The Q-Cycle

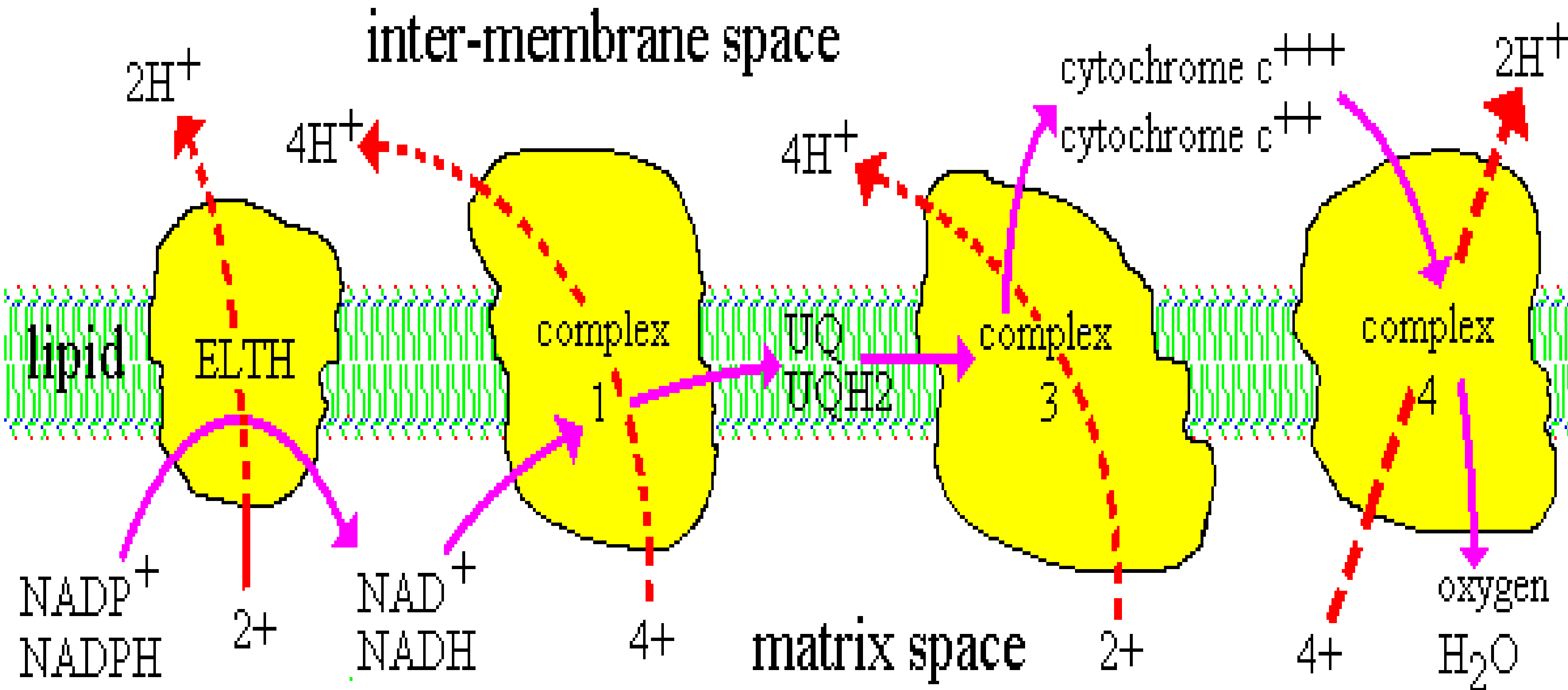
A contribution to Dr. Keith Garlid’s Bioenergetics course on the proton-translocating bc_1 complex (Complex III)

by Ian West (6th May 2004)

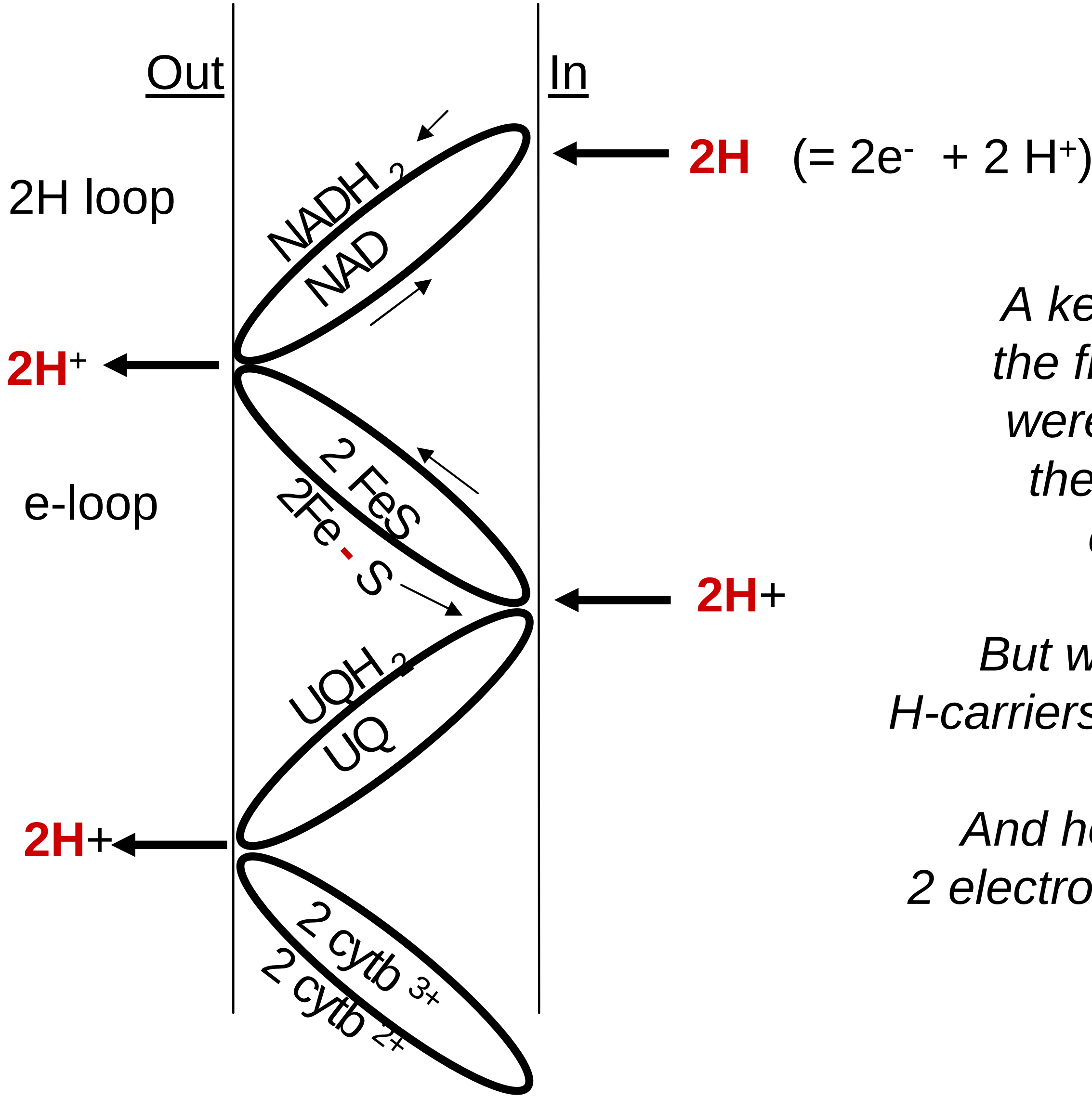
Handy web addresses

- http://www.life.uiuc.edu/crofts/bc-complex_site/
- http://www.life.uiuc.edu/crofts/bioph354/index.html
- http://www.bmb.leeds.ac.uk/illingworth/oxphos/index.htm
- http://www.cmb.uab.edu/courses/Lectures/brooks2.pdf
- http://fig.cox.miami.edu/~cmallery/255/255etc/CoQ.jpg
- www.**medphys**.ucl.ac.uk/research/borl/research/IR_topics/**spectra/spectra**.htm

http://www.bmb.leeds.ac.uk/illingworth/oxphos/index.htm



Mitchell's suggestion of how electron flow might be coupled to proton-translocation "Direct-Coupling"



A key idea was that the flow of e- and H^+ were co-linear, and the stoichiometry one-to-one.

But what could be the H-carriers, and the e-carriers?

And how can cyt b take 2 electrons from e.g. UQH_2?

Redox Components

FMN (2e, 2 H^+)?

FeS2 FeS1

FeS3

UQ_{10} (2e, 2 H+)?

FeS4
FeS5
FeS6
FeS7
FeS8
FeS9

(1e

$NADH^+ + H^+$
(2e, 1 H+)

Cyt b -- cyt $\boldsymbol{b_L}$
cyt $\boldsymbol{b_H}$
Cyt c -- cyt $\boldsymbol{c_1}$
cyt $\boldsymbol{c_1}$
Cyt a -- cyt $\boldsymbol{a}$
cyt $\boldsymbol{a_3}$

(1e)

What is a redox midpoint potential ?

CH_3COOH ? CH_3COO^- + H^+

$pH = pK_A + \text{Log}(CH_3COO^- / CH_3COOH)$

Cyt c(II)$^{2+}$? Cyt c(III)$^{3+}$ + ne^-

$$E_h = E_0' + \frac{2.3RT}{nF} \text{Log}(\text{Cyt c(III)}^{3+} / \text{Cyt c(II)}^{2+})$$

So, E_h is the "activity" of the electon relative to a standard which is that of electrons in a mix of H_2 gas and 1 M H^+

While E_0' is a constant that reflects the affinity of X^+ for e^-

Succinate (E_0'=+30 mV) can give electrons to UQ (E_0'=+70 mV) ; but not (spontaneously) to NAD^+ (E_0'=- 320 mV)

UQH_2 cannot give one electron (E_0'=+230 mV) to cyt bL (E_0'= - 50 mV), or even to cyt b_H (E_0'= +50 mV).

Redox Midpoints (E_0')

(all in mV)

FMN
- 220

FeS2
- 20

FeS1
- 220

FeS3

UQ_{10} --- +70

FeS4
FeS5
FeS6
FeS7
FeS8
FeS9

$NADH^+ + H^+$
- 320

Cyt b -- cyt $\boldsymbol{b_L}$ --- - 50
cyt $\boldsymbol{b_H}$ --- +50

Cyt c -- cyt $\boldsymbol{c_1}$ --- +220
cyt ***c*** --- +260

Cyt a -- cyt ***a*** --- +300
cyt $\boldsymbol{a_3}$ --- +400

Redox Midpoints (E_0')

(all in mV)

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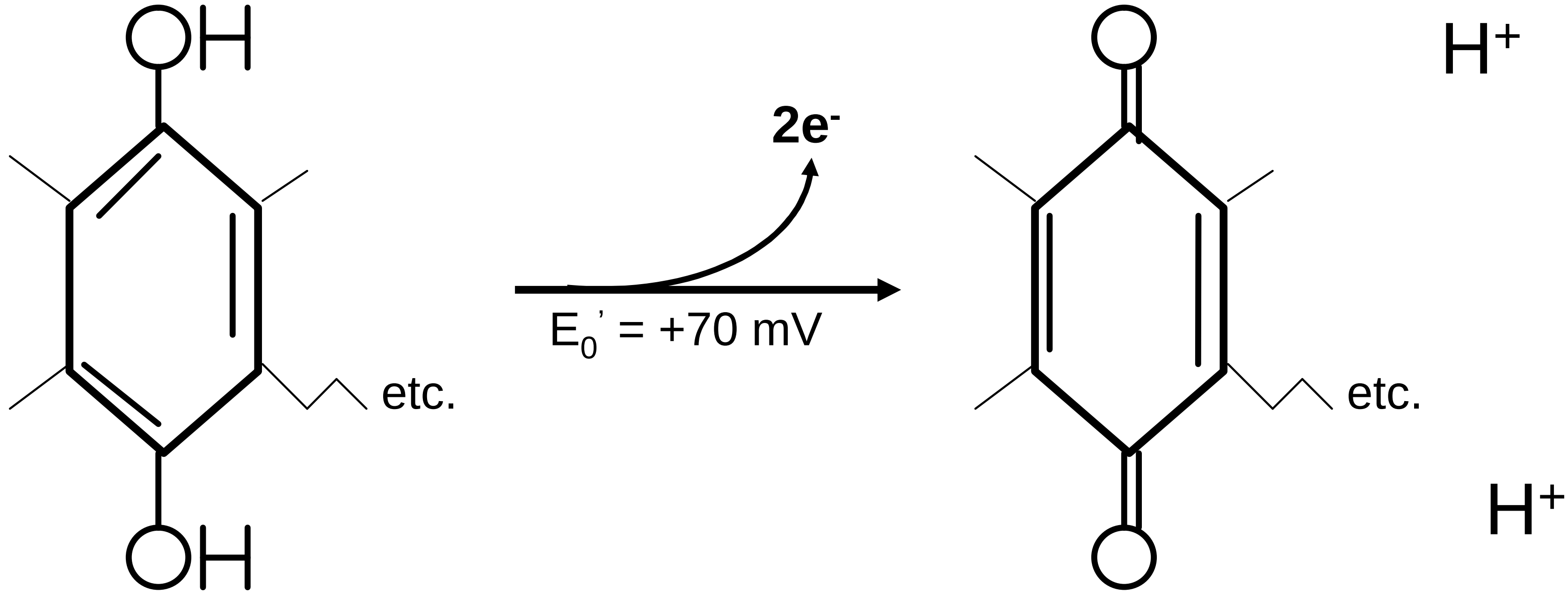
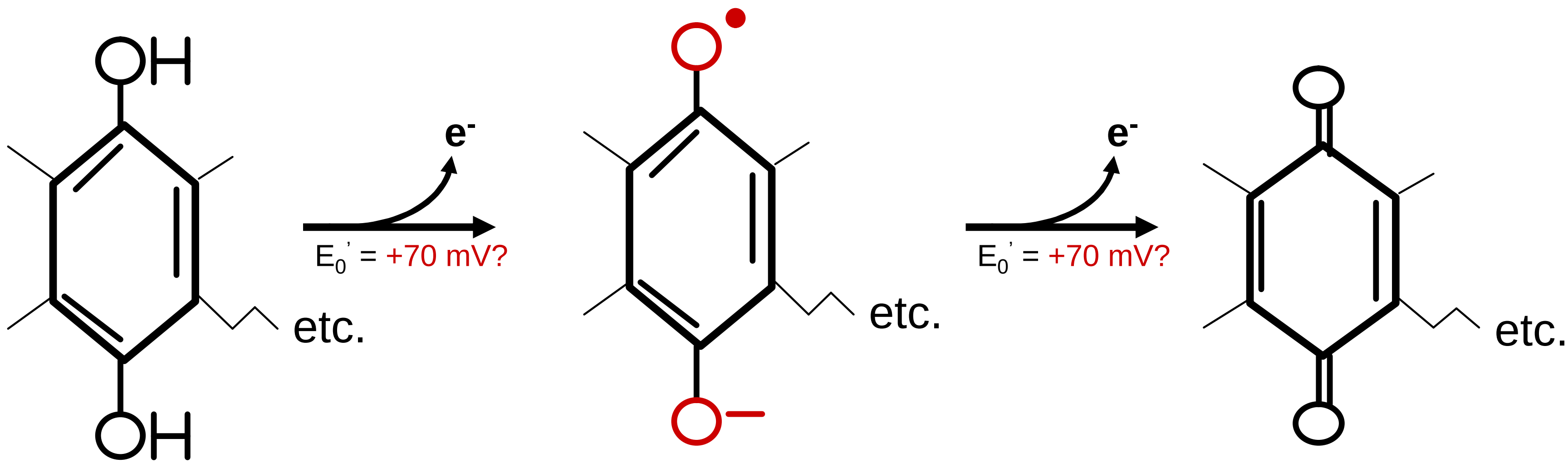
UQ-negative mutants

- In bacteria there are various cytchromes and quinones
- UQ-negative mutants cannot synthesize ubiquinone, or synthesize very little
  - Gibson F: The introduction of Escherichia coli and biochemical genetics to the study of oxidative phosphorylation. Trends.Biochem.Sci 25:342-344, 2000
  - Cox GB, Gibson F: Studies on electron transport and energy-linked reactions using mutants of Escherichia coli. Biochim.Biophys.Acta 346:1-25, 1974
- (I think) they showed that both the **reduction** and the **oxidation** of b-cytochrome(s) are slowed

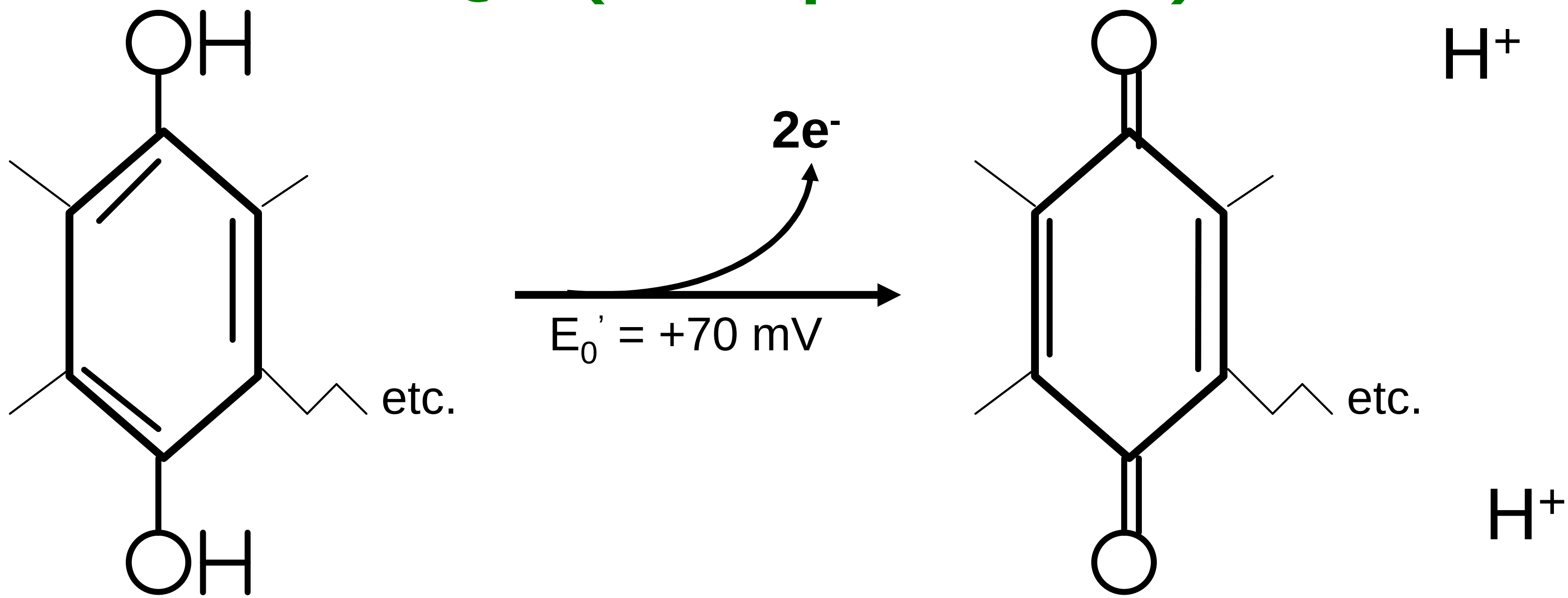
UQ (ubiquinone)

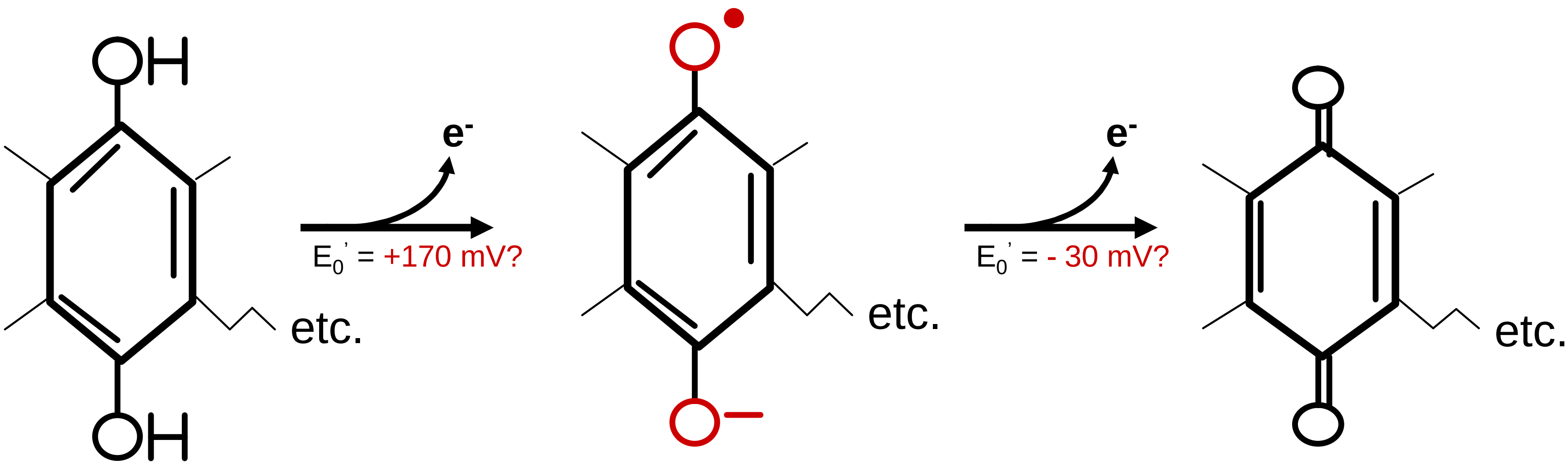




Ubiquinol | Semiquinone radical anion | Ubiquinone

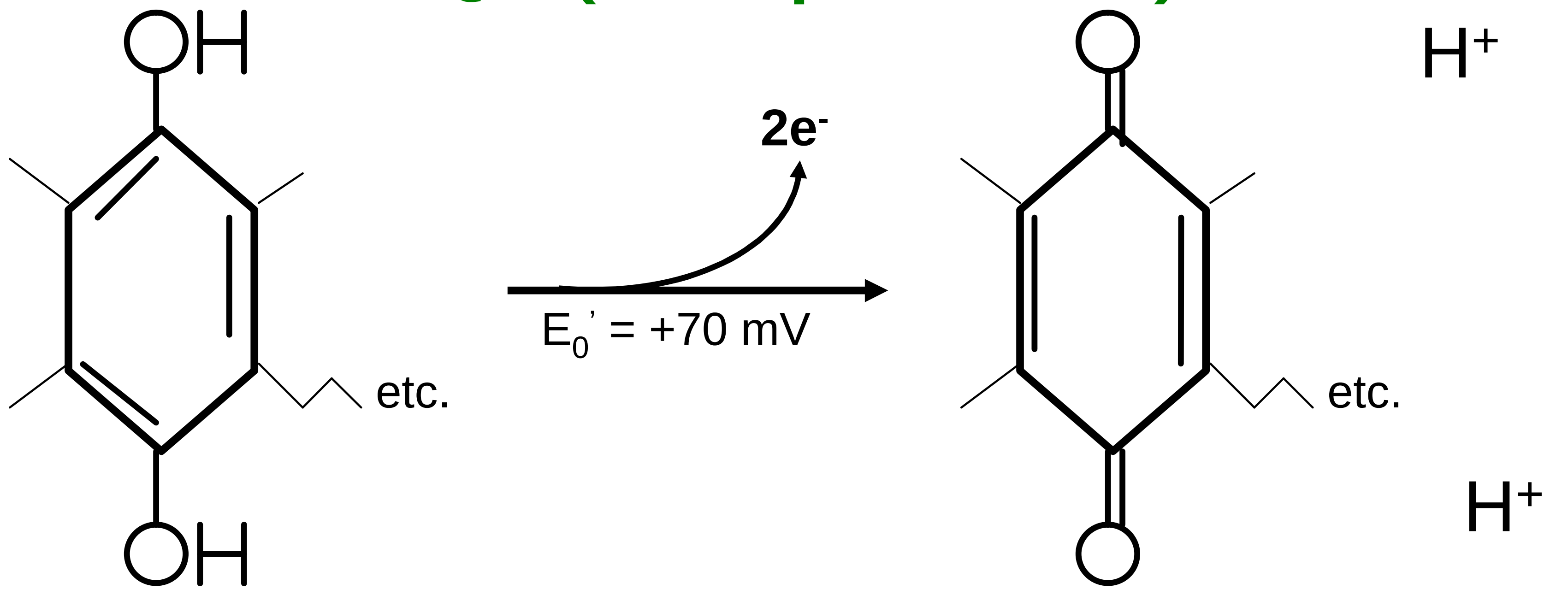
UQ (ubiquinone)

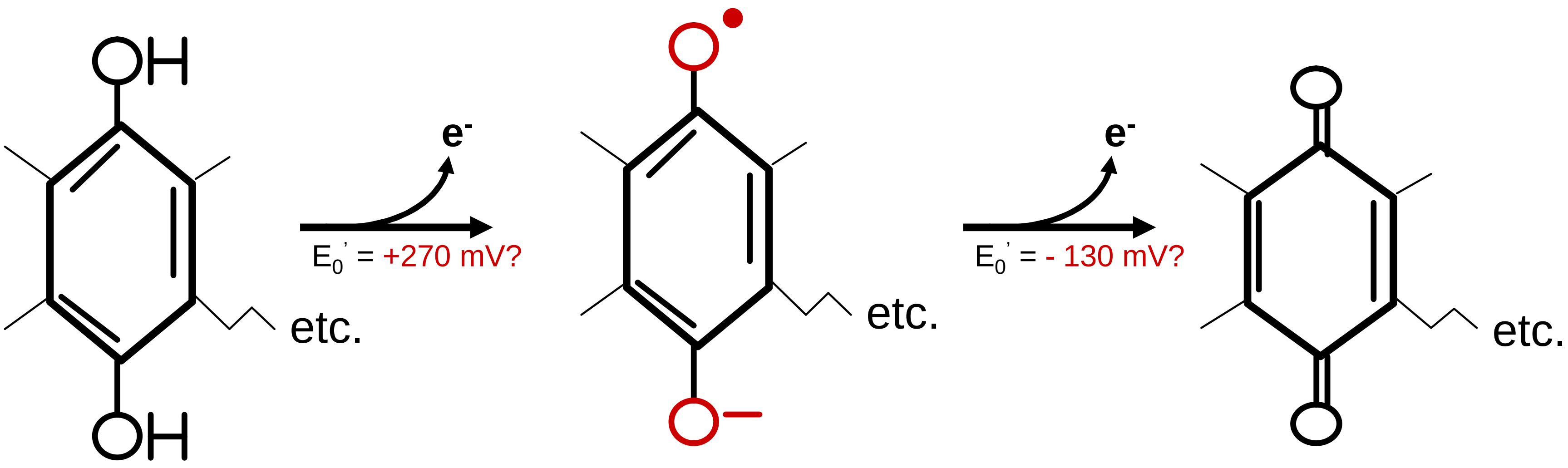




Ubiquinol Semiquinone radical anion Ubiquinone

UQ (ubiquinone)

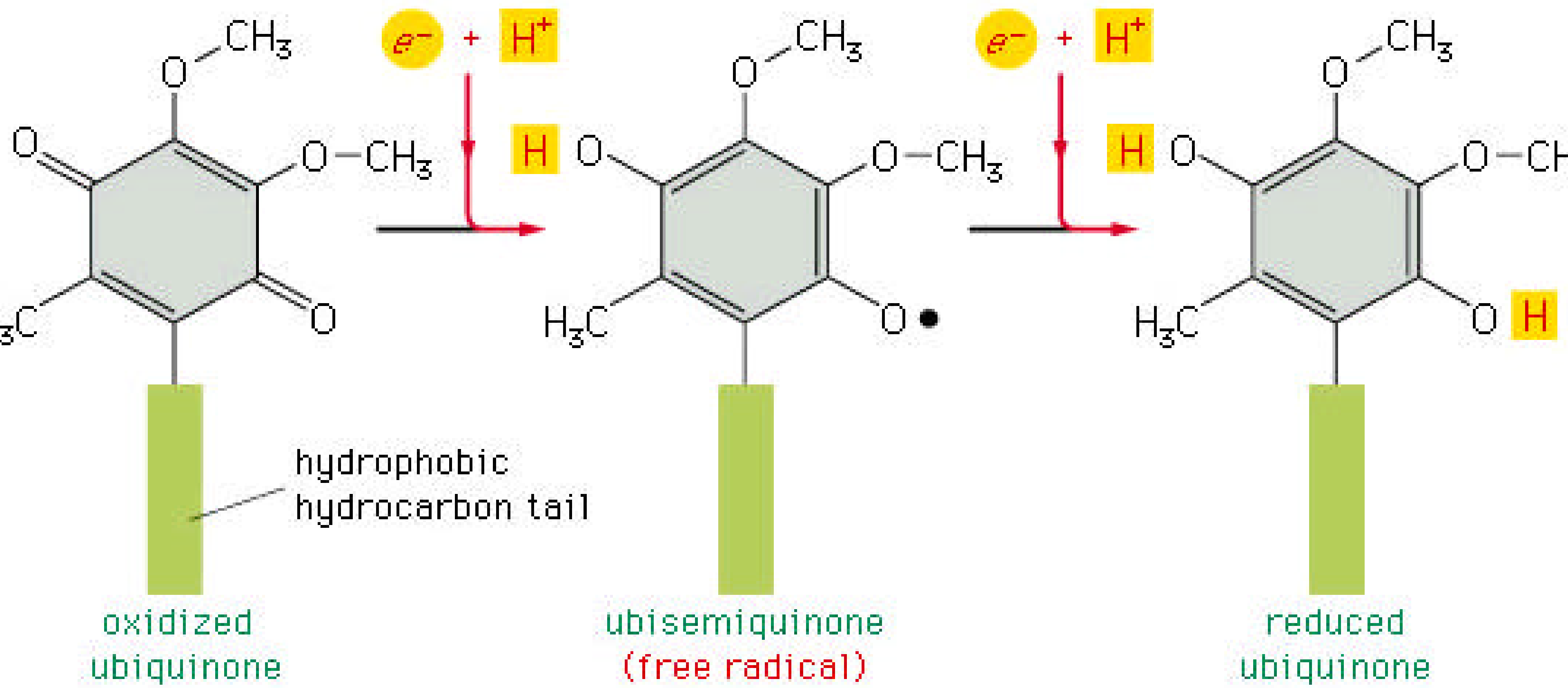




Ubiquinol | Semiquinone anion radical | Ubiquinone

Ubiquinone 10

- http://fig.cox.miami.edu/~cmallery/255/255etc/CoQ.jpg



Redox Midpoints (E_0')

(all in mV -- these are from memory!!)

FeS1
- 220

FeS2
- 20

FMN
- 220

FeS3

FeS4
FeS5
FeS6
FeS7
FeS8
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UQ_{10} --- +70

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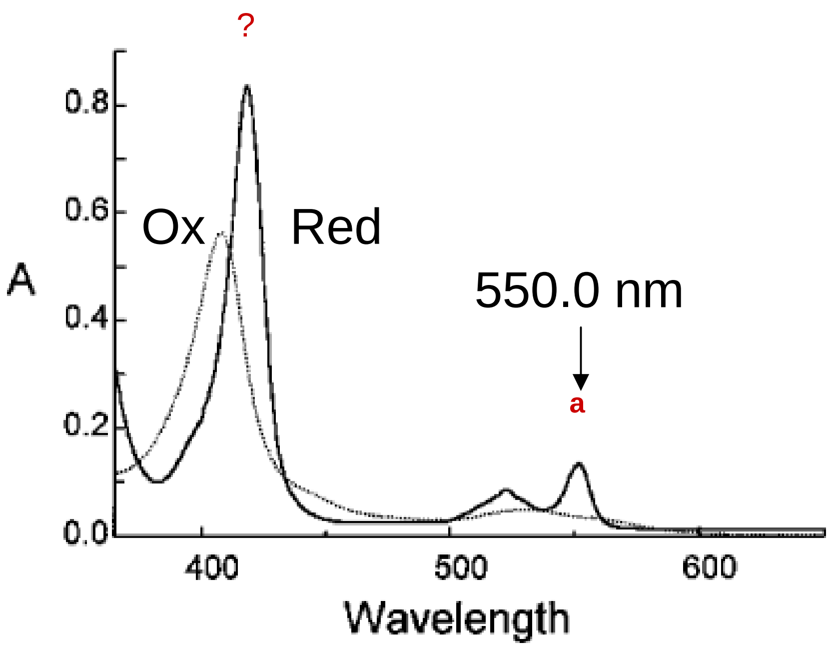
cyt ***c*** --- +260
Cyt a -- cyt ***a*** --- +300
cyt $\boldsymbol{a_3}$ --- +400

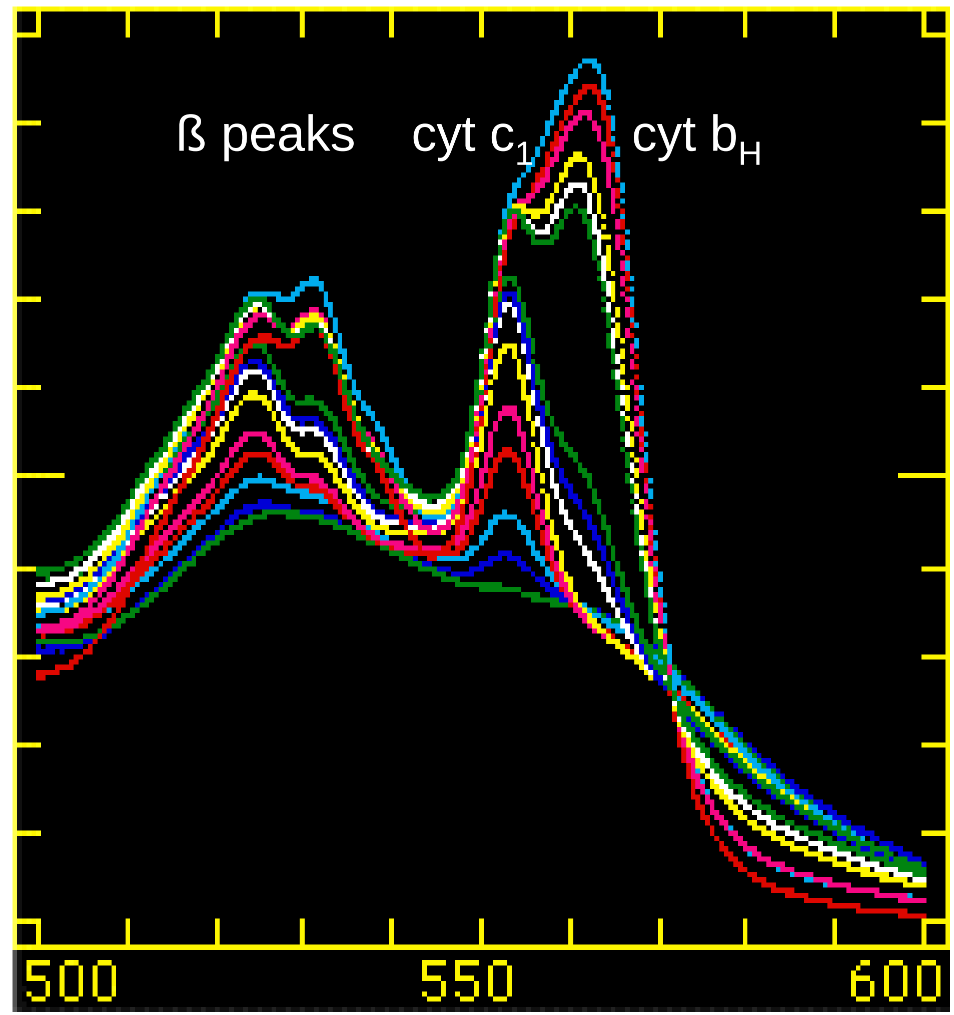
$Fe(CN)_6$(III)/(II) -- +430 (360)
O_2/ $2H_2O$ -- +820

Cytochrome spectra

Like litmus indicating pH, many compounds change colour on reduction

Cytochrome c spectra





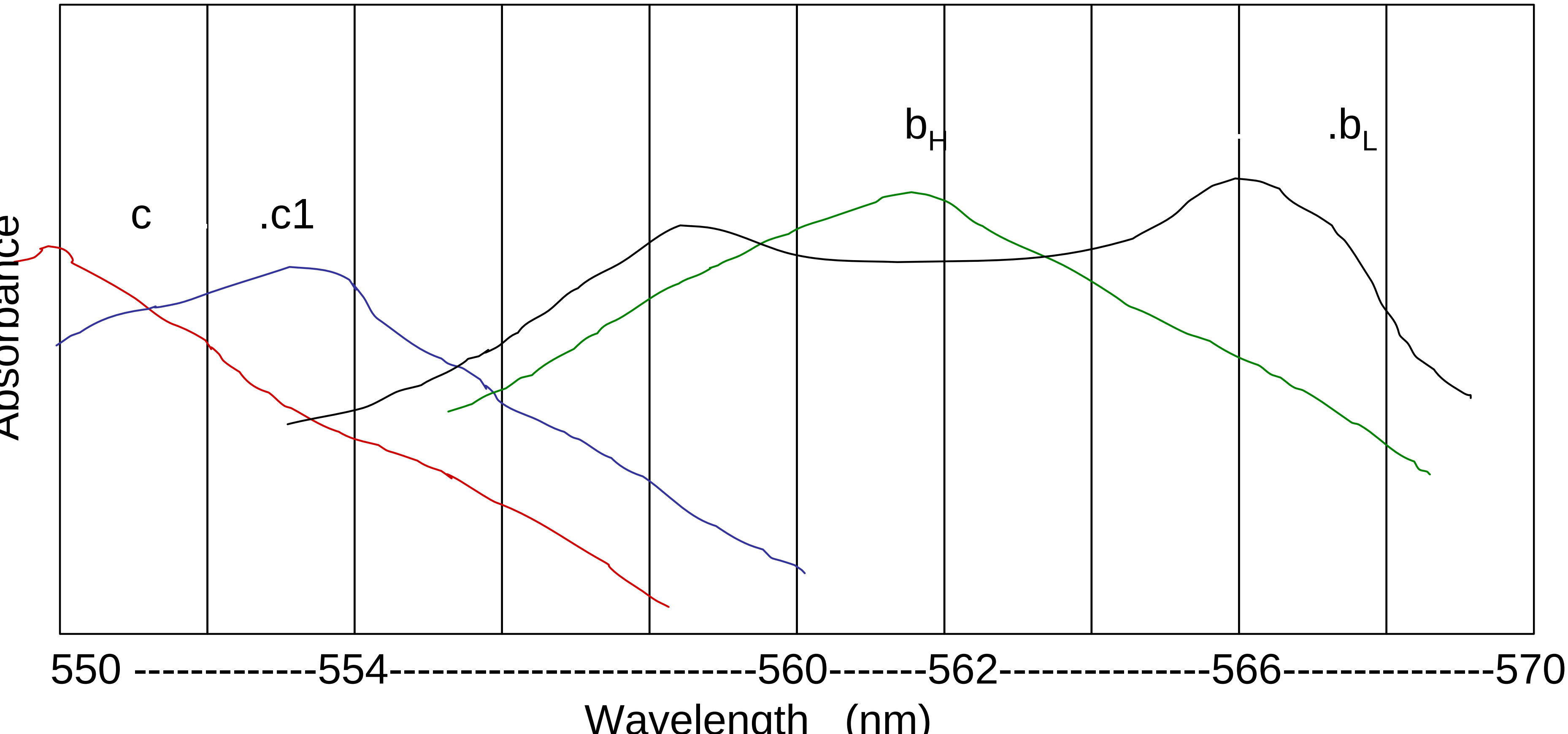
http://www.life.uiuc.edu/crofts/bc-complex_site/

Cytochrome spectra (2)

Like litmus indicating pH, many compounds change colour on reduction

This is a rough sketch of the alpha peaks only.

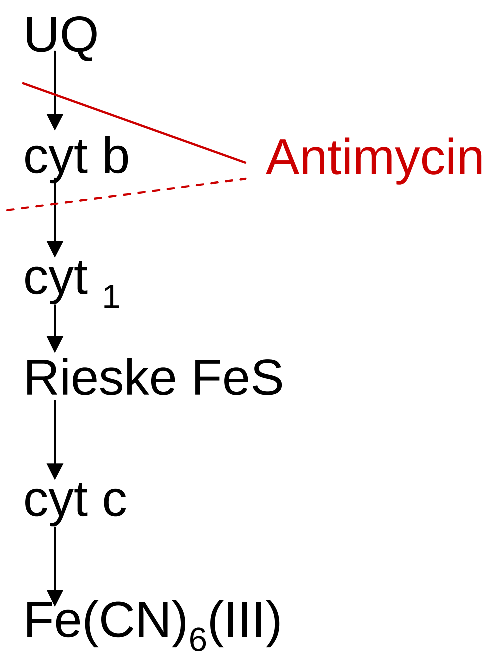
See West et al (1988) Biochim.Biophys.Acta 933:35-41.



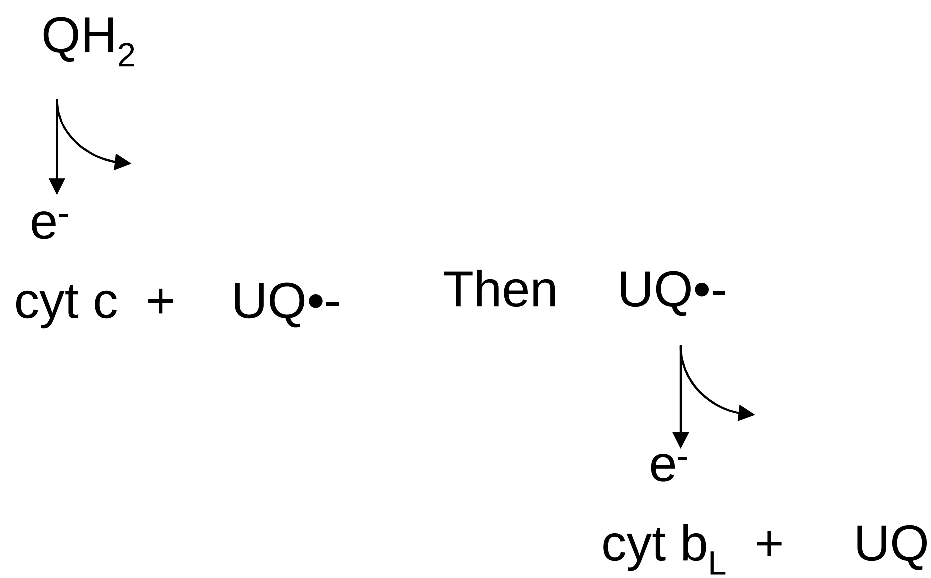
Wickström’s see-saw

- Wikstrom (1972) showed that (in antimycin-inhibited mitochondria) adding an oxidant of cyt *c* caused reduction of cyt $b_?$??

The Puzzle



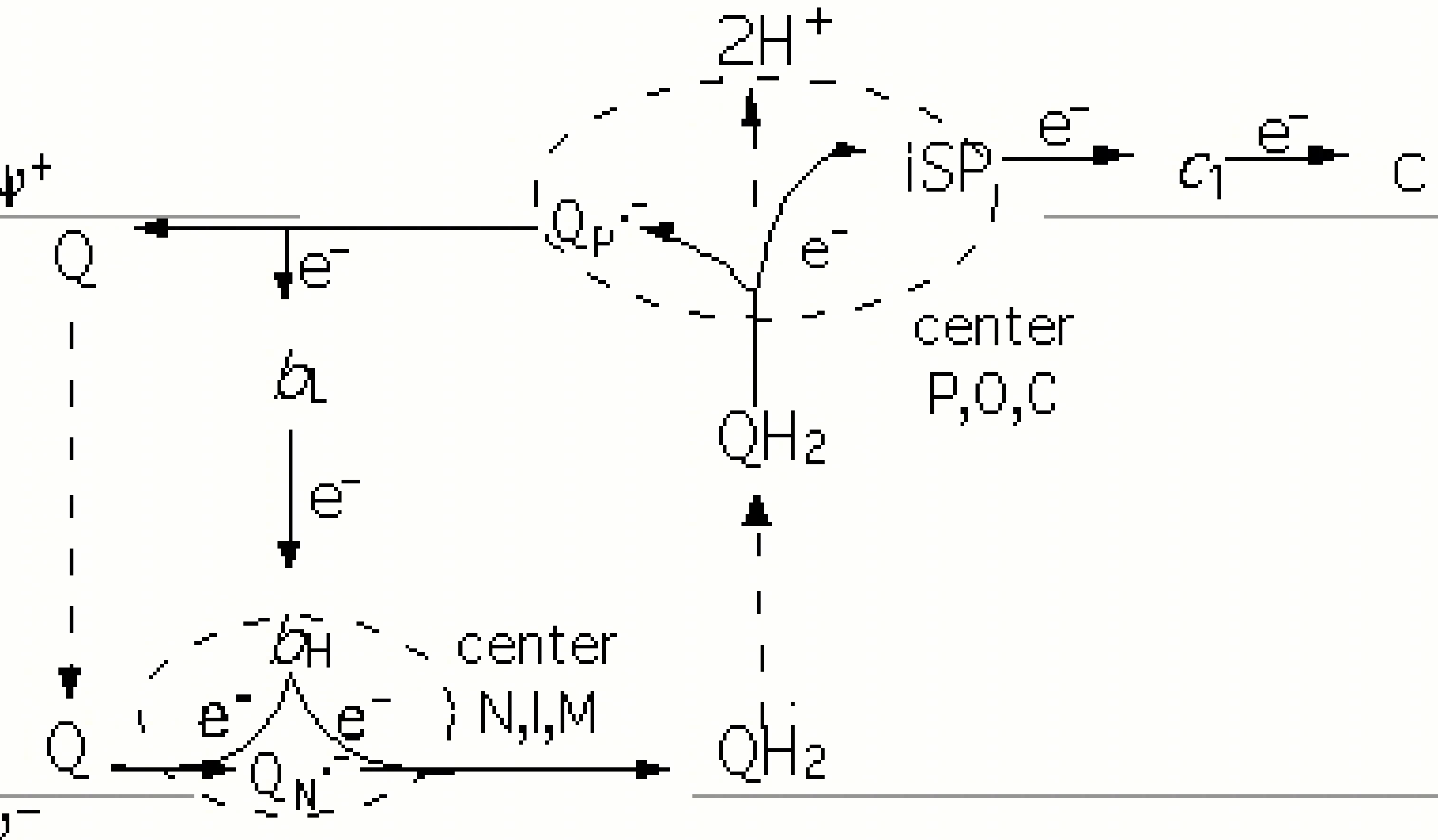
Wickström’s inspired suggestion



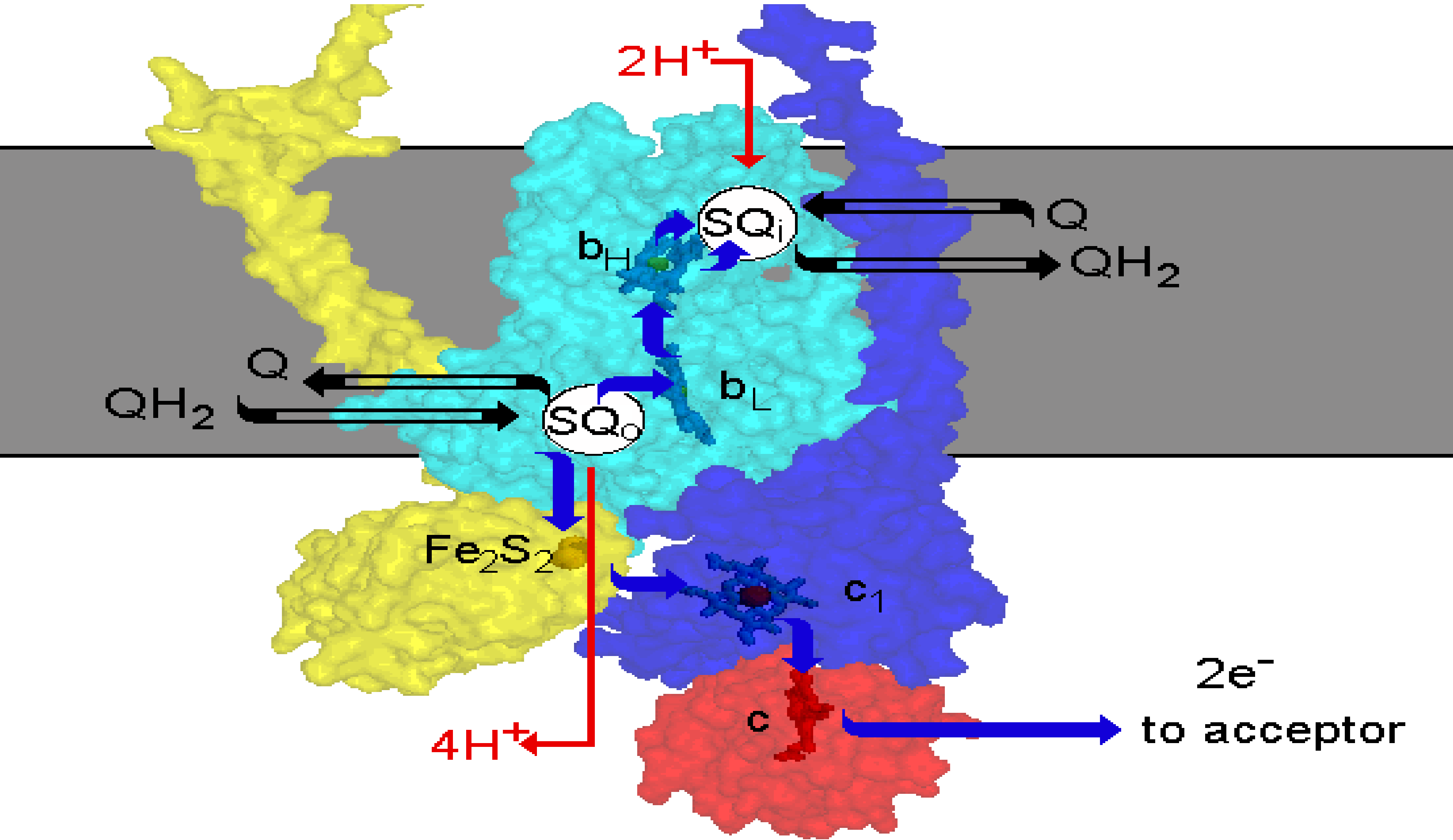
Wikström, M.K.F. and Berden, J.A. (1972) "Oxidoreduction of Cytochrome b in the Presence of Antimycin", Biochim. Biophys. Acta 283, 403-420.

Mitchell's Q-cycle

(according to Yu Chang-An)



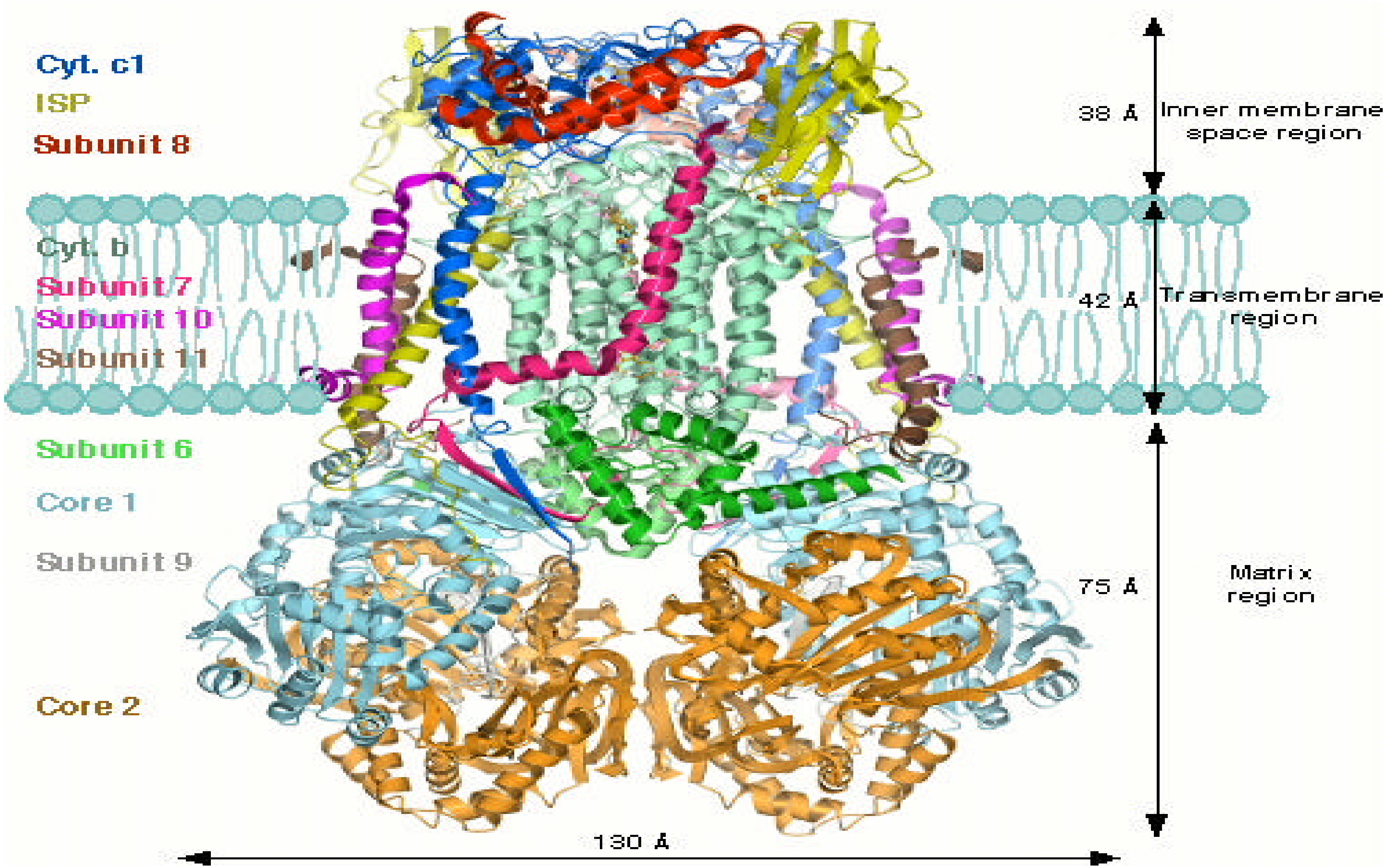
Mitchell's Q-cycle
(According to Tony Crofts)



The overall stoichiometries

- The o-site turns over twice: 4 H^+ to “o”
- The i-site turns over once: 2 H^+ from “i”
- 2 UQH_2 are oxidized but 1 is reduced
- So, overall fuel consumption: 1 UQH_2
- 2 electrons flow to cyt c (and on to O_2)
- 2 electrons flow across membrane
  (generating ? ?)
- Of the $4H^+$ to “o”, 2 come from “i” while 2
  come from ....

‘Google’-search “Q-cycle”



The bc1-complex from beef heart mitochondria

Subunit (no.		Mr(beef)	Function
I	Core	53.6	No catalytic, protein transport Core
II	Core	46.5	No catalytic, protein transport
III	Cyt b	42.6	donor to Qi-site , acpt from SQ at Qo-site (**8**)
IV	c1	27.3	donor to cyt c (**1**)
V	Rieske's 2Fe.2S	21.6	acceptor from QoH2 , donor to cyt c1 Subunit (**1**)
VI	none	13.3	none known
VII	none	9.5	none known (**1**)
VIII	none	9.2	hinge protein (interacts with c1)
IX	none	8.0	none known
X	none	7.2	none known (**1**)
XI	none	6.4	none known (not present in chicken)

http://www.life.uiuc.edu/crofts/bioph354/bc-complex_summary.html

A.R. Crofts' Q-cycle web addresses

- http://www.life.uiuc.edu/crofts/bioph354/index.html
- http://www.life.uiuc.edu/crofts/bioph354/bc-complex_summary.html
- http://www.life.uiuc.edu/crofts/bc-complex_site/
- http://www.life.uiuc.edu/crofts/bc1_in_chime/bcc.html
- http://www.life.uiuc.edu/crofts/bc-complex_site/etp-model_annotated.html
- http://www.life.uiuc.edu/crofts/bioph354/index.html