Plastids better red than dead

SIR — Beyond the end of the genetic rainbow of plastids discussed in News and Views by Palmer[1] lies a dwarf plastid-like genome he failed on that occasion to mention — that of the malaria parasite (but see ref. 2). Palmer's description of the reduced genome of the parasitic plant *Epifagus* as "nearly extinct" (its genetic content is tiny by comparison with ordinary plastids), might lead some to assume that the malarial plastid remnant, which is only half its size again, is equally moribund or even dead. But for various reasons I believe it is still vital.

Since Palmer's News and Views was published, we have obtained further evidence[3] supporting the plastid ancestry of the malarial 35-kilobase circular DNA. The DNA encodes an open reading frame (ORF470) whose predicted peptide product is about 50% identical with a plastid ORF so far reported only in the red algae *Antithamnion spp.*[4], *Cyanidinium caldarum* (K. Zetsche, personal communication) and *Porphyra purpureum* (M. Reith, personal communication). The high level of conservation strongly suggests that ORF470 is a functional gene retained in the highly reduced malarial plastid remnant — its presence thus would fall in line with Palmer's rationale for retention of plastid genomes in non-photosynthetic plants[5]. This likelihood is strengthened by our finding that transcripts of ORF470 are readily detected in total malarial RNA, whereas transcripts of other ORFs encoded by the malarial plastid-like DNA, those encoding elements of the transcriptional machinery — ribosomal proteins and so on — are much rarer.

A second notable feature of the plastid-like DNA of the malaria parasite (still incompletely sequenced), is the retention, unlike *Epifagus*, of at least some elements of the plastid *rpo* operon[6,7]. The malarial *rpoB* gene has undergone considerable evolutionary 'drift' compared with extant chloroplast counterparts, yet it is both complete and expressed at a low level.

Finally, it is striking that a homologue of the 35-kb plastid DNA remnant of *Plasmodium* (malaria) has been retained in other parasites in the ancient phylum Apicomplexa, such as *Toxoplasma* and *Eimeria*, which are now phylogenetically distant to *Plasmodium*[8]. The degree of conservation of this plastid remnant remains largely to be discovered, but in the three genera mentioned above, the plastid-like DNA has a highly characteristic inverted ribosomal RNA repeat that can form a large cruciform structure containing spatially conserved sequences[9].

I suggest that whatever the case for the "nearly extinct" *Epifagus* molecule, the malarial plastid DNA remnant, which we have linked phylogenetically to the non-green end of the currently known spectrum of plastid DNAs, is not dead and that its function is succinct rather than extinct.

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Scientific Correspondence
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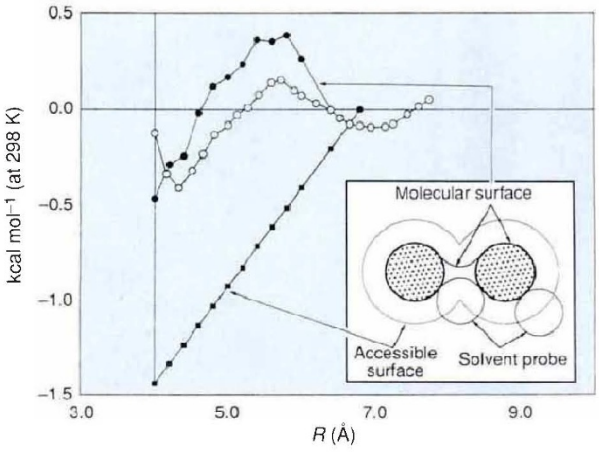
Protein surface area defined

SIR — Weber[1] in scientific correspondence suggested that the entropy of systems as diverse as proteins in solution and black holes are dependent on surface area. Langmuir[2] in 1925 observed that molecular surface area is related to the free energy of processes in solution. We believe that the definition of the surface area is critical in describing the energetics of association in solution. Accessible surface area (see figure) is widely used in protein modelling to describe the entropy-driven hydrophobic effect, but the approach fails to represent even the simpler manifestations of hydrophobicity[3].



Schematic of two methane molecules in close contact, representing the solvent accessible (ASA) and molecular surface areas (MSA) as trace out by a solvent probe. Potential of mean force for the dimerization of two methane molecules in water at 298 K, as represented by spheres of radius 2 and 1.4 Å, respectively. ■, Calculated using ASA with a surface tension of 24 cal mol^{-1} Å^{-2}; ●, using MSA with a surface tension of 102 cal mol^{-1} Å^{-2}. For comparison, ○ was taken from a Monte Carlo statistical mechanics simulation of the dimerization of methane[6].

Interactions in the condensed phase are characterized by an energy barrier for solutes separated by less than a single solvent molecule. Consider the dimerization of methane in water (figure). The potential of mean force generated by a linear relationship between accessible surface area and free energy is in disagreement with theoretical calculations and statistical mechanics simulations. Indeed, the force derived from the accessible surface area is attractive at close separation, because the surface must always be greater for two separated molecules than when they are in van der Waals contact.

In contrast, molecular surface area (see figure) reproduces the energy barrier. We have argued that for a given area and solvent, surface tension described by molecular surface area is shape-independent[4], in contrast to surface tension relating to accessible surface area[5]. The apparent differences in measures of microscopic and macroscopic surface tension can be resolved using molecular surface area, without the need to invoke a marked curvature dependence of surface tension.

This proposal has important implications for modelling surface-area dependence of protein–protein interactions , as calculations show that accessible surface area is not simply related to molecular surface area by a constant of proportionality.

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