neurons), (ii) hepatocyte growth factor/nerve growth factor/transforming growth factor–β(TGFβ)/glial cell line–derived neurotrophic factor: 36 ± 13 min^{-1} (n = 12), (iii) TGF α/glial growth factor: 8 ± 5 min^{-1} (n = 8), and (iv) neurotrophin-3/plate-derived growth factor–AA: 16 ± 6 min^{-1} (n = 12). Each of these factors promoted cell survival, proliferation, or differentiation in other assays performed in our lab. To test the effect of extracellular matrix components, we cultured RGCs on Matrigel (Collaborative Biomedical Products) (mean EPSC frequency of 21 ± 11 min^{-1}; n = 7) or in serum-free medium containing chondroitin sulfate proteoglycan (5 μg/ml; Collaborative Biomedical Products) (mean frequency 2 ± 2 min^{-1}; n = 6). Both components were active, as they fasciculated neurites of RGCs.

15. Astrocytes (7) and oligodendrocytes [B. A. Barres *et al.*, *Cell* **70**, 31 (1992)] were purified by immunopanning from postnatal rat optic nerves as described, because these glial cell types cannot be purified from other brain areas. Microglial cells were purified from the superior colliculus of P8 rats by immunopanning with a goat anti-rat immunoglobulin G antibody (Jackson ImmunoResearch Laboratories) and a rat anti-mouse Thy 1.2 antibody (Boehringer). RGCs were cultured with each glial cell type at a ratio of three to five glial cells per neuron in the defined serum-free medium (*8*). In order to avoid contact between neurons and glial cells, we cultured RGCs on cover slips above glial feeding layers.
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17. Miniature EPSCs were isolated by adding TTX (10 μM, Sigma), bicuculline methylchloride (50 μM, RBI), and D-2-amino-5-phosphonopentanoic acid (50 μM, RBI) to the extracellular recording solution.
18. The average whole-cell resting membrane potential in RGCs cultured for 10 to 15 days without (−48 ± 1 mV, n = 22) or with glial cells (−49 ± 1 mV, n = 19) was not different. This, however, does not rule out that glial cells increased quantal release by depolarizing nerve terminals.
19. For electron microscope analysis, cultures were fixed with glutaraldehyde (2.5% in phosphate-buffered saline for 30 min), treated with osmium tetroxide (1% for 30 min), dehydrated, and embedded in Epon 812 (Polysciences). For each culture, ultrathin sections were cut from at least two blocks with a glass knife, stained with lead citrate and uranyl acetate, and examined with a Phillips EM 410. Ultrastructural criteria to identify synapses were a pre- and a postsynaptic density, a synaptic cleft, and more than two synaptic vesicles in the presynaptic active zone. We counted synapses in photomicrographs (×18,500 magnification) from randomly chosen areas in one to seven sections per block. The number of neurons in glia-free cultures was estimated by counting neuronal cell bodies in the sections. Because the density of neurons was similar in glia-free and in cocultures, we could directly compare the number of synapses in equal numbers of micrographs from each culture condition.
20. In three glia-free cultures, we counted 168, 104, and 43 synapses in 109, 60, and 61 micrographs with approximately 20, 29, and 8 neurons. In the corresponding cocultures with glia, we found 373, 179, and 87 synapses in 104, 57, and 44 micrographs, respectively. Thus, glial cells increased the number of synapses per micrograph by 2.3, 1.8, and 2.8, respectively.
21. EPSCs were evoked by extracellular stimulation as described [F. W. Pfrieger, K. Gottmann, H. D. Lux, *Neuron* **12**, 97 (1994)]. Briefly, a glass pipette (tip diameter: 1 μm), filled with extracellular solution was placed near a neurite, where brief (100 μs) current pulses (0.2 mA) evoked EPSCs in the postsynaptic neuron clamped at a holding potential of −70 mV. At each stimulation site, two trains of 20 stimuli were applied at 1, 5, 10, and 25 Hz, respectively. Action potentials in the postsynaptic neuron were blocked by including the lidocaine derivate QX-314 (10 mM, RBI) in the intracellular recording solution. For the analysis of EPSCs, membrane currents were integrated over a time window of 8 ms beginning at the EPSC onset. For each stimulus, the presence of an EPSC or a stimulation failure was determined by the experimenter. In order to normalize failure rates at 5 and 10 Hz, for each RGC we subtracted the failure percentage at 1 Hz and divided by the rate at 25 Hz. To test the reliability of extracellular stimulation, we performed current-clamp recordings with 6,7-dinitroquinoxaline-2,3-dione (10 μM) added extracellularly to exclude action-potential induction by synaptic currents.
22. The binomial model of transmitter release [see E. M. McLachlan, in *International Review of Physiology: Neurophysiology III, Volume 17*, R. Porter, Ed. (University Park Press, Baltimore, MD, 1978), pp. 49–117] was used to estimate whether the different failure rates in glia-free cultures and in cocultures can be explained by the difference in the number of synapses. According to the binomial equation, the number of trials without release (x_0) in a series of N trials is given by $x_0 = N \cdot q^n$, and the failure rate is $f = x_0/N = q^n$, with q denoting the mean probability of no release ($q = 1 - p$) and n the number of release sites. Assuming that glial cells do not change the release probability ($q_{+glia} = q_{-glia}$), we can calculate the increase in the number of release sites that would cause the observed changes in the failure rates according to $n_{+glia}/n_{-glia} = \log (f_{+glia})/\log (f_{-glia})$. The values for n_{+glia}/n_{-glia} are 2.8 at 1 Hz, 4.0 at 5 Hz, and 4.8 at 10 and 25 Hz. The ratios at higher frequencies exceeded the observed twofold increase in the synapse number, indicating that glial cells enhanced the efficacy of individual release sites.
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25. Supported by the Human Frontier Science Program Organization and the Deutsche Forschungsgemeinschaft (F.W.P.) and by The Searle Scholar Program/The Chicago Community Trust (B.A.B.). We thank T. L. Schwarz and R. W. Tsien for valuable comments on the manuscript, S. Shen for ultrathin sections, F. Thomas for kind help with the electron microscope, and R. Scheller for generously providing an anti-synaptotagmin antibody. We also thank Regeneron for the kind gift of recombinant BDNF and CNTF.

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TECHNICAL COMMENTS

"Killer" Impacts and Life's Origins

The recent report by Christopher P. McKay and William J. Borucki (*1*) brought the consequences of impact shocks for the origin of life on Earth into focus anew. One could, however, imagine further positive consequences of large and small impacts for the prebiotic environment.

If one accepts the "RNA-world" scenario (*2*) for the origin of life on Earth, one has to assume a massive production of activated ribonucleotides or RNA-oligonucleotides. Whereas nucleotide bases and sugars could be produced from hydrogen cyanide (HCN) and formaldehyde—for which plausible prebiotic synthesis-mechanisms in the early Earth atmosphere exist (*3*)—the triphosphate part of the ribonucleotide would have to be mobilized from the lithosphere and brought into contact with the sugars and bases. Furthermore, a ready source of free enthalpy would be required to drive the cycles of polymerization (reproduction) and destruction (selection) of RNA chains until ribozymes (or even enzymes) arose that could couple the self-replicating RNA system to other, not so easily available sources of free energy, like, for example, solar radiation. Several researchers have proposed polyphosphate as this primary source of free enthalpy [see references in (*4*)].

In this respect, the paper by Yamagata *et al.* (*5*) about polyphosphate synthesis by heating of phosphate rocks with water vapor of over 1000°C and subsequent rapid cooling is most instructive. But instead of a synthesis route consisting of production of HCN and formaldehyde by lightning or ultraviolet radiation followed by rain out and subsequent reaction with polyphosphates produced in volcanoes (*5*), a second, maybe more efficient, way of ribonucleotide synthesis should be examined, which is also in line with current thought about the accretion of the Earth by planetesimals and its continuing bombardment even after the oceans and atmosphere had formed.

Fegley *et al.* (*6*) demonstrated the synthesis of HCN by meteoric impact on Earth's early atmosphere, while Sleep *et al.* (*7*) described the consequences of large impacts for the prebiotic enviroment. Large impacts could have repeatedly vaporized not only the entire ocean of the early Earth, but also enough rock to create 100 bar of rock vapor and suspended droplets with a temperature of 2000°C (*7*). Smaller impacts that vaporize only the photic zone of the oceans were also discussed by Sleep *et al.* (*7*). It would be interesting to examine whether, under these conditions, (poly-)phosphates would be produced and in what quantities. Probably no activated polyphosphate would survive the cooling time after a so-called "ocean blaster" had vaporized the whole ocean, but even after somewhat smaller impacts the resulting rock vapor probably produced polyphosphates like the heated phosphate rock/basalt mixure used by Yamagata *et al.* (*5*). As the extraction efficiency rises with increasing temperature (*5*), the higher temperatures should compensate for the fact that natural occurring rocks contain over one order of magnitude less phosphate than the model substances (*4*). The ocean would boil under the influence of the infrared radiation of the rock vapor, but the ocean depths would remain cool (*7*) and could act as a cold trap as in Yamagata's experiment.

The polyphosphate yield of this process would be determined not only by the production, but also by the (hydrolytic) destruction rate of polyphosphate before it could reach the deep ocean. A detailed discussion has to take into account the following considerations (*8*), among others: Phosphate would condense out of rock vapor after much of the silicate had condensed. So, rock rain would concentrate phosphate in the remaining air. The rock rain drops would fall through the surface layer and would be quenched in seconds in the ocean. Water rain would not fall until later, when the atmosphere became cooler than the critical point. This water rain would initially be buoyant on saline water and cool slowly.

In a reduced rock vapor with metallic iron, P is not volatile; it condenses in solid solution, and then as Fe_3P. This would happen in a major impact, when metallic iron is present. Phosphorous becomes a lithosphile at lower temperatures as phosphate. If iron drops quench, then P might react at low temperature. On the other hand, iron phosphide in Fe metal drops may be a good starting material for interesting prebiotic reactions. In a more oxidizing impact of silicate without metallic iron, phosphate may become concentrated more in the final vapor. [The moon is somewhat depleted in P relative to the Earth, so the final vapor that was lost to space was somewhat enriched in P (*9*)].

Finally, a further point has to be taken into account: Keefe and Miller (*4*) pointed out that if the partial pressure of water vapor exceeds 6 bar, the entropy-driven condensation reaction of phosphate into polyphosphate and water would be driven in the reverse direction. This limits the size of the impactor useful for producing polyphosphates to about 90-km diameter (*8*). Much bigger blasts in earlier times (even bigger than ocean blaster) would have destroyed any complex molecules, including polyphosphates, [the water vapor atmosphere lasts 3000 years (*7*)], but could still be beneficial for the later origin of life by reworking the upper crust thoroughly and "leaching out" the phosphate fraction. Because phosphate probably remained airborne longer than the rock fraction (*8*), it would be more concentrated in the upper layers of the Earth's crust after re-condensation. There it could be mobilized again by not so massive and deep penetrating impacts. Such large impactors, however, would have an iron core. So the above-described process has to compete with iron droplets in a large impact. Most of the Earth's P today is in the core (*8*).

The admittedly optimistic scenario described above could be a counterargument to Miller's computation (which was intended as a reductio ad absurdum) that even if the phosphate of the upper 1 km of Earth's crust could be extracted, the resulting solution in the ocean would be only 0.03 M (*4*). Of course, the circumstances described above would be difficult to simulate in a laboratory, but it would be interesting if the outcome of such experiments supported the hypothesis that those "killer impacts," through repeated "fractionation" and enrichment of polyphosphates in the future biosphere, got life started in the first place (*10*).

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10. The rapid cooling of the re-condensed rock vapor would also probably lead to increased fracturing of the rock droplets. A big surface area would be provided. Glass reacts quickly, and could assist in the polymerization of oligonucleotides, as shown by the experiments of J. P. Ferris *et al.* [*Nature* **81**, 59 (1996)]. Also, Fe metal droplets will react and become FeS_2 or FeS templates with P readily available (*8*). Thus, there could be a connection between this process and the iron-sulfur-world scenario for the origin of life [G. Wachtershauser, *Progr. Biophys. Mol. Biol.* **58**, 85 (1992)].
11. I am thankful to N. H. Sleep for answering numerous questions.

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The Usefulness of NMR Quantum Computing

Quantum computing—the manipulation of a quantum mechanical system to do information processing—has attracted considerable recent attention, largely triggered by Shor's proposed algorithm for finding prime factors in polynomial instead of exponential time (*1*). The importance of this problem has also led to numerous attempts to realize quantum computers, including systems such as trapped ions and quantum dots. In their Research Article, Gershenfeld and Chuang (*2*) propose the use of a much less exotic system—nuclear magnetic resonance (NMR) of molecules in a room-temperature solution. They demonstrate that such a "bulk spin-resonance" system is capable in principle of doing quantum computation, and they discuss the generation of 6 to 10 quantum bits ("qubits"), which would be a daunting, but not impossible task with today's technology. Of course, solution NMR was used in the 1950s to study equally small molecules, yet today we study proteins with thousands of spins. If an NMR quantum computer were ultimately scalable to larger numbers of qubits (say 100), the implications for computational science would be exciting.

There is doubt, however, that solution NMR quantum computing will ever be useful. Ensembles of uncoupled two-level systems (magnetic resonance or any other form) have quite classical dynamics, as shown by Feynman (*3*). Thus the clock cycles for any nonclassical dynamics, including all of the computing operations in the report (*2*) and in any other conceivable treatment, require times on the order of the reciprocal of the spin-spin couplings (≈200 Hz for directly bonded atoms, ≈10 Hz for protons on nearest-neighbor carbons) per step. Many such steps would be needed for logic operations between two separated spins. Dipolar couplings (for example, in solids) can increase the couplings by another factor of 10, but then the eigenstates are not the simple spin product states, and each logical manipulation will be much more complex. The slowest limit of speed estimated by Gershenfeld and Chuang (*2*) (10 logic gates per second) is thus grossly overoptimistic for a reasonably sized molecule.

Speed is not an important problem for demonstration experiments; perhaps new quantum algorithms will be found that compensate for the enormous slowdown. However, NMR is the premier spectroscopic example, not of quantum mechanics, but of quantum *statistical* mechanics including ensemble averaging. For a macroscopic sample (say $N \approx 10^{22}$ spins) the evolution is essentially deterministic. For example, all modern spectrometers routinely measure I_x and I_y simultaneously, despite the Uncertainty Principle. Fluctuations from the expectation value scale as $1/\sqrt{N}$, or about 10^{11} $\hbar$ (10^{-11} of the magnetization, but as I show below, this is still not good enough for solution NMR quantum computing). In addition, in NMR the energy difference between the two spin states of each atom is small,