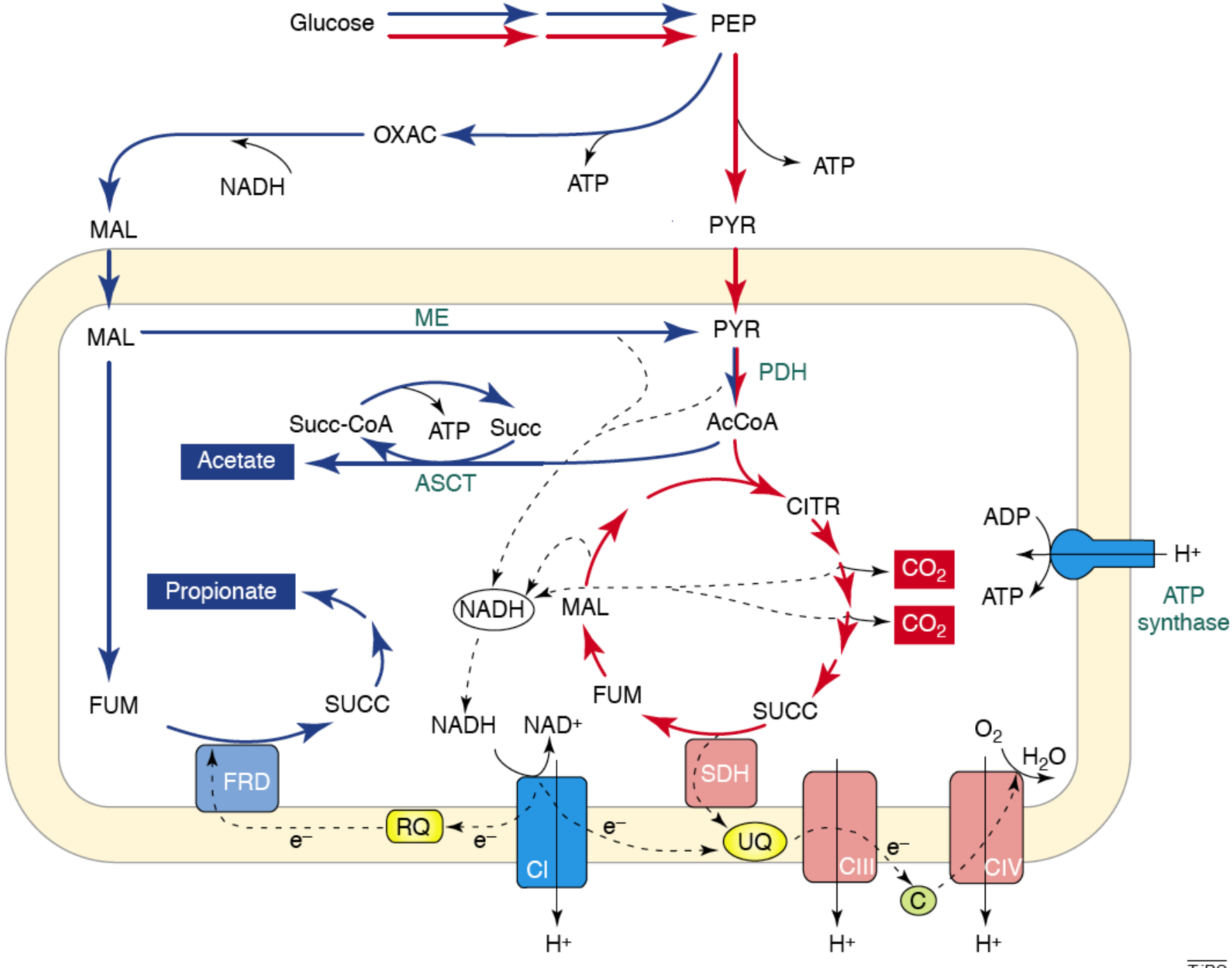
- An energy-converting series of coupled oxidation-reduction reactions in which an inorganic chemical compound or element is the terminal electron acceptor

Fermentation

- An energy-converting series of coupled oxidation-reduction reactions in which an organic chemical compound is the terminal electron acceptor

Mitochondria as we didn't know them

- Some mitochondria carry out anaerobic respiration and anaerobic oxidative phosphorylation

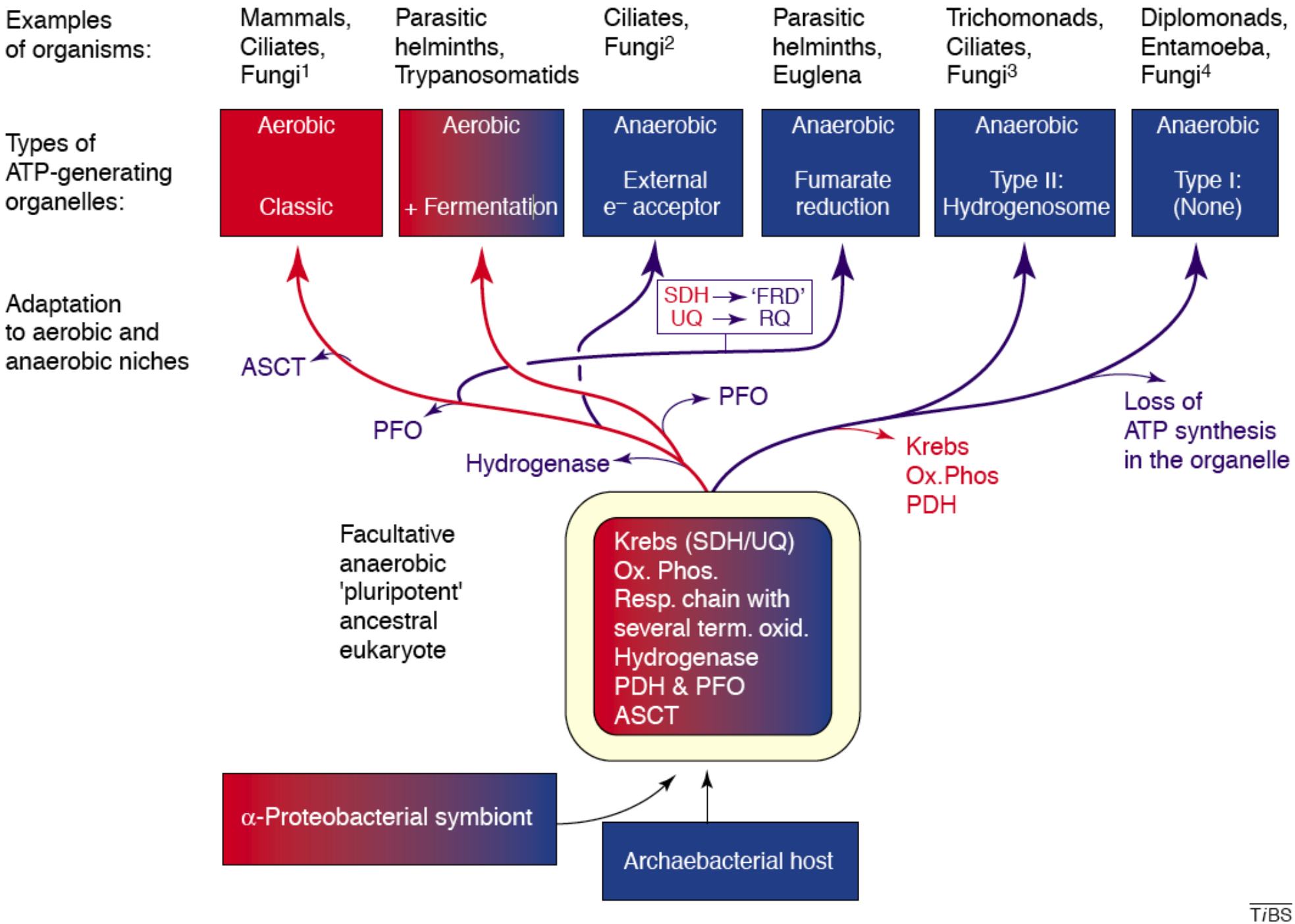


Comparison of mitochondrial carbohydrate metabolism in aerobically and anaerobically functioning mitochondria. As an example, the main pathways of aerobic (red arrows) and anaerobic (blue arrows) metabolism in Fasciola hepatica are shown [11]. Transport of electrons is shown in dashed arrows and end products are shown in boxes. Abbreviations: AcCoA, acetyl-CoA; ASCT, acetate:succinate CoA-transferase; C, cytochrome c, C I, complex I; C III, complex III; CIV, complex IV; CITR, citrate; FRD, fumarate reductase; FUM, fumarate; MAL, malate; ME, malic enzyme; OXAC, oxaloacetate; PDH, pyruvate dehydrogenase; PEP, phosphoenolpyruvate; PYR, pyruvate; RQ, rhodoquinone; SDH, succinate dehydrogenase; SUCC, succinate; Succ-CoA, succinyl-CoA; UQ, ubiquinone.

	Examples	Group	Respiratory Chain		Main end products[a]	Characteristic components[b]	Refs
			e^- donor	e^- acceptor			
Aerobic (classical)							
Unicellular	*Saccharomyces*	Yeast	$NADH, FADH_2$	O_2	CO_2, H_2O	–	[56]
Metazoa	*Homo, Arabidopsis*	Mammals, plants	$NADH, FADH_2$	O_2	CO_2, H_2O	–	

Characteristics of various types of mitochondria

Tielens, Rotte, Hellemond & Martin (2002) Mitochondria as we don't know them. *Trends Biochem Sci* 27: 564-572.



Evolutionary relations between distinct energy generating organelles

Abbreviations: ASCT, acetate:succinate CoA-transferase; FRD, fumarate reductase; Ox.Phos., oxidative phosphorylation; PDH, pyruvate dehydrogenase; PFO, pyruvate:ferredoxin oxidoreductase; Resp., respiratory; RQ, rhodoquinone; SDH, succinate dehydrogenase; term. oxid., terminal oxidases; UQ, ubiquinone.

Summary

- Mitochondria are central to the cell's energy metabolism
- Mitochondria are highly dynamic and continuously fuse and divide
- Mitochondria play an essential role in the assembly of FeS clusters
- Mitochondria can perform *anaerobic respiration*

Reading

- Lane & Martin (2010) *The energetics of genome complexity.* Nature 467: 929-934.
- Frey & Mannella (2000) The internal structure of mitochondria. *Trends Biochem Sci* 25: 319-324.
- Lill & Muhlenhoff (2005) Iron-sulfur-protein biogenesis in eukaryotes. *Trends Biochem Sci* 30:133-141.
- Tielens, Rotte, Hellemond & Martin (2002) Mitochondria as we don't know them. *Trends Biochem Sci* 27: 564-572.
- Martin & Müller (1998) The hydrogen hypothesis for the first eukaryote. *Nature* 392: 37-41.

Lecture 4

Why do chloroplasts and mitochondria have genomes?