Chirality and cold origin of life

SIR – Recent comments on the possible non-racemic nature of extraterrestrial amino acids[1,2] have implications for the origin of life. Two scenarios have been postulated: a terrestrial origin (the Oparin–Haldane model) and an extraterrestrial origin (initiated by Svante Arrhenius's 'panspermia' hypothesis). Neither of these, however, provides an explanation of the chiral purity of the terrestrial biosphere.

We have previously proposed an extraterrestrial origin which we term the 'cold prehistory of life'. This is based on the phenomenon of molecular tunnelling[3,4] — the existence of a finite limiting chemical reaction rate at low temperatures resulting from quantum tunnelling[5,6]. Experiments on formalydehyde polymerization[3] provide evidence for such a process. Recently we reached three conclusions concerning the role of chirality in any model[7]:

(1) The chiral purity observed in the biosphere was achieved at the stage of prebiotic evolution and was a necessary condition for the subsequent development of self-replication.

(2) Chiral purity resulted not from the gradual (evolutionary) accumulation of an enantiomeric excess, but by a process in which mirror symmetry was broken spontaneously[8,9].

(3) The sign of chiral purity in the bio-organic world (L-amino acids and D-sugars) is random[10,11] rather than predetermined by some 'global advantage factor' (for example, by the non-conservation of parity in weak interactions, particularly weak neutral currents[12]).

Spontaneous racemization at low temperatures by D⇄L tunnelling is predicted by Hund's paradox (that is, the fact that the symmetric ground state for a chiral species is the racemic mixture). But in the 'cold prehistory of life' it is possible to inhibit D⇄L conversion[13,14] even at temperatures sufficient for cryochemical reactions to occur, such as those found in space.

The study by Engel *et al.*[1] on the stereoisomer and isotope (^{13}C) composition of amino acids in the Murchison meteorite is of great interest in this regard. Engel *et al.* reported enantiomeric excesses of the L-isomer for alanine (D/L ratio of 0.85 ± 0.03) and glutamic acid (0.54), accompanied by a ^{13}C enrichment typical of extraterrestrial organic materials (up to 30 ‰). They concluded that optically active (or rather, deracemized) compounds were present in the early Solar System.

This conclusion is consistent with point (1) above. Moreover, if this partially deracemized state represents an intermediate stage in the transition to a chirally pure state, the results can provide an indication of the timescale required for the symmetry-breaking process in point (2): according to ref. 15 it could be as short as 10^6–10^7 years, whereas the whole prebiotic stage of the Earth's history lasted 2×10^8–5×10^8 years.

In view of the totality of data that led us to our conclusions (2) and (3), the possibility mentioned in ref. 1 that β-decay of ^{14}C could provide a mechanism for deracemization of amino acids in meteorites must, in our opinion, be excluded.

Finally, in regard to the question of whether extraterrestrial amino acids can be delivered intact to the Earth by a large impactor[2,16], we note that shock waves with amplitudes of as much as 500 kbar need not destroy amino acids but can instead initiate their condensation into oligopeptides[17].

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1. Engel, M. N., Macko S. A. & Silfer J. A. *Nature* **348,** 47(1990).
2. Chyba, C. F. *Nature* **348,** 113 (1990).
3. Goldanskii, V. I., Frank-Kamenetskii, M. D. & Barkalov, I. M. *Science* **182,** 1344 (1973).
4. Goldanskii, V. I. *Nature* **268,** 612 (1977); **269,** 583 (1977); **279,** 109 (1979).
5. Bell, R. P. *Proc. R. Soc.* A**139,** 466 (1933); **148,** 241 (1935); **158,** 128 (1937).
6. Goldanskii, V. I. *Doklady Akad. Nauk SSSR* **124,** 1261 (1959); **127,** 1037 (1959).
7. Goldanskii, V. I. & Kuzmin, V. V. *Sov. Phys. Uspekhi* **32,** 1 (1989).
8. Frank, F. *Biochim. biophys. Acta* **11,** 459 (1953).
9. Morosov, L. L. *Origins of Life* **9,** 187 (1979).
10. Avetisov, V. A., Kuzmin, V. V. & Anikin, S. A. *Chem. Phys.* **112,** 179 (1987).
11. Grossmann, S. & Mikhailov, A. S. *Z. Phys.* B**78,** 1 (1990).
12. Kondepudi, D. K. & Nelson, G. W. *Nature* **143,** 438 (1985).
13. Harris, R. A. & Stodolsky, L. *Phys. Lett.* B**78,** 313 (1978); **116,** 464 (1982).
14. Berlin, Yu.A. *et. al. Doklady AN SSSR* **306,** 844 (1989).
15. Morosov, L. L., Kuzmin, V. V. & Goldanskii, V. I. *Doklady-Biophys. (Proc. Acad. Sci. USSR)* **274,** 55 (1984); **275,** 71 (1984).
16. Zahnle, K. & Grinspoon, D. *Nature* **348,** 157 (1990).
17. Goldanskii. V. I. *et. al. Doklady-Biochemistry (Proc. Acad. Sci. USSR)* **207,** 218 (1972).

DNA strand asymmetry

SIR – We reported[1] an apparent inequality in the mutation rates of the two strands of DNA. Our analysis was based on seven DNA sequences in an intergenic region within the β-globin gene complex of six primate species. Our observation was in good agreement with an independent study of the φη region, 4 kilobases away[2]. Since then, the DNA spanning a 11.5-kb region that encompasses the two subregions has been sequenced; analysis of the whole region[3] does not show the trend observed in the two subregions[1,2]. We have partitioned this data into four subregions for more detailed analysis.

The results show that the inequality in ref. 1 is restricted to the last 3 kb. The other three subregions all show weak asymmetry in the opposite direction (C.-I. W. and T. Baldanzi, unpublished results). One explanation is that the locations of replication origins, at least in the germ cells, have not been conserved since the divergence of these species. As a consequence, regions of homologous DNA strands may be replicated as a leading strand in one species and as a lagging strand in another species, obscuring the asymmetry reported in ref. 1.

This possibility becomes greater when a longer sequence is examined. Umek *et al.*[4] have reviewed cases of nonspecific and stochastic usage of replication origins in higher eukaryotes. It is also possible that mammalian male germ cells may recruit many secondary origins for rapid replication. For sequence analysis, it is therefore most promising to compare molecules with known fixed origins, such as bacterial chromosomes or mitochondrial DNA.

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1. Wu, C.-I. & Maeda, N. *Nature* **327,** 169–170 (1987).
2. Koop, B. F., Goodman, M., Xu, P., Chan, K. & Slighton, J. L. *Nature* **319,** 234–238 (1986).
3. Goodman, M., Koop, B. F., Czelusniak, J., Fitch, D. H. A. & Slighton, J. L. *Genome* **31,** 316–335 (1989).
4. Umek, R. M., Linskens, M. H. K., Lowalski, D. & Huberman, J. A. *Biochem. biophys. Acta* **1007,** 1–14 (1989).

AZT before AIDS

SIR – Our early work on azidothymidine (AZT) provided the first demonstration of its antiretroviral activity and indeed constituted the only research of the time to suggest what would later turn out to be efficacy at treating people with AIDS.

AZT was born via chemical synthesis by J. Horwitz *et al.* (*J. org. Chem.* **19,** 2076; 1964). After a relatively uneventful childhood, its biological potential was first clearly recognized in the early 1970s and by its tenth birthday firmly established (W. Ostertag *et al. Proc. natn. Acad. Sci. U.S.A.* **71,** 4980; 1974). In those experiments, we examined the effect of AZT on the replication of a murine retrovirus complex consisting of spleen focus-forming and leukaemia viruses and made the crucial observation that AZT interfered with virus replication quite dramatically but had very little hinderance of cell growth even at relatively high concentrations of 2.5×10^{-4}M.

These observations, showing AZT's high toxicity for the virus but low toxicity for the cell, suggested for it a career of high promise. Indeed, on its twenty-first birthday it came of age when H. Mitsuya *et al.* (*Proc. natn. Acad. Sci. U.S.A.* **82,** 7096; 1985) demonstrated its usefulness against human T-lymphotropic virus type III. It is gratifying that the effects of AZT in a murine retrovirus system have faithfully reproduced with a human retrovirus and, once again, mouse has proved its worth to man.

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