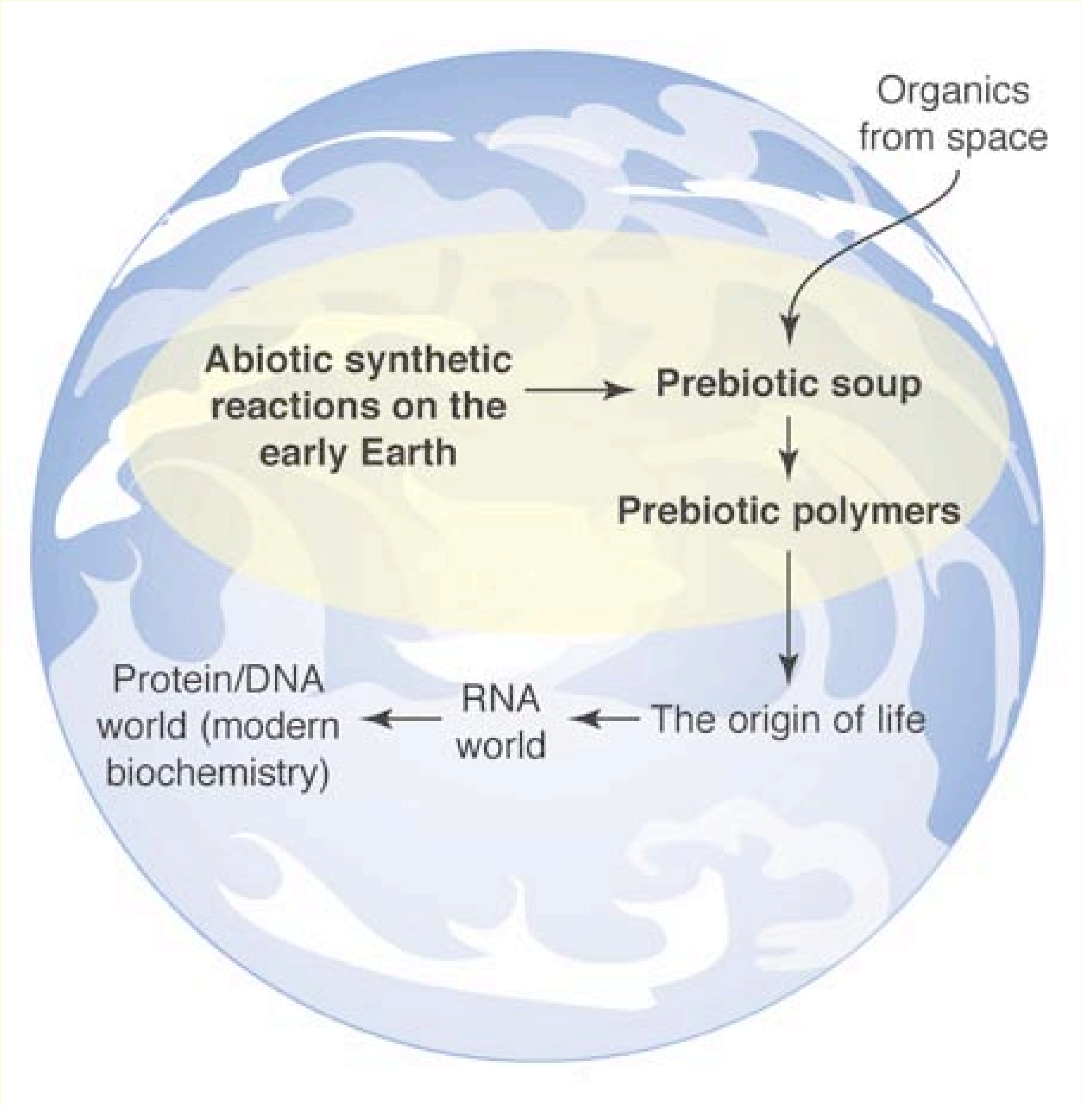
We want to understand how something like the sequence of events shown below could have occurred. To do this we need to know what the Earth was like very early in its life.



This is the genetic code used by nearly every organism on Earth today. The “code” refers to the manner in which codons are assigned. (Note: there are a few exceptions.) However the overall universality of this code, and especially the similar genes (sequences of codons that specify a function) found from bacteria to fruit flied to humans suggests that there was a common ancestor.

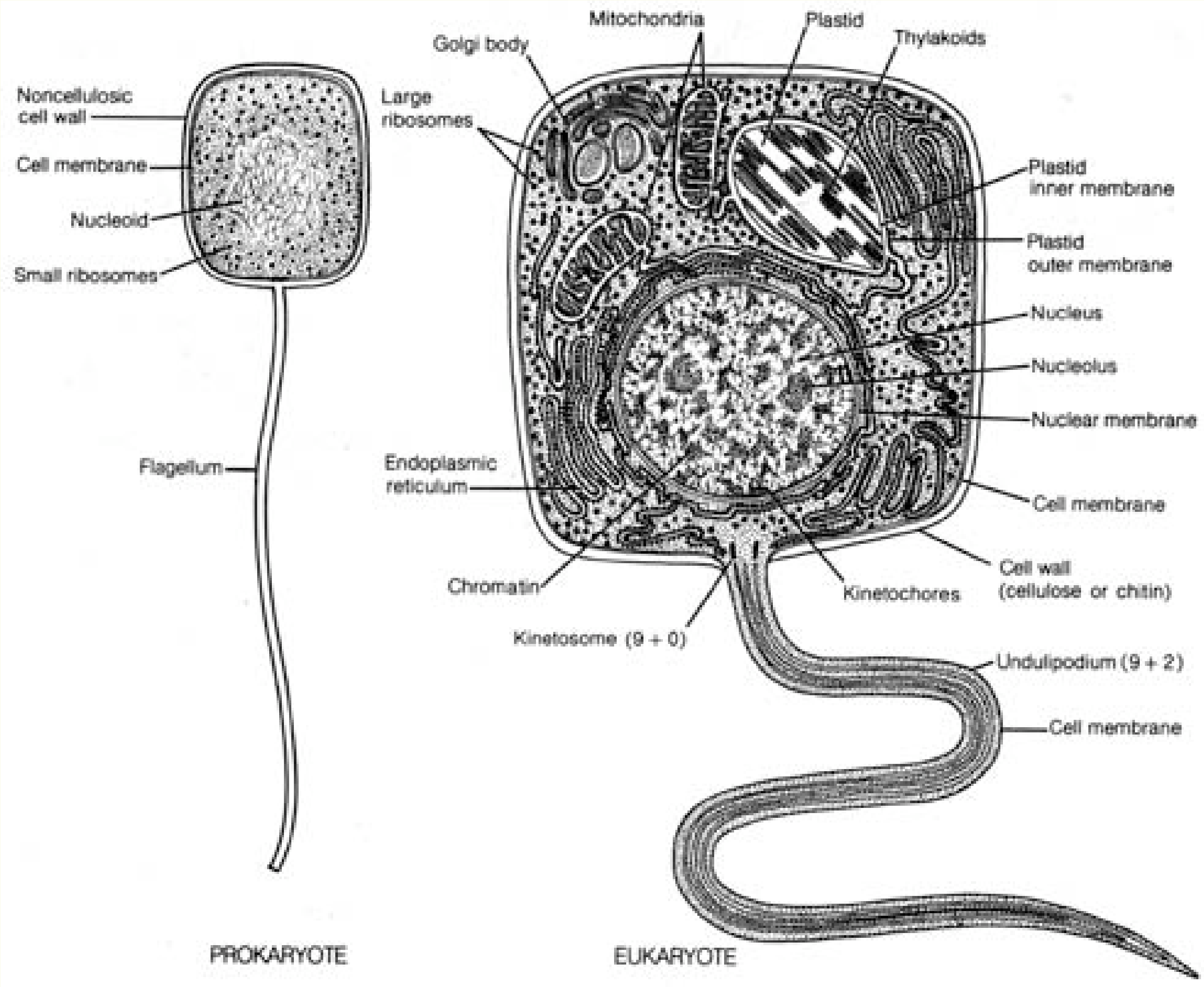
The Genetic Code

First Letter		Second Letter: U		C		A		G		Third Letter
U		UUU	phe	UCU	ser	UAU	tyr	UGU	cys	U
		UUC		UCC		UAC		UGC		C
		UUA	leu	UCA		UAA	stop	UGA	stop	A
		UUG		UCG		UAG	stop	UGG	trp	G
C		CUA	leu	CCU	pro	CAU	his	CGU	arg	U
		CUC		CCC		CAC		CGC		C
		CUA		CCA		CAA	gln	CGA		A
		CUG		CCG		CAG		CGG		G
A		AUU	ile	ACU	thr	AAU	asn	AGU	ser	U
		ACU		ACC		AAC		AGC		C
		AUA		ACA		AAA	lys	AGA	arg	A
		AUG	met	ACG		AAG		AGG		G
G		GUU	val	GCU	ala	GAU	asp	GGU	gly	U
		GUC		GCC		GAC		GGC		C
		GUA		GCA		GAA	glu	GGA		A
		GUG		GCG		GAG		GGG		G

Abbreviations:

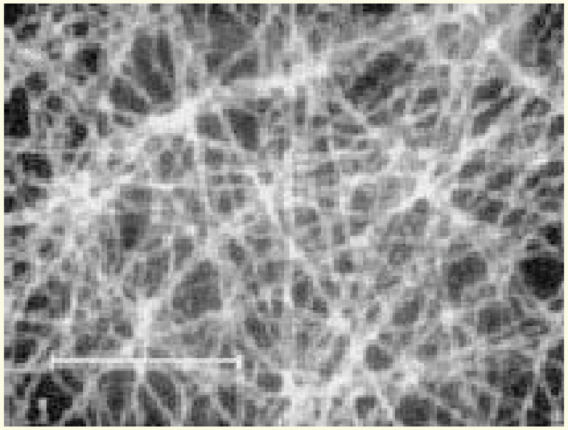
ala = alanine	gln = glutamine	leu = leucine	ser = serine
arg = arginine	glu = glutamic acid	lys = lysine	thr = threonine
asn = asparagine	gly = glycine	met = methionine	trp = tryptophan
asp = aspartic acid	his = histidine	phe = phenylalanine	tyr = tyrosine
cys = cysteine	ile = isoleucine	pro = proline	val = valine

Prokayotic vs. Eukaryotic cells. Notice nuclear membrane, organelles (e.g. mitochondria), cytoskeleton (not shown--next slide). Clearly the jump to eukaryotes was a large increase in complexity, and it only occurred relatively recently (compared to the origin of life).

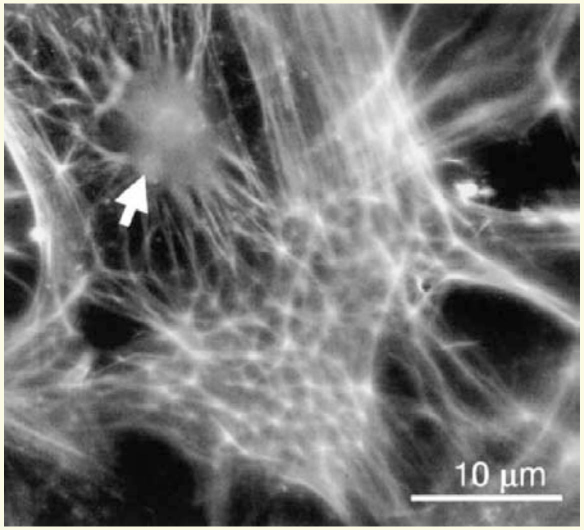


Eukaryotic cells all have a **cytoskeleton**, an amazing network of filaments (mostly made of actin and tubulin proteins) that participate in a large number of cellular activities such as cell support and nutrient transport. The network deforms, flows, and reforms continuously. Recently discovered that bacteria actually make similar proteins, so there is continuity between prokaryotes and eukaryotes.

A typical actin network



Human airway actin network



Giant cell cytoskeleton (microtubules)

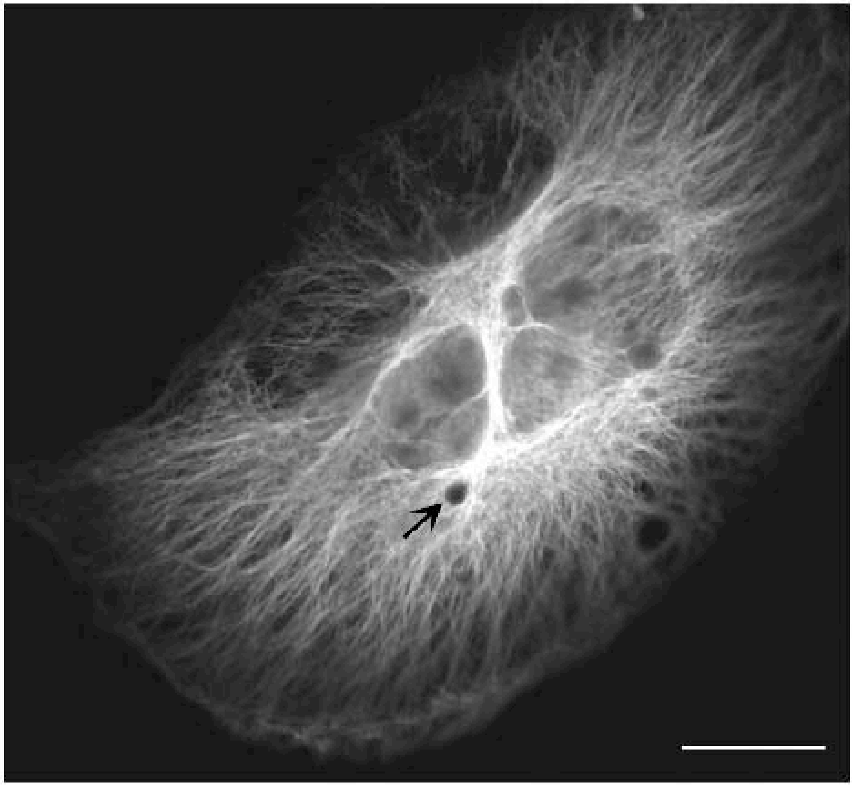
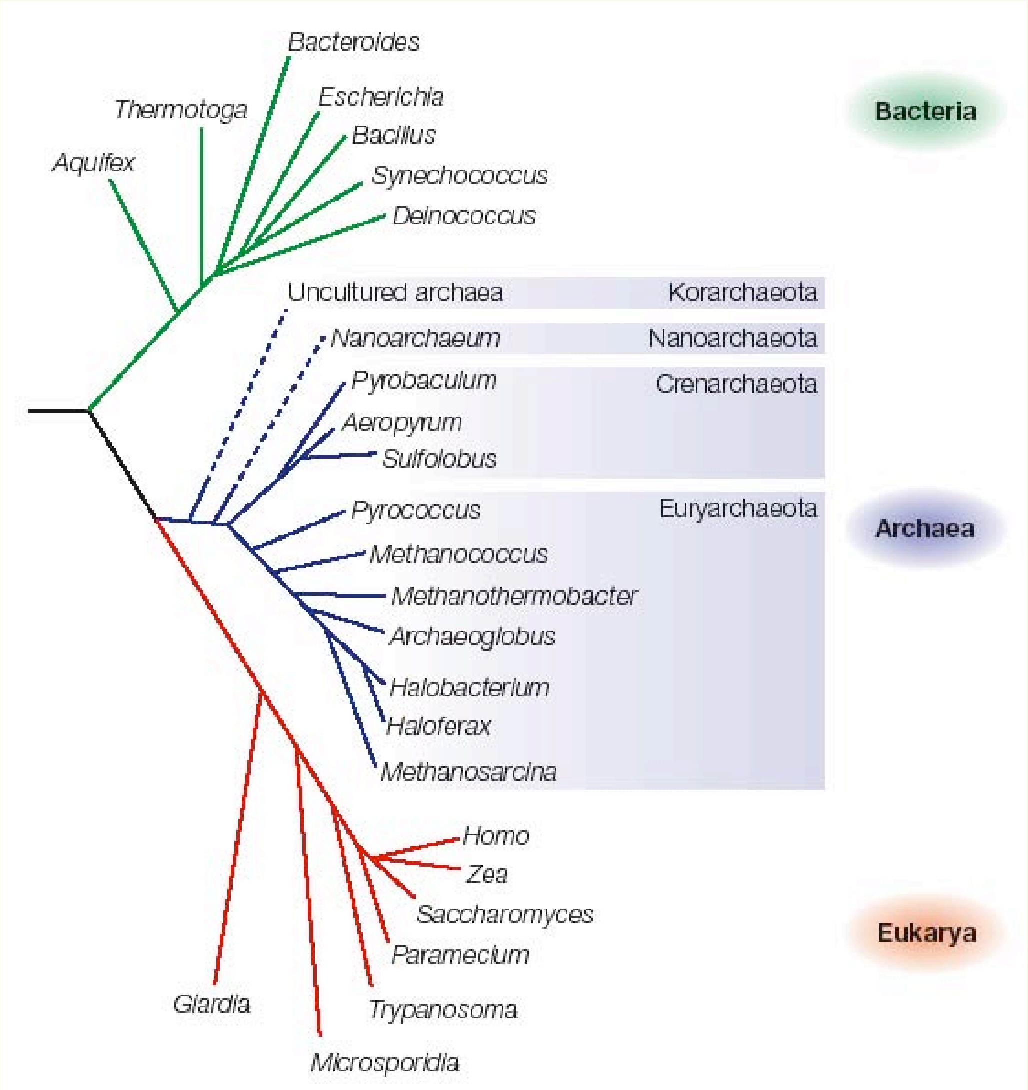


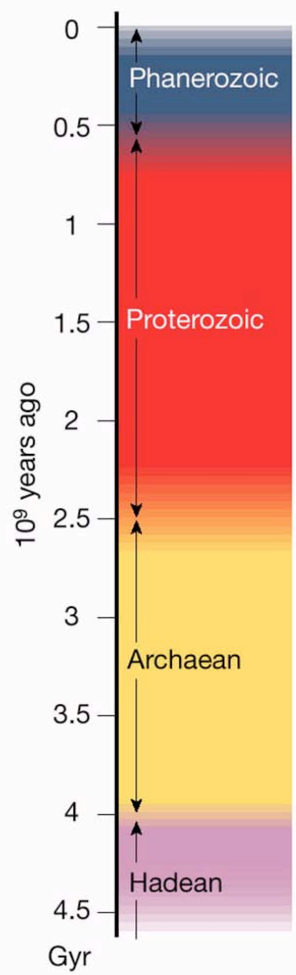
FIG. 3. Immunoflorescence image (Olympus Fluoview confocal microscope, PlanApo ×60/1.4 objective) of a multinuclear giant cell fixed and stained to show the microtubules [16] following measurement on the indicated bead; scale bar 20 μm.

Three domains of life, all with similar basic biochemistry and genetic code



We are interested in the first billion years (Gyr) or so of Earth's history. This encompasses the "Hadean" and "Archaean" eras.

Geological timescales



In discussing geological time, 1 Gyr is 10^9 years, 1 Myr is 10^6 years (the 'ago' is implicit and often omitted, such that Gyr and Myr refer to both time before present and duration). There are four aeons. The Hadean is taken here as the time from the formation of the Solar System and early accretion of the planet (4.6–4.5 Gyr), to the origin of life (probably sometime around 4.0 ± 0.2 Gyr). The Archaean, or time of the beginning of life, is from about 4–2.5 Gyr; the Proterozoic from 2.5 Gyr to about 0.56 Gyr; and the Phanerozoic since then.

Overview of the various processes that were probably occurring on the very young Earth.
How could life arise in such a tumultuous environment?

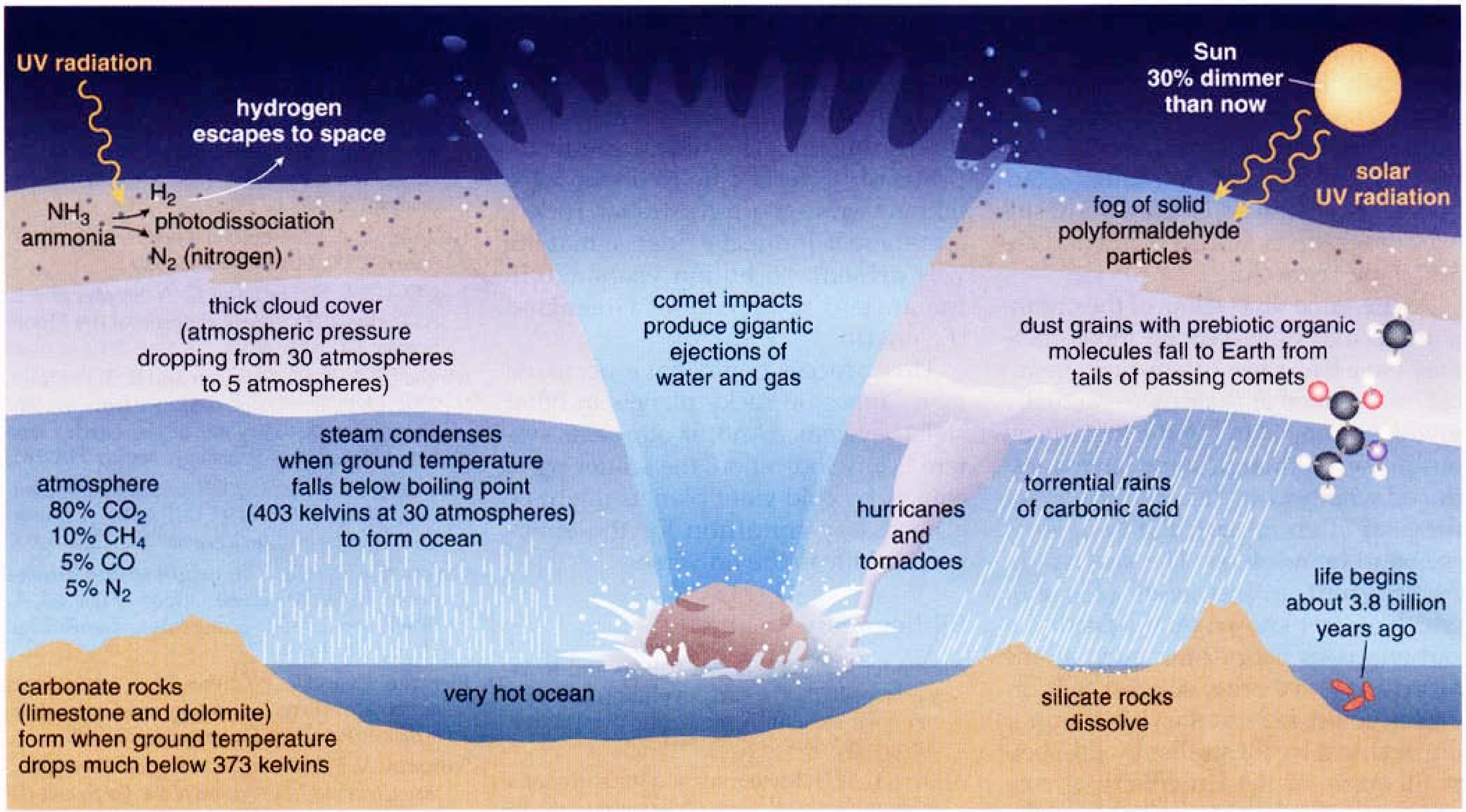
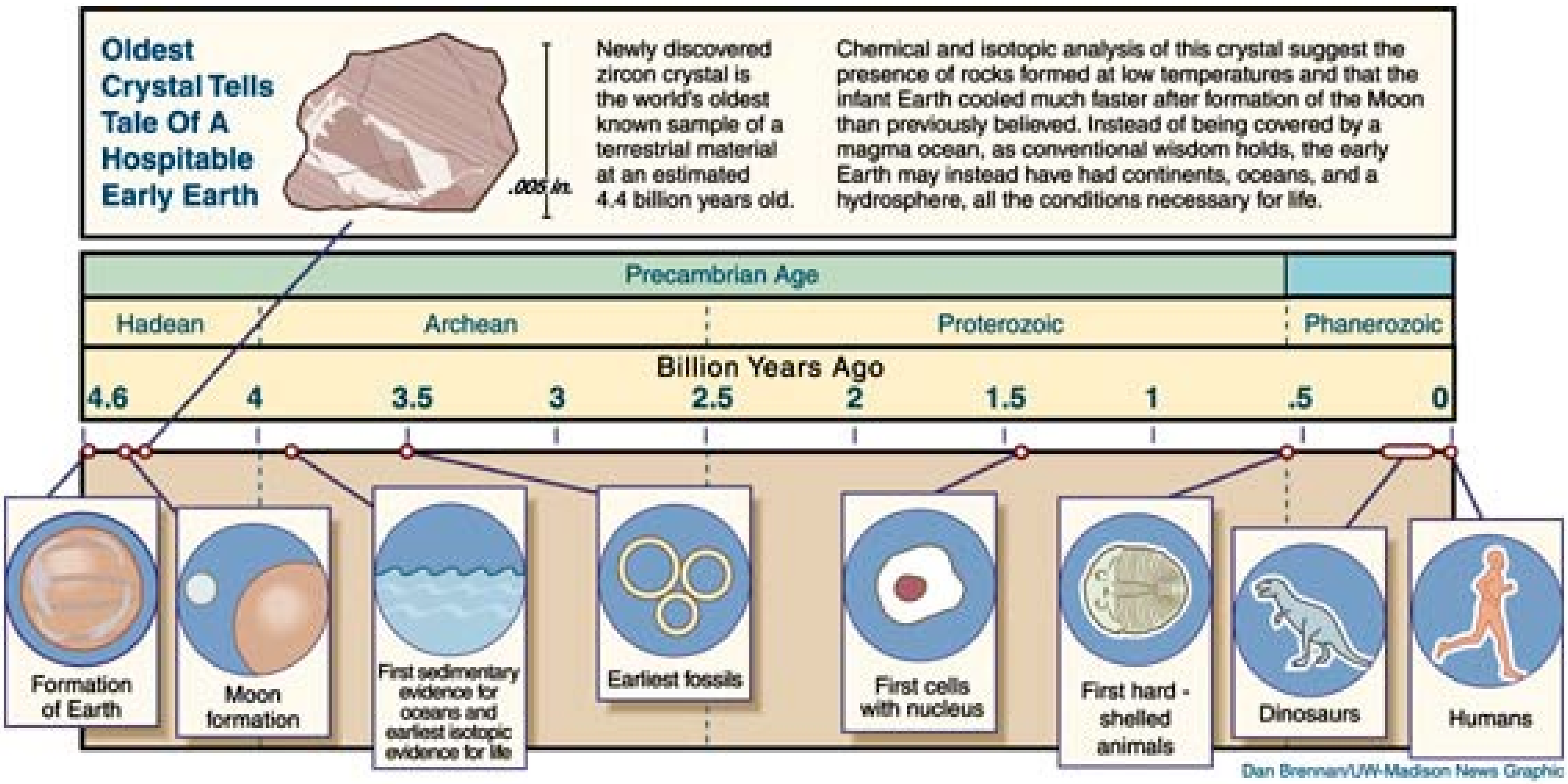
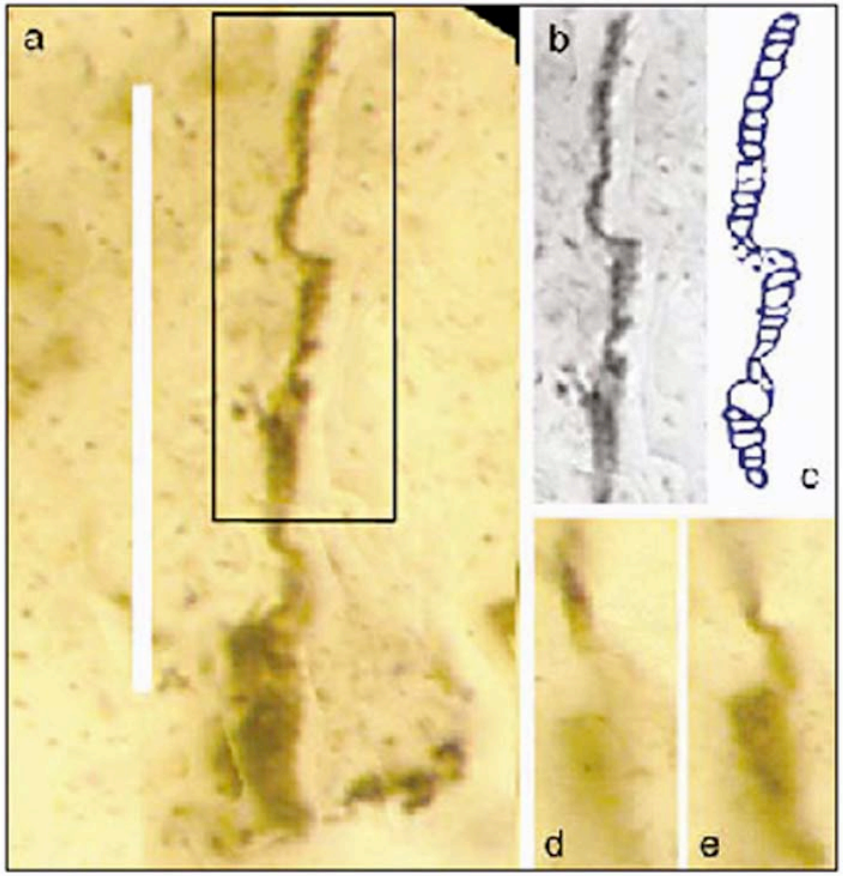


Figure 11. The primeval biosphere awoke to a tempestuous world of intermittent comet impacts, a steaming-hot ocean, a very thick atmosphere and torrential acid rains. Giant comet impacts would have ejected large amounts of material into space and spun off violent hurricanes and tornadoes. Although the atmosphere was originally rich in carbon dioxide (CO_2), photodissociation would have gradually increased the proportion of nitrogen in the atmosphere, while releasing hydrogen into space. Silicate rocks, dissolved by the acidic rain, would have been gradually replaced by carbonate rocks. Prebiotic organic molecules, delivered by the comets, would have provided the "seed" for the evolution of the first life.

Zircon crystals from 4.4 Gyr ago--Earth may have already had continents, oceans, instead of covered by a magma ocean as previously thought.

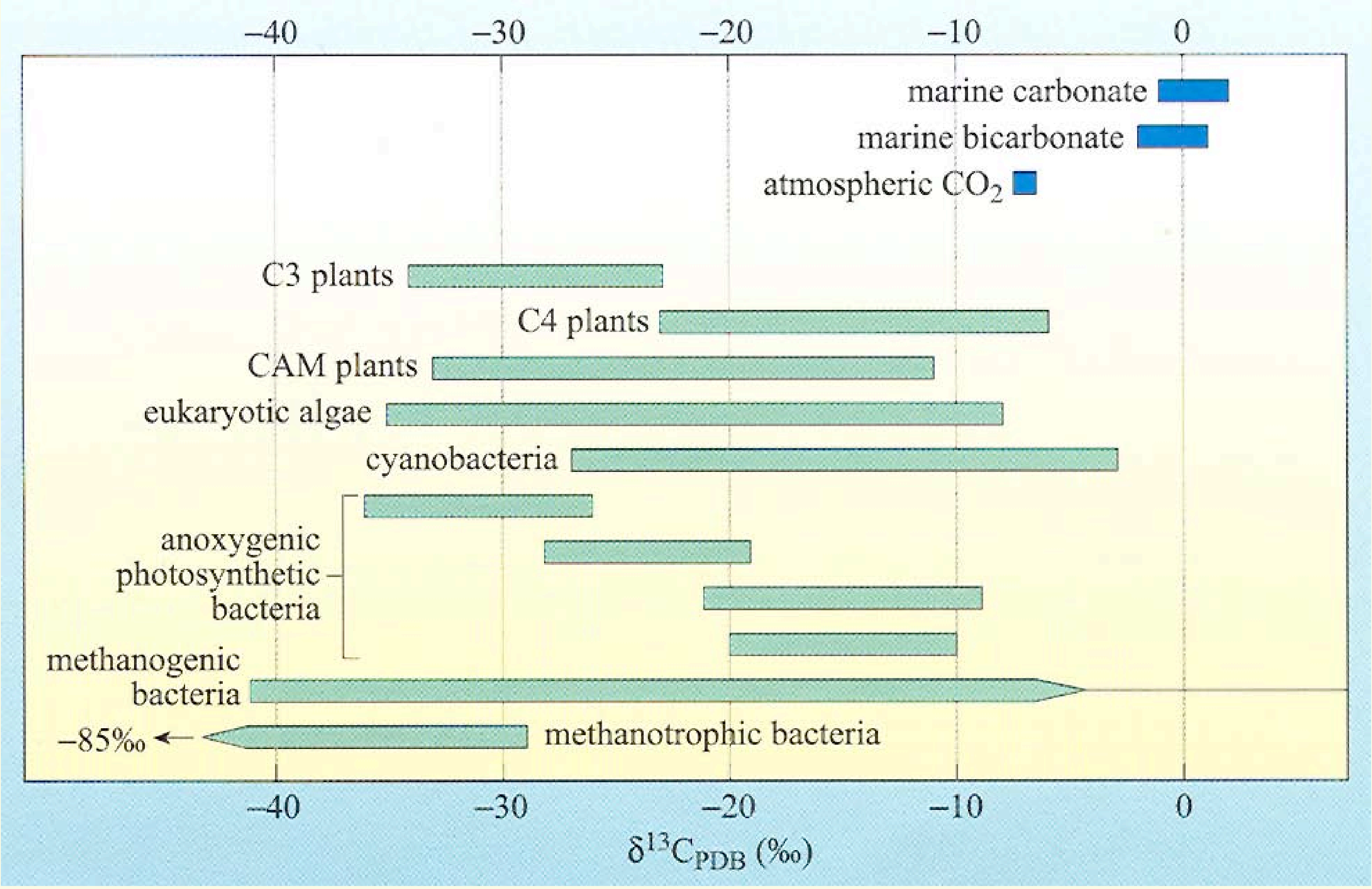


When did the first life arise? Direct evidence: until recently the “microfossil” imprints found in 3.5 Gyr rocks were considered strong evidence not only for early life, but even for photosynthesis (Schopf 1993). Reanalysis (Brasier et al. 1999) strongly questions that interpretation. See picture, where inset is the part shown by Schopf.

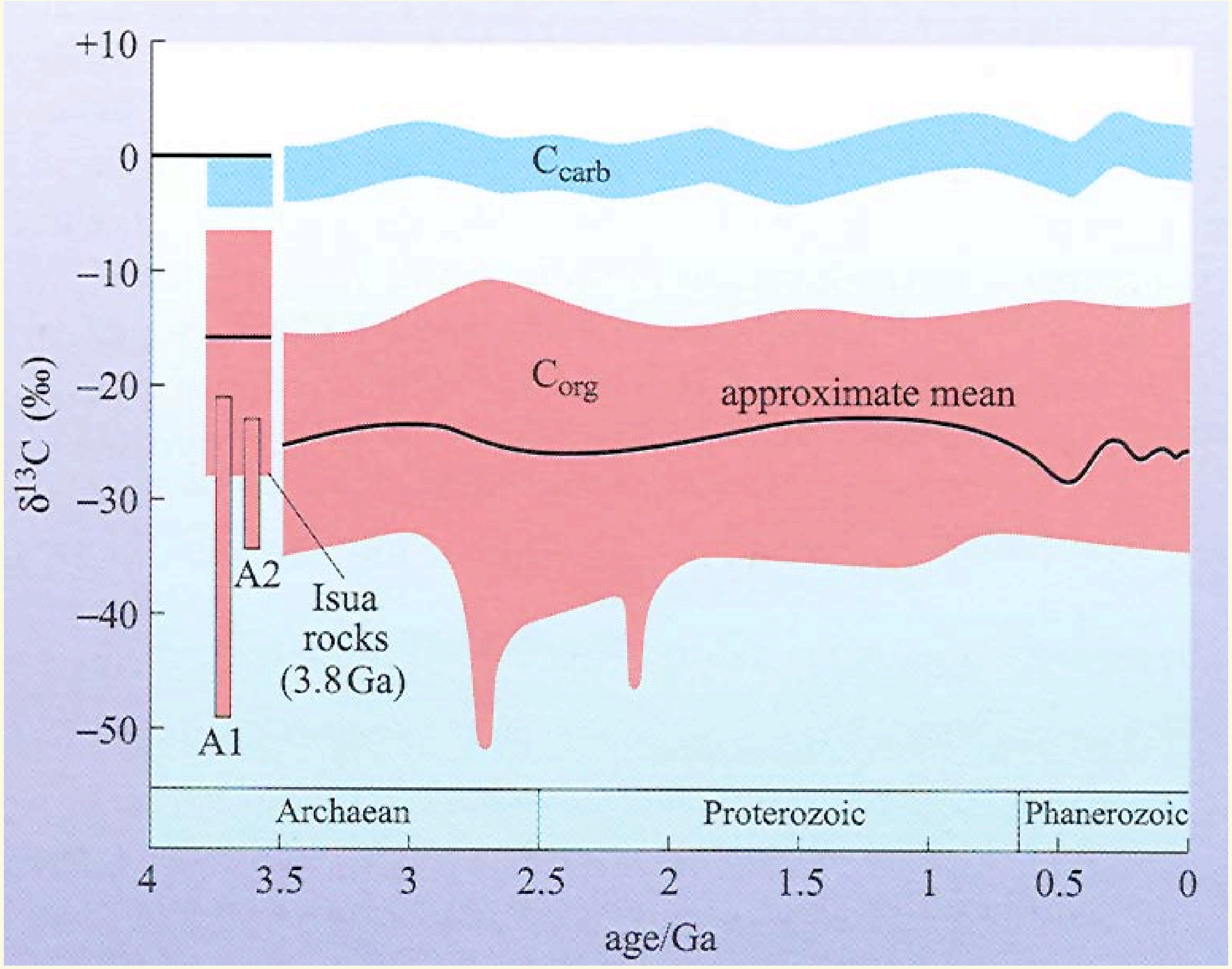


A new view. By compositing in-focus views from a range of depths, a putative microfossil described by William Schopf (b, c) extends and balloons into (a).

Biological organisms selectively use C12 over C13 and so have a 5 to 50% deficit of C13 relative to C12. This deficit is denoted δ 13CO.

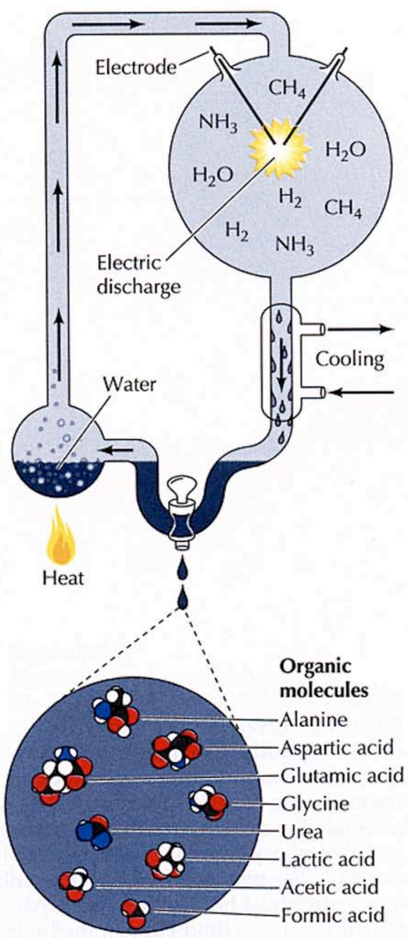


An indirect indicator of biological activity: the "delta C-13" index. Most living organisms use C-12 more than C-13, so they show a deficit of C-13 by 10 to 40%. Illustration shows average value and spread for (blue) inorganic carbonate minerals and (red) keratin pigment from biological fossils as a function of time in the past. Note the recent results for the 3.8 Gyr-old Isua rocks!



The Miller-Urey experiment

Figure 1.2
Spontaneous formation of organic molecules Water vapor was refluxed through an atmosphere consisting of CH_4, NH_3, and H_2, into which electric sparks were discharged. Analysis of the reaction products revealed the formation of a variety of organic molecules, including the amino acids alanine, aspartic acid, glutamic acid, and glycine.

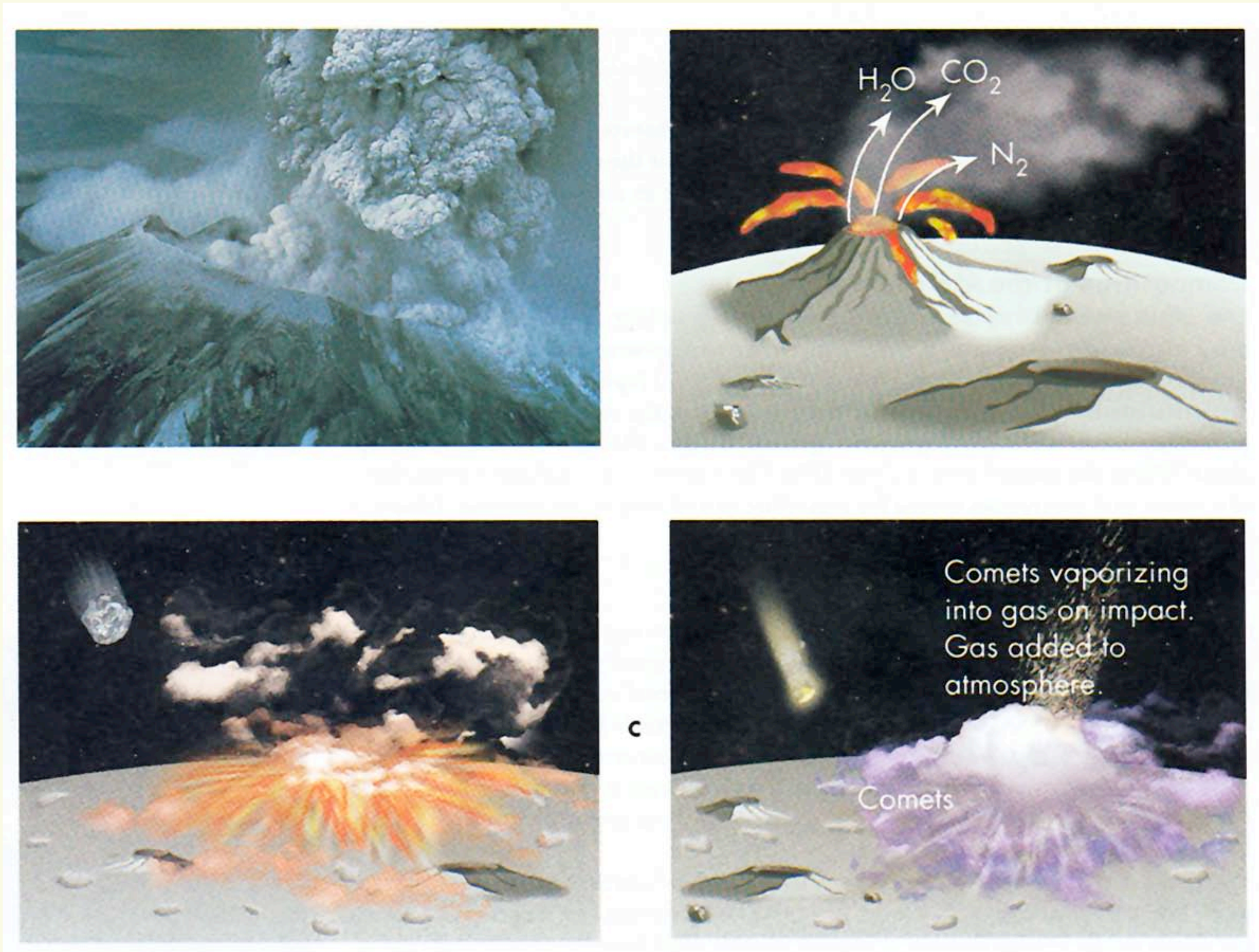


Energy sources: plenty available. That is not a problem for Miller-Urey-type experiments (although different energy sources do give somewhat different results.

Present-day sources of energy averaged over the Earth.

Source	Energy /J m^{-2} yr^{-1}
total radiation from the Sun	1090000.0
ultraviolet light	1680.0
electric discharges (lightning)	1.68
cosmic rays	0.0006
radioactivity (to 1 km depth)	0.33
volcanoes	0.05
shock waves (atmospheric entry)	0.46

The problem is that the experiments only give large yields of interesting organics (amino acids, nucleic acids, sugars) if the gas is H-rich (highly reducing). What was the source of the early Earth's atmosphere? Outgassing from the crust due to volcanoes (top two) or planetesimal impact (lower left), or comet vaporization (lower right)?



Interesting pre-biological molecules are found in meteorites as well as in Miller-Urey-type experiments (and in comets too!)

Abundances of amino acids synthesized in the Miller–Urey experiment and those found in the Murchison meteorite. The number of dots represents relative abundance. Those amino acids used by life (i.e. in proteins) are indicated.

Amino acid	Abundance of amino acids		Found in proteins on Earth
	synthesized in the Miller–Urey experiment	Found in the Murchison meteorite	
glycine	●●●●	●●●●	yes
alanine	●●●●	●●●●	yes
α-amino-*N*-butyric acid	●●●	●●●●	no
α-aminoisobutyric acid	●●●●	●●	no
valine	●●●	●●	yes
norvaline	●●●	●●●	no
isovaline	●●	●●	no
proline	●●●	●	yes
pipecolic acid	●	●	no
aspartic acid	●●●	●●●	yes
glutamic acid	●●●	●●●	yes
β-alanine	●●	●●	no
β-amino-*N*-butyric acid	●●	●●	no
β-aminoisobutyric acid	●	●	no
γ-aminobutyric acid	●	●●	no
sarcosine	●●	●●●	no
N-ethylglycine	●●	●●	no
N-methylalanine	●●	●●	no

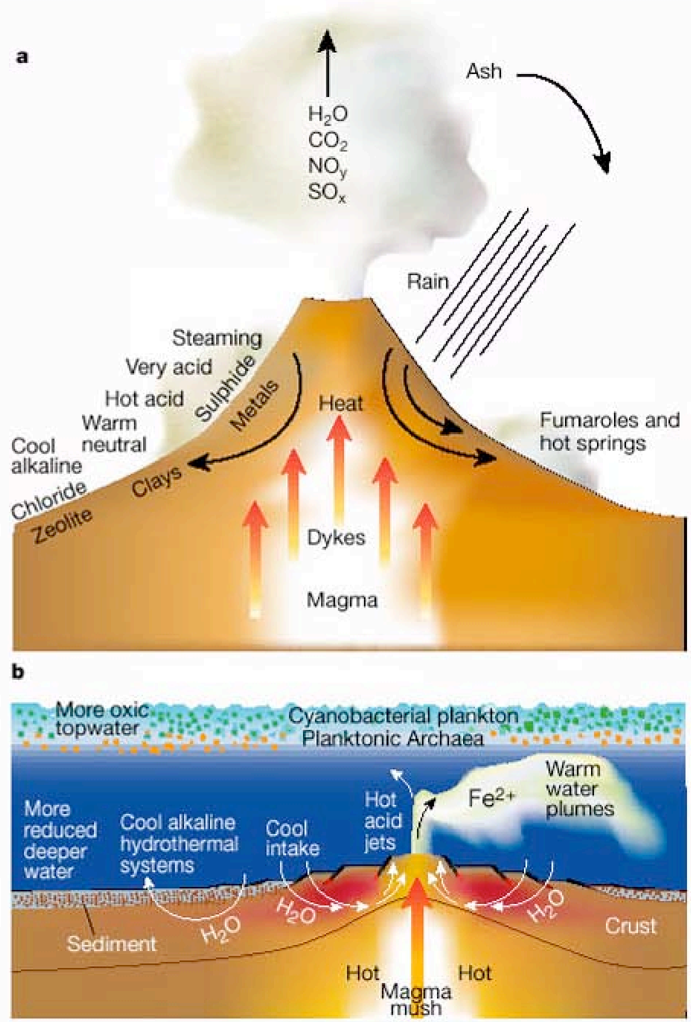
Another potential source of prebiological organics (and methane!): deep-sea **hydrothermal vents**

Hydrothermal systems

Hydrothermal systems occur wherever magma reaches the surface. Water is heated by the magma, becomes less dense, and rises to be replaced by incoming cool fluid. As it moves it interacts chemically with the rock matrix, leaching metals. When it emerges and suddenly cools, these are redeposited. Around volcanoes on land, rainwater-fed systems form hot pools and fumaroles of varying pH. At mid-ocean ridges, in water 2.5–3 km deep, vigorous circulation includes 'black smokers' emitting jets of very acid water at temperatures up to 400 °C, which are crucial in ocean chemistry, especially metal supply and pH control[106,107]. Many minerals offer internal surfaces that are organophilic and catalytic[108].

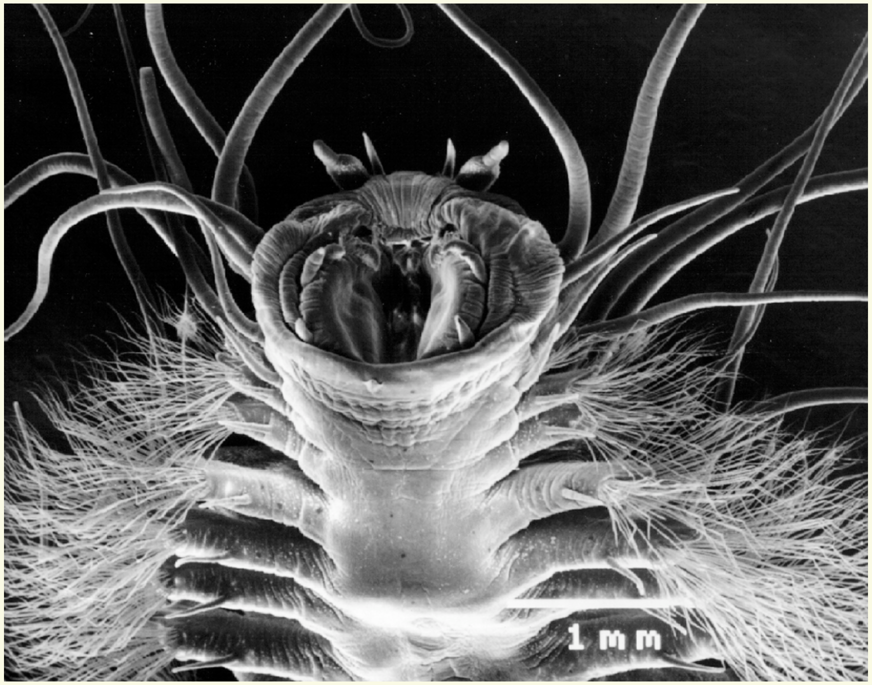
Modern subaerial hydrothermal pools are widely colonized by hyperthermophile bacteria and archaea. Subaerial systems are very diverse, with a wide range of pH possible. Near-surface magma can heat steam to >600 °C, with highly acidic, vigorously boiling hot springs. Fluids heated by basaltic magmas degassing at depth can form near neutral to alkaline springs. If the country rock is ultramafic (magnesium-rich), very alkaline systems can occur. Komatiite shield volcanoes may have produced many alkaline systems. At high levels in the volcano both fluid and vapour phases can occur. Country rock is altered to clay, and sulphide deposition (usually iron sulphide) is widespread. Komatiites host nickel sulphide deposits[28].

Submarine systems[107] include diffuse vents as well as black smokers, which emit iron and manganese oxides. Typically, hydrothermal fluids that have interacted with magma in some way are more reduced than overlying sea water. Sulphur has a key role. Some is volcanic, but in modern systems much of the sulphur is from seawater sulphate (which derives from sulphur gases via photosynthetic oxidation). The sulphate is reduced bacterially (for example, against organic matter, or against more reduced chemical species) as the water enters the hydrothermal circulation, further reduced in the circulation system, and then reoxidized by bacteria as the water leaves vents and mixes with ambient oxidized water. Similarly, nitrate is reduced, such that ammonium minerals are found in deposits. Before photosynthesis, the supply of sulphate and nitrate (that is, oxidized species of sulphur and nitrogen) to oceanic water was probably far less than today, coming from, respectively, oxidation of sulphur gases by OH in the upper air, and lightning fixation of nitrogen, and returned by volcanism.

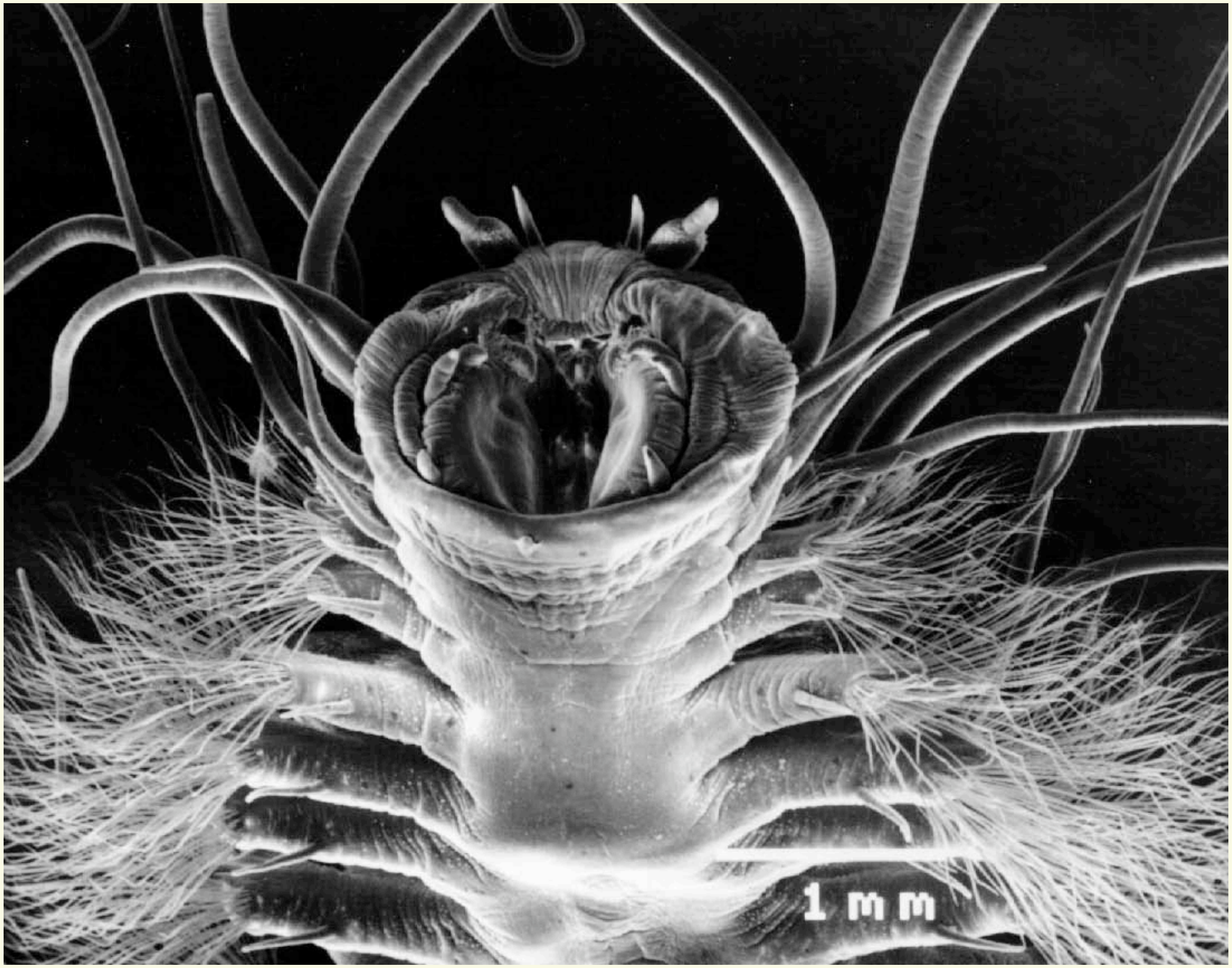


Box 2 Figure Hydrothermal systems. **a**, On land, around a volcano. **b**, On seafloor, at a mid-ocean ridge. (Not to scale.)

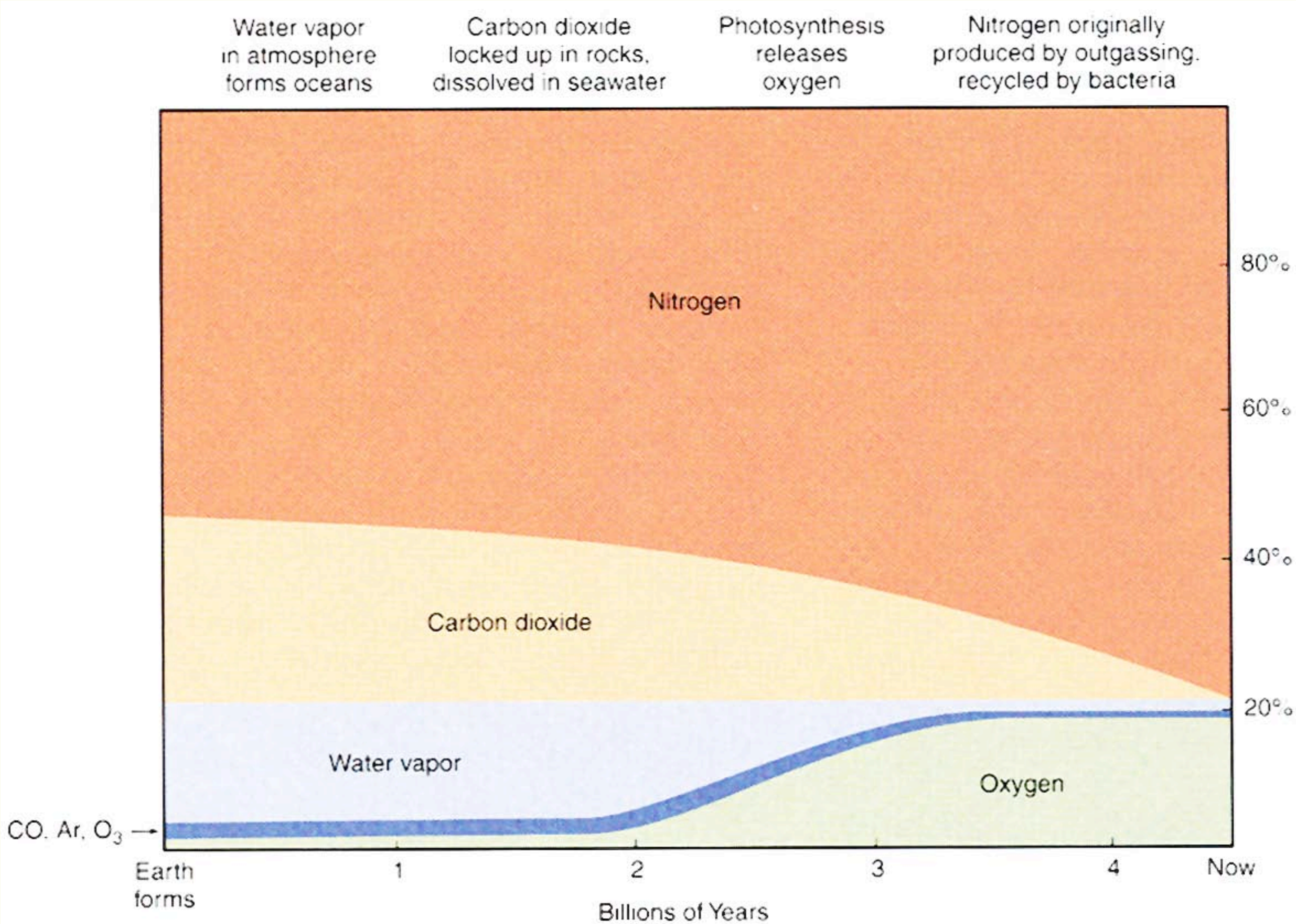
Deep hydrothermal vents are *hot* and have produced a variety of strange life forms (e.g. "tubeworms" lower right), many of which do not rely on oxygen, and some of which produce methane and other reducing (H-rich) gases (see "black smoker" top left)



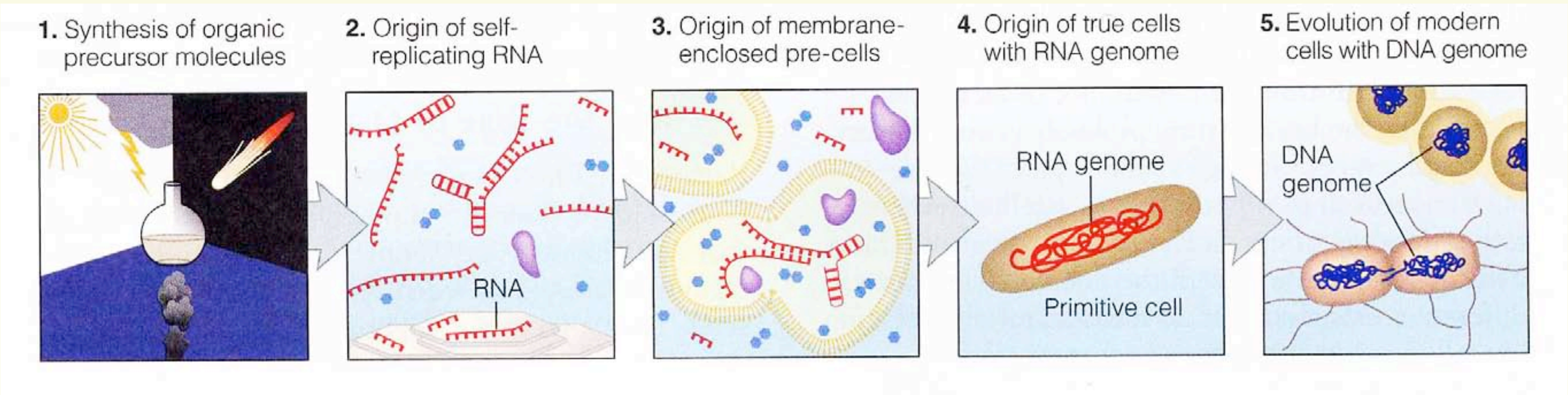
My favorite hydrothermal vent organism



Most likely evolution of the Earth's atmosphere. Note that oxygen could only rise after photosynthesis AND after the crust was saturated with oxygen.



Review--we are trying to understand how life got from the formation of prebiological organic molecules (left) to modern cells with a DNA genome (right). So far we have discussed (1) below, but what is evidence for RNA-first, how did RNA evolve, and what preceded it?



Some major experimental results leading to the "RNA world":

Spiegelmann (1960s): Qβ virus (long RNA) + enzyme ("replicase") + free nucleotides ➙ serial transfer ➙ short RNAs. **This was direct demonstration of evolution at molecular level**.

Eigen (1970s): enzyme + free nucleotides + salts (but no Qβ RNA) ➙ short RNA random replicator. Eigen called thee "quasi-species." But could not grow longer than about 100 nucleotides because of "error catastrophe" associated with mutations.

Cech et al.(1980s): **self-catalytic RNA** = "ribozymes", RNA that can act as its own enzyme. This suggested likelihood of an "RNA world," discussed in your textbook.

1994: Joyce et al. made synthetic RNA that can copy part of itself (given right proteins)

1997: Two studies claim experimental evidence for enzymes that convert between RNA and DNA

2001: Johnston et al. discover an RNA that can catalyze its own polymerization needed for RNA replication without (protein enzymes). Major support for RNA world idea.

Problems: [1.and 2. are discussed in more detail in class notes]

1. How does 1st RNA form by chance encounter between ~ 100 nucleotides?
2. Water opposes polymerization reaction.
3. Error rate (due to mutations, copying errors) too large to allow growth to longer RNAs without an enzyme, but RNA enzymes are long ➙ "error catastrophe"

These are discussed in more detail in the class notes; there is also discussion of pre-RNA candidates but you don't have to know details about that for the exam, only that there are several proposed pre-RNA candidates (next slide).

Since it is difficult to form RNA, there may have been earlier forms that developed into RNA. Some suggestions are shown below (see notes for discussion)

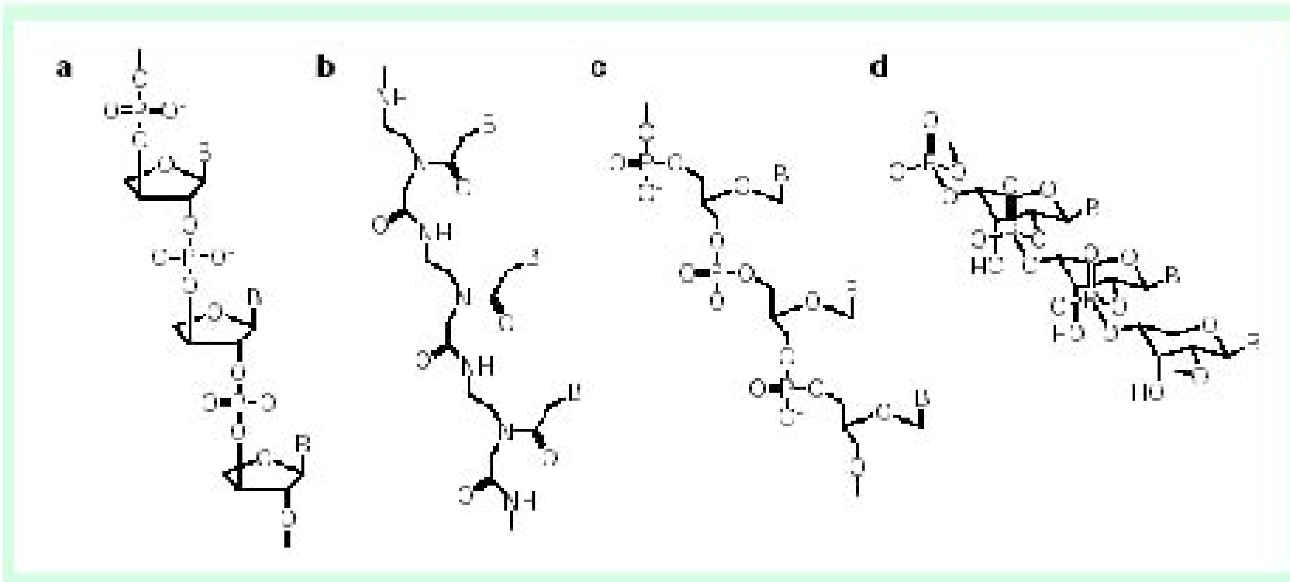


Figure 3 Candidate precursors to RNA during the early history of life on Earth. **a**, Threose nucleic acid; **b**, peptide nucleic acid; **c**, glycerol-derived nucleic-acid analogue; **d**, pyranosyl-RNA. B, nucleotide base.

Proteins first?

Sydney Fox (1960s-1970s): heated (dry) amino acids (maybe deserts, volcano rims), got "proteinoids."
When he dissolved these in warm water and then cooled, got "**proteinoid microspheres**"

Pro: ϑ Sizes and appearance like single-celled organisms (see photo in your textbook)
- ϑ Can catalyze chemical reactions
- ϑ Surfaces "like cell membranes"
- ϑ Can produce electrical responses "like nerve cells"
- ϑ Sensitive to light
- ϑ Can "proliferate" (fission and form buds) and evolve by natural selection (really?)

Con: ϑ Many microscopic inorganic particles have these traits (like dust grains in the room)
ϑ They don't grow, reproduce, and evolve **by copying their own internal organization**, like all other living things we know of.

Also, many biologists biased against "protein-first" simply because they work on nucleic acids, and more recently because of the demonstration of self-catalyzing RNA (ribozymes). And how would you get from proteins to a genetic code?? Today: proteins may or may not have come first, but they were *not* the first *living* molecule.
Fox's view: S. Fox, The Emergence of Life: Darwinian Evolution from the Inside.

There *are* continued suggestions in the direction of how proteins came to be, although not in the sense of the first life. For example Keefe et al. (1995 Nature, part of S. Miller's group) synthesized **pantethine** in an environment like evaporating bodies of water besides beaches and lagoons (again this brings up the importance of tidepools, and hence our large Moon). Pantethine is part of "coenzyme A that helps link amino acids together.

Cairns-Smith: Life begins as minerals, then “organic takeover”?
Illustration shows complex structure seen in some clay minerals.

Plate 5 A mixture of clay crystals showing complex patterns of grooves and shearings. Other clays can form tubes and spheres and membranes. Could such structures have formed the architecture of the first simple, inorganic forms of life?

More suggestions (discussed in notes and in class):

- Clays as first life (or at least as a helper)
- Hydrothermal vents as site of first life
- Panspermia ("An infected world?" in notes)

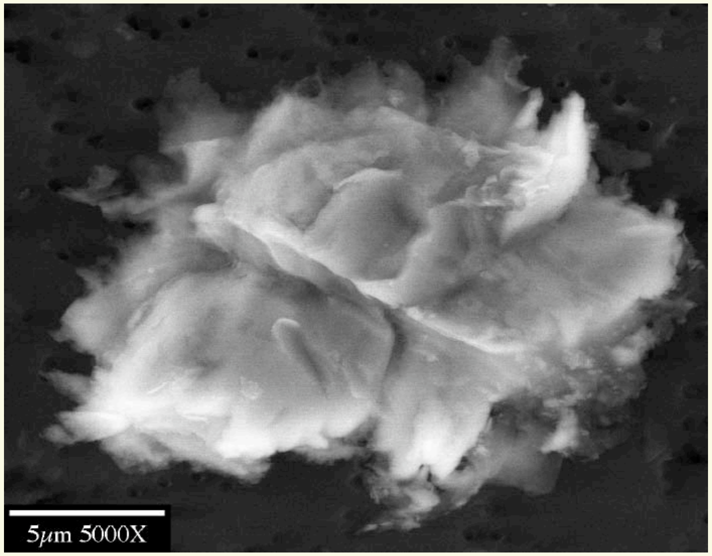
Extremophiles

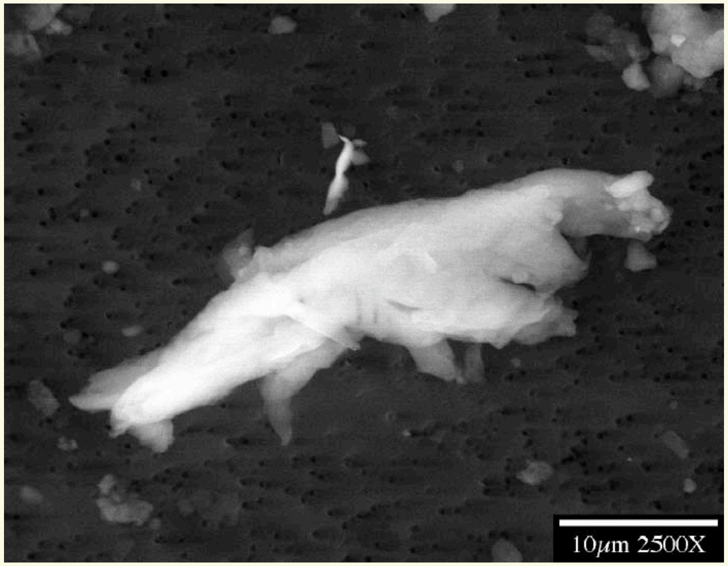
Unexpected organisms and ecologies found in unlkely environments

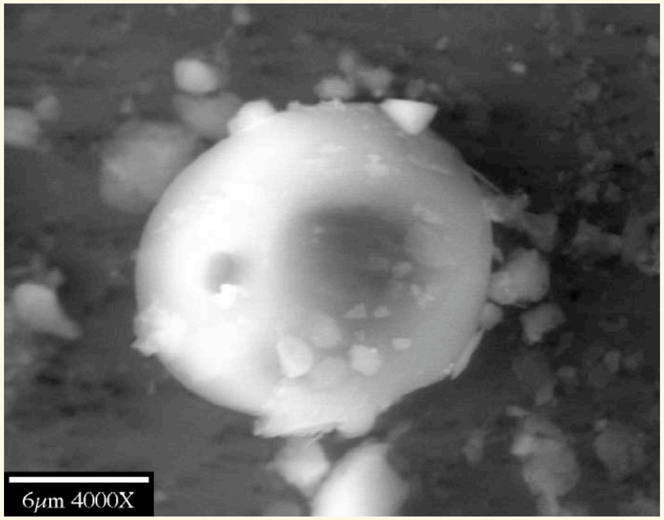
Discovered in 1970s in Yellowstone Park hot springs (above) by Thomas Brock, who decided to study microorganisms in natural environments, rather than in the lab. Found thermophiles (e.g.*thermus aquaticus*, up to 180 F) and acidophiles (e.g. *sulfolobus acidocaldarius*,turns out to be an **archaeon**, like many extremophiles). Now know of extremophiles in even more extreme environments, like *methanopyrus* which lives around black smoker **hydrothermal vents**, produces **methane** gas, and is near the "bottom" of the evolutionary tree.

See e.g. http://www.theguardians.com/Microbiology/ or http://www.astrobiology.com/extreme.html

Ice lovers: examples of microorganisms found up to two miles deep in ice cores beneath Lake Vostok, Antarctica.





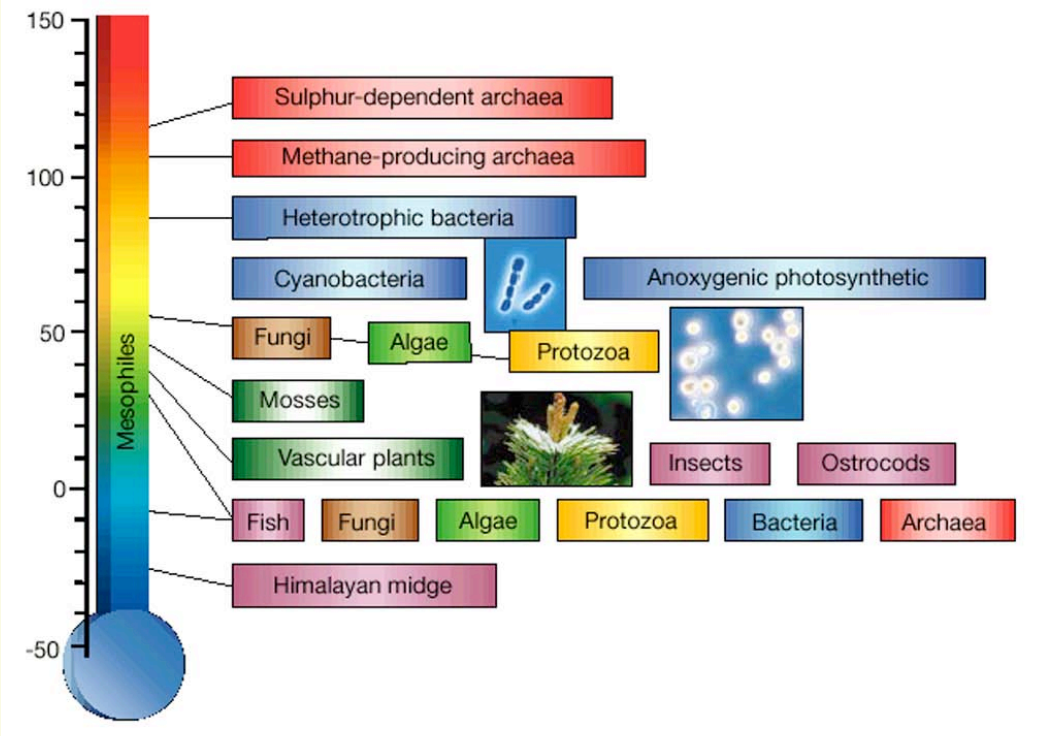


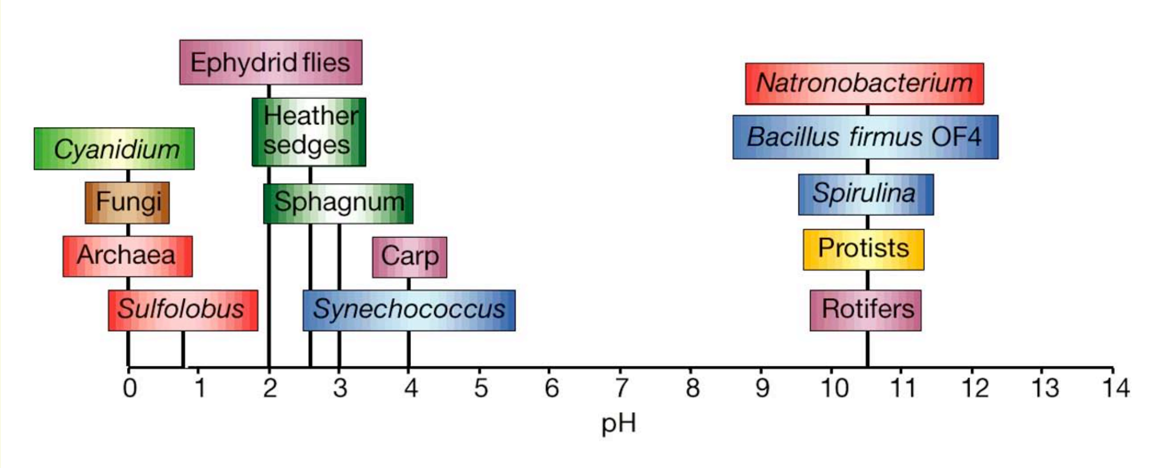
Extremophiles: life can apparently thrive in the most "hostile" of environments. But did it originate there, or does this only show adaptation?

Table 1 Classification and examples of extremophiles

Environmental parameter	Type	Definition	Examples
Temperature	Hyperthermophile Thermophile Mesophile Psychrophile	Growth >80 °C Growth 60–80 °C 15–60 °C <15 °C	*Pyrolobus fumarii*, 113 °C *Synechococcus lividis* *Homo sapiens* *Psychrobacter*, some insects
Radiation			*Deinococcus radiodurans*
Pressure	Barophile Piezophile	Weight-loving Pressure-loving	Unknown For microbe, 130 MPa
Gravity	Hypergravity Hypogravity	>1*g* <1*g*	None known None known
Vacuum		Tolerates vacuum (space devoid of matter)	Tardigrades, insects, microbes, seeds
Desiccation	Xerophiles	Anhydrobiotic	*Artemia salina*; nematodes, microbes, fungi, lichens
Salinity	Halophile	Salt-loving (2–5 M NaCl)	Halobacteriaceae, *Dunaliella salina*
pH	Alkaliphile Acidophile	pH > 9 low pH-loving	*Natronobacterium, Bacillus firmus* OF4, *Spirulina* spp. (all pH 10.5) *Cyanidium caldarium*, *Ferroplasma* sp. (both pH 0)
Oxygen tension	Anaerobe Microaerophile Aerobe	Cannot tolerate O_2 Tolerates some O_2 Requires O_2	*Methanococcus jannaschii* *Clostridium* *H. sapiens*
Chemical extremes	Gases Metals	 Can tolerate high concentrations of metal (metalotolerant)	*C. caldarium* (pure CO_2) *Ferroplasma acidarmanus* (Cu, As, Cd, Zn); *Ralstonia* sp. CH34 (Zn, Co, Cd, Hg, Pb)

Temperature (top), pH (acid/base) (bottom)





Three domains of life, all with similar basic biochemistry and genetic code