elements—four α-helices, two 3_{10} helices and three turns—is based on the three-dimensional structure of *Rhodospirillum rubrum* cytochrome c_2 (ref. 6) deposited with the Brookhaven Protein Data Bank.) The two matrices computed in this way clearly differ from one another (see Table 1). When phylogenetic trees[7] are constructed of them (Fig. 1), these also differ.

There are 135 amino acid positions in the cytochromes c_2, half of which (69) form helices and turns, the other half (66) being involved in unstructured loops. There is therefore no bias in favour of any of the two groups considered. They do differ evolutionarily, however, in that the secondary structure segments predominantly evolved by amino acid replacements whereas the unstructured loops harbour two-thirds of the deletions responsible for a distinction of the short, medium and long cytochromes c_2.

Thus, the following important points emerge as far as evolution of cytochromes c_2 is concerned. (1) Different phylogenies can be proposed for different segments of homologous primary structures, the phylogeny of the whole structure being a weighted average of the partial ones. (2) Because the differences can be correlated with typical features of the secondary structure, they seem to result from structural, rather then genetic causes.

Bacterial phylogeny is a notoriously difficult subject. Dickerson[8] and Woese *et al*[9]. have already tried to reconcile the cytochrome c_2 dilemma; this note, far from attempting to solve all the existing questions, aims at delineating a new approach to them.

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Methotrexate binding to dihydrofolate reductase

RECENTLY, in discussing dihydrofolate reductase, Gready[1] described, with the emphasis on our paper[2], the finding that the inhibitor, methotrexate, binds to the enzyme with its pteridine ring 'upside down' with respect to the substrates dihydrofolate and folate. It is essential to point out that the most important observations leading to this conclusion were made by others.

In their report of the crystal structure of the enzyme–methotrexate–NADPH complex, Matthews *et al.*[3] discussed the implications for the stereochemistry of the reaction and specifically recognized the possibility that the substrates might bind the other way up. Shortly thereafter, Fontecilla-Camps *et al.*[4] determined the absolute configuration of 5,10-methenyl-tetrahydrofolate (which can be related to that of tetrahydrofolate itself; see ref. 2). This revealed the stereochemistry of reduction of dihydrofolate at C6, and by comparison with the results of Matthews *et al.*, showed that dihydrofolate does bind the other way up from methotrexate. This was pointed out by Hitchings[5]. Our NMR experiments extended this to folate, showing that both substrates have the same orientation on the enzyme, which, from the crystallographic work, differs from that adopted by methotrexate.

The interesting finding that substrates and structurally analogous inhibitors bind to dihydrofolate reductase in quite different orientations thus arises from a comparison of a number of separate observations.

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Effects of the Earth's rotation rate on climate

HUNT'S[1] investigation of the meteorological effects of a faster rotating Earth has application to palaeoclimatology, but his findings cannot explain the occurrence or character of the several late Precambrian glaciations.

Hunt's[1] article does not distinguish between middle and late Precambrian. Late Precambrian glaciation occurred $0.95–0.60 \times 10^9$ yr ago[3–5], whereas glaciation is unknown during the middle Precambrian $\sim 1.5 \times 10^9$ yr ago[3]. Pannella's[2] curve of length of year suggests a 19–20-h day during the late Precambrian. Using Hunt's[1] Fig. 4, an Equator-to-Pole temperature difference of ~41 K and poles ~4 K colder than at present accordingly are indicated for late Precambrian glacial time; these estimations assume an obliquity of the ecliptic near that of today, which geological[3–7] and geophysical[3,5,8] data suggest may be invalid.

In the Precambrian conditions predicted by Hunt's[1] model—an increased Equator-to-Pole temperature gradient, with equatorial regions warmer and polar regions colder than those of today—glaciation would be confined to high palaeolatitudes, while low palaeolatitudes remained ice-free. Available palaeomagnetic data[3,5,8] reveal, however, a dominant picture of low palaeolatitude (~0–40°) glaciation in late Precambrian time; although some of the daata are difficult to interpret[9], circumpolar models of glaciation can be ruled out. Furthermore, Hunt's[1] findings cannot explain the marked episodicity of the seven or more glaciations since the middle Precambrian[3,4].

The major application of Hunt's[1] model lies in testing explanations of low-palaeolatitude glaciation in the late Precambrian. The concept of global glaciation[3,8] as a cause of preferred low-palaeolatitude glaciation is difficult to reconcile with an Earth possessing a warmer Equator and an Equator-to-Pole temperature gradient greater than at present. The alternative hypothesis of an increased obliquity of the ecliptic ($\gtrsim 54°$) in late Precambrian time[3–8] to reduce equatorial insolation and thereby confine glaciation to relatively low palaeolatitudes explains the data better.

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