Articles

Mimicking Photosynthesis

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Although the concept of an artificial photosynthetic reaction center that mimics natural electron- and energy-transfer processes is an old one, in recent years major advances have occurred. In this review, some relatively simple molecular dyads that mimic certain aspects of photosynthetic electron transfer and singlet or triplet energy transfer are described. Dyads of this type have proven to be extremely useful for elucidating basic photochemical principles. In addition, their limitations, particularly in the area of temporal stabilization of electronic charge separation, have inspired the development of much more complex multicomponent molecular devices. The use of the basic principles of photoinitiated electron transfer to engineer desirable properties into the more complex species is exemplified. The multiple electron-transfer pathways available with these molecules make it possible to fine-tune the systems in ways that are impossible with simpler molecules. The study of these devices not only contributes to our understanding of natural photosynthesis, but also aids in the design of artificial solar energy harvesting systems and provides an entry into the nascent field of molecular electronics.

THE HARVESTING OF LIGHT ENERGY BY PLANTS AND ITS conversion to chemically useful forms is not only a fascinating scientific phenomenon, but also of utmost importance to mankind. Photosynthesis, ancient or modern, is responsible for our oxygenic atmosphere and fills most of our food and energy requirements and many of our raw materials needs. Why not, then, construct a synthetic device that derives energy from sunlight by using the basic principles of natural photosynthesis? This idea is not new. Schemes for using energy from the sun have been around for thousands of years, and mimicry of the photosynthetic process in the laboratory has been a goal since the birth of the science of photochemistry (*1*). However, the last few years have seen dramatic progress, including the synthesis of a variety of complex, multicomponent molecular species for artificial photosynthesis. There are several reasons for this. Our knowledge of the molecular basis of photosynthesis has increased tremendously as a result of a host of new investigations, including the x-ray structure determination of a bacterial reaction center that led to the most recent Nobel Prize in chemistry (*2*). In addition, new tools for the investigation of the interaction of light and matter have become available, such as laser-based spectroscopies on the subpicosecond time scale. Third, advances have been made in the synthesis of complex molecules, their separation by chromatographic techniques, and their characterization by nuclear magnetic reasonance (NMR) and mass spectrometry. Finally, substantial progress has been made in our understanding of the theoretical basis of photoinitiated electron transfer, which is at the heart of the photosynthetic process. In this review, we summarize some of the recent work in artificial photosynthesis and illustrate the concepts involved by means of several examples drawn mainly from our laboratory.

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Natural Photosynthesis

Natural photosynthesis encompasses a host of biochemical processes in which sunlight is used to produce energy-rich products, which in turn are used in the synthesis of a variety of materials necessary for the growth of the organism. We focus on the interesting early events in the sequence: the gathering of light energy and its conversion to chemical potential energy in the form of transmembrane electronic charge separation.

The process begins with the absorption of light. Most of this occurs in the antenna system of the organism, which can consist of arrays of chlorophyll molecules, carotenoid polyenes, or other pigments. These materials collect light energy in various regions of the solar spectrum and transfer the resulting excitation energy to a reaction center where the photochemistry occurs. Although there are a variety of types of reaction centers, we discuss the photosynthetic process in terms of the bacterial reaction centers, which are the best understood to date. These molecular assemblies consist of proteins that span a lipid bilayer membrane and a variety of small organic molecules that are bound by intermolecular forces. Typically, these small molecules include four bacteriochlorophylls, two of which are in van der Waals contact and are referred to as the "special pair." The special pair is the trap for singlet excitation. In addition, the reaction center contains two bacteriopheophytins (bacteriochlorophylls which lack the central magnesium atom), a carotenoid polyene and two quinone molecules. These small organic species, which are organized by the protein host, perform the basic photochemistry.

In general, the excited states of molecules are both better electron donors and better acceptors than the ground states. In a reaction center, the excited singlet state of bacteriochlorophyll in the special pair acts as the primary photoreducing agent. The net result of the early steps of photosynthesis is transmembrane charge separation. However, electron transfer over such a large distance (~30 Å) is much too slow to compete with other processes that drain energy from the excited state. Thus, photosynthetic organisms have developed a clever strategy that involves a sequence of short-range, rapid electron-transfer steps. Within about 3 ps (1 ps = 10^{-12} s) after excitation, the special pair donates an electron to a bacteriopheophytin molecule, with the help of a nearby monomeric bacteriochlorophyll. Within a few hundred picoseconds, this bacteriopheophytin passes an electron on to a quinone molecule, which subsequently

donates an electron to a second quinone on the cytoplasmic side of the membrane. The positive charge left behind on the special pair is neutralized by electron transfer from a heme porphyrin of a cytochrome on the opposite, periplasmic side of the membrane. The transmembrane charge-separated state is formed with a quantum yield approaching unity, and has preserved a significant fraction of the energy of the bacteriochlorophyll singlet state. The large separation of the positive and negative charges, enforced by the membrane, prevents rapid charge recombination so that the stored energy can be used to fulfill the needs of the organism.

Simple Artificial Photosynthetic Systems

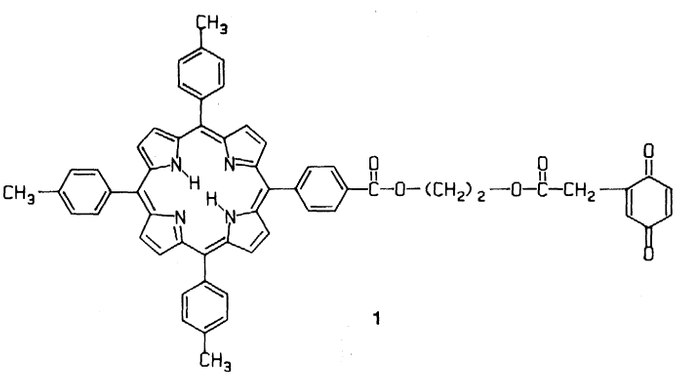
Artificial photosynthetic systems, broadly defined, encompass many fields of science, including solid-state chemistry, materials science, polymer science, organic and inorganic chemistry, and biochemistry. We confine our discussion to systems that use the types of small organic molecules found in the natural system (chlorophylls, quinones, and such) but that do so without the protein component of the reaction center.

The simplest approach to the problem is to dissolve one or more of the organic reaction center components in a solvent and study the resulting solution. This approach has taught us a great deal about the photophysical properties of the pigments in question and their solution photochemistry. However, such systems are in general not very good models for photosynthetic electron transfer. In solution, electron-transfer rates are limited by the rate of diffusion of the donors and acceptors, and rates approaching the picosecond time scales of reaction centers are thus precluded. In fact, although photosynthetic electron transfer involves excited singlet states, most solution studies at normal concentrations are restricted to the much longer lived triplet states of the pigments. In addition, electron transfer is a sensitive function of donor-acceptor separation and orientation. Control of electron transfer therefore requires control of these factors, which is impossible with unlinked molecules in solution. Finally, even if photoinitiated charge separation were achieved, the lifetime of the resulting charge-separated state would be severely limited by diffusion-controlled charge recombination.

Thus, much of the effort in the design and synthesis of artificial photosynthetic systems has involved devising ways to decrease the entropy of the system by imposing the proper constraints on the spatial relations among the pigments, donors, and acceptors. Although there are several approaches to this problem, we concentrate on artificial devices in which the structural role of the reaction center proteins is replaced by covalent chemical linkages that control intercomponent relations.

The simplest such devices are molecular dyads. Although many systems containing linking chromophores have been reported, most of the work in the photosynthesis area has concentrated on three types of systems. In the tetrapyrrole area, the preparation of the first covalently linked porphyrin dimers was described in 1972 (*3*). In 1976, several dimers of chlorophyll derivatives (designed to mimic the reaction center special pair) were reported (*4, 5*). Since that time, a large variety of multicomponent tetrapyrrole species have been prepared and studied (*6*). Carotenoid polyenes linked to porphyrins and chlorophyll derivatives have also been investigated (*7–11*). Some of these dyads successfully mimic the antenna function of carotenoids, wherein the polyene absorbs light in regions of the solar spectrum where chlorophylls are not strong absorbers and transfers singlet excitation to chlorophyll where it may be used for photosynthetic work in the usual way. Other carotenoporphyrins can be used to elucidate the role of carotenoids in photoprotection from singlet oxygen damage. Singlet oxygen ($^1\Delta_g$) is the lowest excited state of the oxygen molecule, and is an extremely reactive species that is deleterious to living tissue. In fact, this is apparently the basis of a new phototherapy for cancer treatment (*12*). Because the triplet states of most chlorophylls are very good sensitizers for the production of singlet oxygen, organisms that perform aerobic photosynthesis must have protection against singlet oxygen damage. Carotenoid polyenes quench chlorophyll triplet states before they can interact with oxygen and also deactivate singlet oxygen itself. The carotenoporphyrin model system studies have helped delineate the structural and energetic requirements for efficient photoprotection. Finally, most of the molecular dyads constructed for the mimicry of photosynthetic electron transfer have been covalently linked porphyrin-quinone (P-Q) systems. We discuss these in some detail and show how they have led to more complex artificial photosynthetic devices.

The earliest P-Q systems (structures **1** and **2**) were prepared by



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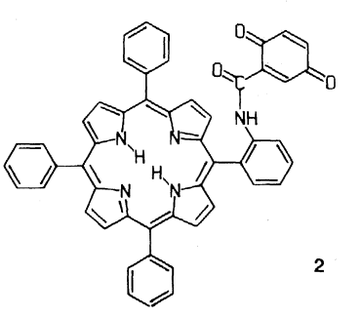

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Kong and Loach (*13*) and by Tabushi and co-workers (*14*), respectively. This early work has been followed by an avalanche of reports on related species; the field has recently been reviewed (*15*). In these systems, the tetraarylporphyrin plays the role of chlorophyll as the excited state electron donor, and the quinone acts as the acceptor. Excitation of the porphyrin generates its first excited singlet state (^{1}P-Q) (Fig. 1). This state may, of course, decay by the usual photophysical processes of intersystem crossing to the triplet state, internal conversion, and fluorescence. Photoinitiated electron transfer competes with these processes to generate a charge-separated state $P^{\cdot+}$-$Q^{\cdot-}$. This state preserves some fraction of the energy of the excited singlet state as chemical potential. The amount of energy stored depends upon the redox properties of the dyad. The quantum yield of the $P^{\cdot+}$-$Q^{\cdot-}$ state depends upon the details of the system, but can approach unity with proper molecular architecture.

Studies of porphyrin-quinone molecular dyads (*15*) and a variety of other ingenious covalently linked donor-acceptor molecules (*16–18*), coupled with theoretical interpretations of the electron-transfer process, have substantially increased our knowledge of the factors that influence electron transfer. In particular, the dependence of the

electron-transfer rate constant on the free-energy change during the reaction (for example, the thermodynamic driving force for conversion of ^{1}P-Q to P$^{\cdot+}$-Q$^{\cdot-}$ in Fig. 1) and the donor-acceptor separation has been investigated. The effects of donor-acceptor orientation, the solvent, the intervening linkage or other medium, and the temperature are also being studied at this time (*15–17*).

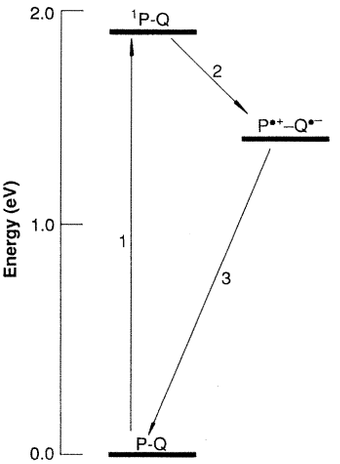


Fig. 1. Energy level diagram for a typical porphyrin-quinone dyad molecule that exhibits photoinitiated electron transfer from the porphyrin first excited singlet state. The photophysical pathways that compete with electron transfer from the singlet state are not shown.

Molecular Triads

As mentioned above, the porphyrin-quinone systems do a good job of modeling certain aspects of photosynthetic electron transfer. However, a conspicuous limitation of these molecules is their inability to achieve temporal stabilization of the photoproduced charge-separated state. A successful artificial reaction center should be able to maintain an energetic charge-separated state long enough to allow extraction of useful work from it. Typically, the P$^{\cdot+}$-Q$^{\cdot-}$ state survives only a few hundred picoseconds or less in solution. The reason for this is that the geometric factors that facilitate rapid and therefore efficient photoinitiated charge separation also favor rapid charge recombination to the ground state. A viable solution to this problem is to mimic the strategy used in the reaction center itself: multistep electron transfers that occur through a series of donors or acceptors or both.

In 1983, two biomimetic molecular triad systems that use this strategy were reported. One of these was carotenoid-porphyrin-quinone **3** (*19, 20*), and the other was a porphyrin-diquinone molecule (*21*). In the latter species, the redox potentials were adjusted in order to favor sequential electron transfer from the porphyrin first excited singlet state to a primary quinone acceptor, and then on to a secondary quinone. The carotenoporphyrin-quinone species achieved by far the greatest temporal stabilization of charge separation and mimicked several other aspects of photosynthesis as well, and is discussed in some detail.

Triad **3** consists of a synthetic carotenoid polyene (C) covalently linked to a porphyrin (P), which in turn bears a benzoquinone electron acceptor (Q). High-resolution ^{1}H NMR experiments (*22*) have shown that the molecule adopts a linear conformation in solution, with the carotenoid and quinone moieties extended out and away from the porphyrin rather than folded back across it. The absorption spectrum of **3** indicates that the porphyrin, carotene, and quinone each act independently, rather than as a single large chromophore. A variety of time-resolved spectroscopic measurements have demonstrated that absorption of light by the porphyrin moiety of **3** is followed by the sequence of events depicted in Fig. 2. The porphyrin first excited singlet state can decay by a number of photophysical pathways, but competing with these is electron transfer to produce C-P$^{\cdot+}$-Q$^{\cdot-}$. As one would expect by analogy to the porphyrin-quinone molecules, the charge recombination reaction that regenerates the ground state and releases the stored energy as heat is very fast. However, a second electron transfer, from the carotenoid to the porphyrin radical cation, competes with charge recombination and produces a new charge-separated state C$^{\cdot+}$-P-Q$^{\cdot-}$. Charge recombination is extremely slow in this species: in dichloromethane the lifetime of C$^{\cdot+}$-P-Q$^{\cdot-}$ is about 300 ns, and in butyronitrile solution it is ~2 μs. Thus, the lifetime of the final charge-separated state in the triad is about four orders of magnitude longer than that in the related porphyrin-quinone systems. This tremendous increase is the result of the biomimetic two-step electron-transfer sequence that rapidly achieves a large spatial separation between the positive and negative charges.

Electrochemical measurements of the redox potentials of **3** and related model compounds show that of the 1.9 eV of energy inherent in the porphyrin first excited singlet state, ~1.4 eV is

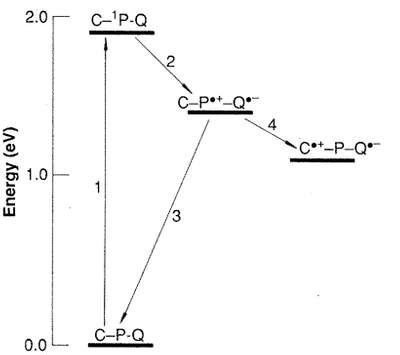


Fig. 2. Energy levels and electron-transfer pathways for a carotenoid-porphyrin-quinone triad. The energies shown here are those estimated for triad **3** from cyclic voltammetric measurements. In these photosynthesis mimics, the final C$^{\cdot+}$-P-Q$^{\cdot-}$ charge-separated state has a long lifetime, and preserves a significant fraction of the energy of the initial excited state.

preserved in the intermediate C-P$^{\cdot+}$-Q$^{\cdot-}$ species, and ~1.1 eV remains in C$^{\cdot+}$-P-Q$^{\cdot-}$. Thus, the final state is a highly energetic species that conserves a substantial portion of the energy of the initial excited state. The quantum yield of C$^{\cdot+}$-P-Q$^{\cdot-}$ ranges up to ~0.25, depending on conditions.

The triad molecule **3** is an example of a fairly complex molecular device that has been assembled from a variety of components (carotenoid, porphyrin, and quinone) joined by chemical linkages. It is thus an excellent candidate for molecular engineering to enhance selected properties. Such engineering involves altering either the moieties themselves (which affects redox properties, absorption spectra, and such) or the linkages (which affects the electronic coupling between the moieties, their conformational mobility, and other properties). We give two examples of the application of this approach below.

Although the quantum yield of long-lived charge separation in reaction centers approaches unity, such high quantum yields were not obtained with **3**. In dichloromethane solution, for example, the quantum yield of C$^{\cdot+}$-P-Q$^{\cdot-}$ was only 0.04. Electron-transfer theories suggest several strategies for overcoming this limitation. One approach relies on the finding that the electron-transfer rate constant (k_{et}) depends exponentially on the donor-acceptor separation r (*16, 18*).

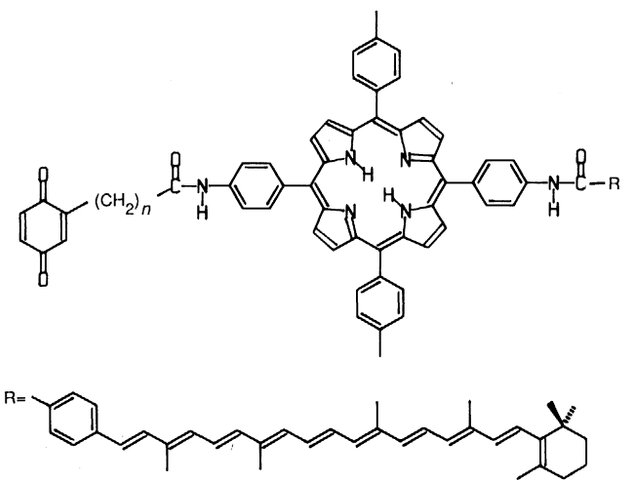
$$k_{et} = \nu \exp(-\alpha r) \quad (1)$$

In a simple donor-acceptor system such as a P-Q molecule, an increase in r can only reduce k_{et} and therefore reduce the quantum yield of charge separation. In the triad, however, things are not so simple. The quantum yield of C$^{\cdot+}$-P-Q$^{\cdot-}$ depends not only upon the quantum yield C-P$^{\cdot+}$-Q$^{\cdot-}$, but also on the ratio of the rate constants for the charge-recombination reaction (step 3 in Fig. 2) and the

second electron-transfer step (step 4). Time-resolved fluorescence measurements reveal that in dichloromethane, the quantum yield of the initial charge separation (step 2) is 0.97. Thus the low overall yield of C^{+}-P-Q^{-} in this solvent must be due to unfavorable partitioning between steps 3 and 4.

The qualitative effects of altering the porphyrin-quinone separation in a molecule such as **3** may be predicted from Eq. 1. Increasing the distance will slow down the initial charge separation (step 2) and the rate of the charge-recombination reaction (step 3), but should have little effect on the rate of step 4 because that step does not involve porphyrin-quinone electron transfer. The net result of these effects could in principle lead to an overall increase or decrease in the quantum yield of the final charge-separated state, depending upon the magnitudes of the rate constants involved.

Triad molecules **4** through **6** and some related porphyrin-quinone dyads were prepared in order to investigate this possibility (*22, 23*). In the series of triads **3** through **6**, the structures of the carotenoid, porphyrin, and quinone moieties are identical, but the porphyrin-quinone linkage has been altered by inserting methylene spacer groups, each of which increments the porphyrin-quinone separation. The time-averaged solution conformations of these molecules were determined from porphyrin-ring-current–induced shifts in the porphyrin ^{1}H NMR resonances of the molecules (*22, 24*). The species were then studied in dichloromethane solution by time-correlated single-photon-counting measurements of fluorescence lifetimes in order to determine the rate constants for the initial electron-transfer step (step 2). The rate constants varied from $9.7 \times 10^{9}\ s^{-1}$ for **3** to $1.5 \times 10^{8}\ s^{-1}$ for **6**, and the results were consistent with the exponential decrease with distance predicted by Eq. 1 (*22*). However, the yield of the final C^{+}-P-Q^{-} state, as determined by laser-induced transient absorption studies, showed more complex behavior. Addition of a second methylene spacer group to the molecule (structure **4**) increased the quantum yield of C^{+}-P-Q^{-} by a factor of 1.44, but inclusion of more spacers as in **5** and **6** decreased the yield below that seen for **3** itself. Thus, although the second methylene group decreases the quantum yield of step 2 somewhat because of the increased donor-acceptor separation, it also decreases the rate of the charge-recombination reaction (step 3) relative to that of step 4. The overall result is an increase in the quantum yield of the final charge-separated state. The molecules with three or four methylene spacers also have a favorable ratio of step 4 to step 3, but the loss of efficiency in step 2 now contributes to an overall reduction in the yield of the final C^{+}-P-Q^{-} state relative to triads **3** and **4**.



3 *n*=1 **5** *n*=3
4 *n*=2 **6** *n*=4

Electron-transfer rate constants in general do not depend linearly on the reaction free-energy changes, which provides a second avenue for molecular engineering in the triads. Marcus has proposed (*16, 25, 26*) that the electron-transfer rate constant is given by Eq. 2.

$$k_{et} = A \exp\left[\frac{-(\Delta G^{\circ}+\lambda)^{2}}{4\lambda k_{b} T}\right] \quad (2)$$

The pre-exponential factor A includes the electronic matrix element that describes the coupling of the reactant state with that of the products, ΔG° is the free-energy change for the reaction, k_b is Boltzmann's constant, λ is the total reorganization energy, which includes both solvent reorganization energy and changes in internal vibrational modes, and T is the absolute temperature. Thus, electron-transfer rates increase with increasing standard free-energy change ("normal" behavior) up to a maximum ($\lambda = -\Delta G^{\circ}$), and then decrease with additional thermodynamic driving force ("inverted" behavior). Investigations of simple porphyrin-quinone systems indicate that for this class of molecules, the dependence of electron-transfer rate constants on thermodynamic driving force is indeed nonlinear (*16, 27, 28*). The maximum electron-transfer rate most probably occurs at about 1 eV.

This dependence may be used to control the quantum yield of charge separation in a triad. For example, raising the energy of the C-P^{+}-Q^{-} state in Fig. 2, while leaving the energies of the other states unchanged, should have three effects:

1) The rate of the initial charge separation (step 2) should decrease (normal Marcus behavior).

2) The rate of electron transfer from the carotenoid to the porphyrin radical cation (step 4) should increase because the driving force for the reaction increases (normal Marcus behavior).

3) The rate of charge recombination (step 3) should decrease, because this reaction is highly exergonic and should exhibit inverted behavior. Proper tuning of the energy of C-P^{+}-Q^{-} might lead to a relatively small decrease in the quantum yield of C-P^{+}-Q^{-} accompanied by a large increase in the efficiency of step 4, and consequently in the quantum yield of the final C^{+}-P-Q^{-} state.

This strategy was tested by preparing an analog of triad **3** in which the two *p*-tolyl substituents on the porphyrin macrocycle were replaced by pentafluorophenyl groups (*29*). The electronegative nature of the fluorinated groups raises the energy of C-P^{+}-Q^{-} by ~0.2 eV relative to the same state in **3**, but the energies of the other states involved are essentially unchanged. Transient spectroscopic studies demonstrate that the substitution has led to a sevenfold increase in the quantum yield of C^{+}-P-Q^{-} (to 0.30 in dichloromethane). Time-resolved fluorescence decay studies show that the efficiency of step 4 has been increased by a factor of 18 (to 0.73).

Multicomponent Devices

The initial work with triad molecules mentioned above was followed in 1985 by a report of a donor-porphyrin-acceptor triad featuring a dimethylaniline donor instead of a carotenoid which also formed a long-lived charge-separated state with a high quantum yield (*30*). This molecule incorporated relatively rigid triptycene-based linkages between the moieties as a means of controlling donor-acceptor distances. A diporphyrin-quinone three-part system was reported in the same year (*31*). With the generality of the concept well established, a variety of three-part molecules for photoinitiated charge separation based on organic or inorganic chromophores have recently been described (*32*), and the research area is extremely active.

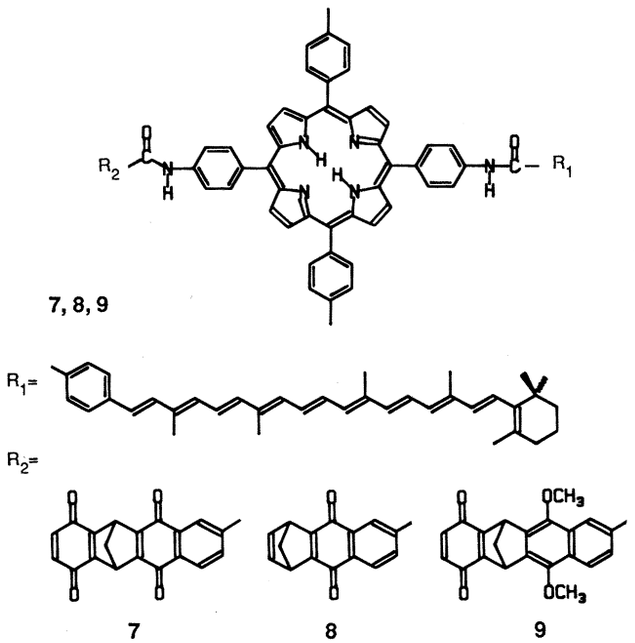
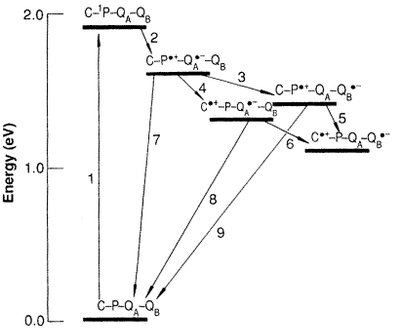


Fig. 3. The tetrad C-P-Q_A-Q_B features two electron-transfer pathways that compete with the first charge-recombination reaction step 7. Both of these ultimately lead to the same final charge-separated state.



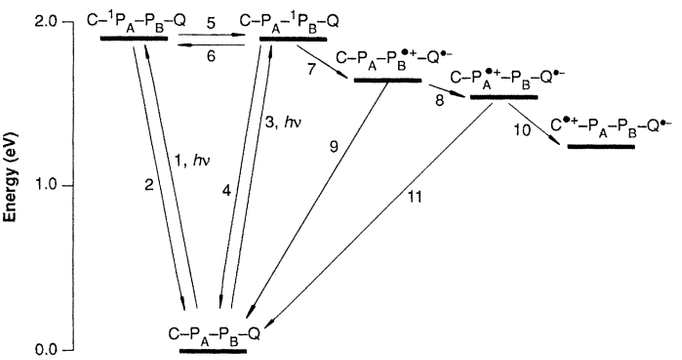


Fig. 4. The C-P_A-P_B-Q tetrad molecule not only undergoes photoinitiated electron transfer, but also demonstrates the transfer of singlet excitation between the porphyrin moieties. Such energy transfer is an important feature of the natural photosynthetic apparatus.

The triad devices have demonstrated that multicomponent molecular species allow investigations of cooperative and competitive physical and chemical phenomena that are precluded with simpler molecules. The synthesis and study of a few still more complex many-component systems have already been reported.

The carotene-porphyrin-diquinone tetrad 7 was prepared in order to explore the strategy of increasing the quantum yield of long-lived charge separation by providing several convergent electron-transfer pathways (*33*). Among the design considerations for this molecule are the saturated, bicyclic bridge which links the two quinone species and the amide bonds that join the porphyrin to the other moieties. These linkages ensure that the molecule remains in an extended conformation in solution, rather than folding up into a geometry that could short-circuit the multistep electron-transfer sequence. This three-dimensional arrangement has been confirmed by ^{1}H NMR spectroscopy. In addition, the benzoquinone moiety (Q_B) at the end of the C-P-Q_A-Q_B chain is a better electron acceptor than the naphthoquinone (Q_A), which is adjacent to the porphyrin. This arrangement favors sequential electron transfer from the porphyrin to the benzoquinone through a naphthoquinone radical anion intermediate.

The response of the tetrad to illumination is diagrammed in Fig. 3. Photoinitiated electron transfer from C-^{1}P-Q_A-Q_B (step 2 in Fig. 3) gives rise to a C-$P^{\cdot+}$-$Q_A^{\cdot-}$-Q_B species similar to those seen with other porphyrin-quinone systems. The rate constant for this process is $\geq 2 \times 10^{10}$ s^{-1}, which ensures a quantum yield near unity for this step. Although C-$P^{\cdot+}$-$Q_A^{\cdot-}$-Q_B should tend to rapidly undergo charge recombination (step 7), two additional electron-transfer reactions (steps 3 and 4) compete with charge recombination to yield two new intermediates, C-$P^{\cdot+}$-Q_A-$Q_B^{\cdot-}$ and C^+-P-$Q_A^{\cdot-}$-Q_B. Steps 5 and 6 compete with recombination of these intermediates to yield the same final charge-separated state C^+P-Q_A-$Q_B^{\cdot-}$. In dichloromethane solution at 295 K, this final state is formed with a quantum yield of 0.23 and a lifetime of 460 ns. At 240 K, the quantum yield increases to 0.50.

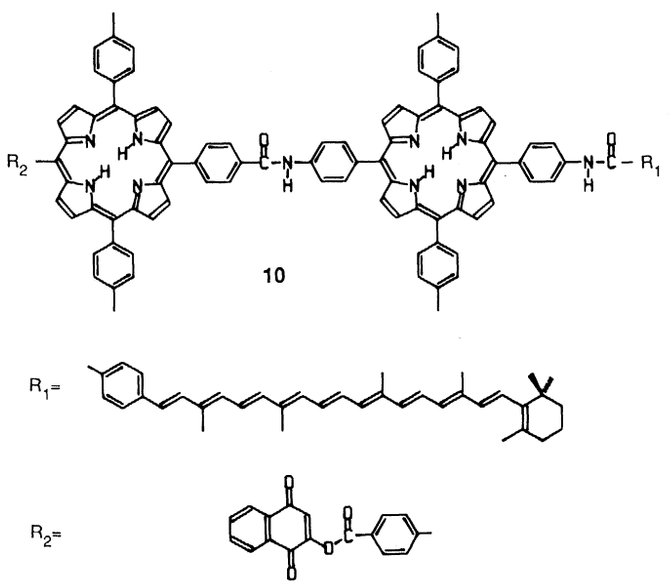
The consequences of the multiple electron-transfer steps available to 7 can best be appreciated by comparison of the results for this molecule with those obtained for related species **8** and **9**. Triad **8** is similar to 7, but lacks the terminal benzoquinone moiety (Q_B). Excitation of the porphyrin leads to the production of C-$P^{\cdot+}$-$Q_A^{\cdot-}$ with a quantum yield near unity, as is the case with 7. However, the final charge-separated state $C^{\cdot+}$-P-$Q_A^{\cdot-}$ is formed with a yield of only 0.04 because only a single, relatively inefficient electron-transfer path (analogous to step 4 in Fig. 3) competes with charge recombination of C-$P^{\cdot+}$-$Q_A^{\cdot-}$. Tetrad 7 has two electron-transfer pathways competing with charge recombination (one of them evidently relatively effective), and thus the final quantum yield is much higher.

Molecule **9** also resembles 7, but the electron-accepting properties of the naphthoquinone moiety have been substantially reduced by its conversion to a dimethoxynaphthalene derivative. Excitation of this molecule gives a final charge-separated state $C^{\cdot+}$-P-Q_A(OMe)$_2$-$Q_B^{\cdot-}$ with a quantum yield of 0.11 (Me, methyl). The decreased quantum yield of **9**, relative to 7, is due to several factors, one of which is that two short-range, efficient electron-transfer pathways (steps 2 and 3 in Fig. 3) have been replaced by one long-distance electron-transfer pathway that is less efficient and that yields C-$P^{\cdot+}$-Q_A(OMe)$_2$-$Q_B^{\cdot-}$ directly from C-^{1}P-Q_A(OMe)$_2$-Q_B.

A second example of a complex multicomponent molecular system for artificial photosynthesis is C-P_A-P_B-Q tetrad **10** (*34*). The two porphyrin moieties have essentially identical absorption spectra, and therefore their first excited singlet states are nearly isoenergetic. However, they differ in their redox properties because of the different substituents on the porphyrin rings. This difference leads to the interesting sequence of photochemical events shown in Fig. 4. Excitation of the molecule in anisole solution with 590-nm laser light leads to essentially equal populations of the two porphyrin first excited singlet states. Kinetic analysis of the decay of the porphyrin fluorescence of **10** and related model systems indicates that singlet excitation is transferred back and forth between the porphyrins at a rate faster than or comparable to the rates of the

other processes that depopulate the singlet states. Such singlet energy transfer is also observed in the antenna systems of photosynthetic organisms and is the means by which excitation energy is funneled to the reaction centers. In addition to the other decay pathways indicated in Fig. 4, C-P_A-^1P_B-Q decays by electron transfer to the quinone (step 7, $k_7 = 2.4 \times 10^8\ s^{-1}$). The resulting C-$P_A$-$P_B^{\cdot+}$-$Q^{\cdot-}$ species is partitioned between charge recombination (step 9) and additional electron transfer to yield a final $C^{\cdot+}$-P_A-P_B-$Q^{\cdot-}$ state. The final species is formed with a yield of 0.25, and has a lifetime of 2.9 μs.

The energetics shown in Fig. 4 suggest the formation of an intermediate C-$P_A^{\cdot+}$-P_B-$Q^{\cdot-}$ species. However, these energetics were derived from cyclic voltammetric studies and do not allow for any stabilization of the charges involved by coulombic forces. If such stabilization is great enough to drop the energy of C-P_A-$P_B^{\cdot+}$-$Q^{\cdot-}$ significantly below that of C-$P_A^{\cdot+}$-P_B-$Q^{\cdot-}$, then the latter species might not be a discrete intermediate in the electron-transfer process. However, the porphyrin P_A might still facilitate electron transfer through superexchange interactions, which would involve the participation of electronic orbitals of P_A in the coupling between the acceptor $P_B^{\cdot+}$ and the carotenoid electron donor. Such superexchange interactions may also play a role in bacterial reaction centers, where a bacteriochlorophyll monomer may mediate electron-transfer interactions between the special pair and the bacteriopheophytin acceptor (*35*).



Conclusions

As the examples discussed above illustrate, the sophistication of synthetic multicomponent species that mimic natural photosynthesis has increased tremendously in recent years. Chemists now have the tools necessary to construct complicated molecular devices, determine their structure, and study their spectroscopic, photochemical, and photoelectrochemical properties. The number and complexity of such systems should increase rapidly in the next few years. What can we learn from these devices? The most obvious application is to photosynthesis itself. Model systems of the type discussed here allow one to abstract certain aspects of the natural reaction center and study them in a well-defined environment from which unnecessary complications have been eliminated. Thus studies of artificial photosynthetic systems complement studies of the natural apparatus. Second, artificial photosynthetic molecules should help point the way to the design of new devices to harvest solar energy that use the basic chemistry and physics of photosynthesis as well as some of the strategies for exploiting these basic principles that have evolved in natural systems. Simple, well-designed dyads and triads are ideal for elucidating the basic principles of photoinitiated electron transfer, whereas the more complex devices allow one to study cooperative and competitive effects in systems like the reaction center that have a variety of potential electron- and energy-transfer pathways.

Finally, complex molecular devices such as those discussed here may provide an entry into the field of molecular electronics. Molecular electronics, broadly defined, is the design of electronic devices at the molecular level, rather than the materials level. In the limit, one could envision electronic circuits constructed from molecule-sized components. For example, a shift-register memory based on porphyrin-diquinone molecules has recently been proposed (*36*). In addition, the physical size of the devices described above (a length of ~75 Å for tetrad **10**) is adequate to cross boundaries such as monolayers or lipid bilayers (*37*), and approaches that necessary to span the distance between microfabricated electrical contacts. Although the concept is fascinating, the problems inherent in the design and preparation of molecular electronic devices are formidable. In this context, the natural photosynthetic reaction center is an efficient photovoltaic device on the molecular level, and can serve as a paradigm for man-made devices.

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38. Much of the work performed at Arizona State University was supported by the National Science Foundation (CHE-8515475, INT-8514252, and INT-8701663) and by the Division of Chemical Sciences, Office of Basic Energy Sciences, Office of Energy Research, U.S. Department of Energy (DE-FG02-87ER13791). We gratefully acknowledge the contributions of the many colleagues, students, and postdoctoral associates who have contributed to the work reviewed here, and whose names are listed in the references. Publication no. 9 from the Arizona State University Center for the Study of Early Events in Photosynthesis. The Center is funded by U.S. Department of Energy grant no. DE-FG02-88ER13969 as part of the USDA/DOE/NSF Plant Science Center program.

The Purine Path to Chemotherapy

GERTRUDE B. ELION

Research on antimetabolites of nucleic acid purines led to drugs for the treatment of acute leukemia (6-mercaptopurine and thioguanine), gout and hyperuricemia (allopurinol), and herpesvirus infections (acyclovir), and for the prevention of organ transplant rejection (azathioprine).

IN 1944, WHEN I JOINED THE WELLCOME RESEARCH LABORATORIES, the state of knowledge of nucleic acids was rather rudimentary. The prevailing theory was that there were two purines and two pyrimidines in each tetranucleotide and that these tetranucleotides were strung together in some fashion, but the sequences were not known. The nature of the internucleotide linkage had not been established and the helical structure of DNA had not yet been proposed.

In 1940 Woods (*1*) and Fildes (*2*) had put forth the antimetabolite theory to explain the action of sulfonamides on bacteria, suggesting that the sulfonamides interfered with the utilization of a necessary nutrient, para-aminobenzoic acid. Hitchings theorized that, since all cells required nucleic acids, it might be possible to stop the growth of rapidly dividing cells (for example, bacteria, tumors, and protozoa) with antagonists of the nucleic acid bases. One might hope to take advantage of the faster rate of multiplication of these cells compared with normal mammalian cells and eventually sort out the biochemical differences between various types of cells by the way they responded to these antimetabolites (*3, 4*). It was my assignment to work on purines, pteridines, and some other condensed pyrimidine systems.

It was, of course, necessary to have some biological systems to determine the potential activities of the new compounds. Essentially nothing was known at that time about the anabolic pathways leading to the utilization of purines for nucleic acid synthesis. A number of catabolic enzymes were known: nucleases, nucleotidases, nucleosidases, deaminases (for guanine, adenine, adenosine, and adenylic acid), xanthine oxidase, and uricase. In 1947 Kalckar described the reversibility of nucleoside phosphorylase (*5*). The enzymes guanase and xanthine oxidase were useful in our laboratory to examine the purines as substrates or inhibitors of these enzymes (*6, 7*). However, it was the microorganism *Lactobacillus casei* upon which we mainly relied. This organism could grow on adenine, guanine, hypoxanthine, or xanthine, provided the pyrmidine thymine was added. It could also synthesize purines and thymine, if given a source of folic acid in the form of liver powder. [The structure of folic acid was not elucidated until 1946 by the Lederle group (*8*)]. Hitchings and Falco had devised a screening test in which it was possible to determine whether a compound could substitute for thymine (*9*) or a natural purine (*4, 10*) or inhibit its utilization, and they could also determine whether a compound was a folic acid antagonist (*11*).

Few chemists were interested in the synthesis of purines in those days and I relied on methods in the old German literature. The transformation reactions were carried out mainly by the methods of Emil Fisher and the syntheses from pyrimidine intermediates by the methods of Traube. The direct replacement of oxygen by sulfur by the method of Carrington (*12*) also proved to be exceedingly useful for synthesizing the mercaptopurines (*13*).

In 1948 we found that 2,6-diaminopurine inhibited the growth of *L. casei* very strongly and that the inhibition was reversed specifically by adenine, but not by the other natural purines (*4, 14*). However, low concentrations of diaminopurine could also be reversed by folic acid, an attribute that diaminopurine had in common with other diaminopyrimidines and diaminopyrimidine condensed systems (*10*). Studies on a diaminopurine-resistant strain of *L. casei* revealed that it grew poorly on adenine as a source of purine. We deduced that adenine and 2,6-diaminopurine must be anabolized by the same enzyme, and that the product of diaminopurine anabolism interfered with purine interconversion (*15*). That enzyme was reported by Kornberg *et al.* in 1955 to be adenylate pyrophosphorylase (adenine phosphoribosyltransferase) (*16*). When

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