Part 2. The Vital Force

Proton power and the origin of life

Birth of oxygen dependent life
Life also depends on energy

Chemiosmotic hypothesis by Peter Mitchell
Mitchondrial contribution to the evolution of all higher forms of life

4. The meaning of respiration
5. Proton power
6. The origin of life

4. The meaning of respiration

16th century alchemist Paracelsus: ‘Man dies like a fire when deprived of air’
Lavoisier: ‘father of modern chemistry’, respiration is combustion (respiration to heat)
1843 James Prescott Joule and William Thompson (Lord Kelvin): the first law of thermodynamics
1847 Hermann von Helmholtz: energy from respiration is used to generate the force in the muscles

conversion of chemical energy to a potential energy and to a biological energy

concept of currency

1870 German physiologist Eduard Pflüger: cell respiration
1912 B.F. Kingsbury: mitochondria respiration
1949 Eugene Kennedy and Albert Lehninger: respiratory enzymes in mitochondria

Colors in the cell: look for energy currencies

How the energy released by the oxidation of glucose is coupled to the energetic demands of life?
Oxygen is thermodynamically reactive but kinetically stable: requirement of activation energy

1884 Charles MacMunn: a respiratory pigment inside tissues
1925 David Keilin: rediscovery of the pigment and named cytochromes (a, b, c)

but none of them reacted directly with oxygen

Otto Warburg: binding of CO to iron compounds in the dark and its dissociation when illuminated

observation of absorption spectrum change

The respiratory chain

Warburg: one-step process of releasing all the energy bound in glucose

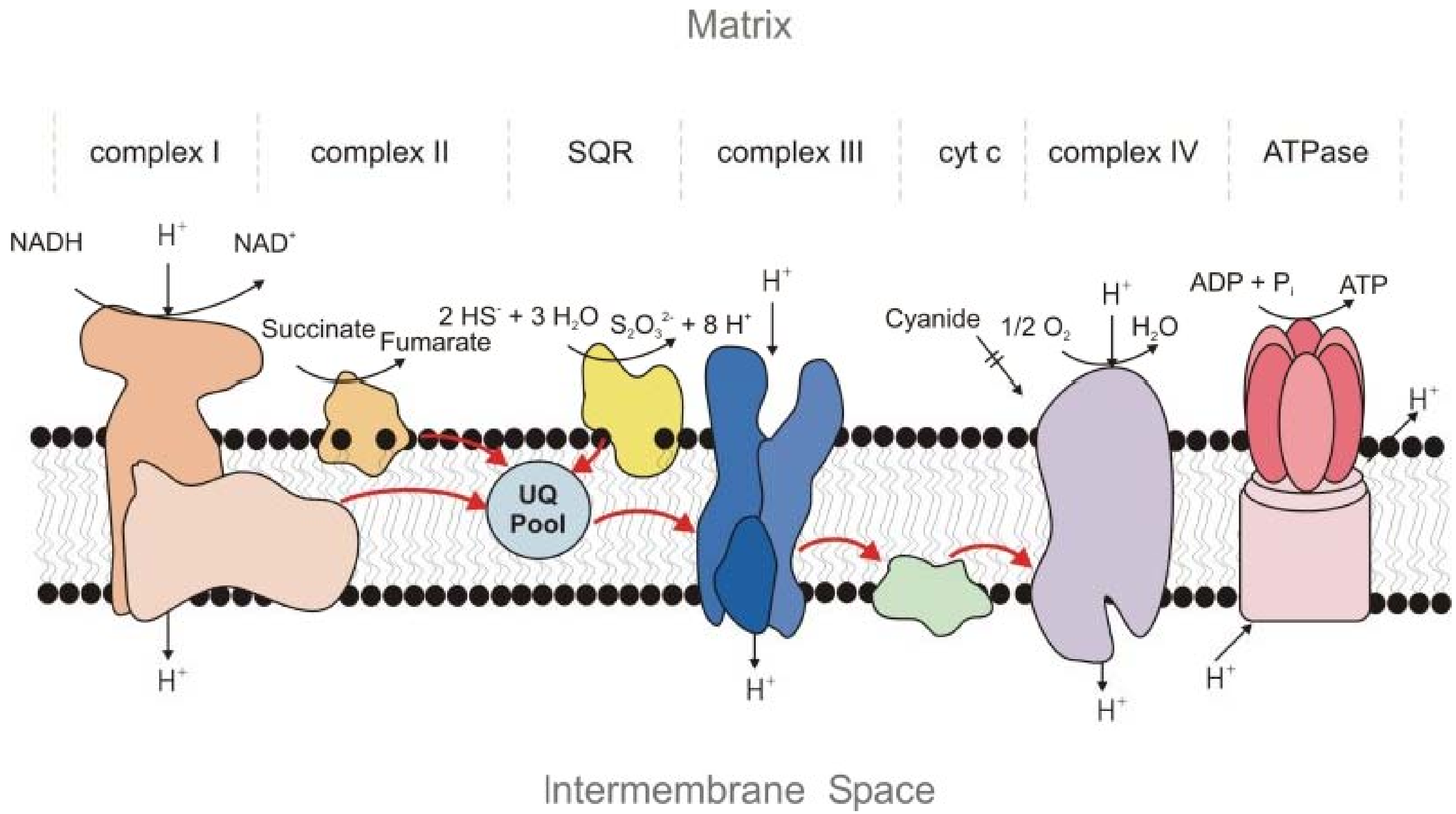
Keilin: the idea of a respiratory chain

passing down of protons and electrons to a chain of cytochromes

finally reacting with oxygen to form water

manageable amount of energy release at each step

1930s Warburg: discovery of additional non-protein components of the chain



ATP: he universal energy currency

How energy is conserved? presence of an intermediate molecule

Respiratory chain is the Mint, where the new currency is produced

The first glimpse of answer from studies of fermentation

Lavoisier: fermentation as a chemical process

19th century: a living process

Louis Pasteur: fermentation as ‘life without oxygen’

1897 Eduard Buchner: fermentation outside of cell

- finding of enzyme
- the end of vitalism

Sir Arthur Harden and Hans von Euler: unraveling of succession of steps in fermentation

1924 Otto Meyerhof: the same process in muscle cells and the final product lactate

- the fundamental unity of life

By the end of 1920s: fermentation to generate energy when oxygen respiration fails

- fermentation and respiration are parallel processes

1929 Karl Lohman: discovery of ATP and its synthesis in fermentation

1930s Vladimir Engelhardt: ATP for muscle contraction and its conversion to ADP

- ATP production in the process of oxygen respiration

Severo Ochoa: 38 ATP molecules from oxygen respiration

- in average person, 9×10^{20} molecules/sec, turnover rate of 65 kg/day

1941 Fritz Lipmann and Herman Kalckar: ATP as the universal energy currency

The elusive squiggle: ‘high-energy bond’

ATP from ADP in cells

How ATP is actually formed?

1940s Efraim Racker: fermentation generates high-energy phosphate intermediates

they in turn transfer their phosphates to form ATP

discovery of ATPase (a giant enzyme complex)

1964: visualized as studded particles in the inner mitochondrial membrane

how respiratory chains transfer the energy to the ATPase to generate ATP

Respiratory chain reactions are physically separated from ATPase

high-energy intermediate from the chain and move to ATPase

Searching for the high-energy intermediate for two decades

A variable and noninteger number of electrons for the production of ATP

Respiration requires membrane

without membrane respiration is uncoupled: glucose oxidation proceeds but no ATP synthesis

chemical uncouplers

1961 Peter Mitchell

5. Proton power

Peter Mitchell

He studied bacterial transport systems

1961 Nature: respiration in cells worked by chemiosmotic coupling

coupling of chemical reaction with osmotic gradient

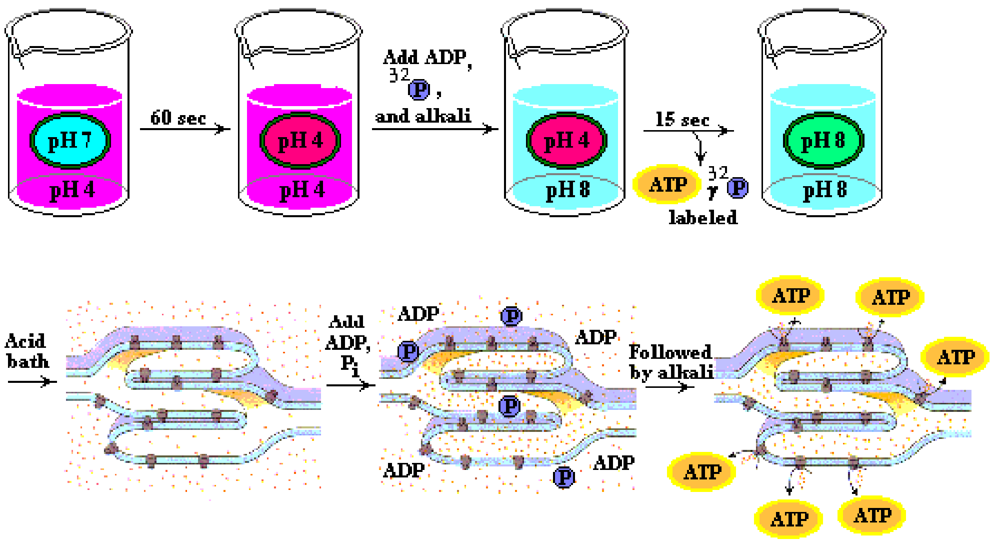
<u>The explanatory power of proton power</u>

Why a membrane is necessary

How the uncoupling agent work

Why ATPase is not physically linked to respiratory chain

predictions and proofs



The deeper meaning of respiration

the proton-motive force: fundamental to many aspects of life besides ATP formation

active transport of molecules

heat production

bacterial locomotion

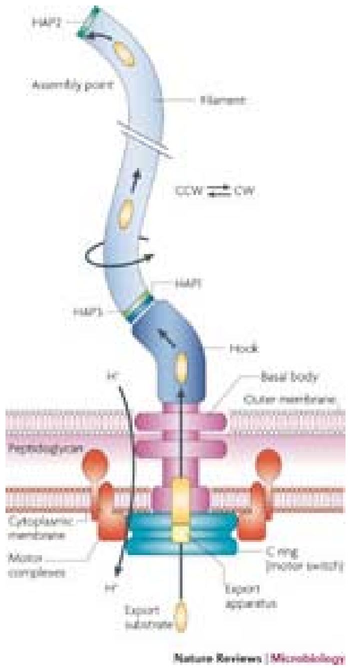
if respiration fails, bacteria generate ATP by fermentation and

then ATPase breakdown ATP to pump protons and

all other ATP-dependent tasks must wait

the main purpose of fermentation might be to maintain the proton-motive force

A fundamental property of life: common to all life and central to all aspects of life
Therefore, the origin of life may have tied to the natural energy of proton gradients



6. The origin of life

Why so fundamental is a proton-motive force in bacteria?

RNA world

- two serious problems with the RNA world
  - ribozymes are not very versatile catalysts, while minerals are
  - where comes the energy for ribozyme replication and turnover?

The idea of a primordial soup

- Stanley Miller and Harold Urey: abiotic synthesis of organic compounds
- primordial soup
- life of fermentation
- birth of autotrophs ($H2S$ photosynthetic bacteria)
- birth of oxygen respiring bacteria

Several problems with fermentation

1. Ran out of fermentable substrates
   - There is a gap of at least several hundred million yrs
   - Life origin at least 3.85 billion yrs ago
   - Photosynthesis between 3.5 and 2.7 billion yrs go

2. Fermentation is not a primitive process
   - too complex a process requiring 12 enzymes

3. LUCA: the last universal common ancestor of all known life on earth
Classical fermentation did not exist in LUCA
Photosynthesis evolved in cyanobacteria never found in any archaea
Both the archaea and bacteria do ferment
    but they do so by using different unrelated enzymes

The first cell

If proton pumping is fundamental to life, it should be present in both bacteria and archaea
- Both have respiratory chains with similar components
- Both share an ATPase that is basically similar in its structure and function

Respiration is far simpler than fermentation
- electron transport (just a redox reaction)
- a membrane
- a proton pump
- an ATPase

The problem of membrane
- the membranes of bacteria and archaea have very little in common
- meaning difference in the enzymes involved in the synthesis

Martin & Russell: LUCA could not have had a lipid membrane
- inorganic membrane: a thin, bubbly layer of iron-sulfur minerals

Full metal jacket

Iron-sulfur minerals such as iron pyrites

Black smokers in the deep sea
The smoke composed of iron and hydrogen sulphide, which precipitate as iron-sulphur minerals

Iron-sulfur minerals: well-known catalyst in organic reaction and in proteins

<u>Gunter Wachtershauser, late 1980s and 1990s</u>
Suggested iron-sulfur minerals to reduce CO2 to a plethora of organic molecules
Hydrothermophiles as the most ancient groups

Supported by genetic evidence but questioned by thermodynamics problems
- dissociation of reaction products after being generated on the surface of iron-sulfur

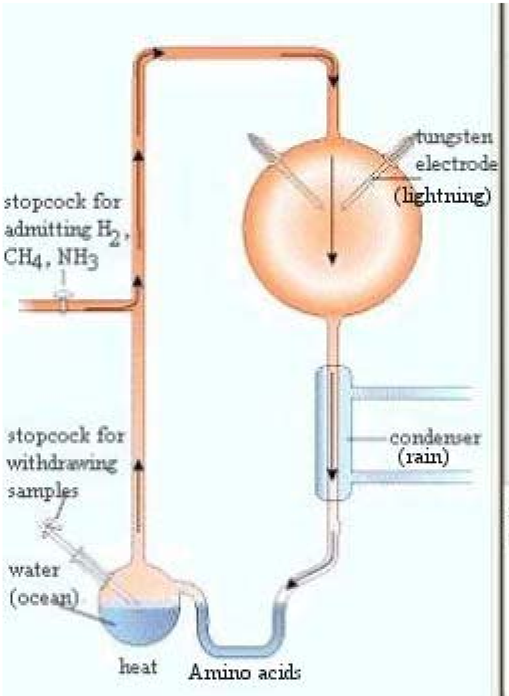
<u>Mike Russell, late 1980s</u>
- Finding of minerals forming huge numbers of tubular structures
  - in 350 million yrs old iron-pyrites at Tynagh in Ireland
  - A possible reaction scenario in the menacing black smoker
  - Demonstrated in laboratory (Fig. 8)
- Highly probable in the points that
  - Cells are naturally chemiosmotic
  - Conduction of electrons in the bubbly membranes of iron-sulfur crystals

Prebiotic broth theories

self-assembly of high-molecular weight structures such as RNA, proteins, and vesicles in a cold prebiotic broth of preaccumulated modules

Iron-sulfur world theory

Autotrophic metabolism of low-molecular weight constituents in an environment of iron-sulfur and hot magmatic exhalations

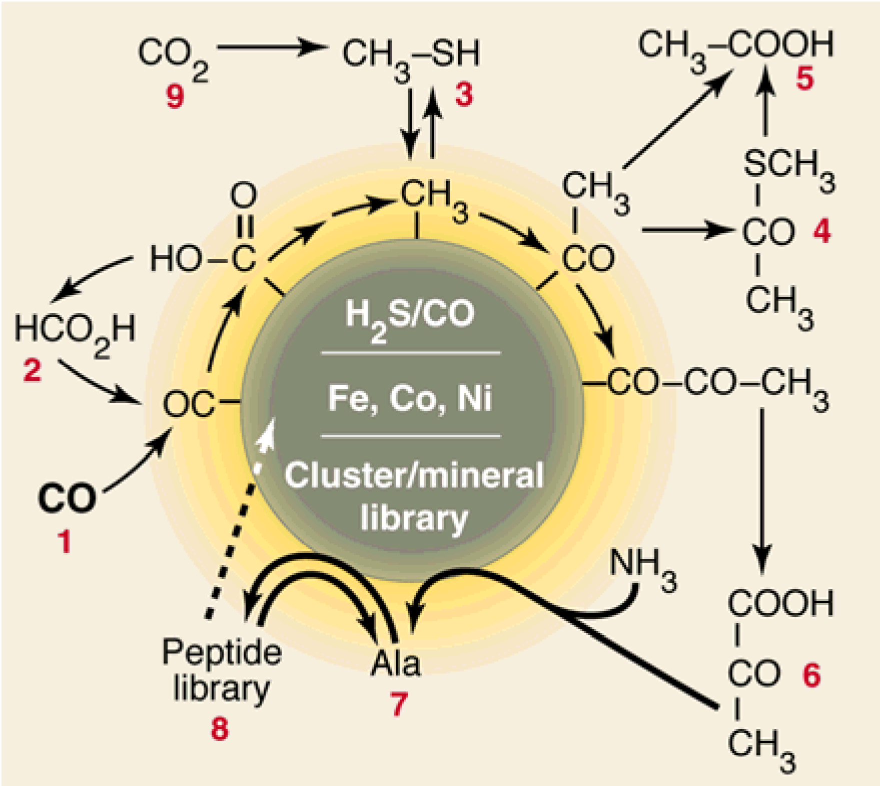


Some Products Formed under Prebiotic Conditions

Carboxylic acids	Nucleic acid bases	Amino acids
Formic acid	Adenine	Glycine
Acetic acid	Guanine	Alanine
Propionic acid	Xanthine	α-Aminobutyric acid
Straight and branched fatty acids (C_4–C_{10})	Hypoxanthine	Valine
Glycolic acid	Cytosine	Leucine
Lactic acid	Uracil	Isoleucine
Succinic acid		Proline
	Sugars	Aspartic acid
	Straight and branched pentoses and hexoses	Glutamic acid
		Serine
		Threonine

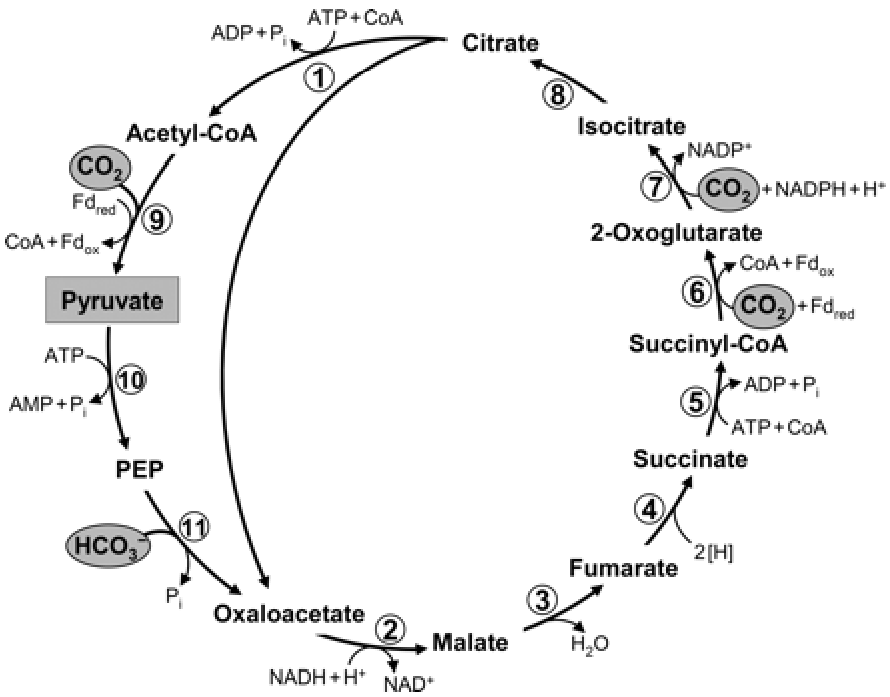
Source: From Miller, S.L. (1987) Which organic compounds could have occurred on the prebiotic earth? *Cold Spring Harb. Symp. Quant. Biol.* **52**, 17–27.

Reactions in the iron-sulfur world
(Cody et al., 2000. Science)



$$FeS + H_2S \rightarrow FeS_2 + 2H^+ + 2e^-$$

The reductive (reverse) citric acid cycle as it functions in green sulfur bacteria



The pathway of acetyl-CoA assimilation to pyruvate, phosphoenolpyruvate (PEP), and oxaloacetate is shown as well. For deviations from this variant of the cycle, see the text. Enzymes: 1, ATP-citrate lyase; 2, malate dehydrogenase; 3, fumarate hydratase; 4, fumarate reductase (natural electron donor is not known); 5, succinyl-CoA synthetase; 6, ferredoxin (Fd)-dependent 2-oxoglutarate synthase; 7, isocitrate dehydrogenase; 8, aconitate hydratase; 9, Fd-dependent pyruvate synthase; 10, PEP synthase; 11, PEP carboxylase.

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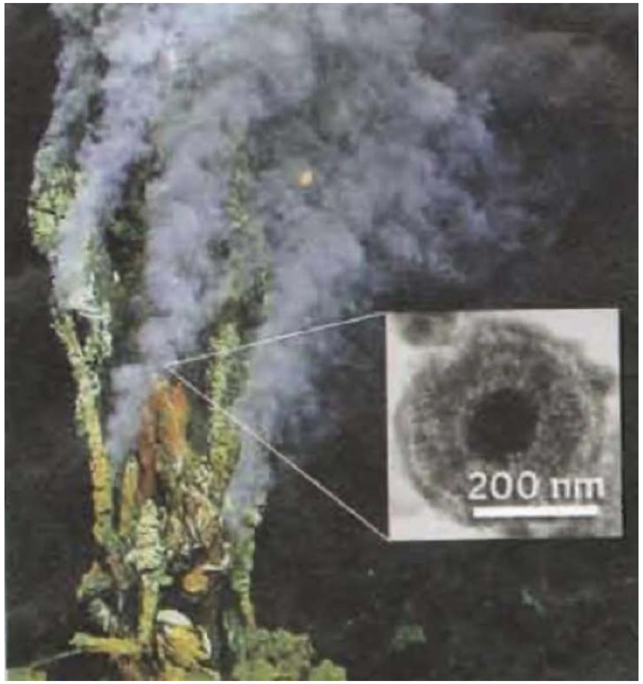
Pyrite nanoparticles exploding out of deep-sea vents help feed iron-craving deep-ocean creatures



Bacteria and plankton hungry for iron in the deep ocean can't just pop over to the nearest pharmacy to buy a multivitamin or dig into a juicy steak. Instead, new research shows that they may be getting their daily allowance of iron from pyrite (FeS2 nanoparticles delivered over long distances after erupting from hydrothermal vents *(Nat. Geosci., DOl: 10.1038/ngeo1148). In the* past, researchers believed that a majority of the iron bursting out of these deep-sea vents would immediately precipitate nearby as the hot vent fluid mixed with cold seawater. Biogeochemists subsequently discovered that some hydrothermal vent iron remained dissolved and was transported farther from the vents than expected. A team led by George W. Luther III and Mustafa Yiicel of the University of Delaware now report that hydrothermal vents are "nanofactories" that produce stable pyrite nanoparticles up to 200 nm wide. Formed before erupting from vents, the nanoparticles remain suspended and slowly oxidize to release iron for deep-sea creatures farther afield. This incarnation of pyrite, also known as fool's gold for its deceptively shiny yellow appearance, appears to be priceless to the ocean food chain, the researchers say.