4. R. Pacanowski, K. Dixon, A. Rosati, Modular Ocean Model Users' Guide (Geophysical Fluid Dynamics Laboratory, National Oceanic and Atmospheric Administration, Princeton, NJ, 1991).
5. K. Bryan, *J. Comput. Phys.* **4,** 347 (1969); M. D. Cox, *GFDL Ocean Group Tech. Rep. No. 1* (1984).
6. R. Bleck, H. P. Hanson, D. M. Hu, E. B. Kraus, *J. Phys. Oceanogr.* **19,** 1417 (1989); R. Bleck, C. Rooth, D. M. Hu, L. T. Smith, *ibid.* **22,** 1486 (1992); D. M. Hu, *ibid.* **27,** 96 (1997)
7. R. Pacanowski and S. G. H. Philander, *ibid.* **11,** 1443 (1981).
8. E. B. Kraus and J. S. Turner, *Tellus* **19,** 98 (1967).
9. S. Levitus, *Climatological Atlas of the World Ocean* (NOAA Professional Pap. No. 13, Government Printing Office, Washington, DC, 1982).
10. S. Hellerman and M. Rosenstein, *J. Phys. Oceanogr.* **13,** 1093 (1983).
11. Y. Chao and L.-L. Fu, *J. Geophys. Res.* **100,** 24965 (1995).
12. L.-L. Fu and Y. Chao, *Geophys. Res. Lett.* **24,** 1783 (1997).
13. The OAM variation was calculated by assuming the spurious mass change to be distributed uniformly over the oceanic surface layer, following R. J. Greatbatch, *J. Geophys. Res.* **99,** 12767 (1994). The results obtained by assuming the spurious mass change to be distributed uniformly over the oceanic interior are similar.
14. J. C. McWilliams, *Annu. Rev. Fluid Mech.* **28,** 215 (1996); for a general discussion of Earth rotation excitation by geophysical fluids see R. T. H. Barnes, R. Hide, A. A. White, C. A. Wilson, *Proc. R. Soc. London, Ser. A* **387,** 31 (1983). We found that the barotropic component of the MOM model produces OAM variations, which are very similar to the full MOM results, indicating a dominant role for barotropic dynamics in seasonal and shorter OAM variations. The rapid adjustment time of the barotropic modes [R. M. Ponte, *J. Geophys. Res.* **95,** 11369 (1990)] enables the OGCMs to produce realistic OAM variations in spite of the incomplete equilibration of the model fields evident in Fig. 1, A and B.
15. R. S. Gross, in *1996 IERS Annual Report*, M. Feissel, Ed. (Observatoire de Paris, France, 1997), p. 1129.
16. S. D. Desai, thesis, University of Colorado (1996).
17. AAM values were provided by the Sub-Bureau for Atmospheric Angular Momentum of the International Earth Rotation Service [D. A. Salstein, D. M. Kann, A. J. Miller, R. D. Rosen, *Bull. Am. Meteorol. Soc.* **74,** 67 (1993)], based on operational analyses from ECMWF and JMA. Data from the NCEP/NCAR 40-Year Reanalysis Project were used to calculate the NCEP AAM series; see D. A. Salstein and R. D. Rosen, in *7th Conference on Climate Variations* (American Meteorological Society, Boston, MA, 1997), p. 344. AAM values above 10 hPa were computed from gridded wind data taken from the UK Meteorological Office's Assimilated Data for Upper Atmosphere Research Satellite files and provided by the BADC; for details, see R. Swinbank and A. O'Neill, *Mon. Weather Rev.* **122,** 686 (1994).
18. For the atmosphere, variations in axial angular momentum arising from moment-of-inertia changes are about an order of magnitude smaller than those driven by zonal winds (*1*) and involve mass fluctuations due to water vapor. Although these effects are large enough to significantly affect closure of the global budget, their consistent treatment requires full consideration of the hydrological cycle and is beyond the scope of this study.
19. R. Hide, in *Dynamics of Earth's Deep Interior and Earth Rotation*, J.-L. Le Mouel, D. E. Smylie, T. Herring, Eds. (American Geophysical Union, Washington, DC, 1993), pp. 109–112.
20. R. S. Gross, S. L. Marcus, T. M. Eubanks, J. O. Dickey, C. L. Keppenne, *Geophys. Res. Lett.* **23,** 3373 (1996).
21. R. M. Ponte and R. D. Rosen, *J. Phys. Oceanogr.* **24,** 1966 (1994); F. O. Bryan, *Dyn. Atmos. Oceans* **25,** 191 (1997). Both of these studies found sizable annual signals in 1-year samples of OAM taken from OGCM runs forced by monthly mean climatological winds; however, no comparisons using synoptic geodetic or atmospheric data were made.
22. D. Hu and Y. Chao, *Mon. Weather Rev.*, in press.
23. We thank M. Ghil, R. Gross, R. Hide, and two anonymous reviewers for useful comments on the manuscript. We are very grateful to D. Hu, who helped with the MICOM integration, and to D. Dong for the OAM calculation. Computations were performed on the Cray J-90 computer through the JPL Supercomputing project. The work of the authors was carried out by the Jet Propulsion Laboratory, California Institute of Technology, under contract with NASA.

11 May 1998; accepted 28 July 1998

Energetics of Amino Acid Synthesis in Hydrothermal Ecosystems

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Thermodynamic calculations showed that the autotrophic synthesis of all 20 protein-forming amino acids was energetically favored in hot (100°C), moderately reduced, submarine hydrothermal solutions relative to the synthesis in cold (18°C), oxidized, surface seawater. The net synthesis reactions of 11 amino acids were exergonic in the hydrothermal solution, but all were endergonic in surface seawater. The synthesis of the requisite amino acids of nine thermophilic and hyperthermophilic proteins in a 100°C hydrothermal solution yielded between 600 and 8000 kilojoules per mole of protein, which is energy that is available to drive the intracellular synthesis of enzymes and other biopolymers in hyperthermophiles thriving in these ecosystems.

Recently, Woese (*1*) suggested that the ancestor of all life on Earth was not a discrete entity but rather a community of cells with a shared physical history. Over time, as the universal tree of life radiated outward from the root, three primary domains of organisms arose. Although interpretations of the complete genomes of over a dozen microbes have raised questions regarding the classification of various organisms within this phylogenetic tree (*2*), general properties of members belonging to the deepest branches of the Bacteria and Archaea lineages indicate that the earliest life was autotrophic not heterotrophic, relied on chemosynthesis rather than photosynthesis, and required high temperatures for growth (*3*). On the basis of these findings, ancient hydrothermal systems have been proposed as likely sites for the origin of life (*4–6*). This view is consistent with the results of hydrothermal experiments that were aimed at identifying the primordial chemosynthesis reactions for life's origin (*7*).

In the speculative arena of the origin and the early evolution of life, quantification of the energetics of biosynthesis reactions in microorganisms belonging to the deepest branches in the phylogenetic tree is of interest. However, the determination of these energetics in hydrothermal systems on early Earth (*4, 8, 9*) is hindered somewhat by poorly constrained chemical and physical properties of the earliest oceans, including the redox state, pH, temperature, and concentrations of CO_2, NH_4^+, and H_2S. On the other hand, ample data are available from active hydrothermal ecosystems, which are hosts to the deepest branches of thermophilic, chemoautotrophic Archaea and Bacteria. Analyses of seawater and vent fluids together with reliable equations of state for aqueous organic and inorganic compounds permit well-constrained calculations of the energetics of biosynthesis reactions in hydrothermal ecosystems. Once such a framework for evaluating the energetics of biosynthesis is in place, analogous calculations can be carried out to account for likely conditions on early Earth.

Chemical disequilibria in hydrothermal ecosystems provide substantial amounts of energy, which can drive anabolic reactions in thermophilic and hyperthermophilic chemoautotrophs (*8, 10*). Furthermore, the formation of many aqueous organic compounds is favored at high temperatures over low temperatures (*11–13*). We calculated the overall Gibbs free energies (ΔG_r) of net amino acid synthesis reactions (*r*) for hydrothermal systems and contrasted them with the energy requirements of synthesis reactions in surface seawater. We then used these calculations to explore the ramifications for the synthesis of thermophilic proteins, and we considered the implications for early life.

Amino acid synthesis pathways in extant microorganisms, although highly diverse, share two basic features: (i) the nitrogen of α-amino groups in amino acids originates from NH_4^+ and (ii) the sources of skeletal carbons are intermediates of the tricarboxylic acid cycle and the other major metabolic

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pathways that are ultimately linked, in autotrophs, to the assimilation of inorganic carbon in the form of CO_2. These features allow us to write net reactions for the autotrophic synthesis of the 20 naturally occurring amino acids (Table 1). Implicit in all the calculations presented here is the assumption that the appropriate enzymes for each step in the amino acid synthesis pathways are present and active.

The net energetics of amino acid synthesis can be determined by combining standard-state Gibbs free energies of synthesis reactions (ΔG_r°) with products of intracellular activity. Although the intracellular concentrations of the essential reactants and products are poorly known, we can place constraints on the amounts of energy released or required during amino acid synthesis from CO_2, H_2, NH_4^+, and H_2S by autotrophic microbes in natural ecosystems using extracellular activity products. The diffusion of neutral molecules and the transfer of ions by transport proteins establish chemical links across cell membranes between the host aqueous environment and the intracellular fluid. The energetic consequences of differences between the extracellular and intracellular activities of the reactants and products can be assessed when the energetic demands that organisms place on their geochemical environments are established. Even if the activities of free amino acids, for example, are orders of magnitude higher within the cell than in the natural environment, values of ΔG_r for their synthesis can be computed.

We calculated values of ΔG_r for all 20 net amino acid synthesis reactions in submarine hydrothermal solutions with a temperature (100°C) between that of cold (2°C) seawater and very hot (350°C) vent fluid; this temperature was achieved by mixing these end members in the subsurface. The amounts of energy associated with the reactions in Table 1 can be calculated from the expression

$$\Delta G_r = \Delta G_r^\circ + RT \ln Q_r \quad (1)$$

where ΔG_r and ΔG_r° are as defined above; R and T represent the gas constant and temperature in kelvin, respectively; and Q_r denotes the activity product. The values of Q_r that are required to evaluate ΔG_r with Eq. 1 can be determined from

$$Q_r = \prod a_i^{\nu_{i,r}} \quad (2)$$

where a_i stands for the activity of the ith species and $\nu_{i,r}$ represents the stoichiometric reaction coefficient of the ith species in reaction r, which is negative for reactants and positive for products (*14*).

The standard-state term (ΔG_r°) can be computed at any temperature and pressure by combining the apparent standard Gibbs free energies of formation (ΔG_i°) of the ith species in r (*15*) at these conditions in accord with the expression

$$\Delta G_r^\circ = \sum \nu_{i,r} \Delta G_i^\circ \quad (3)$$

The values of ΔG_i° at the temperature and pressure of interest for the aqueous species in the reactions given in Table 1 are readily calculated using thermodynamic properties and parameters for the revised Helgeson-Kirkham-Flowers equation of state (*16*) together with the SUPCRT92 software package (*17*). For all 20 reactions, the values of ΔG_r° at 250 bar and at temperatures from 0° to 150°C are negative and exhibit substantial temperature dependencies, increasing with increasing temperature (Fig. 1).

Evaluating $RT \ln Q_r$ (Eq. 1) for the reactions in Table 1 requires the activities of the reactants and products under the environmental conditions of interest. For example, a 100°C hydrothermal solution can be generated if ~2.55 kg of 2°C seawater are mixed with 1 kg of 350°C vent fluid (*10*). The calculated activities of the aqueous species CO_2, H_2, H_2S, H^+, and NH_4^+ are given in Table 2 for a 100°C mixed hydrothermal solution and surface seawater at 18°C. The activities of the free amino acids in these two fluids were determined with the same mixing model, assuming, however, that the only contribution was from free amino acids in seawater (Table 3) (*18*).

The value of ΔG_r in the 100°C mixed solution for each net amino acid synthesis reaction can now be calculated (Table 3). As an example, we describe the approach used for the synthesis of alanine, represented by the first reaction in Table 1. At 100°C and 250 bar (see Fig. 1 and text above), ΔG_1° is equal to −155.34 kJ mol^{-1}, and Q_1, determined from

Table 1. Net amino acid synthesis reactions (*23*).

$3CO_2(aq) + NH_4^+ + 6H_2(aq) \rightarrow$ alanine(aq) $+ H^+ + 4H_2O$
$6CO_2(aq) + 4NH_4^+ + 11H_2(aq) \rightarrow$ arginine$^+ + 3H^+ + 10H_2O$
$4CO_2(aq) + 2NH_4^+ + 6H_2(aq) \rightarrow$ asparagine(aq) $+ 2H^+ + 5H_2O$
$4CO_2(aq) + NH_4^+ + 6H_2(aq) \rightarrow$ aspartate$^- + 2H^+ + 4H_2O$
$3CO_2(aq) + NH_4^+ + H_2S(aq) + 5H_2(aq) \rightarrow$ cysteine(aq) $+ H^+ + 4H_2O$
$5CO_2(aq) + NH_4^+ + 9H_2(aq) \rightarrow$ glutamate$^- + 2H^+ + 6H_2O$
$5CO_2(aq) + 2NH_4^+ + 9H_2(aq) \rightarrow$ glutamine(aq) $+ 2H^+ + 7H_2O$
$2CO_2(aq) + NH_4^+ + 3H_2(aq) \rightarrow$ glycine(aq) $+ H^+ + 2H_2O$
$6CO_2(aq) + 3NH_4^+ + 10H_2(aq) \rightarrow$ histidine(aq) $+ 3H^+ + 10H_2O$
$6CO_2(aq) + NH_4^+ + 15H_2(aq) \rightarrow$ isoleucine(aq) $+ H^+ + 10H_2O$
$6CO_2(aq) + NH_4^+ + 15H_2(aq) \rightarrow$ leucine(aq) $+ H^+ + 10H_2O$
$6CO_2(aq) + 2NH_4^+ + 14H_2(aq) \rightarrow$ lysine$^+ + H^+ + 10H_2O$
$5CO_2(aq) + NH_4^+ + H_2S(aq) + 11H_2(aq) \rightarrow$ methionine(aq) $+ H^+ + 8H_2O$
$9CO_2(aq) + NH_4^+ + 20H_2(aq) \rightarrow$ phenylalanine(aq) $+ H^+ + 16H_2O$
$5CO_2(aq) + NH_4^+ + 11H_2(aq) \rightarrow$ proline(aq) $+ H^+ + 8H_2O$
$3CO_2(aq) + NH_4^+ + 5H_2(aq) \rightarrow$ serine(aq) $+ H^+ + 3H_2O$
$4CO_2(aq) + NH_4^+ + 8H_2(aq) \rightarrow$ threonine(aq) $+ H^+ + 5H_2O$
$11CO_2(aq) + 2NH_4^+ + 23H_2(aq) \rightarrow$ tryptophan(aq) $+ 2H^+ + 20H_2O$
$9CO_2(aq) + NH_4^+ + 19H_2(aq) \rightarrow$ tyrosine(aq) $+ H^+ + 15H_2O$
$5CO_2(aq) + NH_4^+ + 12H_2(aq) \rightarrow$ valine(aq) $+ H^+ + 8H_2O$

Table 2. Activities of aqueous inorganic species in mixed hydrothermal solution and surface seawater.

Aqueous species	Activity in 100°C hydrothermal solution*	Activity in 18°C surface seawater
CO_2	2.2×10^{-3}	1.0×10^{-4}†
NH_4^+	2.9×10^{-6}	5.0×10^{-8}‡
H_2	3.4×10^{-4}	2.0×10^{-9}‡
H^+	1.9×10^{-6}	5.0×10^{-9}†
H_2S	1.6×10^{-3}	b.d.§

*Calculated by McCollom and Shock (*10*) using chemical analyses for deep seawater and hot vent fluid as given by Von Damm (*24*), except that the value for NH_4^+ was determined in this study with activities in deep seawater and hot vent fluid equal to 5.0×10^{-8} and 1.0×10^{-5}, respectively (*25*). †Calculated in this study at the temperature in this table from the pH and total CO_2 given in (*26*). ‡(*25*). §Below detection, b.d.; a value of 10^{-15} was used to perform the calculations described in the text.

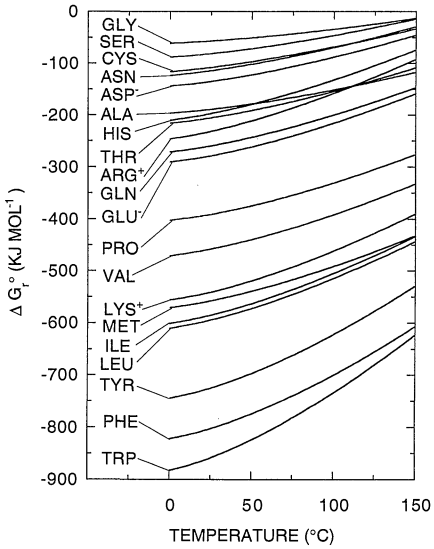

Fig. 1. Values of ΔG_r° of the net amino acid synthesis reactions (see Table 1) in aqueous solution as a function of temperature at 250 bar. This pressure was chosen to approximate conditions in deep-sea hydrothermal systems.

$$Q_1 = \frac{a_{\text{alanine}} a_{H^+}}{(a_{CO_2})^3 a_{NH_4^+} (a_{H_2})^6} \quad (4)$$

using activities a given in Tables 2 and 3, is equal to 1.1×10^{20}. Combining these values, as in Eq. 1, gives $\Delta G_r = -12.12$ kJ mol^{-1}. Therefore, the net synthesis of 1 mol of alanine in a 100°C mixed hydrothermal solution releases 12.12 kJ of energy, which is available to drive otherwise endergonic anabolic reactions such as peptide and protein synthesis.

The value of ΔG_r is negative for 11 of the 20 net amino acid synthesis reactions in a 100°C mixed hydrothermal solution that supports the growth of hyperthermophilic microbes (Table 3). The formation of these 11 amino acids from inorganic precursors lowers the energy state of the system at the conditions that occur in this subsurface ecosystem. The net synthesis reactions for the remaining nine amino acids are endergonic and must be coupled to exergonic reactions in order to proceed. By comparison, the net synthesis reactions of all 20 amino acids are strongly endergonic in cooler (18°C), oxidized, surface seawater. The values of ΔG_r (Table 3) for the reactions in Table 1 under these conditions were generated with the values of ΔG_r° at 18°C and 1 bar together with activity products for seawater computed with data from Tables 2 and 3. Comparisons of ΔG_r for the two distinct environments show differences of 65 to 470 kJ mol^{-1} of amino acid produced.

Table 3. Activities of amino acids in surface seawater (*27*) and in mixed hydrothermal solution, values of ΔG_r for net amino acid synthesis reactions (Table 1) in these two fluids, and mean nominal oxidation states of the carbon atoms (Z_C) in the amino acids.

Amino acid	Concentration* in seawater (nm) (*28*)	Activity in 100°C hydrothermal solution	ΔG_r for 100°C hydrothermal solution (kJ mol^{-1})	ΔG_r for 18°C surface seawater (kJ mol^{-1})	Z_C
Alanine	3.9	2.8×10^{-9}	−12.12	113.66	0.00
Arginine$^+$	0.7	5.0×10^{-10}	197.52	409.46	0.33
Asparagine	1.1	7.9×10^{-10}	83,53	201.56	1.00
Aspartate$^-$	3.3	2.4×10^{-9}	32.78	146.74	1.00
Cysteine	0.5†	3.6×10^{-10}	60.24	224.67	0.67
Glutamate$^-$	3.8	2.7×10^{-9}	−1.43	172.13	0.40
Glutamine	1.0	7.2×10^{-10}	44.03	223.36	0.40
Glycine	5.8‡	4.2×10^{-9}	14.89	80.49	1.00
Histidine	1.2	8.6×10^{-10}	154.48	350.52	1.00
Isoleucine	0.7	5.0×10^{-10}	−96.40	213.93	−1.00
Leucine	0.8	5.7×10^{-10}	−105.53	205.03	−1.00
Lysine$^+$	1.0	7.2×10^{-10}	−28.33	258.56	−0.67
Methionine	2.8§	2.0×10^{-9}	−174.71	113.22	−0.40
Phenylalanine	0.5	3.6×10^{-10}	−114.54	303.64	−0.44
Proline	0.5†	3.6×10^{-10}	−38.75	192.83	−0.40
Serine	4.6	3.3×10^{-9}	69.47	173.73	0.67
Threonine	5.8‡	4.2×10^{-9}	53.51	216.50	0.00
Tryptophan	0.6	4.3×10^{-10}	−38.99	431.17	−0.18
Tyrosine	0.9	6.5×10^{-10}	−59.53	334.20	−0.22
Valine	2.8§	2.0×10^{-9}	−70.12	178.00	−0.80

*Owing to the low amino acid concentrations, activity coefficients equal to unity are used to convert to activity. †Measured values were not reported; those given here correspond to the lowest measured concentrations of the other amino acids. ‡Glycine and threonine commonly coelute; the reported value is the maximum value. §Methionine and valine commonly coelute; the reported value is the maximum value.

Table 4. Values of ΔG_r in a 100°C mixed hydrothermal solution for the net synthesis of the amino acids that constitute nine proteins from thermophilic and hyperthermophilic Archaea and Bacteria. This is not the net energy for protein synthesis. Numbers in brackets are the number of amino acid residues. GAPDH, glyceraldehyde phosphate dehydrogenase; OMP, orotidine 5′-phosphate.

Thermophilic organism	Protein	ΔG_r (kJ per mole of protein)
Pyrococcus furiosus	Rubredoxin [53] (*29*)	−722
Thermococcus litoralis	Ferredoxin [59] (*30*)	−664
Pyrococcus furiosus	Ferredoxin [66] (*30*)	−931
Thermotoga maritima	GAPDH [332] (*31*)	−3171
Thermotoga maritima	OMPα [380] (*32*)	−5022
Thermotoga maritima	Elongation factor–Tu [400] (*33*)	−4237
Thermus thermophilus	Elongation factor–Tu [406] (*33*)	−2438
Thermotoga maritima	Glutamine synthase [439] (*34*)	−5335
Pyrococcus woesei	Glutamine synthase [439] (*34*)	−7892

If the concentrations of free amino acids were, for example, three orders of magnitude higher, values of ΔG_r (Table 3) would increase for each amino acid synthesis reaction by 21.43 and 16.72 kJ mol^{-1} at 100° and 18°C, respectively. As a result, 9 instead of 11 net amino acid synthesis reactions would be exergonic in the 100°C hydrothermal solution. At millimolar concentrations, an increase in ΔG_r of 42.86 and 33.44 kJ mol^{-1} can be calculated at the two temperatures. In this case, six net amino acid synthesis reactions have negative values of ΔG_r at 100°C.

These results support the argument that hydrothermal vent environments are well suited for organic synthesis (*5, 11, 19*). Even biomolecules such as amino acids can be synthesized exergonically in hydrothermal ecosystems. The environmental conditions that permit the exergonic formation of amino acids are entirely geochemically and geologically controlled. The temperature, pressure, and activities of reactants and products that exist in hydrothermal systems determine the energetics discussed above.

Although values of ΔG_r° for the reactions in Table 1 are strongly temperature dependent (see Fig. 1), it is an inescapable consequence of the reducing potential of mixed hydrothermal solutions that synthesis of the more reduced amino acids is favored over the synthesis of the more oxidized ones. In a 100°C hydrothermal solution, negative values of the mean nominal oxidation state of the carbon atoms (Z_C) (*20*) in the amino acids correspond to negative values of ΔG_r (Table 3). In fact, the net synthesis reactions are exergonic for the 10 most reduced (lowest values of Z_C) amino acids (Leu, Ile, Val, Lys$^+$, Phe, Met, Pro, Tyr, Trp, and Ala) and are endergonic for 9 of the 10 most oxidized (highest values of Z_C) amino acids (His, Asn, Asp$^-$, Gly, Cys, Ser, Gln, Arg$^+$, and Thr). In contrast to the 100°C mixed hydrothermal solution, all values of ΔG_r in 18°C surface seawater are positive (endergonic). These observations support the notion that, under oxidizing near-surface conditions, the autotrophic synthesis of amino acids driven by photosynthesis requires a tremendous external energy source (solar radiation), which is not necessary in ecosystems of high or even moderate reducing potential.

The energy yield from the autotrophic synthesis of amino acids in a 100°C mixed hydrothermal fluid (see Table 3) may ultimately be used to overcome the energy requirements of protein synthesis. To calculate this energy yield, we combined sequence data for thermophilic proteins with the thermodynamic evaluation discussed above. For example, from the sequence of rubredoxin from the hyperthermophilic Archaeon *Pyrococcus furiosus* (53 residues) and the values of ΔG_r for all 20 amino acids (Table 3), we computed

that, in a 100°C mixed hydrothermal solution, the net synthesis of the amino acids constituting 1 mol of this protein releases 722 kJ. The values of ΔG_r for the net amino acid synthesis of this and eight other thermophilic proteins (Table 4) are all negative (exergonic). Combined with the conclusion that peptide bond formation is energetically favored with increasing temperature (*12*), an argument can be made that thermophilic chemoautotrophs, such as those occupying the deepest branches in the universal tree of life, expend considerably less energy for the synthesis of macromolecules, such as proteins, than do their mesophilic counterparts. Depending on the amino acid composition of the protein, the synthesis of the monomers from CO_2, H_2, and other inorganic precursors in hot, reduced aqueous solutions may provide substantial surplus energy that can be harnessed to drive intracellular synthesis of enzymes and other polymers.

Our results might start to explain the phenomenal rates of biomass production around hydrothermal vents (*21*) and also how hyperthermophilic Archaea in natural or laboratory high-temperature systems are able to synthesize all required intracellular biomolecules in time periods ranging from minutes to hours as their population doubles. Our calculations can be used as a template in concert with constraints on the flow of energy through early hydrothermal systems to determine the potential of such systems as environments where amino acid and protein synthesis, primitive metabolisms, and even the universal ancestor of all extant life emerged. Calculations representing early Earth hydrothermal systems must reflect the differences in geochemistry and geophysics from active analogs. For example, sensitivity tests show that lower O_2 concentrations in seawater and ultramafic host rocks enhance the potential for hydrothermal organic synthesis (*13*), and the same should be expected for amino acid and protein synthesis.

References and Notes

1. C. Woese, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 6854 (1998).
2. E. Pennisi, *Science* **280**, 672 (1998).
3. N. R. Pace, *ibid.* **276**, 734 (1997).
4. E. L. Shock, in *Evolution of Hydrothermal Ecosystems on Earth (and Mars?)*, G. R. Bock and J. A. Goode, Eds. (Wiley, Chichester, UK, 1996), pp. 40–60.
5. M. J. Russell and A. J. Hall, *J. Geol. Soc. London* **154**, 337 (1997).
6. B. M. Jakosky and E. L. Shock, *J. Geophys. Res.*, in press.
7. C. Huber and G. Wächtershäuser, *Science* **276**, 245 (1997); *ibid.* **281**, 670 (1998).
8. E. L. Shock, T. M. McCollom, M. D. Schulte, in *Thermophiles: The Keys to Molecular Evolution and the Origin of Life?*, J. Wiegel and M. W. W. Adams, Eds. (Taylor and Francis, London, in press).
9. ———, *Origins Life Evol. Biosphere* **25**, 141 (1995).
10. T. M. McCollom and E. L. Shock, *Geochim. Cosmochim. Acta* **61**, 4375 (1997).
11. E. L. Shock, *Origins Life Evol. Biosphere* **20**, 331 (1990).
12. ———, *Geochim. Cosmochim. Acta* **56**, 3481 (1992).
13. ——— and M. D. Schulte, *J. Geophys. Res.*, in press.
14. The standard-state convention for aqueous species is unit activity in a hypothetical 1 *m* solution referenced to infinite dilution at any temperature and pressure, and the standard-state convention for H_2O is unit activity of the pure component at any temperature and pressure.
15. The convention for ΔG_f° is to use the standard Gibbs free energy of formation from the elements at 25°C and 1 bar (ΔG_f°) and to integrate from there in temperature and pressure. Because the properties of the elements will cancel in any reaction, using values of ΔG_f° at high temperatures and pressures eliminates the need to calculate the high-temperature and high-pressure values of the standard Gibbs free energies of the elements.
16. H. C. Helgeson, D. H. Kirkham, G. C. Flowers, *Am. J. Sci.* **281**, 1249 (1981); E. L. Shock and H. C. Helgeson, *Geochim. Cosmochim. Acta* **52**, 2009 (1988); ———, D. A. Sverjensky, *ibid.* **53**, 2157 (1989); E. L. Shock, E. H. Oelkers, J. W. Johnson, D. A. Sverjensky, H. C. Helgeson, *J. Chem. Soc. Faraday Trans.* **88**, 803 (1992); J. P. Amend and H. C. Helgeson, *Geochim. Cosmochim. Acta* **61**, 11 (1997); *J. Chem. Soc. Faraday Trans.* **93**, 1927 (1997); E. L. Shock, D. C. Sassani, M. Willis, D. A. Sverjensky, *Geochim. Cosmochim. Acta* **61**, 907 (1997).
17. J. W. Johnson, E. H. Oelkers, H. C. Helgeson, *Comput. Geosci.* **18**, 899 (1992).
18. Because the activities of amino acids in vent fluids are not currently known, we set the activity values to zero. This assumption will introduce only minimal error in mixed hydrothermal solutions unless the concentrations of free amino acids in 350°C vent fluids are substantially higher than the concentrations in seawater.
19. D. E. Ingmanson and M. J. Dowler, *Origins Life Evol. Biosphere* **8**, 221 (1977); J. A. Baross and S. E. Hoffman, *ibid.* **15**, 327 (1985); G. Wächtershäuser, *Syst. Appl. Microbiol.* **10**, 207 (1988).
20. To determine Z_C (*22*) in an amino acid, the sum of the nominal oxidation states for each carbon atom is divided by the total number of carbon atoms in the compound. A carbon atom is assigned a nominal charge of −1 for each bond to a hydrogen atom; 0 for each bond to another carbon atom; and +1 for each bond to an oxygen, nitrogen, or sulfur atom.
21. R. A. Lutz *et al.*, *Nature* **371**, 663 (1994).
22. H. C. Helgeson, *Can. Mineral.* **29**, 707 (1991).
23. At the temperatures and pHs of the two environments considered here, 16 of the 20 amino acids have a net charge of 0, 2 are present as anions (aspartate$^-$ and glutamate$^-$), and 2 are cations (arginine$^+$ and lysine$^+$).
24. K. L. Von Damm, *Annu. Rev. Earth Planet. Sci.* **18**, 173 (1990).
25. M. Lilley, personal communication.
26. T. Takahashi, W. S. Broecker, A. E. Bainbridge, R. F. Weiss, *Tech. Rep. CU-1-80* (Lamont-Doherty Geological Observatory, Palisades, NY, 1980).
27. Although likely to be lower, the activities of amino acids in deep seawater are conservatively estimated to be equal to the activities of amino acids in surface seawater.
28. R. G. Keil, in preparation.
29. P. R. Blake *et al.*, *Biochemistry* **30**, 10885 (1991).
30. S. C. Busse *et al.*, *ibid.* **31**, 11952 (1992).
31. V. Schultes, R. Deutzmann, R. Jaenicke, *Eur. J. Biochem.* **192**, 25 (1990).
32. A. M. Engel, Z. Cejka, A. Lupas, F. Lottspeich, W. Baumeister, *EMBO J.* **11**, 4369 (1992).
33. M. Bachleitner, W. Ludwig, K. O. Stetter, K. H. Schleifer, *FEMS Microbiol. Lett.* **57**, 115 (1989).
34. A. M. Sanangelantoni, G. Forlani, F. Ambroselli, P. Cammarano, O. Tiboni, *J. Gen. Microbiol.* **138**, 383 (1992).

35. We thank two anonymous reviewers for their insightful critique of an earlier version of this manuscript and H. Helgeson, G. Olsen, R. Keil, M. Lilley, T. McCollom, M. Schulte, J. Deming, J. Baross, M. Summit, A. Playsunov, M. Zolotov, P. Prapaipong, and G. Chan for many helpful discussions. Financial support was provided by NSF grant OCE-9714288 and by NASA grant NAG5-4002. This is GEOPIG contribution 162.

22 May 1998; accepted 3 August 1998

Crystal Structure of the Catalytic Domain of Human Plasmin Complexed with Streptokinase

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Streptokinase is a plasminogen activator widely used in treating blood-clotting disorders. Complexes of streptokinase with human plasminogen can hydrolytically activate other plasminogen molecules to plasmin, which then dissolves blood clots. A similar binding activation mechanism also occurs in some key steps of blood coagulation. The crystal structure of streptokinase complexed with the catalytic unit of human plasmin was solved at 2.9 angstroms. The amino-terminal domain of streptokinase in the complex is hypothesized to enhance the substrate recognition. The carboxyl-terminal domain of streptokinase, which binds near the activation loop of plasminogen, is likely responsible for the contact activation of plasminogen in the complex.

The activation of human plasminogen (Plg) to plasmin (Pm) in blood plasma is the central event that results in the dissolution of the fibrin clot by proteolysis. Human Plg, a single-chain protein of 791 residues, contains five kringle domains and a serine protease domain (*1*). Plg activation by physiological activators, for example, tissue-type plasminogen activator (TPA), is accomplished by the hydrolysis of the Arg^{561}-Val^{562} bond in Plg (*2*). Plg activators, TPA and streptokinase (SK), are widely used as thrombolytic agents