disrupting helical structure[6,7], are conserved within a central 115 amino acid stretch of each URF. This region, which is bounded by characteristic decapeptide motifs, is thus likely to play a key part in determining both protein structure and enzymatic function, as does a region immediately downstream, in which numerous *trans*-recessive mutations affecting splicing have been identified[9,10].

Two indirect observations concerning maturase function are important. First, intron mutants, with defective mitochondrial maturases, generally accumulate only high molecular weight, intron-containing pre-mRNAs[12,13]. Second, nuclear mutants defective in mitochondrial splicing reactions have been isolated and partially characterized. The defects are surprisingly specific, often involving an inability to cut or ligate the ends of a single intron in the gene for cytochrome *b* or subunit I of cytochrome *c* oxidase. In one group of cytochrome *b*-deficient mutants recently studied by Diekmann *et al.*[18], transcripts consisting of bI_4 linked to downstream exon sequences accumulated, indicating first that a nuclear gene product is required for scission of the bI_4–exon boundary and second, by implication, that the bI_4 maturase may itself be involved in the initial scission at the upstream exon–bI_4 border.

With such an intricate systems for RNA processing, it is remarkable that many individual introns and their maturases are dispensable, in that various yeast strains, either found in nature[19] or constructed in the laboratory[8,15], can lack them entirely and suffer no ill-effect. So, why have introns?

One view is that they are evolutionary relics, left over from a primitive, genes-in-pieces type of genome organization. Indeed, the high homology observed between introns in mtDNA of yeast and *Aspergillus nidulans*[4,5] indicates that at least some introns pre-date the common ancestor of these fungi. On the other hand, whatever role introns may have had in the evolution of mitochondrial genes, their continued retention in fungal mtDNAs cannot be an accident. The distribution of introns is highly non-random: two of the seven major protein-coding genes, one of the two rRNA genes and none of the tRNA genes contain introns. The maintenance of the introns requires a large number of genes involved in splicing; this complex system must be vulnerable to disruption by mutation. Nature is not without means to eliminate this costly genetic investment, because it can produce mtDNAs with fewer or no introns. The introns in the fungal mtDNAs must therefore confer a selective advantage now.

Among possible advantages, the most plausible is that additional splicing steps allow a more precise control over mitochondrial gene expression. This could permit, for example, the selective suppression of the synthesis of mitochondrial components during growth in the presence of fermentable sugars. Such an explanation may not, however, hold for all introns and all fungi. The gene for the mitochondrial large rRNA contains an intron plus URF, yet accurate splicing is possible in the absence of the URF product[20] (albeit somewhat inefficiently) and rRNA synthesis does not seem to be selectively repressible. Again, *Aspergillus* has also retained introns and their reading frames in the genes for cytochrome *b* and subunit I of cytochrome *c* oxidase, yet does not repress mitochondrial synthesis. There is obviously room for further speculation about the selective advantage of having mitochondrial introns and maturases.

Finally, where do the introns and their maturases come from? We suggested previously[21] that they might have arisen from insertion elements which lost their mobility in the course of evolution and this idea remains plausible. First, the sequence homologies found between the URFs of yeast mtDNA argue for a common origin with subsequent dispersal around the genome[7]. Second, the hypothesis correctly predicts that sequences homologous to intronic reading frames may also be found outside genes[22]. Third, all yeast URFs display codon usage which deviates markedly from the characteristic pattern observed in genes for known, major translation products[3,23]. Such usage could be the last visible trace of a separate genetic orgin of URF sequences. □

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Where has that Moon been?

from Kurt Lambeck

THAT tidal forces play a most significant part in the dynamical evolution of the Earth–Moon system is beyond dispute. What is in dispute is the time scale of this evolution. One more attempt at resolving this vexing question has recently been discussed by Webb in the *Geophysical Journal of the Royal Astronomical Society* (**70**, 261; 1982).

That this ancient subject continues to draw the attention of scientists in diverse disciplines may seem curious but is a reflection of the important ramifications of tidal evolution models as well as their intellectually satisfying nature. Few other subjects require one to delve into the rigours of celestial mechanics or into the ambiguity of an observational record that includes eighteenth century telescope observations, ancient records of eclipses and the life styles of Palaeozoic corals. It requires investigations into the solid Earth's structure, into ocean tides, speculations on the evolution of the Earth and an initiation into the mysteries of lunar chemistry.

A central difficulty in modelling the past orbital and spin configurations of the Moon and Earth is to extrapolate from present-day tide models and tidal accelerations. It is inescapable that most of the tidal energy is dissipated in the oceans[1] and that this must have been so for much of the Earth's past history. Any extrapolation backwards into geological time is, therefore, only as good as the assumption that past and present tides are identical or that past tides can be characterized by some mathematically convenient law. Such extrapolations lead to the conclusion that the Moon must have been very close to the Earth some 1.5–2 billion years ago. This conclusion is unsavoury to most lunar scientists[2].

Can this close approach, so late in the Earth's history, be avoided without invalidating the orbital evolution calculations?. Is it possible to push it back into the Earth's remote past? This is the problem that Webb sets out to solve; how to compute representative tidal dissipation estimates for past epochs when the requisite detailed oceanic data are

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unavailable. His approach is not to consider detailed models at specific geological epochs as others have attempted[3]. Instead Webb adopts an 'average' ocean model and then investigates how dissipation may vary in response to the evolving Earth–Moon system. In particular, he investigates the dependence of dissipation on the frequency of the tide-raising force. His important result is that the rate of tidal energy dissipation has been less in the past than it is now and that the calamitous consequences of a close approach of the Moon can be readily averted.

Present rates of energy dissipation are now quite well established as about 4.0×10^{12} Watts (ref. 4). It is also clear that at least 90 per cent of this energy is dissipated in the oceans. What remains less obvious is the mechanism by which this dissipation takes place. Is it by bottom friction in a few shallow seas, or by a more global mechanism such as the breaking of tidal waves along shorelines or the scattering of tidal waves into internal modes? Advocates of all mechanisms can be found but it seems that the actual assumptions made have little influence on the numerical solutions or interpolations of the Laplace tidal equations. Compare, for example, the recent tidal models for the dominant lunar tide[5-8]. All solutions require that dissipation is fairly uniformly distributed through the world's oceans, and all give very comparable results once corrections for the solid tide are made where appropriate[4]. That this is so is at least partly because all solutions are either explicitly or implicitly constrained by observations of the tides. But it makes Webb's approach of considerable interest for he does not have to make assumptions about the detailed ocean geometry. Instead, he considers tides on a hemispherical ocean[9] whose orientation with respect to the Earth's rotation axis is allowed to vary through all possible values. Dissipation is introduced by requiring that the decay time of tidal energy equals the average observed value. For a given frequency of the tide — defined by the Earth–Moon distance and the Earth's spin rate — Webb averages the power estimates over all orientation angles with the acceptable rationale that the time constant for plate tectonics is much less than the age of the oceans. The variation in the ocean geometry with time is therefore accounted for in this statistical manner. At any one frequency, strong resonances are encountered as a function of the orientation but Webb finds that, when averaged, these isolated resonances are smoothed out and that any resonances in the averaged power curve occur at frequencies that are lower than present and past values: the further one goes into the past the greater becomes the separation between the forcing and resonance frequencies.

Consequentially, past rates of orbital evolution will be less than if the Q or dissipation function of the ocean had been held constant, and Webb concludes that the close approach may never have occurred at all. Quantitatively his results may not be very significant but the general trend that emerges is. Evidence for reduced dissipation in the geological past has also been found in palaeontological records of the Earth's rotation where growth rhythms in corals and bivalves point to less dissipation over the past 400 million years than occurs at present[4]. A similar conclusion was also reached from explicit model studies of past ocean tides[3].

A word of caution seems appropriate however. The resonance frequencies of the ocean basins depend on the ocean scale as well as on the ocean depth. Thus by fixing the decay time, Webb also assumes that these factors have not changed much. The approximate period of the free oscillation is given by $2L/(gh)^{1/2}$ where L is the characteristic length scale, h the average depth and g is gravity. If, on the average, L is greater than today, as when the oceans were clustered into the Pangea continent, then the driving force will have been further away from resonance than it is now. If the ocean depths were less in the past, if the present basins evolved only relatively late in the Earth's history, then the difference between the forcing and resonance frequencies also increases. Thus some cancellation of Webb's result may occur. I rather doubt that this will be significant and those who argue that the Moon formed close to the Earth can sleep in peace. □

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From CoA to complement: thioesters as the spring in the molecular mouse trap

from John Fothergill

To most biochemists, thioesters mean coenzyme A and fatty acid metabolism. They are remarkable for their high free energy of hydrolysis and their participation as metabolic intermediates. With this background, the discovery of thioesters in proteins came as something of a surprise.

There is now good evidence that two of the complement proteins, C3 and C4, and the plasma proteinase inhibitor α_2-macroglobulin contain an internal thioester formed from the side chains of a cysteinyl and a glutamyl residue four positions apart on the polypeptide chain. In the native protein, the thioester is apparently buried, but on activation of the protein by proteolytic cleavage the thioester is exposed to the surroundings, readily generating a free thiol and an active acyl group that can react with nucleophilic amino or hydroxyl groups. This leads to covalent attachment of the thioester protein to adjacent protein or carbohydrate. Thus a single proteolytic cleavage of the protein containing the thioester leads to covalent linking of the activated protein to a nucleophilic group in its immediate environment. What are we to make of this 'molecular mouse trap'?

It has been known for a long time that complement components, once activated, adhere strongly to cell surfaces. This was explained as an interaction between a hydrophobic region on the complement component, revealed during proteolytic activation, and the cell membrane. The relatively short half life of the activated complement components was explained in terms of conformational rearrangement of this hydrophobic binding region. The first evidence[1] that the reaction could be a covalent one came from the detection of proteins in SDS-polyacrylamide gel electrophoresis that had higher molecular weights than the C3 polypeptide chains they were known to contain. Similar evidence has been obtained for the covalent binding of C4 (ref. 2) and C3 (ref. 3) to antigen–antibody aggregates. During the last two years evidence for this internal thioester has been accumulating rapidly. Publications have been overwhelmingly confirmatory, if somewhat repetitious.

Much of the evidence for the thioester in C3 has come from the work of Janatova

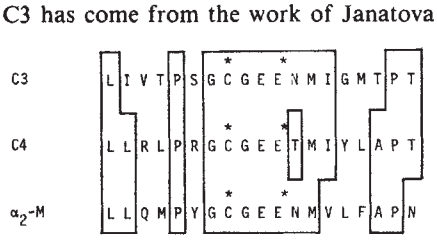

Fig. 1. Amino acid sequences around the thioester site of C3 (ref. 4), C4 (ref. 5) and α_2-macroglobulin (ref. 6). The cysteinyl and glutamyl residues contributing to the thioester are marked by an asterisk.

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