The abiotic synthesis of nucleosides, nucleotides and RNA in hydrothermal systems

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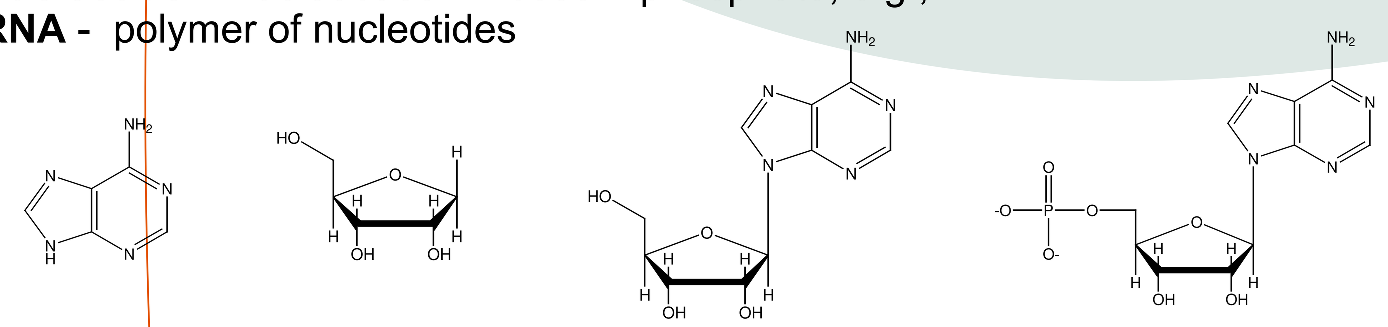
1. Abstract

Recent calculations have shown that the abiotic synthesis of nucleobases, ribose and deoxyribose from formaldehyde (CH_2O) and hydrogen cyanide (HCN) under hydrothermal conditions are thermodynamically favored [1]. Yet, to form the nucleosides, and ultimately by the addition of phosphate, nucleotides, that constitute RNA, a thermodynamic drive (negative Gibbs energy) must also be available for the condensation reactions among these fundamental building blocks. In this study, the energy required for these reactions and the polymerization of RNA at high temperatures and pressures has been quantified Results reveal that none of these reactions are thermodynamically favored under the low concentrations of nucleobases, ribose and deoxyribose that would likely exist on the early Earth. A concentrating step of the building block molecules, likely driven by the steep thermal gradients that exist in some hydrothermal systems, is required to overcome this energetic limitation. Building on work by Baaske et al. [2], who calculate that nucleotides can be concentrated in hydrothermal environments through a combination of convection and thermal diffusion in narrow pore spaces, we show that adenosine, ribose, and phosphate can be concentrated under hydrothermal conditions to sufficiently high concentrations to overcome the condensation energy barrier. Calculations of this kind strongly support the notion that hydrothermal systems played a fundamental role in the origin of life.

[1] LaRowe, D.E. and Regnier, P. (2008) *Orig. Life Evol. Bios.*, DOI 10.1007/s11084-008-9137-2 [2] Baaske, P. et al. (2007) *PNAS* 104, 9346-9351.

2. Glossary

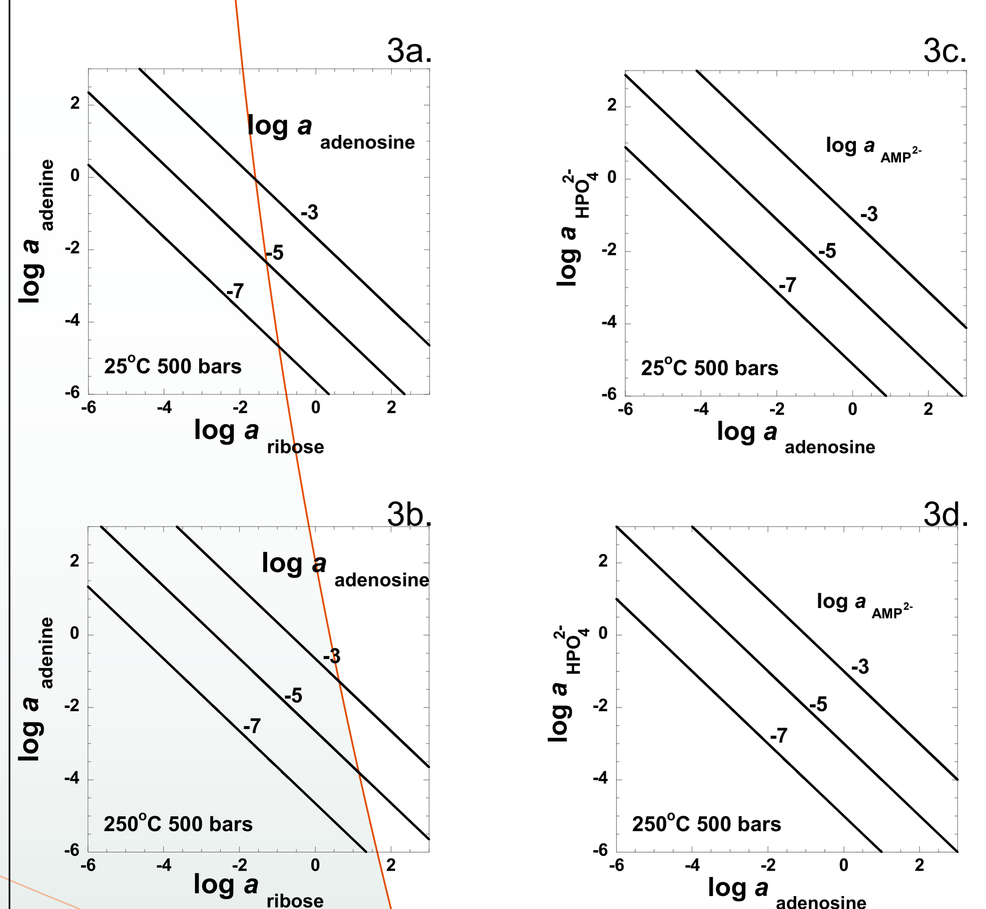
Nucleobase - partially aromatic heterocyclic compound, e.g., adenine
Ribose - 5-carbon carbohydrate
Nucleoside - nucleobase + ribose, e.g., adenosine
Nucleotide - nucleobase + ribose + phosphate, e.g., AMP^{2-}
RNA - polymer of nucleotides

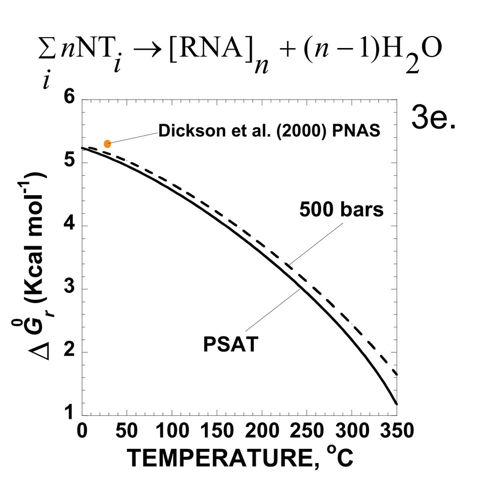


Adenine Ribose Adenosine AMP^{2-}

3. Condensation Reactions

Figures 3a-d show activities of adenosine and AMP^{2-} that are in equilibrium with variable activites of adenine and ribose (Figs. 3a & b) and phosphate and adenosine (Figs. 3c & d) at 25°C and 250°C and 500 bars. Large activities (~1) of each of the reactant compounds are required for appraciable activities (~10^{-3}) of the condensed, product molecules to coexist.





$$\sum_i n\mathrm{NT}_i \rightarrow [\mathrm{RNA}]_n + (n-1)\mathrm{H_2O}$$

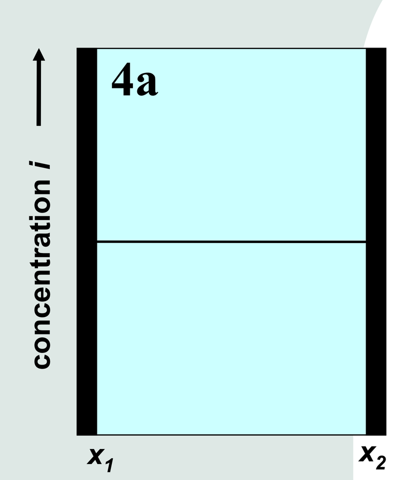
Figure 3e depicts the standard molal Gibbs energy of reaction required to polymerize nucleotides (NT) into RNA using the amino acid polymerization model established in Dick, LaRowe and Helgeson (2006).

These plots were made using thermodynamic data taken from LaRowe and Helgeson (2006) using the the SUPCRT software package (Johnson et al., 1992).

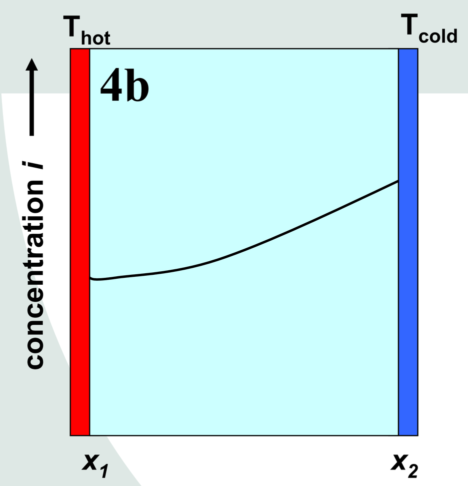
4. Concentrating Biomolecules

Because it is unlikely that ribose, adenine and phosphate existed at concentrations on the priobiotic earth high enough for significant reactions among them to occur, a concentration mechanism for them is required. The mechanism preposed below (after Baaske et al., 2007) combines thermodiffusion (the Soret effect) with convection in a hydrothermal pore system.

The Soret effect

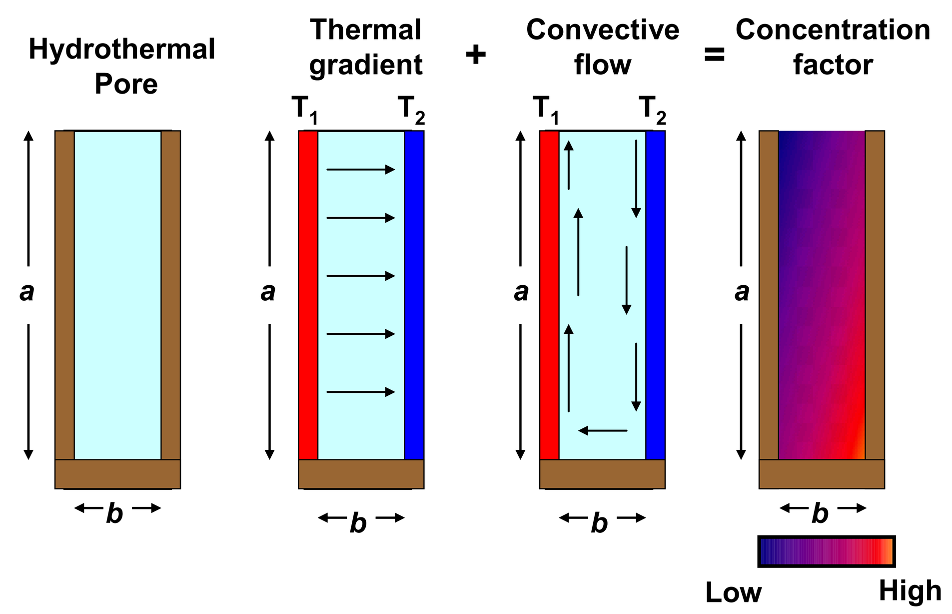


The Soret effect, or thermodifffusion, is a non-equilibrium phenomenon in which a concentration gradient is established in response to a sustained temperature gradient. In Fig. 4a, the concentration of *i* is constant throughout an isothermal solution. However, when a thermal gradient is imposed on the solution, species *i* is concentrated onone side of the system.



Consider a temperature gradient in a hydrothermal pore:

A hydrothermal pore of length *a* and width *b* characterized by a thermal gradient, ∇T, that is open at the top and closed at the bottom can concentrate biomolecules through a combination of the Soret effect and convection.. In this scenario, the bulk fluid, conatining a small concentration of a biomolecule, enters the pore and due to the thermal gradient, thermodiffusion and convection act in concert to concentrate the biomolecule in a subcompartment of the system:



5. Quantifying Concentration

The concentration factors reported here were calculated using the COMSOL Multiphysics finite element code for hydrothermal pores corresponding to the following specifications:

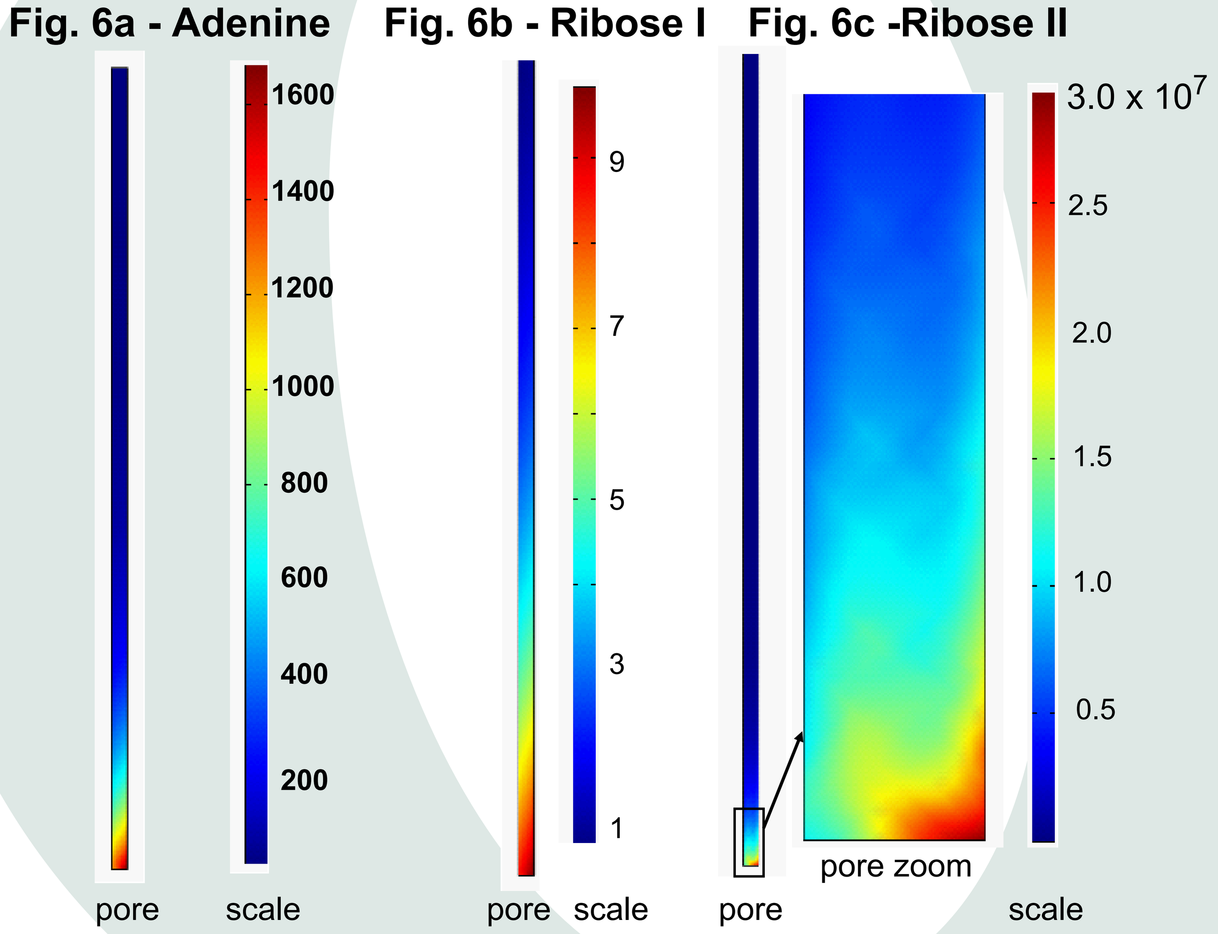
model hydrothermal pore:

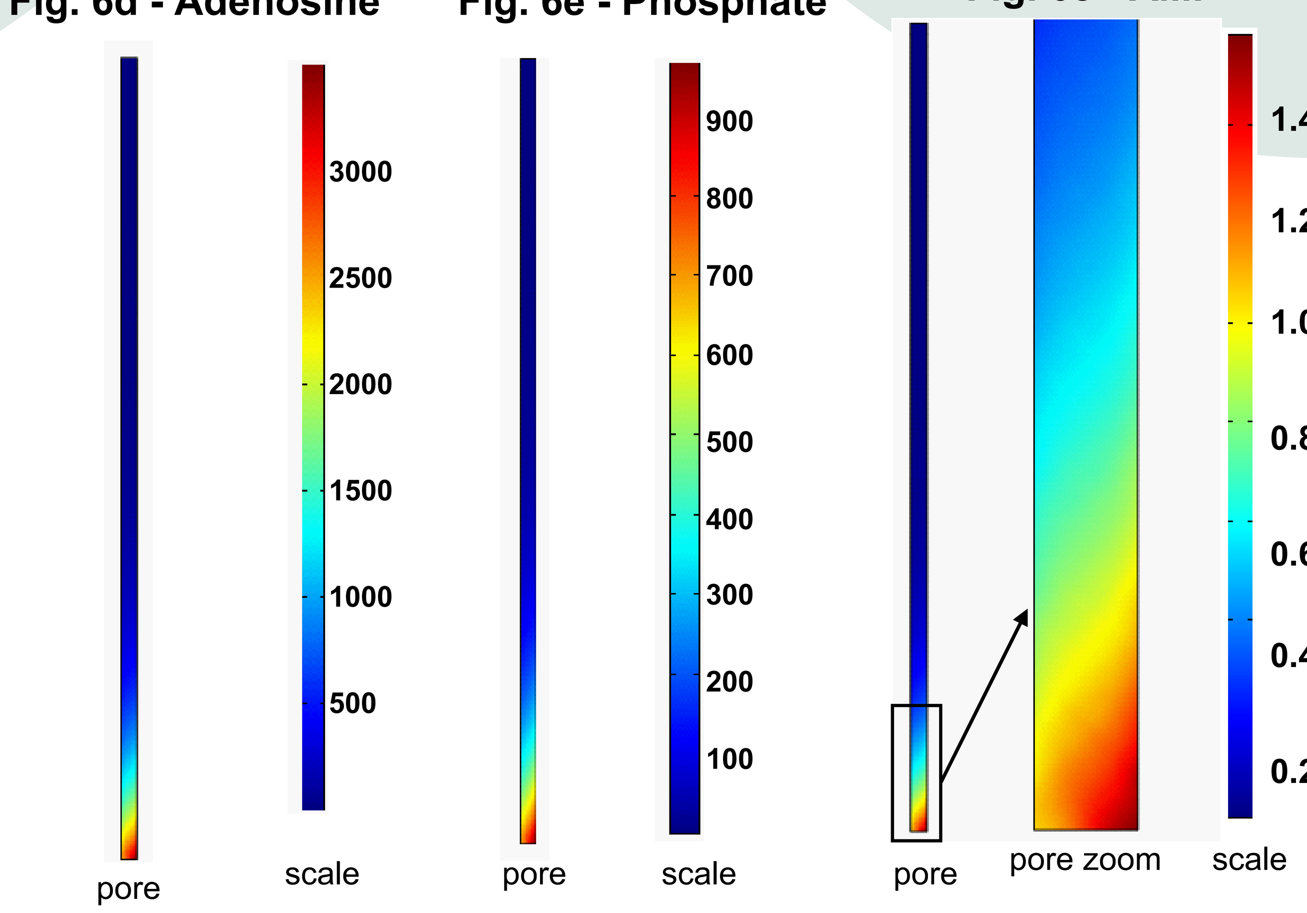
- Width: 140 μm
- Length: 7mm
- Ratio: 50
- Mesh: 644 elements
- Temperature gradient: 30 K (linear)
- Left side temperature: 323 K
- Equation systems considered:
  - Incompressible Navier-Stokes
  - Heat Transfer
  - Mass & Thermal Diffusion

6. Model Results: Concentration factors

The figures shown below display the concentration factors for phosphate, adenine, ribose, adenosine and AMP^{2-} in the model pore described in Section 5a.

It can be seen in Figs. 6a-e that each of the molecules considered in this study can be concentrated many times their bulk solution concentration due to the combined effects of thermodiffusion and convection. However, the scale to which they can be concentrated is very sensitive to the values of the mass diffusion coefficients used. For instance, a nearly seven order of magnitude difference in concentration factor for ribose can be seen in Figs. 6b & c The value of the mass diffusion coefficient is altered by a factor of 10 (10^{-9} vs.10^{-10} $m^2\ s^{-1}$, respectively).



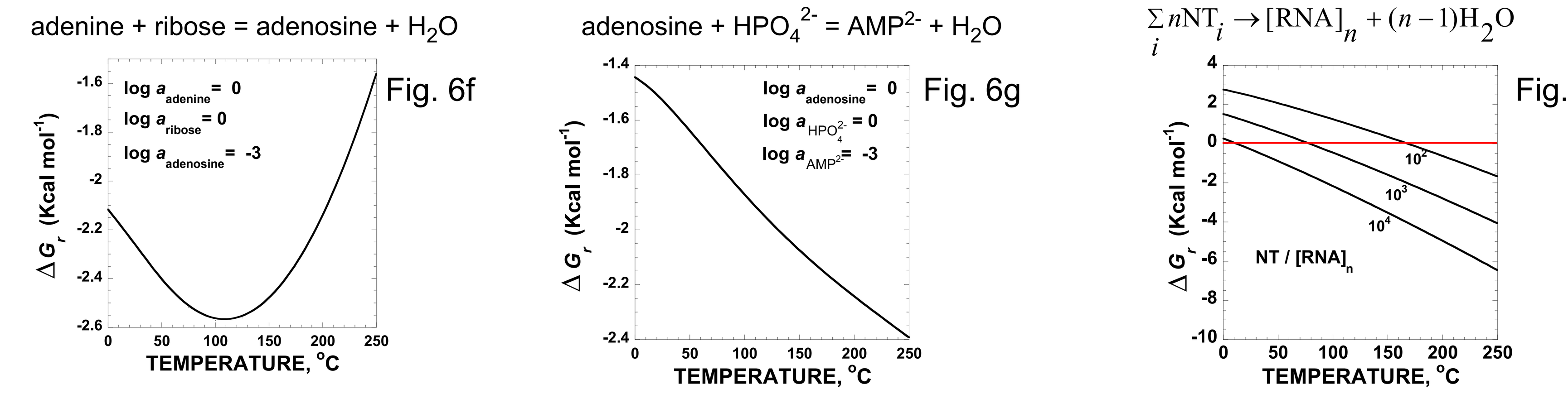


Figures 6f-h depict the energetic consequences of concentrating the molecules considered in this study as a function of temperature. It can be seen in Figs. 6f & g that the Gibbs energy of the reactions written above these panels is negative for activities of the reactants equal to 1. Similarly, the polymerization of RNA, shown in Fig. 6h, becomes favorable as the temperature increases and as the concentration of nucleotides increases by only a couple of orders of magnitude.

adenine + ribose = adenosine + H_2O

adenosine + HPO_4^{2-} = AMP^{2-} + H_2O

$$\sum_i n\mathrm{NT}_i \rightarrow [\mathrm{RNA}]_n + (n-1)\mathrm{H_2O}$$



7. Concluding remarks

Although the condensation reactions among phosphate, nucleobases, and ribose that form nucleosides, nucleotides and RNA are not thermodynamically favored unless high concentrations of these reactants persist, the combined force of thermally-driven convection and the non-equilibrium Soret effect can work in concert to concentrate these biomolcules. The thermal gradient required for these phenomena to act in concert can be achieved in hydrothermal pores. These results support that notion that fundamental biomolecules, if not life itself, originated in hydrothermal systems. **Acknowledgements** This work is supported by the by the Netherlands Organization for Scientific Research (NWO) grant number 815.01.008. We are indebted to Philipp Baske and Dieter Braun for providing the COMSOL Multiphysics files that were modified to produce the concentration factor plots.