Simple Models for the Dynamics of Biomolecules: How Far Can We Go?

William Bialek,[a] Robert F. Goldstein,[b] and Steven Kivelson[c]

a) Institute for Theoretical Physics, University of California
Santa Barbara, California 93106
b) Department of Cell Biology, Stanford University School of Medicine
Stanford, California 94305
c) Department of Physics, State University of New York
Stony Brook, New York 11794

Biological macromolecules exhibit a remarkable variety of dynamical phenomena. As experimental methods for characterizing these phenomena have improved in the last decade, two theoretical questions have been brought into focus: To what extent are the observed dynamics relevant to biological function?, and Can we develop a simple physical picture of the functionally important dynamics?

Simple models have had impressive success in describing the dynamics of non-biological macromolecules, such as polyacetylene and other quasi-one-dimensional materials (1). In biological systems the most convincing success thus far has been the analysis of a particular photosynthetic electron transfer reaction in *Chromatium vinosum* (2) in terms of two electronic states coupled to a few key intra-molecular vibrational modes (3,4). Another well-studied example is the binding of small ligands to heme proteins, but in this case applicability of simple models (5) is the subject of considerable controversy (4,6). These particular molecules attracted theoretical attention because of their unusual kinetic behavior. Here we give preliminary accounts of our work on two systems which exhibit even more remarkable kinetics, the "activationless" electron transfers of bacterial photosynthesis (7) and the primary events following photon absorption in rhodopsin (8).

Activationless Electron Transfer

The rates of most chemical and biochemical reactions obey the Arrhenius law near room temperature, $k \sim Ae^{-E_a/k_B T}$. At very low T one sometimes observes a T-independent rate (e.g. Ref. 2) which can be understood in terms of quantum mechanical tunneling. For at least two of the electron transfer reactions in bacterial photosynthesis this low-temperature behavior is *not* observed to cross over into an Arrhenius regime; indeed the rate *decreases* slightly as T increases above ~ 200 K (9-11). In the one case which has been checked (12) this "activationless" behavior persists as the energy gap between reactants and products is varied by chemical substitution, and the reaction rate itself varies surprisingly little in response to these substitutions.

We have found a family of very simple models which account for activationless behavior over a wide range of energy gaps and other parameters. In the simplest case these models consist of two electronic states (reactants and products) coupled to two vibrational modes, with strong coupling to the lower mode and weak coupling to the higher mode. If we turn off the coupling to the high-frequency mode we can draw a one-dimensional schematic of the model as in Fig. 1. This single mode model, however, exhibits the conventional temperature dependence as in Ref. (2). The dependence on energy gap is also predicted to be very strong except in a small neighborhood around $\epsilon = \lambda$ (cf. Fig. 1). What is remarkable is that *extremely* weak coupling to a high frequency mode can quench both the Arrhenius T-dependence and the ϵ-dependence of the reaction rate at large ϵ.

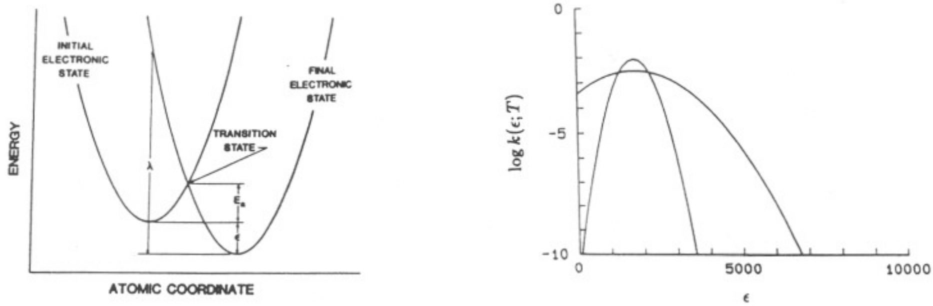

Figure 1: Reaction rates in a single mode model. (a) Coupling of electronic and vibrational states, identifying the energy gap ϵ, the classical activation energy E_a and the reorganization energy $\lambda = S\hbar\Omega$. In this picture the system is 'overcoupled'—$\lambda > \epsilon$, so increasing ϵ decreases the activation energy and increases the rate, as may be seen by pulling the final state energy curve downward while leaving other features of the picture fixed. When $\epsilon = \lambda$ the rate is maximal and E_a vanishes, but if ϵ increases further the rate decreases once again. (b) The reaction rate *vs.* ϵ with $S = 70$ and $\hbar\Omega = 25\,\mathrm{cm}^{-1}$, shown at 30 and 300 K. Note the strong T-dependence at almost all ϵ.

Quantitative calculations of the reaction rate in multi-mode models can be done using methods outlined earlier (13). To understand the effects of a high frequency mode we can make a much simpler argument. Imagine that we have solved the problem with only the lower mode, to give $k_L(\epsilon, T)$. When we add a high-frequency (Ω_H) mode there is a probability $P_n = e^{-S_H} S_H^n/n!$ to emit n phonons into this mode, with S_H the dimensionless electron-phonon coupling,[1] and since $\hbar\Omega_H \gg k_B T$ there are no phonons to absorb. But if n phonons go into the higher mode the lower mode sees an energy gap which is reduced by $n\hbar\Omega_H$. The rate is then

$$k(\epsilon, T) = e^{-S_H} \sum_{n=0}^{\infty} \frac{S_H^n}{n!} k_L(\epsilon - n\hbar\Omega_H, T). \tag{1}$$

If ϵ is large we can see from Fig. 1 that $\epsilon \to \epsilon - n\hbar\Omega_H$ produces a very large increase in $k_L(\epsilon, T)$ and a substantial decrease in the classical activation energy. If S_H is small, there is a penalty $\sim S_H^n/n!$ to pay, but if Ω_H is large enough the gain $k_L(\epsilon - n\hbar\Omega_H)/k_L(\epsilon)$ will always dominate. Indeed, no matter how small S_H may be, if Ω_H is sufficiently large the sum in Eq.

---

[1] If ΔQ_μ is the structural change of the molecule along mode μ between reactants and products, $S_\mu = (\Delta Q_\mu / 2q_\mu^\circ)^2$, with q_μ° the rms quantum zero-point motion along this mode. Typical values for S_μ are discussed in Ref. 4.

(1) will be dominated by terms where the effective energy gap, $\epsilon - n\hbar\Omega_H$ is near the peak of $k_L(\epsilon)$, which is the point where the classical activation energy vanishes! Once the Arrhenius behavior has been eliminated, thermal expansion (9) or other factors can contribute to a slight slowing of the rate with increasing temperature.

These results are illustrated by quantitative calculations in Fig. 2. These plots reproduce the main features of the data in Refs. (9–12), namely the lack of significant Arrhenius T-dependence and weak ϵ-dependence at large ϵ, and this qualitative agreement persists over a wide range of parameters. Discussions of the conditions for activationless behavior and possible tests of our scenario are given in Ref. 7. Perhaps the most important conclusion from these calculations is that quantum mechanical effects associated with a high frequency mode can *qualitatively* change the functional behavior of a biomolecule at room temperature, even though most of the reorganization energy is stored in low frequency (~ classical) degrees of freedom.

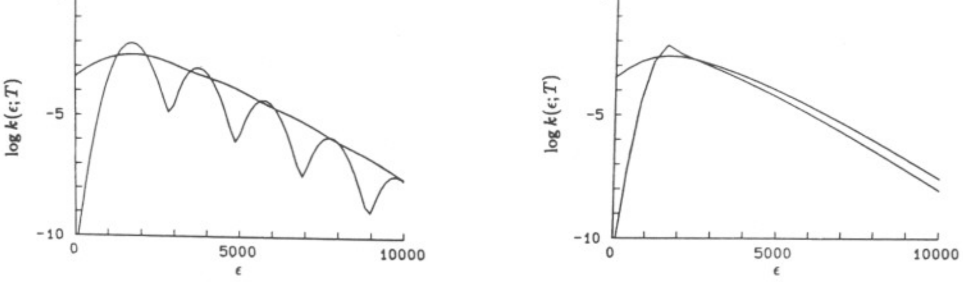

Figure 2: Calculations of the reaction rate for a model of two electronic states coupled to vibrational modes at $\hbar\Omega_L = 25\,\mathrm{cm}^{-1}$ ($S_L = 70$) and $\hbar\Omega_H = 2000\,\mathrm{cm}^{-1}$ ($S_H = 0.1$). (a) Calculations from Eq. (1), where quantum oscillations associated with Ω_H are visible at 30 K but have washed out at 300 K. (b) Calculations which systematically discard the oscillations but are otherwise fully quantum mechanical. These results are more representative of a molecule with several high frequency modes at different frequencies, where the quantum oscillations associated with different modes 'beat' against one another and are essentially unobservable. Rates are again at 30 and 300 K; the higher temperature corresponds to the faster rate near $\epsilon = 0$. Note that in each case the T- and ϵ-dependence of the rate at large ϵ is substantially reduced relative to Fig. 1.

Primary Events in Vision

Photon absorption by rhodopsin triggers *cis/trans* isometrization of the retinal chromophore, and recent experiments indicate that this large structural change is essentially complete in 3 picoseconds with the formation of bathorhodopsin. The time scale of the primary event is even shorter (14): the quantum yield for fluorescence is just 10^{-5}, and with a radiative lifetime of 5 nanoseconds this implies that the initial excited state is irreversibly depleted in less than 50 fs. To understand how irreversibility arises on such a short time scale we have performed simulations of the coupled electronic and vibrational dynamics of retinal using models derived from our understanding of the simplest infinite chain polyene $(\mathrm{CH})_x$ — polyacetylene (1,15). Here we give a qualitative picture of our results.

Although polyacetylene is conjugated, its ground state exhibits bond-alternation: successive C-C bonds are alternatively short and long. As a result there are two inequivalent ground states — short/long/short/long... and long/short/long/short... . We can imagine that portions of the molecule are in one state and other portions in the other; at the boundaries of these regions there must be "kinks" in the atomic configuration, which are termed solitons. These kinks bind a single electronic state, and these localized soliton-bound levels dominate the low-energy dynamics and optical spectra. If we excite the electrons with an optical photon, the excited electron will "dig a hole" in the atomic structure of the molecule, creating a configuration which corresponds to a pair of solitons. What is remarkable is that the excess energy of the soliton pair as it develops following photon absorption is almost completely trapped as kinetic energy in a single collective coordinate corresponding to the inter-soliton separation; "leakage" into other vibrational modes occurs only after hundreds if not thousands of large amplitudes oscillations of this collective coordinate.

Electrons can hop from one soliton-bound state to another, so with a soliton pair these states hybridize into "bonding" $|B\rangle$ and "anti-bonding" $|A\rangle$ levels; the three lowest-lying electronic states are schematically $|BB\rangle, |AB\rangle$ and $|AA\rangle$, corresponding to three ways of placing two electrons in two orbitals to form a spin singlet. Photon absorption from the ground state is forced, by certain approximate symmetries of the molecule, to be largely $|BB\rangle \rightarrow |AB\rangle$. Small asymmetric perturbations cause very small spectral shifts but allow mixing $|AB\rangle \leftrightarrow |AA\rangle$ on a very rapid time scale ($\sim$ 20 fs) if the ground vibrational level of $|AA\rangle$ lies below the excited vibrational state of $|AB\rangle$ which one reaches by photon absorption (16). The key point is that the state $|AA\rangle$ is unstable to molecular rotations.

To understand this instability we recall that the bonding and anti-bonding levels are symmetric and anti-symmetric combinations of the two localized states, but which combination "bonds" depends on the sign of the overlap between the two localized electronic wavefunctions. Since the π_z orbitals of the carbon atoms have a polarity, this sign depends on the relative orientation of neighboring C-C bonds — the bonding level of a *cis* molecule is the anti-bonding level of the corresponding *trans* molecules, and vice versa. By rotating from *cis* to *trans* we can turn the anti-bonding level into a bonding level, so the state $|AA\rangle$ is massively unstable to *cis/trans* isomerization! One the molecule begins to isomerize the energy of state $|AA\rangle$ rapidly falls below that of state $|AB\rangle$ and there can be no "mixing back", which quenches the fluorescence $|AB\rangle \rightarrow |BB\rangle$.

To test these ideas we have done simulations of the SSH (15) model for $(\mathrm{CH})_x$ as applies to a finite chain which models the conjugated portion of retinal and extended this model to include molecular rotations (8). Parameters were fixed at the best estimates in $(\mathrm{CH})_x$ itself (1). All of the results are consistent with the scenario described above, so the qualitative features of solitons in polyacetylene are apparently applicable to this system. We draw attention to the following points:

[1] The quality of the collective coordinate corresponding to inter-soliton separation is

remarkable. Photon absorption leaves behind 0.87 eV of vibrational energy, and after ten periods of oscillation in this coordinate (~ 0.3 ps) we so no tendency toward equipartition of energy with other modes, within an accuracy of ~ 0.01 eV.

[2] The energy of state $|AA\rangle$ is indeed less than the photon energy at the absorption maximum, as required for our scenario. The rotational dynamics of this state include several unstable modes, with the time scale for growth of the instabilities ~ 40 fs.

[3] If rhodopsin absorbs a very long wavelength photon it will not have enough energy to mix into $|AA\rangle$ and the quantum efficiency for photo-isomerization will be reduced. This was observed many years ago (17) and should be re-investigated.

[4] As in $(\mathrm{CH})_x$ a significant portion of the long wavelength tail in optical absorption should arise from quantum fluctuations rather than thermal activation (1). This can be detected as a large isotope effect upon substitution of the C or H atoms.

[5] Since the state reached by photon absorption is a superposition of localized states it is highly dipolar, in agreement with Stark effect measurements (18). Since the dipole moment depends on mixing of $|AB\rangle$ and $|AA\rangle$, the Stark effect should be wavelength-dependent.

We thank M. Gunner, A. Heeger, D. Kleinfeld, J. Ohnuchic, and R. Shopes for helpful discussions. Work at Santa Barbara was supported by the NSF under Grant No. PHY82-17852, supplemented by funds from NASA. Work at Stanford was supported by the NIH under Grant No. GM 24032 and a National Eye Institute Post-Doctoral Fellowship to R.F.G.. Work at Stony Brook was supported by the NSF under Grant No. DMR83-18051 and by a Sloan Fellowship to S.K..

References

1. Kivelson, S. (in press) in *Solitons* (Trullinger, S., ed.), North-Holland, Amsterdam.
2. DeVault, D. and Chance, B. (1966) Biophys. J. 18, 311.
3. Hopfield, J.J. (1974) Proc. Nat. Acad. Sci. (USA) 71, 3640.
4. Goldstein, R.F. and Bialek, W. (in press) Comments Mol. Cell. Biophys..
5. Bialek, W. and Goldstein, R.F. (1985) Biophys. J. 48, 1027
6. Frauenfelder, H. and Wolynes, P. (1985) Science 229, 337
7. Goldstein, R.F. and Bialek, W. (in preparation).
8. Bialek, W. and Kivelson, S. (in preparation).
9. Kleinfeld, D. (1984) Thesis, University of California at San Diego.
10. Kiramaier, C., Holten, D., and Parson, W.W. (1985) Biochim. Biophys. Acta 810, 33.
11. Shopes, R.J. and Wraight, C.A. (1986) Biophys. J. 49, 586a.
12. Gunner, M., Dutton, P.L., Woodbury, N.W., and Parson, W.W. (1986) Biophys. J. 49, 586a.
13. Goldstein, R.F. and Bialek, W. (1983) Phys. Rev. B 27, 7431.
14. Doukas, A.G., *et al.* (1984) Proc. Nat. Acad. Sci. (USA) 81, 4790.
15. Su, W.P., Schrieffer. J.R., and Heeger, A.J. (1980) Phys. Rev. B 22, 2099.
16. Wu, W.K. and Kivelson, S. (in press) Phys. Rev. B.
17. St. George, R.C.C. (1952) J. Gen. Physiol. 35, 495.
18. Matheis, R. and Stryer, L. (1976) Proc. Nat. Acad. Sci. (USA) 73, 2169.