

School of Chemistry and Molecular Biosciences  
University of Queensland  
18th February 2009

# Why organelle genomes? Costs and benefits of DNA in mitochondria and chloroplasts

John F. Allen

Australian Academy of Science Rudi Lemberg Travelling Fellow

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[jfallen.org](http://jfallen.org)



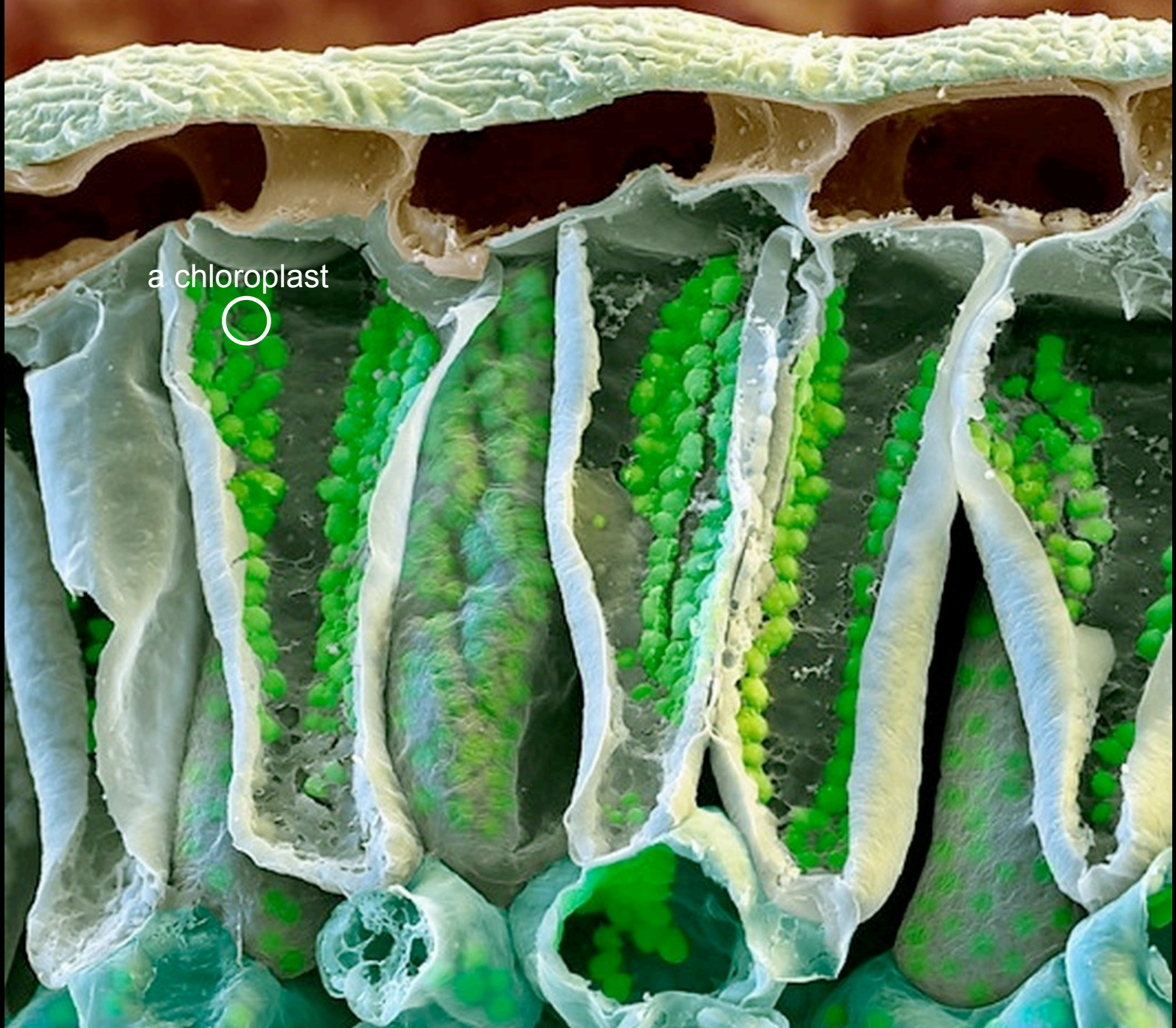
Queen Mary  
University of London



Max Rudolph Lemberg

1896-1975

# Genes in organelles



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



30th  
2000

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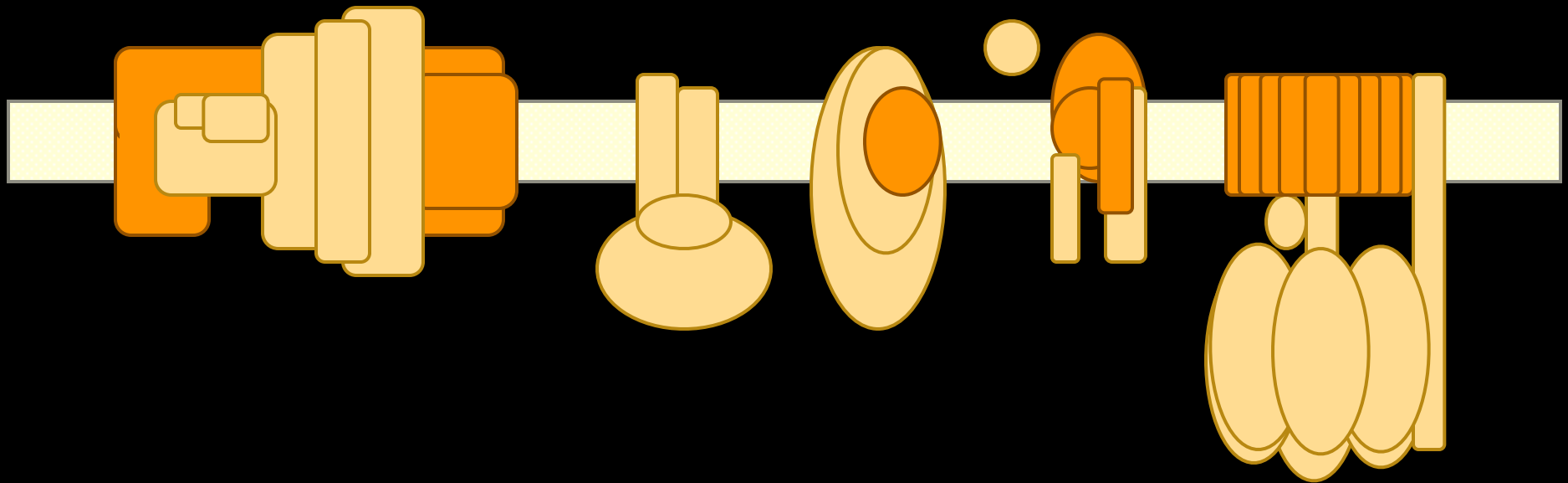
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**Why?**





Inter-membrane space

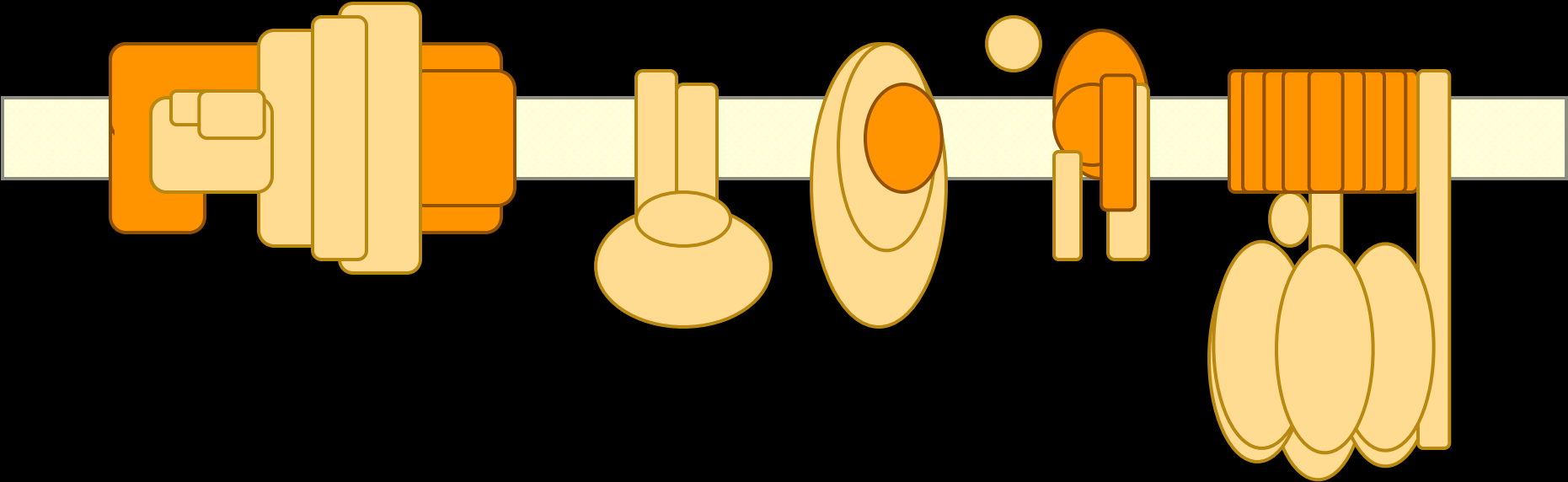
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II

III

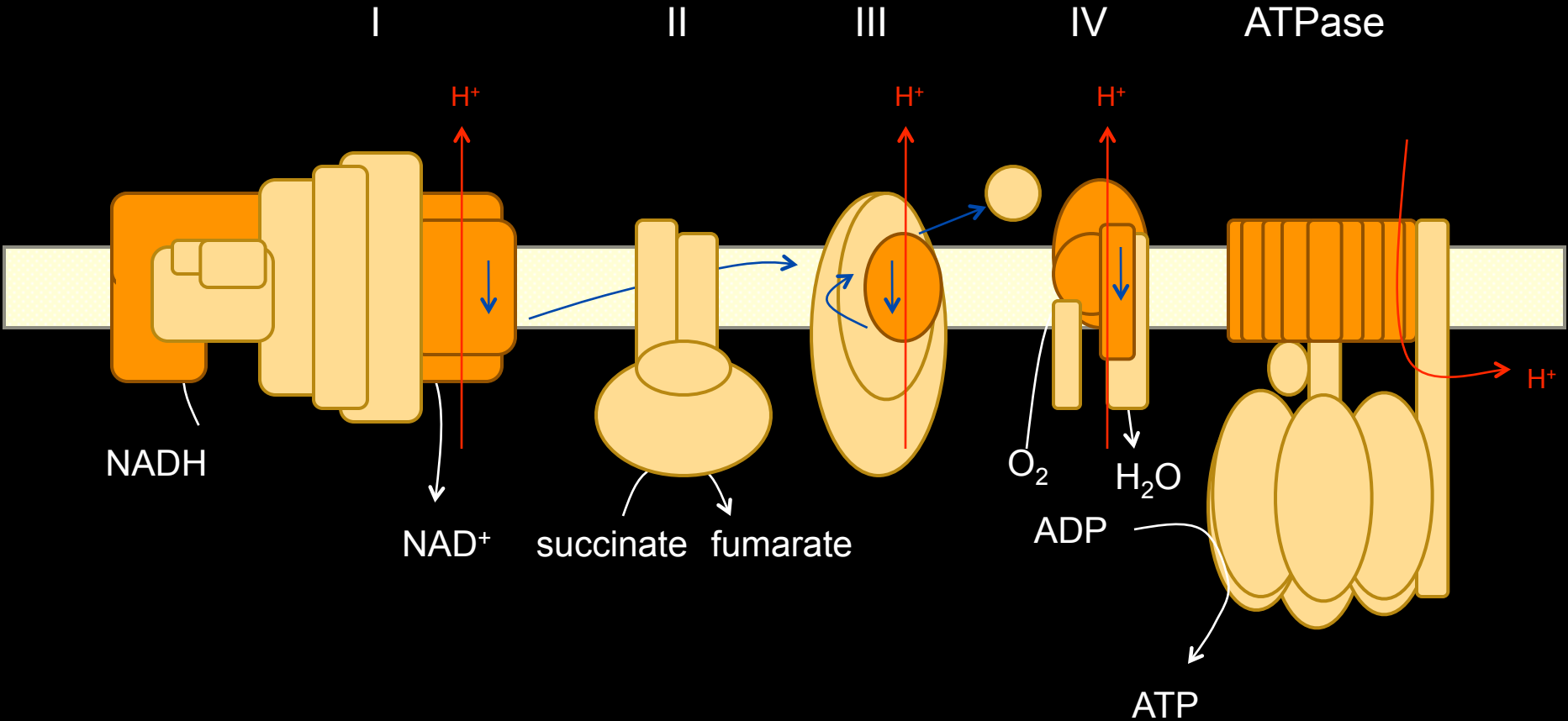
IV

ATPase

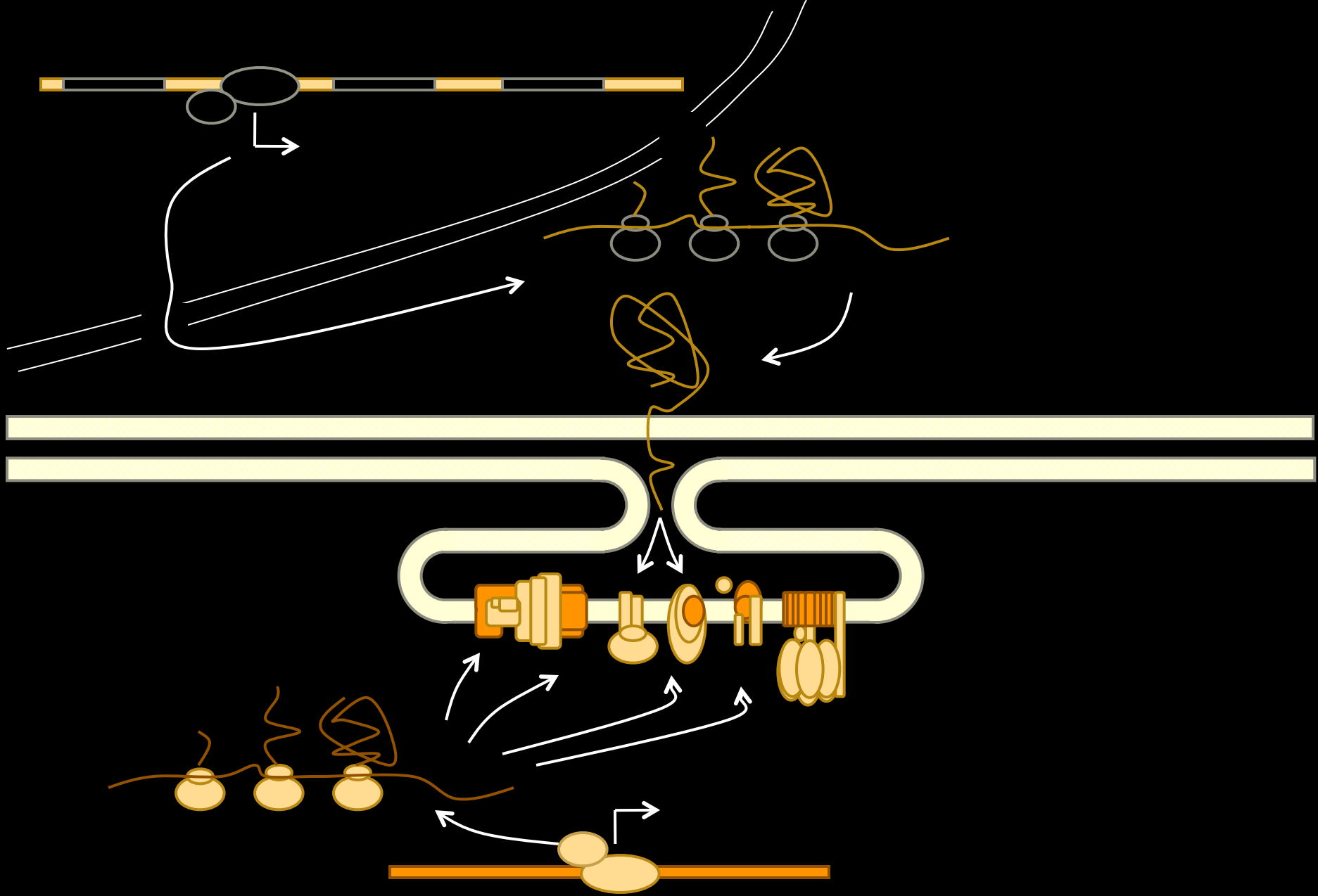


Mitochondrial matrix

Inter-membrane space



Mitochondrial matrix





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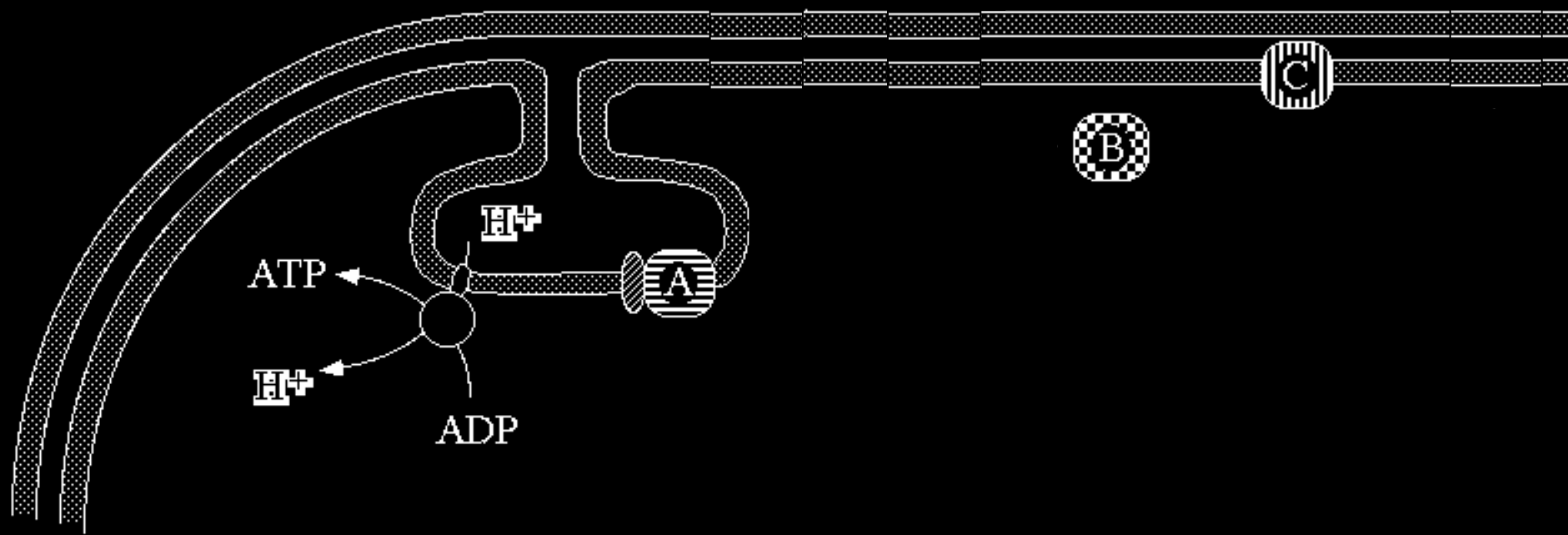
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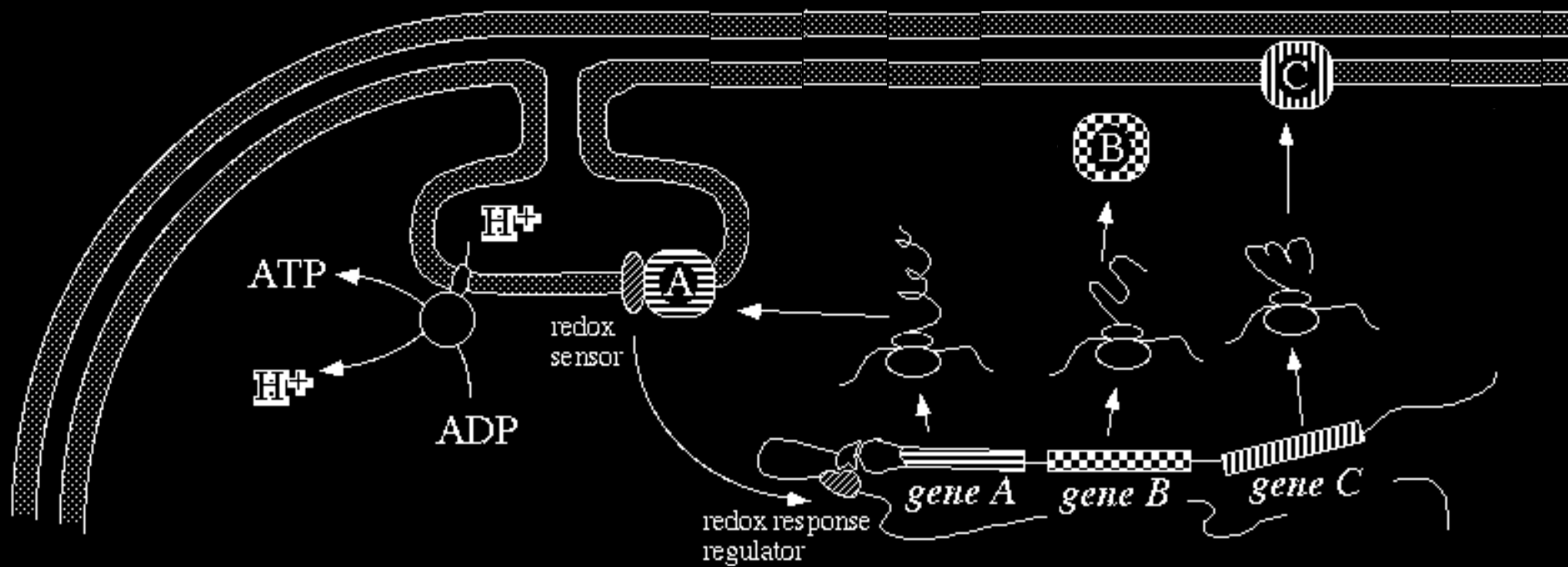
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\*Redox reactions are chemical reaction in which an electron is transferred from one molecule to another - the basis of biological energy conversion.



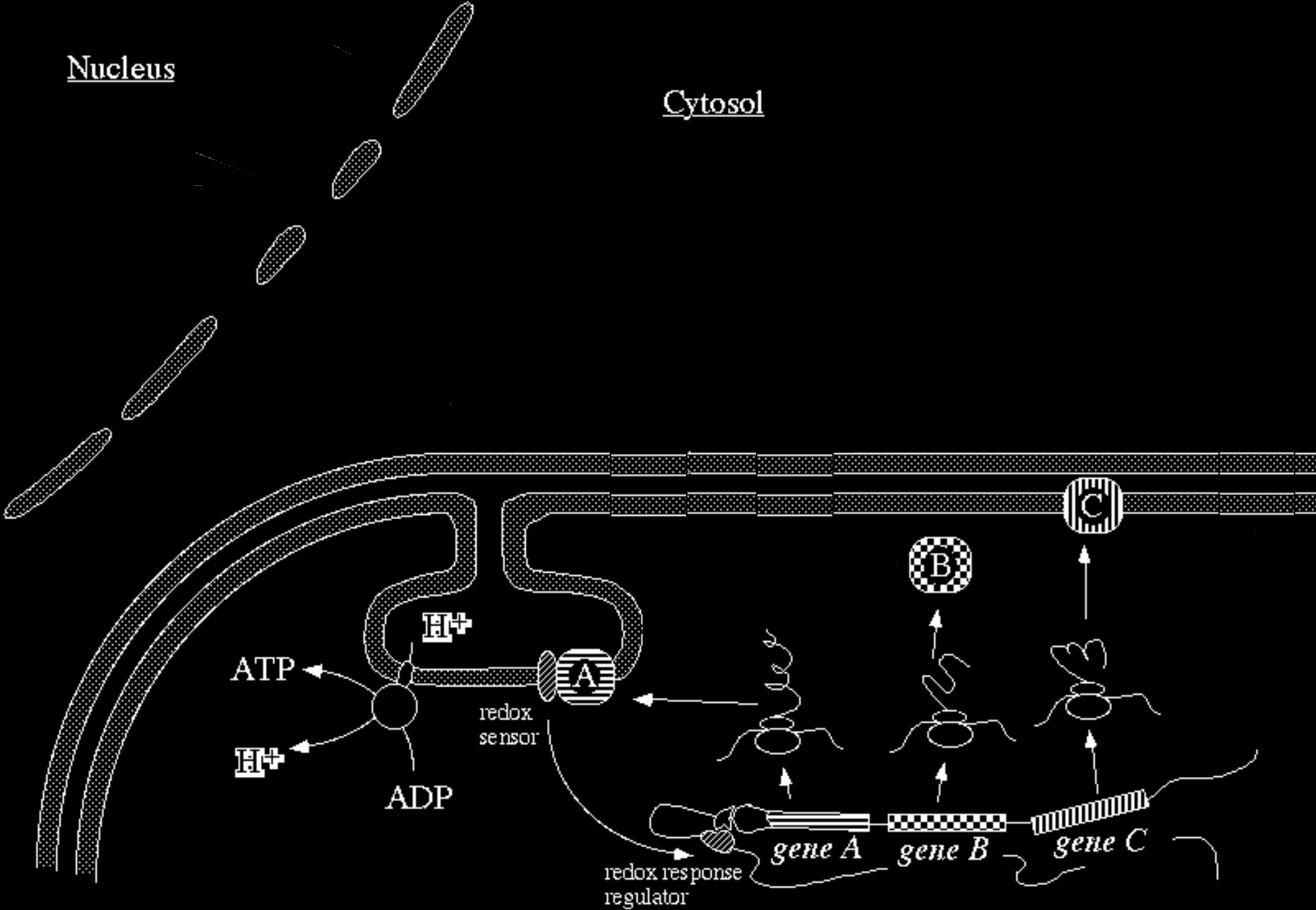




Bacterium

Nucleus

Cytosol



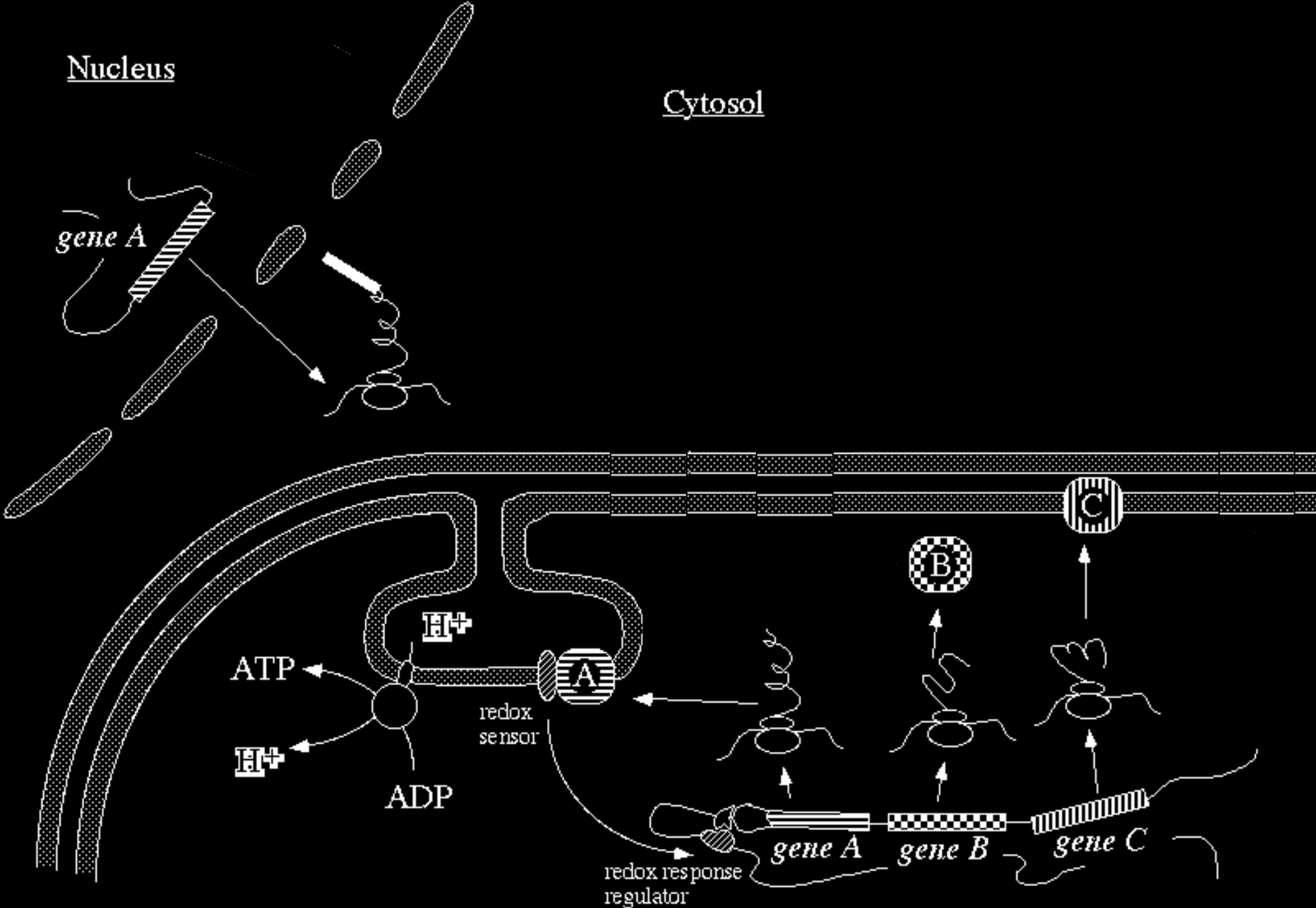
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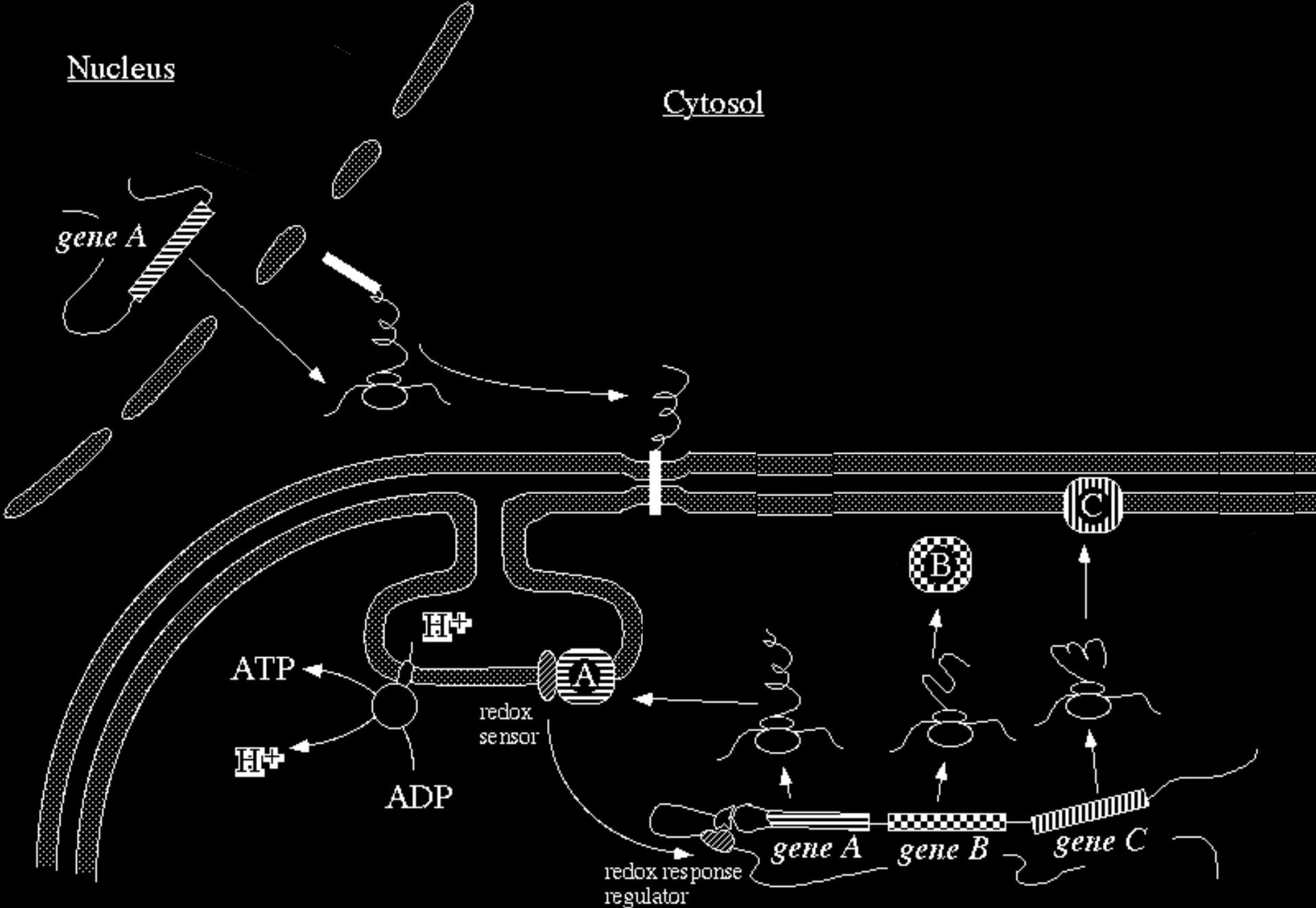
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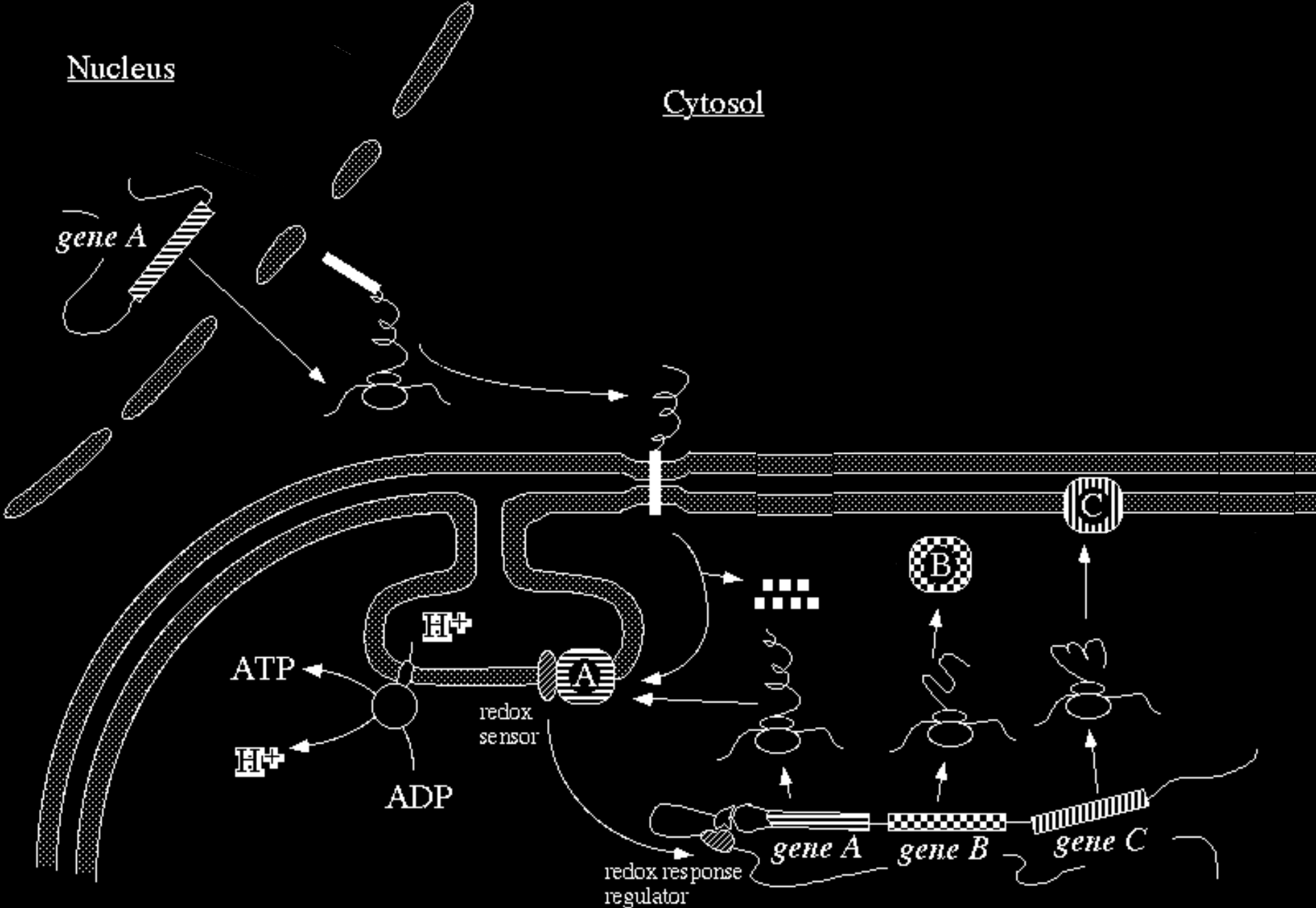
*gene A*



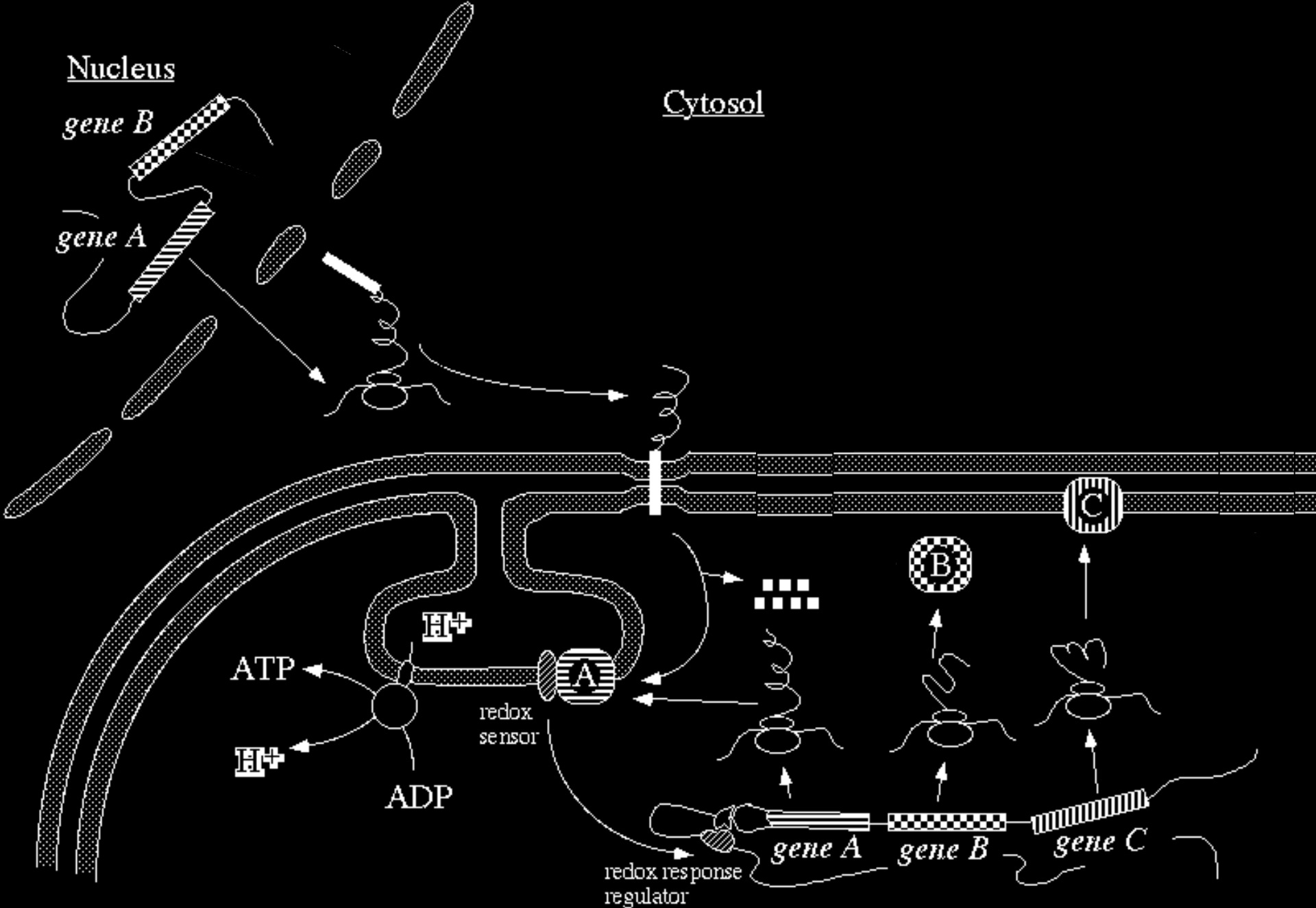
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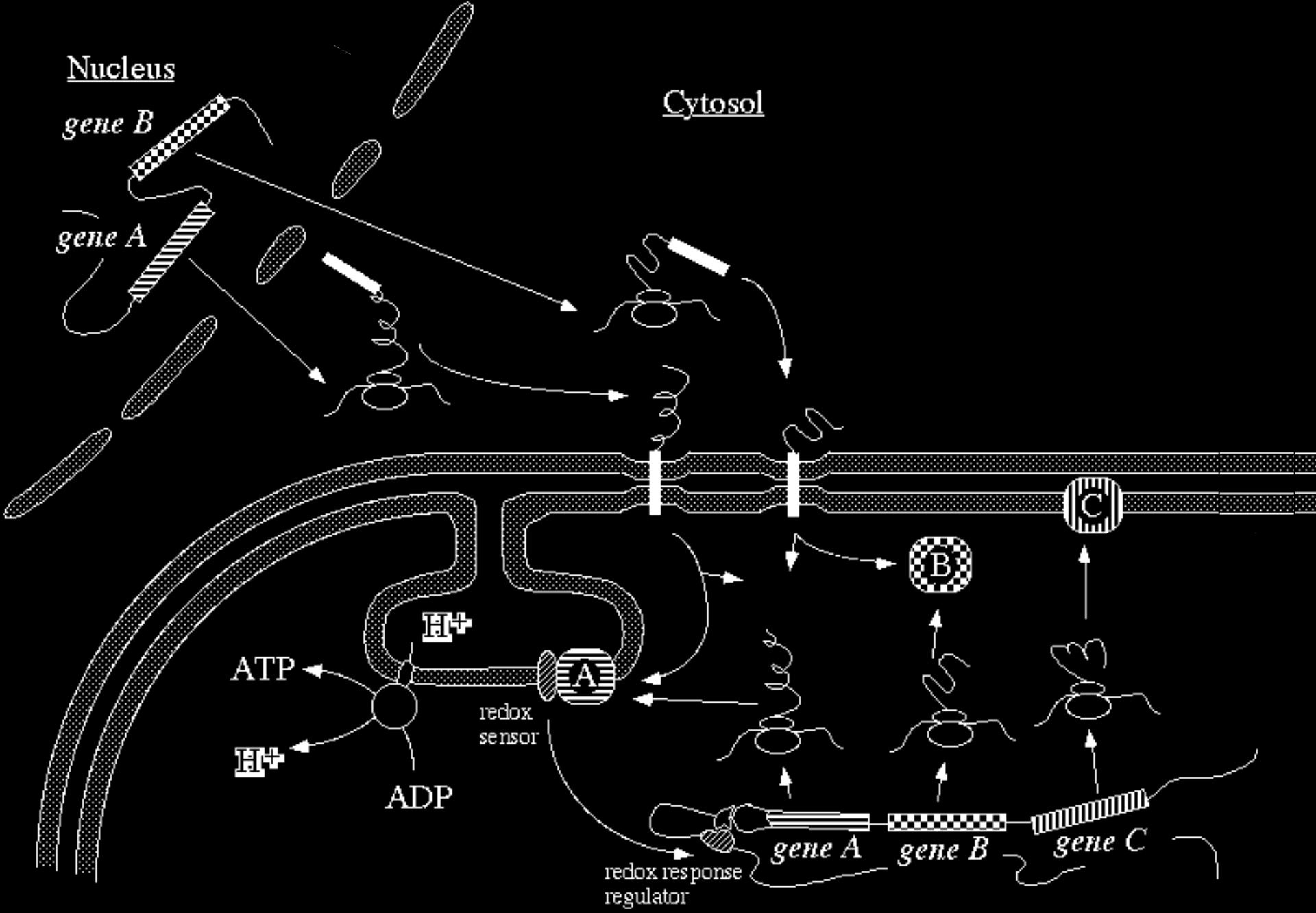
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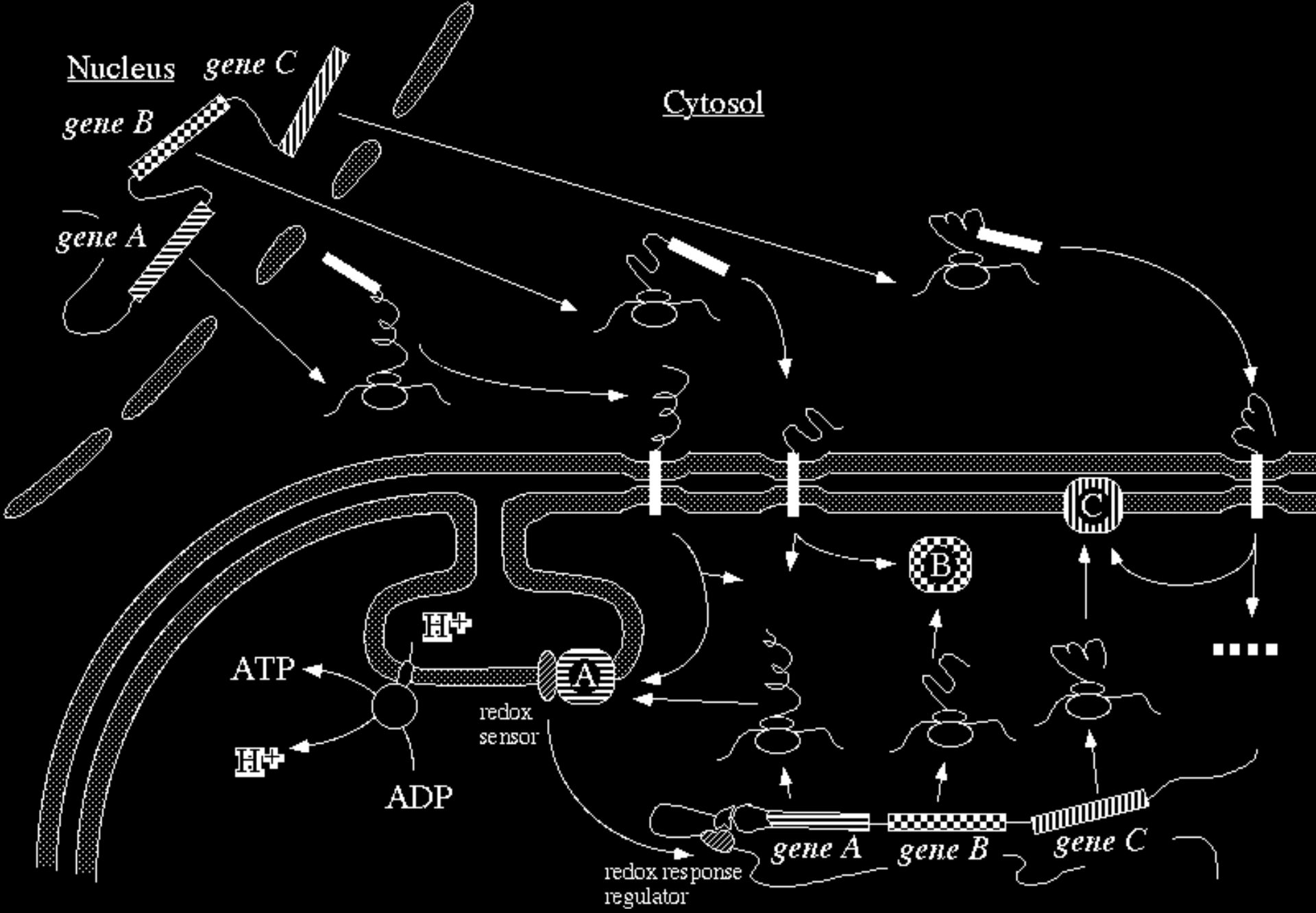
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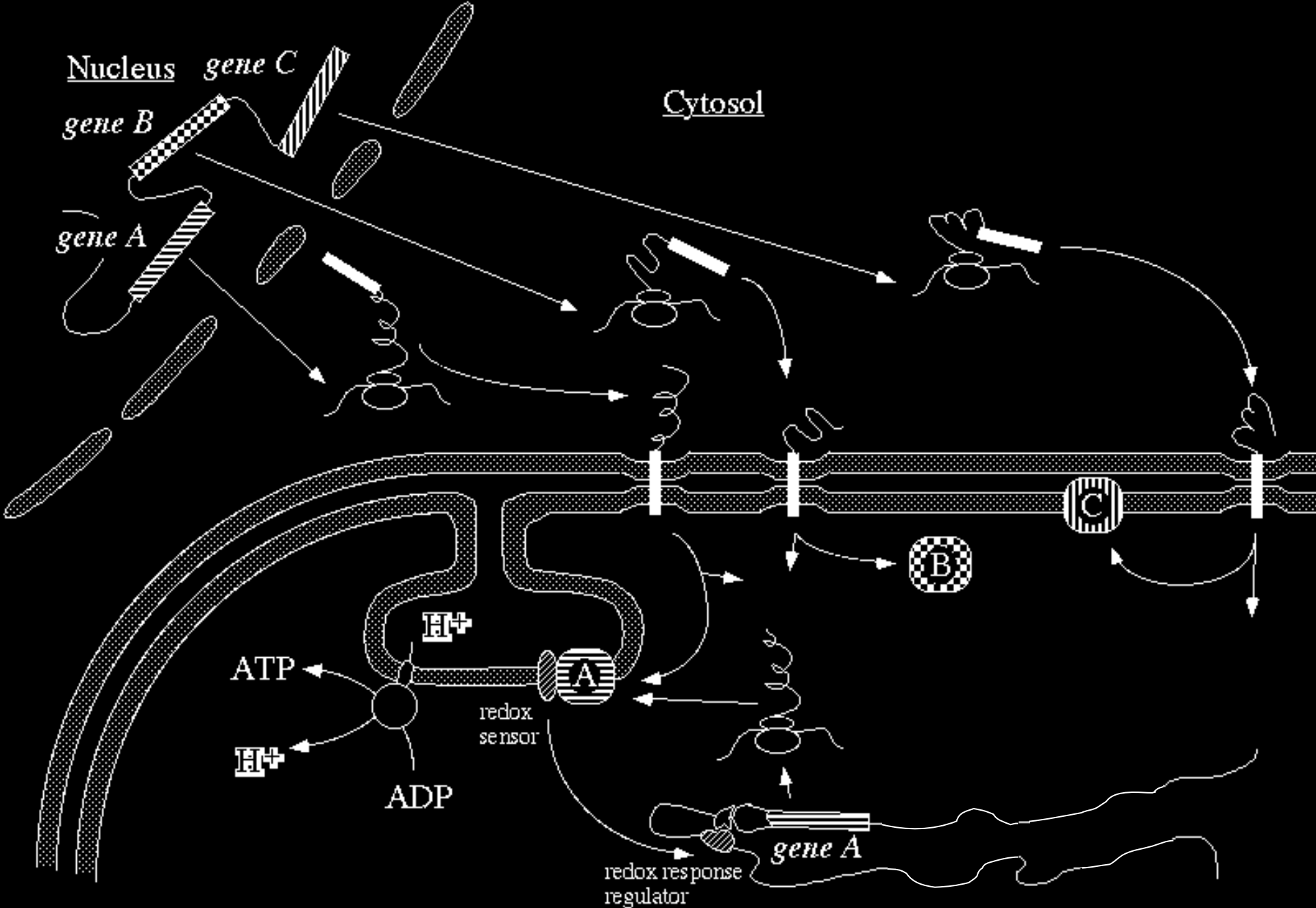
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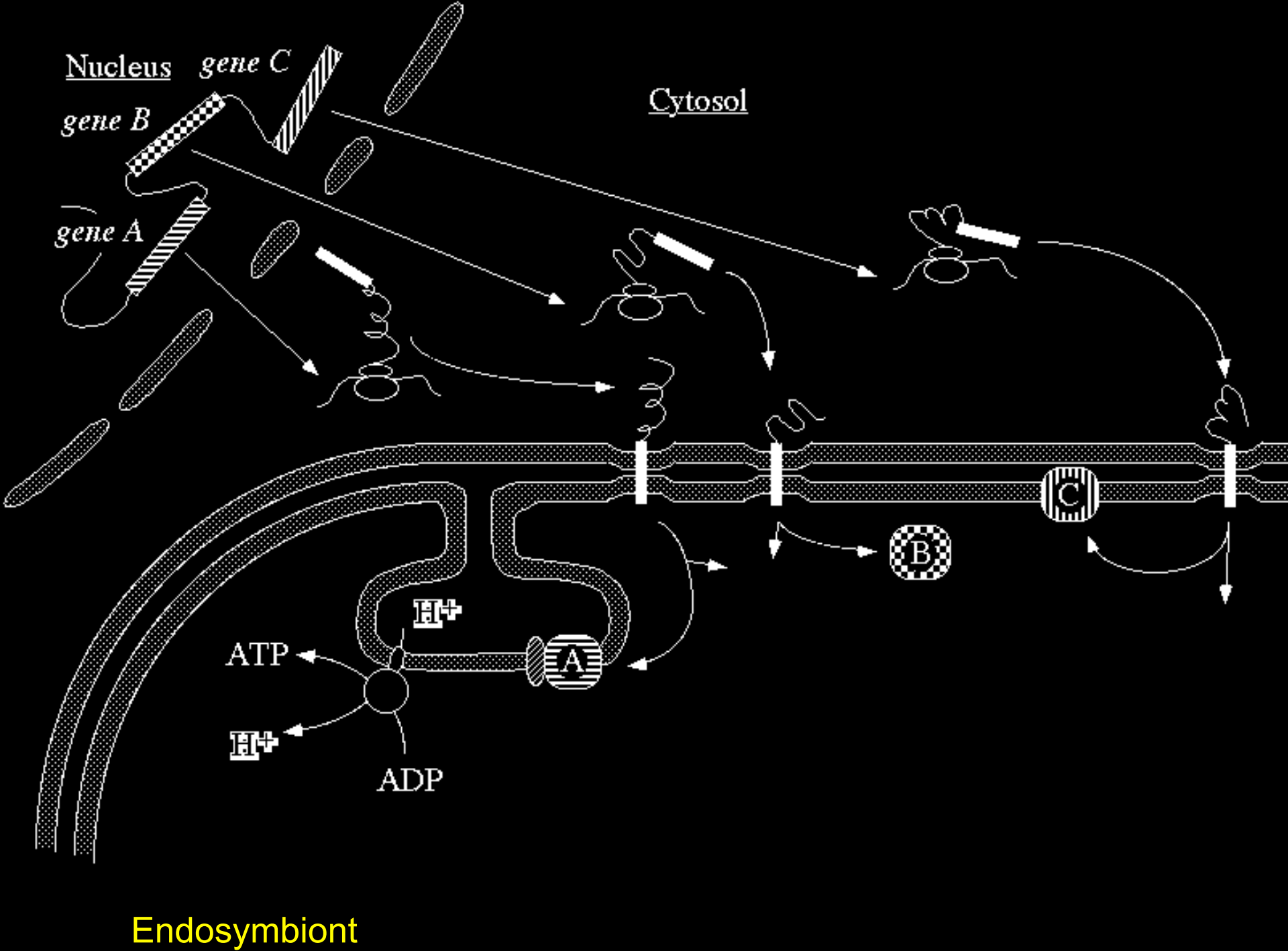
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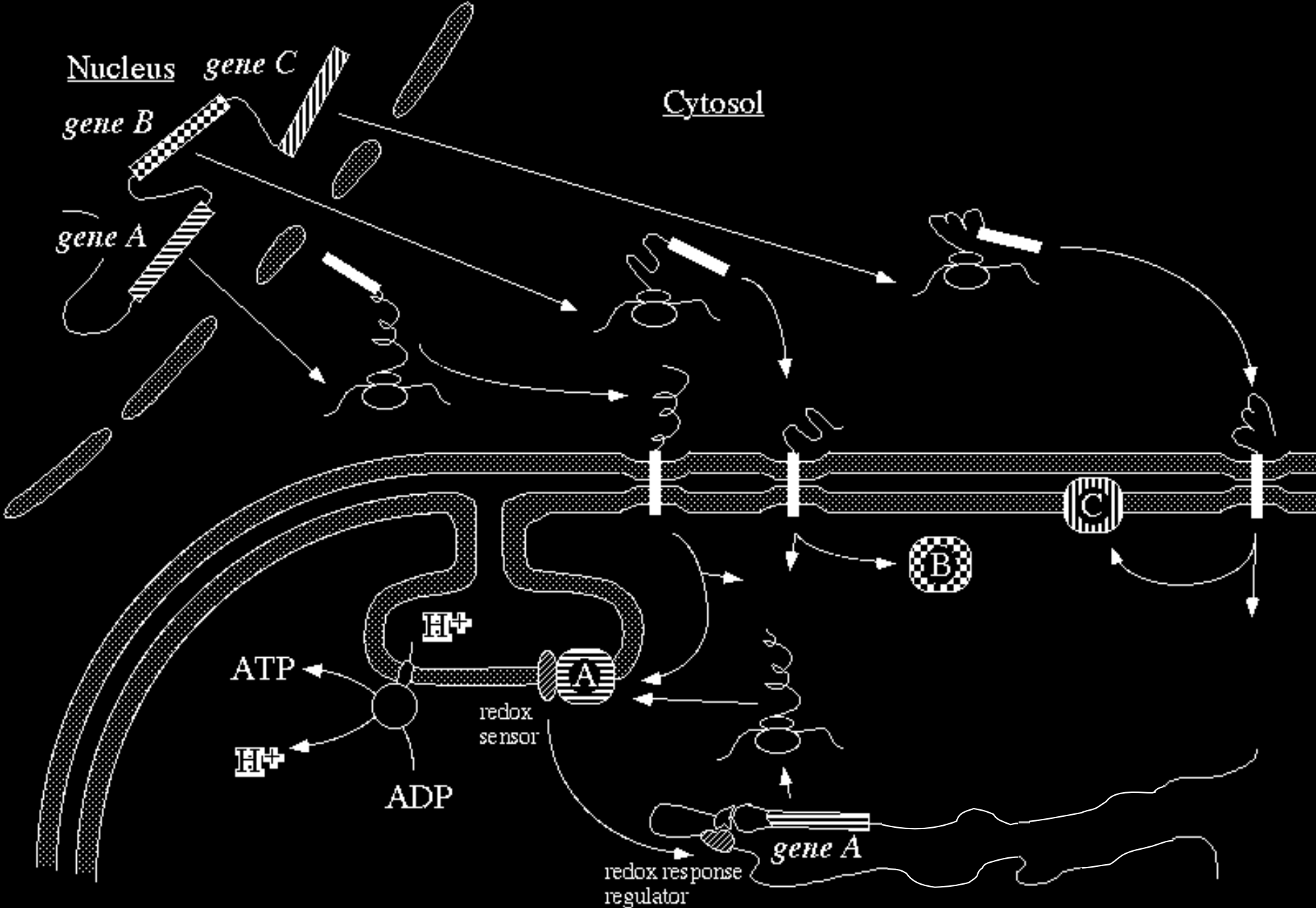


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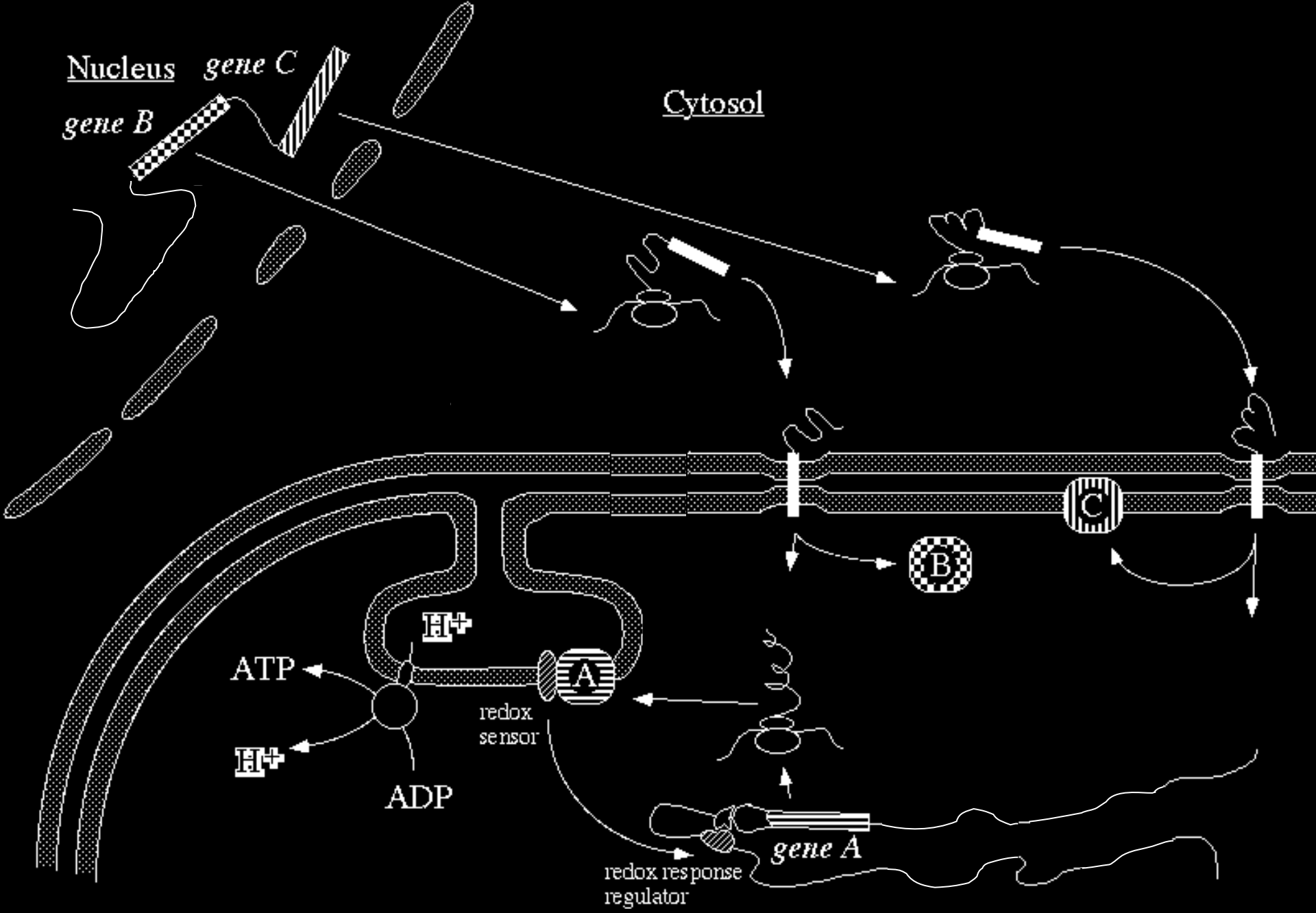


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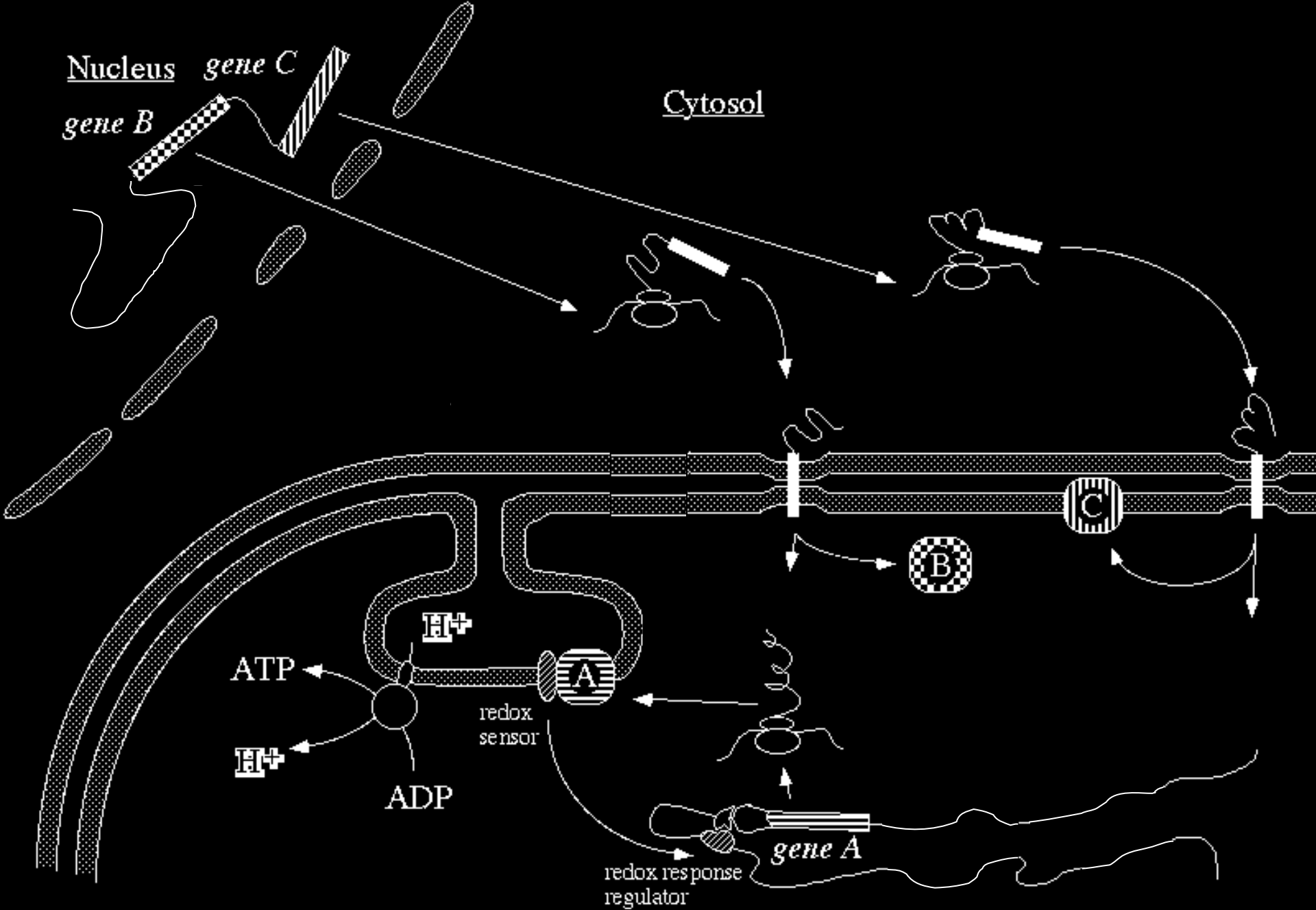




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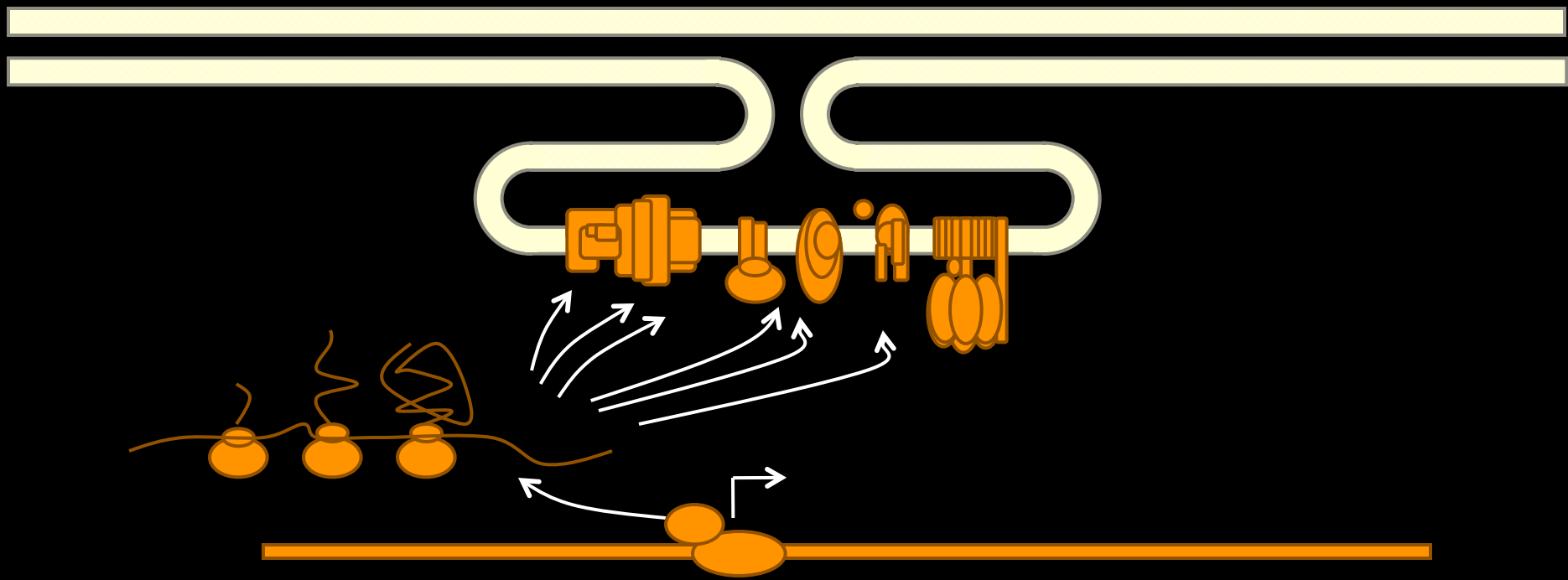


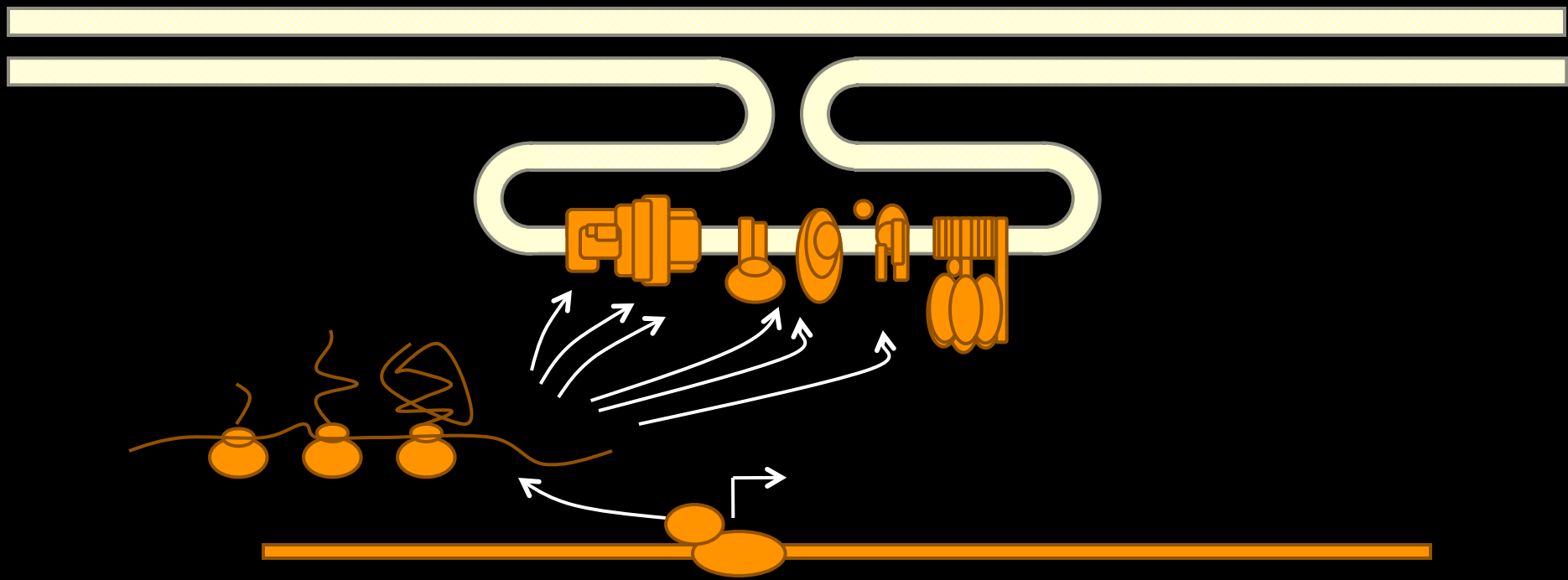
Bioenergetic organelle



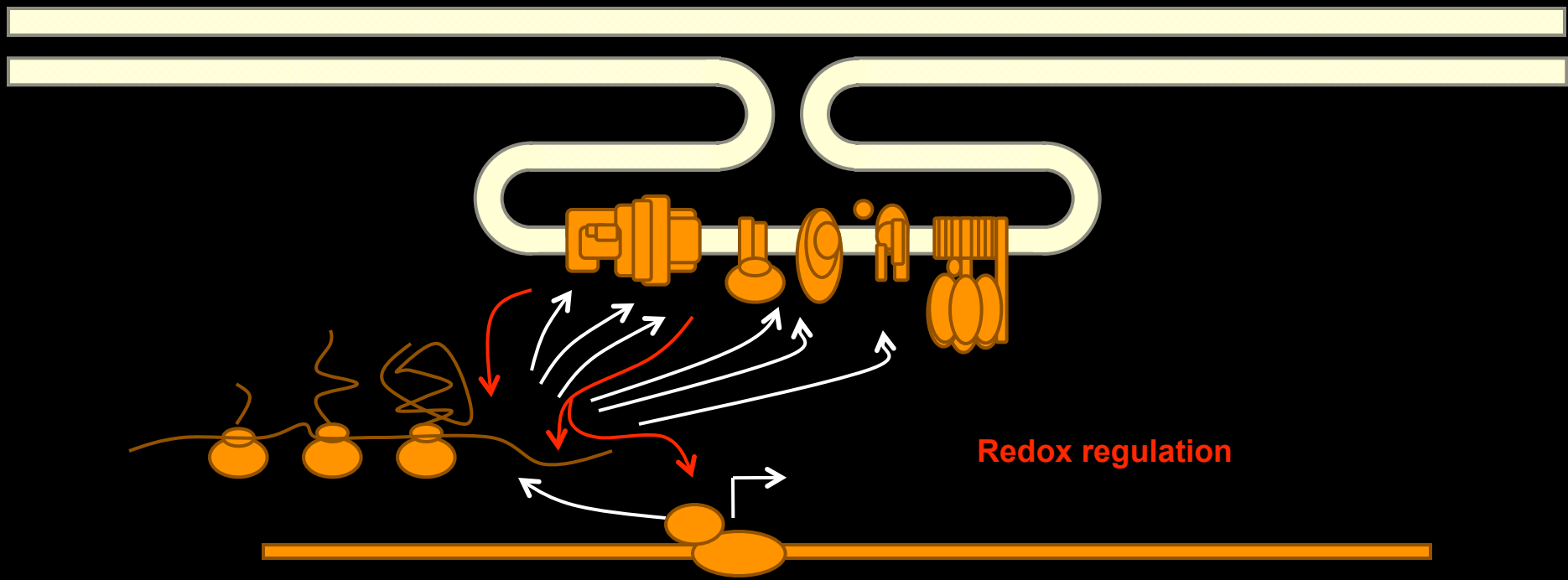
## Bioenergetic organelle

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

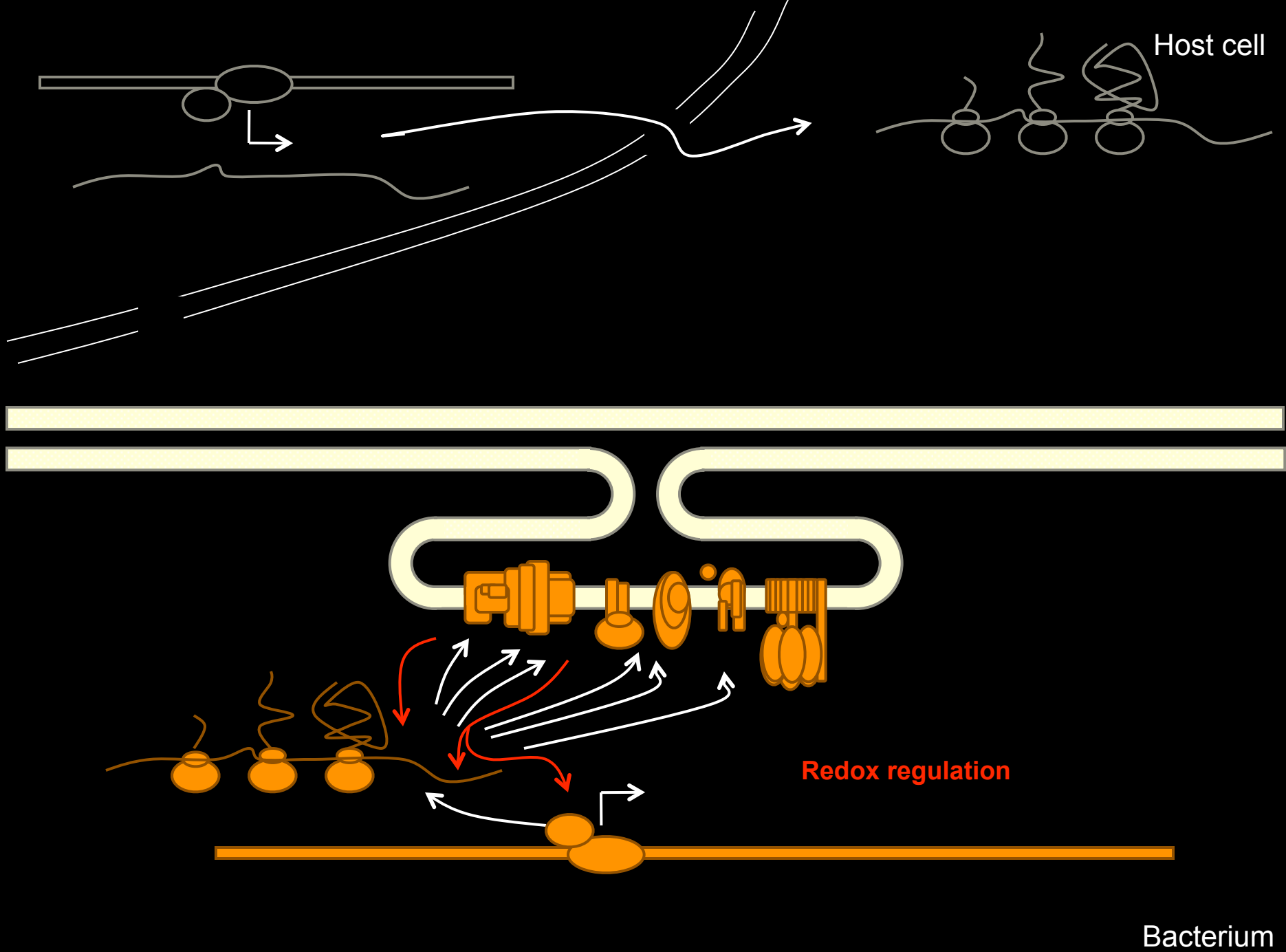




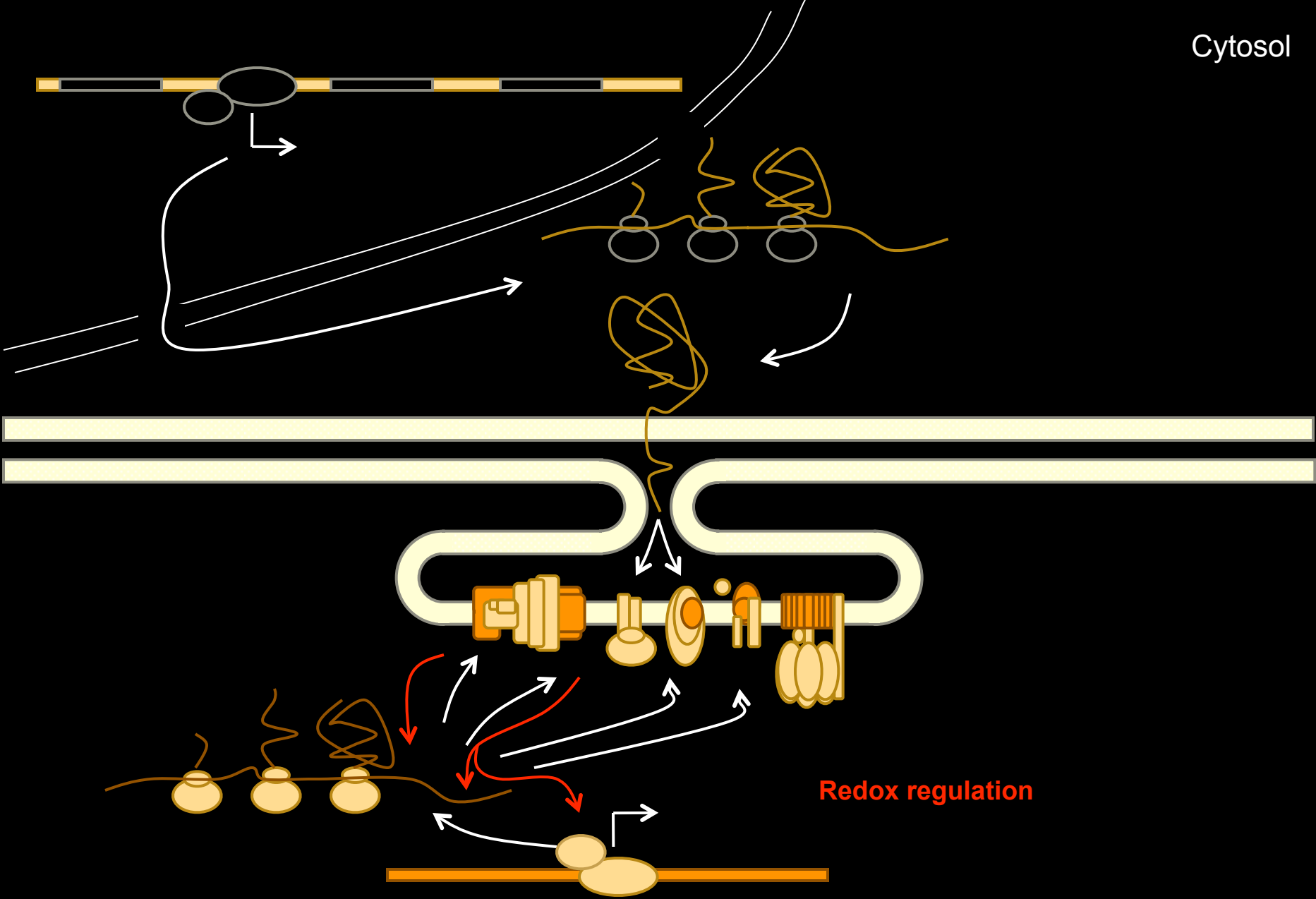
Bacterium



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Cytosol



Mitochondrial matrix

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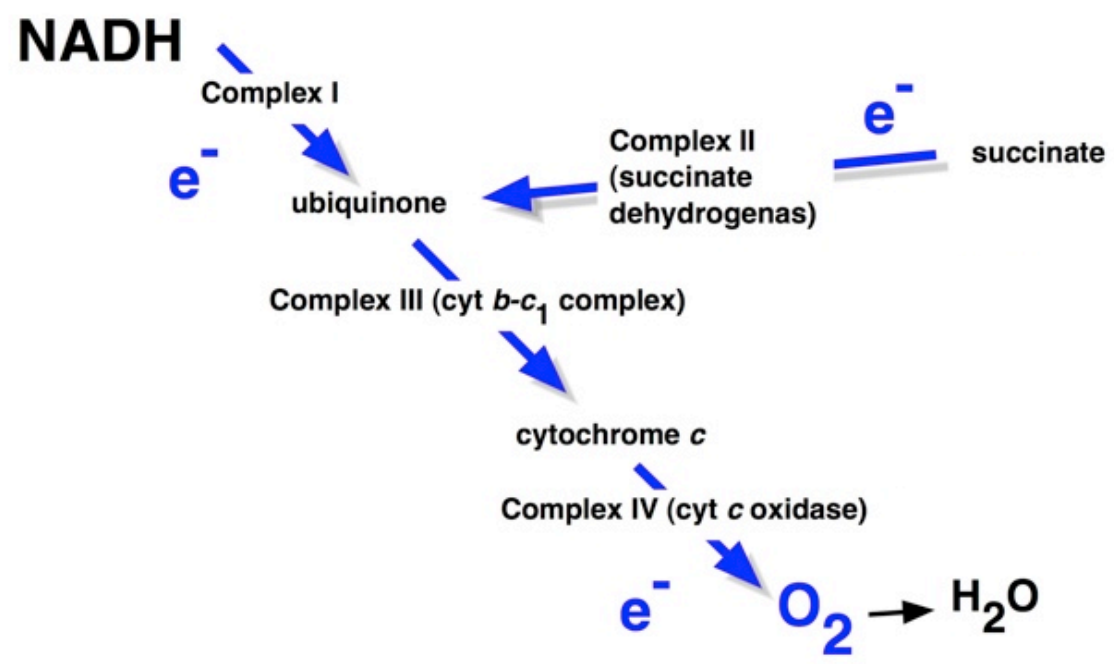
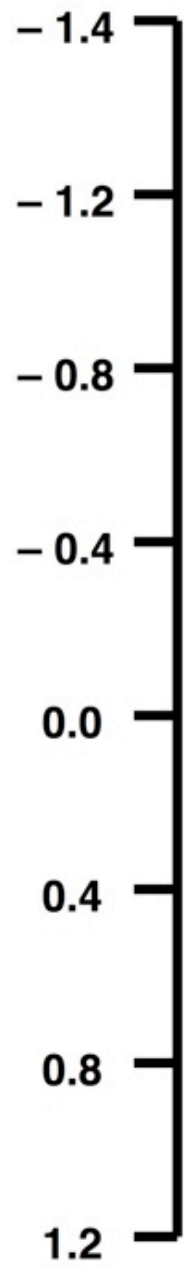
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# Co-location for Redox Regulation - CoRR

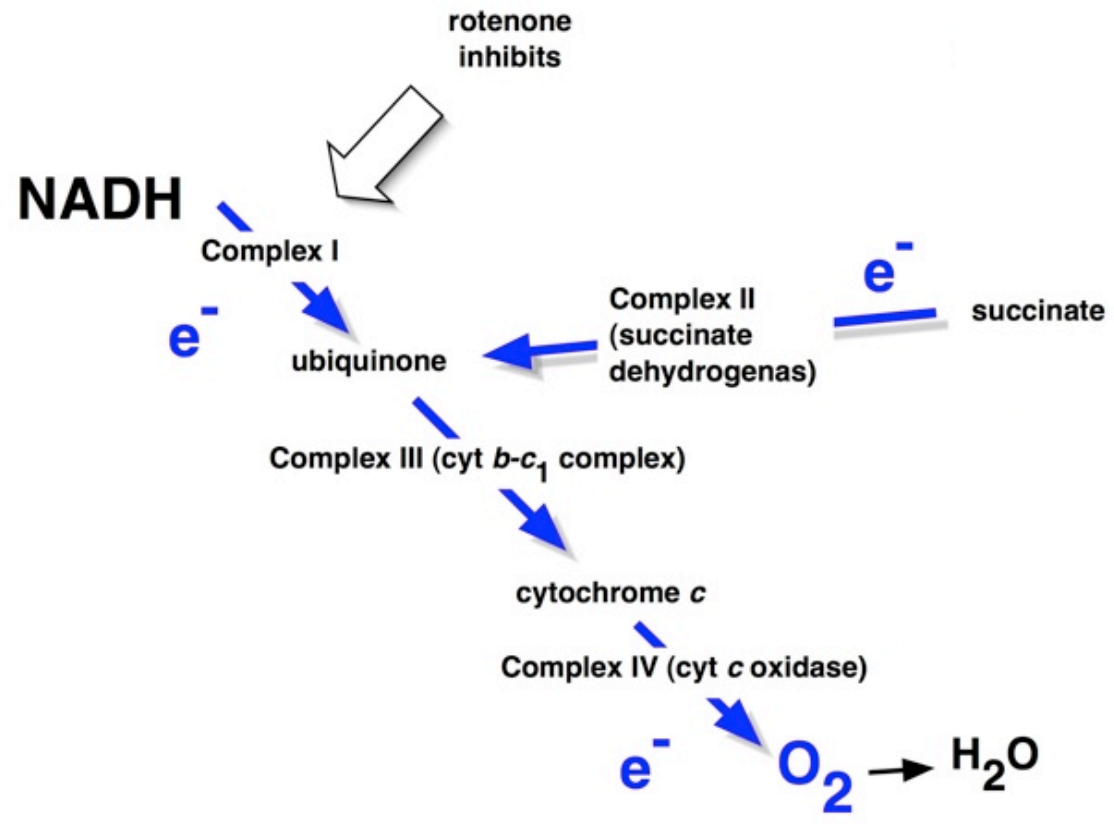
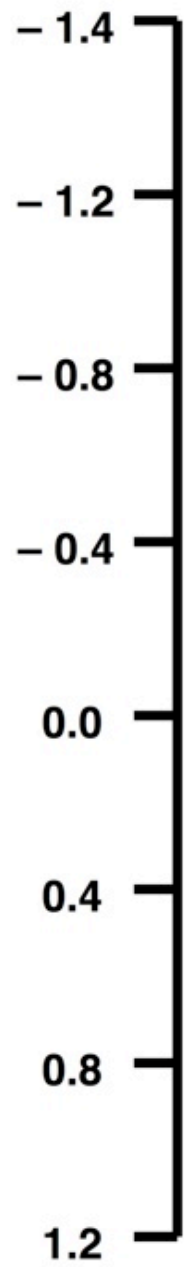
Prediction

Experimental results

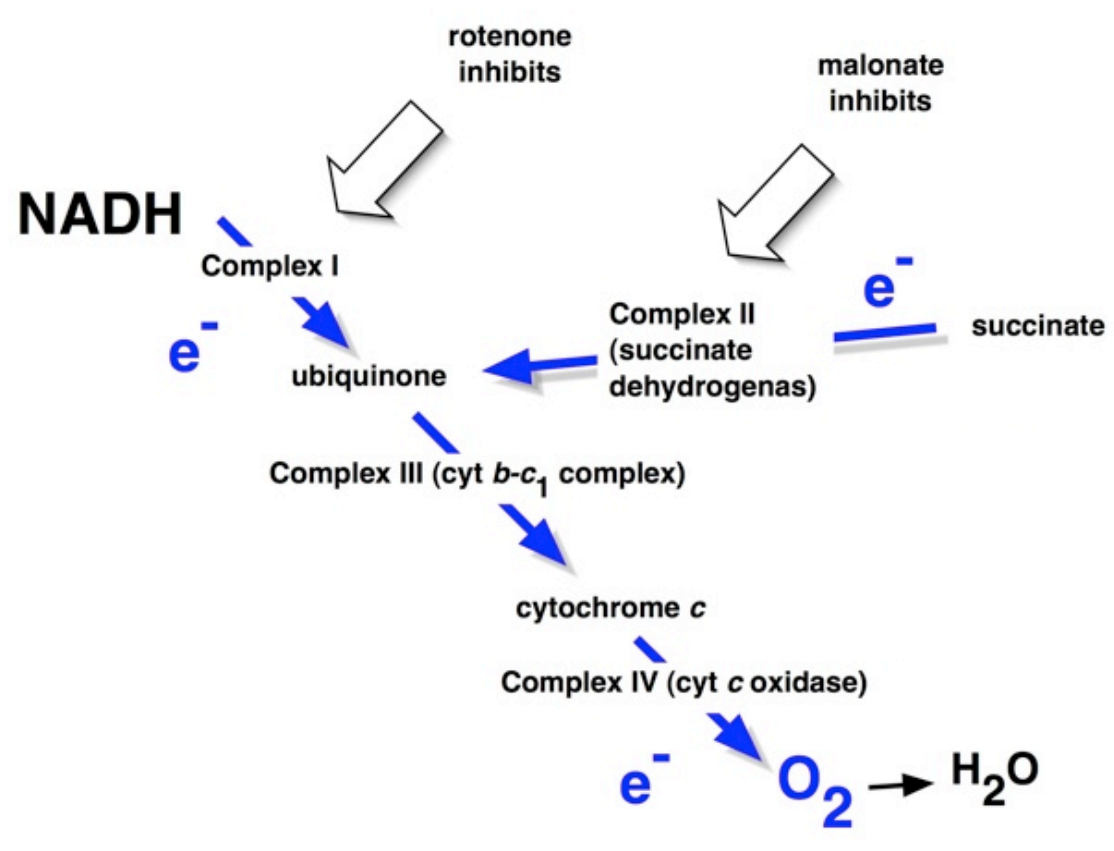
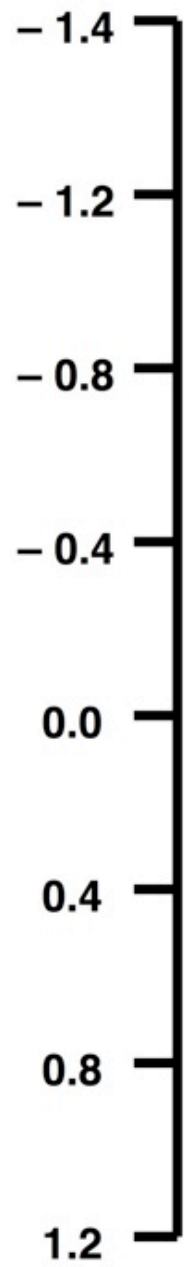
Redox regulatory control of mitochondrial and chloroplast gene expression



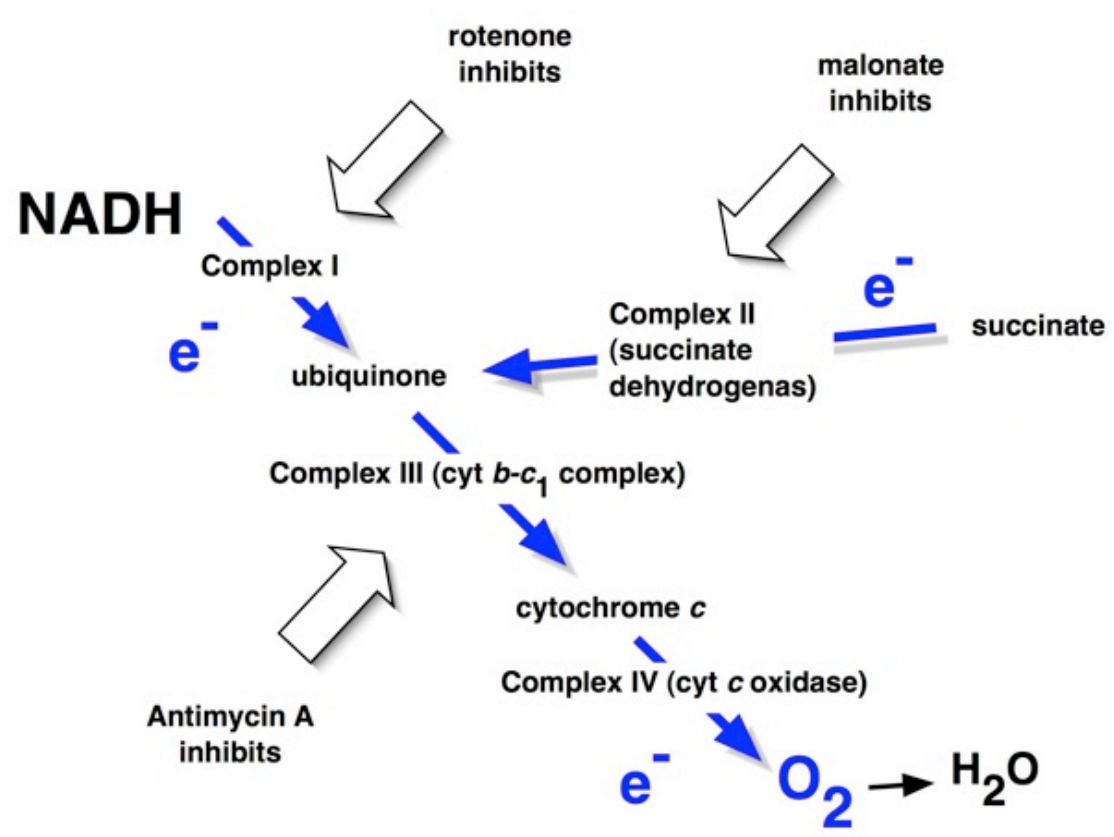
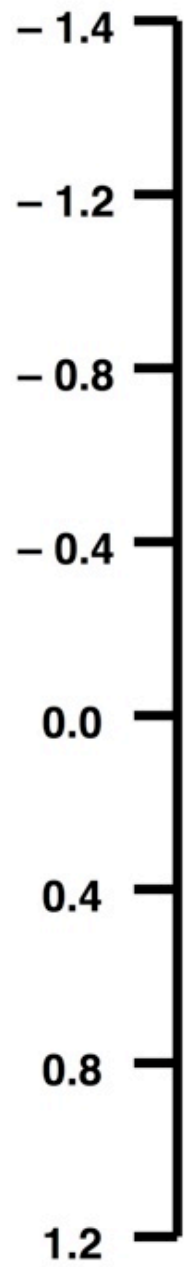
standard redox potential, volts



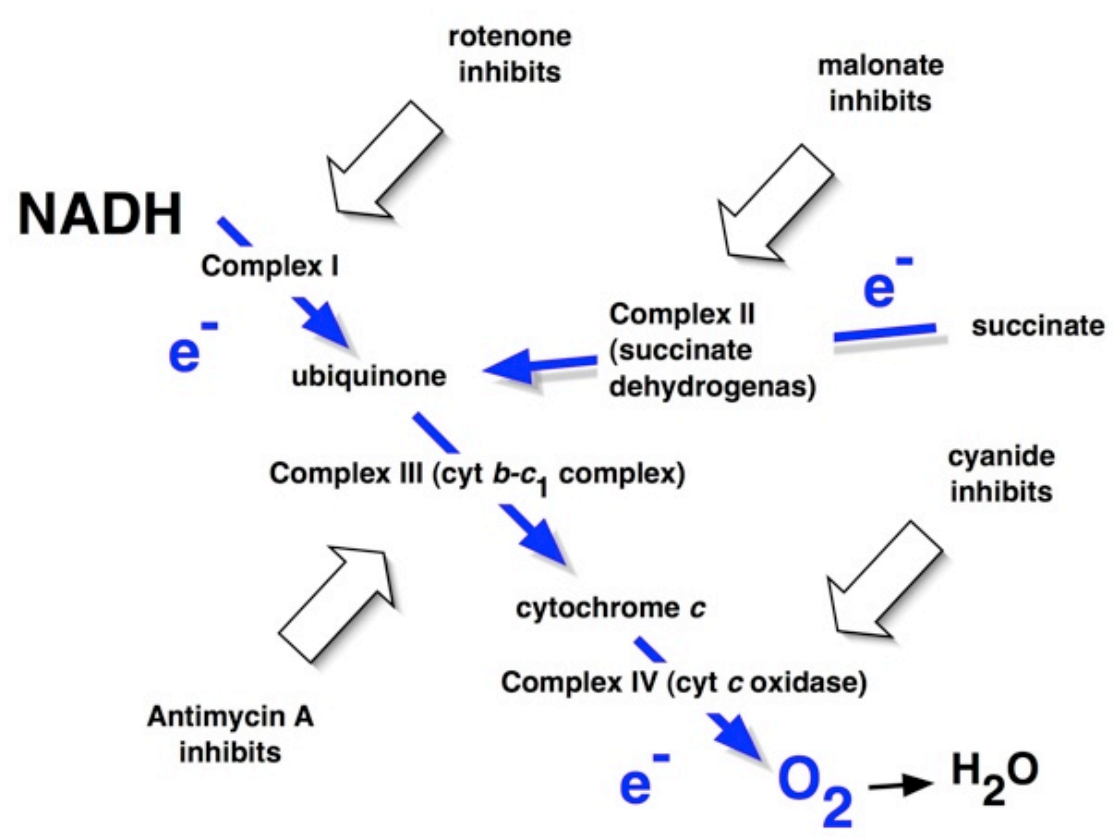
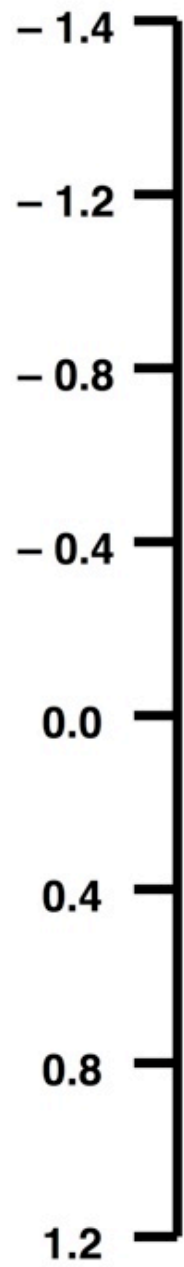
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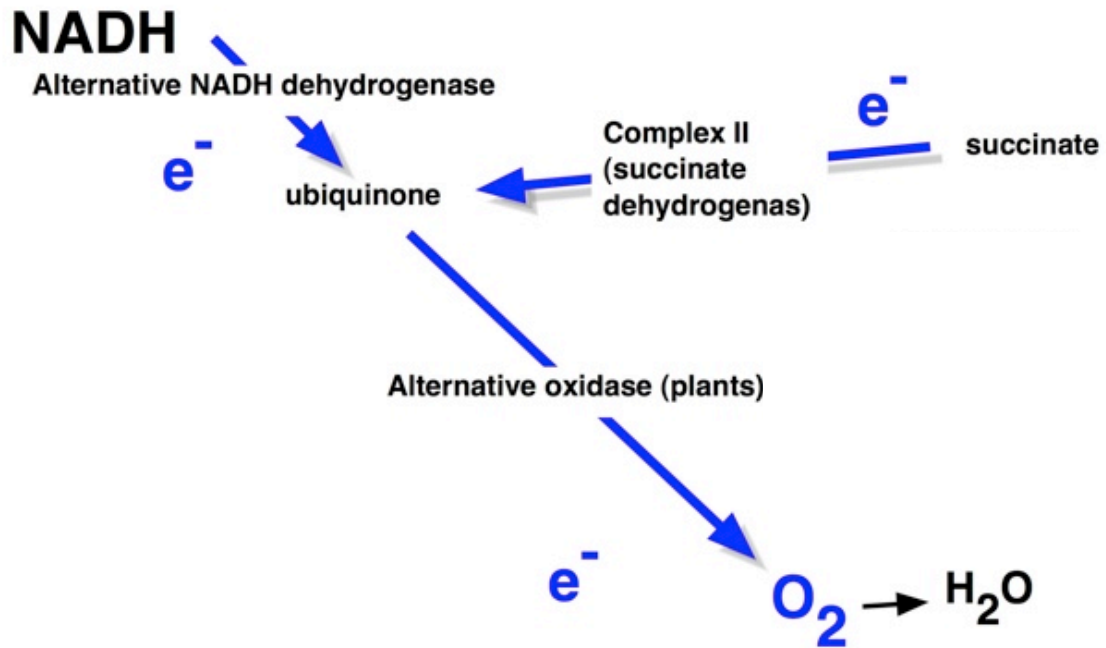
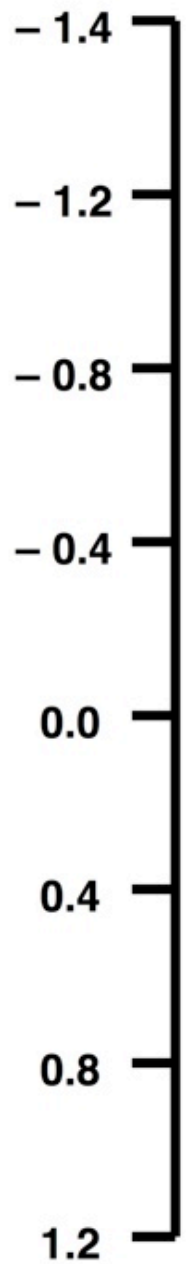
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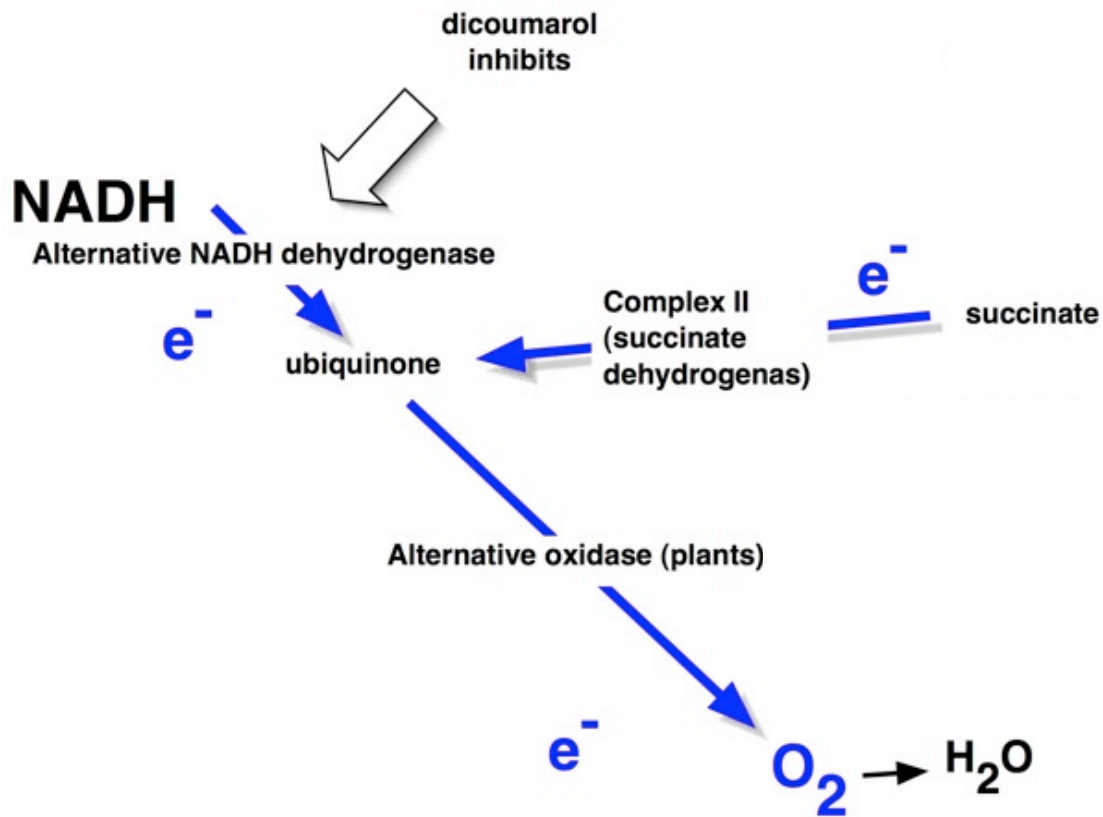
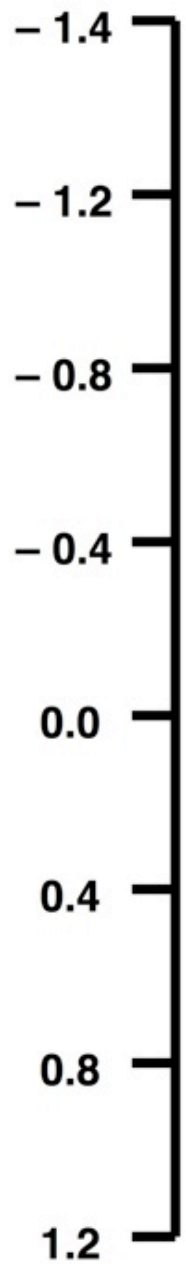
standard redox potential, volts



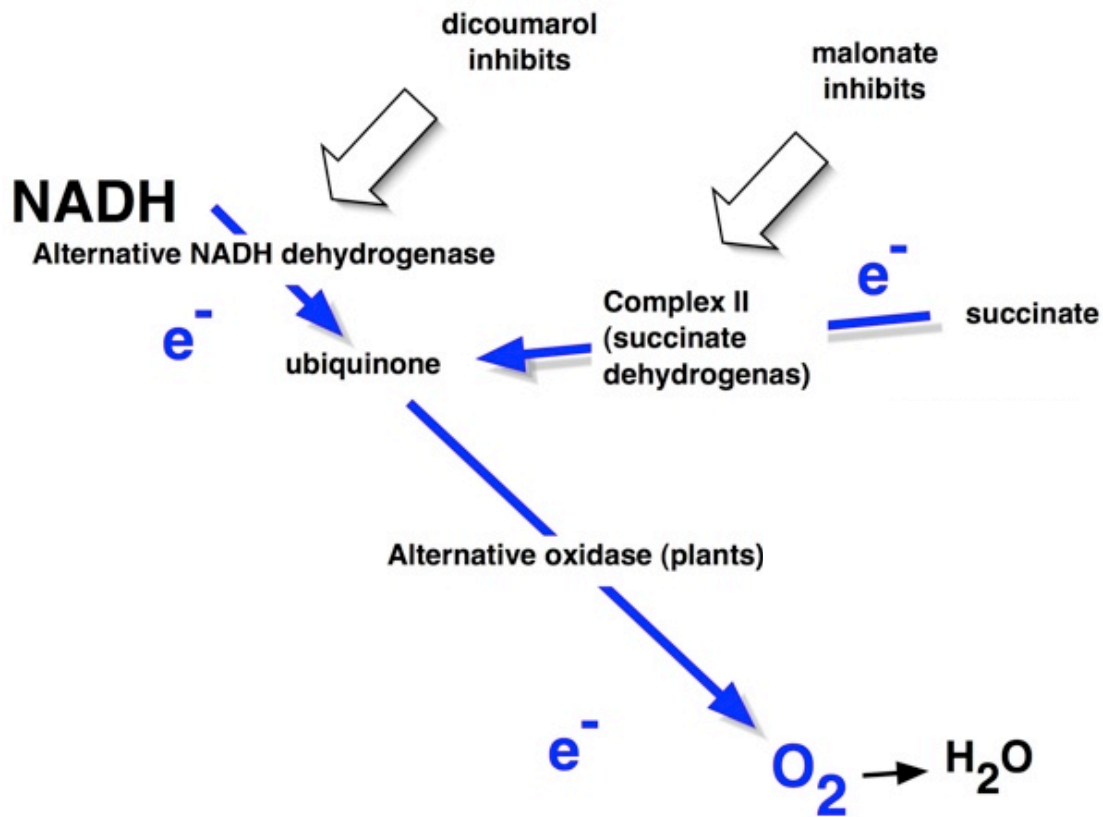
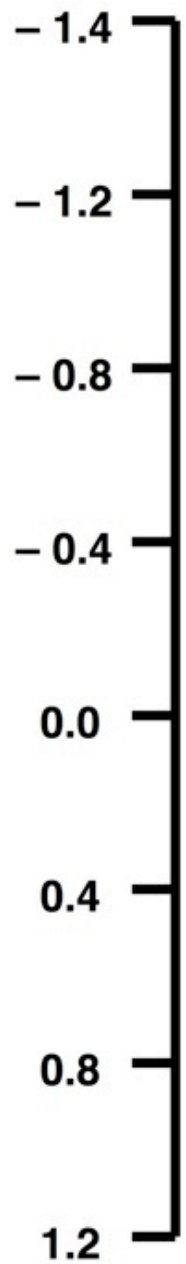
standard redox potential, volts



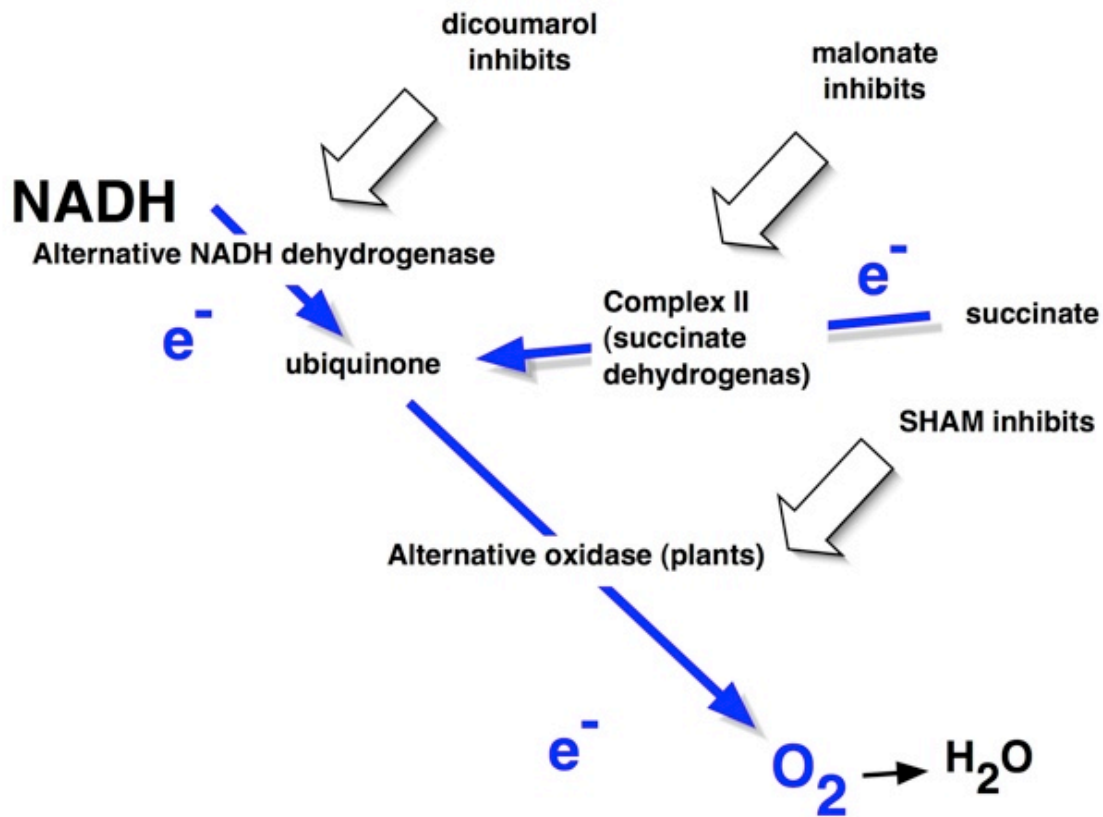
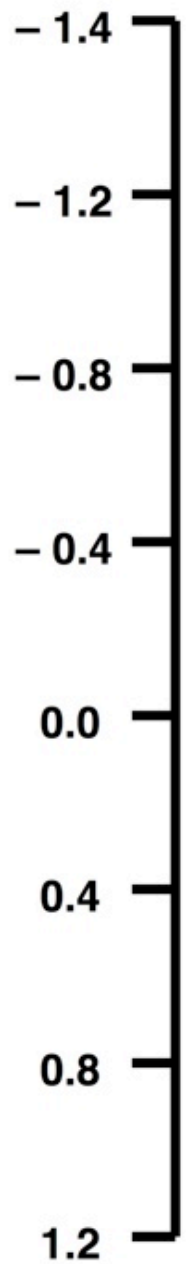
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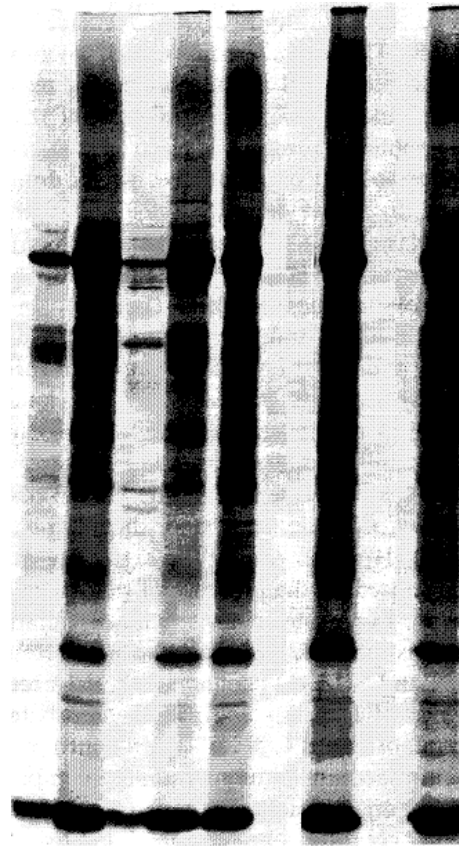


standard redox potential, volts



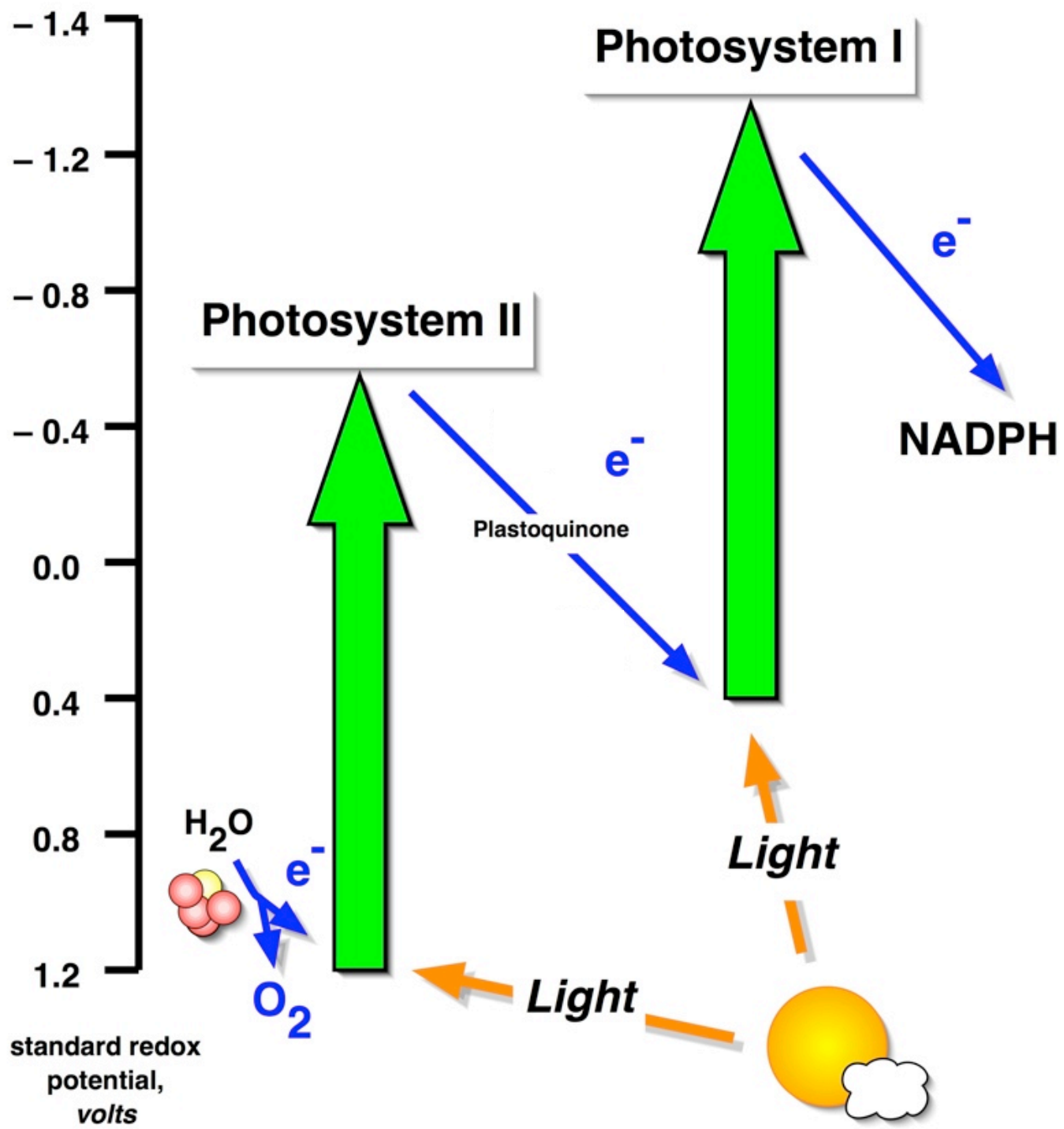
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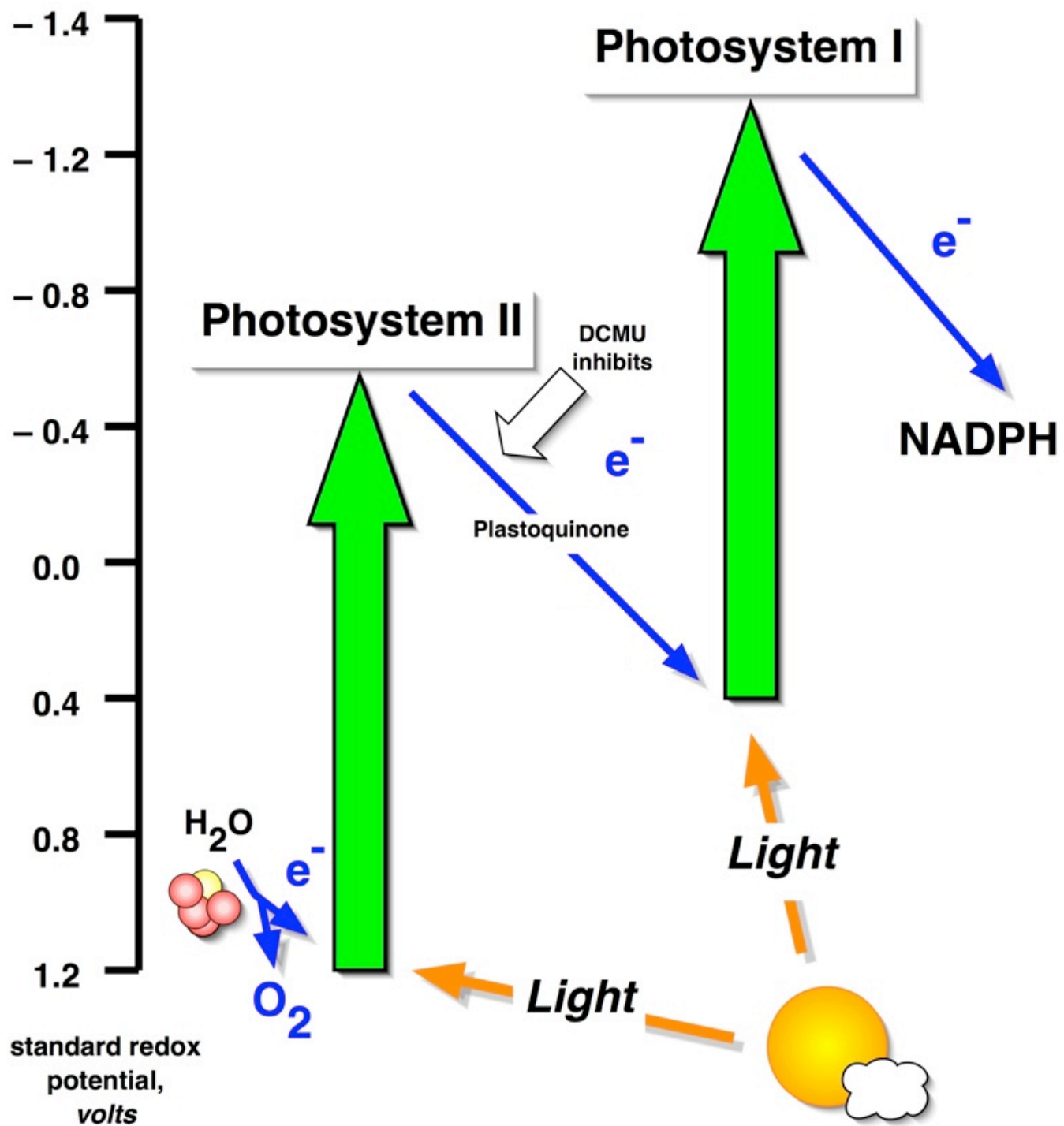
+ ferricyanide  
 + ascorbate  
 + dithiothreitol  
 + dithionite  
 + duroquinol  
 + rotenone, malonate.,dicumarol  
 + cyanide, SHAM

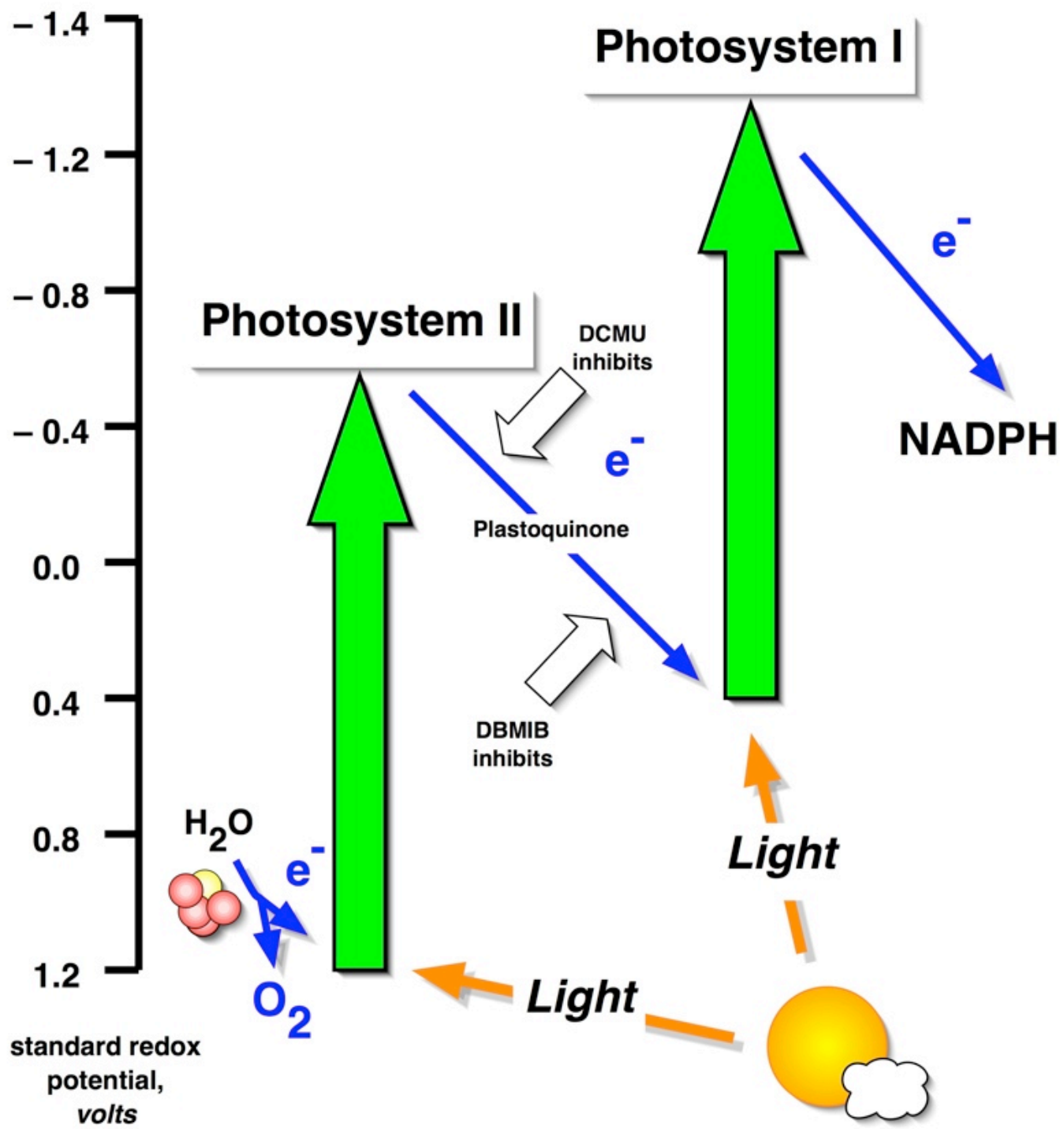


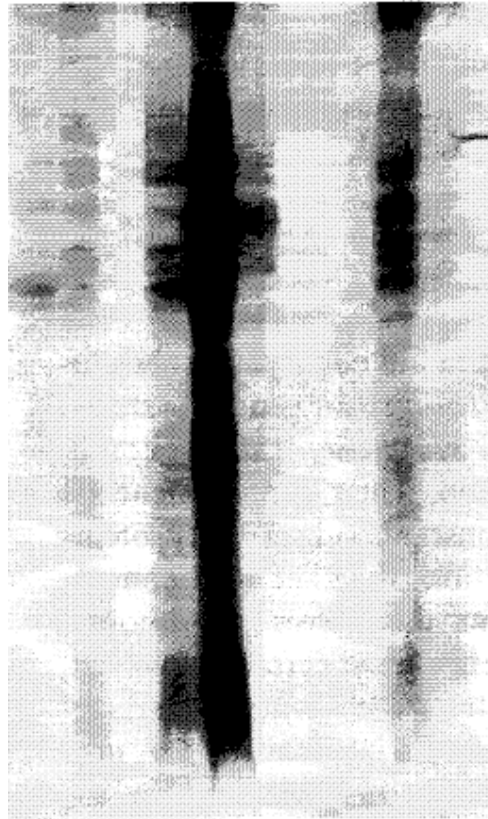
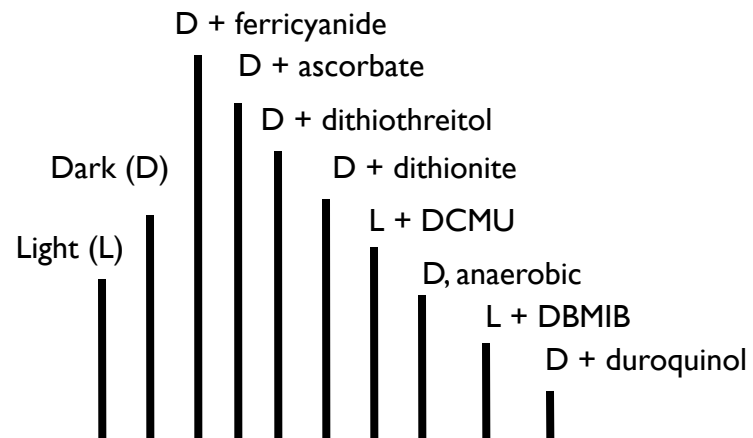
Allen, C.A. et al  
 Redox Report 1, 119-123

<sup>35</sup>S-methionine labelling of newly synthesised proteins in pea leaf mitochondria



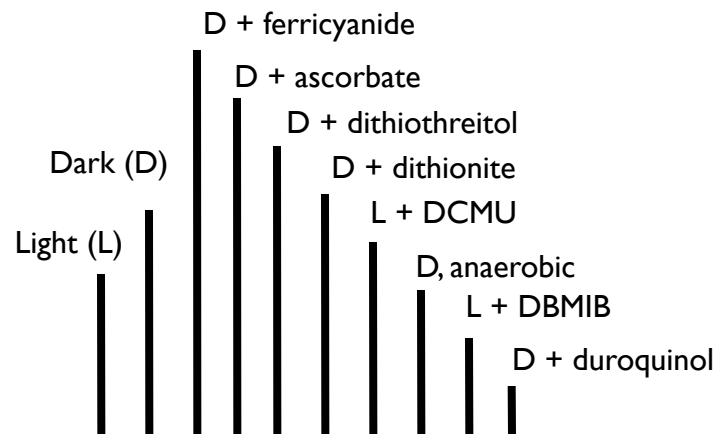






Allen, C.A. et al  
 Redox Report 1, 119-123

<sup>35</sup>S-methionine labelling of newly synthesised proteins in pea leaf thylakoids



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

<sup>35</sup>S-methionine labelling of newly synthesised proteins in pea leaf chloroplast stroma

# Co-location for Redox Regulation - CoRR

Prediction

Experimental results

Redox regulatory control of chloroplast and  
mitochondrial transcription

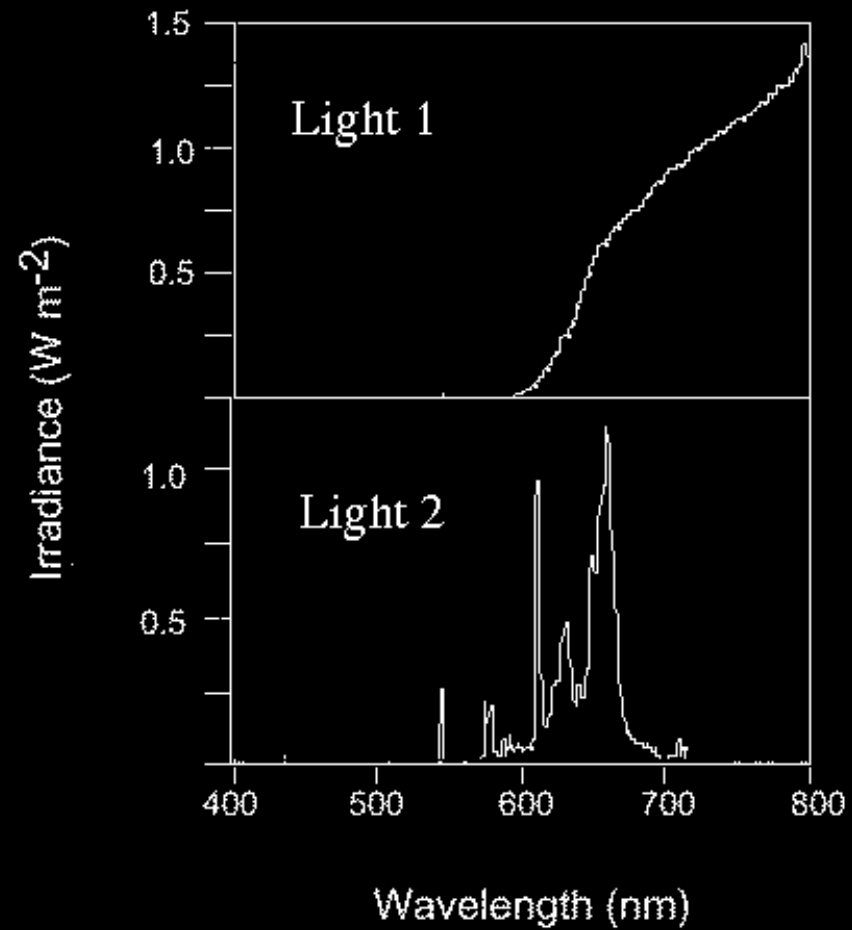


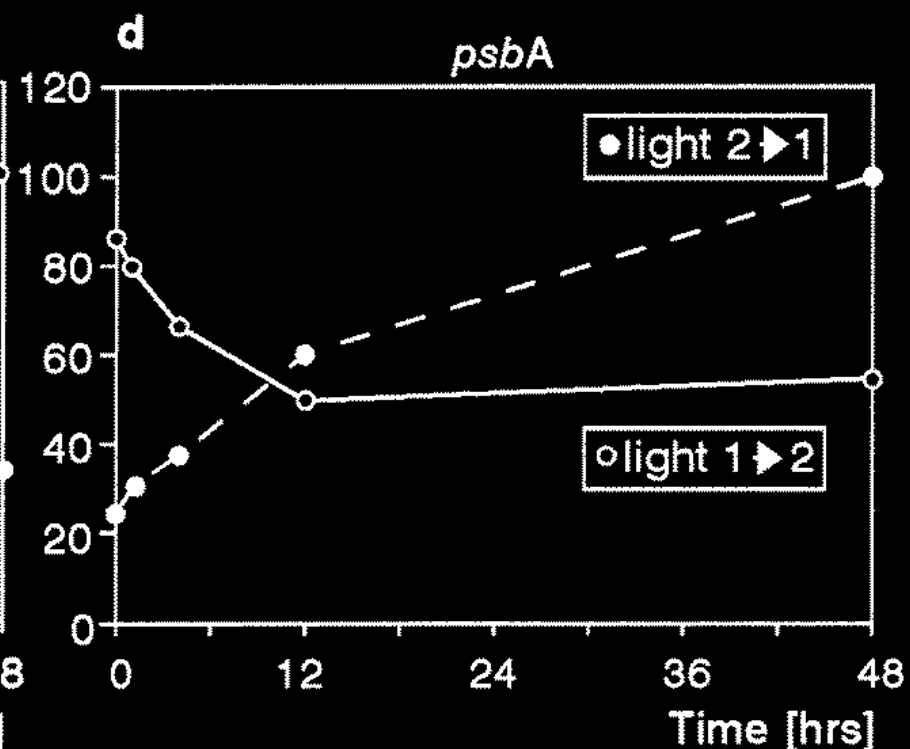
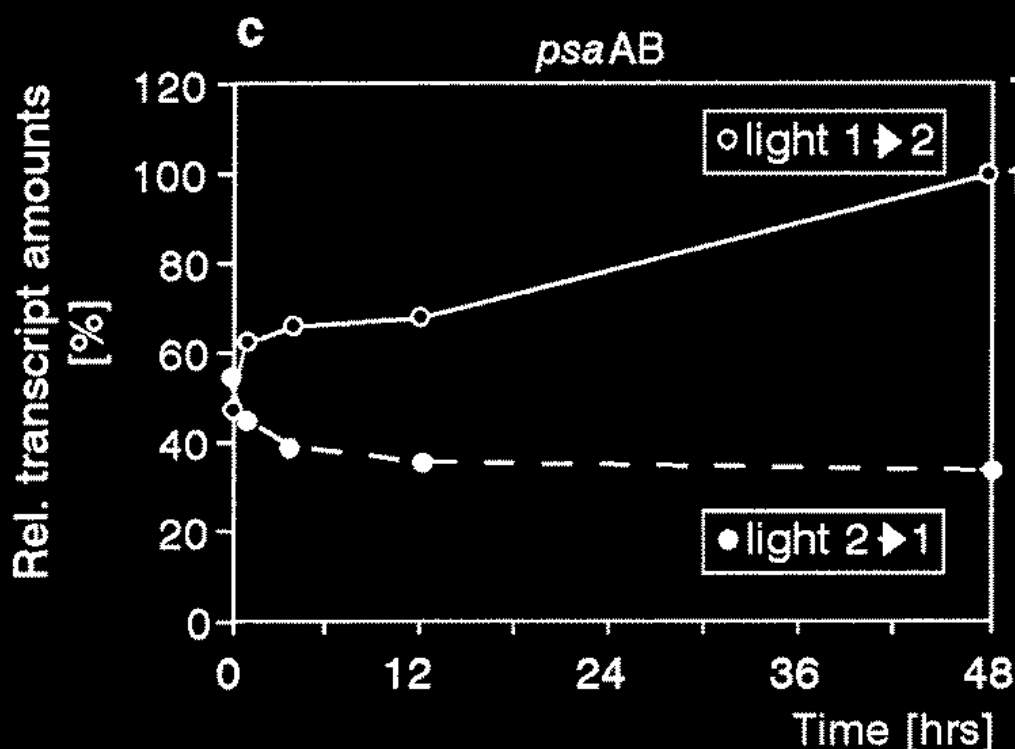
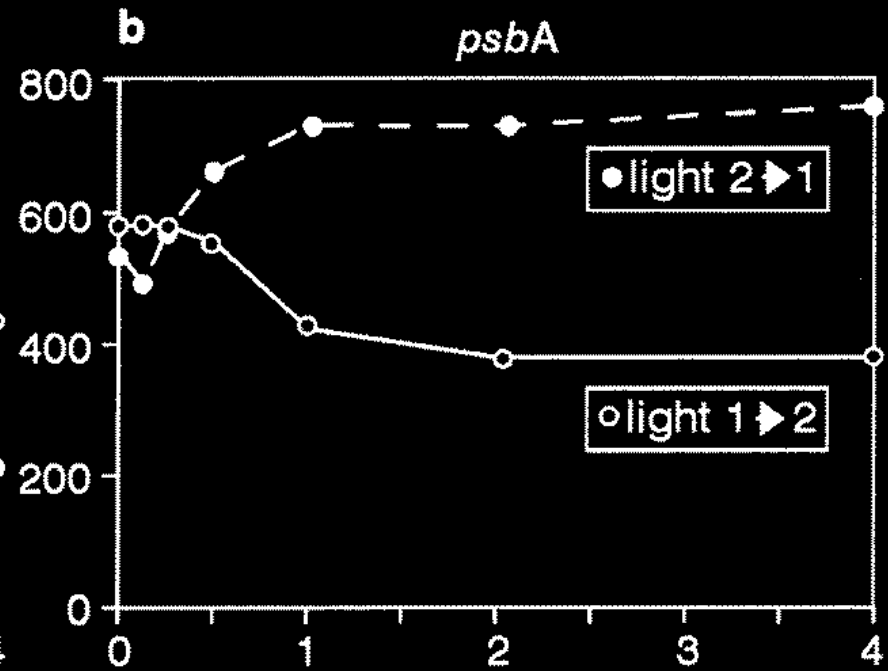
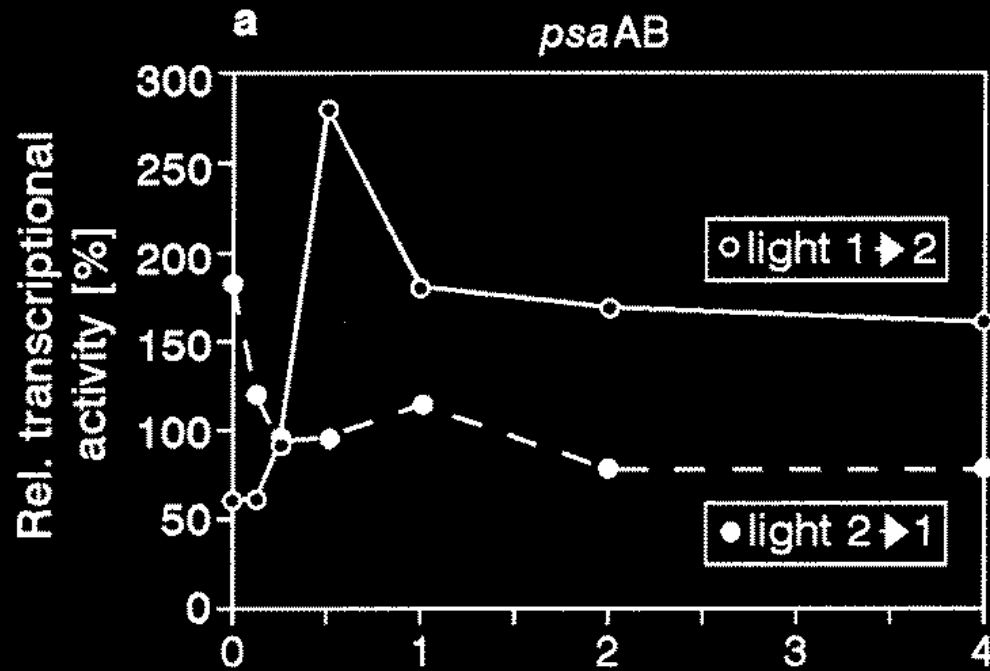
31. 7. 2001











# Co-location for Redox Regulation - CoRR

Prediction

Experimental results

Persistence of “bacterial” redox signalling components  
in chloroplasts and mitochondria

# The ancestral symbiont sensor kinase CSK links photosynthesis with gene expression in chloroplasts

Sujith Puthiyaveetil\*, T. Anthony Kavanagh<sup>†</sup>, Peter Cain<sup>‡</sup>, James A. Sullivan\*, Christine A. Newell<sup>§</sup>, John C. Gray<sup>§</sup>, Colin Robinson<sup>‡</sup>, Mark van der Giezen<sup>¶</sup>, Matthew B. Rogers<sup>¶</sup>, and John F. Allen\*<sup>||</sup>

\*School of Biological and Chemical Sciences, Queen Mary, University of London, Mile End Road, London E1 4NS, United Kingdom; <sup>†</sup>Smurfit Institute of Genetics, Trinity College Dublin, Dublin 2, Ireland; <sup>‡</sup>Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, United Kingdom; <sup>§</sup>Department of Plant Sciences, University of Cambridge, Downing Street, Cambridge CB2 3EA, United Kingdom; and <sup>¶</sup>Centre for Eukaryotic Evolutionary Microbiology, School of Biosciences, University of Exeter, Exeter EX4 4QD, United Kingdom

Communicated by Elisabeth Gantt, University of Maryland, College Park, MD, April 25, 2008 (received for review February 15, 2008)

We describe a novel, typically prokaryotic, sensor kinase in chloroplasts of green plants. The gene for this chloroplast sensor kinase (CSK) is found in cyanobacteria, prokaryotes from which chloroplasts evolved. The CSK gene has moved, during evolution, from the ancestral chloroplast to the nuclear genomes of eukaryotic algae and green plants. The CSK protein is now synthesised in the cytosol of photosynthetic eukaryotes and imported into their chloroplasts as a protein precursor. In the model higher plant *Arabidopsis thaliana*, CSK is autophosphorylated and required for control of transcription of chloroplast genes by the redox state of an electron carrier connecting photosystems I and II. CSK therefore provides a redox regulatory mechanism that couples photosynthesis to gene expression. This mechanism is inherited directly from the cyanobacterial ancestor of chloroplasts, is intrinsic to chloroplasts, and is targeted to chloroplast genes.

limited to a few examples in certain nongreen algal groups, where there are just one or two two-component genes of uncertain function in the chloroplast genome itself (8).

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Author contributions: S.P. and J.F.A. designed research; S.P., T.A.K., P.C., C.A.N., and J.F.A. performed research; S.P., T.A.K., J.A.S., and M.v.d.G. contributed new reagents/analytic tools; S.P., T.A.K., P.C., J.C.G., C.R., M.v.d.G., M.B.R., and J.F.A. analyzed data; and S.P. and J.F.A. wrote the paper.

The authors declare no conflict of interest.

Freely available online through the PNAS open access option.

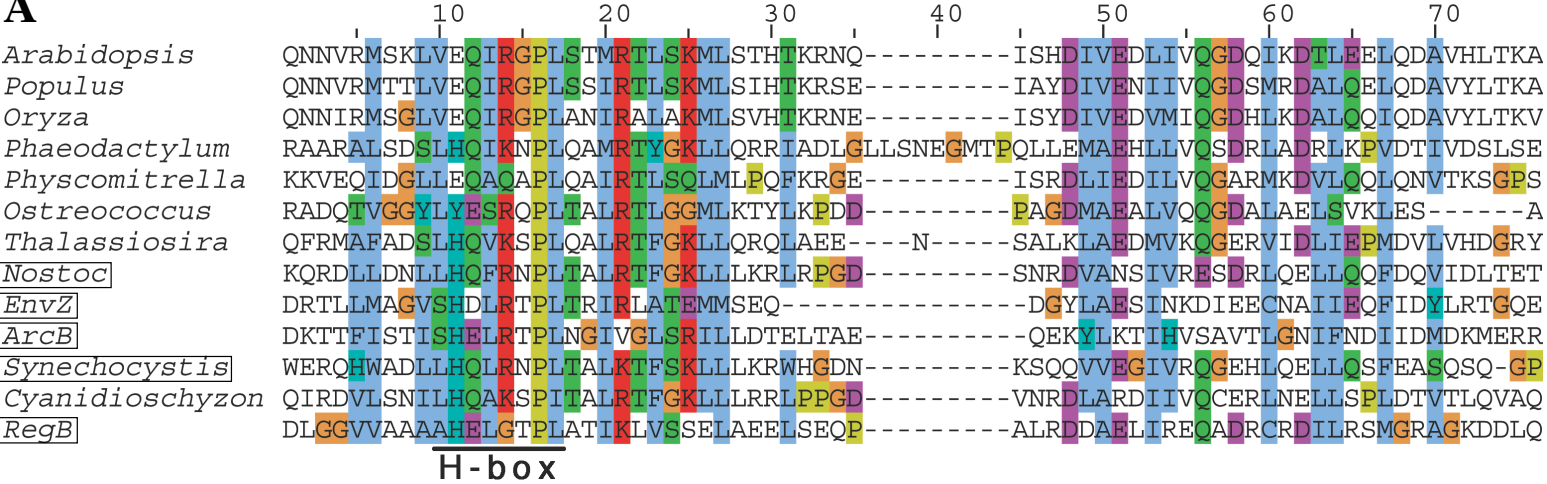
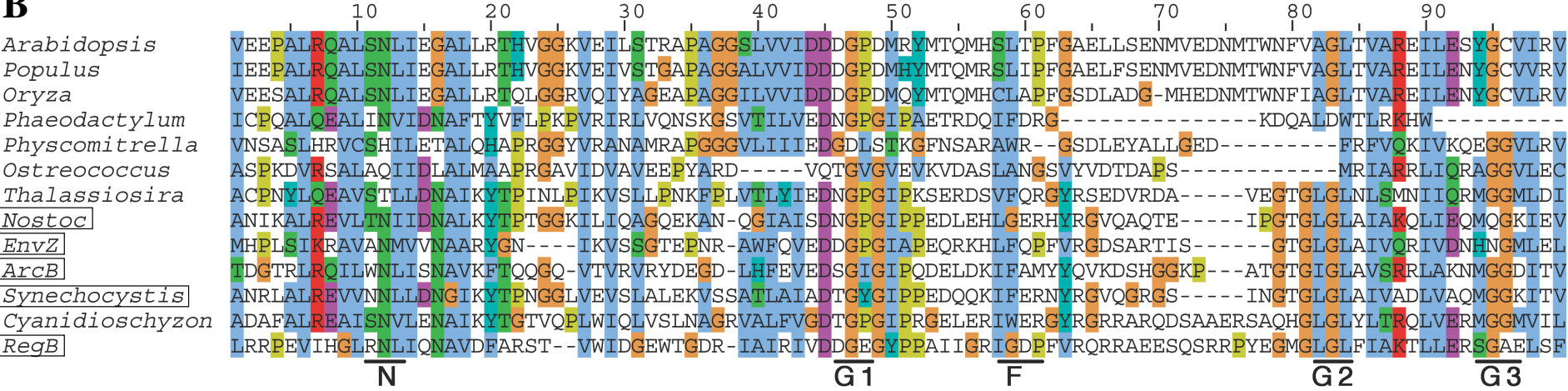
<sup>||</sup>To whom correspondence should be addressed. E-mail: j.f.allen@qmul.ac.uk.

This article contains supporting information online at [www.pnas.org/cgi/content/full/0803928105/DCSupplemental](http://www.pnas.org/cgi/content/full/0803928105/DCSupplemental).

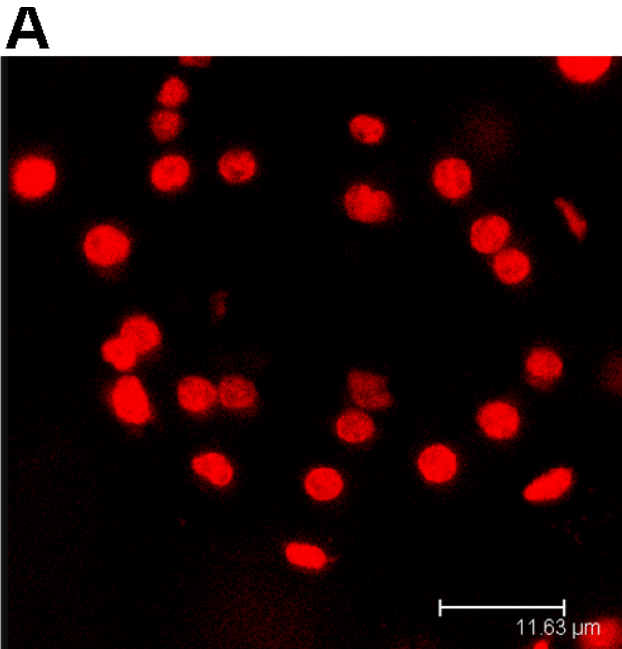
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# CSK

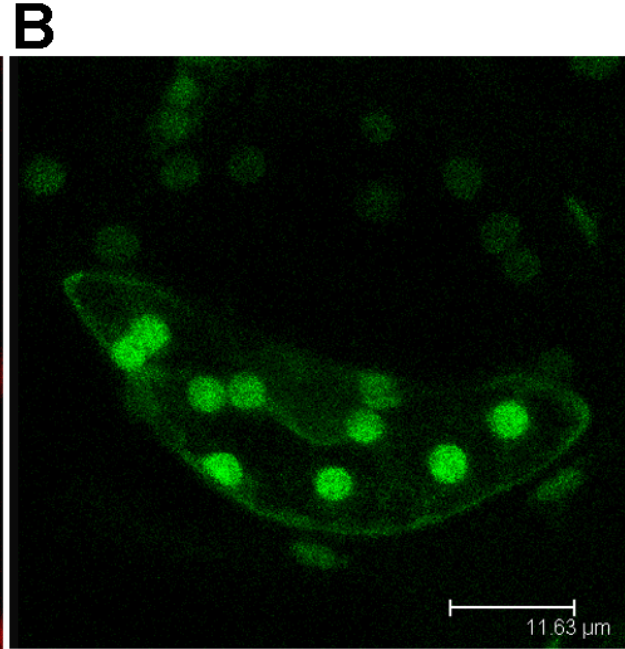
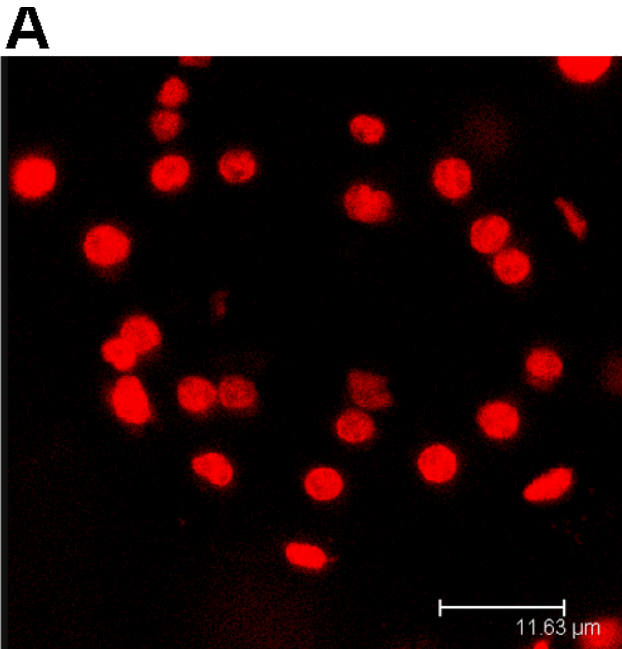
- **Chloroplast Sensor Kinase**
- A Histidine sensor kinase homologous with Hik2 of cyanobacteria
- *A Redox Sensor*
- Sujith Puthiyaveetil

**A****B**

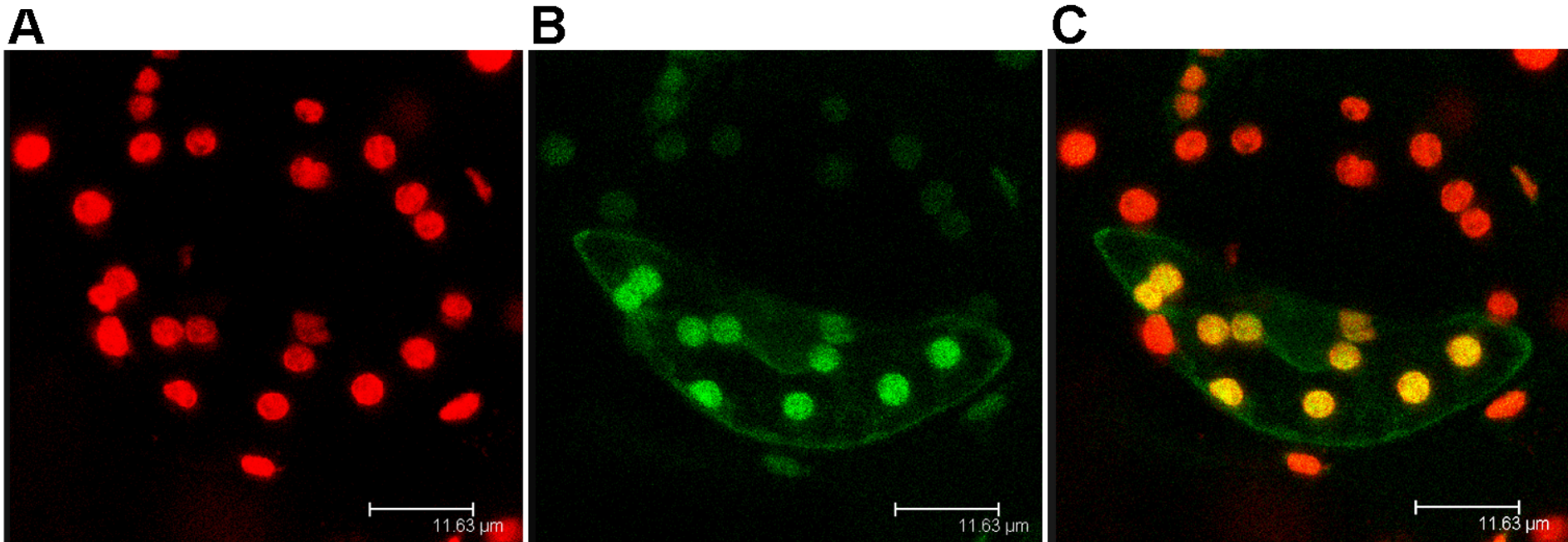
Puthiyaveetil S, Kavanagh TA, Cain P, Sullivan JA, Newell CA, Gray JC, Robinson C, van der Giezen M, Rogers MB, Allen JF (2008) The ancestral symbiont sensor kinase CSK links photosynthesis with gene expression in chloroplasts. *Proceedings of the National Academy of Sciences of the United States of America* 105: 10061-10066.



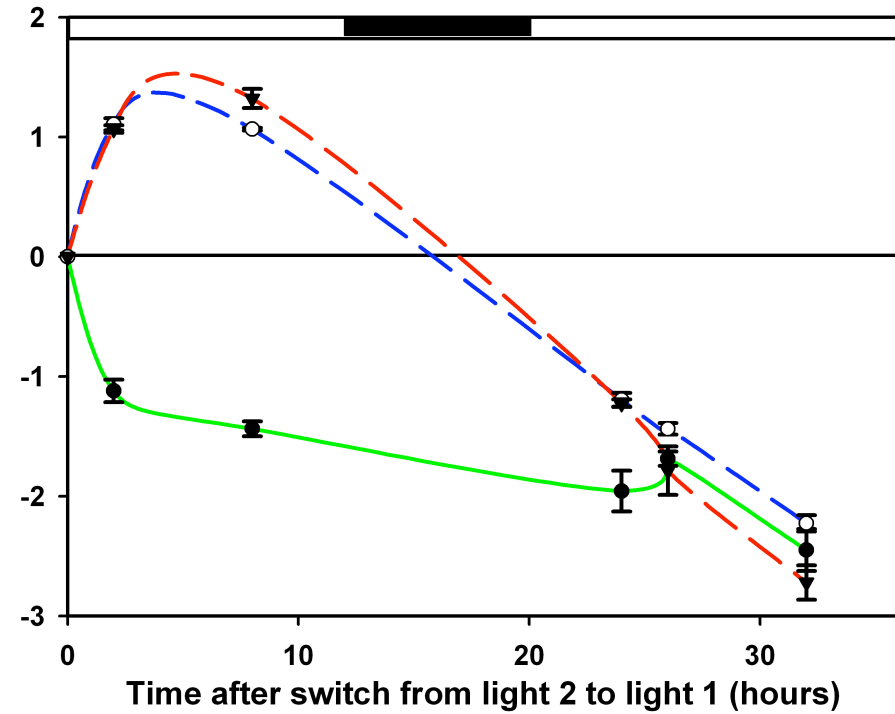
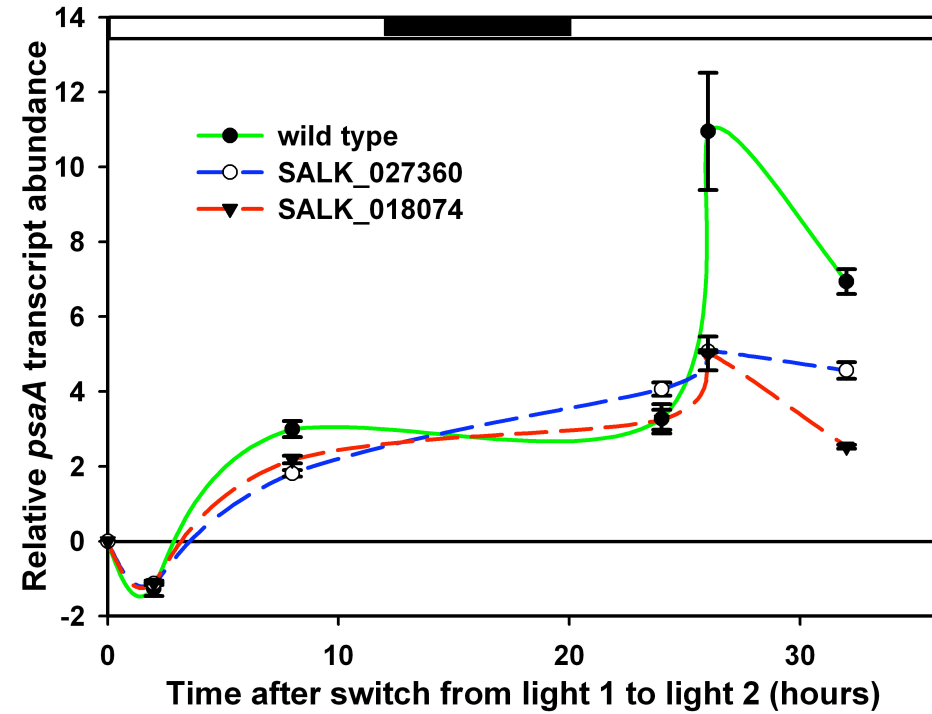
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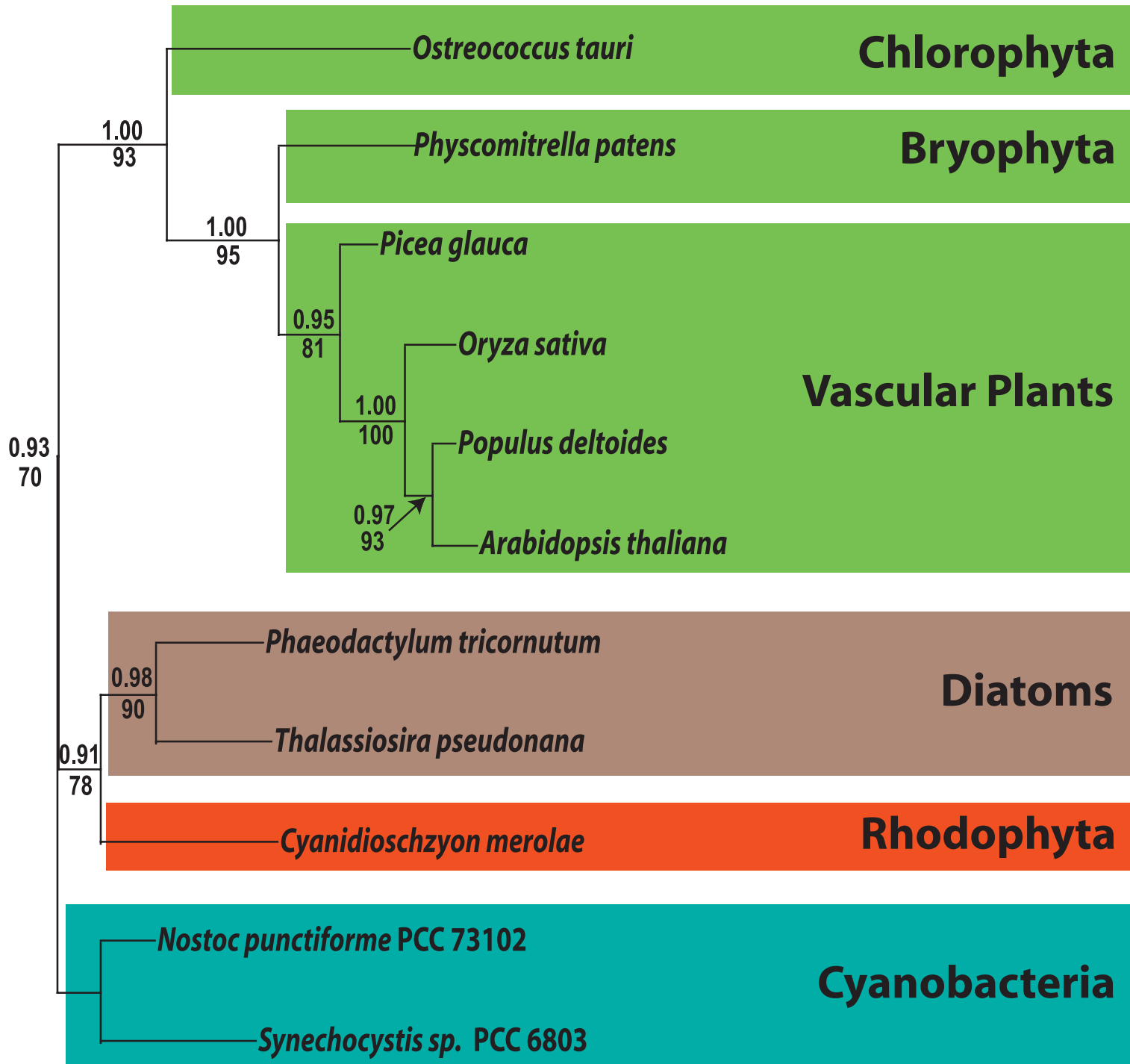
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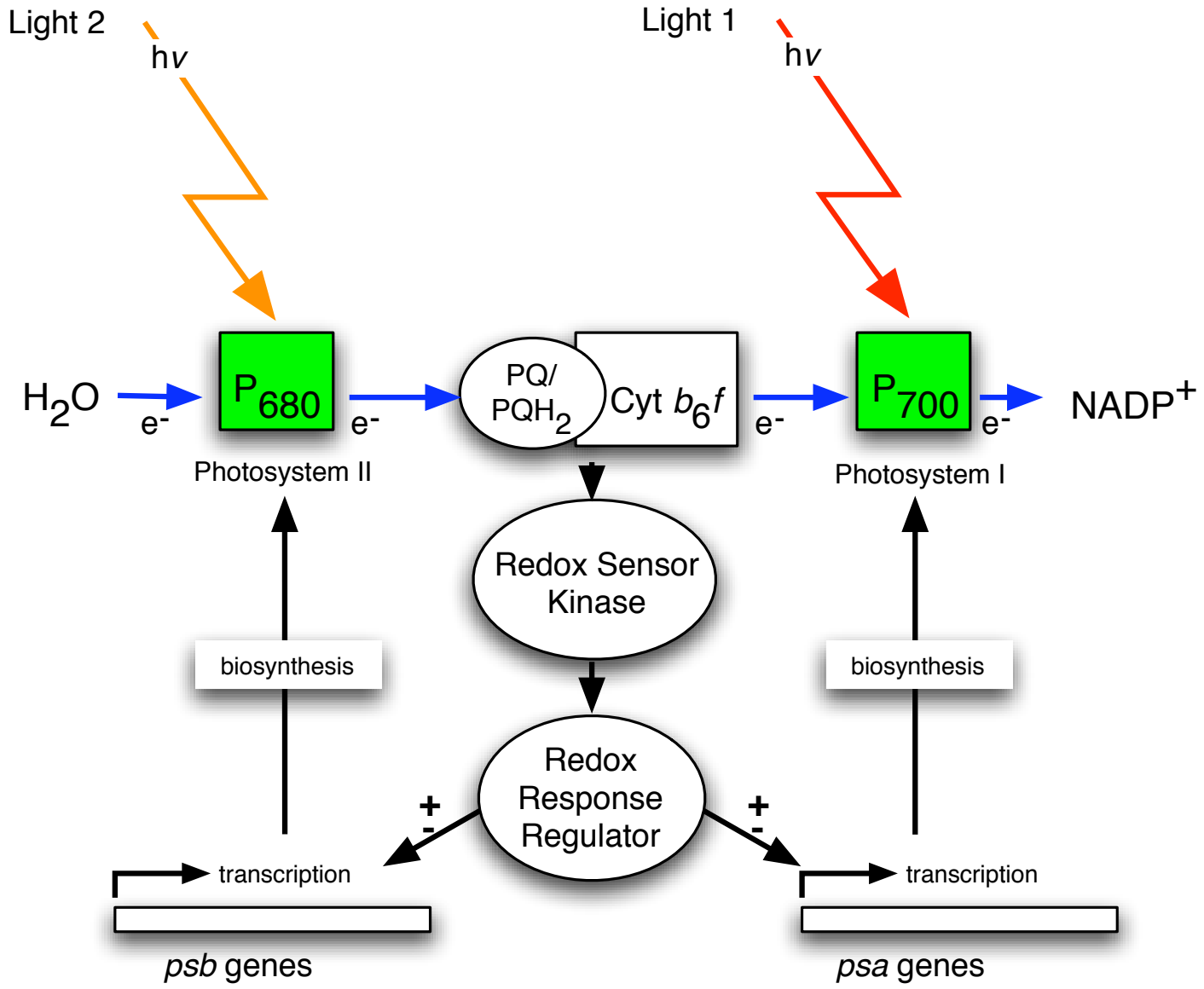


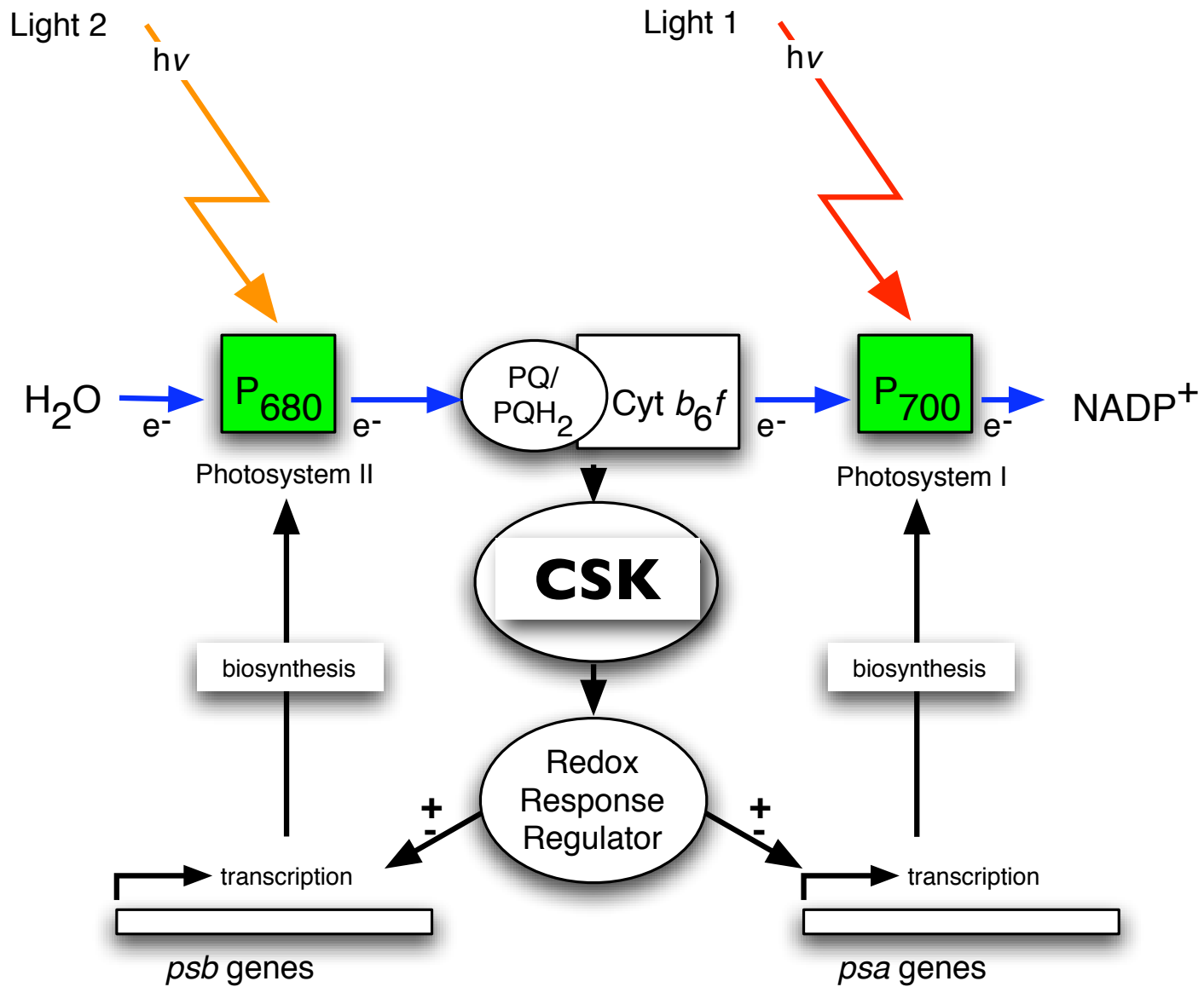
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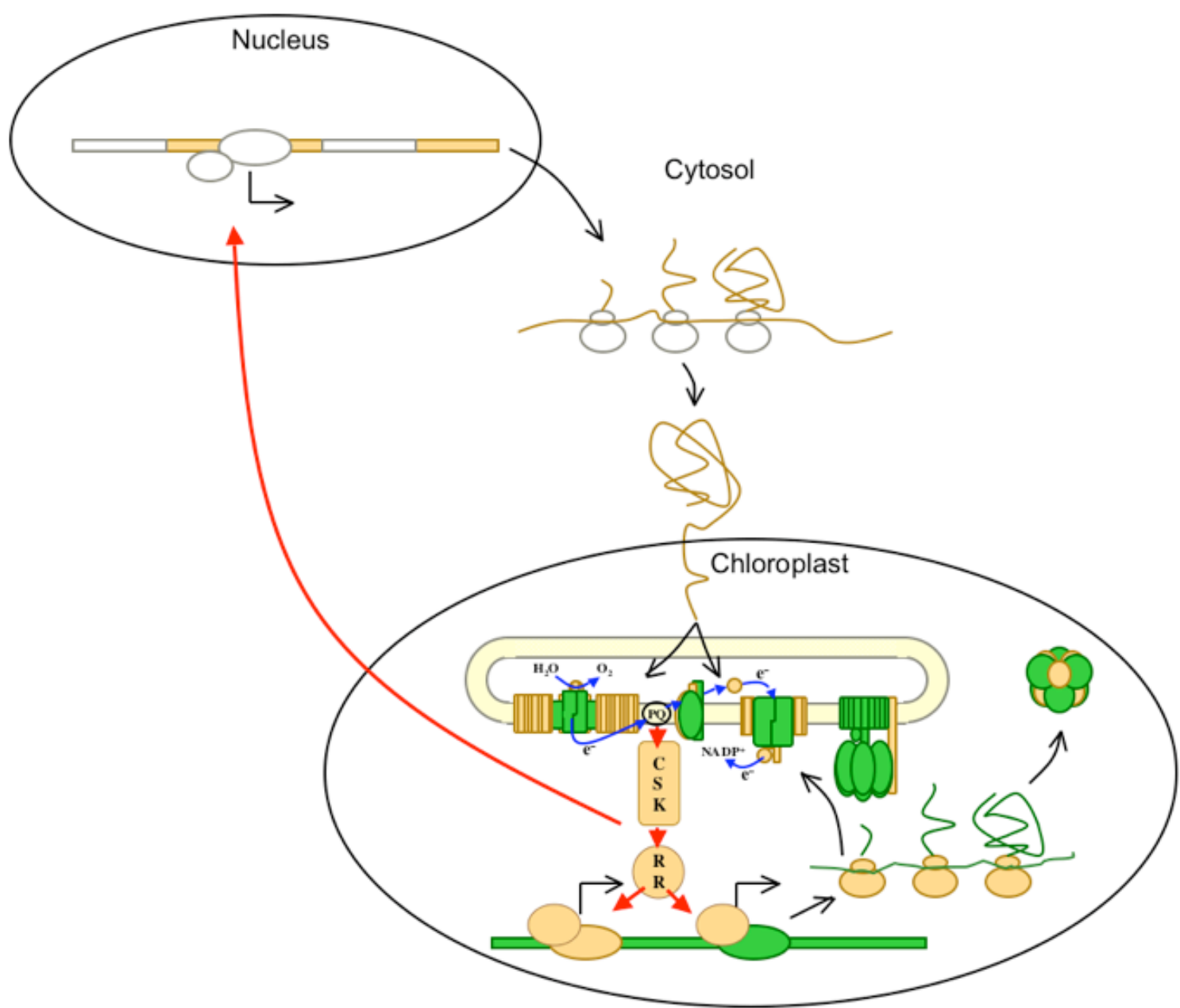


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Puthiyaveetil S and Allen JF (2009)  
 Chloroplast two-component systems: evolution of the link between photosynthesis and gene expression  
*Proceedings of the Royal Society B-Biological Sciences. In press*

# The costs of DNA in mitochondria

The mitochondrial theory of  
ageing (“aging” - U.S.)

# The mitochondrial theory of ageing

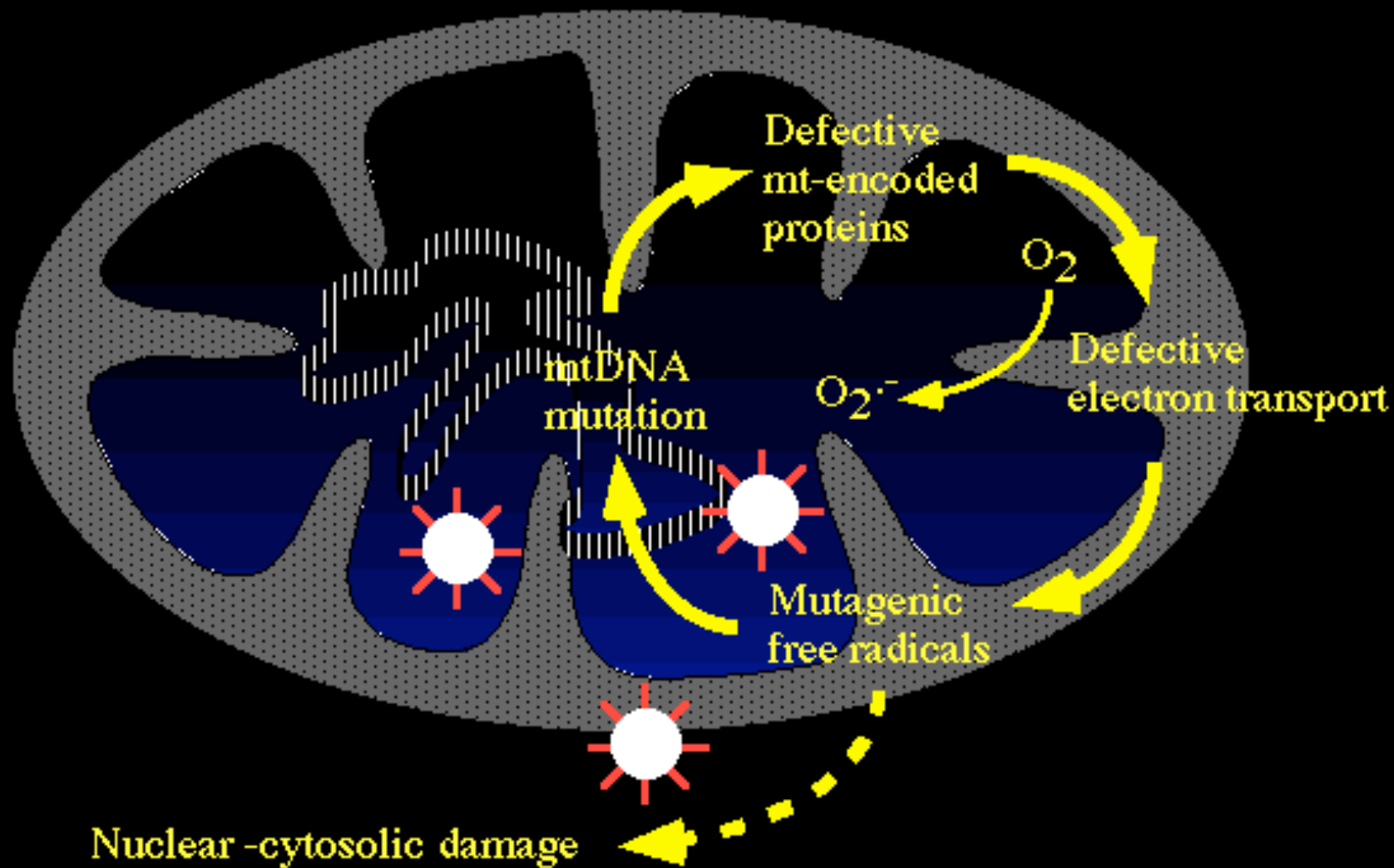
# The mitochondrial theory of ageing

“Errors” in electron transfer - transfers to the “wrong” electron acceptor - occur at fixed frequency.

# 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.



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

Douglas C. Wallace

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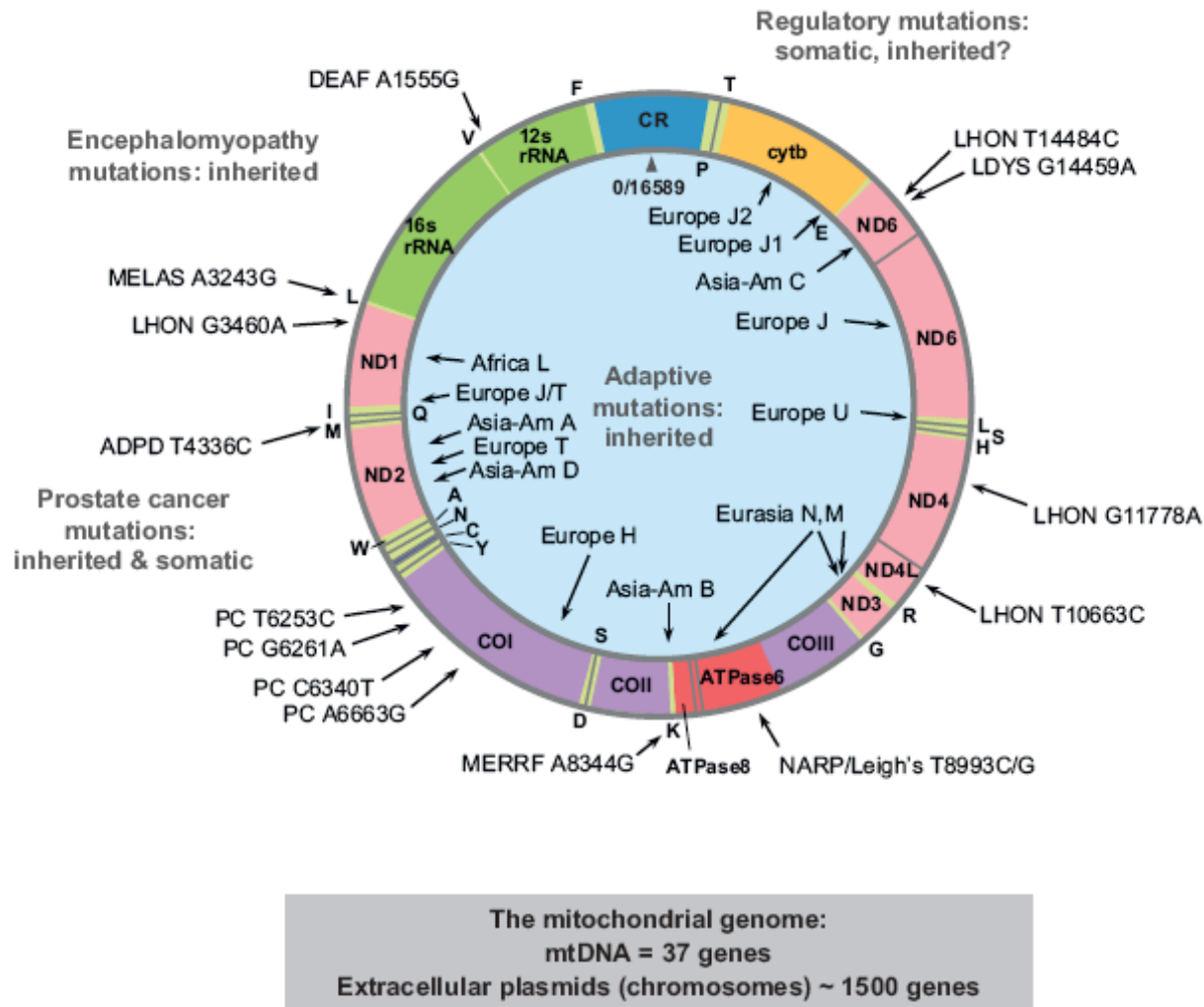
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## Key Words

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 ( $\Delta P$ ).  $\Delta P$  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.

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The mitochondrion is the worst  
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Whatever the reason for the persistence of mitochondrial genomes, it had better be a good one.

Separate sexes as  
mitochondrial division of labour

# Why there are two sexes

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**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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**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).

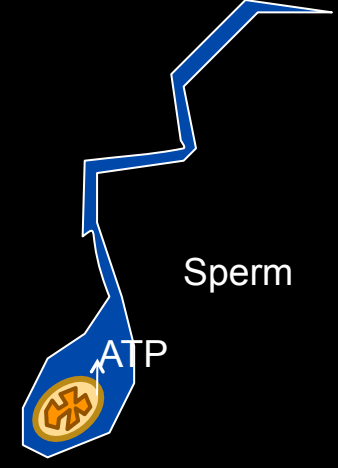
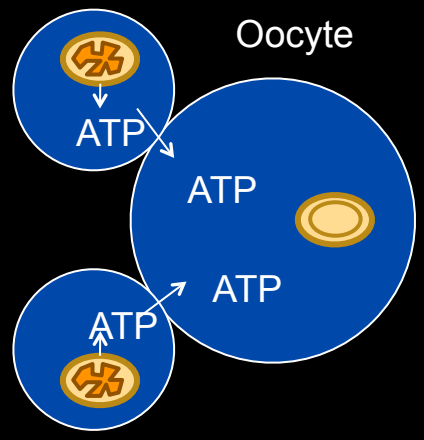
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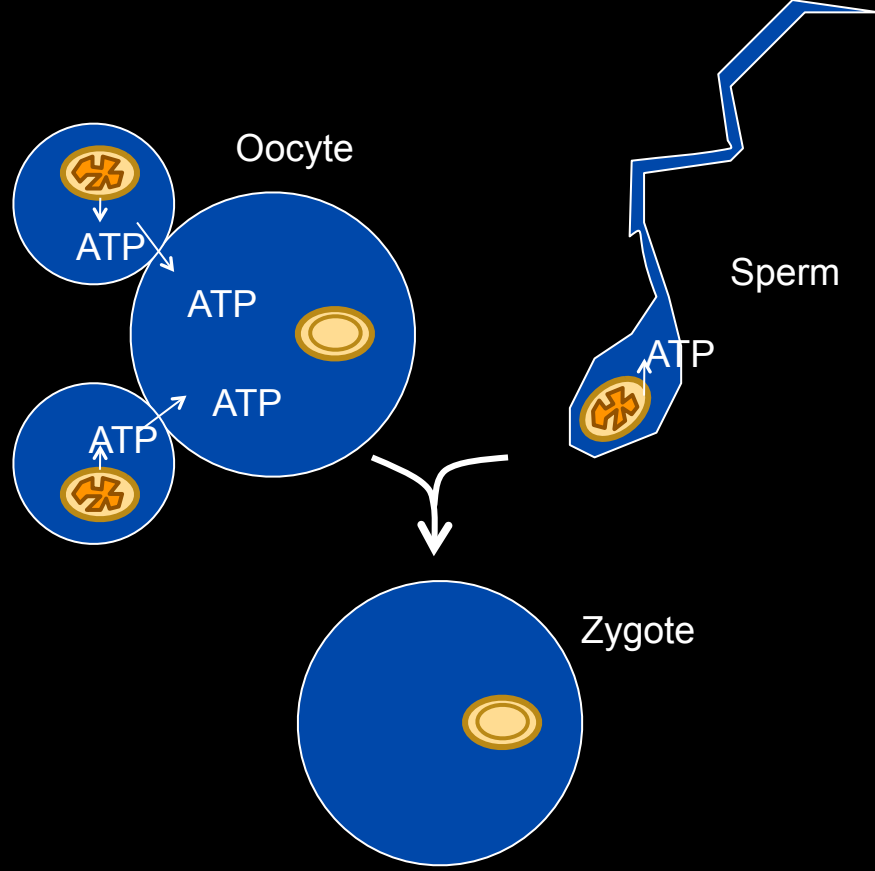
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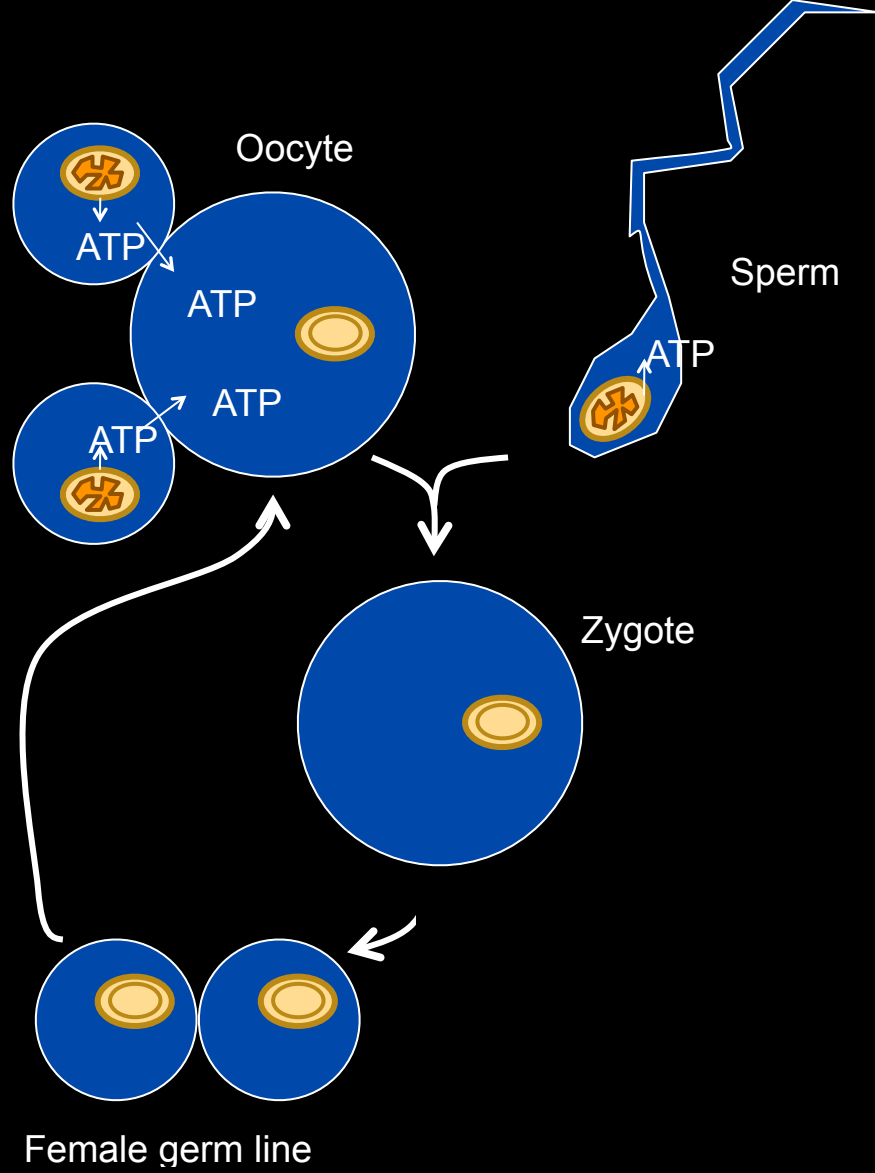
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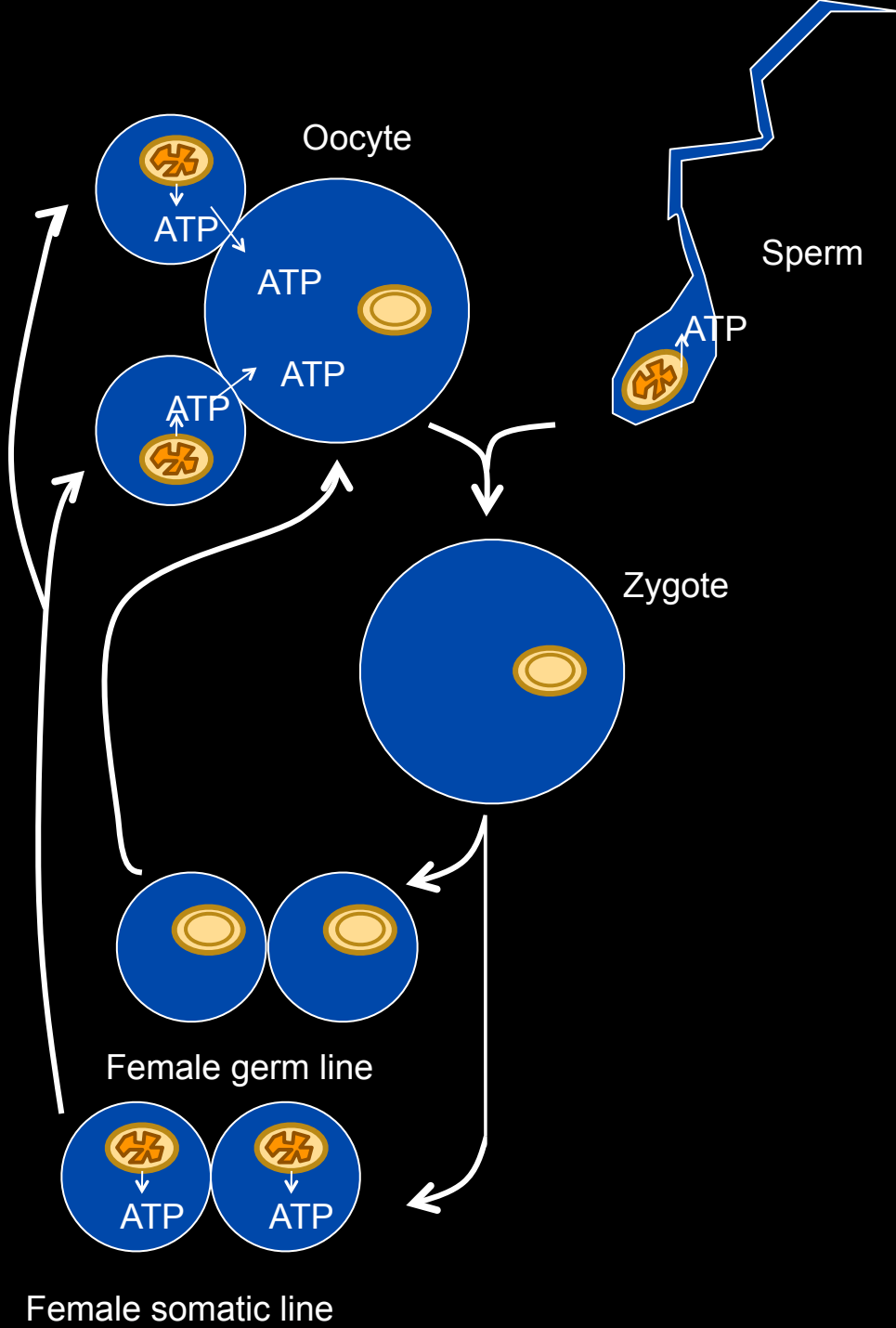
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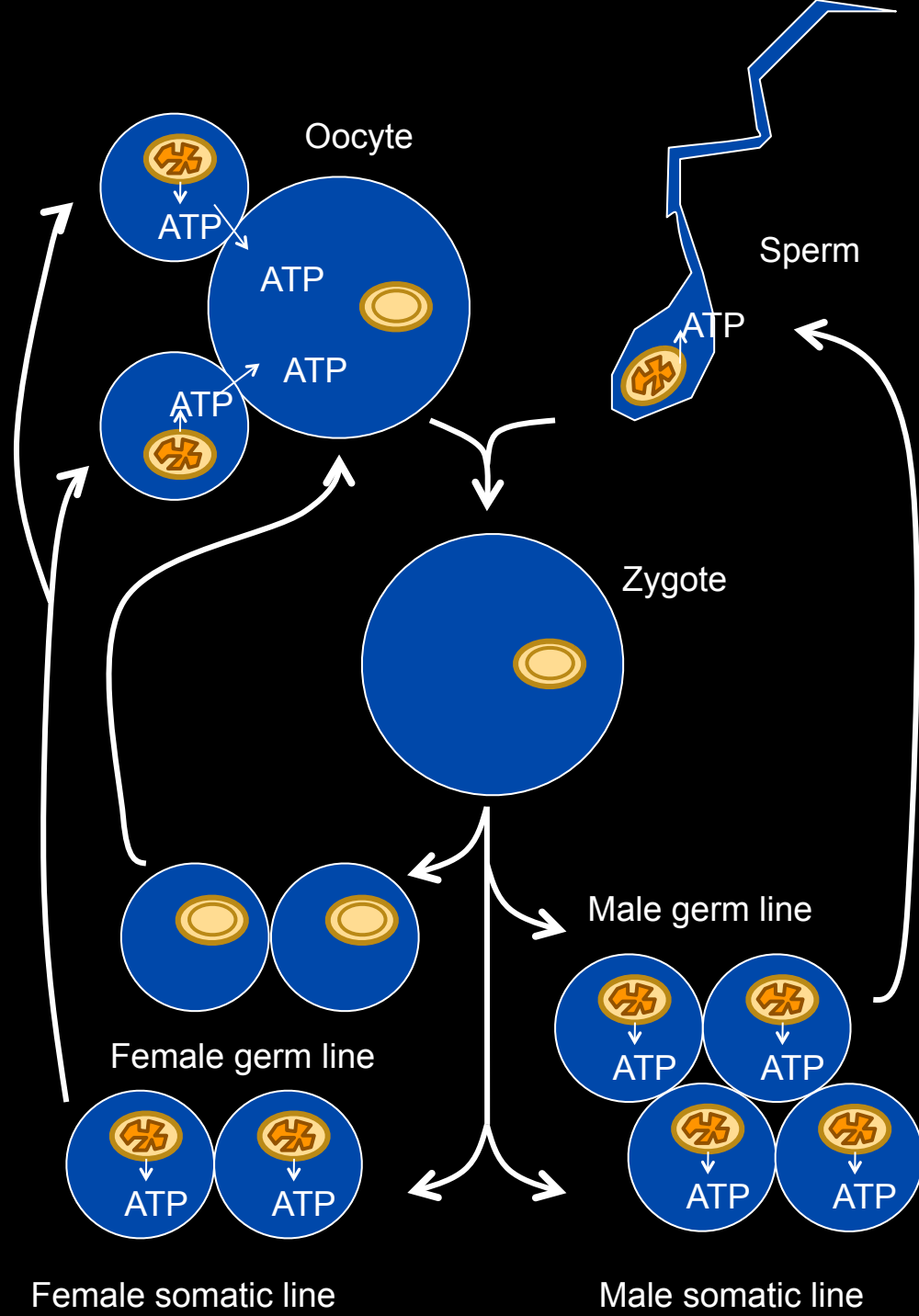
And they can never be both.

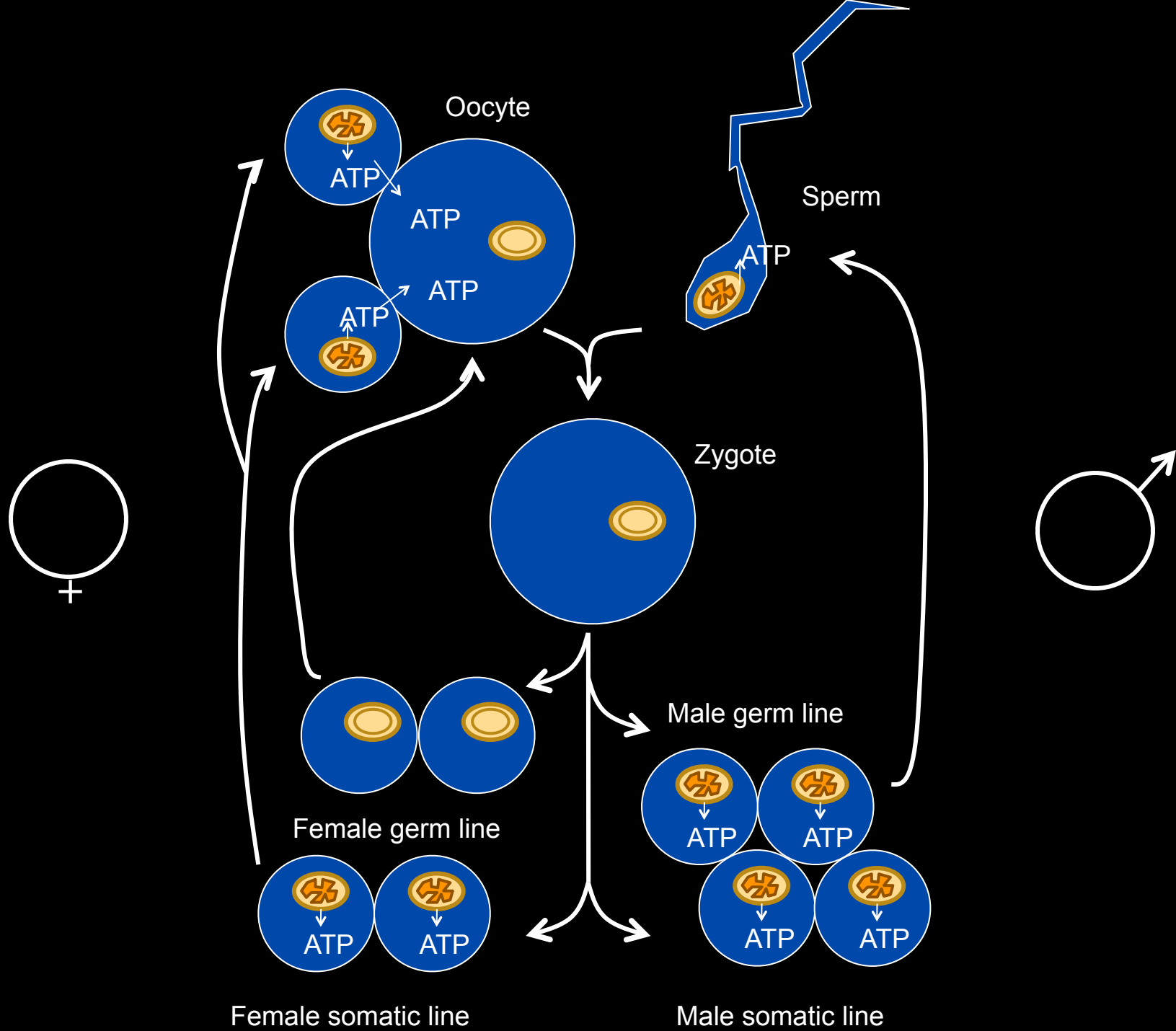


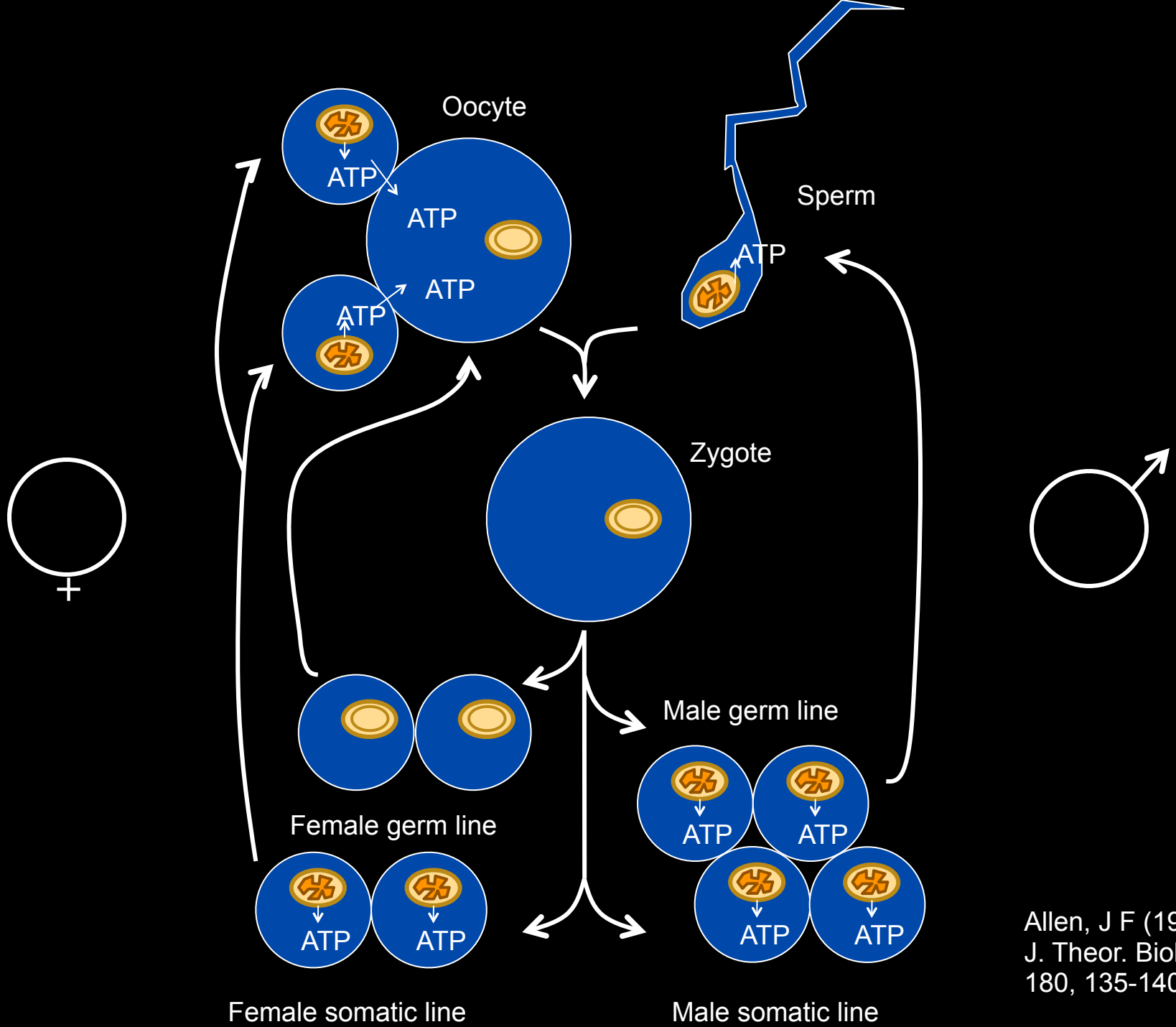












Allen, J F (1996)  
 J. Theor. Biol.  
 180, 135-140

# Separate sexes as mitochondrial division of labour

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

# Summary

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- mostly destroy themselves (and, eventually, us) in consequence
- but are predicted to 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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Mitochondria:

– “...are not part of the genetic material that we consider makes us as human beings.”

“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.”

Coda. Two views of mitochondria

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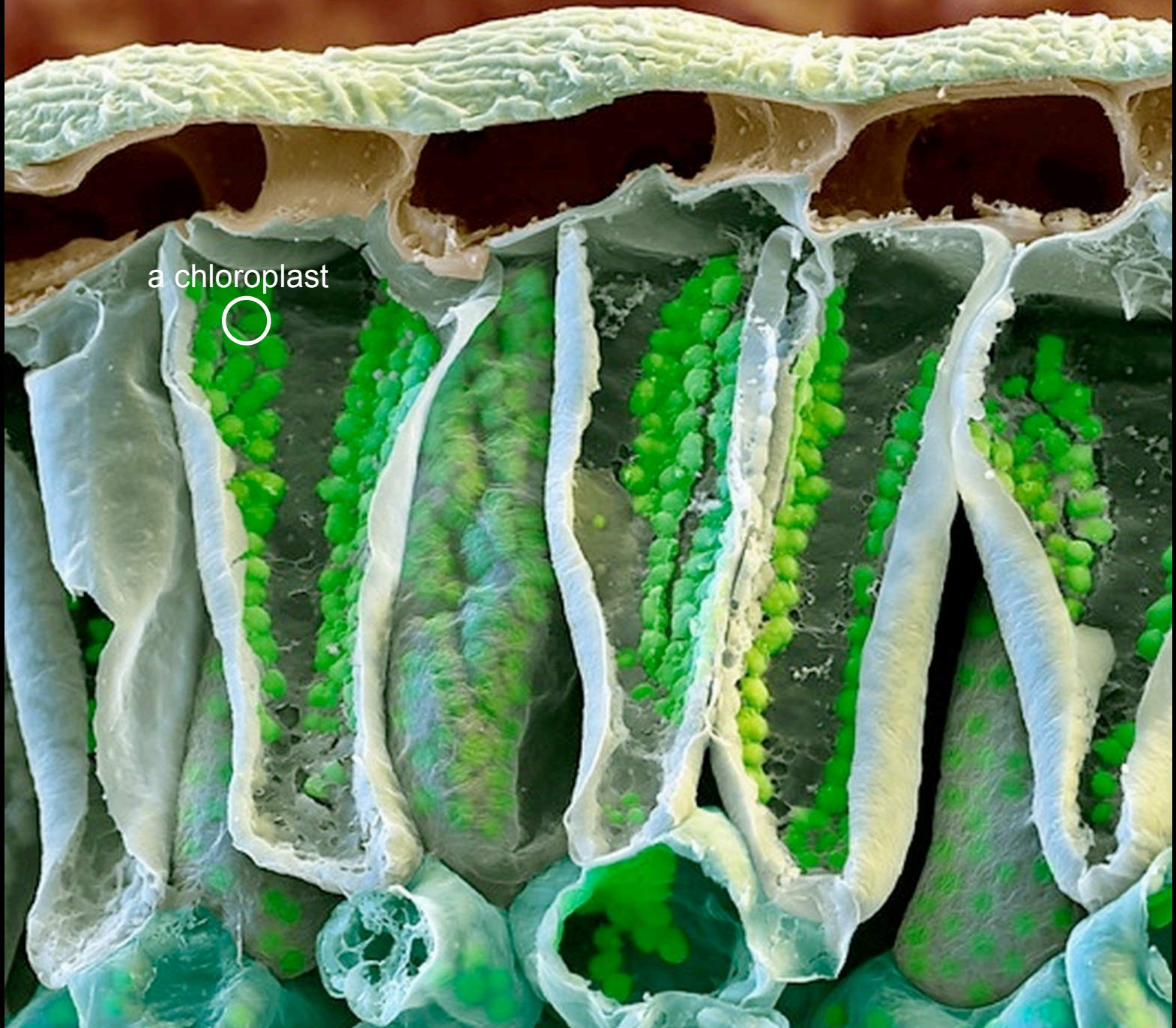
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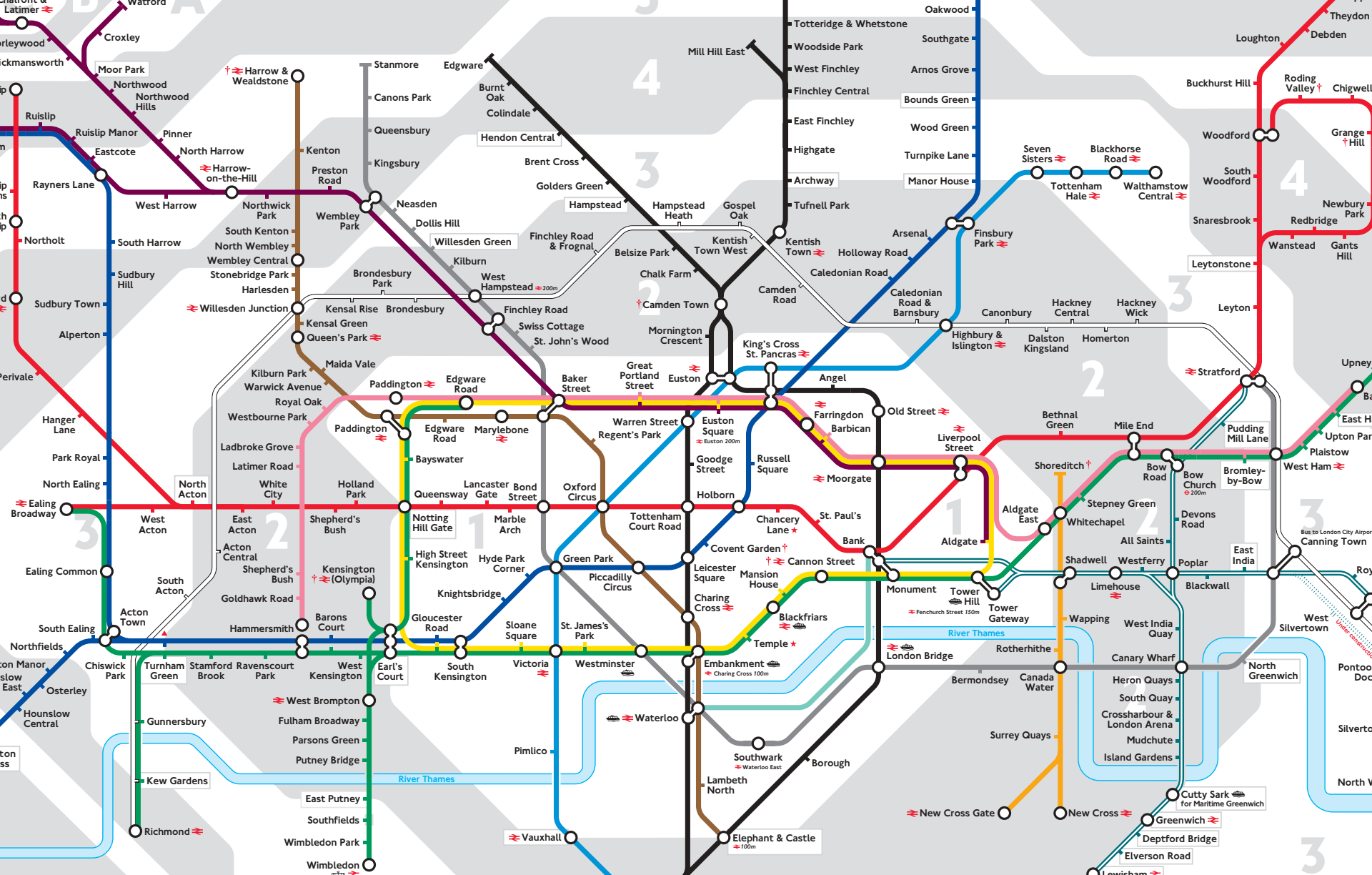
– “...give striking new insights into why we are here at all, whether we are alone in the universe, why we have our sense of individuality, why we should make love, where we trace our ancestral roots, why we must age and die—in short, into the meaning of life.”



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



30th  
2000



### Land symbols

- Northern
- Piccadilly †
- Victoria
- Waterloo & City  
restricted service - see opposite key
- Dockslands Light Railway
- National Rail
- Interchange stations
- Connections with National Rail
- Connections with riverboat services
- Airport interchange
- Connection with Tramlink
- Closed Sundays
- Under construction

### Explanation of zones

D	Station in Zone D	Bakerloo	Special fares apply for single and return tickets to and from Harrow & Wealdstone.	Hammersmith & City	No service late evening
C	Station in Zone C	Central	No service Woodford - Hainault after 2000 daily.	Metropolitan	For Chesham on most trains
B	Station in Zone B	Circle	Cannon Street open until 2100 Mondays to Fridays. Closed Saturdays and Sundays.	Northern	On Sundays Camden Town
A	Station in Zone A	District		Piccadilly	No entry to between 130 Heathrow to Mondays to
6	Station in Zone 6 - see opposite key	District		Waterloo & City	No service Uxbridge to 0615 to 2130
5	Station in Zone 5	East London	Shoreditch - Whitechapel open 0700 to 1000 and 1530 to 1900 Mondays to Fridays.		
4	Station in Zone 4				
3	Station in Zone 3				
2	Station in Zone 2				

### † Points to remember

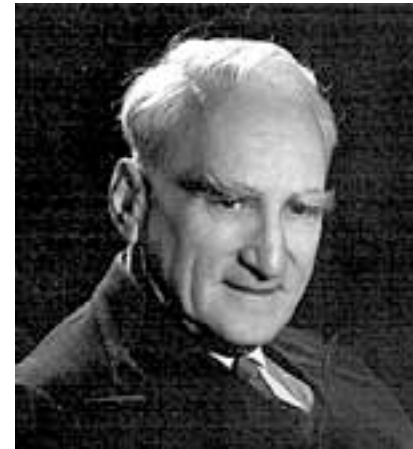
- Earl's Court - Kensington (Olympia) 0700 to 2345 Mondays to Saturdays, 0800 to 2345 Sundays.
- Shoreditch - Whitechapel open 0700 to 1000 and 1530 to 1900 Mondays to Fridays.
- Cannon Street open until 2100 Mondays to Fridays. Closed Saturdays and Sundays.
- Special fares apply for single and return tickets to and from Harrow & Wealdstone.
- No service Woodford - Hainault after 2000 daily.







CELEBRATING 350 YEARS



Rudi Lemberg  
1896-1975



Ebikabowei Bozimo Carol A. Allen Iskander Ibrahim John F. Allen Azma Shiyam Thomas Buckland Sujith Puthiyaveetil



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The end. Thank you for listening.

