Electron Bifurcation
life's 3rd mechanism of energy conversion

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A brief history of earth and life

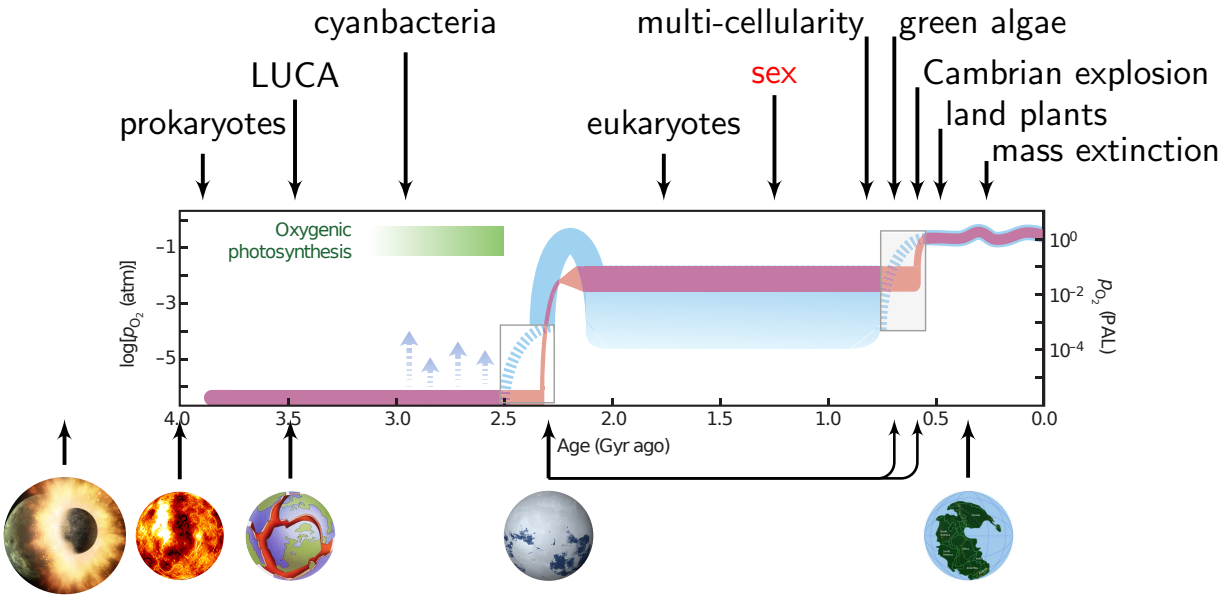


Figure modified from **Lyons TW, Reinhard CT & Planavsky NJ (2014)**, The rise of oxygen in Earth's early ocean and atmosphere, *Nature* **506**:307-315 | doi:10.1038/nature13068

Redox reaction

$$2\,H_2 \longrightarrow 4\,H^+ + 4\,e^- \quad \text{(donor)}$$
$$O_2 + 4\,H^+ + 4\,e^- \longrightarrow 2\,H_2O \quad \text{(acceptor)}$$
$$2\,H_2 + O_2 \longrightarrow 2\,H_2O \quad \text{(overall reaction)}$$

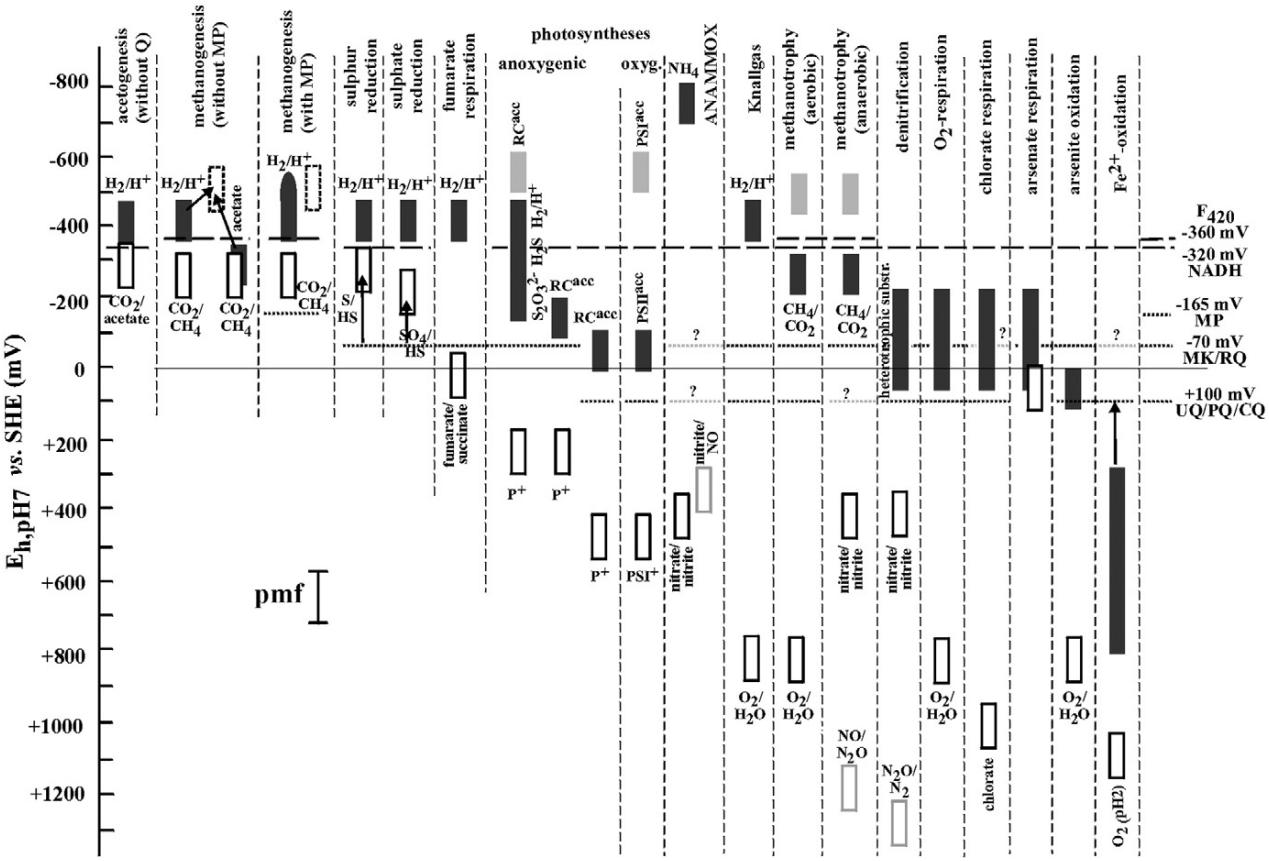
Obviously, not all couples of redox substrates yield the same amount of energy.

ΔG depends on the difference in standard electrochemical potential ΔE_m between e^- donor and acceptor and concentration (Nernst-Equation).

$$E_{h,7} = E_{m,7} + \frac{1}{n} \cdot 59\text{mV} \cdot \log([ox]^a/[red]^b)$$

$E_{m,7}$ ... redox midpoint potential at pH 7
n ... number of transferred electrons.
a, b ... stoichiometric coeffitions of oxidized donor / reduced acceptor
Electrochemical driving force for redox equilibrations between a donor (D) and an acceptor (A) molecule: $\Delta E_h = E_h(A) - E_h(D)$; Gibbs free energy of redox reaction: $\Delta G = nF\Delta E_h$ with n, number of transferred electrons and F, Faraday constant

Life on the redox-scale



black/white boxes are electron donors/acceptors; proton motive force (pmf)
energetically favorable is from more negative to more positive electrochemical potential.

Schoepp-Cothenet B et al (2013), On the universal core of bioenergetics, *Biochim Biophys Acta* **1827**:79-93 | doi:10.1016/j.bbabio.2012.09.005

The core of bioenergetics

Life's ability to create order from randomness rests on disequilibria:

1. chemical ($\mathrm{ATP/ADP{+}P_i}$).
2. electrochemical ($\mathrm{NAD(P)H}$/oxidizing environment).

$$-\frac{\Delta G}{kT} = \ln\left(\frac{[\mathrm{ATP}]/[\mathrm{ADP}][\mathrm{P}_i]}{[\mathrm{ATP}]_{\mathrm{eq}}/[\mathrm{ADP}]_{\mathrm{eq}}[\mathrm{P}_i]_{\mathrm{eq}}}\right) \approx 20 - 24$$

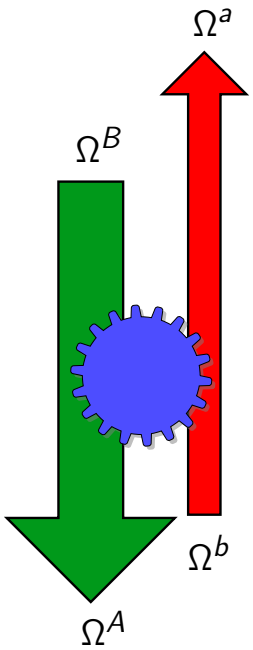
$\Delta G_{\mathrm{ATP}} \sim 50 - 60\,\mathrm{kJ/mol}$; $kT \sim 3\,\mathrm{kJ}/mol$; unit activities are assumed

Implying that the *ratio* of concentrations of ATP to it's hydrolysis products $\mathrm{ATP{+}P_i}$ *is in the order of* $10^9 - 10^{11}$!!!

- ATP is **actively driven** out of equilibrium with respect to $\mathrm{ADP{+}P_i}$.
- This astronomical disequilibrium provides the "driving force".
- The disequilibrium is **constently dissipated** to maintain structure.

Branscomp E & Russell MJ (2017), Escapement mechanisms and the conversion of disequilibria; the engines of creation, *Phys Rep* **677**:1-60 | doi:10.1016/j.physrep.2017.02.001

What is energy conversion?



$$S = k \log \Omega$$

$$\Omega^A > \Omega^B \quad \text{and} \quad \Omega^a < \Omega^b$$

2nd Law requires

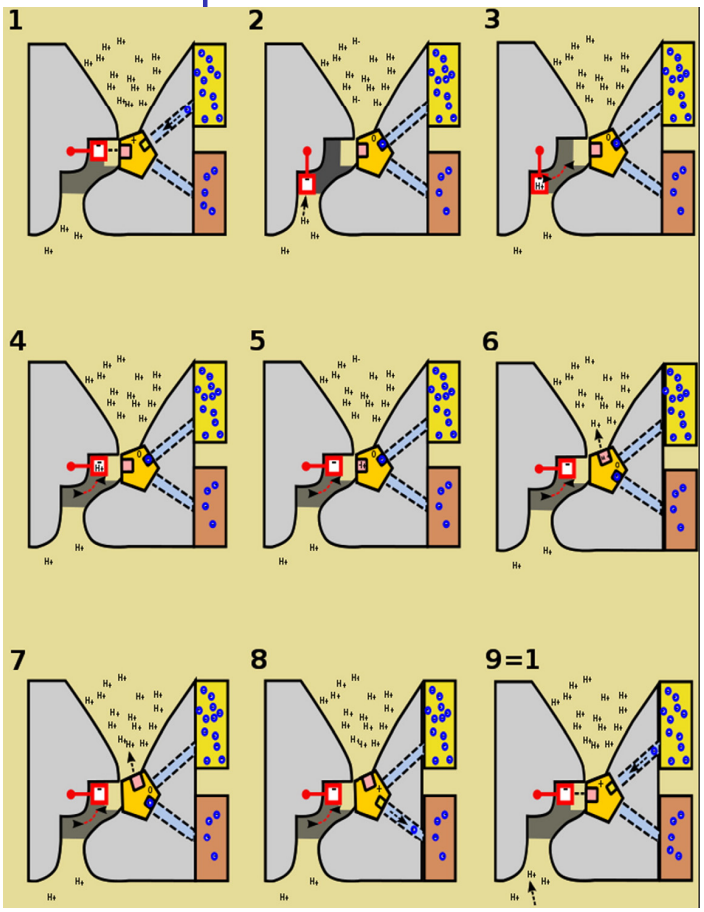
$$\Delta S^{\mathrm{driver}} \geq \Delta S^{\mathrm{driven}}$$

The **gear** symbolizes a **molecular coupling** tying the two individual processes into a **single thermodynamic process**.

driven process, driven process, S entropy, Ω total mircostate count

Branscomb E & Russell MJ (2013), Turnstiles and bifurcators: The disequilibrium converting engines that put metabolism on the road, *Biochim Biophys Acta* **1827**:62-78 | doi:10.1016/j.bbabio.2012.10.003

Example: Ferredoxin I from *Azotobacter vinelandii*



Moving parts:

- box (CO_2^--moiety).
- pentagon ($3Fe4S$-cluster).

dark gray channel blocks H^+.
yellow box redox donor.
brown box redox acceptor.

Figure modified from Branscomb & Russell 2013;
Chen K et al (2000), Atomically defined mechanism for proton transfer to a buried redox centre in a protein, *Science* **405**:814-817 | doi:10.1038/35015610

The electron transfer puzzle

Hydrogenotropic methanogenesis

$$4\,H_2 \;+\; CO_2 \longrightarrow CH_4 \;+\; 2\,H_2O \qquad \Delta G = -134\text{kJ/mol } CH_4$$

Thermodynamic conundrum:

Crucial electron transfer steps go steeply uphill against a substantial unfavorable redox midpoint potential difference.

Solution:

Energy conserving electron bifurcation[†].

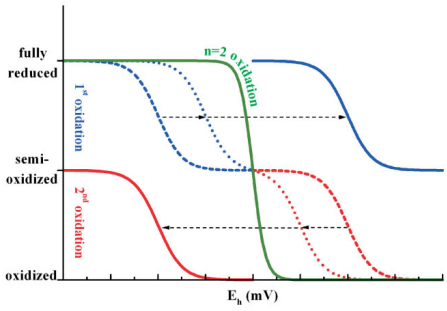
Mechanism:

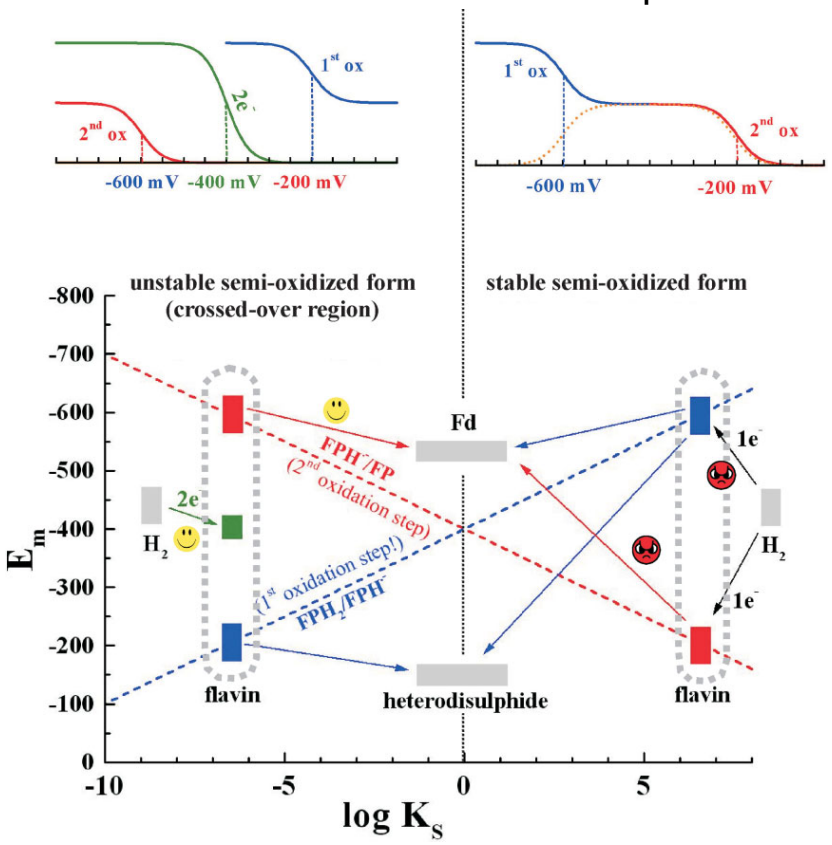
The highly exergonic electron transfer to the high potential acceptor compensates the endergonic reduction of an acceptor substantially more negative than the flavin.

[†] The hypothesis put forward by Buckel, Thauer, and colleagues in essence stipulates that the 2-electron carrier, flavin, bifurcates its two electrons towards acceptors with much lower and much higher redox potentials than that of the average (2-electron) transition of flavin.

Mechanism of redox-bifurcation

Cross-over of individual redox transitions in 2-e^- redox compounds.





"Magic" Cofactors:

- flavins
- quinones

Figures modified from **Nitschke W & Russell MJ (2011)**, Redox bifurcations: Mechanisms and importance to life now, and at its origin, Bioessays **34**:106-109 | doi:10.1002/bies.201100134

Example: Methanogenic heterodisufide reductase complex

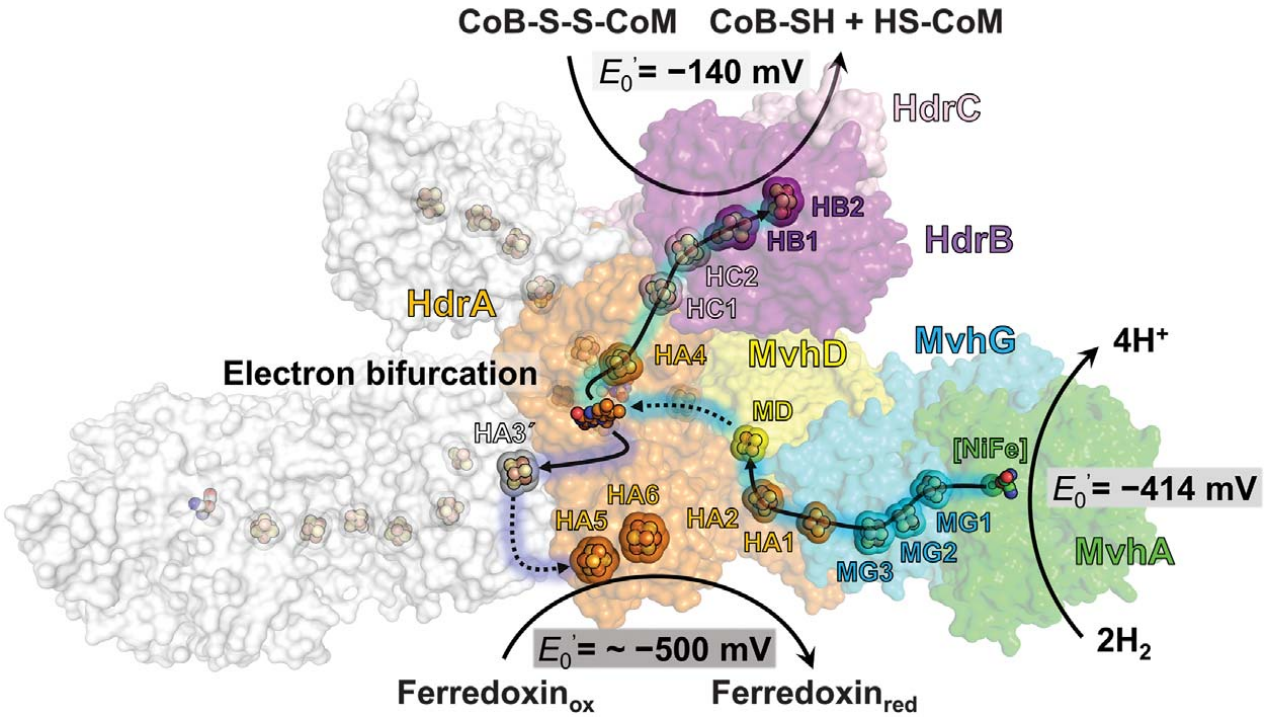


Figure modified from **Wagner T et al (2017)**, Methanogenic heterodisulfide reductase (HdrABC-MvhAGD) uses two noncubane [4Fe-4S] clusters for reduction, *Science* **357**:1-4 | doi:10.1126/science.aan0425

Further Reading


Buckel W & Thauer RK. **Energy conservation via electron bifurcating ferredoxin reduction and proton/Na^+ translocating ferredoxin oxidation.** Biochim Biophys Acta (2013), 1827:94-113 | doi:10.1016/j.bbabio.2012.07.002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Peters J, Miller A-F, Jones AK, King PW & Adams MWW. **Electron bifurcation.** Curr Opin Chem Biol (2016), 31:146-152 | doi:10.1016/j.cbpa.2016.03.007


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