Distant charge transport

Highlighting this issue of PNAS is a special feature comprising a Perspective and five research articles on the theme of long-range electron transfer. Distant electron transfers play key roles in aerobic respiration and photosynthesis, which work in concert: The oxygen that is evolved by photosynthetic organisms is the oxidant that sustains life in aerobic microbes and animals; and, in turn, the end products of aerobic respiratory metabolism, carbon dioxide and water, nourish photosynthetic organisms. Electron flow through proteins and protein assemblies in the respiratory and photosynthetic machinery commonly occurs between redox active cofactors that are separated by large molecular distances, often on the order of 10–25 Å. Although these cofactors are weakly coupled electronically, the reactions are remarkably rapid and specific. Understanding the underlying physics and chemistry of these distant electron transfer processes has been an overarching goal of theorists and experimentalists for many years.

Over 60 years ago, Szent-Györgyi (1) proposed that electrons travel between redox enzymes immobilized in membranes by using energy bands analogous to those found in semiconductors. Evans and Gergely (2) took issue with this proposal a few years later, arguing that the very large band gaps in polypeptides rule out thermal semiconductivity as the mechanism of biological electron flow. Long before atomic-resolution structures were available, it was suspected that many of the redox centers embedded in biological membranes were separated by relatively long molecular distances. So, how are electrons transferred between these centers? One possibility, suggested by Chance and Williams in 1956 (3), is that protein conformational changes could bring distant redox cofactors into contact, thereby facilitating oxidation-reduction reactions. Millisecond times for dioxygen reduction by cytochrome oxidase would require electron transfers to occur in microseconds or less. How far can an electron travel through biological material in a few microseconds? Measurements of cytochrome oxidation rates in reaction centers by DeVault and Chance in the 1960s (4, 5) were interpreted by Hopfield in 1974 (6) in terms of a thermally activated electron tunneling kinetics model; and, in 1982, experiments on Ru-modified cytochrome *c* demonstrated that electron tunneling can occur on biologically relevant time scales over distances of 15–20 Å (7). Much subsequent work has established that long-range electron transfer reactions are key steps in the energy transduction pathways of all living organisms.

More than a half century of research has produced a remarkably detailed picture of the factors that regulate these electron tunneling processes. Systematic investigations of electron transfer in frozen glasses and designed donor(bridge)-acceptor complexes have played a central role in this effort (8). The paper by Wasielewski, Ratner, and coworkers (9) is an outstanding contribution in this area. Investigations of metal-modified proteins have elucidated the effects of distance and driving force on the rates of long-range electron transfers (10). As described by Beratan and coworkers (11), these modified proteins now serve as models for studies of the role of polypeptide dynamics on electron tunneling reactions. Electron transfers across protein–protein interfaces have been very actively investigated; articles in this issue by Hoffman and colleagues (12) and by Onuchic and colleagues (13) deal with this subject. Distant redox chemistry also is critically important in DNA, as discussed in the paper by Barton, David, and coworkers (14).

This collection of papers on long-range electron transfer is part of a series of PNAS special features highlighting forefront areas of multidisciplinary science, with a particular focus in the chemical sciences. Previous topics for special features have included: Bioinorganic Chemistry, Supramolecular Chemistry and Self-Assembly, Asymmetric Catalysis, Rapid Climate Change, Astrobiology, Science and Technology for Sustainable Development, Social and Behavioral Sciences, and, most recently, Natural Product Synthesis. An objective of these special feature issues is to advance the journal's initiative to expand its coverage of mathematics, physical sciences, and social sciences. PNAS continues to encourage submission of exceptional research articles in all areas of the natural sciences, social sciences, and mathematics.

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1. Szent-Györgyi, A. (1941) *Science* **93,** 609–611.
2. Evans, M. G. & Gergely, J. (1949) *Biochim. Biophys. Acta* **3,** 188–197.
3. Chance, B. & Williams, G. R. (1956) *Adv. Enzymol.* **17,** 65–134.
4. DeVault, D. & Chance, B. (1966) *Biophys. J.* **6,** 825–846.
5. DeVault, D., Parkes, J. H. & Chance, B. (1967) *Nature* **215,** 642–644.
6. Hopfield, J. J. (1974) *Proc. Natl. Acad. Sci. USA* **71,** 3640–3644.
7. Winkler, J. R., Nocera, D. G., Yocom, K. M., Bordignon, E. & Gray, H. B. (1982) *J. Am. Chem. Soc.* **104,** 5798–5800.
8. Wenger, O. S., Leigh, B. S., Villahermosa, R. M., Gray, H. B. & Winkler, J. R. (2005) *Science* **307,** 99–102.
9. Goldsmith, R. H., Sinks, L. E., Kelley, R. F., Betzen, L. J., Liu, W., Weiss, E. A., Ratner, M. A. & Wasielewski, M. R. (2005) *Proc. Natl. Acad. Sci. USA* **102,** 3540–3545.
10. Gray, H. B. & Winkler, J. R. (2005) *Proc. Natl. Acad. Sci. USA* **102,** 3534–3539.
11. Skourtis, S. S., Balabin, I. A., Kawatsu, T. & Beratan, D. N. (2005) *Proc. Natl. Acad. Sci. USA* **102,** 3552–3557.
12. Hoffman, B. M., Celis, L. M., Cull, D. A., Patel, A. D., Seifert, J. L., Wheeler, K. E., Wang, J., Yao, J., Kurnikov, I. V. & Nocek, J. M. (2005) *Proc. Natl. Acad. Sci. USA* **102,** 3564–3569.
13. Miyashita, O., Okamura, M. Y. & Onuchic, J. N. (2005) *Proc. Natl. Acad. Sci. USA* **102,** 3558–3563.
14. Yavin, E., Boal, A. K., Stemp, E. D. A., Boon, E. M., Livingston, A. L., O'Shea, V. L., David, S. S. & Barton, J. K. (2005) *Proc. Natl. Acad. Sci. USA* **102,** 3546–3551.