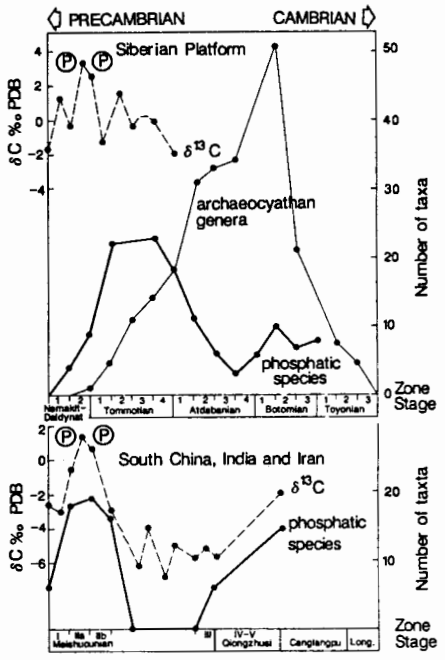

Contrasting diversity of oligotrophic archaeocyathan genera and 'phosphophilic' phosphatic skeletal species, compared against published carbon isotopes curves from Siberia and south China. P, phosphogenic events.

archaeocyathans diversified explosively[5]. The latter were seldom associated with phosphatic shells or phosphorites, and a preference for oligotrophic conditions may be implied by analogy with recent reefal biotas plus evidence for close associations with cyanobacterial mounds. Symbiotic recycling of phosphorus, nitrogen and organic compounds is inferred.

The peak of archaeocyathan diversity coincided with maximum transgression during the early Cambrian, and declined during a eustatic regression[5]. A return to more phosphogenic conditions and heavier stable isotopes during and after this demise raises important questions about the role of nutrient excess in evolution, like that currently destroying coral reefs.

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Erratum

In the Scientific Correspondence "The law beats Maxwell's demon" by Paul A. Samuelson (*Nature* **347**, 24–25; 6 September 1990) the equation

$$D[\dot{x}, 1/2] = \dot{x} \text{ for } \dot{x} < 0$$

should have read

$$D[\dot{x}, 1/2] = -\dot{x} \text{ for } \dot{x} < 0. \quad \square$$

HIV mutation rate

SIR—The human immunodeficiency virus (HIV) evolves at a rate about a million times as great as that of eukaryotic DNA genomes[1]. This ratio is reflected in the replication accuracies of the corresponding enzymes: the typical error rate of DNA polymerization is somewhere around 10^{-10} and 10^{-9}; the measured average error rate per site for the HIV-1 reverse transcriptase is between 10^{-4} and 10^{-3} (refs 2,3). This implies that the reverse transcriptase makes on average 1–10 errors during the replication of the HIV genome (10^4 bases). This high mutation rate might be an important factor for the virus to escape destruction by the immune system.

An interesting feature of HIV-1 infections is the high genetic variability found in virus populations. Sequential virus isolations from the same infected patients have shown that mutation *in vivo* is rapid: many related but distinguishable mutants evolve during chronic infection[1,4–6]. The selection pressure exerted by the immune response might represent the main force to generate this genetic variability.

The existence of neutralizing antibodies against HIV has been well documented[7,8]. The immunodominant loop (V3 loop), a region of about 30 amino acids within the viral envelope protein gp120, mediates most of the neutralization phenomena in infected humans. This part of the envelope protein seems to mutate rapidly in infected patients. Immunological selection (propagation of new resistant mutants in the presence of specific neutralizing agents) has been observed *in vitro*[9]. The generation of new neutralization resistant mutants might result from a single point mutation in the envelope gene[10]. This production of escape mutants by antigenic drift has also been reported for other lentiviruses.

It seems to be essential for the virus to change its immunodominant epitopes as fast as possible. An obvious question is: what is the optimal mutation rate that maximizes the probability to produce escape mutants?

If the average replication accuracy of the reverse transcriptase is denoted by q, the probability that replication of the whole genome is done without error is given by $Q = q^n$, where n is the total length of the genome. For HIV, $n \sim 10^4$ for one single strand. Let m be the number of sites within the genome such that a mutation in at least one of these sites results in the production of an escape mutant (m might be the length of the immunodominant loop or so, but the particular value for m will not influence our result, as long as m is much smaller than n, which is clear). The probability to obtain an escape mutant (the probability of obtaining a mutant with no errors in $n - m$ sites and at least one error in the m sites) is given by $P = q^{n-m}(1 - q^m)$. This probability has a maximum for $q^* = (1 - m/n)^{1/m}$ which is well approximated by $q^* = 1 - 1/n$. This result is independent of m. Therefore, the optimal mutation rate is given by $e^* = 1 - q^* = 1/n$, which is for HIV around 10^{-4}.

This result could be shifted slightly to higher values if we consider the effect of neutral sites in the genome. Additional mutation in the neutral sites will not change the fitness of an escape mutant. If r is the fraction of neutral sites in the whole genome, then $P = q^{n(1-r)-m}(1 - q^m)$ and $e^* = 1/n(1-r)$. If r lies somewhere between 0 and 0.9, then e^* is found between 10^{-4} and 10^{-3}.

My argument is based on the assumption that the human immune response against HIV favours variation in some parts of the viral genome. If this is true, then there is an optimal mutation rate which maximizes the probability of producing new resistant mutants due to errors in viral replication. This optimal mutation rate is in good agreement with the measured replication accuracy of the HIV-1 reverse transcriptase.

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Radiating bodies

SIR—H. Aspden (*Nature* **347**, 25; 1990) describes a procedure for driving sensible energy from a cooler body to a hotter body, in contravention of thermodynamics. This is done by the use of a mirror to focus radiation from the cooler body A onto the surface of the hotter body B.

This procedure will fail. If the only radiating bodies involved are the bodies A and B, then body B will radiate heat back to body A faster than A radiates to B, so bringing the two bodies to the same temperature, as required by thermodynamics. It would be necessary in practice to enclose both A and B by additional surfaces, but in order that these should make no net contributions to the energy exchanges between A and B, these too would have to be at the same temperature as A and B.

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