RESUME

Gone fishing

THE changing ratios of strontium isotopes in sea water can be used to establish the chronology of marine sediments. But an ingenious scheme to correlate this record with continental sediments proved too slippery to handle (P. L. Koch *et al. Earth planet. Sci. Lett.* **108**, 227–287; 1992). Strontium replaces calcium in vertebrate bone, and if samples of bone formed in the oceans could be found in continental sediments, this bone could help correlate the disjunct land and ocean geological records. Koch *et al.* came up with the very thing — 15-million-year-old migratory salmon. Strontium isotope ratios from the continental fossils of mature salmon should reflect those of their adopted marine homes. But sad to say, it turned out that the vagaries of diagenesis mean that strontium ratios in fossils reflect the sediments in which they are found rather than the oceans once inhabited by the fish.

Getting the point

A CIRCLE of diagnostic understanding of Duchenne muscular dystrophy has been closed by R.G. Roberts *et al. (Proc. natn. Acad. Sci. U.S.A.* **89**, 2331–2335; 1992). About two-thirds of the mutations to the dystrophin gene, the underlying cause of muscular dystrophy, are large-scale rearrangements which can be directly characterized and used in screening; the remainder, however, have proved hard to identify because the gene is so large and complex. Roberts *et al* analysed the coding sequence of genes from seven patients showing no gross defects. In each they identified a point mutation which would cause a premature termination of transcription and be enough to account for the disease.

Any which way

THE source of astronomical γ-ray bursts remains a puzzle, despite the furious rate at which the satellite-borne Compton Observatory is identifying them. Only in January, operators reported an analysis of the first 153 bursts detected. Now C.A. Meegan *et al.* (*IAU Circ.* 5478; 1992) describe over 100 more. But still the message is ambiguous. The bursts are distributed isotropically over the sky, and because our Galaxy is a flattened disk, that suggests the bursts originate beyond its confines, in other galaxies. But there seems to be a paucity of the faintest (most distant) bursts, implying that they are more common nearby than far away. Nor is an excess of bursts evident when looking towards the Large Magellanic Cloud or towards Andromeda, our galactic neighbours. With the errors in the burster distribution growing as data accumulate, there is plenty of scope for inventive solutions.

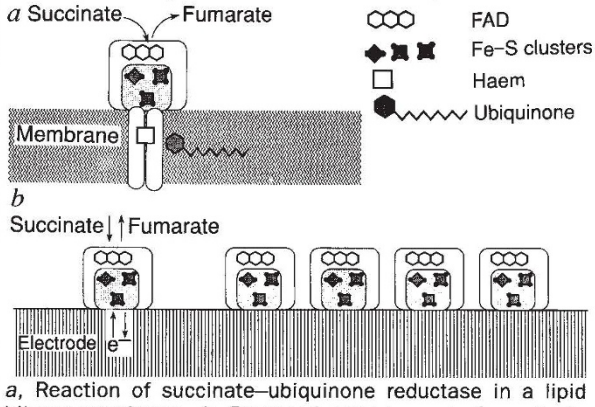
BIOLOGICAL ELECTRON TRANSFER

Plug in a molecular diode

Richard Cammack

ON page 361 of this issue[1] Sucheta and colleagues describe a remarkable enzymatic reaction which appears to behave like a diode; this property may turn out to be of physiological significance.

The protein concerned is succinate dehydrogenase, a mitochondrial enzyme that catalyses the oxidation of succinate to fumarate[2,3]. Redox reactions of proteins can be observed by dynamic electrochemical methods, but such methods usually require the addition of compounds known as promoters (to assist binding of the proteins to the electrodes) or mediators (to assist electron transfer)[4,5]. Sucheta *et al.* demonstrate that succinate dehydrogenase can bind to the surface of a graphite electrode, and can display rapid electron transfer without assistance. Unexpectedly, the enzyme prefers to conduct electrons only one way — it catalyses the oxidation of succinate to fumarate very well, but when a strong reducing potential is applied it catalyses the reverse pathway only poorly. It acts, as the title of the paper declares, like a molecular diode. This effect may be of physiological importance in helping to prevent the Krebs cycle from back-pedalling, and it may also point the way to the development of new types of bio-electronic device.



a, Reaction of succinate–ubiquinone reductase in a lipid bilayer membrane. *b*, Proposed arrangement of succinate dehydrogenase dimers as a monolayer on a graphite electrode surface.

Succinate dehydrogenase is the only membrane-bound enzyme of the Krebs citric acid cycle. It forms part of a respiratory complex, succinate–ubiquinone reductase. The final oxidant for succinate is not, as students used to be taught, the flavin FAD, but a membrane-bound carrier, ubiquinone[6]. To carry out this apparently straightforward transfer of two hydrogen atoms, the enzyme has a complex electron-transfer system, consisting of FAD, three iron–sulphur clusters and a *b*-type cytochrome (see *a* in the figure). The enzyme comprises two hydrophilic protein subunits, which react with the soluble succinate:

$$\text{succinate} \rightleftharpoons \text{fumarate} + 2H^+ + 2e^-$$

The electrons are then fed through the protein to the two hydrophobic subunits in the membrane, where they recombine with two hydrogen ions and ubiquinone:

$$\text{ubiquinone} + 2H^+ + 2e^- \rightleftharpoons \text{ubiquinol}$$

Armstrong, Hill and others[4,5] have adapted the conventional techniques of voltammetry to measure redox potentials and redox reactions of the proteins, making it possible to study the kinetics of electron transfer in the millisecond time range. The method has also been used to follow the rapid interconversions of iron–sulphur clusters of the [3Fe–4S] and [4Fe–4S] types within proteins[7], and even the insertion of unusual metal ions such as thallium[8].

With succinate dehydrogenase, Sucheta *et al.* found that a graphite electrode presents a particularly receptive surface of hydrophobic patches and negatively charged carboxylate groups. The enzyme readily catalysed the oxidation of succinate to fumarate, giving electrons to the electrode surface, just as it does in the mitochondrial membrane. But when the enzyme's capability to catalyse the reverse reaction was addressed, fumarate reduction proceeded rapidly only under conditions of small driving force. Application of a more negative potential (which from classical considerations should accelerate the reduction) resulted instead in a dramatic attenuation of catalytic activity. This atypical behaviour contrasts with that of fumarate reductase, a closely related enzyme, which in anaerobic bacteria catalyses the reverse reaction from fumarate to succinate, and which shows reversible redox chemistry at the electrode (ref. 5 and F. A. Armstrong, personal communication). The intriguing behaviour of succinate dehydrogenase seems to be an intrinsic property of the enzyme, and is consistent with observations from steady-state kinetics of the enzyme in solution[1,9].

A tendency towards unidirectional electron transfer is also evident in other electron-transfer proteins, such as the hydrogenases, which catalyse the production or consumption of hydrogen gas by microorganisms. Some of these en-