



COLLÈGE
DE FRANCE
—1530—

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THE JOHNSON RESEARCH FOUNDATION, SCHOOL OF MEDICINE,
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First principles design of water-soluble photochemical proteins engineered for solar energy conversion in living cells

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BIOGRAPHY

Les Dutton, Ph.D., formally known as P. Leslie Dutton, is the Eldridge Reeves Johnson Professor of Biochemistry and Biophysics, the director of the Johnson Foundation for Molecular Biophysics, and former chair of the Department of Biochemistry and Biophysics in the Perelman School of Medicine. After earning his doctorate in biochemistry at the University of Wales in 1967, he came to Penn the following year – and has been here ever since. The John Scott Award is by no means the only honor he has accrued in his carrier. Named a Fellow of the Royal Society in 1990, he is also a Fellow of the University College, Wales. Germany's Max Planck Institute presented him with the Frontiers in Biological Chemistry Award, and he has received the IBM Partnership Award. From Oxford University: the Senior Visiting Fellowship. From Cambridge University: the First Sir William Dunn Scholar.

ABSTRACT

We are designing and testing entirely novel photochemical proteins to be incorporated into the genome of living cells to provide a self-sustaining way to convert solar energy into useful chemical fuels. By intercepting light energy and initiating charge separation from the excited singlet state, while avoiding competing functions normal to natural photo-systems, these manmade photochemical proteins promise maximized engineering efficiencies solely directed to fuel production. We design these simply folded, light and redox active cofactor binding proteins, called maquettes, to meet photochemical requirements in the aqueous compartments of the cell. This simplifies expression, assembly, transport, and future catalytic steps of fuel production, ideally using water as a source of electrons.

Maquette design applies first principles of protein folding and cofactor assembly, with cofactor placement inspired by natural protein engineering. The creation of an oxygen transport maquette analogous to the hemoglobins, but without any sequence or fold similarity, is proof that a basic understanding of mechanistic engineering in complex natural proteins can clear the way to functional reproduction in simply designed maquettes. We are now applying first-principles molecular electron tunneling engineering drawn from a collective assessment of natural photo-systems.

This elementary molecular engineering of solar energy conversion we have revealed removes many difficulties in the construction of photochemical maquettes working in living microorganisms. While there are significant hurdles still to surmount, early developments are promising. A wide variety of maquettes are readily expressed in high, scalable yield. Maquettes integrate with the *in vivo* machinery of cofactor biogenesis and ligation of bilins, hemes and chlorophyll. They are compatible with membrane transport by either Tat or Sec transporters. Maquettes have also been fused with natural light-harvesting proteins (biliproteins) to support multi-cofactor light energy transport.