

The University of Adelaide
School of Molecular and Biomedical Science
Molecular Life Sciences Building, 11th March 2009

Genes in organelles

Mitochondria, ageing, and sex – energy versus fidelity

John F. Allen* and Carol A. Allen

*Australian Academy of Science Rudi Lemberg Travelling Fellow

School of Biological and Chemical Sciences, Queen Mary, University of London

www.jfallen.org



Queen Mary
University of London

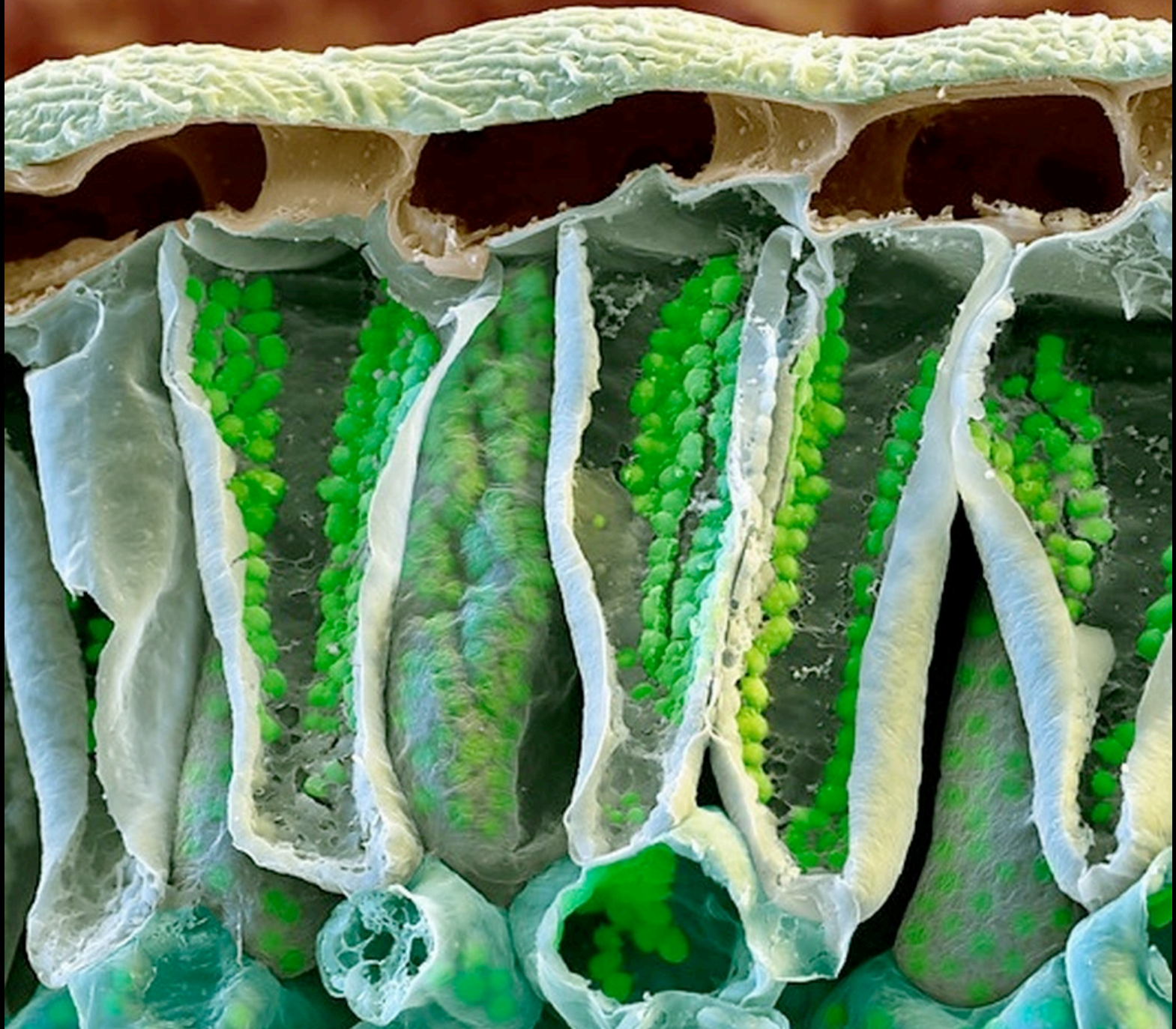


Max Rudolph Lemberg

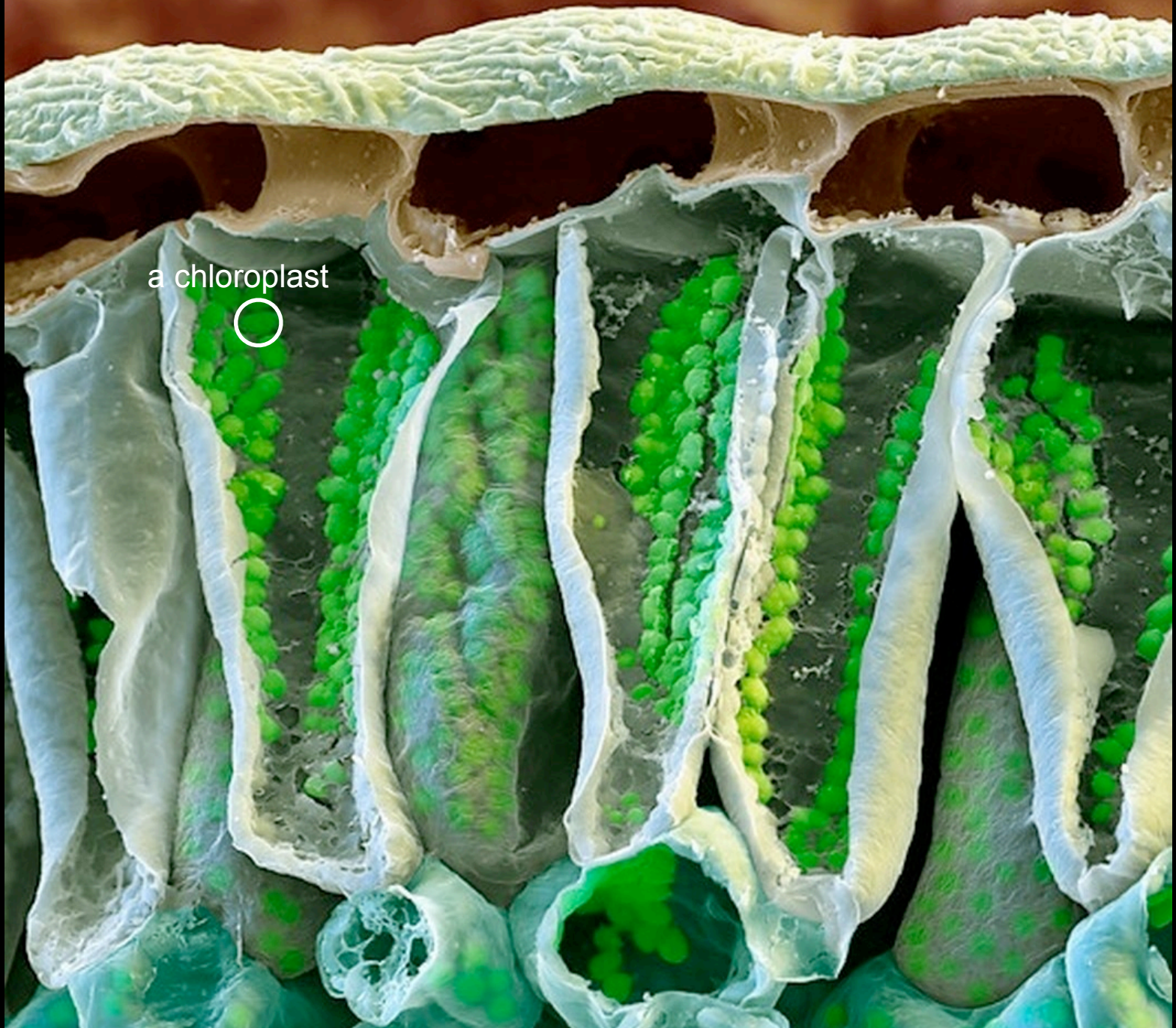
1896-1975

A watercolor illustration of a cell. The cell is depicted as a large, irregular shape with a brownish-orange interior. A large, dark brown circular nucleus is located in the upper left quadrant. The cytoplasm is filled with numerous small, yellow, oval-shaped organelles, likely mitochondria, scattered throughout. The cell is surrounded by a light yellow background. Several dark blue, irregular shapes are scattered around the cell, possibly representing other organelles or molecules. The text "Genes in organelles" is written in a bold, yellow, sans-serif font across the center of the cell.

Genes in organelles



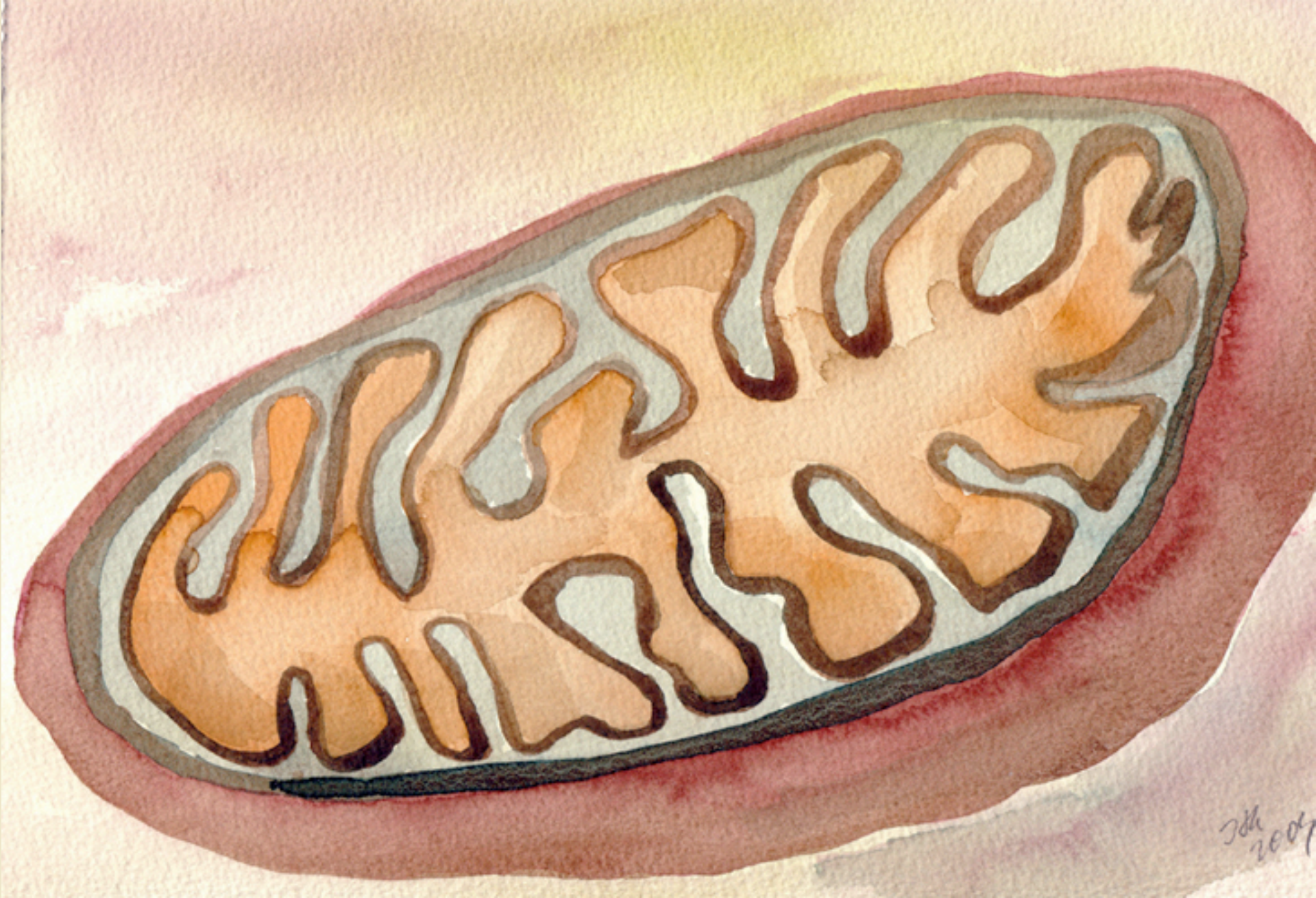
'Christmas-Rose' leaf SEM cross-section; Science Photo Library (SPL)



a chloroplast



'Christmas-Rose' leaf SEM cross-section; Science Photo Library (SPL)



A mitochondrion—one of many tiny power-houses within cells that control our lives in surprising ways

© Ina Schuppe-Koistinen

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Why?

Inter-membrane space

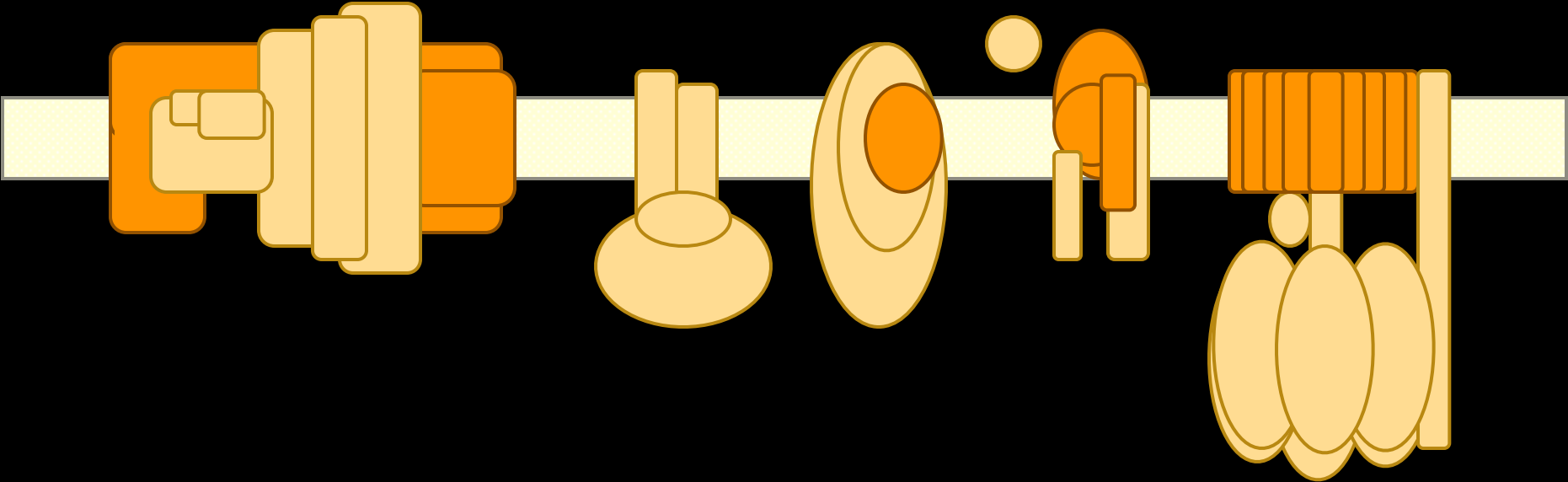
I

II

III

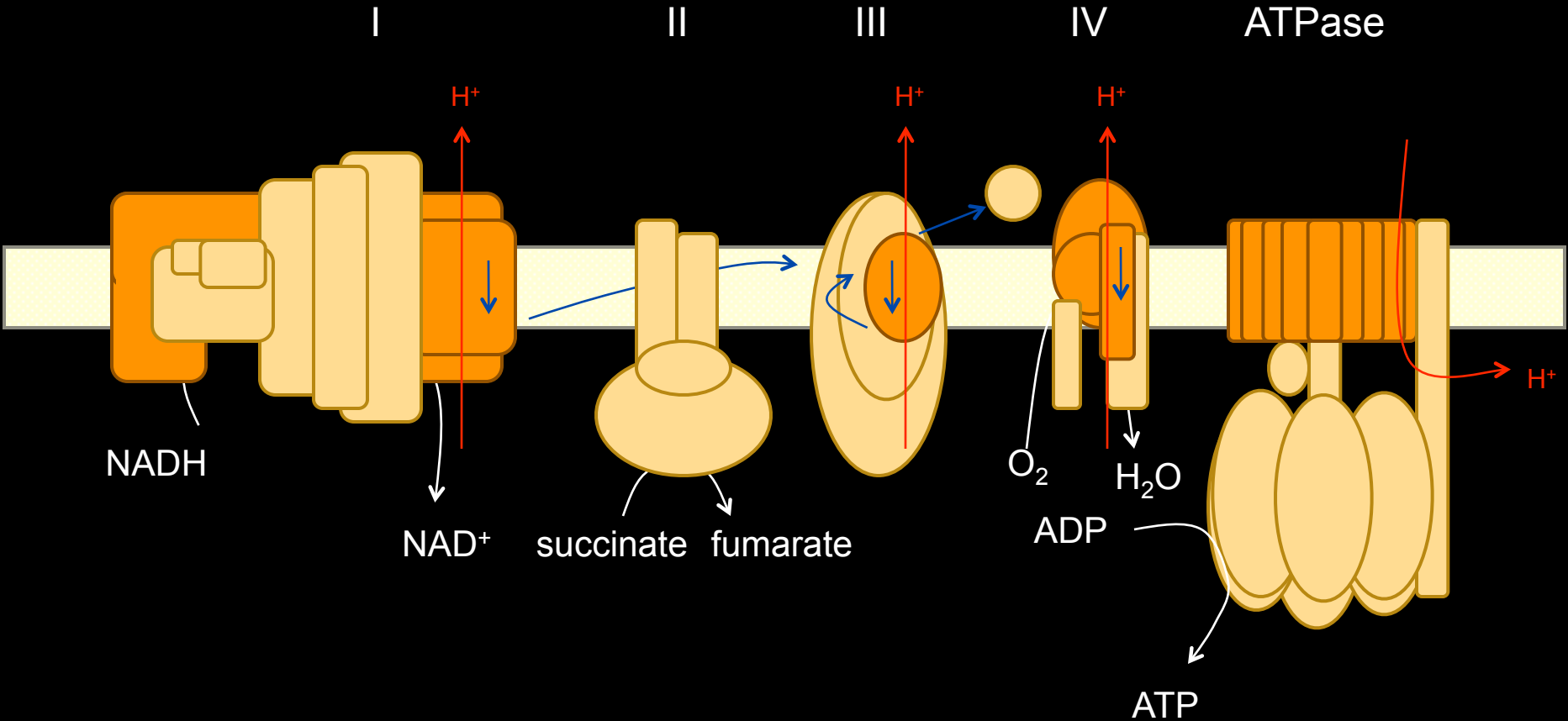
IV

ATPase

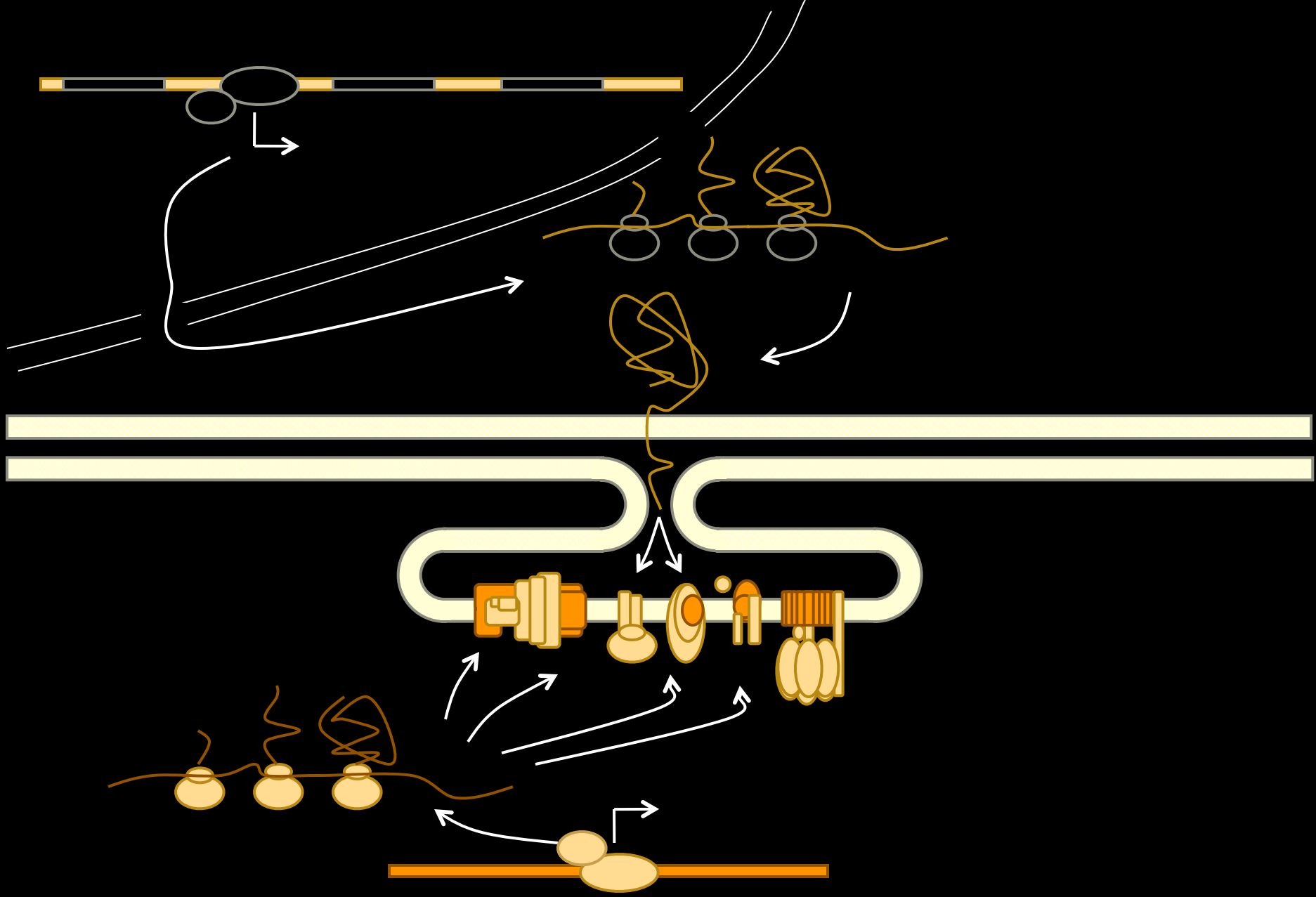


Mitochondrial matrix

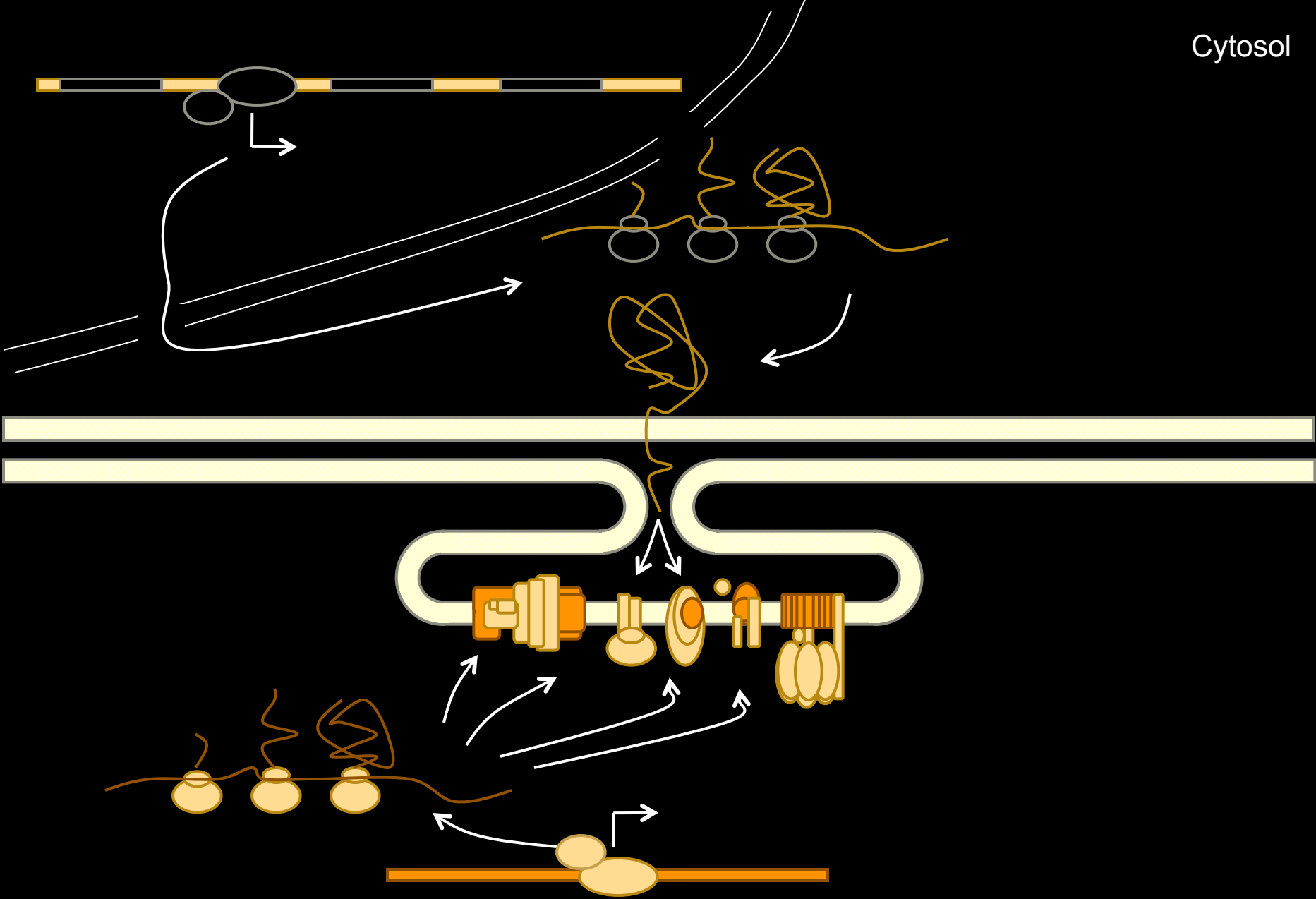
Inter-membrane space



Mitochondrial matrix



Cytosol



Mitochondrial matrix

Why Do Mitochondria and Chloroplasts Have Their Own Genetic Systems?

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Mitochondrial DNA is a relic of ancient history. It is a legacy from a single aerobic bacterium that took up residence in the cytoplasm of a primitive cell that ultimately became an ancestor of all eukaryotic cells. Most of the genes of this ancient symbiont were either lost or transferred over the course of evolution to the nucleus of the host cell, leaving only a handful of genes to encode some of the most hydrophobic proteins of the inner mitochondrial membrane.

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At one time, it was suggested that some proteins have to be made in the organelle because they are too hydrophobic to get to their site in the membrane from the cytosol. More recent studies, however, make this explanation implausible. In many cases, even highly hydrophobic subunits are synthesized in the cytosol.

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Molecular Biology of the Cell

Alberts B, Johnson A, Lewis J, Raff M, Roberts K, and Walter P Molecular Biology of the Cell. Fifth Edition. New York and London: Garland Science; 2007

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Hypothesis: The location of these genetic systems has a selective advantage, since energy conversion, in order to be both safe and efficient, requires a set of proteins whose genes reside with them, in the same compartment of the cell.

CoRR - **Co**-Location for **Redox*** **R**egulation.

CoRR applies equally to mitochondria and chloroplasts

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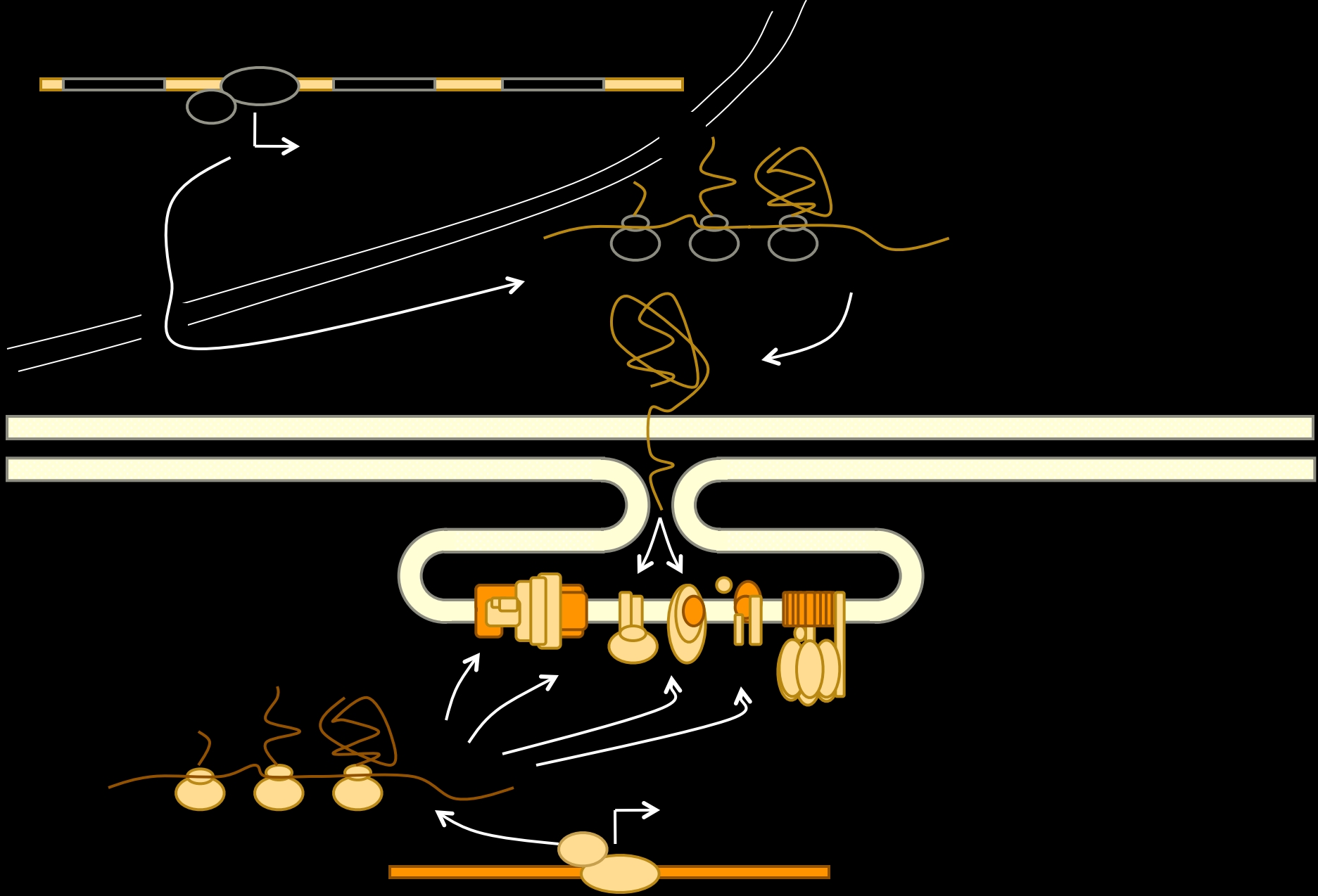
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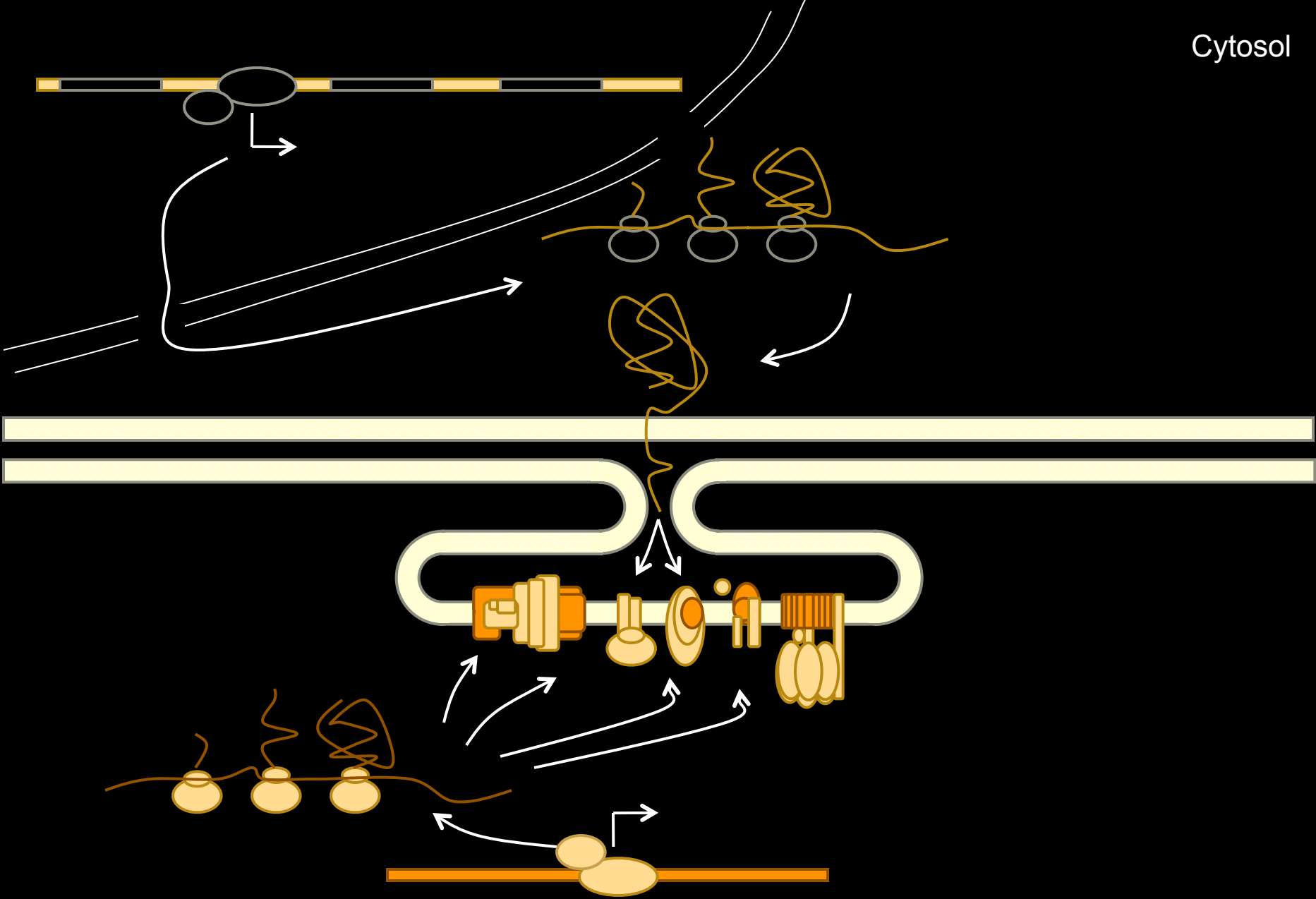
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Allen JF (1993) Control of Gene Expression by Redox Potential and the Requirement for Chloroplast and Mitochondrial Genomes. *Journal of Theoretical Biology* **165**: 609-631

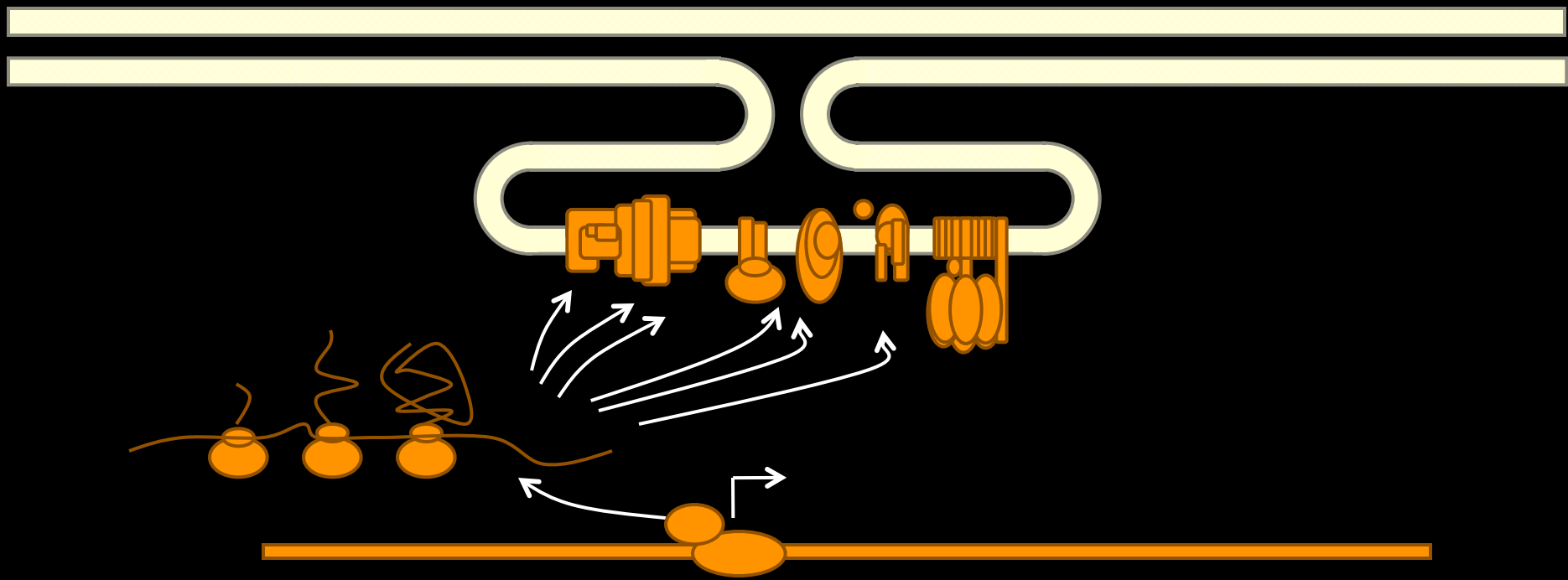
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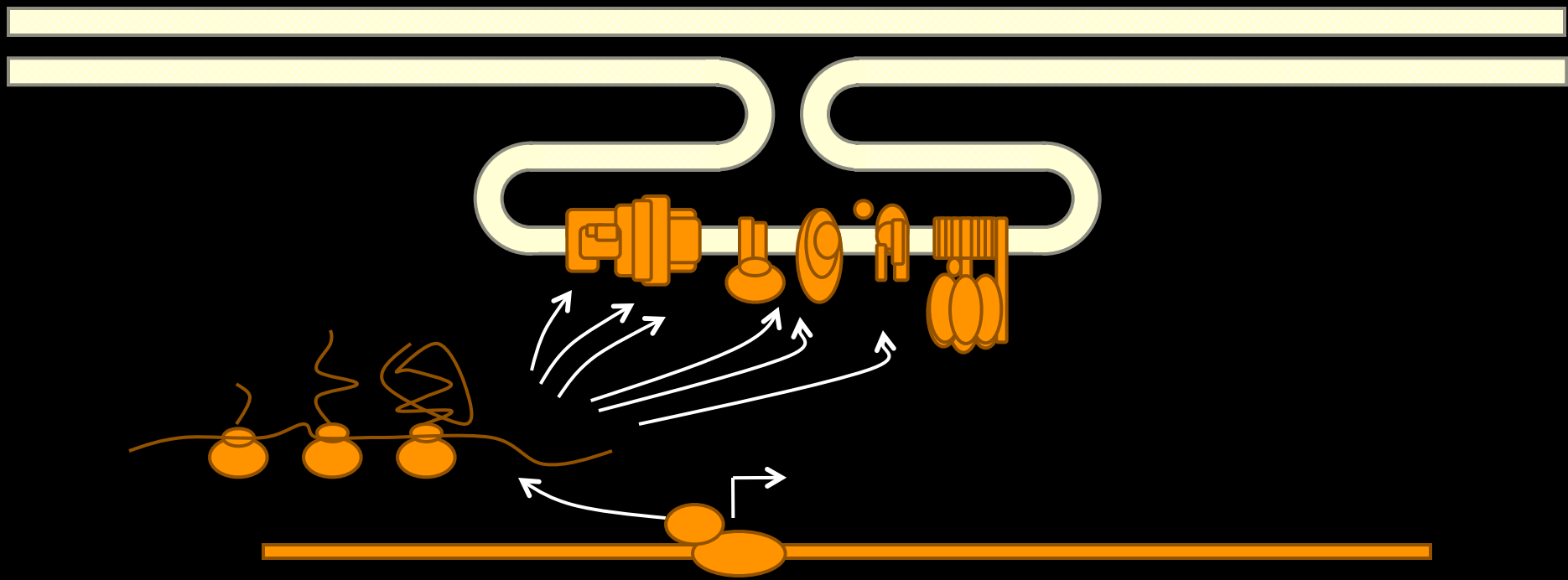


Cytosol

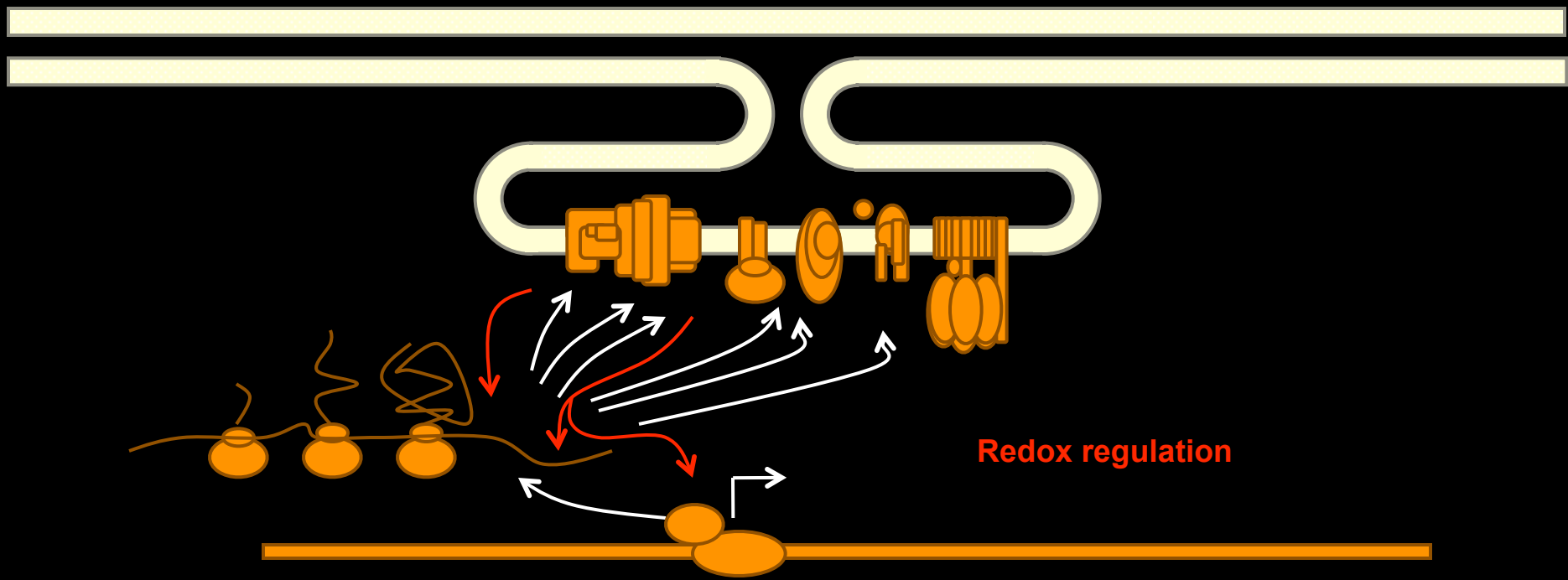


Mitochondrial matrix



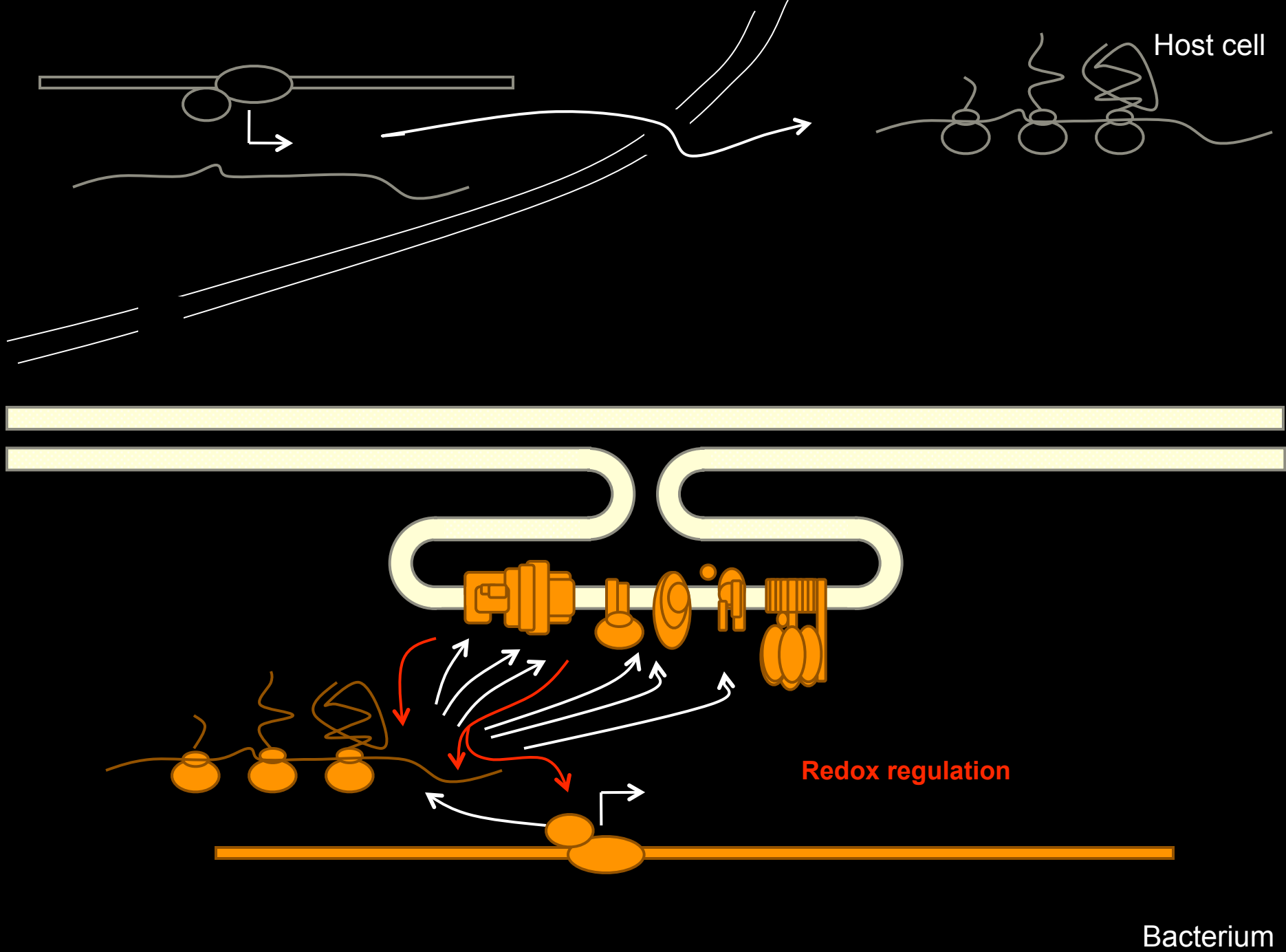


Bacterium

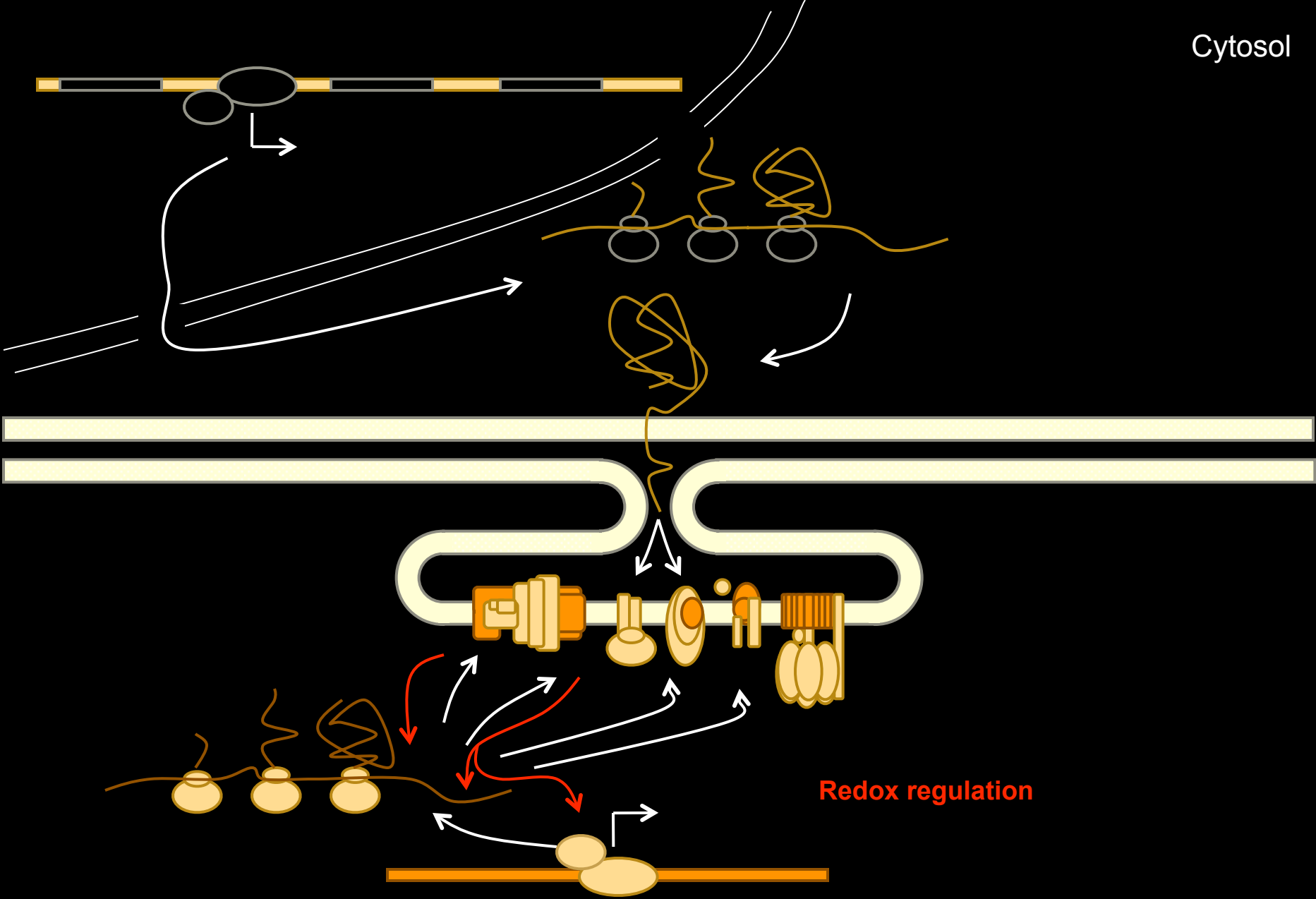


Redox regulation

Bacterium



Cytosol



Redox regulation

Mitochondrial matrix

CoRR

Co-Location (of gene and gene product)
for **R**edox **R**egulation

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Predictions of the **CoRR** hypothesis include:

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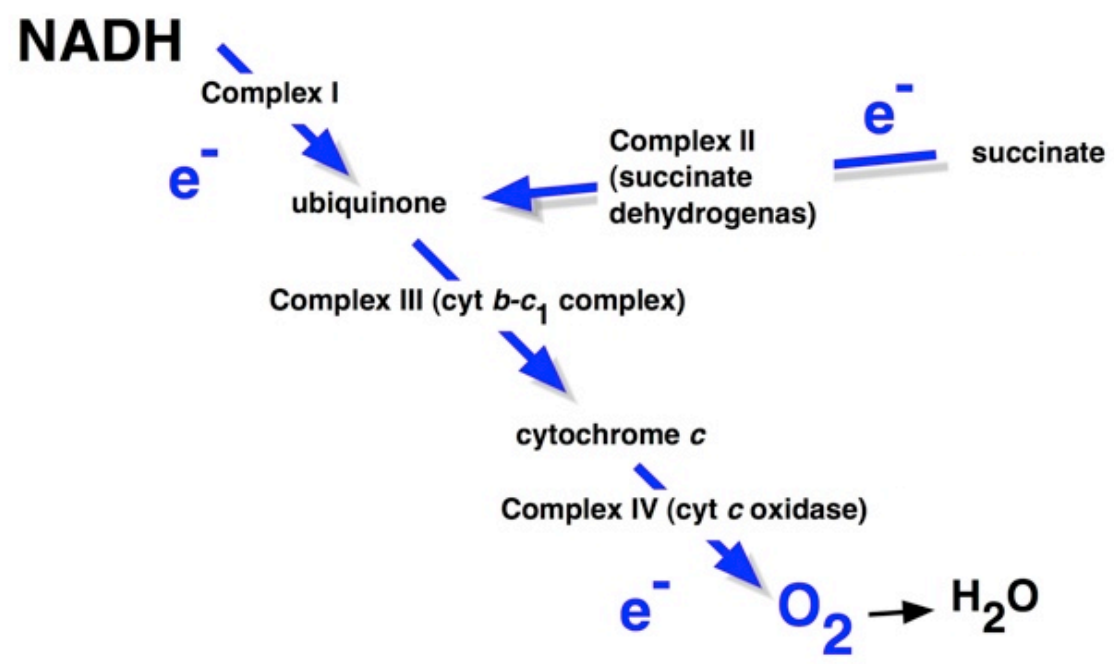
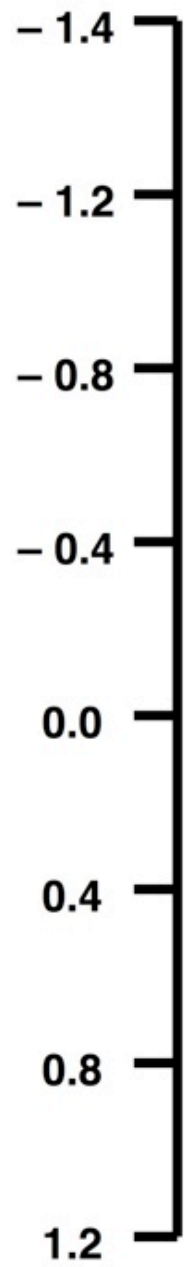
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- 5.....

Co-location for Redox Regulation - CoRR

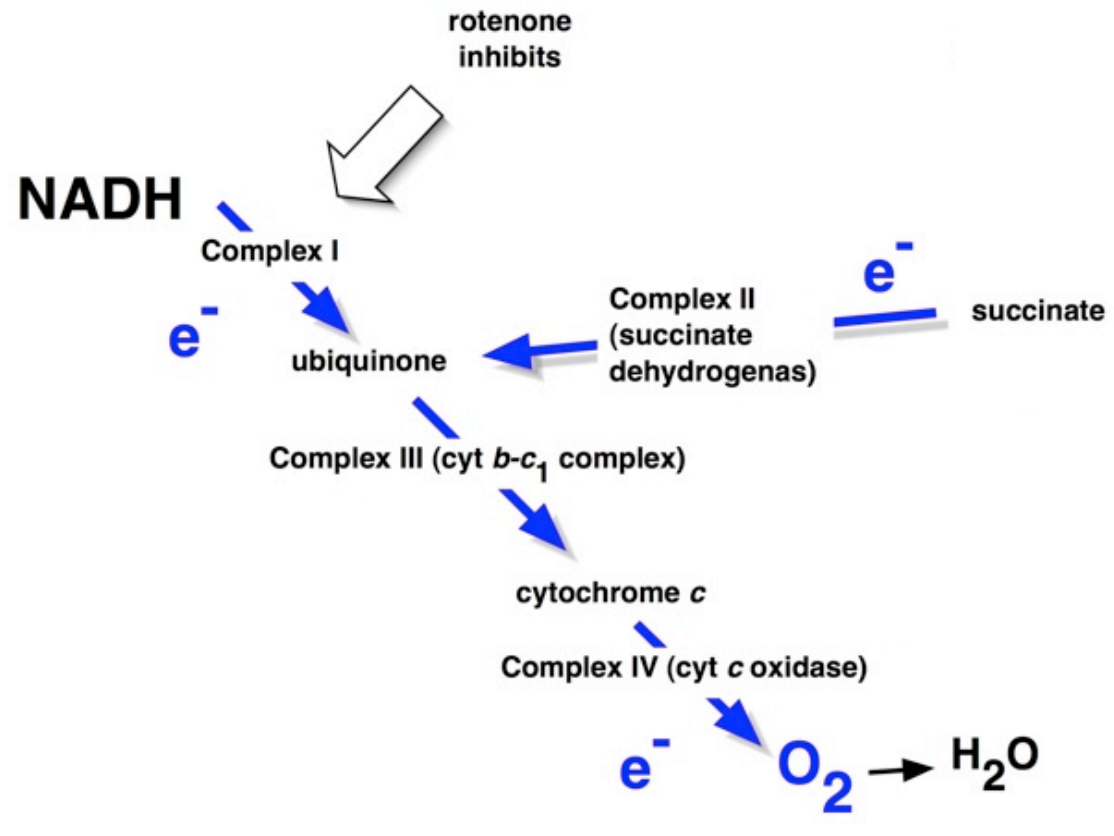
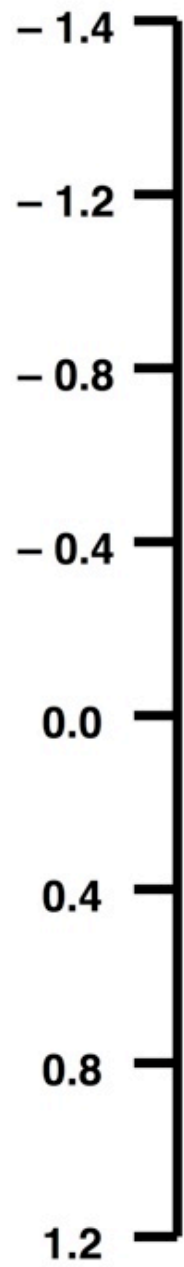
Prediction

Experimental results

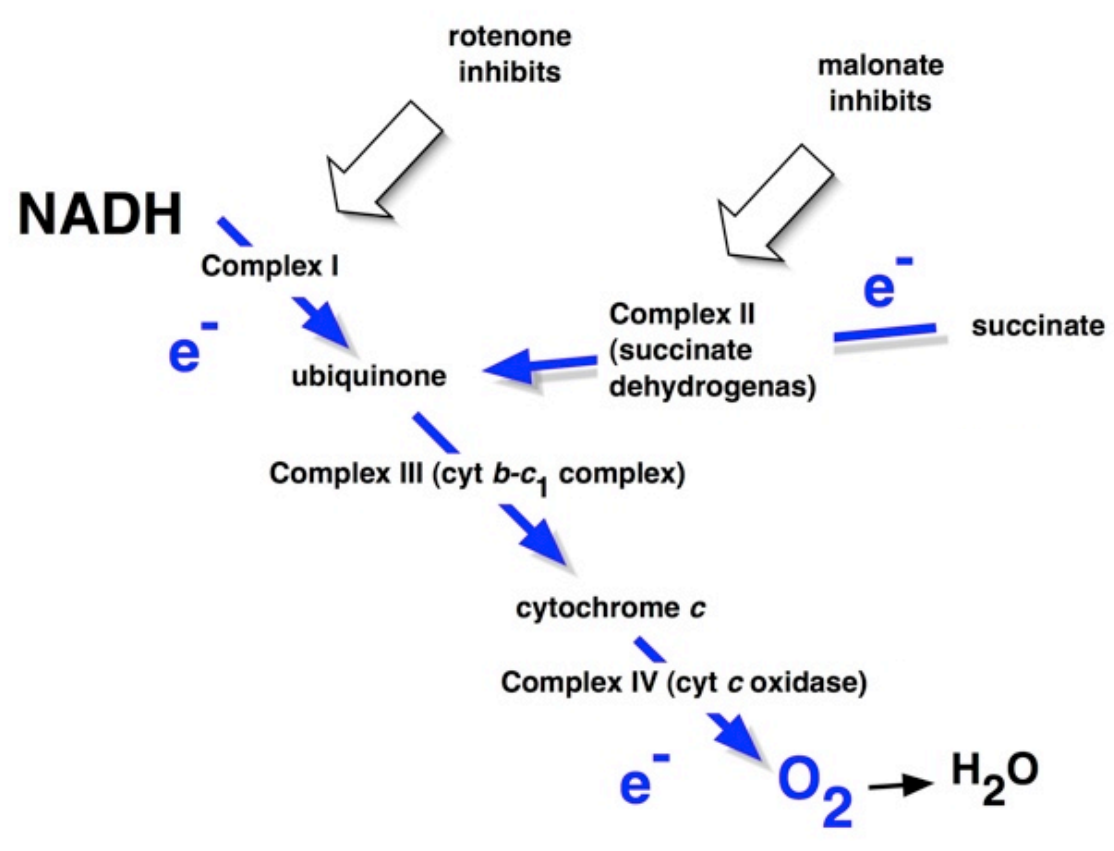
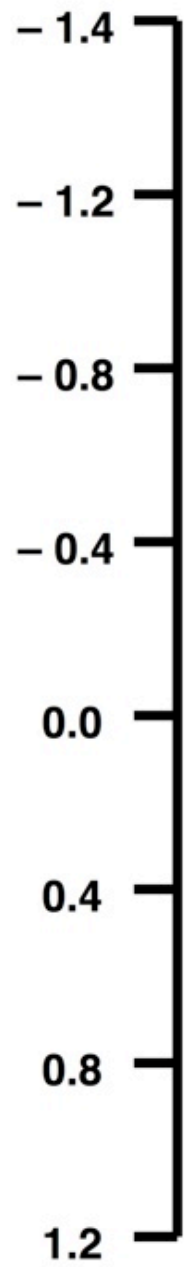
Redox regulatory control of mitochondrial and chloroplast gene expression



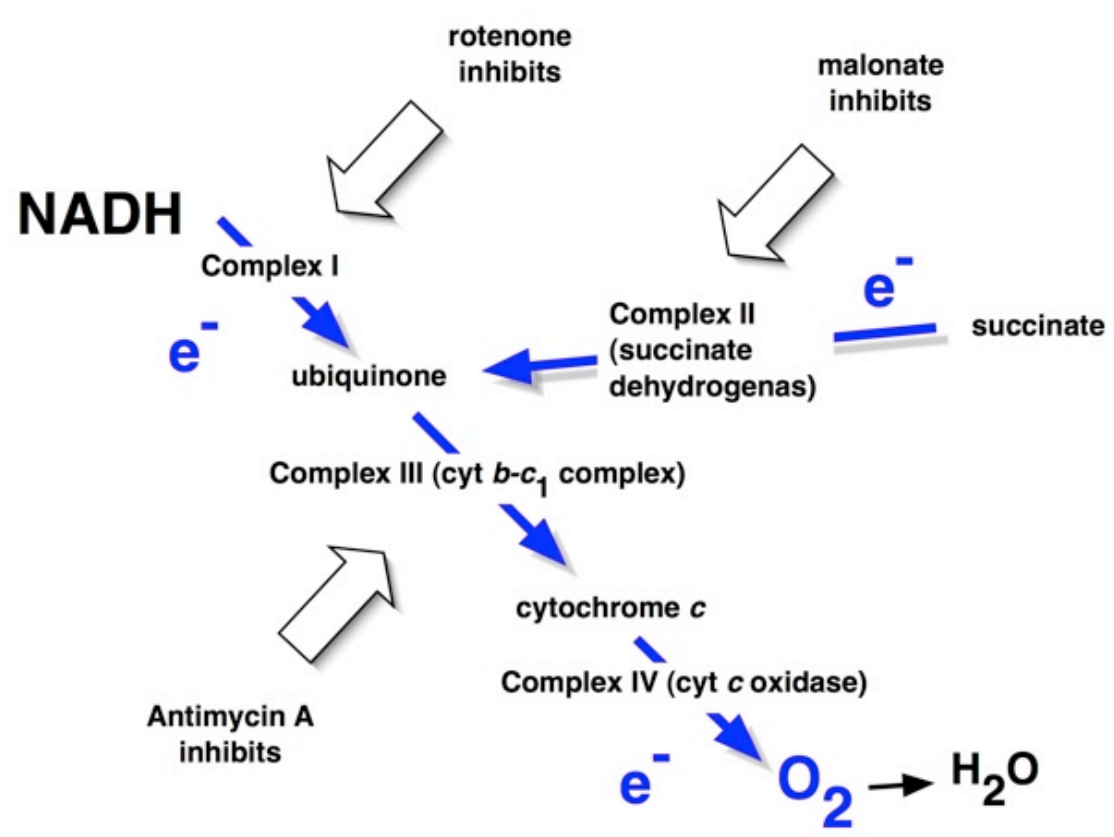
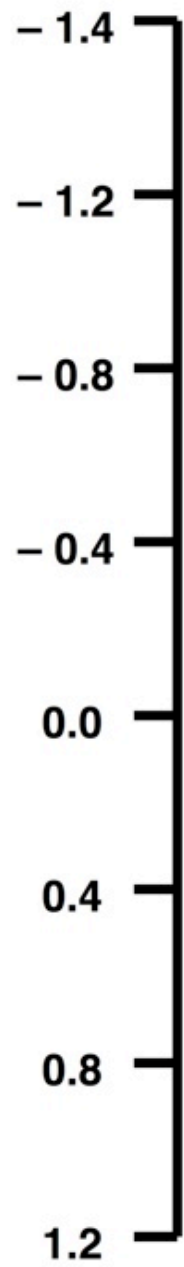
standard redox potential, volts



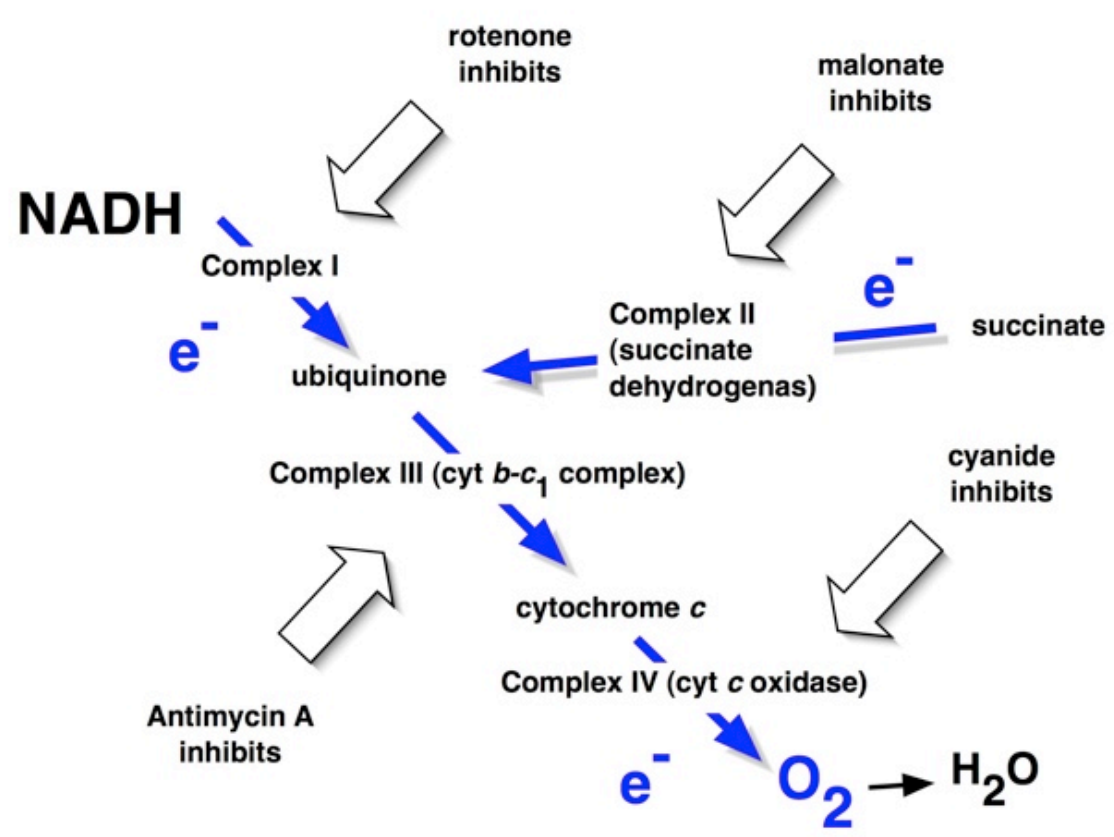
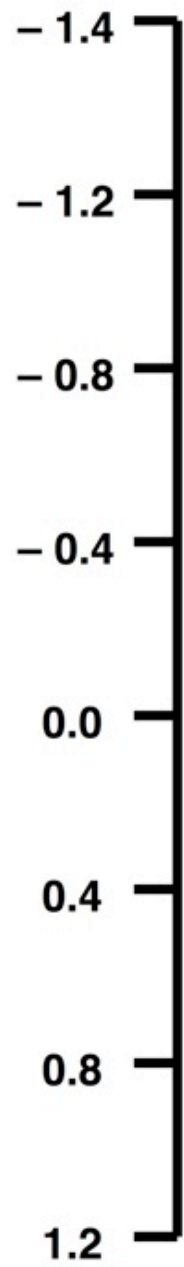
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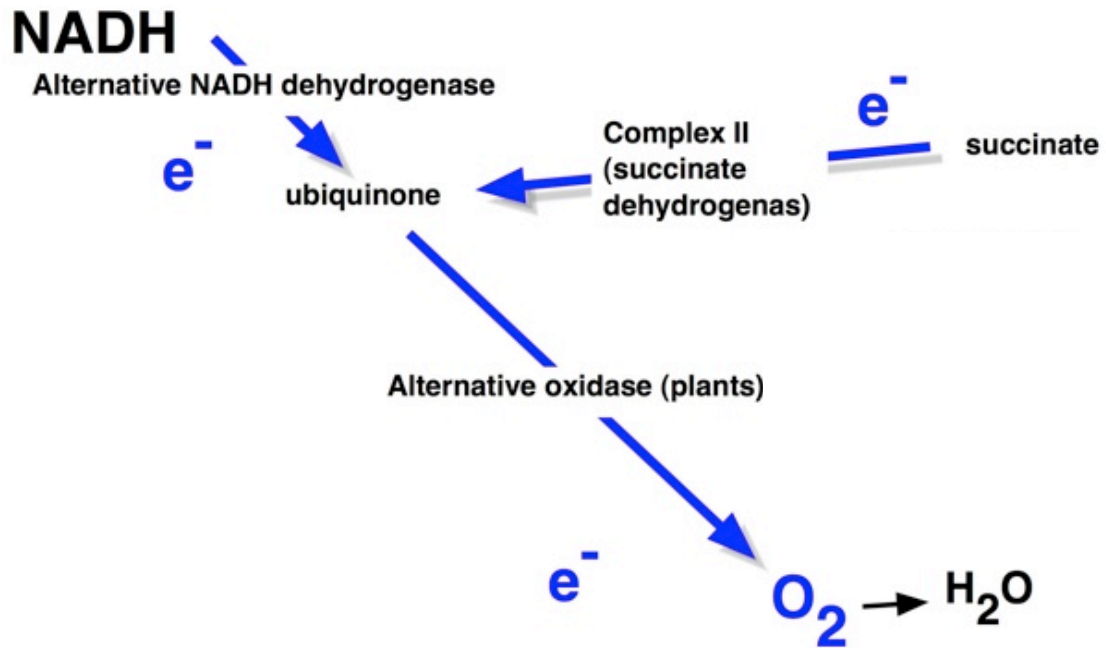
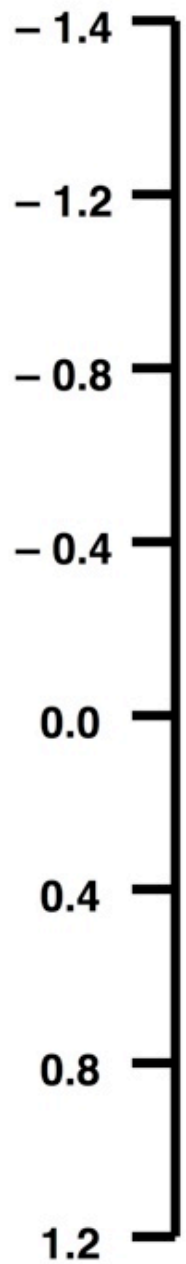
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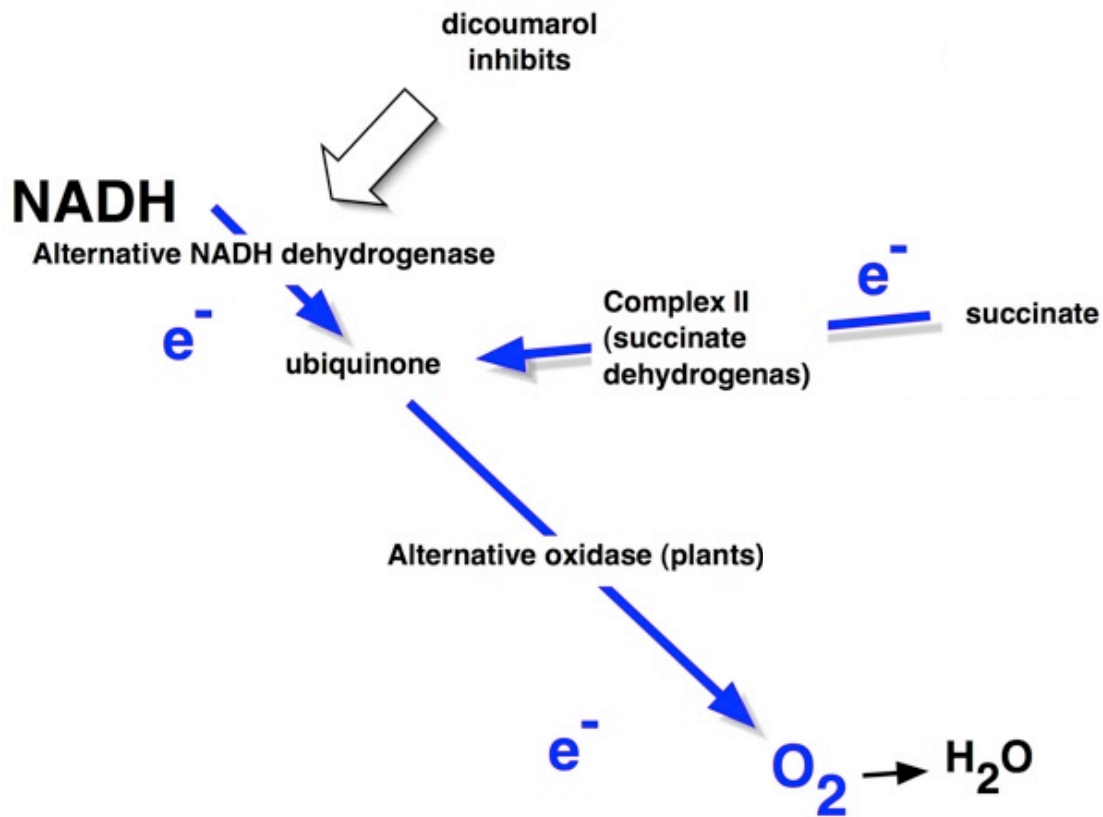
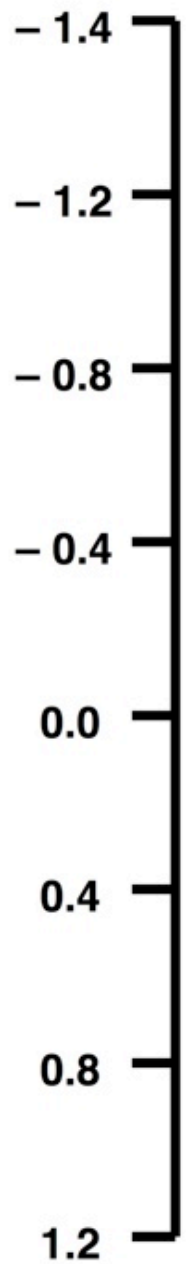
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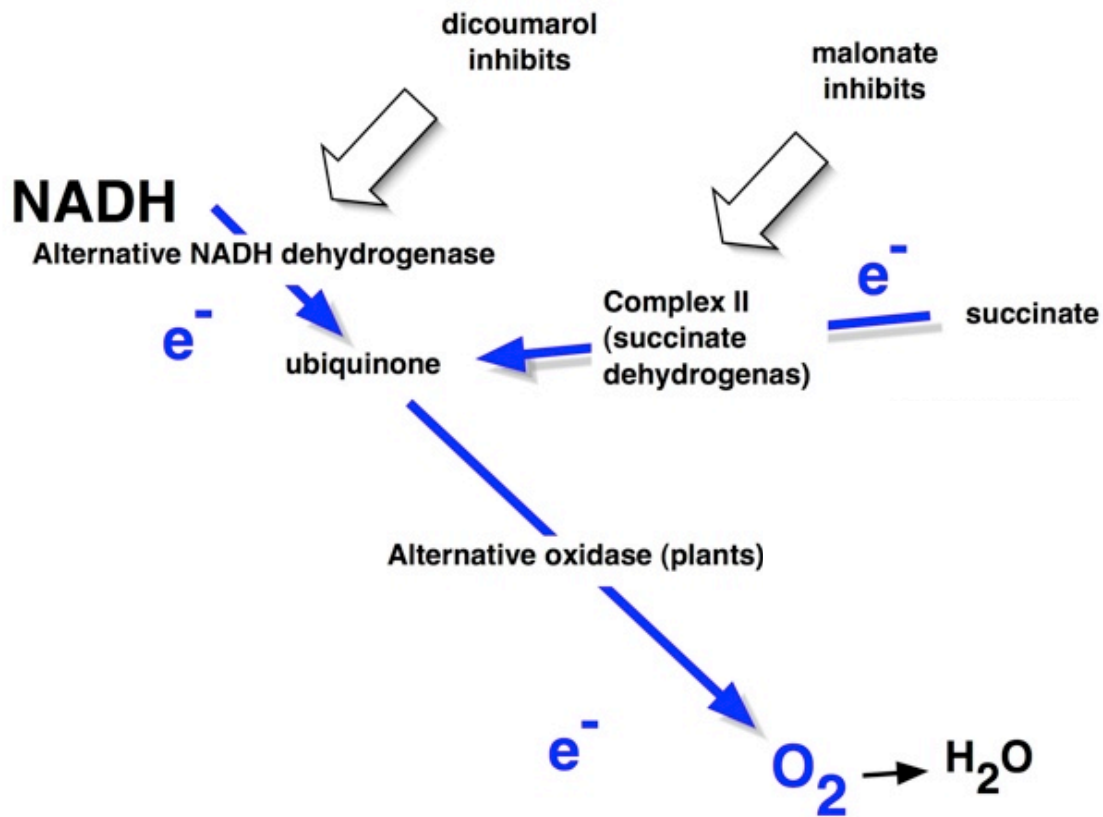
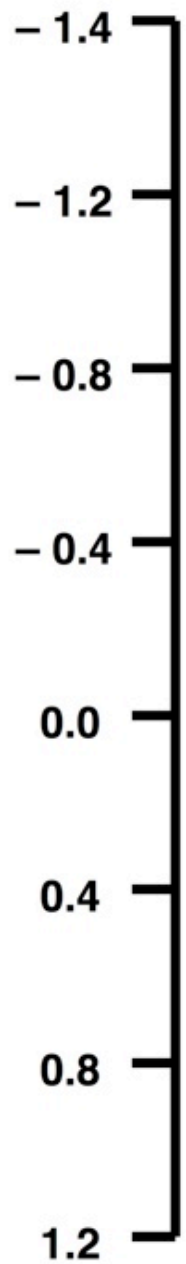
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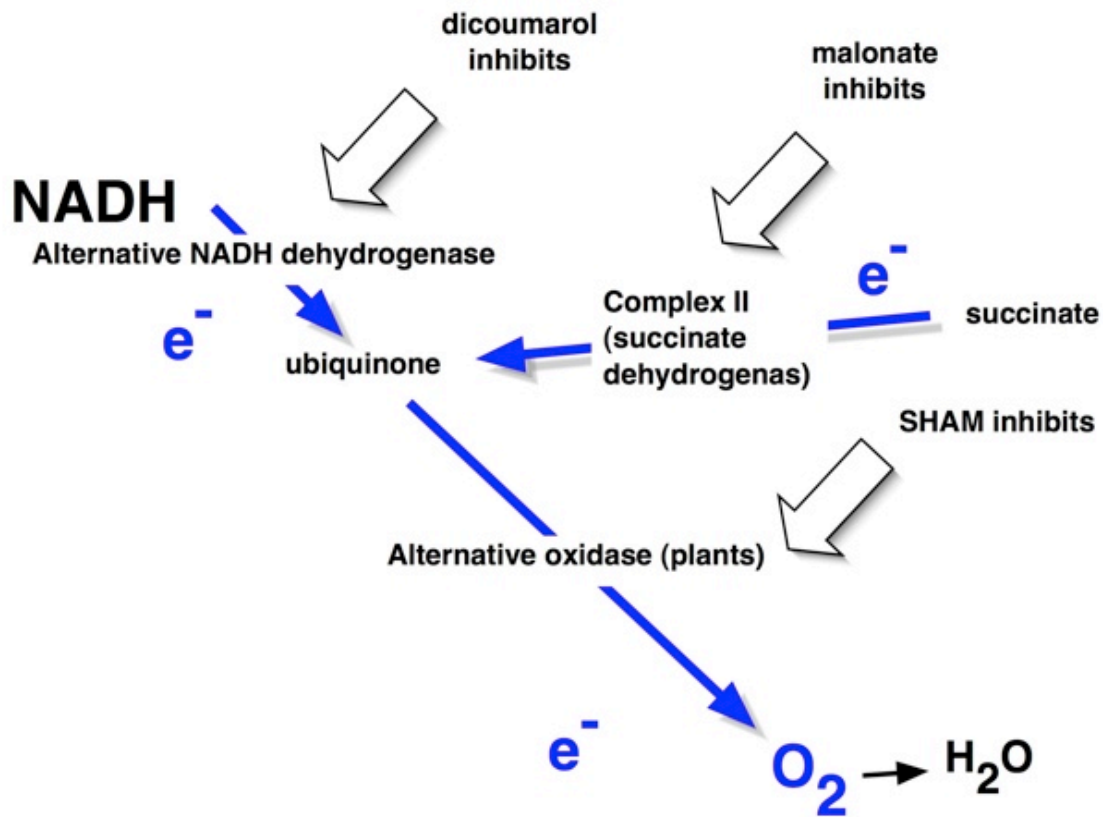
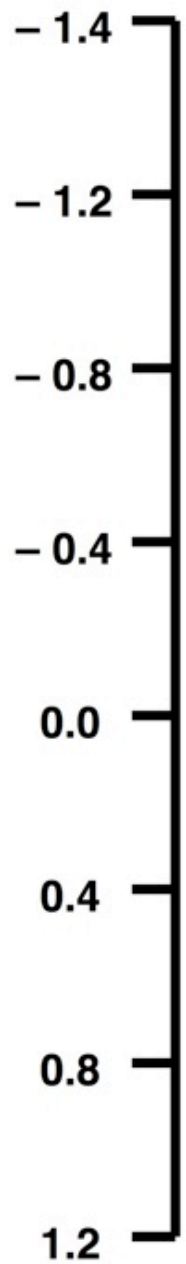
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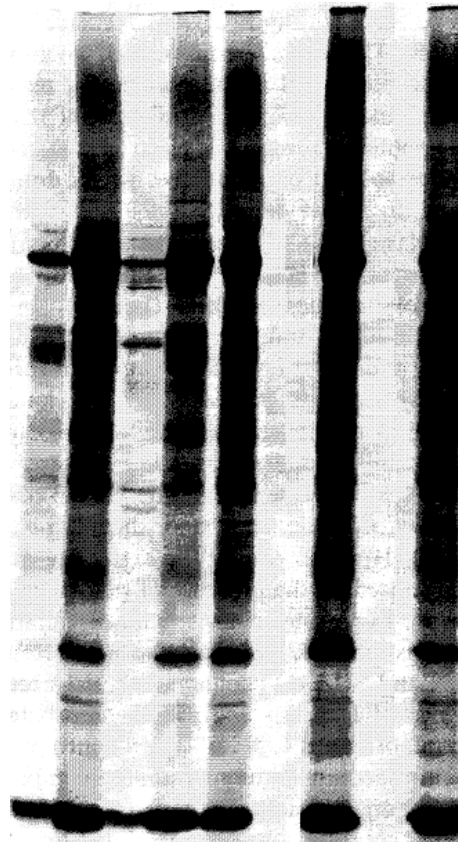
standard redox potential, volts



standard redox potential, volts

+ ferricyanide
 + ascorbate
 + dithiothreitol
 + dithionite
 + duroquinol
 + rotenone, malonate.,dicumarol
 + cyanide, SHAM

pyruvate, malate
 control



Allen, C.A. et al
 Redox Report 1, 119-123

³⁵S-methionine labelling of newly synthesised proteins in pea leaf mitochondria

Co-location for **R**edox **R**egulation - **CoRR**

Advertisement.....

**Photosynthesis explains cytoplasmic inheritance.
CoRR!**

The University of Adelaide

Mawson Lecture Theatre, Medical School North

Friday 13th March 2009

2.00 p.m.

Coffee & Cake 3.00 – 3.30 in the first floor breakout space,
Molecular Life Sciences Building



Mitochondria,
ageing, and sex –
energy versus fidelity

A watercolor illustration of a mitochondrion. The central part is a large, light-colored oval with a darker, wavy border representing the inner membrane. Inside this oval, there is a dense, tangled mass of dark grey lines representing mitochondrial DNA. The background consists of various washes of color, including light blue, green, and brown, suggesting a cellular environment. In the bottom right corner, there is a small signature and the year '2004'.

Costs of DNA in mitochondria

2004

Why Do We Still Have a Maternally Inherited Mitochondrial DNA? Insights from Evolutionary Medicine

Douglas C. Wallace

Center for Molecular and Mitochondrial Medicine and Genetics, Departments of Biological Chemistry, Ecology and Evolutionary Biology, and Pediatrics, University of California, Irvine, California 92697-3940; email: dwallace@uci.edu

Annu. Rev. Biochem. 2007. 76:781-821

The *Annual Review of Biochemistry* is online at biochem.annualreviews.org

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Key Words

adaptation, genomic evolution, mitochondrial disease, mtDNA, oxidative phosphorylation, proton-translocating OXPHOS complexes

Abstract

The human cell is a symbiosis of two life forms, the nucleus-cytosol and the mitochondrion. The nucleus-cytosol emphasizes structure and its genes are Mendelian, whereas the mitochondrion specializes in energy and its mitochondrial DNA (mtDNA) genes are maternal. Mitochondria oxidize calories via oxidative phosphorylation (OXPHOS) to generate a mitochondrial inner membrane proton gradient (ΔP). ΔP then acts as a source of potential energy to produce ATP, generate heat, regulate reactive oxygen species (ROS), and control apoptosis, etc. Interspecific comparisons of mtDNAs have revealed that the mtDNA retains a core set of electron and proton carrier genes for the proton-translocating OXPHOS complexes I, III, IV, and V. Human mtDNA analysis has revealed these genes frequently contain region-specific adaptive polymorphisms. Therefore, the mtDNA with its energy controlling genes may have been retained to permit rapid adaptation to new environments.

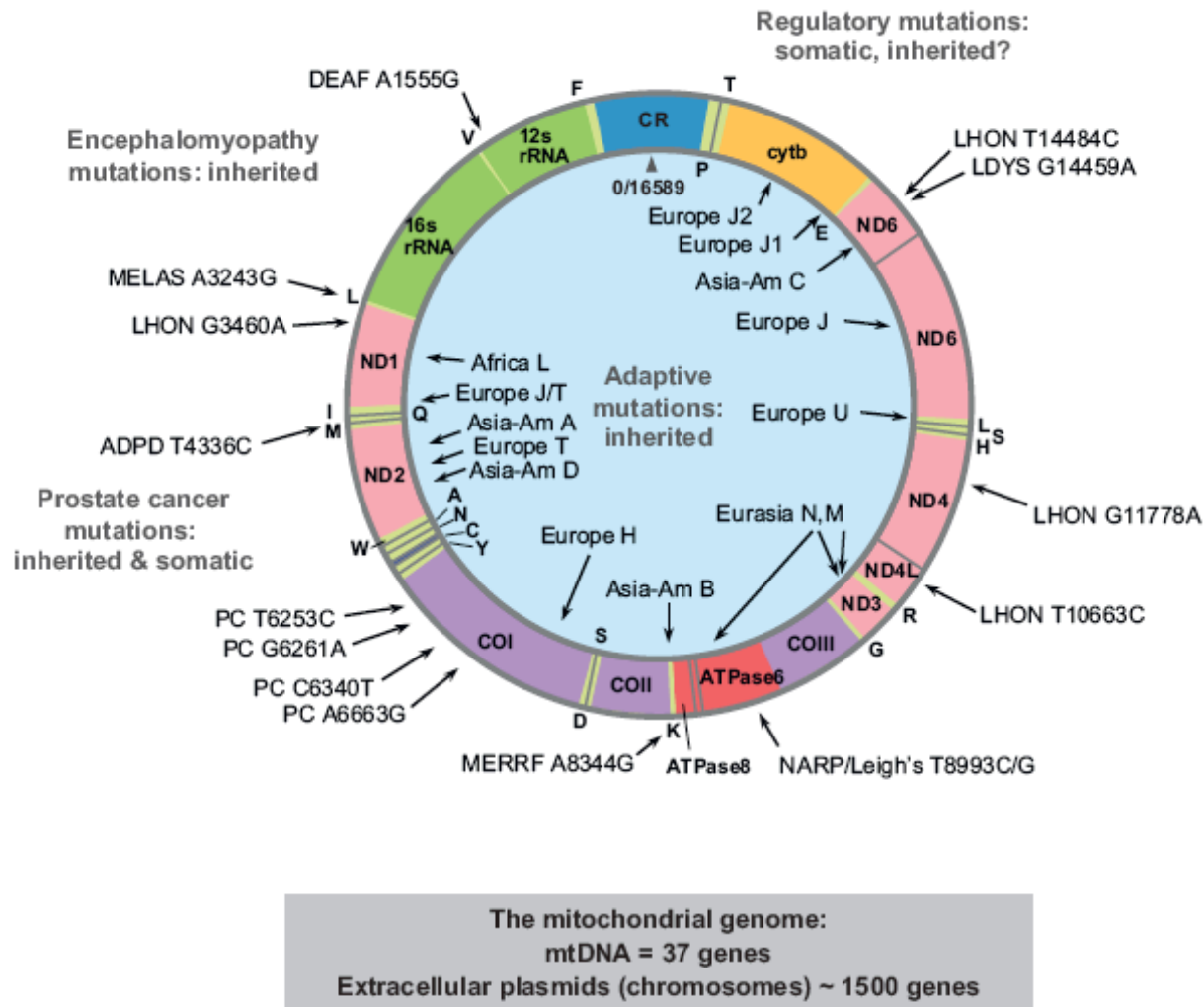


Figure 2

The human mtDNA map. The human mtDNA encompasses three classes of clinically relevant mutations: recent maternally inherited disease-causing mutations, examples of which are shown on the outside of the circular map; ancient geographically correlated and frequently adaptive polymorphic variants, examples presented inside the circle; and somatic mutations that accumulate with age in postmitotic tissues and provide the aging clock. Letters around the outside perimeter indicate cognate amino acids of the tRNA genes. Letters within the ring represent the proteins encoded by the gene sector, all of which are integral membrane components of the proton-translocating complexes of OXPHOS. The polypeptides, corresponding gene, and complexes are ND1-4, -4L, -5, and -6 (*nad1-4*, *-4l*, *-5*, and *-6* gene) of complex I; *cytb* or cytochrome *b* (*cob* gene) of complex III; COI-III (*cox1-3* genes) of complex IV; and ATP6 and ATP8 (*atp6* and *atp8* genes) of complex V.

A watercolor illustration of several cells. The cells are rendered in shades of blue, green, and brown. Each cell contains numerous small, dark green, oval-shaped structures representing mitochondria. The background is a light, textured pinkish-white. The text 'The mitochondrial theory of ageing' is overlaid in the center in a bright yellow, sans-serif font.

The mitochondrial theory of ageing

2002
MPC

The mitochondrial theory of ageing

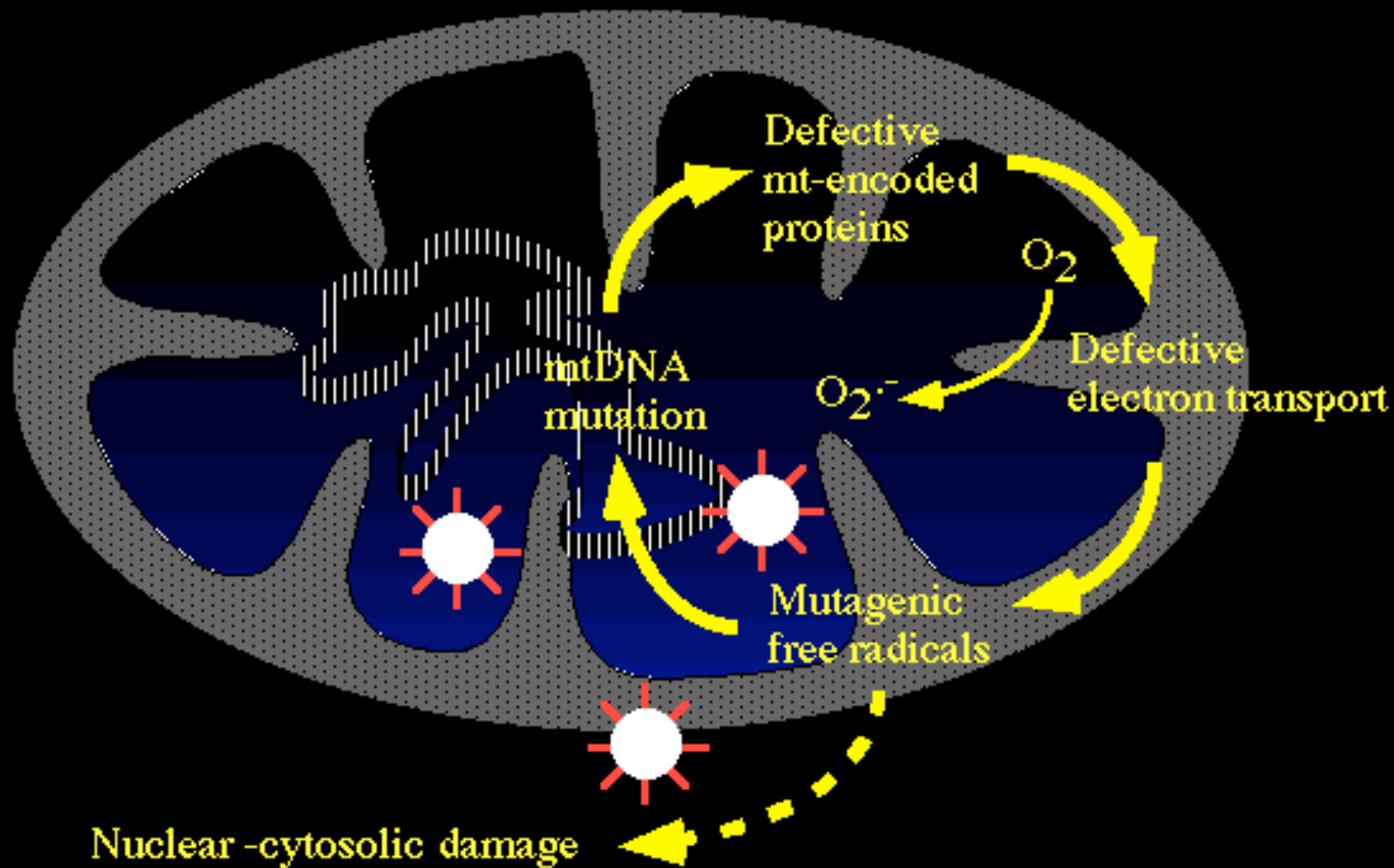
The mitochondrial theory of ageing

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The products of these reactions damage mitochondrial genes, which then produce defective proteins, which then make more "errors" in electron transfer....damaging more genes, making more defective proteins....and so on.





Separate sexes as
mitochondrial division of
labour

Why there are two sexes

Why there are two sexes

Problem: Mitochondrial Ageing predicts that offspring should inherit their mothers' acquired state of accumulated damage, but they evidently do not. Babies are not born at the physical age of their mothers.

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How can this be?

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Proposed solution (hypothesis): Separation of two sexes allows specialisation of mitochondria **either** as genetic templates (female germ line) **or** as energy-converters (male germ line).

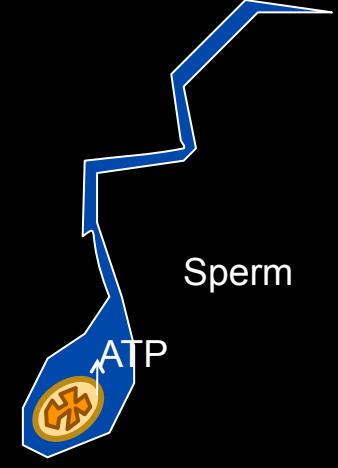
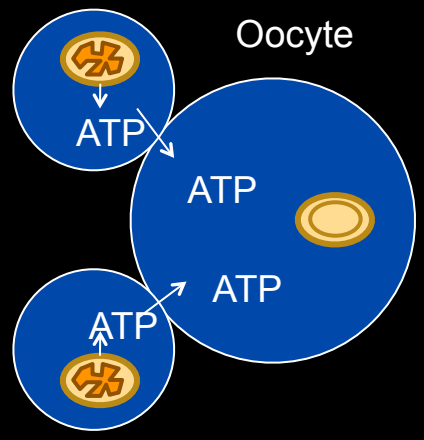
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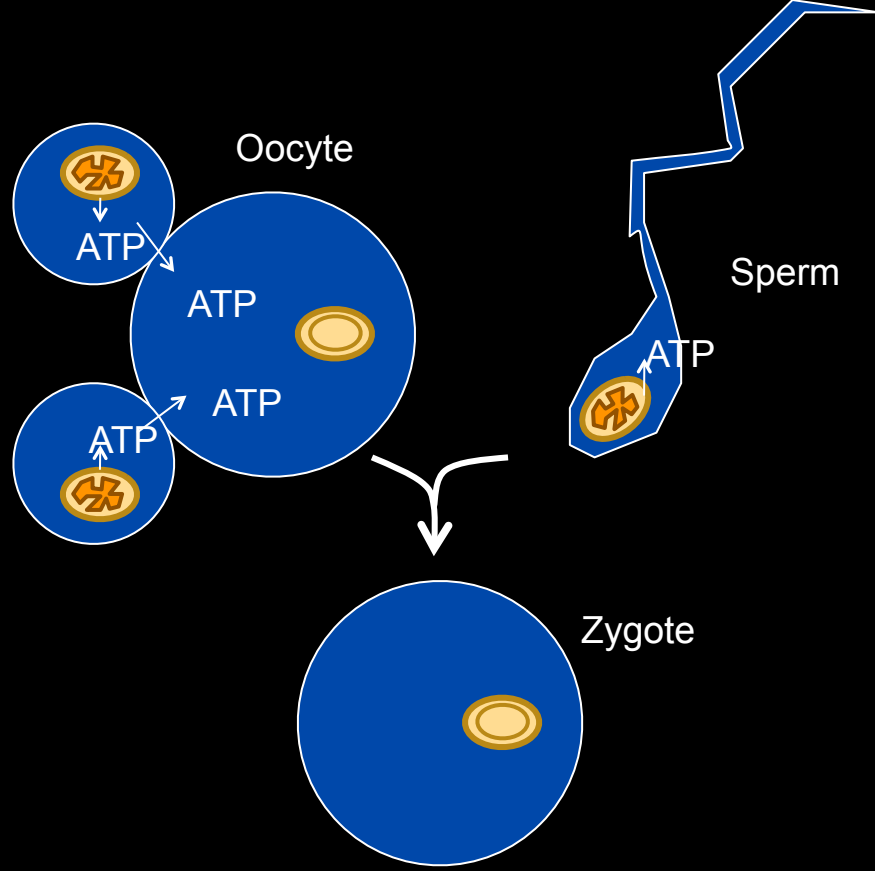
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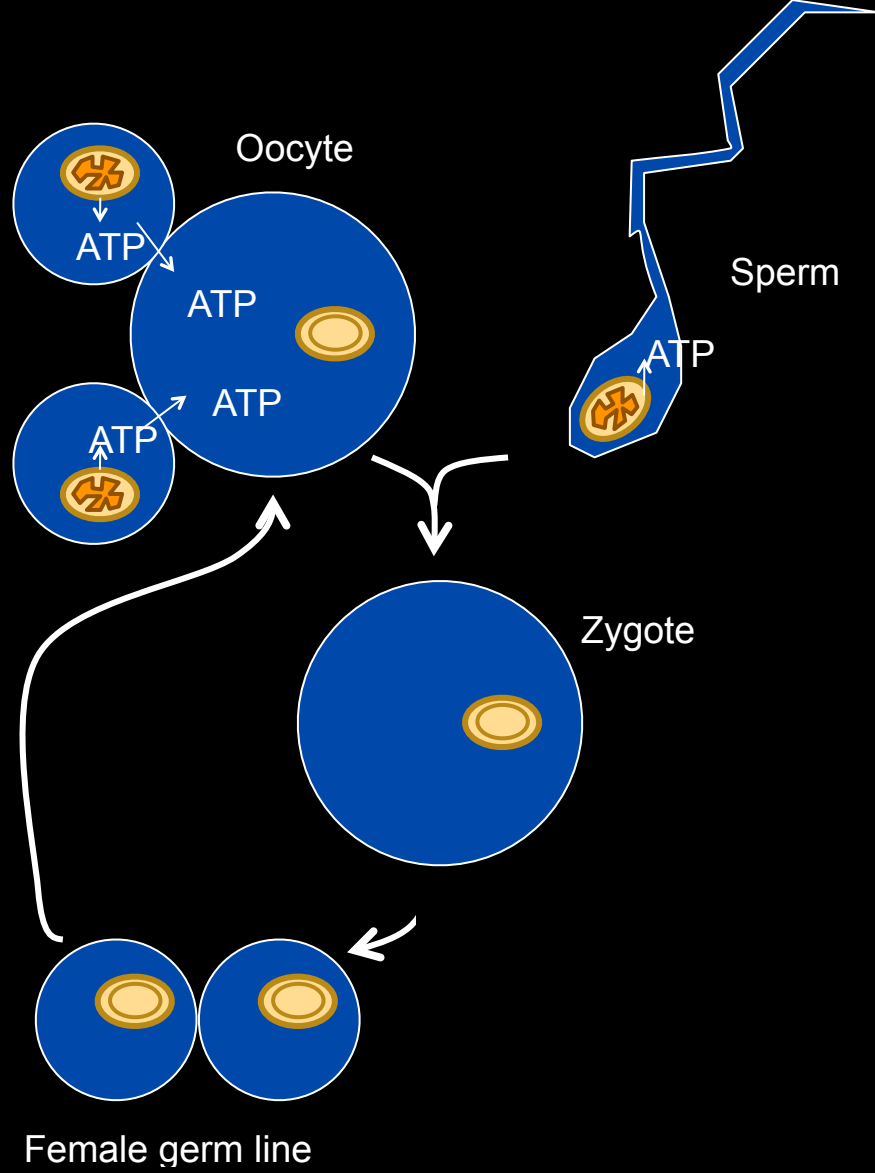
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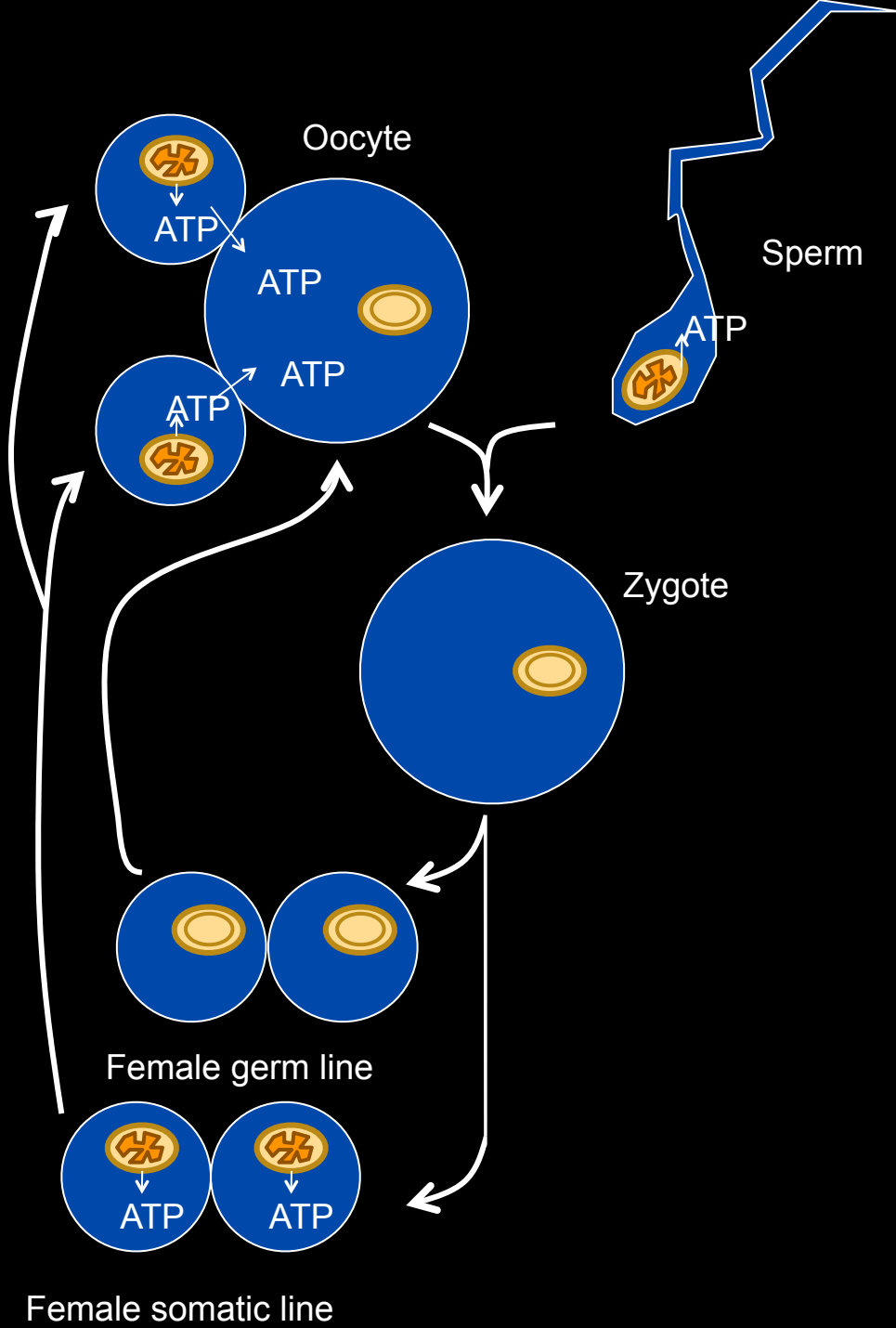
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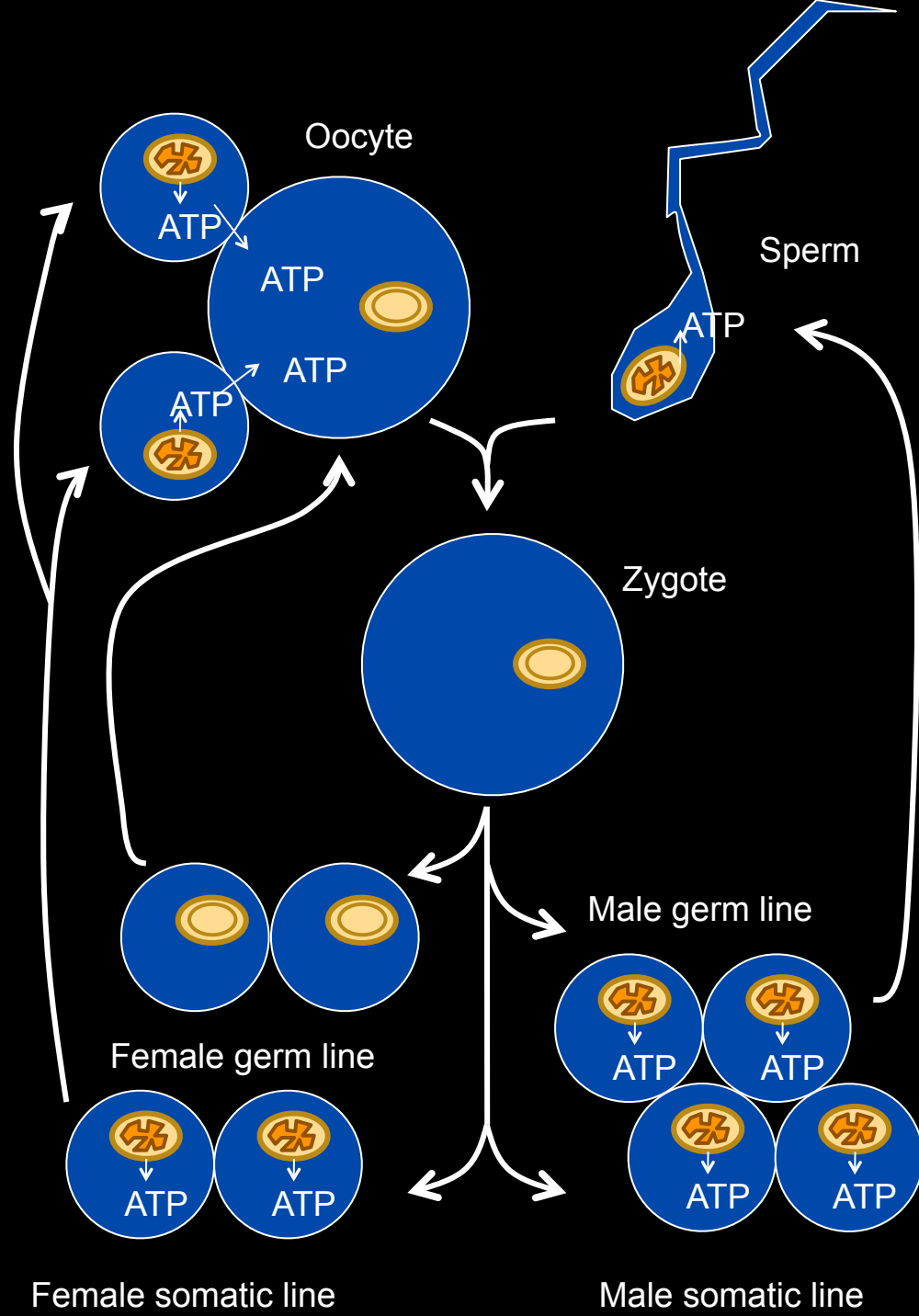
And they can never be both.

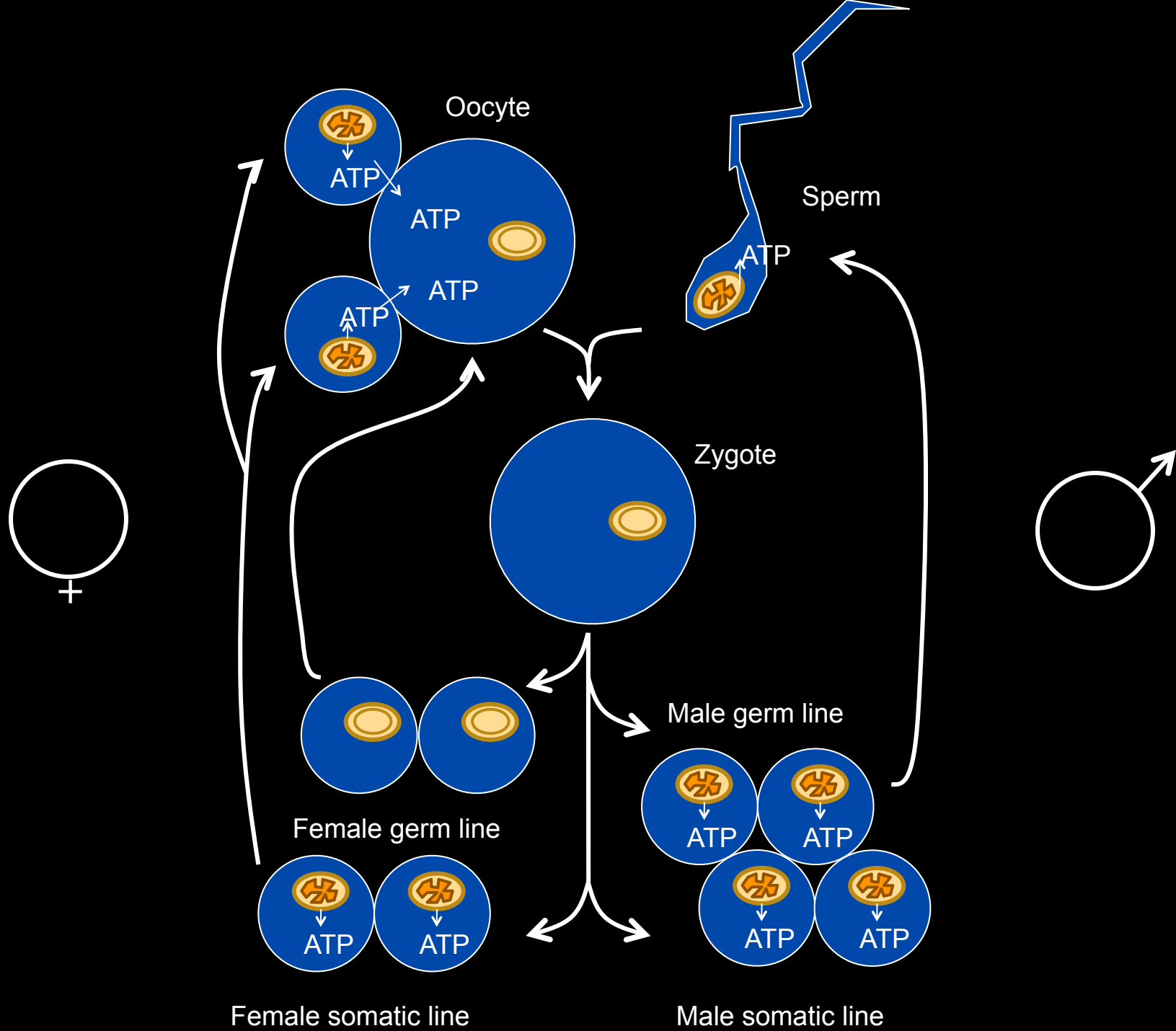


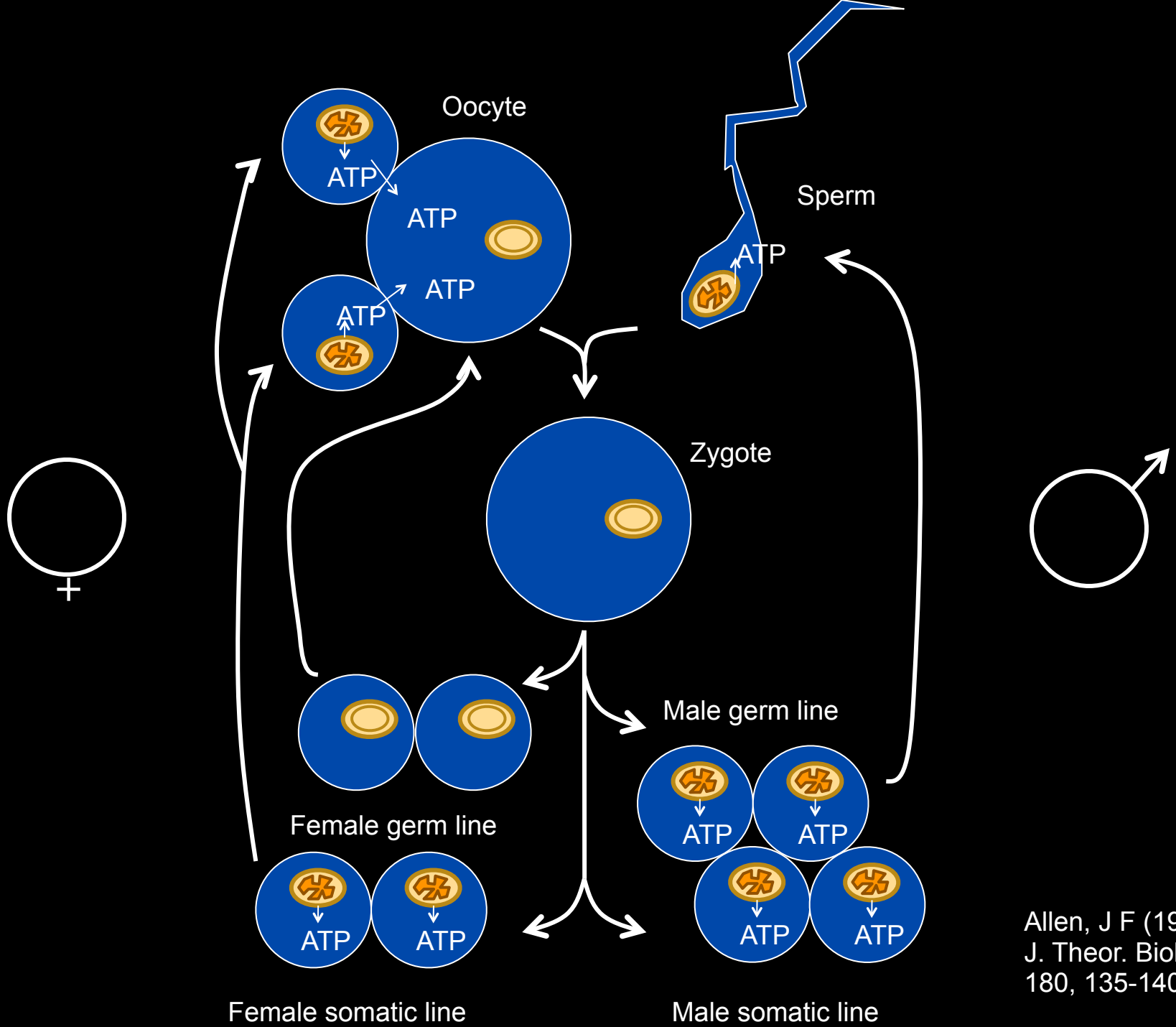




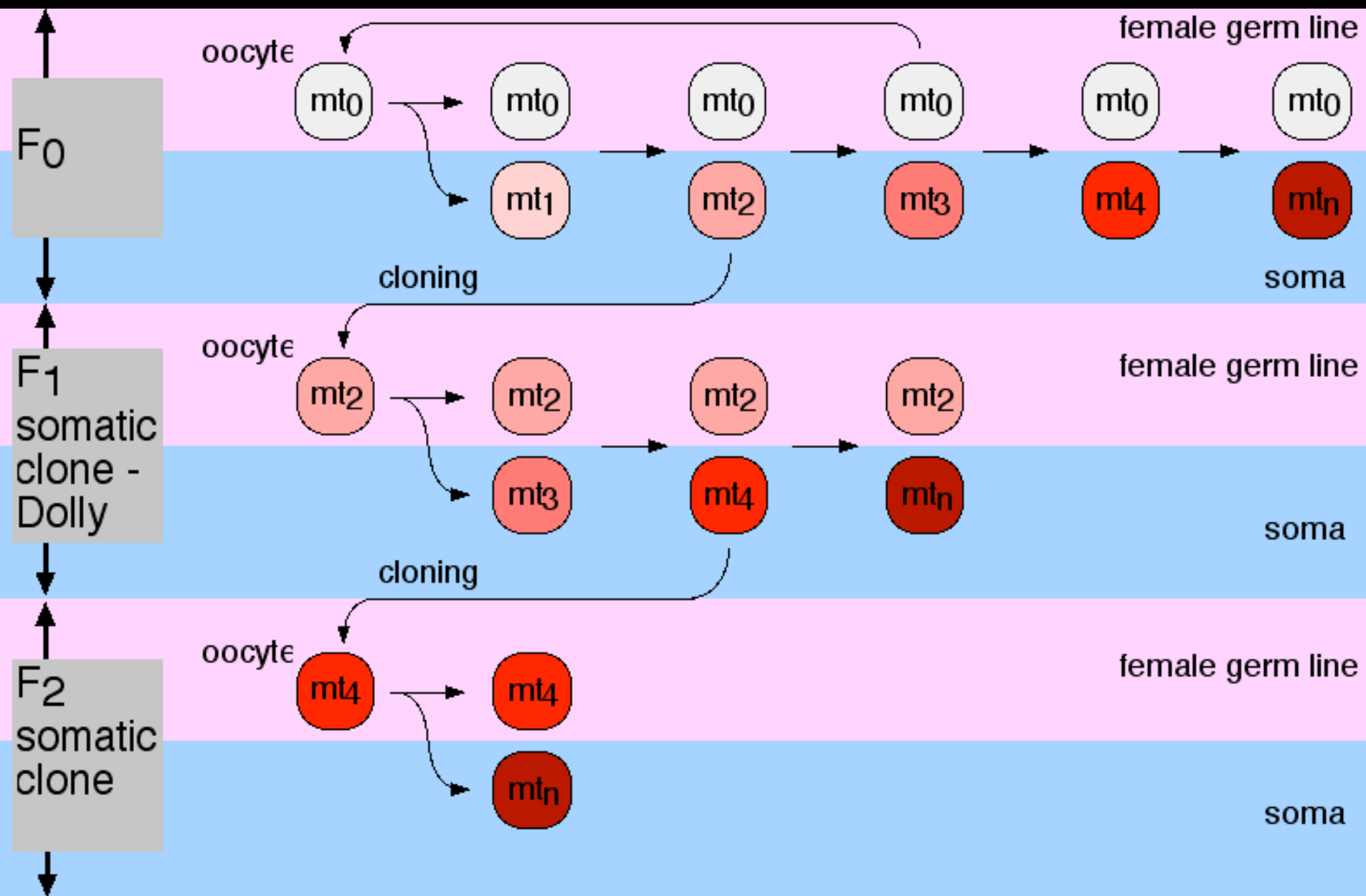








Allen, J F (1996)
 J. Theor. Biol.
 180, 135-140



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Obituary: Dolly the Sheep

<http://www.nature.com/nsu/030210/030210-15.html>

Separate sexes as mitochondrial division of labour

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- An immortal line of genetic template mitochondria in the female germ line; ... from egg back to egg

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Co-location for Redox Regulation
- mostly destroy themselves (and, eventually, us) in consequence
- but might exist also in female germ lines as protected genetic templates, incapable of energy conversion, and from which all other mitochondria and chloroplasts derive

Coda. Two views of mitochondria

View 1

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John Burn (Newcastle Institute of Clinical Genetics). Quoted in *The Times*, 9th September 2005

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“My belief is that what we are doing is changing a battery that doesn't work for one that does....Changing the mitochondria won't affect the important DNA.”

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View 2

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Nick Lane. *Power, Sex, Suicide. Mitochondria and the Meaning of Life*. Oxford University Press. 2005.

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Mitochondria:

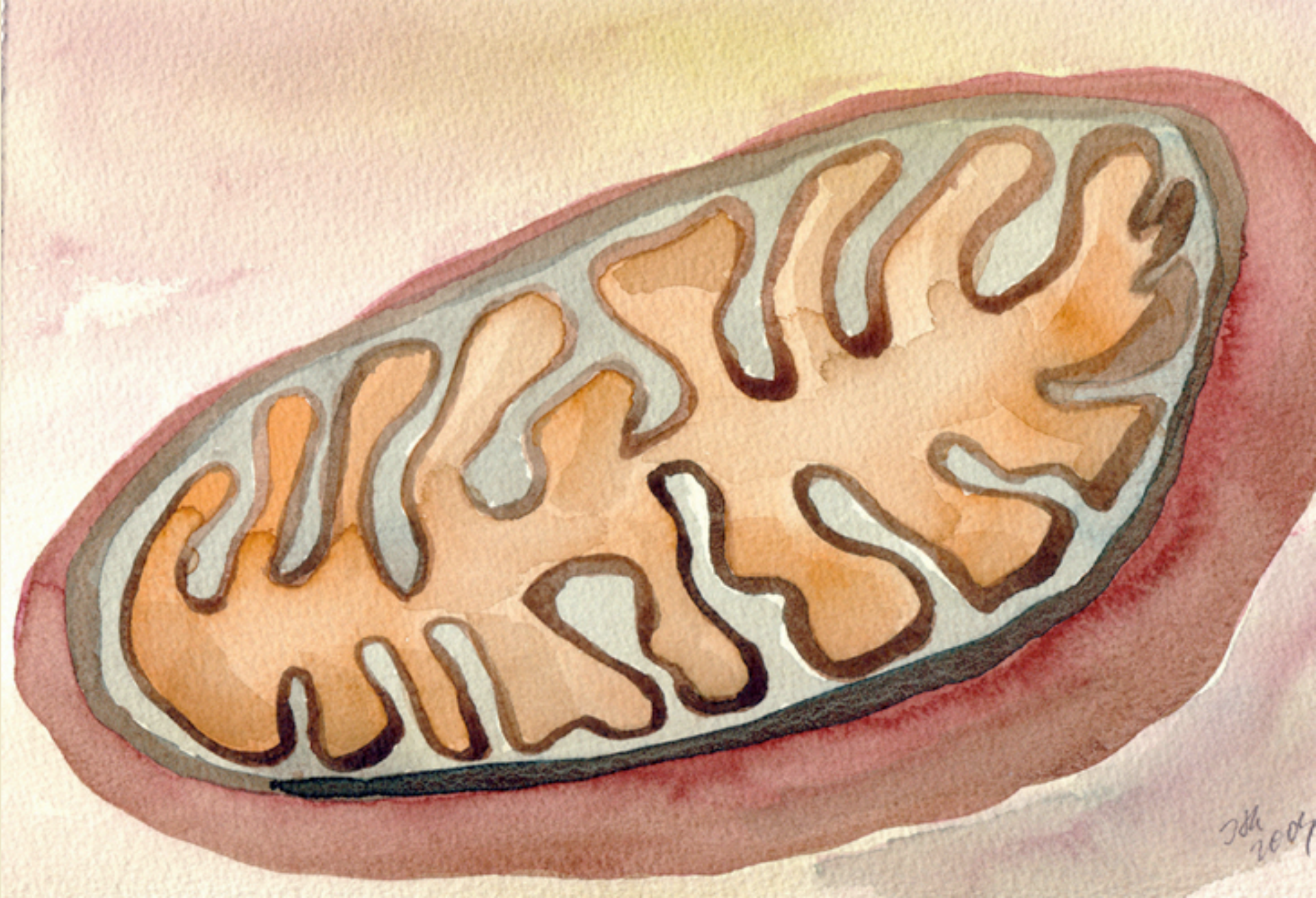
Coda. Two views of mitochondria

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Mitochondria:

– “...give striking new insights into why we are here at all, whether we are alone in the universe, why we have our sense of individuality, why we should make love, where we trace our ancestral roots, why we must age and die—in short, into the meaning of life.”



A mitochondrion—one of many tiny power-houses within cells that control our lives in surprising ways

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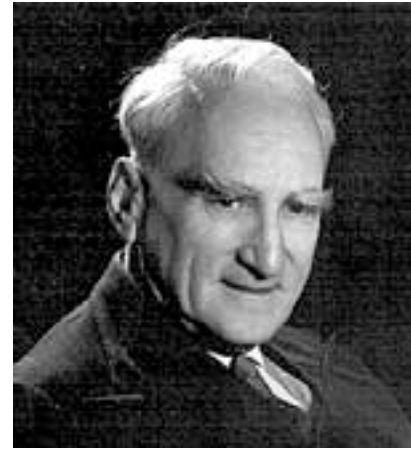


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The end. Thank you for listening.



