Did nature also choose arsenic?

Felisa Wolfe-Simon[1*], Paul C.W. Davies[2], and Ariel D. Anbar[1,3]

[1]Metallomics Laboratory, Department of Chemistry and Biochemistry, Arizona State University, Tempe, AZ 85287, USA; [2]BEYOND: Center for Fundamental Concepts in Science, Arizona State University, Tempe, AZ 85287, USA; [3]School of Earth and Space Exploration, Arizona State University, Tempe, AZ 85287, USA

One sentence summary: Life as we do not know it: arsenic based biology.

---

[*] Present address: Department of Earth and Planetary Sciences, Harvard University, 20 Oxford St, Cambridge, MA 02138, USA

All known life requires phosphorus (P) in the form of inorganic phosphate (PO_4^- or P_i) and phosphate-containing organic molecules[1]. P_i serves as the backbone of the nucleic acids that constitute genetic material and as the major repository of chemical energy for metabolism in polyphosphate bonds. Arsenic (As) lies directly below P on the periodic table and so the two elements share many chemical properties, although their chemistries are sufficiently dissimilar that As cannot directly replace P in modern biochemistry. Arsenic is toxic precisely because As and P are similar enough that organisms attempt this substitution. We hypothesize that ancient biochemical systems, analogous to but distinct from those known today, could have utilized arsenate in the equivalent biological role as phosphate. Organisms utilizing such "weird life" biochemical pathways may have supported a "shadow biosphere" at the time of the origin and early evolution of life on Earth or on other planets. Such organisms may even persist on Earth today, undetected, in unusual niches.

P ranks just behind H, O, C and N in a quantitative list of the most important elements in biology. However, P is usually less available to life than these other elements, particularly in the oceans. H and O are available in any aqueous solution, while C and N can be found in gaseous compounds that are readily distributed through the atmosphere and can be converted to highly soluble chemical forms. In contrast, while P is a relatively common element in the Earth's crust (0.1% by weight)[2], there is no gas phase P compound analogous to CO_2, CH_4, N_2 or NH_3, and common phosphate minerals such as apatite ($Ca_5(PO_4)_3(OH, F, Cl)$) are only sparingly soluble[3]. The distribution of bioavailable P at the Earth's surface is therefore extremely heterogeneous. In this way, P is similar to many of the so-called "micronutrient" elements (e.g., Fe, Cu, Mn, Zn, etc.) that are required in biology in trace amounts. As a result, the distribution of life at the Earth's surface is often determined by the distribution of P, which is why phosphate (PO_4^{3-}) fertilizers are commonly used to compensate for low P concentrations.

Twenty years ago, Westheimer explained why life as we know it is based on P[4]. A critical feature is the acid-base chemistry of P(V) in the form of phosphoric acid (H_3PO_4), which dictates that the dominant soluble forms of P at biological pH (~7-8) are the charged species $H_2PO_4^-$ and HPO_4^{2-} (collectively, these species and H_3PO_4 are referred to as "inorganic phosphorus" or P_i). Charged molecules are contained within lipid membranes more easily than are uncharged molecules, and hence evolution selected for biomolecules that include functional groups derived from P_i and other weak acids such as carboxylic acids and amino acids[5]. However, P_i is unique even among these weak acids because it can maintain a negative charge at physiological pH even when bonded to two other molecular units. Hence, as the building block for ATP and ADP, P_i prevents chemically-stored energy from escaping the cell. Similarly, the repeating phosphodiester linkages in DNA effectively make DNA a polyanion, so that P_i helps cells retain their

genetic material. The negative repeating charge of DNA is also a key factor in its physical stability in the way it prevents folding of the linear strand, thereby protecting template-like behavior[6]. Hence, P_i is well suited as a component of both metabolic and genetic molecules.

However, other elements share key chemical properties with P. Of these, As in the (V) oxidation state warrants closer inspection. Inorganic As(V), like P(V), is negatively charged over a range of physiological pH conditions, as AsO_4^{3-}, $HAsO_4^{2-}$ or $H_2AsO_4^-$ (i.e., arsenate or As_i). In fact, the dissociation constants for H_3AsO_4 are so similar to those of H_3PO_4 that As_i and P_i follow strikingly similar speciation patterns (Figure 1A-B). Also, like P_i, As_i is capable of retaining a negative charge even when it bonds to two other molecules. Because of these similarities, known life cannot easily distinguish As_i from P_i. Thus, arsenate is taken up by cells via phosphate transporters and can substitute for P_i in the early steps of many P_i based metabolic pathways (see Table I). Although As is generally thought to decouple oxidative phosphorylation, oxygen uptake continues in phosphate-deplete, arsenate-rich mitochondrial particles, suggesting that arsenate is substituting for phosphate in the early steps of this process[7]. These similarities account in large measure for the biological toxicity of As_i.

Why, despite these similarities, has the possibility of As-based life been discounted? The primary chemical objection is that As_i-based compounds hydrolyze much more rapidly than their P_i counterparts[4]. In particular, polyarsenates hydrolyze orders of magnitude faster than do polyphosphates. However, this objection is not decisive because both chemically exceptional aquatic environments and natural selection offer solutions, particularly when considered in the context of prebiotic chemistry and the evolution of early life[8].

The relative instability of polyarsenates does not rule out a role for As_i in environments in which it is present at much higher concentrations than P_i. Such settings could sustain elevated steady-state concentrations of polyarsenates and other As-based biomolecules vs. P-based analogs despite the former's faster reaction rates. Intriguingly, such environments include both terrestrial and deep sea hydrothermal systems[9-11] where life is conjectured to have originated[12,13] and where the last common ancestor may have avoided surface-sterilizing meteor impacts of the Late Heavy Bombardment[14-16]. In these systems, As and many other elements react with hydrogen sulfide to precipitate as sulfide minerals, forming the famous "chimneys" of undersea "black smoker" volcanoes. The surfaces of these minerals, rich in bioessential trace metals and S, and bathed in fluids containing dissolved volatiles like CO_2 and N_2[17], are widely recognized as a promising environment for prebiotic catalytic chemistry and early life[18,19]. Importantly, As forms sulfide minerals, unlike P, rendering it far more accessible than P for (bio)chemical reactions occurring on hydrothermal sulfide mineral surfaces. Although present in these minerals in a highly reduced form, measurements in modern, As-rich environments such as Mono Lake indicate that As thermodynamics drive conversion to arsenate and arsenite (AsO_3^{3-}) at pH > 7 even in anoxic waters. In fact, arsenate is favoured over arsenite in waters that are so dysoxic that NO_3^- and Fe^{3+} are absent[20-26], as would have been the case for the deep oceans on the early Earth. If arsenate is present then, like their P_i analogs, As_i biomolecules can form spontaneously. For example, *in vitro* mixtures of adenosine (or a deoxy analog) and As_i readily form As-nucleosides and As-nucleotides[27] (Figure 2). Furthermore, these synthetic 5'AMAs can substitute for 5'AMP in reactions catalyzed by myokinase and adenylate deaminase[27]. Thus, rapid hydrolization per se is unproblematic in environments rich in As, as key molecules may be quickly replenished.

It is interesting to speculate that the reactivity of polyarsenates vs. polyphosphates might have actually been a virtue in prebiotic chemical systems or ancestral organisms. Because of the stability of P_i compounds, all known organisms require sophisticated enzymes to catalyze the removal or addition of P_i (phosphatases and kinases, respectively). As_i compounds might have needed less molecular machinery to fulfil their biochemical roles in ancient systems, facilitating the development of P_i-like metabolism. It is perhaps no coincidence that it is relatively simple, through site-directed mutagenesis, to change an arsenate reductase to a phosphatase[28]. One interpretation of this similarity is that reductases derive from phosphatases. However, an equally plausible interpretation is that the fundamental biochemistry of P_i-based life emerged in an As-rich environment.

Natural selection could have stabilized As_i biomolecules, analogous to ways that P_i biomolecules have evolved stability against hydrolysis. The phosphodiester bonds of RNA, for example, are stabilized *in vivo* by 5' and 3' end modifications as well as by numerous protein interactions[29-31]. Without these mechanisms, the phosphodiester linkages to ribose hydrolyze within seconds under biological conditions[32,33]. Moreover, *in vitro* studies replicating thermophilic environments where early life may have resided show RNA hydrolysis steadily increases as temperatures rise from 65 to 200ºC[34], approaching reaction rate values which are comparable to those for short strands of polyarsenates[35-39]. It is therefore plausible that As-based life emerged in As-rich environments and, once established, evolved strategies that would enable it to persist there.

A second objection to As raised by Westheimer is that it is easily reduced from As(V) to As(III), whereas P is rarely reduced from P(V) at the Earth's surface[4]. Although this difference poses some challenges to As-based metabolism, it also implies

some benefits because the redox properties of As provide possible bioenergetic pathways. Indeed, some extant microorganisms exploit this metabolic opportunity[40-42]. As_i can serve as an electron acceptor by anaerobic heterotrophic bacteria that oxidize reduced carbon and produce arsenite[20,42-44], or in chemolithoautotrophic arsenite oxidizers that fix inorganic carbon and produce arsenate[45]. Therefore, far from being a liability, the redox character of As potentially makes it more biochemically versatile than P.

Once life ventured forth from its As-rich primordial home, the balance of advantage probably tipped in favour of P because P is typically 10,000 times more abundant than As at the Earth's surface. However, As-based life could even survive today in restricted pockets where As is present in abundance, such as deep sea hydrothermal systems or seasonally relevant episodes at Mono Lake[11,20,25,26].

In conclusion, there seems to be no knock-down argument against As-based life, and considerable circumstantial evidence to suggest its plausibility. In recent years, astrobiologists have devoted considerable attention to exploring the possibility of alternative forms of extraterrestrial life (dubbed "weird life")[46]. Curiously, little thought has been devoted to the possibility that the Earth may have once also harboured weird life. It is a tantalizing prospect that an ancestral, alternative form of life might even continue to lurk in modern As-rich Earth habitats forming an extant "shadow biosphere"[47]. A search of such environments would seem to be a promising initial step to test this hypothesis. In view of the extensive consideration given to the possibility of emergent life on other planets, it would be ironic if we overlooked a candidate right here on Earth.

Table I: Evidence of arsenate substitution for phosphate by modern, extant biochemical processes

Reaction or Enzyme	Arseno-analog	Phosphate compound	Reference
Adenylate deaminase	5'AMAs	5'AMP	[27]
Adenylate kinase	5'AM(CH_2)As	AMP	[48]
Aspartate aminotransferase	pyridoxal arsenate	pyridoxal phosphate	[49]
Chloroplastic electron transport	ADP-As	ATP	[50]
Hexokinase	ADP-As	ATP	[51,52]
Human red blood cell sodium pump	As_i	P_i	[53]
Mitochondrial O_2 consumption	As_i	P_i	[7]
Myokinase	AMAs	AMP	[27]
RNA Polymerase	pyroarsenate	pyrophosphate	[54]
R. rubrum light induced phosphorylation	ADP+As_i	ADP+P_i	[55]
Phosphoenolpyruvate mutase	arsenopyruvate	phosphonopyruvate	[56]
Phosphotransacetylase	As_i	P_i	[57]
Protein synthesis	ADP-As hydrolysis	ATP hydrolysis	[52]
Purine nucleoside phosphorylase	As_i	P_i	[58]

FIGURE LEGENDS

Figure 1. pH and redox potential (pe) are the most important factors controlling arsenic speciation. Phosphate (**A**) and arsenate (**B**) speciation are shown as a function of pH for the (V) oxidation states. H_3PO_4 or H_3AsO_4 (dashed and dotted line), $H_2PO_4^-$ or $H_2AsO_4^-$ (dashed line), HPO_4^{2-} or $HAsO_4^{2-}$ (dotted line) and PO_4^{3-} or AsO_4^{3-} (solid line) are all indicated as % of total P_i or As_i. The distribution curves in A and B show that As_i and P_i have similar charge and speciation under biologically relevant pH[59-61]. Redox speciation is shown on a pe-pH diagram for aqueous arsenic species (**C**) in the systems P-O_2-H_2O and As-O_2-H_2O at 25ºC and 1 bar total pressure. Arsenic (solid red lines) and phosphorus (dashed blue line) species have been overlaid with in the bounds of the O_2 – H_2O redox couple (dotted black lines). On such a diagram, phase boundaries represent the conditions at which the activities of the species on each side of the boundary are equal[62,63]. Under dysoxic conditions (pe ≈ 0) and at neutral to mildly alkaline pH, the dominant As species is $HAsO_4^-$ suggesting that it would be present under conditions possibly relevant to the early evolution of life on Earth.

Figure 2. Examples of both described and yet undetected arsenate containing biological molecules (at pH 7). A, As-deoxyribonucleic acid (As-DNA); B, As-ribonucleic acid (As-RNA); C, adenosine diphosphate arsenate (ADP-As) and D, adenosine monoarsenate (AMAs).

REFERENCES

1 Voet, D. & Voet, J. G. *Biochemistry*. (Wiley, New York, 1990).

2 Winter, M. WebElements: the first periodic table on the WWW. *http://www.webelements.com/* (2007).

3 Stumm, W. & Morgan, J. J. *Aquatic chemistry*. (Wiley New York, 1996).

4 Westheimer, F. H. Why nature chose phosphates. *Science* **235**, 1173 (1987).

5 Davis, B. D. On the importance of being ionized. *Arch. Biochem. Biophys.* **78**, 497-509 (1958).

6 Benner, S. A. & Hutter, D. Phosphates, DNA, and the search for nonterrean life: a second generation model for genetic molecules. *Bioorg. Chem.* **30**, 62-80 (2002).

7 Crane, R. K. & Lipmann, F. The effect of arsenate on aerobic phosphorylation. *J. Biol. Chem.* **201**, 235-243 (1953).

8 Levy, M. & Miller, S. L. The stability of the RNA bases:Implications for the origins of life. *Proc. Natl Acad. Sci. USA* **95**, 7933-7938 (1998).

9 Langner, H., Jackson, C., McDermott, T., & Inskeep, W. Rapid oxidation of arsenite in a hot spring ecosystem, Yellowstone National Park. *Environ. Sci. Technol.* **35**, 3302-3309 (2001).

10 Wilkie, J. A. & Hering, J. G. Rapid oxidation of geothermal arsenic (III) in streamwaters of the Eastern Sierra Nevada. *Environ. Sci. & Technol.* **32**, 657-662 (1998).

11 Damm, K. L. V. Seafloor hydrothermal activity: Black smoker chemistry and chimneys. *Annu. Rev. Earth Planet. Sci.* **18**, 173-204 (1990).

12 Corliss, J. B. *et al.* Submarine thermal springs on the Galapagos Rift. *Science* **203**, 1073-1083 (1979).

13 Martin, W. & Russell, M. J. On the origins of cells: a hypothesis for the evolutionary transitions from abiotic geochemistry to chemoautotrophic prokaryotes, and from prokaryotes to nucleated cells. *Phil. Trans. R. Soc. Lond. B* **358**, 59-85 (2003).

14 Sleep, N. H. & Zahnle, K. Refugia from asteroid impacts on early Mars and the early Earth. *J Geophys Res* **103**, 28529-28544 (1998).

15 Maher, K. A. & Stevenson, D. J. Impact frustration of the origin of life. *Nature* **331**, 612-614 (1988).

16 Miller, S. L. & Bada, J. L. Submarine hot springs and the origin of life. *Nature* **334**, 609-611 (1988).

17 Forrest, M. J. *et al.* Gas geochemistry of a shallow submarine hydrothermal vent associated with the El Requesón fault zone, Bahía Concepción, Baja California Sur, México. *Chem. Geol.* **224**, 82-95 (2005).

18 Schoonen, M. A. & Xu, Y. Nitrogen reduction under hydrothermal vent conditions: implications for the prebiotic synthesis of CHON compounds. *Astrobiology* **1**, 133-142 (2001).

19 Brandes, J. A. & Devol, A. H. A global marine-fixed nitrogen isotopic budget: Implications for Holocene nitrogen cycling. *Global Biogeochem. Cycles* **16**, 1120 (2002).

20 Oremland, R. S., Newman, D. K., Kail, B. W., & Stolz, J. F. Bacterial respiration of arsenate and its significance in the environment. in *Environmental Chemistry of Arsenic*, edited by W.T. Frankenberger (Marcel Dekker, New York, 2002), pp. 391.

21 Berner, R. A. A new geochemical classification of sedimentary environments. *J. Sed. Res.* **51**, 359-365 (1981).

22 Smedley, P. L. & Kinniburgh, D. G. A review of the source, behaviour and distribution of arsenic in natural waters. *Appl. Geochem.* **17**, 517-568 (2002).

23 Oscarson, D. W., Huang, P. M., Defosse, C., & Herbillon, A. Oxidative power of Mn(IV) and Fe(III) oxides with respect to As(III) in terrestrial and aquatic environments. *Nature* **291**, 50-51 (1981).

24 Oremland, R. S. *et al.* Anaerobic oxidation of arsenite in Mono Lake water and by a facultative, arsenite-oxidizing chemoautotroph, strain MLHE-1. *Appl. Environ. Microbiol.* **68**, 4795-4802 (2002).

25 Oremland, R., Stolz, J. F., & Hollibaugh, J. T. The microbial arsenic cycle in Mono Lake, California. *FEMS Microbiol Ecol* **48**, 15-27 (2004).

26 Roesler, C. S. *et al.* Distribution, production, and ecophysiology of *Picocystis* strain ML in Mono Lake, California. *Limnol. Oceanogr.* **47**, 440-452 (2002).

27 Lagunas, R., Pestana, D., & Diez-Masa, J. C. Arsenic mononucleotides. Separation by high-performance liquid chromatography and identification with myokinase and adenylate deaminase. *Biochemistry* **23**, 955-960 (1984).

[28] Rosen, B. P. Biochemistry of arsenic detoxification. *FEBS Lett* **529**, 86-92 (2002).

[29] Deana, A. & Belasco, J. G. Lost in translation: the influence of ribosomes on bacterial mRNA decay. *Genes Dev.* **19**, 2526-2533 (2005).

[30] Petrillo, M. *et al.* Stem-loop structures in prokaryotic genomes. *BMC Genomics* **7** (2006).

[31] Slomovic, S., Laufer, D., Geiger, D., & Schuster, G. Polyadenylation and degredation of human mitochondrial RNA: the prokaryotic past leaves its mark. *Mol Cell Biol* **25**, 6427-6435 (2005).

[32] Selinger, D. W. *et al.* Global RNA Half-Life Analysis in Escherichia coli Reveals Positional Patterns of Transcript Degradation. *Genome Res* **13**, 216-223 (2003).

[33] Lindahl, T. Instability and decay of the primary structure of DNA. *Nature* **362**, 709-715 (1993).

[34] Eigner, J., Boedtker, H., & Michaels, G. The thermal degradation of nucleic acids. *Biochim Biophys Acta* **51**, 165-168 (1961).

[35] Kawamura, K., Nagahama, M., & Kuranoue, K. Chemical evolution of RNA under hydrothermal conditions and the role of thermal copolymers of amino acids for the prebiotic degradation and formation of RNA. *Adv. Space Res.* **35**, 1626-1633 (2005).

[36] Kawamura, K. Hydrolytic stability of ribose phosphodiester bonds within several oligonucleotides at high temperatures using a real-time monitoring method for hydrothermal reactions. *Chem. Lett.* **30**, 1120-1121 (2001).

[37] Kawamura, K. Comparison of the rates of prebiotic formation and hydrolysis of RNA under hydrothermal environments and its implications on the chemical evolution of RNA. *Nucleic Acids Symp. Ser.* **1**, 239-240 (2001).

[38] Nagahama, M. & Kawamura, K. A new approach for the cooperative chemical evolution of nucleic acids and proteins under the primitive earth environment. *Nucleic Acids Symp. Ser.* **2**, 279-280 (2002).

[39] Kawamura, K. Measurement of the rate of RNA hydrolysis in aqueous solution at elevated temperatures using a new monitoring method for hydrothermal reactions. *Nucleic Acids Symp. Ser.* **42**, 289-290 (1999).

[40] Bhattacharjee, H. & Rosen, B. Arsenic metabolism in prokaryotic and eukaryotic microbes. in *Molecular Microbiology of Heavy Metals*, edited by Dietrich H. Nies & Simon Silver (Springer, Berlin, 2007), Vol. 6, pp. 371-406.

41 Rosen, B. P. Biochemistry of arsenic detoxification. *FEBS Lett* **529**, 86-92 (2002).

42 Stolz, J. F. & Oremland, R. S. Bacterial respiration of arsenic and selenium. *FEMS Microbiol Rev* **23**, 615-627 (1999).

43 Dowdle, P. R., Laverman, A. M., & Oremland, R. S. Bacterial dissimilatory reduction of arsenic(V) to arsenic(III) in anoxic sediments. *Appl Environ Microbiol* **62**, 1664-1669 (1996).

44 Oremland, R. S. & Stolz, J. F. The ecology of arsenic. *Science* **300**, 939-944 (2003).

45 Ehrlich, H. L. Bacterial oxidation of As(III) compounds. in *Environmental Chemistry of Arsenic*, edited by William T. Frankenberger (Marcel Dekker, New York, 2002), pp. 313-328.

46 Institute, C. o. t. R. o. t. N. A. Assesment of the NASA Astrobiology Institute. 100 (2007).

47 Cleland, C. E. & Copley, S. D. The possibility of alternative microbial life on Earth. *International Journal of Astrobiology* **4**, 165-173 (2006).

48 Adams, S. R., Sparkes, M. J., & Dixon, H. B. The arsonomethyl analogue of adenosine 5'-phosphate. An uncoupler of adenylate kinase. *Biochem. J.* **221**, 829-836 (1984).

49 Ali, B. R. & Dixon, H. B. Pyridoxal arsenate as a prosthetic group for aspartate aminotransferase. *Biochem. J.* **284 (Pt 2)**, 349-352 (1992).

50 Avron, M. & Jagendorf, A. T. Evidence concerning the mechanism of adenosine triphosphate formation by spinach chloroplasts. *J Biol Chem* **234**, 967-972 (1959).

51 Gresser, M. J. ADP-arsenate formation by submitochondrial particles under phosphorylating conditions. *J Biol Chem* **256**, 5981-5983 (1981).

52 Moore, S. A., Moennich, D. M., & Gresser, M. J. Synthesis and hydrolysis of ADP-arsenate by beef heart submitochondrial particles. *J Biol Chem* **258**, 6266-6271 (1983).

53 Kenney, L. J. & Kaplan, J. H. Arsenate substitutes for phosphate in the human red cell sodium pump and anion exchanger. *J Biol Chem* **263**, 7954-7960 (1988).

54 Rozovskaya, T. A. *et al.* The mechanism of pyrophosphorolysis of RNA by RNA polymerase. Endowment of RNA polymerase with artificial exonuclease activity. *Biochem. J.* **224**, 645-650 (1984).

[55] Slooten, L. & Nuyten, A. Arsenylation of nucleoside diphosphates in *Rhodospirillium rubrum* chromatophores. *Biochim Biophys Acta* **725**, 49-59 (1983).

[56] Chawla, S. *et al.* Synthesis of 3-arsonopyruvate and its interaction with phosphoenolpyruvate mutase. *Biochem. J.* **308 (Pt 3)**, 931-935 (1995).

[57] Kyrtopoulos, S. A. & Satchel, D. P. Kinetic studies with phosphotransacetylase. II. The acetylation of arsenate by acetyl coenzyme A. *Biochim Biophys Acta* **268**, 334-343 (1972).

[58] Kline, P. C. & Schramm, V. L. Purine nucleoside phosphorylase. Catalytic mechanism and transition-state analysis of the arsenolysis reaction. *Biochemistry* **32**, 13212-13219 (1993).

[59] Allison, J. D., Brown, D. S., & Novo-Gradac, K. J. MINTEQA2/PRODEFA2, a geochemical assessment model for environmental systems: Version 3.0 users manual. (1991).

[60] Serkiz, S. M. *et al.* Correcting errors in the thermodynamic database for the equilibrium speciation model MINTEQA2. *Water Res* **30**, 1930-1933 (1996).

[61] Westall, J. C., Zachary, J. L., & Morel, F. M. M. *MINEQL: A Computer Program for the Calculation of Chemical Equilibrium Composition of Aqueous Systems*. (Water Quality Laboratory, Ralph M. Parsons Laboratory for Water Resources and Environmental Engineering sic, Dept. of Civil Engineering, Massachusetts Institute of Technology, 1976).

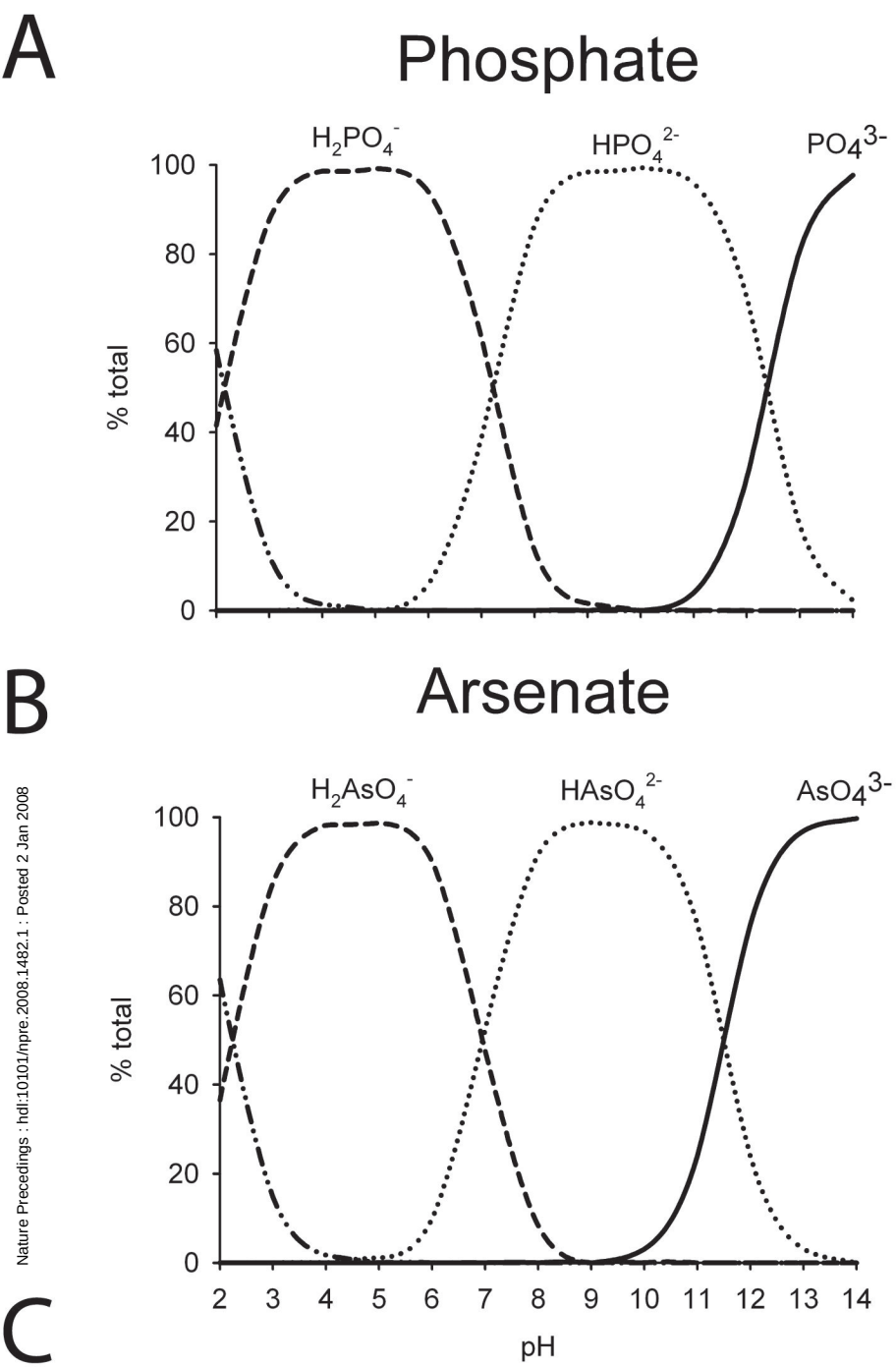
[62] Smedley, P. L. & Kinniburgh, D. G. A review of the source, behaviour and distribution of arsenic in natural waters. *Appl. Geochem.* **17**, 517-568 (2002).

[63] Morel, F. M. M. & Hering, J. G. *Principles and Applications of Aquatic Chemistry*. (John wiley & Sons, Inc., New York, 1993).

Acknowledgments

The authors are especially indebted to Ron Oremland and Barry Rosen for inspirational, thoughtful and supportive discussions. We should also like to thank John Reinfelder for assistance with thermodynamic calculations and discussion, and John Baross, Steve Benner, John Chalmers, Hilairy Hartnett, Andy Knoll, Ann Pearson and Everett Shock for useful discussions and comments. This paper stems from extensive discussions at the workshop "Tree or forest? Searching for an alternative form of life on Earth," held at The Beyond Center, Arizona State University, in December 2006. F.W.-S. was supported during the genesis of these ideas by a National Science Foundation Minority Postdoctoral Fellowship (DBI-0511972).

Correspondence and requests for materials should be addressed to F.W.-S. (wolfe@eps.harvard.edu).



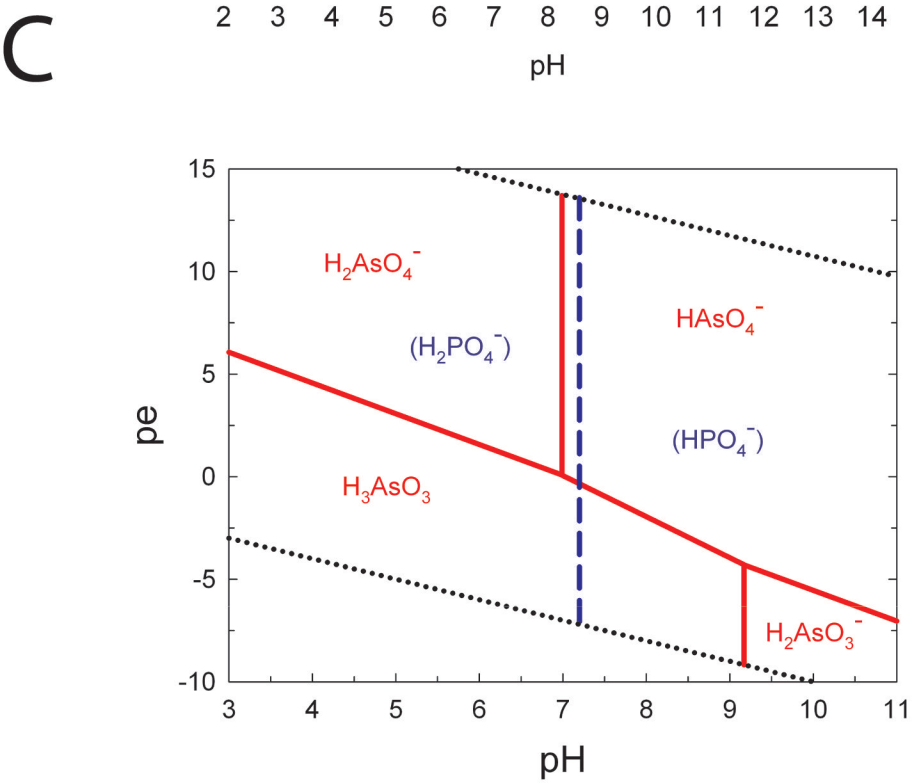


Figure 1.
Wolfe-Simon,
Davies and Anbar

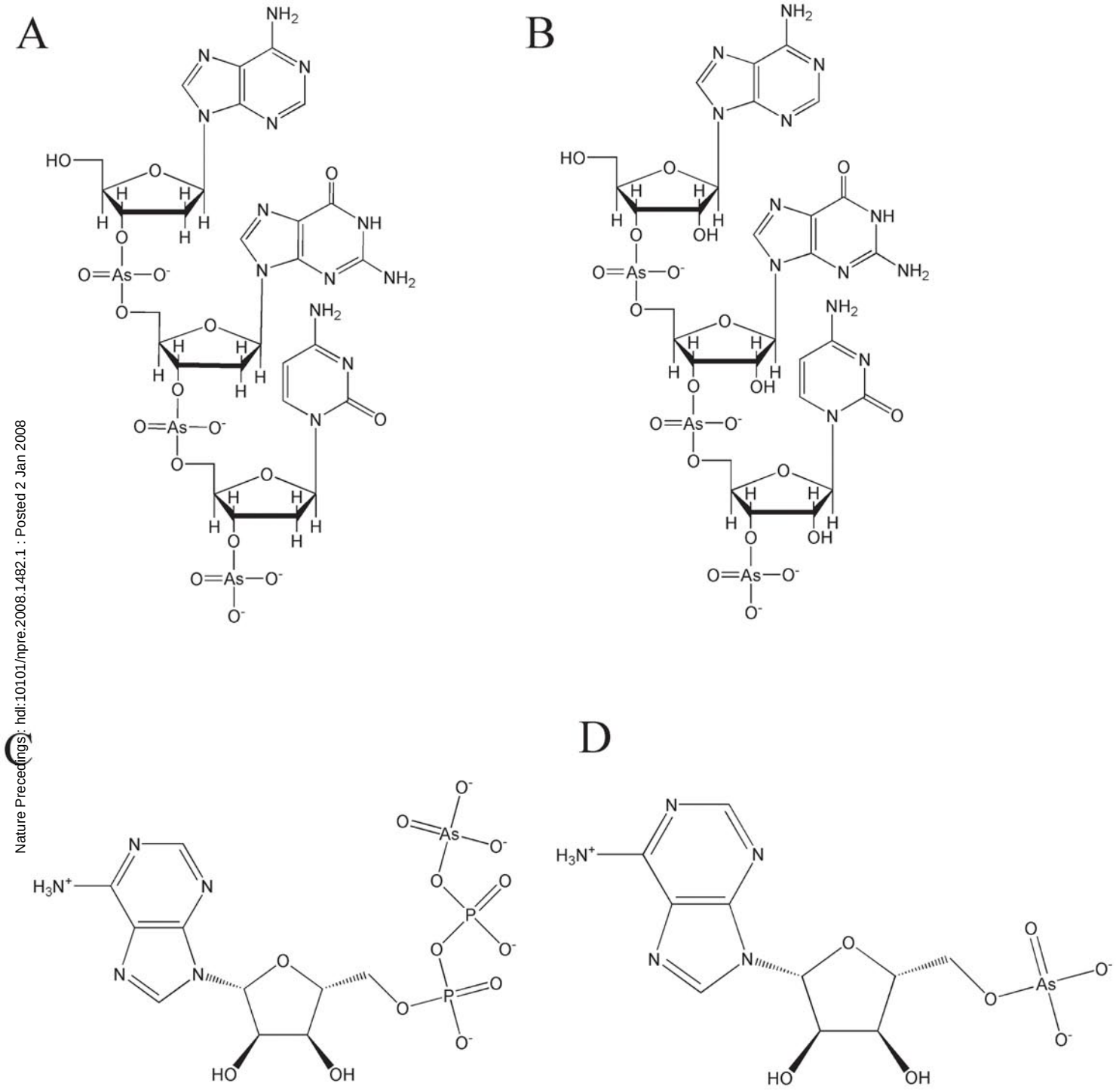


Figure 2.
Wolfe-Simon,
Davies and Anbar