TOPICS IN CURRENT CHEMISTRY 237

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Long-Range Charge Transfer in DNA II

Springer

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In references *Topics in Current Chemistry* is abbreviated Top Curr Chem and is cited as a journal.

Visit the TCC home page at http://www.springerlink.com/

ISSN 0340-1022
ISBN 3-540-20131-9
DOI 10.1007/b14032
Springer-Verlag Berlin Heidelberg New York

Library of Congress Catalog Card Number 74-644622

Springer-Verlag is a part of Springer Science+Business Media

springeronline.com

Printed in Germany

Cover design: KünkelLopka, Heidelberg/design & production GmbH, Heidelberg
Typesetting: Stürtz AG, Würzburg

02/3020 ra – 5 4 3 2 1 0 – Printed on acid-free paper

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Preface

The central role played by DNA in cellular life guarantees a place of importance for the study of its chemical and physical properties. It did not take long after Watson and Crick described the now iconic double helix structure for a question to arise about the ability of DNA to transport electrical charge. It seemed apparent to the trained eye of the chemist or physicist that the array of neatly stacked aromatic bases might facilitate the movement of an electron (or hole) along the length of the polymer. It is now more than 40 years since the first experimental results were reported, and that question has been answered with certainty.

As you will earn by reading these volumes, Long-Range Charge Transfer in DNA I and II, today no one disputes the fact that charge introduced at one location in DNA can migrate and cause a reaction at a remote location. In the most thouroughly studied example, it is clear that a radical cation injected at a terminus of the DNA polymer can cause a reaction at a $(GG)_n$ sequence located hundreds of Ångstroms away.

In the last decade, an intense and successful investigation of this phenomenon has focused on its mechanism. The experimental facts discovered and the debate of their interpretation form large portions of these volumes. The views expressed come both from experimentalists, who have devised clever tests of each new hypothesis, and from theorists, who have applied these findings and refined the powerful theories of electron transfer reactions. Indeed, from a purely scientific view, the cooperative marriage of theory and experiment in this pursuit is a powerful outcome likely to outlast the recent intense interest in this field.

Is the quest over? No, not nearly so. The general agreement that charge can migrate in DNA is merely the conclusion of the first chapter. This hard-won understanding raises many important new questions. Some pertain to oxidative damage of DNA and mutations in the genome. Others are related to the possible use of the charge transfer ability of DNA in the emerging field of molecular-scale electronic devices. Still others are focused on the application of this phenomenon to the development of clinical assays.

It is my hope that these volumes will serve as a springboard for the next phase of this investigation. The foundation knowledge of this field contained within these pages should serve as a defining point of reference for all who explore its boundaries. For this, I must thank all of my coauthors for their effort, insight and cooperation.

Atlanta, January 2004 Gary B. Schuster

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Long-Range Charge Transfer in DNA I

Volume Editor: Gary B. Schuster
ISBN 3-540-20127-0

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Top Curr Chem (2004) 237:1–36
DOI 10.1007/b94471

DNA Electron Transfer Processes: Some Theoretical Notions

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Abstract Charge motion within DNA stacks, probed by measurements of electric conductivity and by time-resolved and steady-state damage yield measurements, is determined by a complex mixture of electronic effects, coupling to quantum and classical degrees of freedom of the atomic motions in the bath, and the effects of static and dynamic disorder. The resulting phenomena are complex, and probably cannot be understood using a single integrated modeling viewpoint. We discuss aspects of the electronic structure and overlap among base pairs, the viability of simple electronic structure models including tight-binding band pictures, and the Condon approximation for electronic mixing. We also discuss the general effects of disorder and environmental coupling, resulting in motion that can span from the coherent regime through superexchange-type hopping to diffusion and gated transport. Comparison with experiment can be used to develop an effective phenomenological multiple-site hopping/superexchange model, but the microscopic understanding of the actual behaviors is not yet complete.

Keywords Electron transfer · Hole transport · Hopping · Superexchange · Coupling to the molecular surroundings

Abbreviations and Symbols

a	Spacing between repeating units of the bridge
A	Adenine
A	Polarization matrix
A_{ij}	Elements of the polarization matrix
b	Transfer integral
B	Bridge connecting a donor and an acceptor
β	Falloff parameter for the distance dependence of the electron transfer rate
c_i	Annihilation operator for a hole at the *i*-th site of the chain describing the stack of Watson–Crick base pairs
c_i^+	Creation operator for a hole at the *i*-th site of the chain describing the stack of Watson–Crick base pairs
C	Cytosine
D	Width of the rectangular barrier
D–A	Donor–acceptor tunneling
(DWFC)	Density of states weighted Franck–Condon factor
DNA	Deoxyribonucleic acid
Δ_b	Barrier height for the adiabatic hole motion
ΔE	Difference in ionization potentials of adenine–thymine and guanine–cytosine base pairs
ΔE_b	Energy barrier between the injection energy and the barrier height
ΔG^0	Driving force for electron transfer
ET	Electron transfer

E	Energy of the particle undergoing a tunneling transition through the rectangular barrier
E_{B_i}	Electronic energy of the bridge state $\|B_i\rangle$
E_{tun}	Electronic energy associated with the "transfer electron" in the activated complex
E_v	Energy of the v-th vibrational state
ε	Dielectric constant of the solvent
g	Conductance
G	Guanine
$\hbar$	Planck constant
H_{DA}	Effective donor–acceptor interaction
HOMO	Highest occupied molecular orbital
k	Rate constant of electron transfer
k_B	Boltzmann constant
k_0	Pre-exponential factor in Eq. 6 for the rate of the elementary hopping step
L	Length of the bridge containing adenine–cytosine base pairs only
LUMO	Lowest unoccupied molecular orbital
λ	Marcus reorganization energy
m	Mass of the tunneling particle
n_i	Population of i-th site of the chain describing the stack of Watson–Crick base pairs
N	Number of sites through which the electron or hole tunnels
NDO SCF	Neglect of differential overlap self-consistent field method
P_G	Products formed in the reactions of water with guanine radical cation G_j^+
P_{GGG}	Product formed in the reaction of water with the hole trapped by the guanine triple GGG
P_v	Probability of the system to be found in the vibrational state v
ω_v	Effective vibronic frequency of the medium
q	Number of base pairs in the adenine–thymine bridge between two guanine sites
r	Spatial donor–acceptor separation
r_0	Spatial donor–acceptor separation in the certain reference state
$\rho_{FCv}(E)$	Generalized Franck–Condon factor
S_{vw}	Franck–Condon overlap factor
σ_0	Conductivity prefactor
T	Thymine
T	Temperature
τ_{LB}	Landauer–Buttiker tunneling time for the rectangular barrier
$\tau_{LB\text{-}M}$	Landauer–Buttiker tunneling time in a molecular orbital representation
τ_t	Tunneling time
U	Height of the rectangular barrier through which the particle is tunneling

$<V^2>$	Average squared electronic mixing between donor and acceptor
V_{BiA}	Hamiltonian term describing the interaction between the bridge state $\|B_i\rangle$ and the acceptor state $\|A\rangle$
V_{DBi}	Hamiltonian term describing the interaction between the donor state $\|D\rangle$ and the bridge state $\|B_i\rangle$
V_{rp}	Half of the effective energy splitting for the electron transfer reaction
v	Set of vibronic states that modulates the electron coupling matrix element
w	Set of vibronic states that does not modulate the electron coupling matrix element
x	Average position of a hole on the chain describing the stack of Watson–Crick base pairs
X_k	Multidimensional coordinate characterizing the polarization of water molecules
X_{opt}	Optimal value of the multidimensional coordinate characterizing the polarization of water molecules

1 Introduction

Electron transfer reactions are among the most widespread and significant in all of chemistry. Electron transfer (ET) within the double helical structure of DNA exhibits an extremely broad range of mechanistic behavior, and its exploration has become a focal point within the chemical community since the key studies of Barton and collaborators [1–3].

The current chapter discusses mechanisms of charge transfer reactions in double-stranded DNA (we will not deal with single-stranded DNA, or with individual bases or base-pair structures). We will also focus on interpretation of excess charge behavior in DNA molecules in terms of accepted theoretical models.

Figure 1 presents a very schematic picture of the DNA double helix, from the viewpoints of physical structure and a model for electronic behavior. Each base pair represents a localization site (actually, the localization is not on a base pair but on an individual base; because of the standard GC/AT hybridization, the language of base-pair localization is often used, when single-base localization is meant). Based on a wealth of evidence, both experimental and theoretical, we have indicated in Fig. 1b that the GC base pair is a more probable place for the hole to be localized—that is, it is easier to oxidize a G than any of the other three DNA bases. In the picture of Fig. 1b, each site (base pair) is assigned a unique energy, although it is clearly true that the energies will be modified by the neighbors with which the individual base pair interacts.

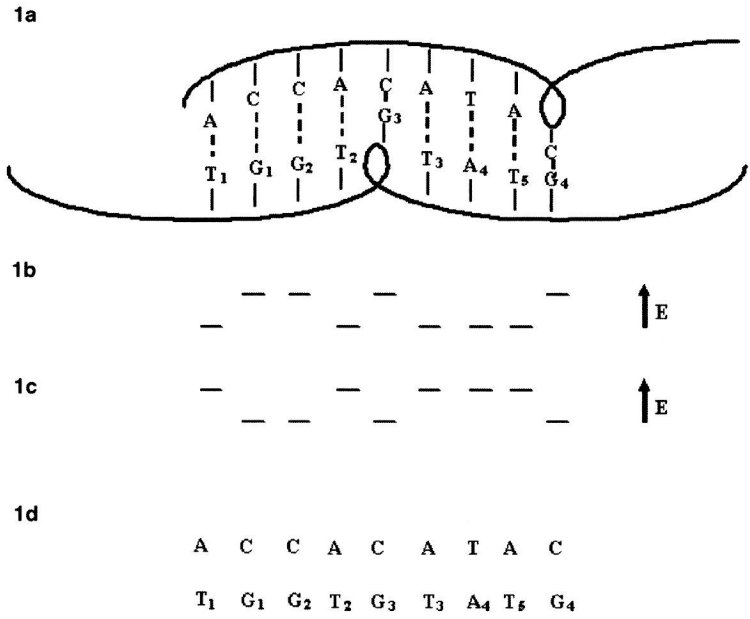

Fig. 1 Schematic illustration of the DNA double helical structure (**a**) and two possible mechanisms (electron-level energies in **b**, hole energies in **c**) of electronic motion in this molecule

Because most charge transfer processes and measurements in DNA actually consist of the motion of an electronic hole (that is, of a positive charge, corresponding to an ionized DNA base), it is more usual and more convenient to replace the picture in Fig. 1b by that of Fig. 1c. The diagram actually shows the energy of the holes, and indicates that the hole is more stable (lower lying energy level) on the GC pair than the AT pair. While this representation is confusing at first, it is both more common in the literature and more useful, and therefore we will depend upon it.

The simplest three mechanisms for motion, then, can be described in terms of the site picture in Fig. 1c. The sites G_1 and G_2 are located next to one another, and are separated by roughly 3.4 Å. Electrons can then tunnel between these two sites due to the overlap of the π-electron wave functions on the two (nearly cofacial) Gs. To move the electron from G_2 to G_3, it has to pass through T_2. Because T_2 is substantially higher in energy (the numbers differ, but a characteristic value between 0.2 and 0.4 eV is suspected), most of the hole wave functions will be localized on the Gs, with very little overlap onto the T site. Therefore, the motion from G_2 to G_3 is best represented as tunneling assisted by the presence of the T bridge, or as superexchange tunneling.

To move from G_3 to G_4, it is necessary for the hole to pass through three AT pairs. We can imagine this might happen in several different ways: the

hole could be thermally excited to the first AT (energetically very costly, as noted above), tunnel down the AT strand, and then decay to G_4. This would correspond to what is often called thermally induced hopping [4]. Alternatively, the hole could try to tunnel directly from G_3 to G_4, but the extent of overlap charge mixing dies off exponentially with distance, and therefore this route should be substantially less efficient. Finally, the hole might actually be delocalized so that it is not simply "on" G_3, but actually extends over G_3, G_1, G_2, T_2, T_3, T_4, and even a bit onto G_4. In this picture, the delocalized hole migrates from having its center on G_3 to have its center on G_4—this is usually referred to as polaron hopping, although the term can be confusing (essentially, there can be small (localized) and large (delocalized) polarons, so that the term polaron motion needs to be more precisely qualified). The three mechanisms of tunneling, hopping, and thermally induced hopping differ in their distance dependence, their temperature dependence, and their rates. Direct tunneling falls off exponentially with distance as does superexchange tunneling; hopping is expected to fall off very slowly with length, as is thermally induced hopping. Tunneling and superexchange should depend on temperature much more weakly as compared with hopping and thermally induced hopping.

Because of the controlled disorder in DNA, all three of these processes can and do occur. Interpretation of any set of experiments, therefore, might be attempted using any of these mechanisms. Careful contrasting between experiment and model is quite necessary, to understand which of the possible charge transfer schemes in fact occurs for a given measurement on a given system under given conditions.

DNA electron transfer centers on two exponential factors: the Boltzmann population of electronic excited states and the distant-dependent probability of electron tunneling. The mechanism of electron transfer is determined by the relative value of these terms. The tunneling factor (for single-step D–A tunneling through the bridge) drops exponentially with the distance. This distance dependence is usually discussed in terms of the falloff parameter β. The Boltzmann factor (for carrier injection) drops exponentially with the energy mismatch between D–A and bridge states. The interplay of these rapidly varying factors defines the transport rate and mechanism, as well as their dependence on the DNA, donor, and acceptor.

2
Computation of Electronic Matrix Elements. Geometry and Energy Dependence

2.1
Preliminaries

Electron transfer through a molecular bridge can occur by single or multiple-step mechanisms [5–7]. The multiple steps may involve real (hopping) or virtual (superexchange) bridging states. Single electron transfer steps

can occur in the strongly coupled (adiabatic) or weakly coupled (nonadiabatic) regimes [7]. In the weak-coupling regime, the electronic structure—including energetics and symmetry of the donor, acceptor, and bridge—determines the ET rate. In addition, the nonadiabatic rate depends on an activation free energy. In contrast, adiabatic ET is controlled by the activation free energies and dynamics of nuclear relaxation.

Transitions between these tunneling and hopping regimes have been probed in molecular wires, and DNA electron transfer systems generally reside near the boundary between these regimes. Whether DNA electron transfer is adiabatic or nonadiabatic depends upon the donor–acceptor distance. Since nearest-neighbor bases in DNA have electronic interaction energies as large as tenths of eV (see below), nearest-neighbor ET is likely adiabatic or nearly adiabatic.

Our attention here focuses on the change in donor–acceptor interaction strength as the number of bases intervening between donor and acceptor grows. In two-state donor–acceptor ET, the coupling matrix element is required for geometries at or near the activated complex in which the donor and acceptor localized electronic states are quasi-degenerate. There are several practical computational schemes to find this energy splitting [7–9]. While these specific schemes are described in greater detail below, it is instructive to introduce a perturbation theory that is commonly employed to lift degeneracy between two states when they do not interact directly with each other [10]. When a state $|\mathrm{D}\rangle$ interacts indirectly with $|\mathrm{A}\rangle$ through a manifold of $|\mathrm{B}_i\rangle$ states, and the Hamiltonian term V describes the D–B and B–A interactions, the effective D–A interaction with a single superexchange step is [5–9]

$$H_{\mathrm{DA}} = \sum_i V_{\mathrm{DB}_i} V_{\mathrm{B}_i\mathrm{A}} / (E_{\mathrm{tun}} - E_{\mathrm{B}_i}) \tag{1}$$

Here E_{tun} is the electronic energy associated with the "transfer electron" in the activated complex. The orbital symmetry dependence arises from the V terms in the numerator. The energy dependence of the coupling—the energy mismatch between the D/A and bridge states—is reflected in the denominator. Note that when donor, acceptor, and bridge are in near resonance, the coupling changes rapidly with detuning of the bridge state energies from resonance with the tunneling energy. When the mismatch energy is large, there is only a weak dependence of coupling on tunneling energy.

2.2 Computing Coupling Elements

There are two qualitative ways to influence H_{DA}. One is to modify the V elements. The V elements are changed by altering the donor–bridge and acceptor–bridge interactions. Pulling D and A away from the helix, for example, weakens the V elements. In DNA, if π-orbital-mediated coupling dominated,