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Charge Transfer, Conductance, and Detection of a Single Mismatch in DNA

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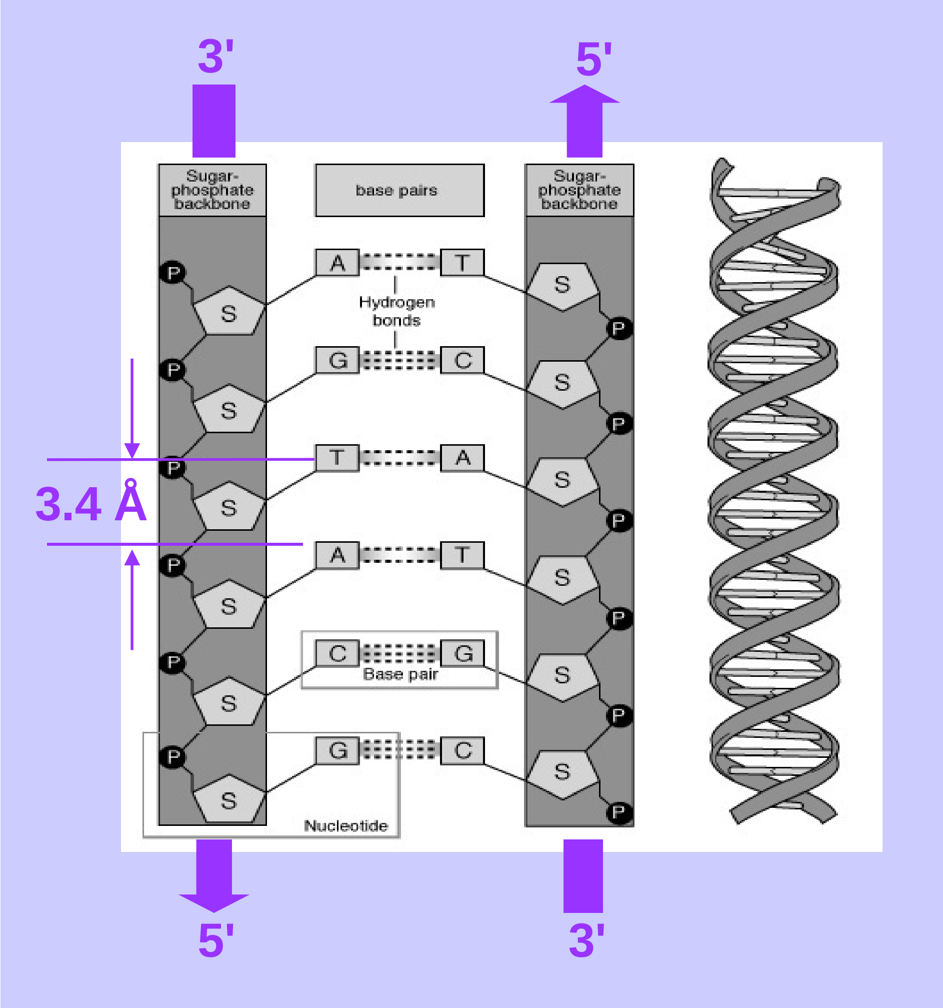
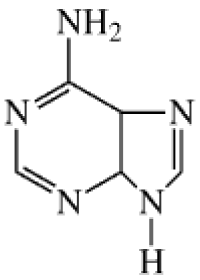
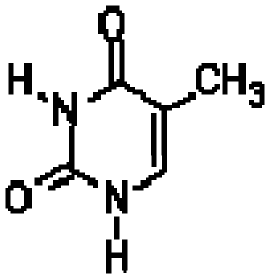
Architecture of DNA



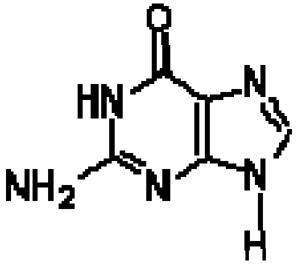
Adenine, A



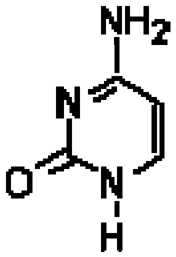
Thymine, T



Guanine, G



Cytosine, C



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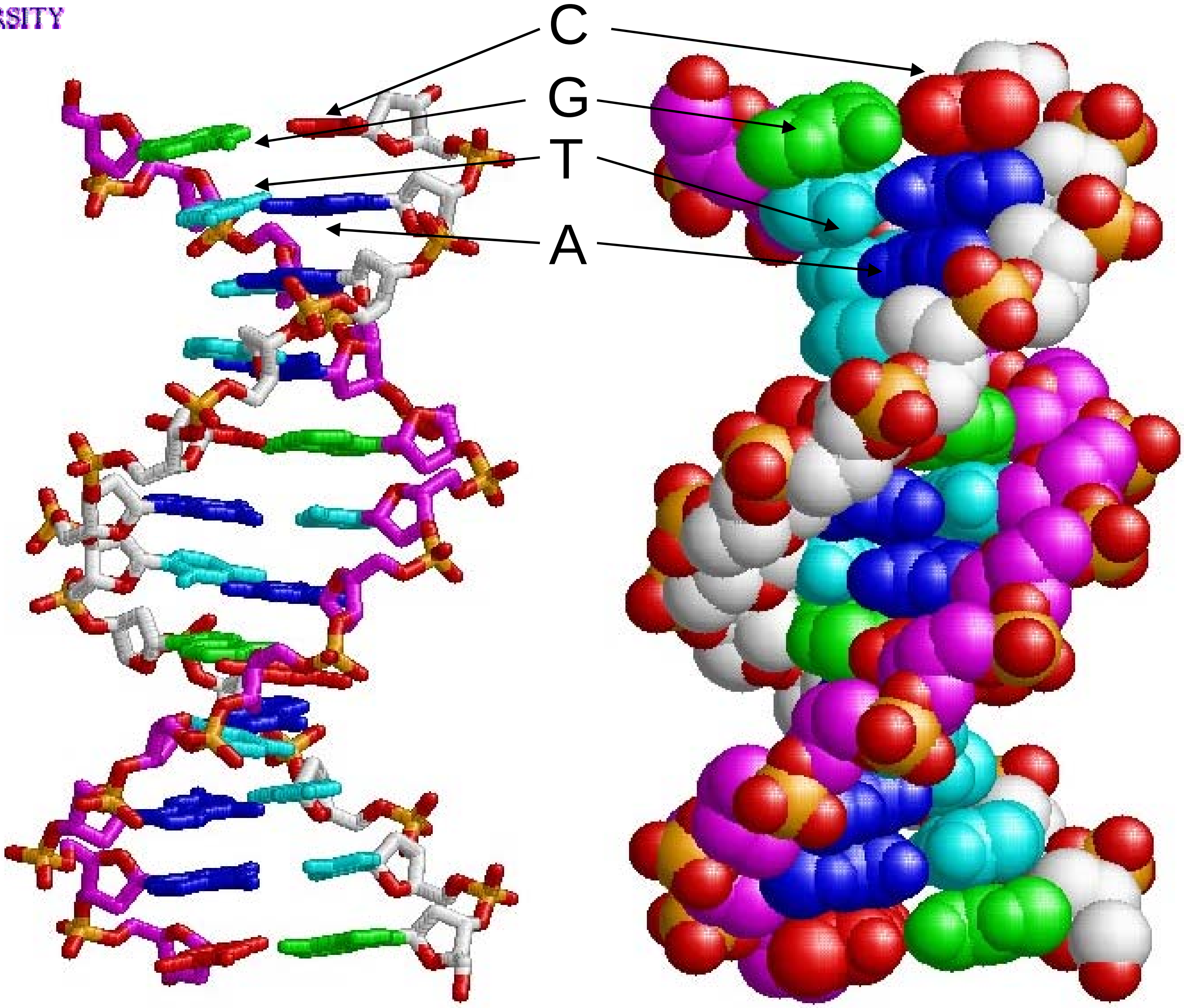
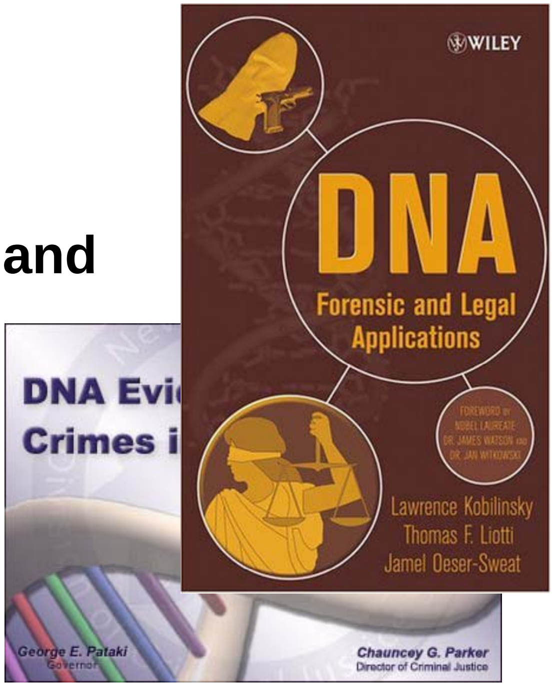
3-D View of DNA



Outcome Including Potential Applications



1. Biological relevance

Generation of damage and mutations

Implications in aging, several types of cancer and diseases such as arteriosclerosis

2. DNA-based molecular technologies

Detection of DNA and electrochemical sequencing techniques

3. Nanoelectronics

DNA as a molecular wire in mesoscopic electronic devices

Molecular computing

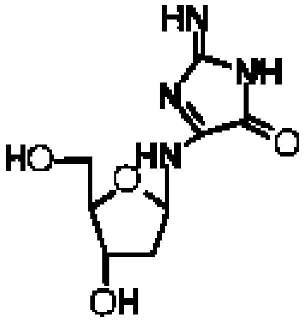
4. Chemistry

Possibility of doing "chemistry at a distance“

Possibility to detect anomalies in the base pair stack

Biological Significance: Radiative Damage

GAG TTGATGT GAGAG
CTC AACTACAC TCTC



2-aminoimidozolone (Iz)

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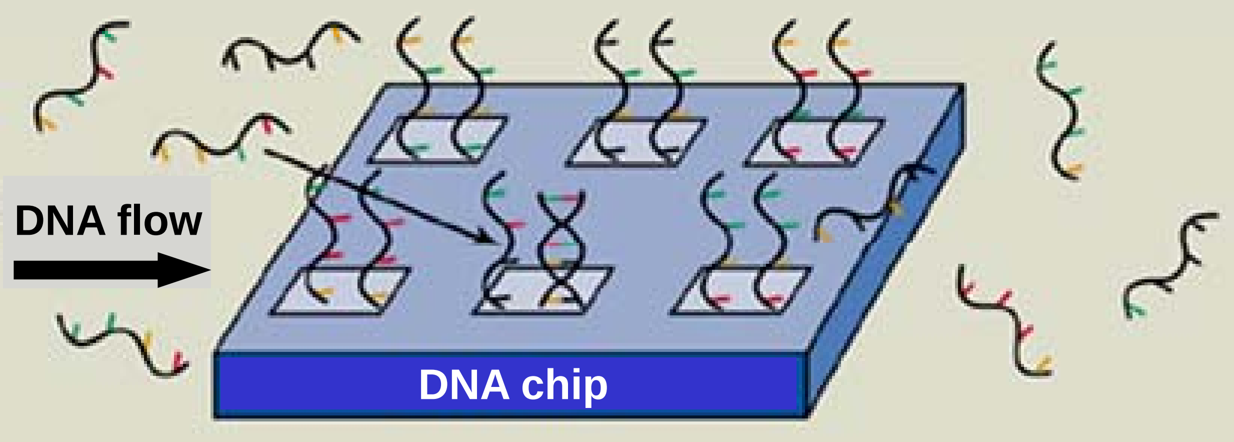
Charge migration and sequencing techniques



DNA chips are patterned with many short snippets of single-strand DNA, each with a different sequence of bases. When DNA has been extracted from a cell, for example, and labelled with a fluorescent marker, it will only bind to the fragments that have exactly the right genetic code. Currently the chips are read out optically by searching for the fluorescent markers, but the electronic properties of DNA can be exploited for this purpose as well.

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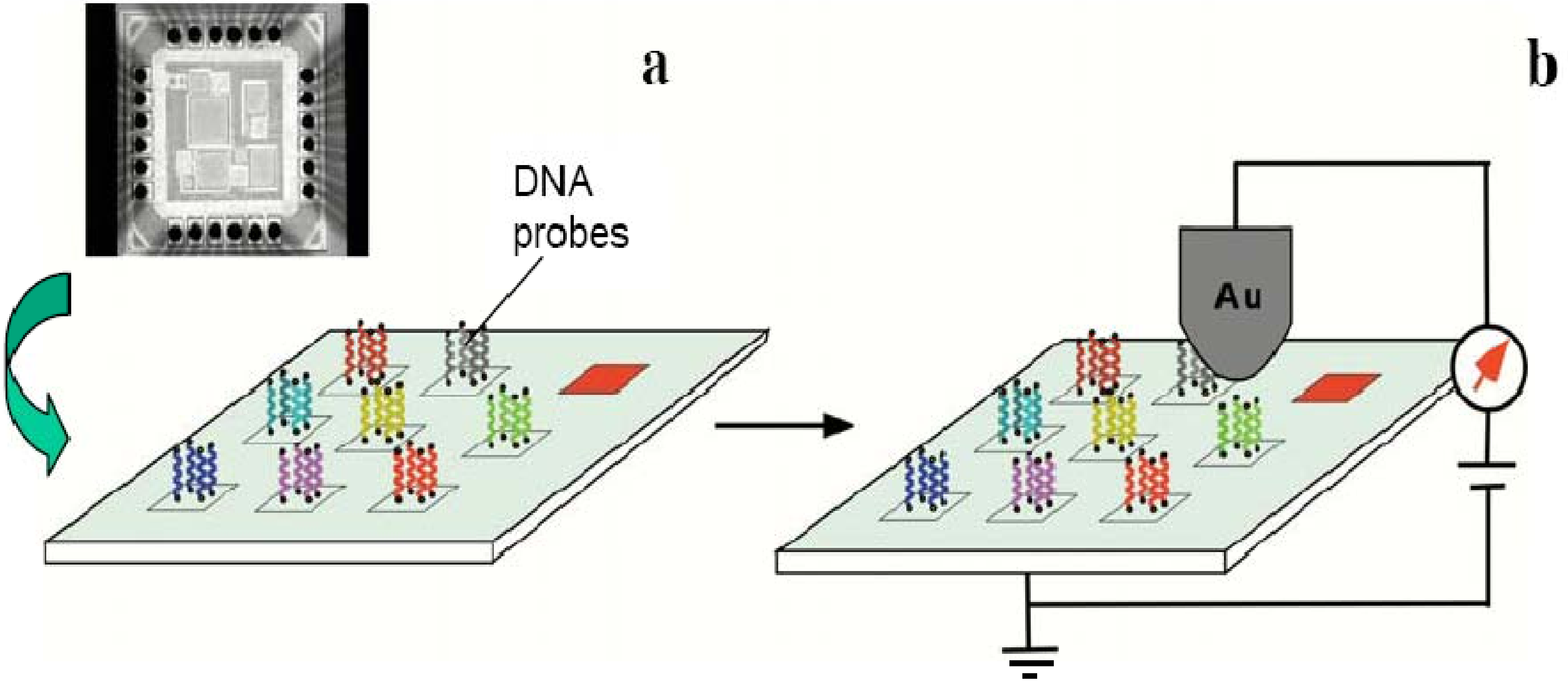
Molecular Detection and Diagnosis Device Based on Electrically Wired Single DNA

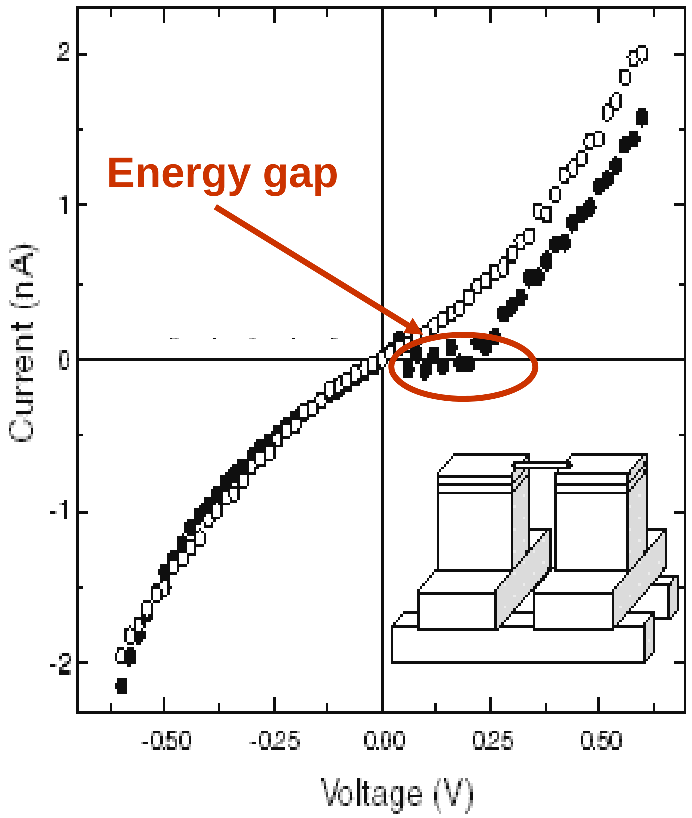


An array of different DNA probes hybridized with target DNA

Rapid screening based on conductance measurement

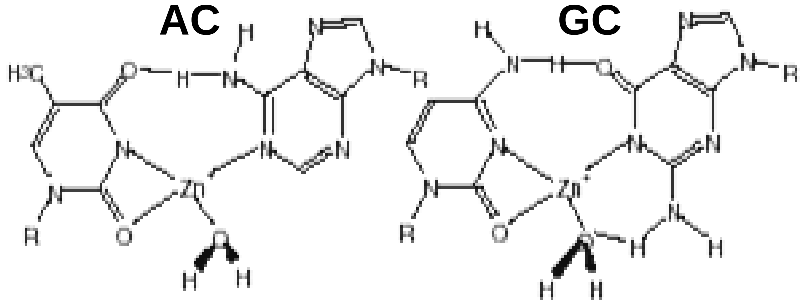
Nanoelectronics: M-DNA

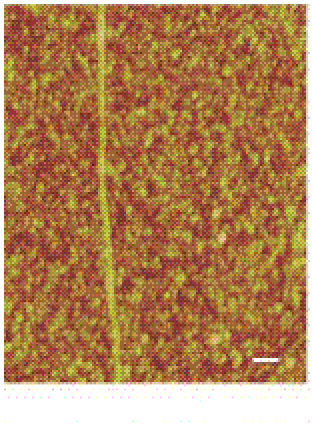
Replacement of imino proton by Zn^{2+}, Co^{2+}, and Ni^{2+}



Energy gap

AC **GC**





Interelectrode spacing: 10 μm

Length of DNA fibers: 15 μm

A. Rakitin et al. *Phys. Rev. Lett.* 86 (2001) 3670

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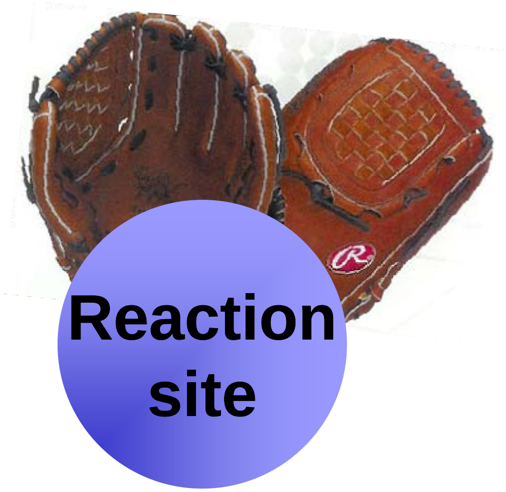
"Chemistry at a Distance"

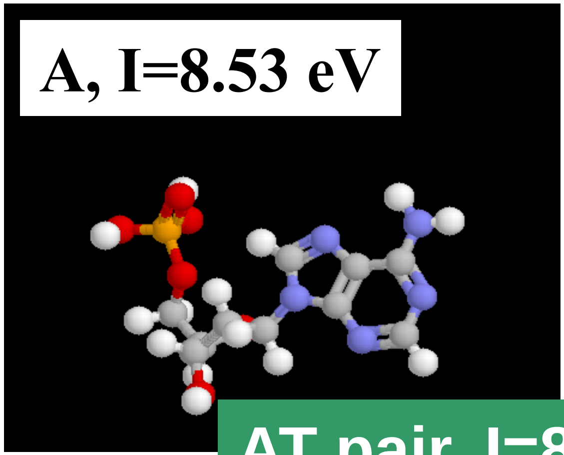
Site
of generation



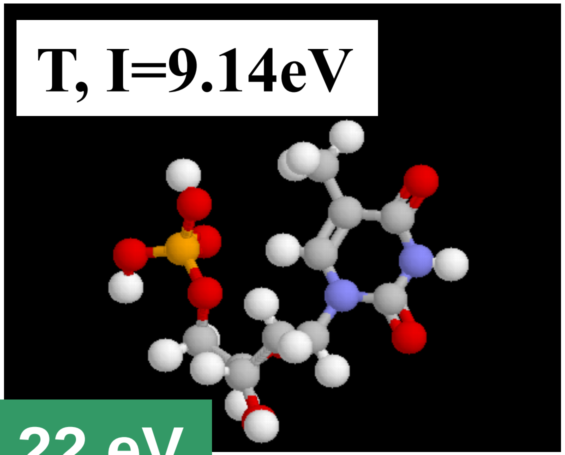
Reaction
site

Energetics of Bases and Base Pairs

A.A.Voityuk, J. Jortner, M.Bixon, and N. Rösch, Chem. Phys. Lett. 324, 430 (2000)

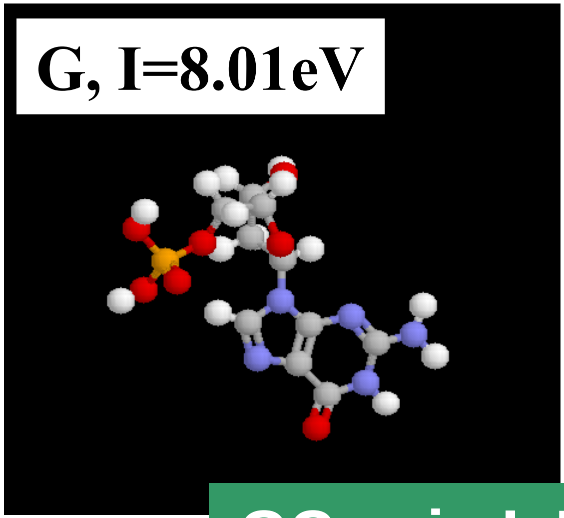


A, I=8.53 eV

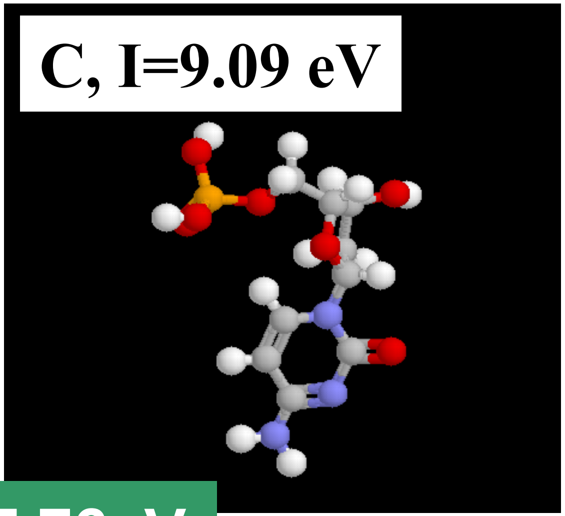


T, I=9.14eV

AT pair, I=8.22 eV



G, I=8.01eV



C, I=9.09 eV

GC pair, I=7.76eV

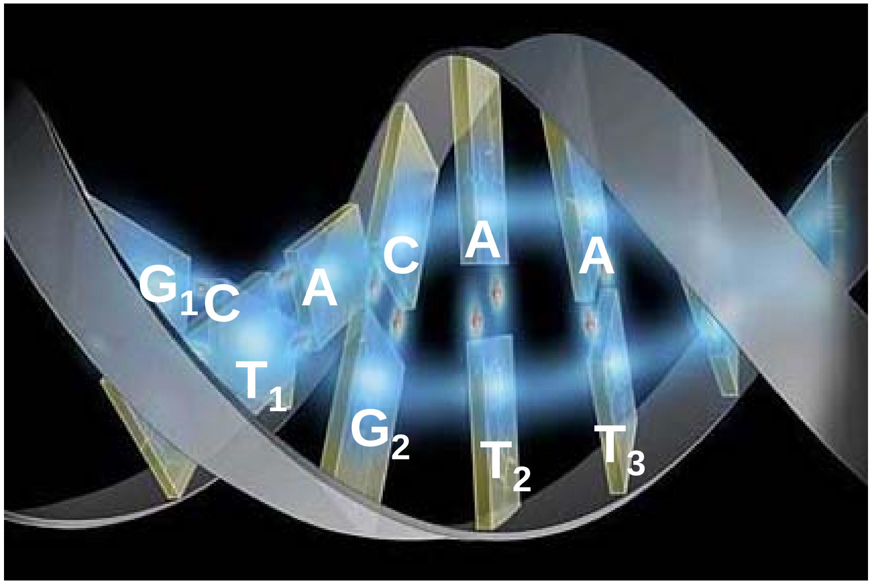
More recent data for
nucleotide triplets

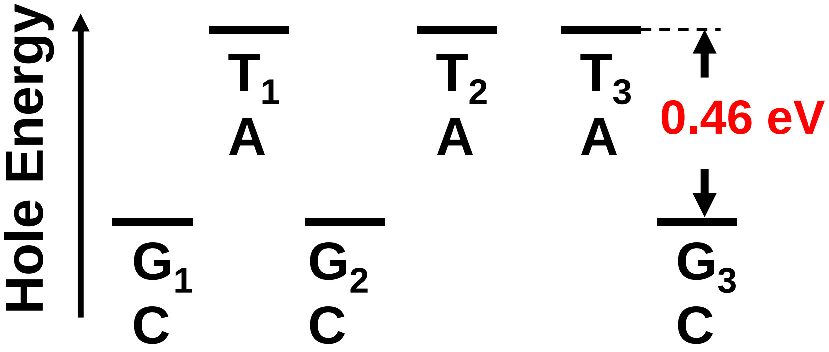
K. Santhilkumar, F. C. Grozema, C. F. Guerra, M. L. Bickelhaupt, F. D. Lewis, Y.A. Berlin, M.A. Ratner, L.D.A. Siebbeles, JACS 127, 14894 (2005)

Neighboring bases in triplets does not affect the hierarchy of ionization potentials

G<A<C<T

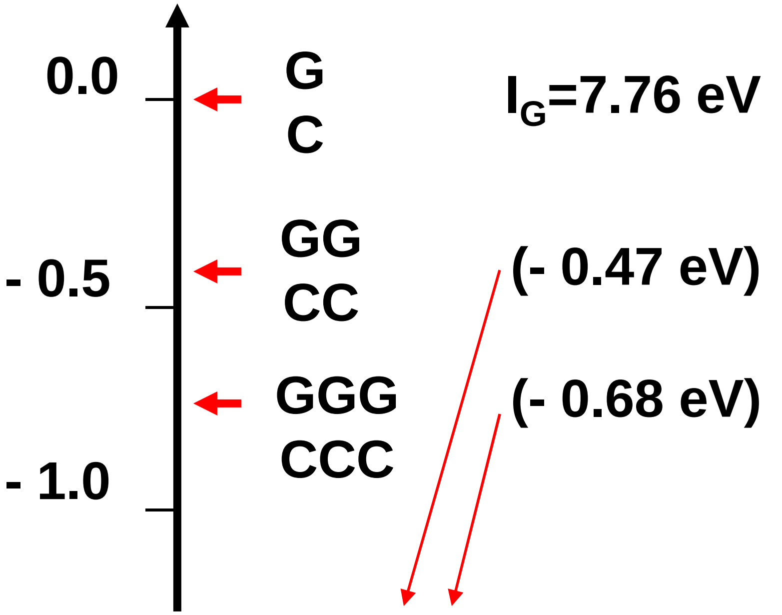
Stack Structure and Energy Profile





So, G bases are resting sites for traveling holes

H. Sugiyama, I. Saito, *JACS* 118, 7063 (1996)



This numbers becomes smaller if the solvation (Beratan et al 2002) and the effect of flanking nucleobases (Berlin, Siebbeles, Ratner et al 2005) are taken into account

GG doublets and GGG triples are traps for traveling holes

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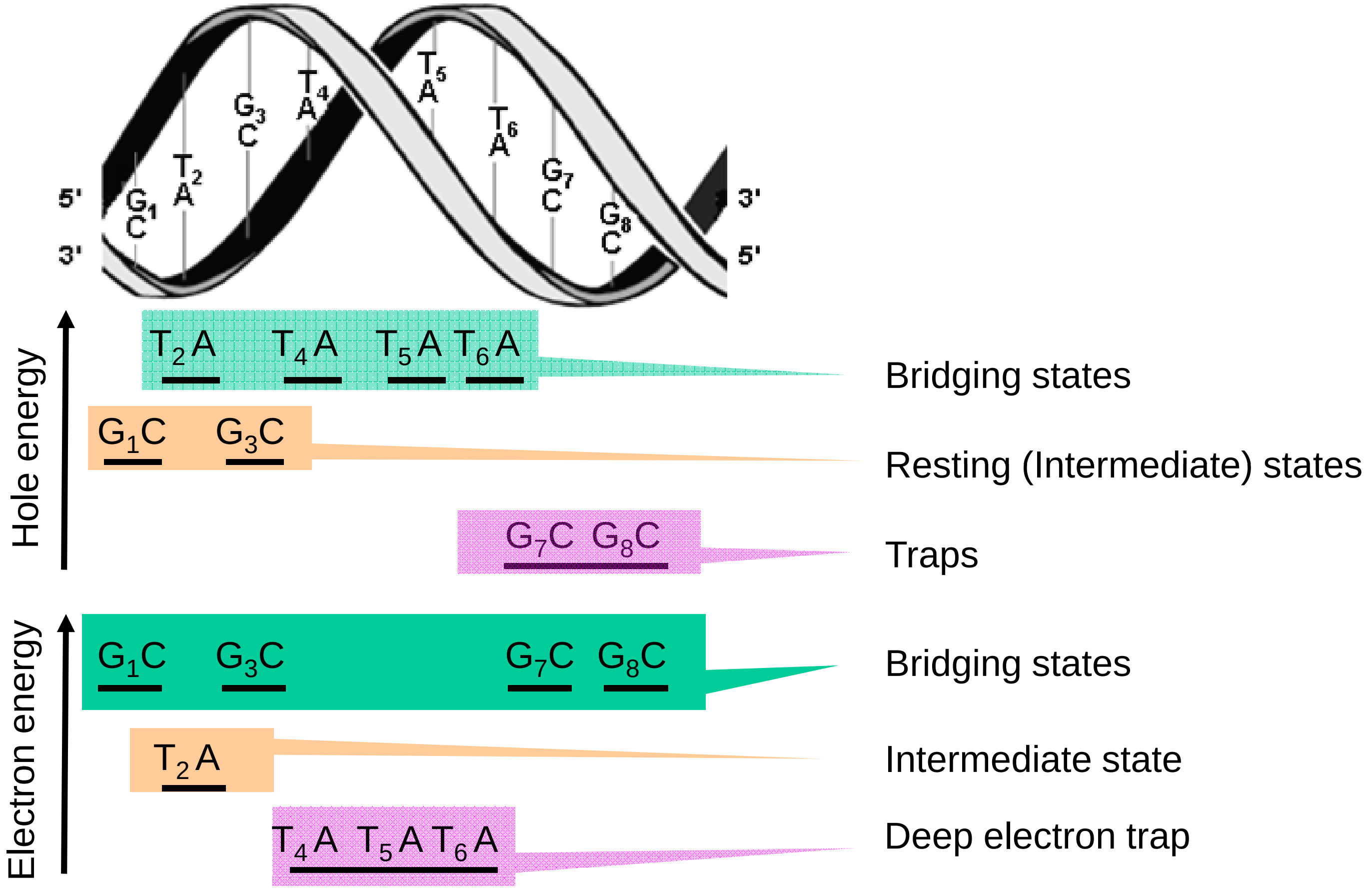
Hole and excess electron states in the DNA energy landscape



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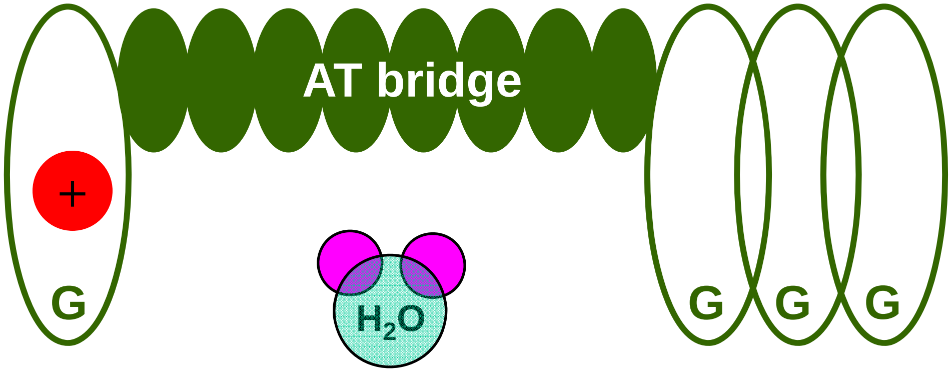
Elementary Processes on Stacks of Base Pairs

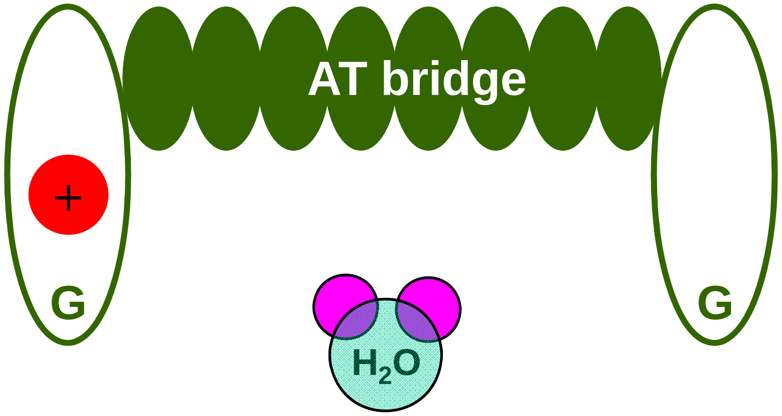
Hole generation

- Intercalated hole injectors (Barton)
- Covalently attached hole-injecting chromophores (Schuster)
- Nucleobase analogue acting as a hole-donating species (Fiebig, Zewail et al., Geacintov et al.)
- Site-selective generation of holes (Giese, Michel-Beyerle)

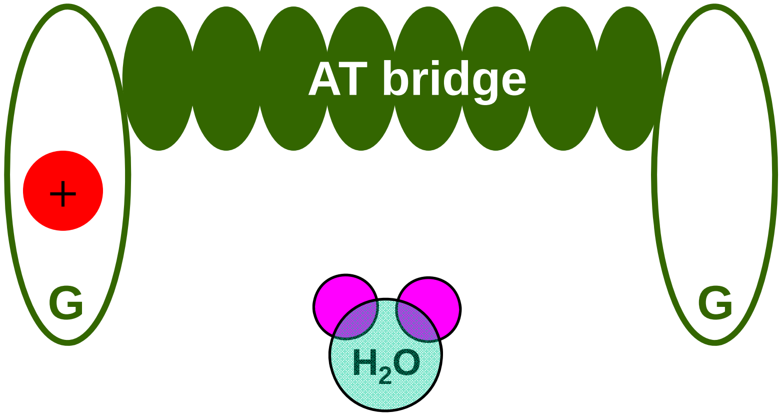
Trapping



Hole transition between resting G states



Side reaction with water



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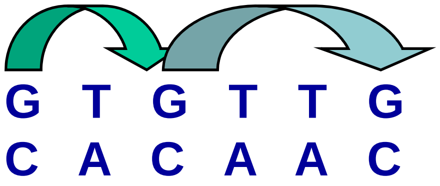
Theoretical Methodology

Macroscopic level: Theoretical analysis of charge migration within the model of sequential charge hopping



Microscopic level: Quantum chemical calculation of parameter controlling the rate, *W,* for elementary hopping step

$$W = \frac{V^2}{\hbar}\left(\frac{\pi}{\lambda k_B T}\right)^{1/2} \exp\left[-\frac{(\Delta G + \lambda)^2}{4\lambda k_B T}\right]$$

Description of charge transport in DNA and its sensitivity to mismatches

Issues

- **Steady-state experiments**
- **Their theoretical analysis**
- **Information available from steady-state studies**
- **Time-resolved measurement**
- **Estimates of rates for elementary process**
- **The effect of conformational dynamics on the rates**

Experimental Approaches

1. Hole transfer through AT bridges

Observable: **the damage ratio $\phi' = P_{GGG}/P_G$**

$G^{\bullet +}$ T T T T G G G

C A A A A C C C

Information: dependence of hole transfer efficiency on the AT bridge length

2. Hole transfer through bridges with AT and GC

Observable: **the damage ratio $\phi = P_{GGG}/\Sigma P_{Gi}$**

$G^{\bullet +}$ T G T T G G G

C A C A A C C C

Information: distance and sequence dependence of hole transfer efficiency

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Key Theoretical Problem

1. To propose a mechanism and a minimal description of hole transfer through AT bridges

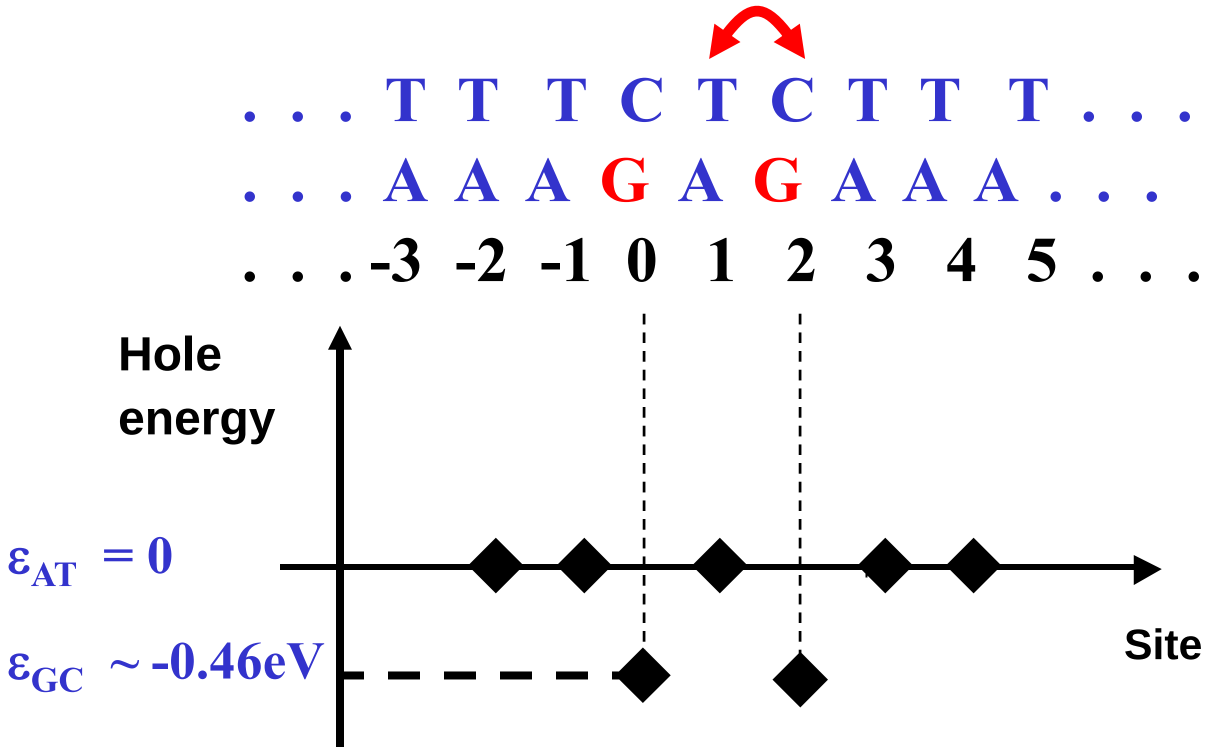
2. To formulate a kinetic model for hole transfer through sequences of AT and GC base pairs

3. To predict the efficiency of hole transfer in DNA

Minimal Theoretical Description of Hole Transfer through AT Bridges

$$H = -b\sum_{i=-\infty}^{+\infty}\left(c_i^{+} c_{i+1} + c_{i+1}^{+} c_i\right) - \varepsilon_G\left(n_0 + n_k\right), \quad n_i = c_i^{+} c_i$$

$b \approx 0.16\,\mathrm{eV}$



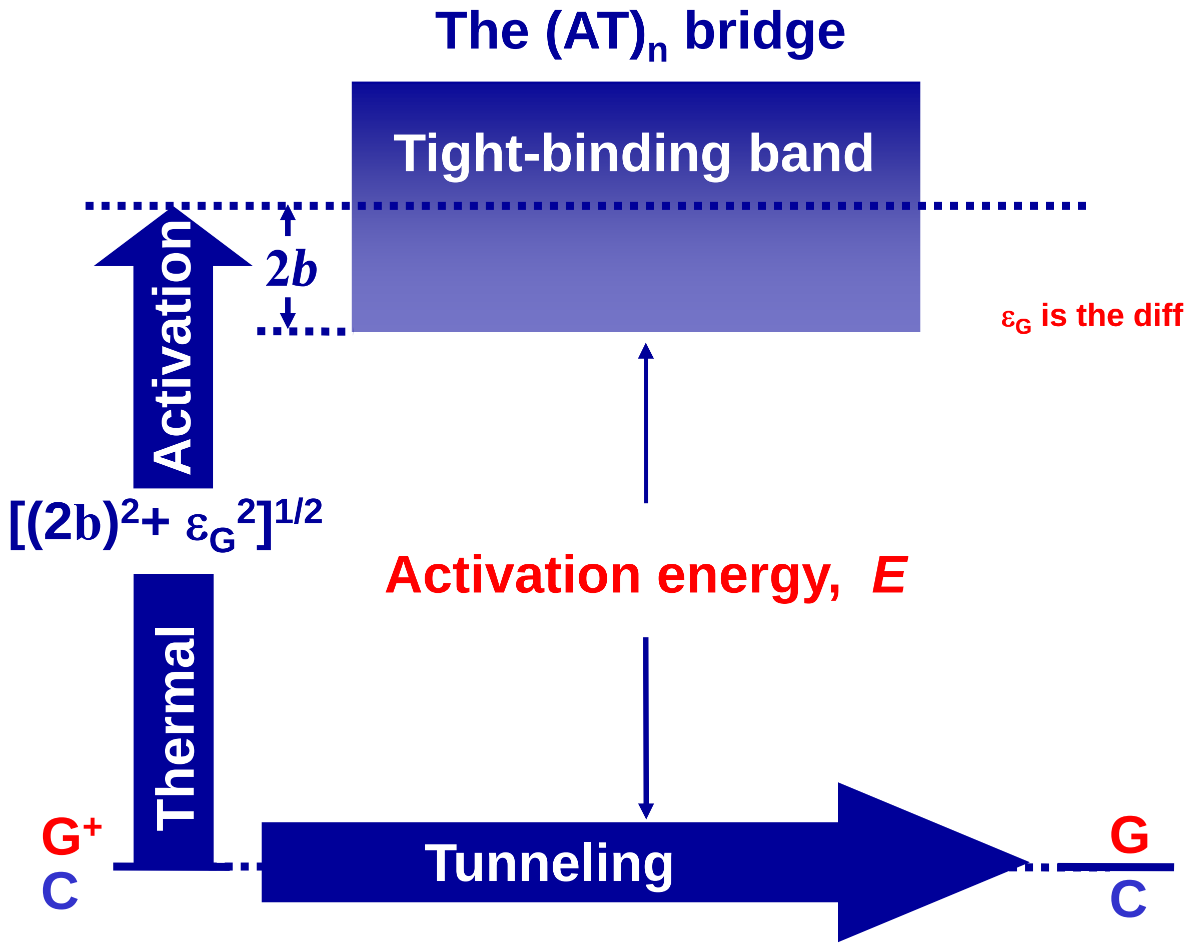
Values of transfer integral, b, and site energy, ε_{GC} were taken from

K. Senthilkumar et al, *J. Am. Chem. Soc.* 127, 1894 (2005)

A. A. Voityuk, et al, *J. Phys. Chem. B* 104, 9740 (2000); *Chem. Phys. Lett*. 324, 430 (2000)

Mechanism of Individual Hopping Steps

Yu. A. Berlin, A. L. Burin and M. A. Ratner,
Chem. Phys. 275, 61 (2002)



The $(AT)_n$ bridge

Tight-binding band

$2b$

Activation

$[(2b)^2 + \varepsilon_G^2]^{1/2}$

Thermal

Activation energy, *E*

G^+
C

Tunneling

G
C

Thermal Activation:

$W_{th} \sim exp[-E/(k_B T)]$

$E = [(2b)^2 + \varepsilon_G^2]^{1/2} - 2b \approx$
$0.24 eV$

ε_G is the difference of ionization potentials for AT and GC

Tunneling:

$W_{tun} \sim exp(-\beta L)$,

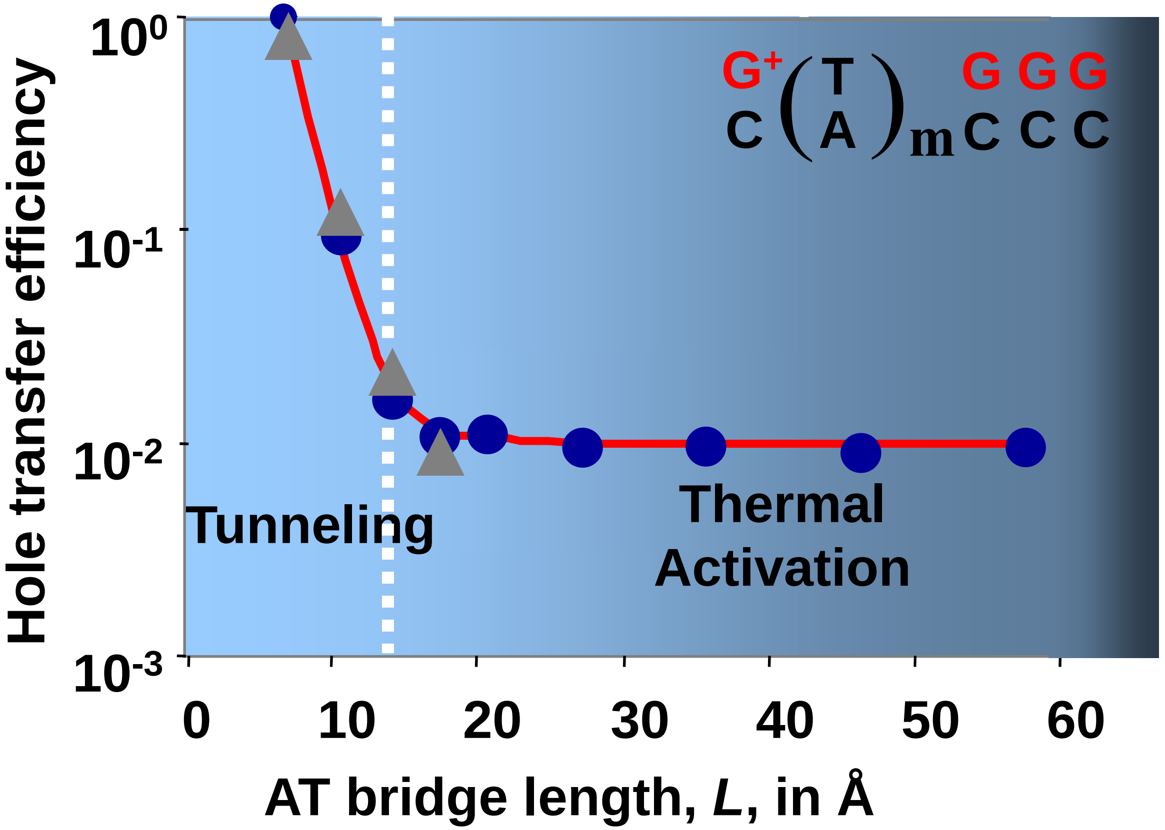
$\beta = (2/a) \ln[x + (1 + x^2)^{1/2}]$,

$x = \varepsilon_G/(2b)$

Total Rate:

$$\boxed{W = W_{th} + W_{tun}}$$

Comparison of Theory and Experiment



Normalized hole transfer efficiency

$$\frac{\exp(-\beta L) + \exp(-E/k_BT)}{\exp(-\beta L_1) + \exp(-E/k_BT)},$$

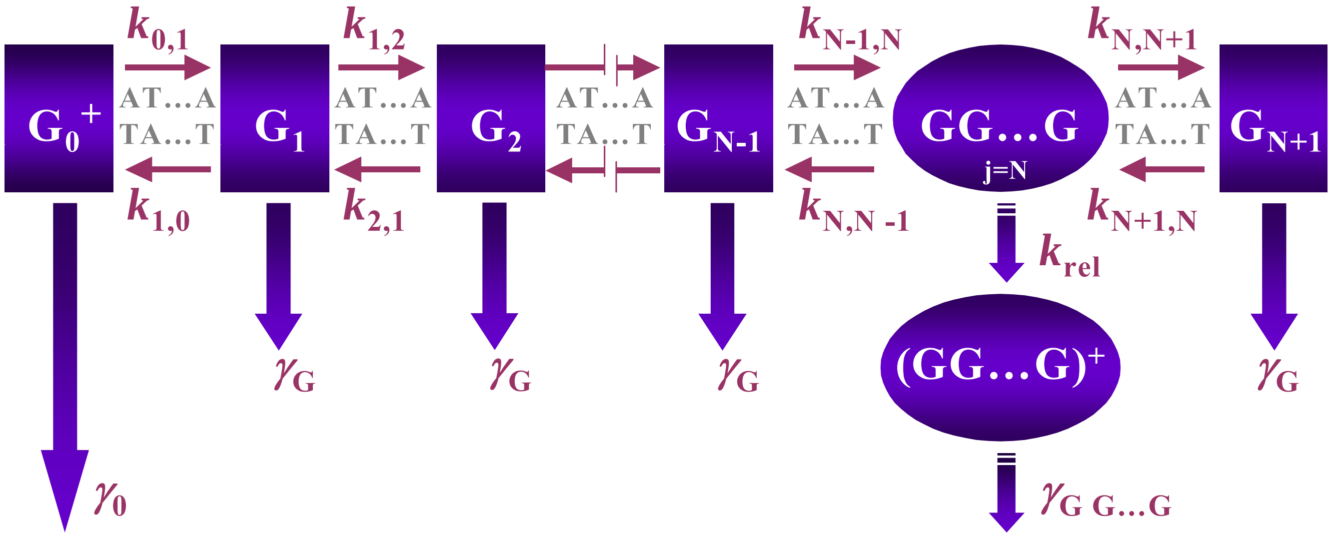
L_1=6.8 Å

━ **theory:** Yu. A. Berlin, A. L. Burin and M. A. Ratner, *Chem. Phys.* 275 (2002) 61

▲ **experiment:** E. Meggers et al, *J.Am.Chem.Soc.* 120 (1998) 12950

● **experiment:** B. Giese et al. *Nature* 412 (2001) 318

Kinetic Modeling



If the main contribution to the damage ϕ ratio comes from the reaction of water with primarily cation G_0^+ and with $(GGG)^+$,

$$\phi = \frac{1}{\gamma_0} \cdot \frac{1}{\left(\frac{1}{k_{0,1}} + \frac{1}{k_{1,2}} + \ldots \frac{1}{k_{N-1,N}} \right)}$$

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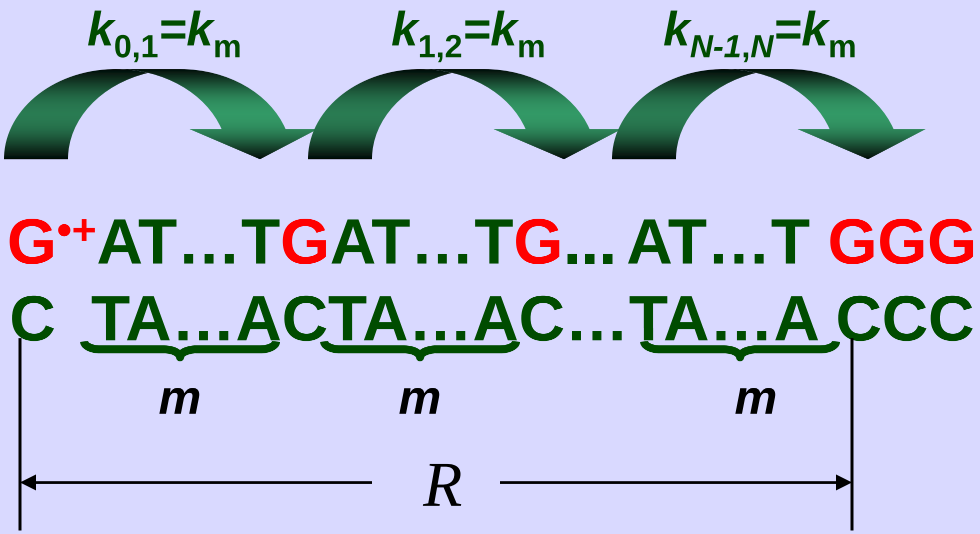
Regular Sequences



$k_{0,1}=k_m$ $k_{1,2}=k_m$ $k_{N-1,N}=k_m$

$G^{\bullet+}$AT…TGAT…TG… AT…T GGG
C $\underbrace{\text{TA…A}}_{m}C\underbrace{\text{TA…A}}_{m}$C…$\underbrace{\text{TA…A}}_{m}$ CCC

R

$$\phi' = \boxed{a(m+1)}\frac{k_m}{R\gamma_0} = \frac{Lk_m}{R\gamma_0}$$

L is the length of elementary hopping step

For comparison, superexchange yields

$$\phi' \sim \exp(-\beta R)$$

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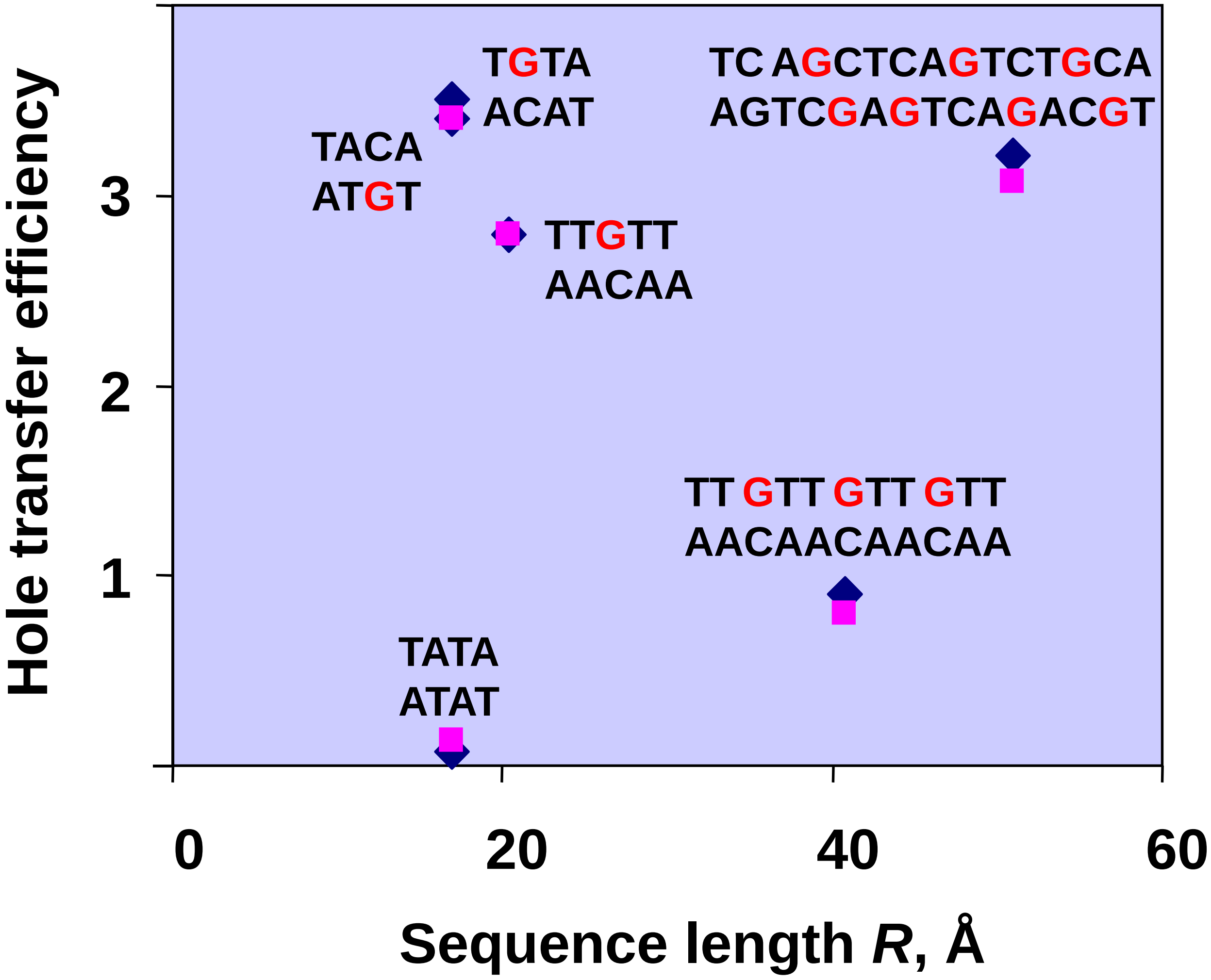
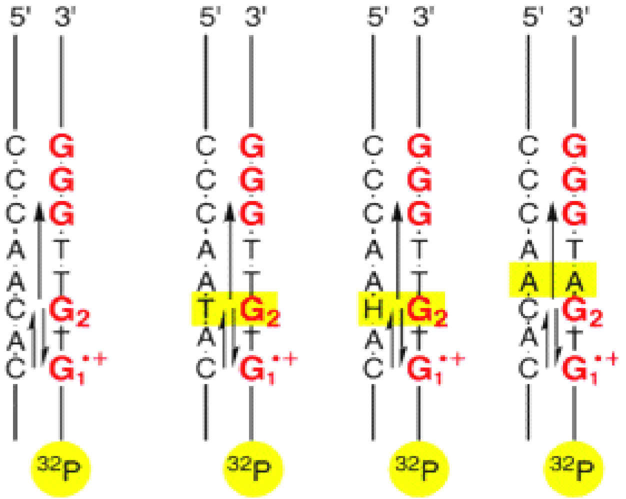
Comparison with Steady-state Experiment

◆ **Experiment:** E. Meggers, et al, *J.Am.Chem.Soc.* 120 (1998) 12950; B. Giese, et al, *Angew. Chem., Int. Ed.* Engl. 38 (1999) 996

■ **Theory:** Yu. A. Berlin, A. L. Burin, M. A. Ratner, *J. Phys. Chem. A*, 104 (2000) 443; *J.Am.Chem.Soc.* 123 (2001) 260



Influence of Mismatches on Hole Transfer: Experimental Evidences



Damage Yield P_{GGG}:

68% 23% 8% 66%

(H is a vacancy on strand)

B. Giese and S. Wessely, *Angew. Chem. Int. Ed.* **39**, 3490 (2000).

- No effect if there is a mismatch in the AT bridge
- Efficiency of charge transfer decreases if there is a mismatch at G site

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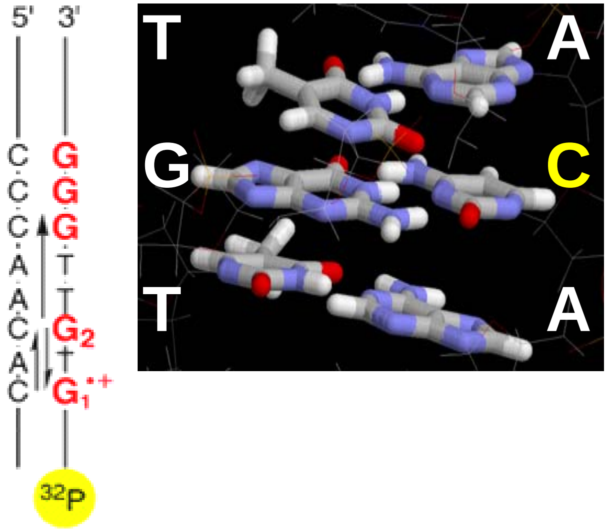
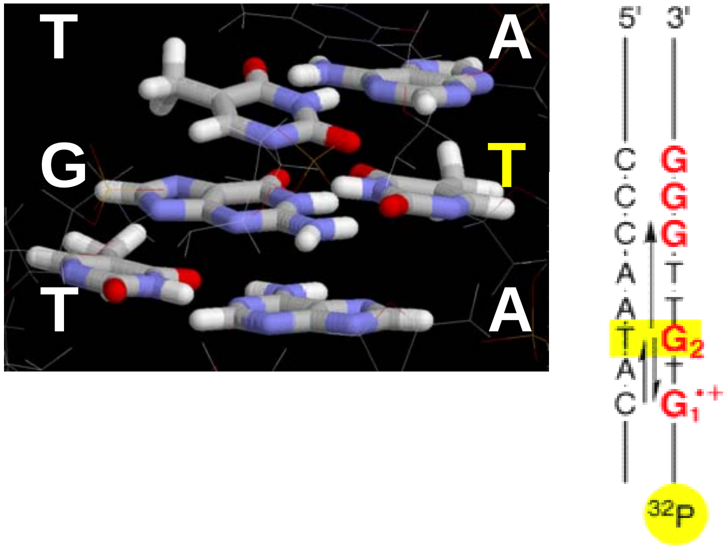
Ionization Potentials of G Paired with Different Nucleobases

Y.A. Berlin, I.V. Kurnikov, M.A. Ratner, in press





Ionization Potential:	**7.31 eV**	**7.74 eV**
Electron coupling:	5.8 10^{-3} eV for G_1TG_2 1.4 10^{-2} eV for G_2TTGGG	2.1 10^{-3} eV for G_1TG_2 3.5 10^{-3} eV for G_2TTGGG
Damage Yield P_{GGG}:	**68 % (theory)** **68% (experiment)**	**21 % (theory)** **23% (experiment)**

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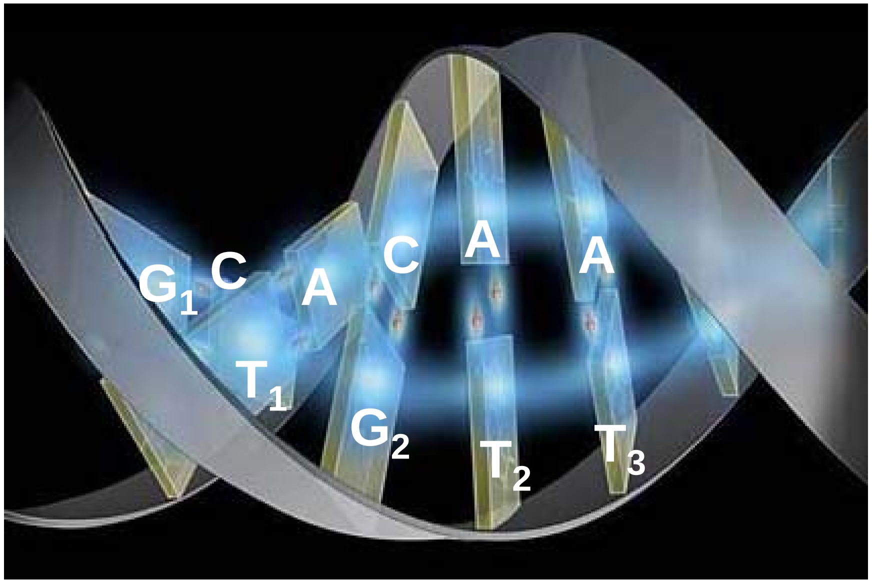
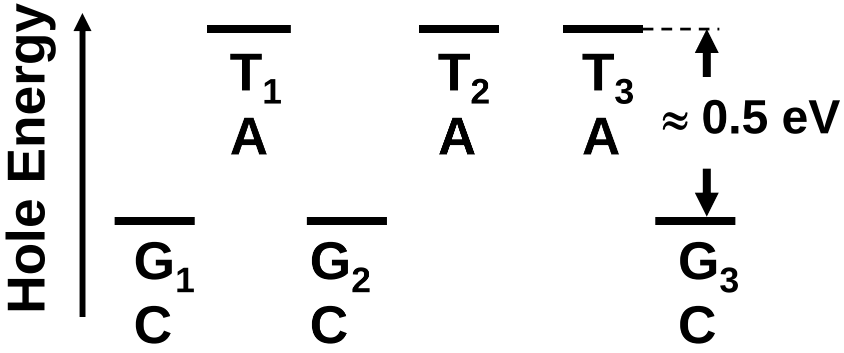
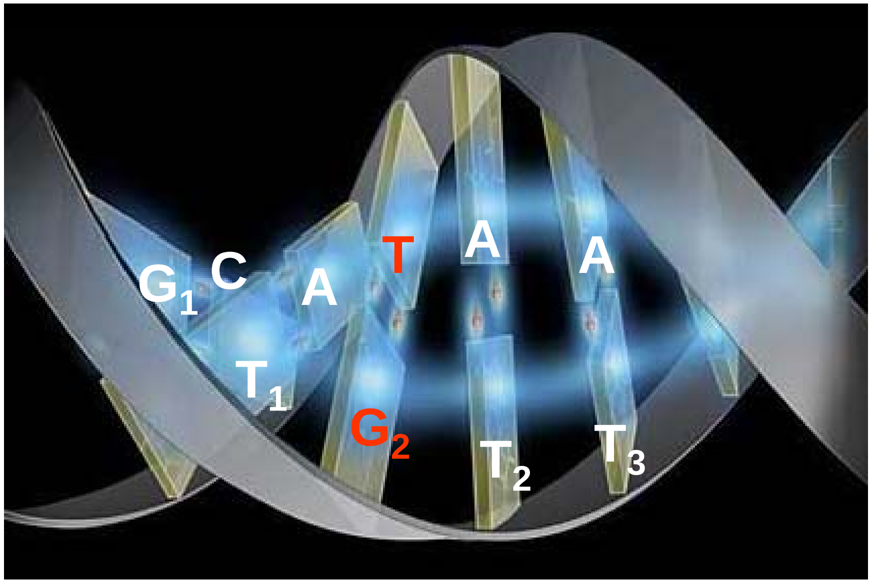
Energy Profiles for Normal Base Pair Stacks and Stacks with a Single Mismatch

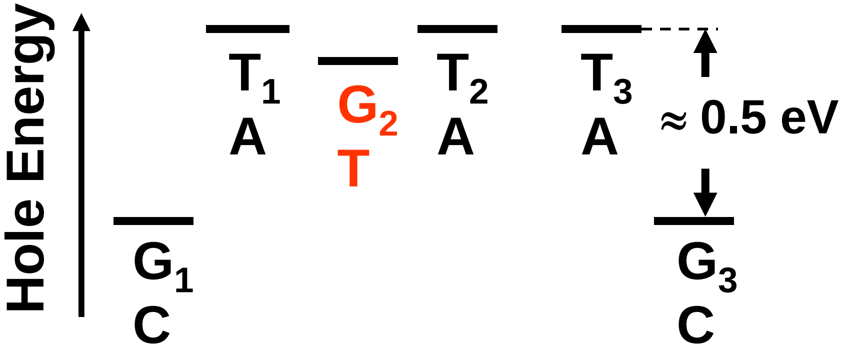
No mismatch



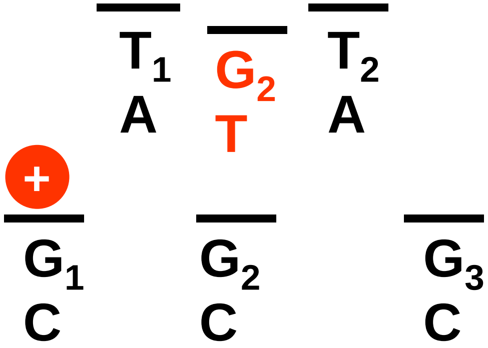


With mismatch

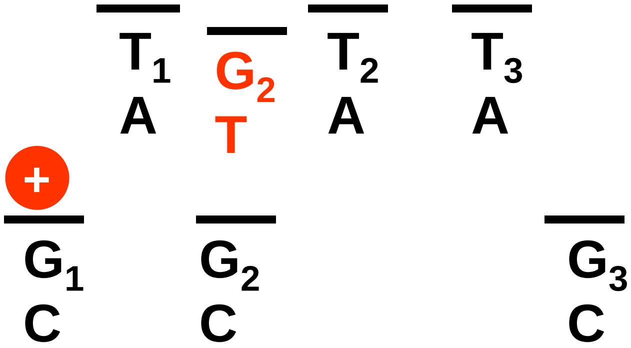




Consequences for Hole Transport in DNA



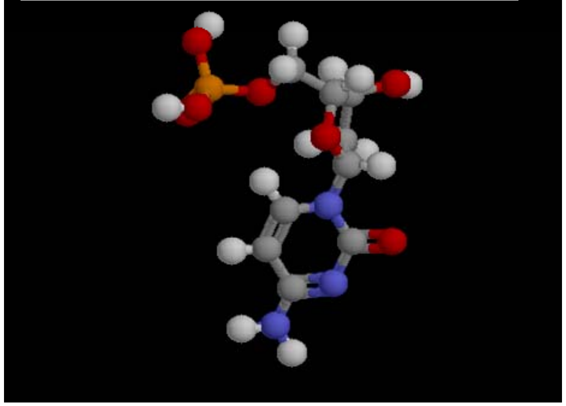
- **Unlike GC pairs, the GT mismatch serves as a bridging state rather than the "resting" state for holes**



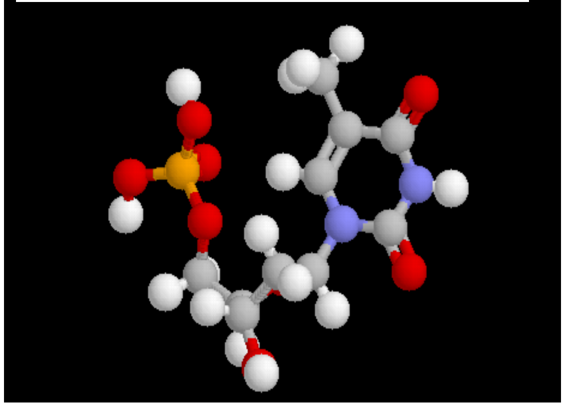
- **Transition from tunneling to the regime of thermally activated hopping**

Energetics of Excess Electron Transfer in DNA

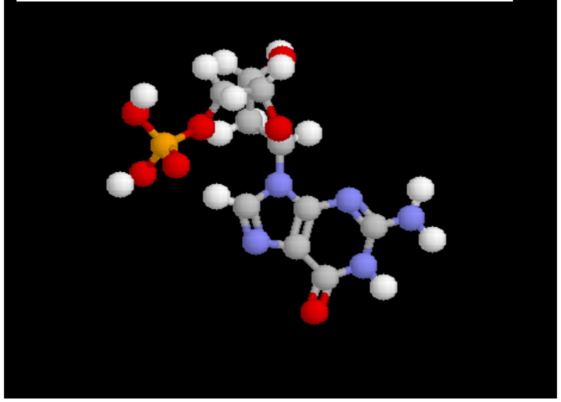
C, EA= +0.36 eV



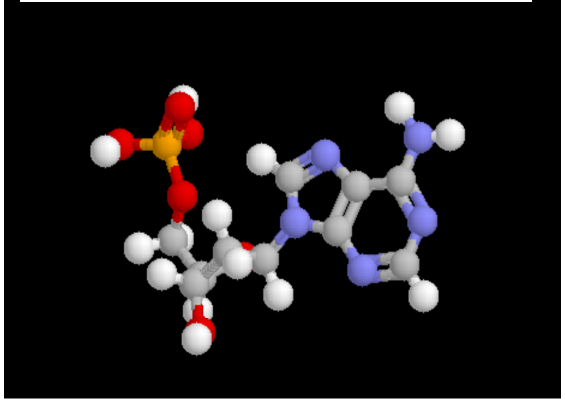
T, EA= +0.28 eV



G, EA= -0.57 eV



A, EA= -0.27 eV



More recent data for nucleotide triplets

A.A. Voityuk, M.E. Michel-Beyerle, N.Rösch, Chem. Phys. Lett. 342, 231 (2001)

Electron affinities decrease in the order

C≈T>>A>G

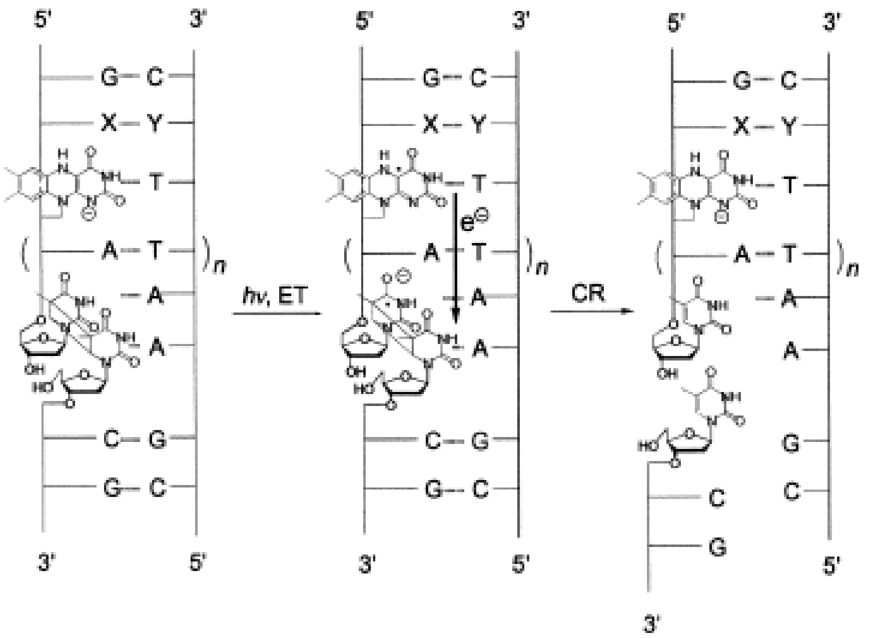
Thus “resting” sites for electrons are C and T.

Excess Electrons in DNA: Steady-State Measurements

C. Behrens, L.T. Burgdorf, A. Schwögler, and T. Carell, Angew. Chem. Int. Ed. 41, 1763 (2002)

1 →2 Photoexcitation initiates electron transfer from flavin injector to the thymine dimer

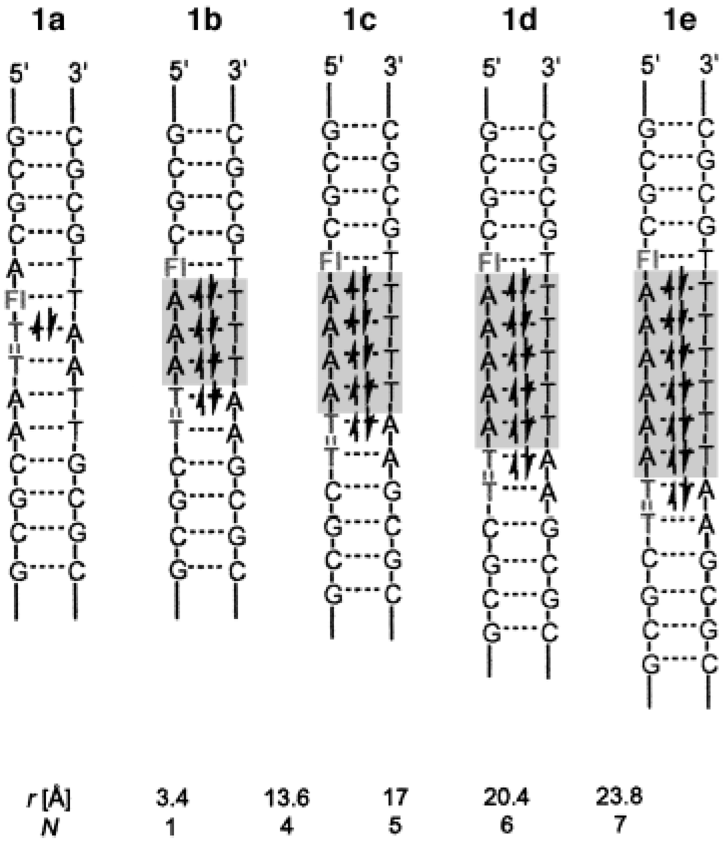
2→3 Electron irreversible trapped by the dimer subsequently triggers a cycloreversion (CR)

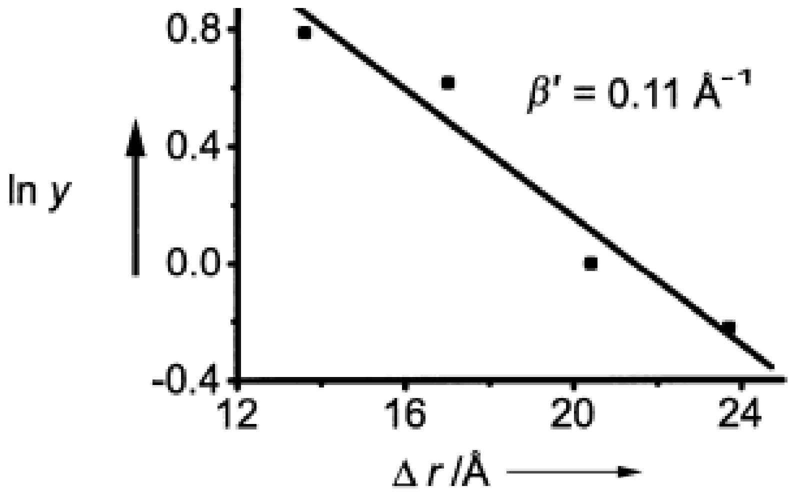


1 2 3

Observable: the yield of the cleaved DNA measured as a function of a number of AT pairs between flavin injector and the tymine dimer

Yield of DNA Cleavage y vs. the Length of AT Bridge between Flavin (Fl) and TT Dimer





Tunneling through A bases located at the same strand

Thymine TT dimer is the electron trap

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Is Electron Transfer from Flavin to TT dimer Sequence Dependent?

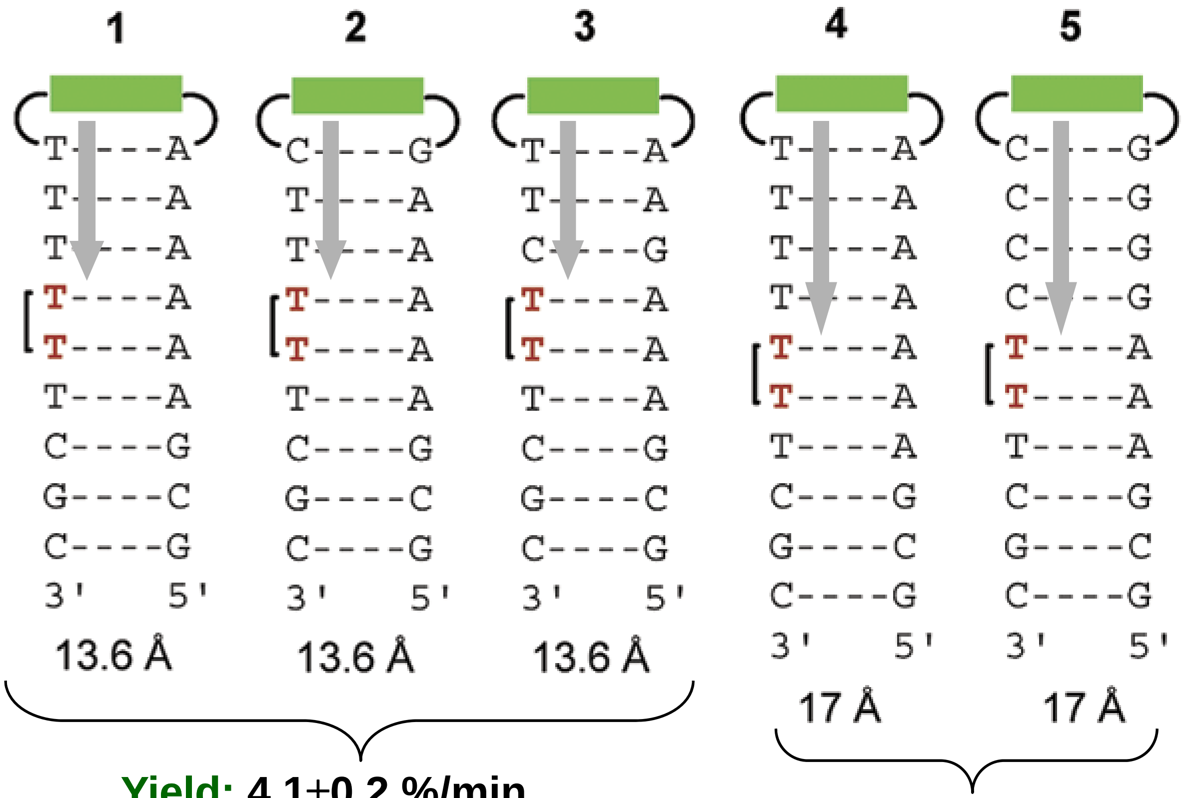
Experiment: S. Breeger, U. Hennecke, T. Carell, JACS 126, 1302 (2004)

🟩 Schematically denotes flavin electron donor

→ Excess electron pathway

In general, electron transfer is expected to be sequence dependent.

The lack of the sequence dependence in this particular case is due to the fact that for sequences 1- 5 electron pathway involves only bases (T and C) with almost the same EA values



Yield: 4.1±0.2 %/min

Yield: 2.7±0.2 %/min

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Summary of Stead-state Studies

Accessible Information

- G base is a resting site for a hole, C and T are resting sites for an excess electron
- Mechanisms of individual hole hops between two neighboring Gs connected by AT bridge
- Charge transfer efficiency in any sequence of Watson-Crick pairs as a function of the sequence structure and length
- How far a hole can travel along the stack

This allows to specify the initiation of chemistry over a large distance in DNA (several hundreds of Å)

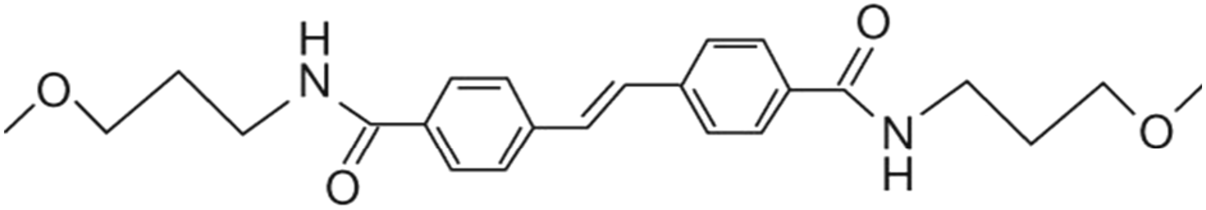
Inaccessible information

- The absolute rates of hole and electron generation, hopping, and trapping
- Influence of DNA dynamics on transport of holes and excess electrons
- How fast a hole and an excess electron can be transferred over a given distance

Issues

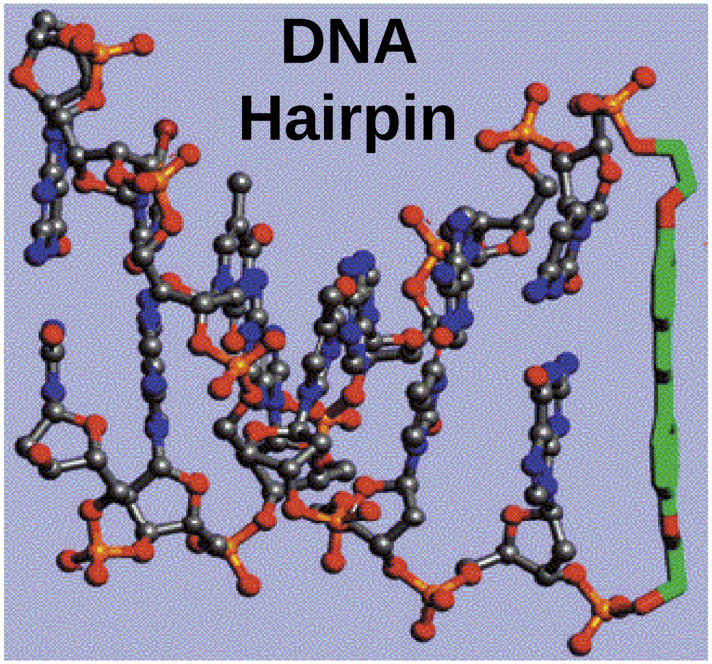
- Steady-state experiments
- Their theoretical analysis
- Information available from steady-state studies
- **Time-resolved measurement**
- **Rates the elementary processes**
- **The effect of conformational dynamics on the rates**

DNA Hairpins



F. D. Lewis, R. L. Letsinger, and M. R. Wasielewski, *Acc. Chem. Res.* 34 (2001) 159

Stilbene-4,4‘-dicarboxamide linker



Analysis of transient absorption of St anion in certain families of hairpins yields rates of hole generation

$St^{*} + G \longrightarrow St^{-} + G^{+}$

and hopping

$G \rightarrow G^{+}$

Hole Transfer Rates for Short AT Bridges

Marcus-Levich-Jortner equation

$$k_{CT} = \frac{2\pi}{\hbar} V^2 FC$$

Electronic coupling V

$$V \approx V_0 \exp\left(-\beta_c L/2\right)$$

β_c is the falloff parameter

L is the donor-acceptor distance

Franck-Condon factor FC

$$FC = (4\pi\lambda k_B T)^{-1/2} \exp\left(-\frac{(\Delta G + \lambda)^2}{4\lambda k_B T}\right)$$

λ is the reorganization energy

ΔG is the change in Gibbs free energy driving charge transfer

Information Needed to Estimate Hopping Rates

- **Electronic coupling V**

  Available from quantum chemical calculations

  K. Santhilkumar, F. C. Grozema, C. F. Guerra, M. L. Bickelhaupt, F. D. Lewis, Y.A. Berlin, M.A. Ratner, L.D.A. Siebbeles, JACS 127, 14894 (2005)

- **Gibbs free energy driving hole transfer ΔG**

  Available from the data on the linker reduction potential, its oxidation potential, and singlet energy

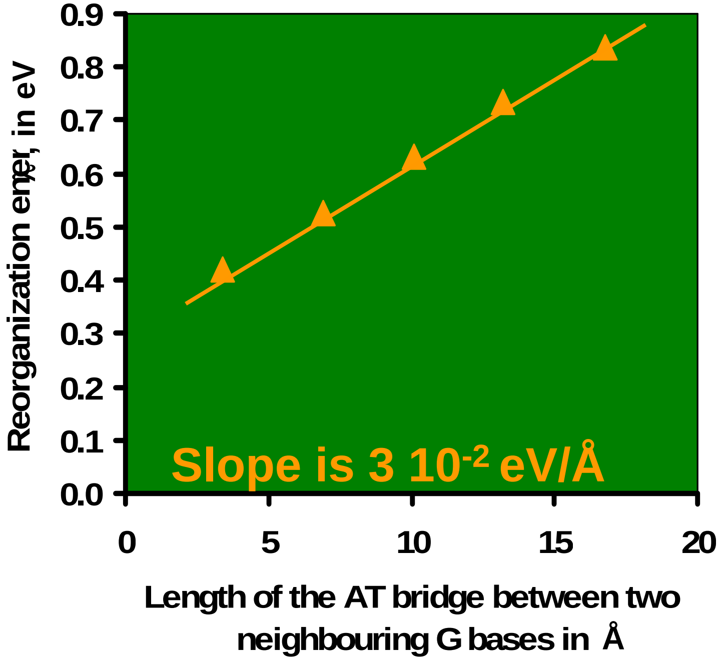
How can the reorganization energy λ be evaluated?

Distance-dependent Reorganization Energy

To calculate λ, a molecular non-local model of solvent response is useful

Advantages:

- **calculations are beyond the continuum approach**
- **molecular correlation length for orientation of permanent dipoles in water can properly be taken into account**



D. N. LeBard, M. Lilichenko, D. V. Matyushov, Yu. A. Berlin, M. A. Ratner, *J. Phys. Chem. B* 107, 14509-14520 (2003)

For further experimental evidences strongly supported this dependence, see S. Hess, M. Gotz, W. B. Davis, M. E. Michel-Beyerle, *J Am. Chem. Soc*. 124, 2422-2423 (2002)

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Consequences from Theoretical Analysis

- Estimate for the hopping rate $G^+ \rightarrow GG$ through one AT base pair

  Theory: $k_h = 1.4\ 10^7\ s^{-1}$ **Experiment:** $k_h = 2.0\ 10^7\ s^{-1}$

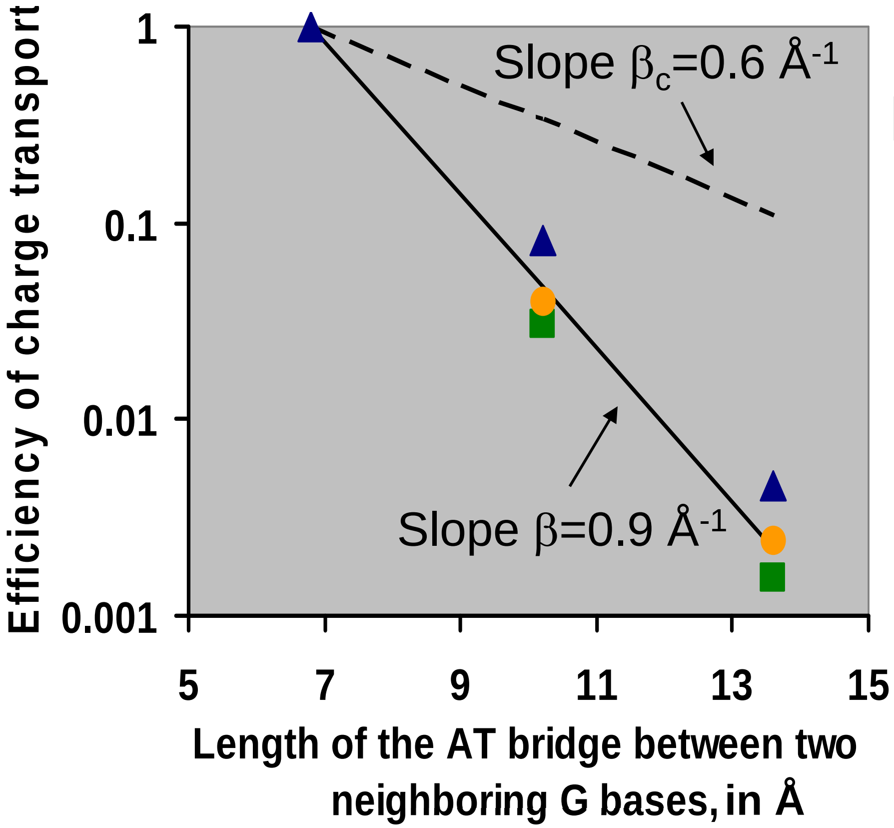
- Distance dependence of the rate results from the distance dependence of electronic coupling

$$V^2 = V_0^2 \exp(-\beta_c L)$$

and the distance dependence of Frank-Condon factor

$$FC \sim \exp(-\beta_r L)$$

Two Contributions to the Distance Dependence of Charge Transfer



Efficiency of charge transfer

$\sim \exp(-\beta L)$

$$\beta = \beta_r + \beta_c$$

● **Experimental data of Lewis et al.**

🟩 **Experimental data of Giese et al.**

▲ **Experimental data of Meggers et al.**

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Possible Mechanisms of Hole Motion in DNA A-tracts

- Polaron motion

According to Voityuk J. Chem. Phys. 122, 204904 (2005) the polar surroundings should essentially suppress the formation of polaron

- Motion in the tight-binding band with the width B

$$B > \hbar / \tau_{scatt}, \quad \text{where} \quad \mu = \frac{e}{m}\tau_{scatt}$$

$$\mu > \frac{e\hbar}{mB} = \frac{e\hbar}{4mb} \square \; 10 \text{ cm}^{2}\text{V}^{-1}\text{s}^{-1}$$

*Estimation based on experimental results of T. Takada et al. JACS **126**.1125 (2004) gives μ =9 10^{-4} $cm^{2}V^{-1}s^{-1}$*

- Sequential A-hopping

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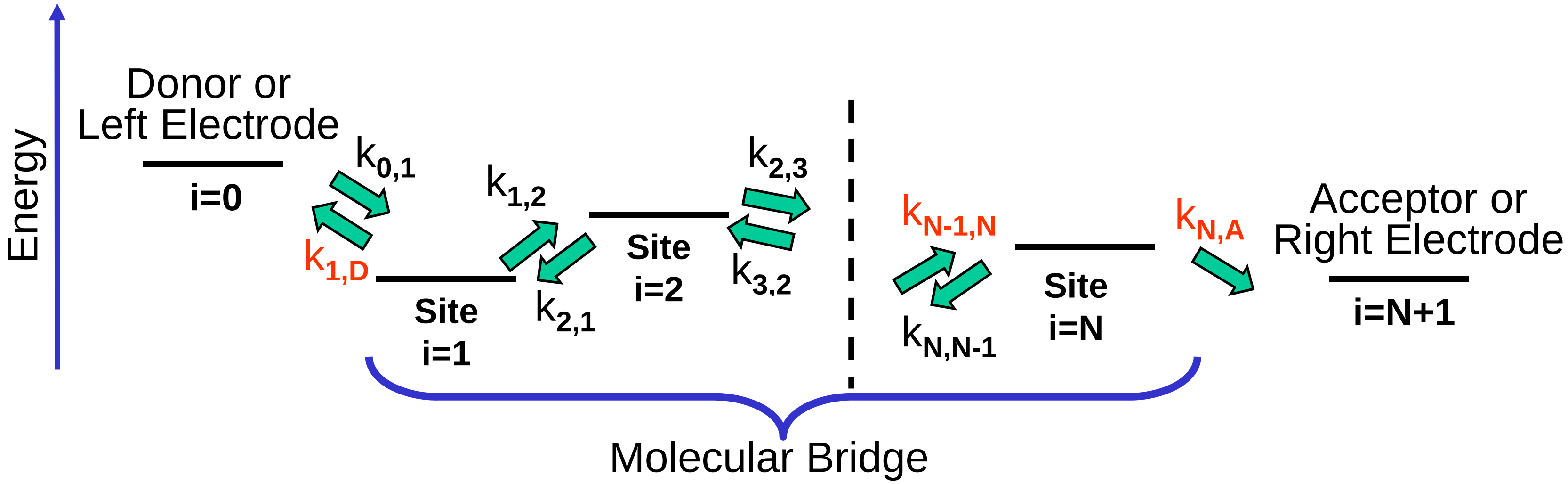
General Kinetic Analysis of Sequential Hopping



$$k_{CT} = \frac{\Psi \exp\left(-\frac{E_{BD}}{k_B T} \right)}{\frac{1}{k_{N,A}} + \frac{\Psi}{k_{1,D}} + \frac{1+\Phi}{k_{N,N-1}}}$$

$$\Psi = \begin{cases} \prod_{q=1}^{N-1} \frac{k_{q,q+1}}{k_{q+1,q}} & \text{for } N > 1 \\ 0 & \text{for } N = 1, \end{cases} \qquad \Phi = \begin{cases} \sum_{s=1}^{N-2} \left(\prod_{q=s}^{N-2} \frac{k_{q+1,q+2}}{k_{q+1,q}} \right) & \text{for } N > 2 \\ 0 & \text{for } 0<N \le 2 \end{cases}$$

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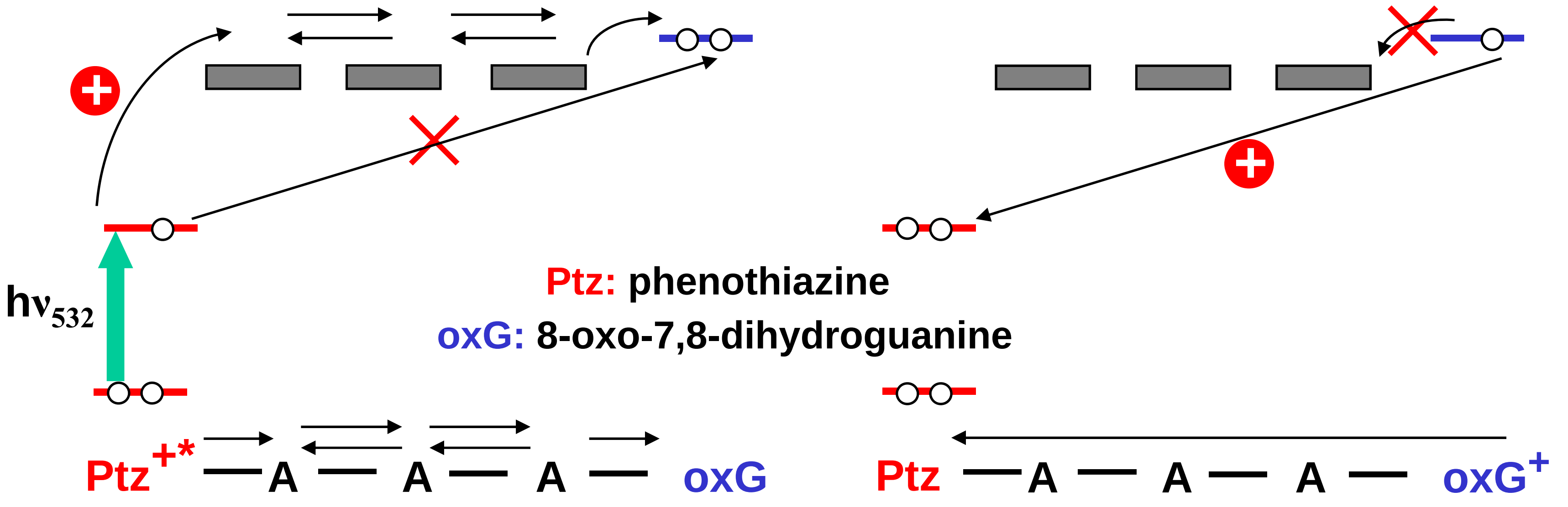
A-hopping vs. Superexchange

Experiment: K. Kawai, T. Takada, S, Tojo, M. Fujitsuka, and T. Majima, JACS 125, 6842 (2003);

T. Takada, K. Kawai, X. Cai, A. Sugimoto, M. Fujitsuka, and T. Majima, JACS 126, 1125 (2004)

Theory: K. Santhilkumar, F. C. Grozema, C. F. Guerra, M. L. Bickelhaupt, F. D. Lewis, Y.A. Berlin, M.A. Ratner, L.D.A. Siebbeles, JACS 127, 14894 (2005)

Forward A-hopping **Backward superexchange**



Ptz: phenothiazine

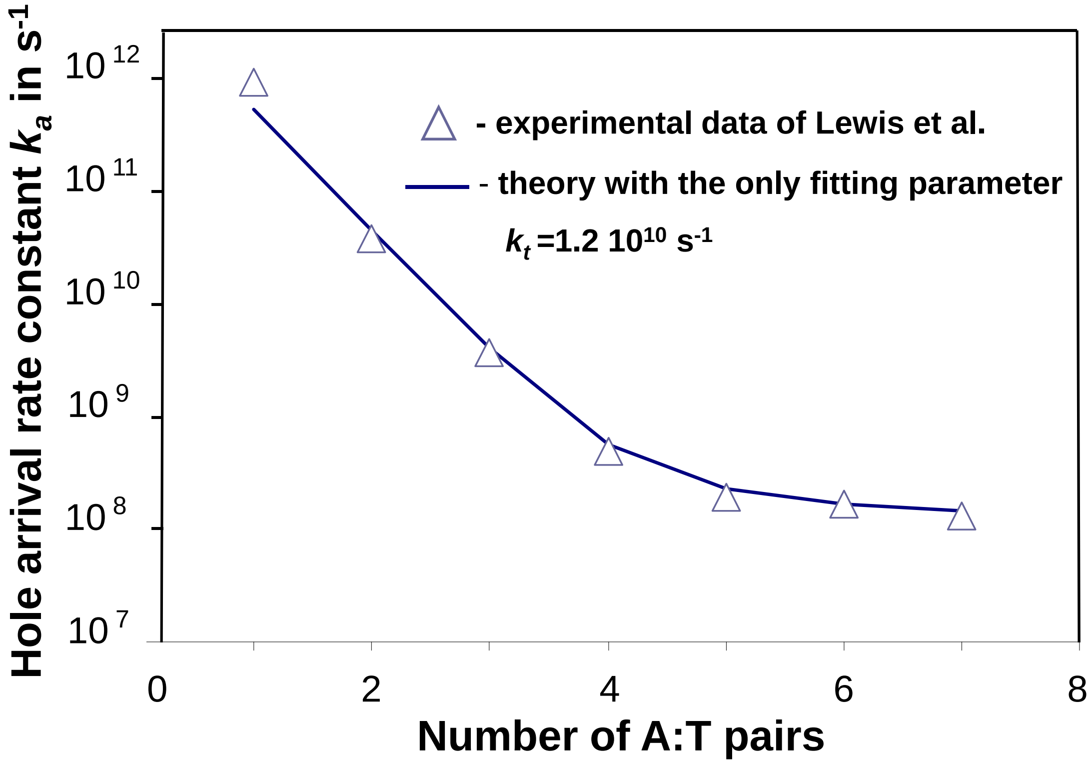
oxG: 8-oxo-7,8-dihydroguanine

Rate of A-hopping

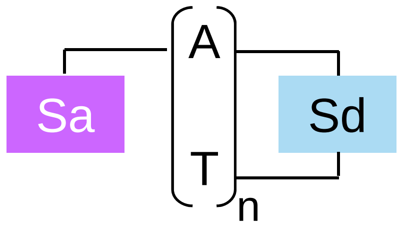
$2\ 10^{10}\ s^{-1}$ (deduced from transient absorption measurements)

$1.8\ 10^{10}\ s^{-1}$ (theory)

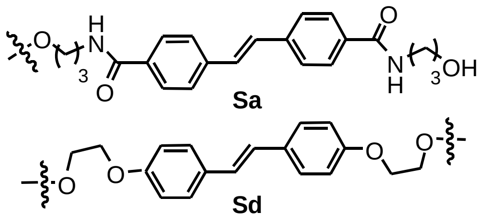
Hole Motion through A-tracts



Model systems studied:



n=1-7



Hole donor

Hole acceptor

$$k_a = \underbrace{W\exp[-\beta a(n+1)]}_{\text{Tunneling}} + \underbrace{\frac{k\exp\left(-\frac{E_{BD}}{k_B T}\right)}{\frac{k}{k_t}+\frac{k}{k_i}\exp\left(-\frac{E_{BD}}{k_B T}\right)+n-1}}_{\text{A-hopping}}$$

$k = 2\ 10^{10}\ s^{-1}$ is the rate of hole hopping between AT pairs (A-hopping)

k_t is the rate of hole trapping by Sd

$k_i = 3\ 10^{10}\ s^{-1}$ is the rate of hole injection on the AT bridge

E_{BD} is the energy gap between the AT bridge and Sa

$\beta = 0.7$ Å^{-1} is the falloff parameter

$a = 3.4$ Å is the mean distance between AT pairs

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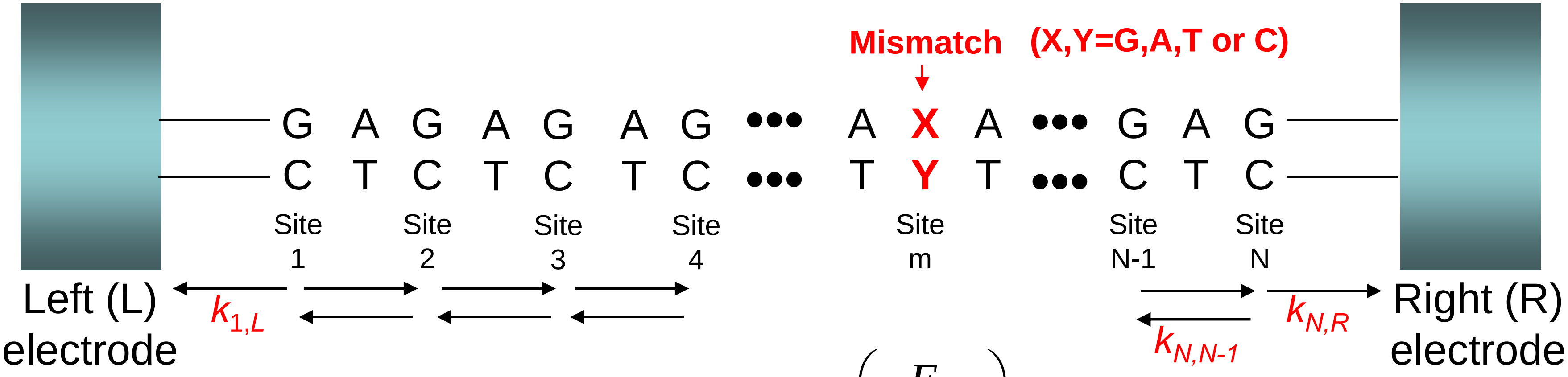
Hopping Conductance


Mismatch **(X,Y=G,A,T or C)**

G A G A G A G ••• A X A ••• G A G

C T C T C T C ••• T Y T ••• C T C

Site 1 Site 2 Site 3 Site 4 Site m Site N-1 Site N

Left (L) electrode

$k_{1,L}$

$k_{N,N-1}$

$k_{N,R}$

Right (R) electrode

$$g = \frac{e^2}{k_B T} \cdot \frac{\Psi \exp\left(-\frac{E_{BF}}{k_B T} \right)}{\frac{1}{k_{N,R}} + \frac{\Psi}{k_{1,L}} + \frac{1+\Phi}{k_{N,N-1}}}$$

$$\Psi = \begin{cases} \prod_{q=1}^{N-1} \frac{k_{q,q+1}}{k_{q+1,q}} & \text{for } N > 1 \\ 0 & \text{for } N = 1, \end{cases} \qquad \Phi = \begin{cases} \sum_{s=1}^{N-2} \left(\prod_{q=s}^{N-2} \frac{k_{q+1,q+2}}{k_{q+1,q}} \right) & \text{for } N > 2 \\ 0 & \text{for } 0 < N \le 2 \end{cases}$$

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Relationship between the Charge Transfer Rate and Molecular Conductance

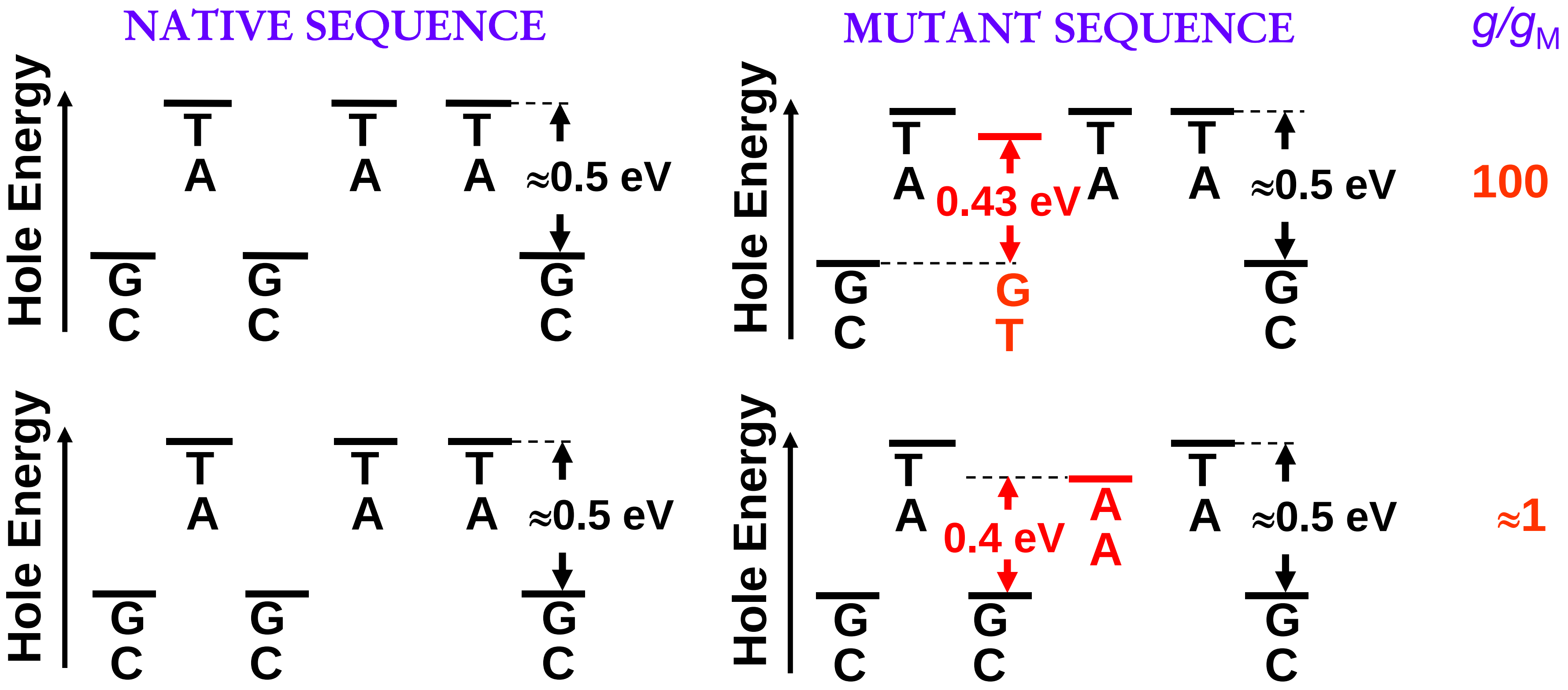
$$g = \frac{e^2}{k_B T} \exp\left[-\frac{\left(E_{BF} - E_{BD}\right)}{k_B T} \right] \frac{k_{N,A}^{-1} + \Psi k_{1,D}^{-1} + (1+\Phi) k_{N,N-1}^{-1}}{k_{N,R}^{-1} + \Psi k_{1,L}^{-1} + (1+\Phi) k_{N,N-1}^{-1}} \cdot k_{CT}$$

For long sequences (wires)

$$N >> \max\left\{ k_{N,N-1}\left(\frac{1}{k_{N,A}} + \frac{1}{k_{1,D}} \right), k\left(\frac{1}{k_{N,R}} + \frac{1}{k_{1,L}} \right) \right\}$$

$$\boxed{g = \frac{e^2}{k_B T} \exp\left[-\frac{\left(E_{BF} - E_{BD}\right)}{k_B T} \right] \cdot k_{CT}}$$

Different Mismatches Modify Energy Landscape for Hole Transport Differently



These results predict the dependence of DNA conductance on the type of the mismatch

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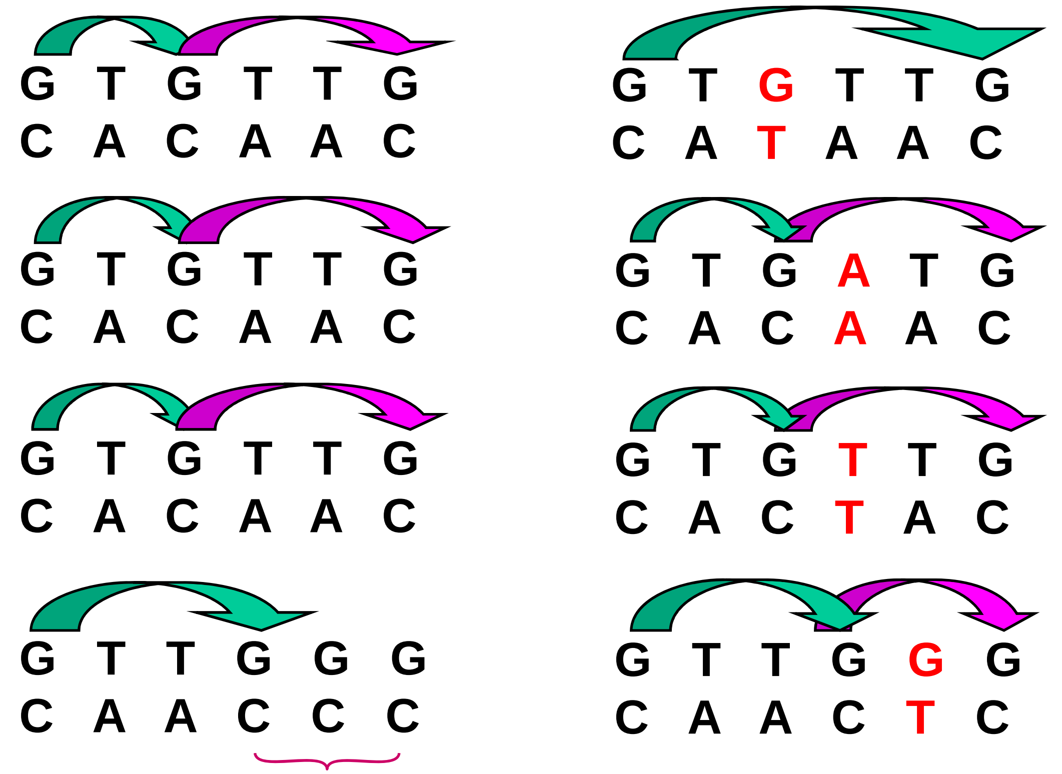
Changes in DNA Conductance Depend on the position of the mismatch within the base pair sequence



MISMATCH LOCATION	NATIVE SEQUENCE WITH CONDUCTANCE *g*	MUTANT SEQUENCE WITH CONDUCTANCE *g*	g/g_M
Single G site	G T G T T G C A C A A C	G T G T T G C A T A A C	100
AT bridge	G T G T T G C A C A A C	G T G A T G C A C A A C	≈1
AT bridge	G T G T T G C A C A A C	G T G T T G C A C T A C	≈1
GGG triplet	G T T G G G C A A C C C	G T T G G G C A A C T C	<1

Hole trap

No hole trap

Conclusions

1. The proposed model of variable range hopping adequately describes sequence and distance dependencies of charge transfer in DNA
2. Analysis of the mechanism governing the elementary step of hopping motion shows that for short AT bridges hole transfer between neighboring G bases proceeds via tunneling. By contrast, hopping over longer bridges requires thermal activation
3. These two mechanisms allow a hole to travel along the stack of Watson-Crick base pairs over long distances (several hundreds of angstroms)
4. The reorganization of the environment slows down hopping motion, so that a hole needs at least 0.1 μs to cover this distance
5. Theoretical analysis shows that within the model of variable range hopping the rate of charge transfer and molecular conductance are interrelated. Using this relationship we predict that measurements of DNA conductance allow the detection of single mismatch. The change in conductance caused by mismatch depends on the position of “mutant” pair in the sequence and on the type of the mismatched base pair. Recently these theoretical findings were supported by experiments of N. Tao and co-workers (Arizona).
6. For hopping motion, the effect of DNA dynamics on the rate of hole transfer can be taken into account by averaging the square of the electron coupling matrix element over fast conformational changes

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Acknowledgement

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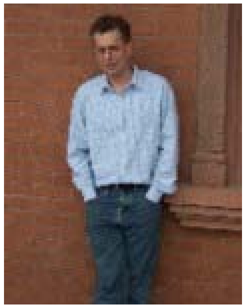
(Regensburg)

for the opportunity to present this talk and for hospitality

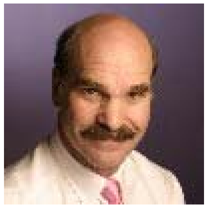


Prof. Dmitry Matyushov
(Arizona)

Prof. Laurens Siebbeles
(Delft)

Prof. Alex Burin
(New Orleans)

Prof. Fred Lewis



Prof. Mark Ratner

for collaborative studies of particular aspects of the problem

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(Munich)

for valuable discussions

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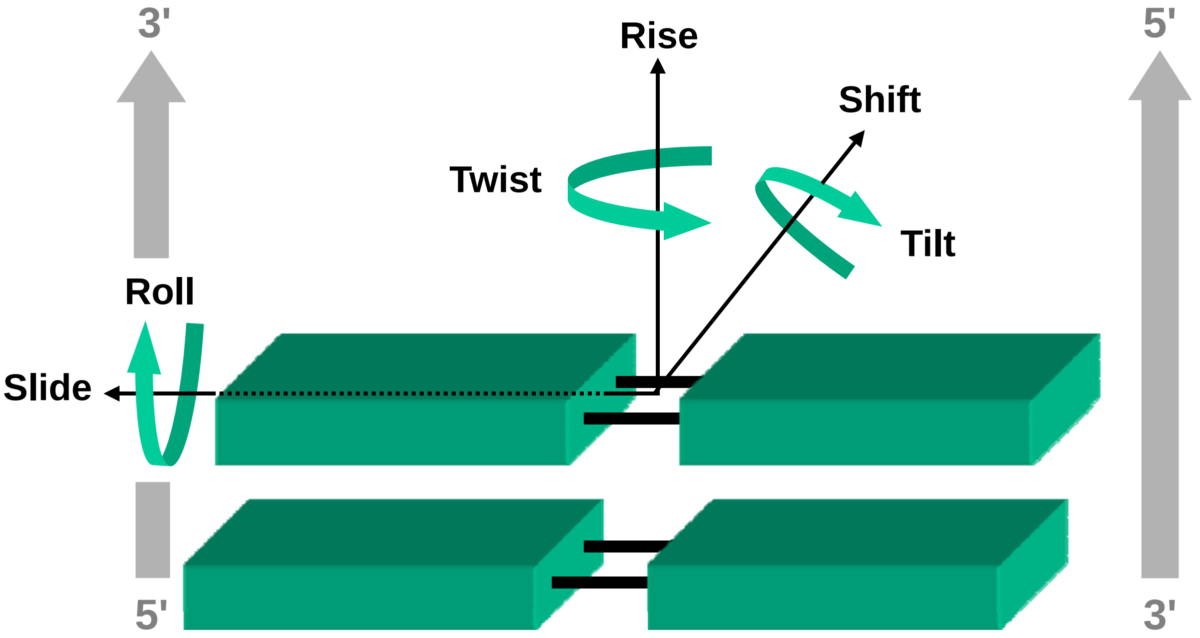
Last but not the least

Chemistry Devision of the Office of Naval Research,

the Department of Defense MURI and DURINT programs,

the NASA University Research, Engineering and Technology Institute (URETI) program

Conformational Degrees of Freedom



Real structure (X-ray data for 400 base pairs):

Rise=3.2÷3.6 Å,

Shift=-1.0 ÷ 1.6 Å,

Slide=-2.4 ÷ 2.8 Å

Twist=20 ÷41 º,

Tilt=-7.8 ÷ 6.6 º,

Roll=-8.6 ÷ 25 º

Ideal structure: Rise=3.38 Å, twist=36º,
all other parameters are zero

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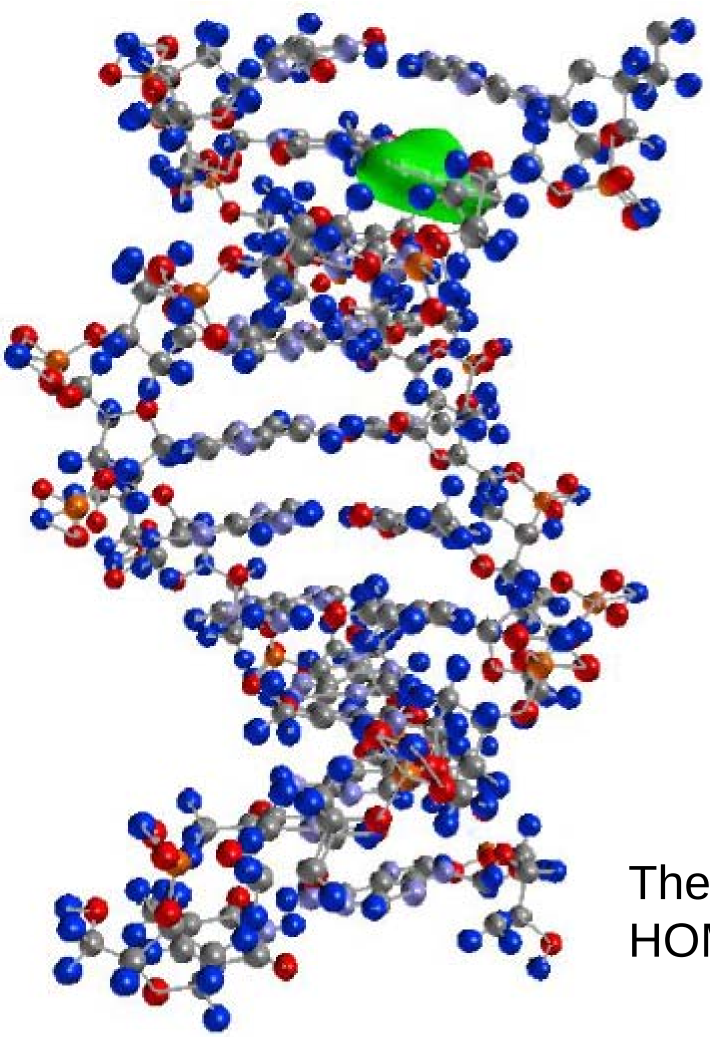
Charge Carriers in Dynamic DNA



The charge density of
HOMO is shown in green

Is Charge Transport Conformationally Dependent?

Time scale of hopping: $\tau_h \sim 10^{-8}$ s

Time scale of conformational motion: $\tau_m \sim 10^{-11} - 10^{-10}$ s

T. E. Cheatham,III and P. A. Kollman, *Ann. Rev. Phys. Chem.* 51 (2000) 435

So, $\tau_h \gg \tau_m$ and averaging over the spectral density function yields

$$k_{CT} = k^{(0)} + \underset{0}{k^{(1)}} + k^{(2)} + \ldots$$

$$k^{(0)} = \frac{\langle V^2 \rangle}{\hbar} \sqrt{\frac{\pi}{\lambda k_B T}} \exp\left(- \frac{\left(\lambda + \Delta E^0\right)^2}{4 \lambda k_B T} \right)$$

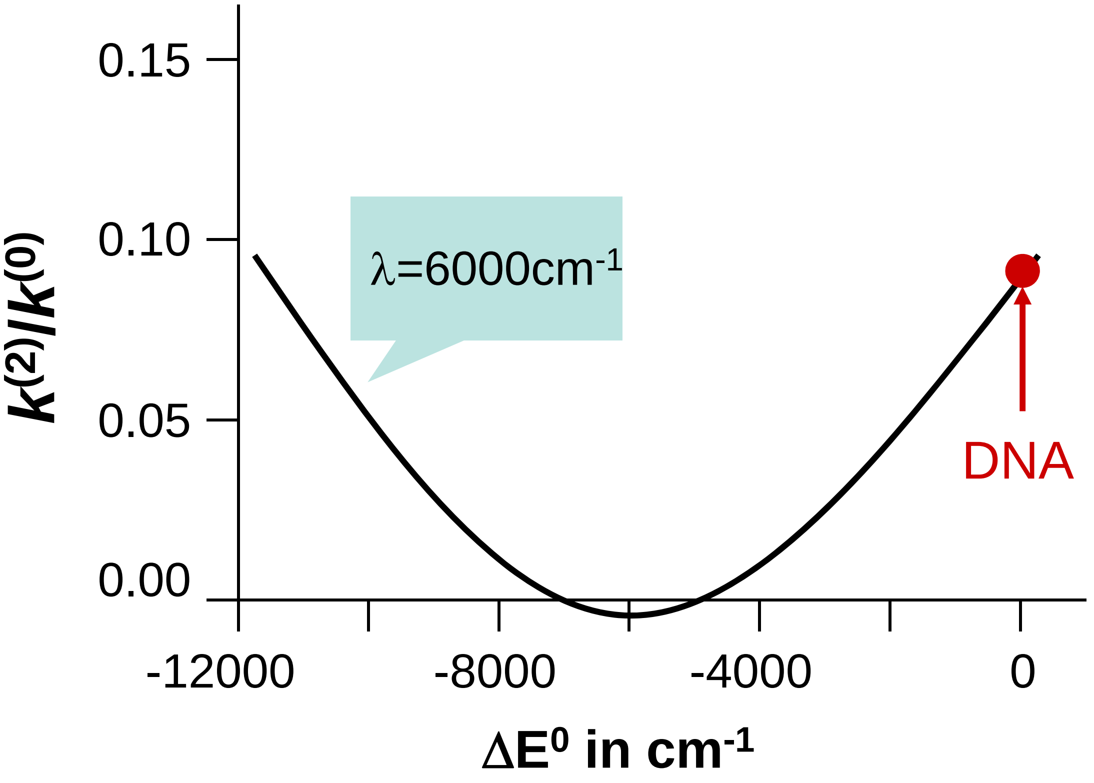
**Marcus equation
with V² replaced by <V²>**

$$k^{(2)} = k^{(0)} 2 \frac{\hbar^2}{\tau_c^2} \left[\frac{\left(\lambda + \Delta E^0\right)^2 - 2 \lambda k_B T}{\left(4 \lambda k_B T\right)^2} \right] \left(1 - \frac{\langle V \rangle^2}{\langle V^2 \rangle} \right)$$

Correction for fluctuations

Is the Correction Important?

$$\frac{k^{(2)}}{k^{(0)}} = 2\frac{\hbar^2}{\tau_c^2}\left[\frac{\left(\lambda+\Delta E^0\right)^2 - 2\lambda k_B T}{\left(4\lambda k_B T\right)^2}\right]\left(1-\frac{\langle V\rangle^2}{\langle V^2\rangle}\right)$$



$$\hbar/\tau_C = 200\,\text{cm}^{-1}$$

T=300K

$\langle V\rangle$=0

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Problems for Further Investigations

- Effect of mismatches and binding events involving repair enzyme on charge transport (more experiments and calculations of energetics are needed)
- Electron migration in DNA (more experiments are needed)
- Localization of charge vs delocalization
  - *Large polaron formation* - Schuster, 1999; Conwell, 2000
  - *Small polaron formation* - Beratan, 2002
  - *Localization of holes on individual G's* - Voityk, 2005
- Solvent response to charge motion
- Adiabatic vs. non-adiabatic mechanism of charge transfer
- DNA-nanopartical interfaces