Charge transfer through DNA

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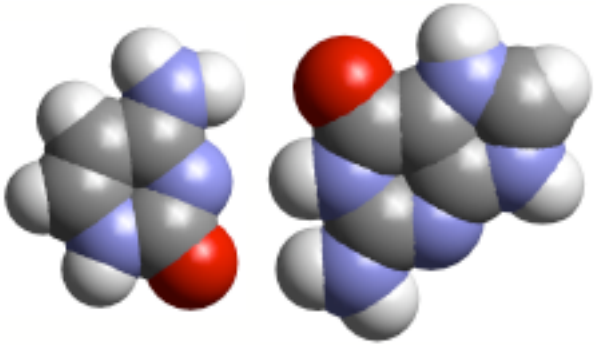
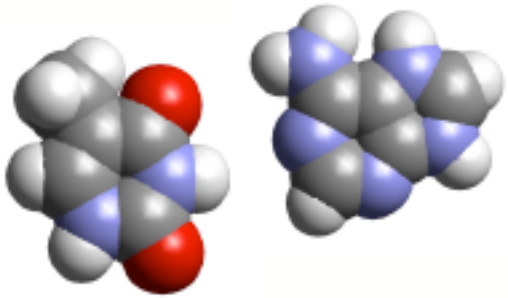
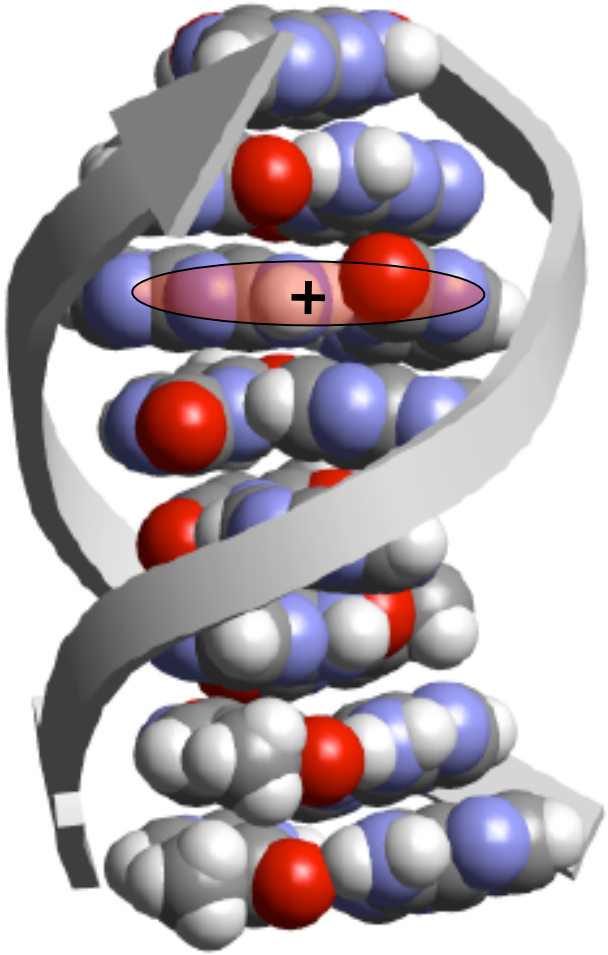
Base pair stacking in DNA



C:G



T:A



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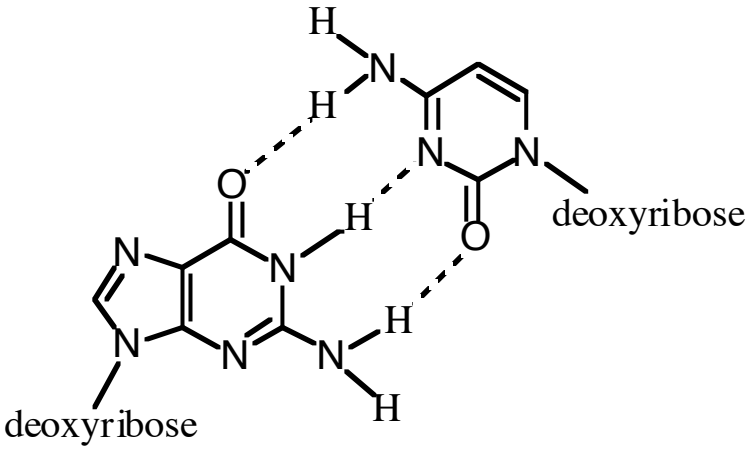
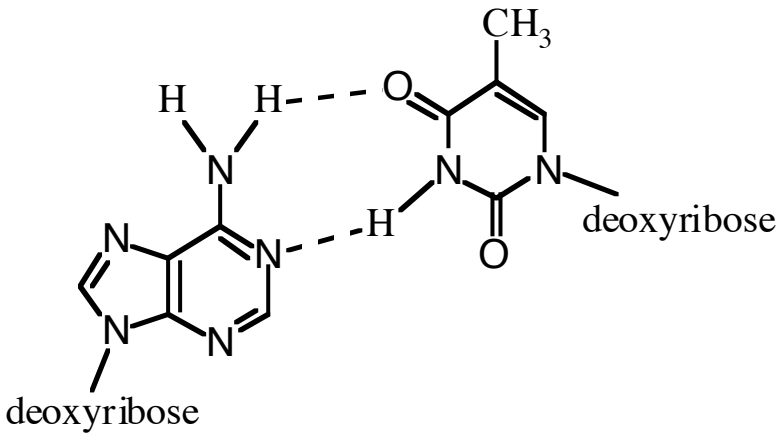
G:C and A:T base pairing



G:C



A:T

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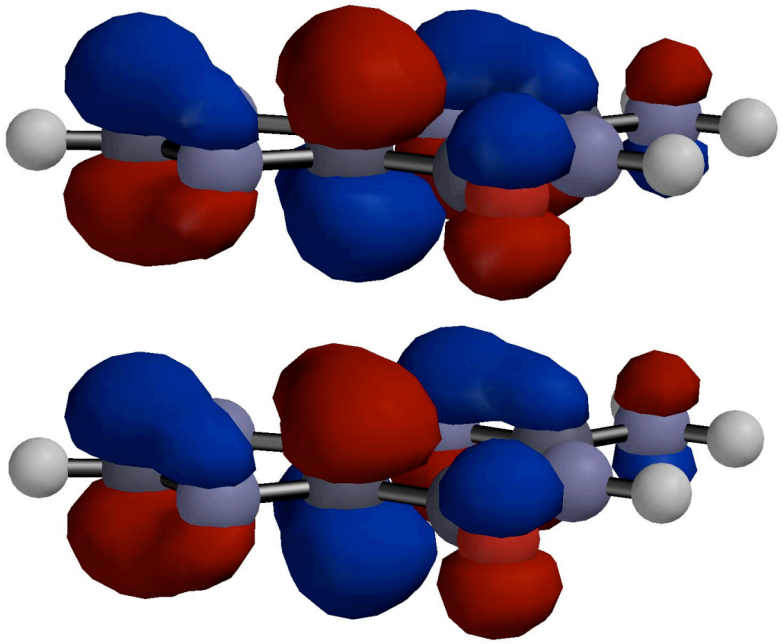
π-orbitals on adjacent bases interact and can provide pathway for charge transport

two stacked guanines



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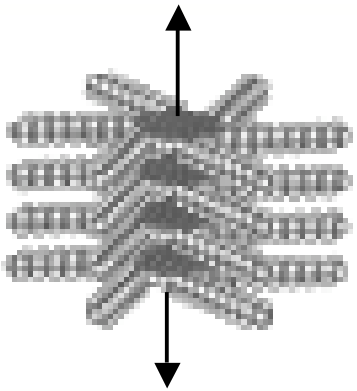
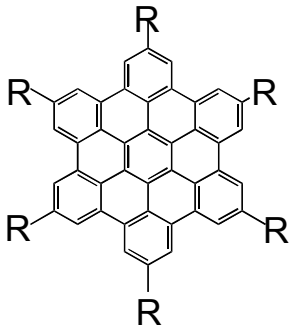
DNA analogous to discotic liquid crystalline materials

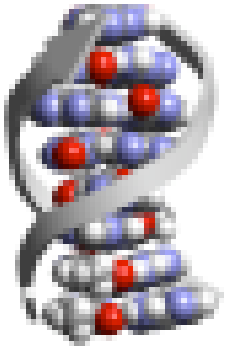
discotic liquid crystals

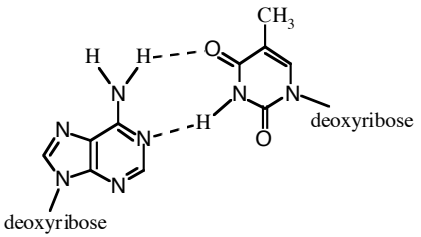
mobility 0.01 - 1 cm^2/Vs





DNA ?





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Charge migration in DNA

Electrons and holes can be created in DNA by:

- radiation (UV, high-energy radiation)
- chemical reactions
- injection from electrodes

Insight into charge migration along DNA is important for:

1. **Understanding biological damage due to charges**
   - radiation induced mutations
   - oxidative reactions

2. **Application in nanoscale molecular electronics**
   - DNA used as a molecular wire
   - DNA used as a scaffold for conducting wire

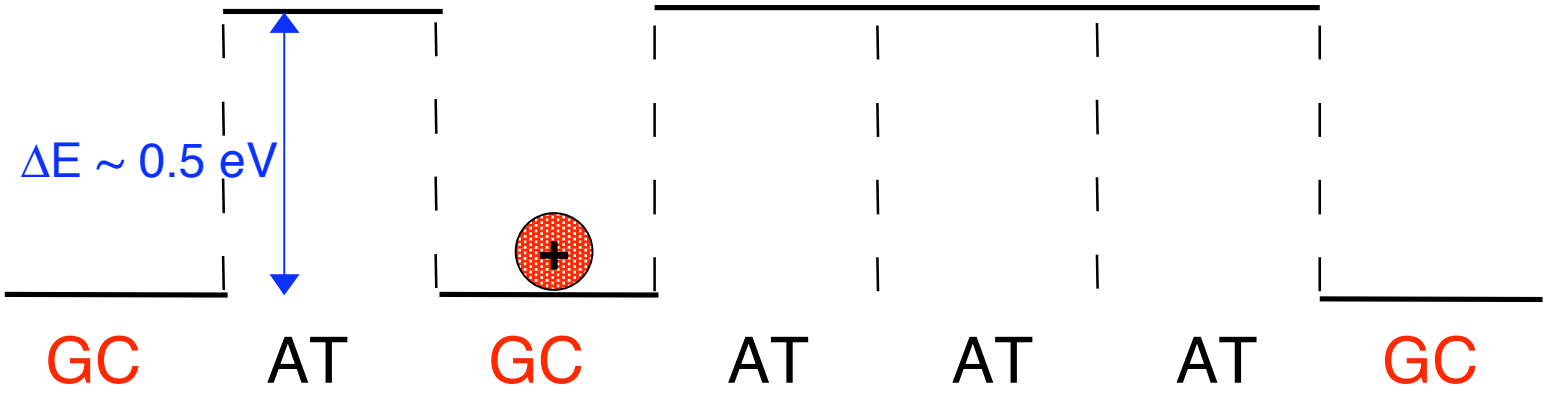
Present work

1. Charge transfer in Donor-DNA-Acceptor systems

2. Mobility of charges on DNA

3. Selective photo-oxidation of specific guanines

Positive charges reside on guanine



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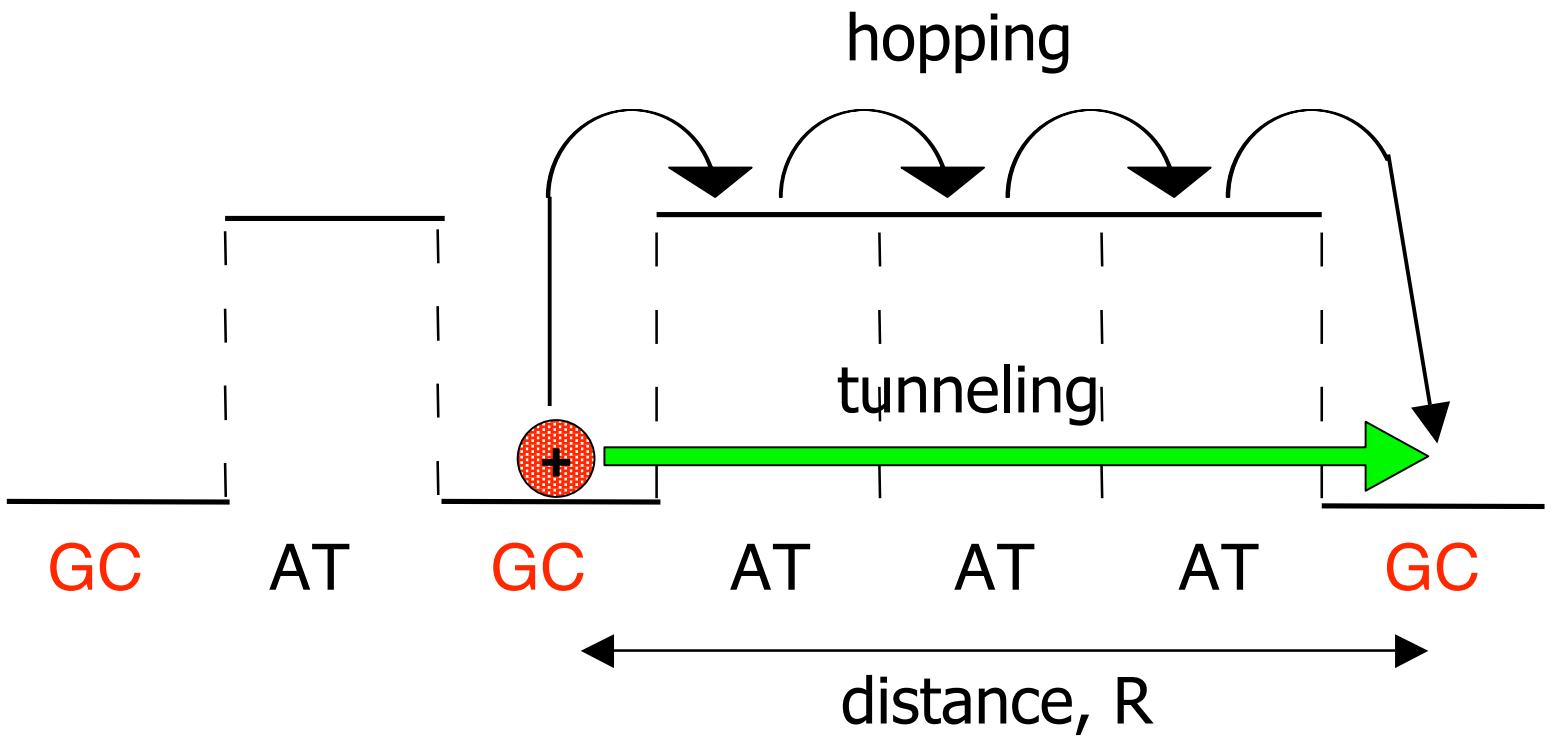
Mechanism of charge migration between G's ?



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Guanine-DNA-Guanine

Charge transfer rate often decays exponentially with distance:

$$k \propto e^{-\beta R}$$

R: Distance between donor and acceptor

β: Fall of rate characterizes distance dependence

Aim of theoretical studies

- Explain high (~ 1.0 $Å^{-1}$) and low (~ 0.1 $Å^{-1}$) experimental values of β

- Provide insight into factors governing absolute values of charge transfer rates

Quantum mechanical model

- Wavefunction of the charge is superposition of HOMO's on nucleobases

$$\psi(t) = \sum c_k(t)\Phi_k$$

- Hamiltonian contains site-energies and electronic couplings from DFT (ADF) calculations

E_{ij} : on-site energy

J_{ij} : electronic coupling

Γ : decay parameter at acceptor site

$$\hat{H}_{el} = \begin{pmatrix} E_{11} & J_{12} & 0 & 0 \\ J_{21} & E_{22} & J_{23} & 0 \\ 0 & J_{32} & E_{33} & J_{34} \\ 0 & 0 & J_{43} & E_{44} - i\Gamma \end{pmatrix}$$

- Electronic couplings vary in time due to motion of base pairs (described classically)

Charge is initially localized on donor site and delocalizes when wavefunction is propagated in time

$$i\hbar \frac{\partial \psi(t)}{\partial t} = \hat{H}\psi(t)$$

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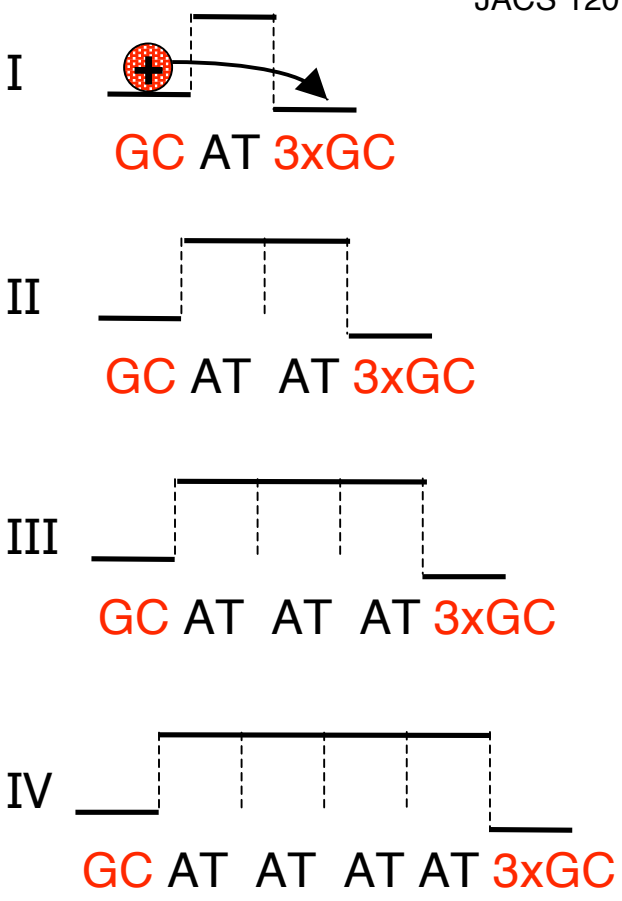
Distance dependence

Experimental studies by Meggers et al.

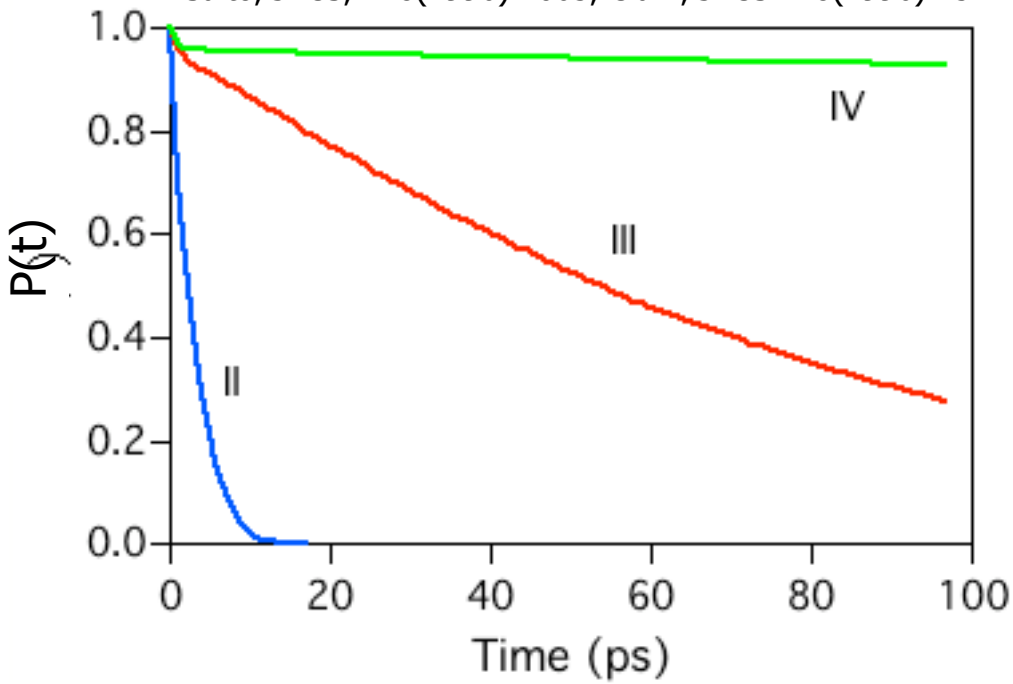
JACS 120 (1998) 12950



Theoretical results

J = 0.11 eV, E_{AT} - E_{GC} = 0.55 eV

Saito, JACS, 118(1996) 7063, Clark, JACS 118(1996) 7574



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Decay of charge: $P(t) = e^{-k(R)t}$

In case $k(R) = k_0 e^{-\beta R}$

One gets linear behavior for

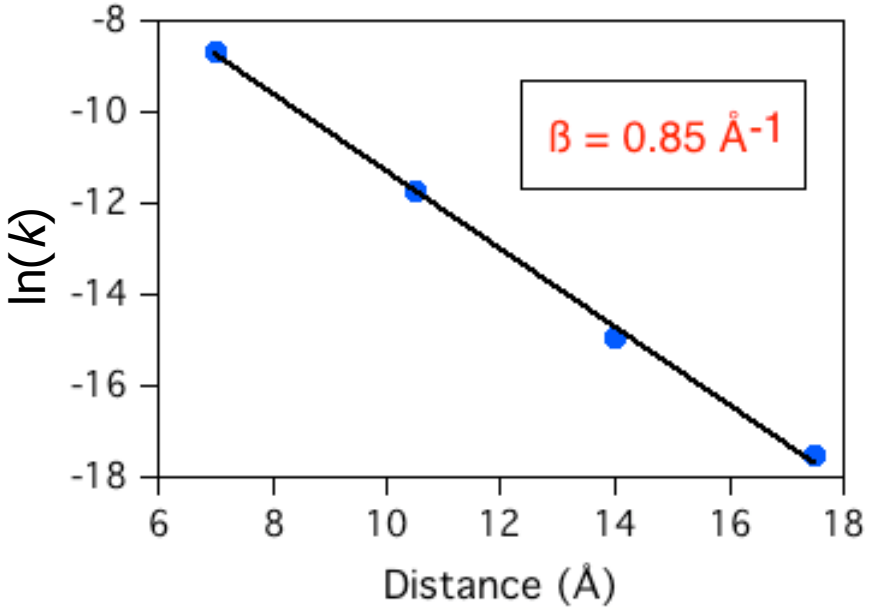
$$\ln[k(R)] = -\beta R + \ln[k_0]$$

Distance dependence

Charge migration rate through sequences I-IV shows exponential dependence on distance

Theoretical β value (0.85Å^{-1}) is close to experimental value (0.7Å^{-1}) of Meggers et al.

Charge tunnels through classically forbidden region of AT base pairs



F.C. Grozema et al., Int. J. Quant. Chem. **75**, 1009 (1999)

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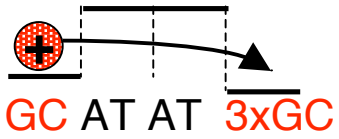
Sequence dependence

Sequences of AT's interrupted with GC base pairs

Experiments by Giese et al. *Angew. Chem. Int. Ed.*, 38(1999) 996

A



B

C

D

Small distance dependence observed: $\beta = 0.07$ Å^{-1}

Hopping between GC base pairs ???

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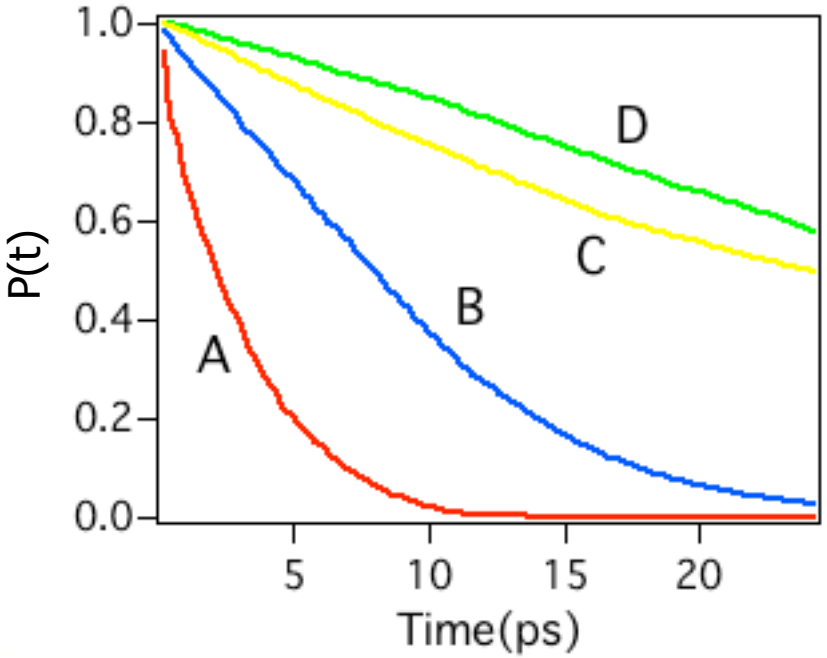
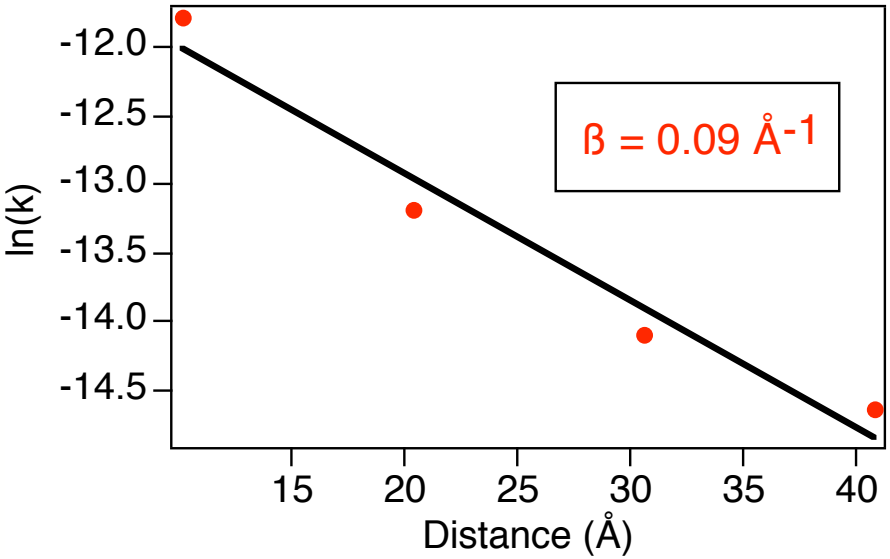
Sequence dependence - Theoretical results



Weak distance dependence



Theoretical β value (0.09 Å^{-1}) agrees with experimental value (0.07 Å^{-1}) of Giese et al.

F.C. Grozema et al., J. Am. Chem. Soc. **122**, 10903 (2000)

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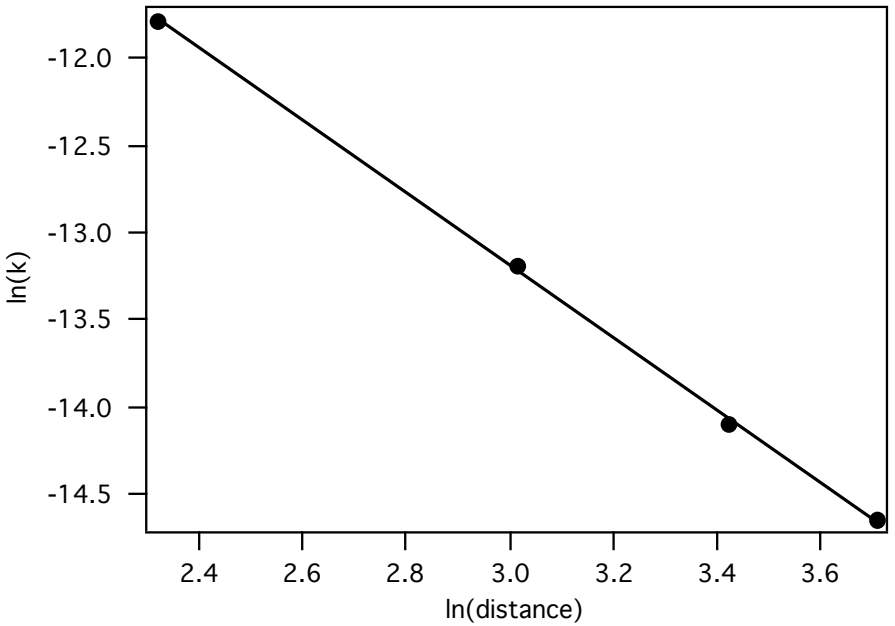
Transfer rate - Multi-step hopping

Charge transfer rate according to multi-step hopping:

$$k_{ct} \sim R^{\eta}$$

$$\Rightarrow \ln k_{ct} \propto -\eta \ln R$$

The fit gives $\eta = 2.09$



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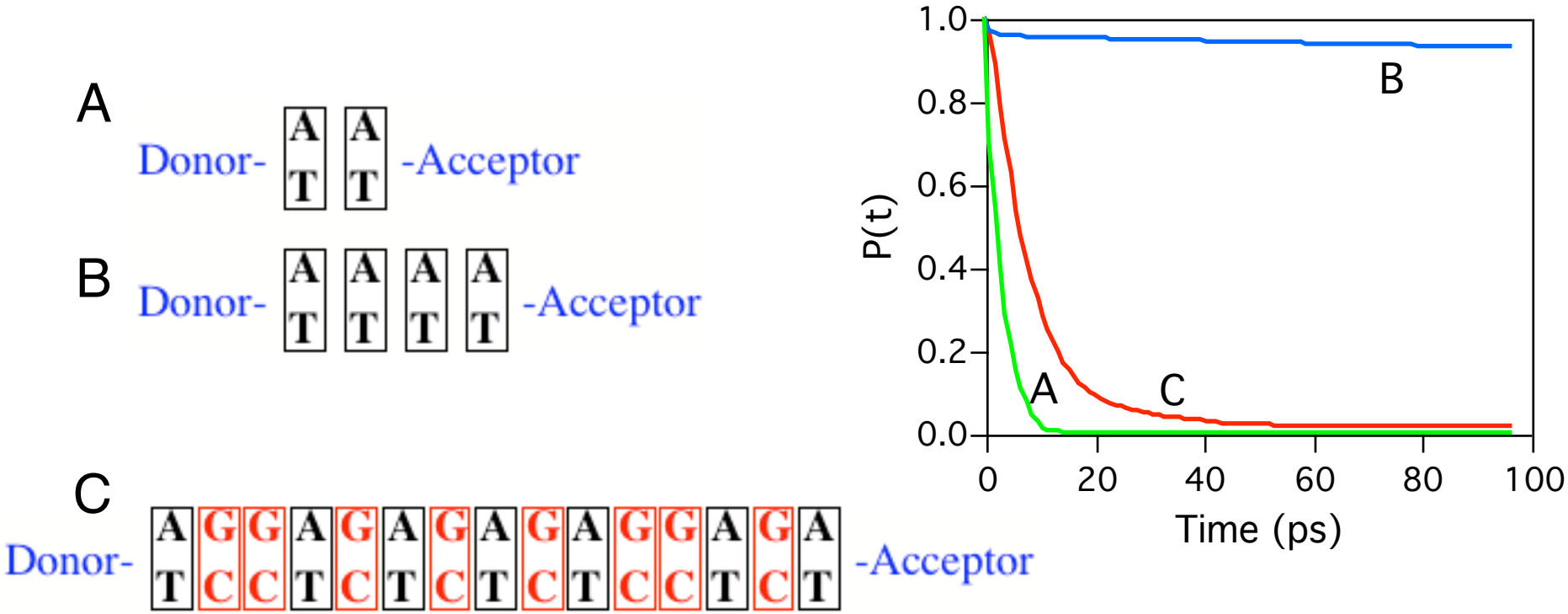
Sequence dependence



Charge migration over 54 Å in sequence C is nearly as efficient as over 10 Å in sequence A (agrees with expts. of Meggers)

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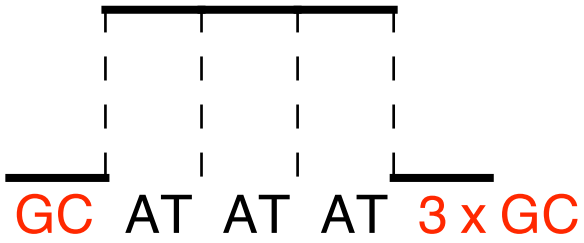
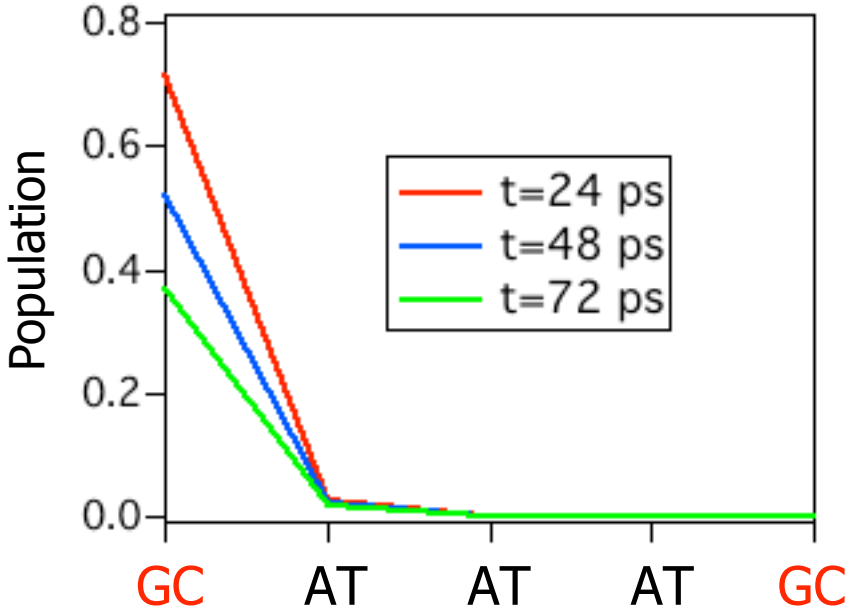
Population analysis

Charge distribution at three different times





Population on AT bridge is negligible at all times

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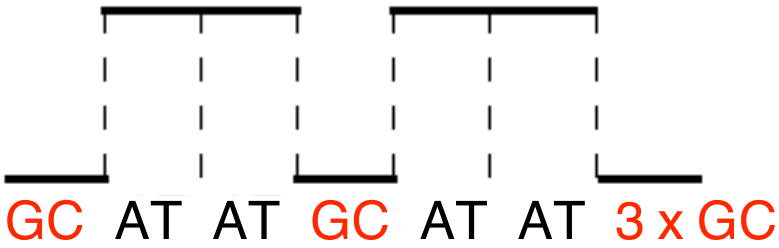
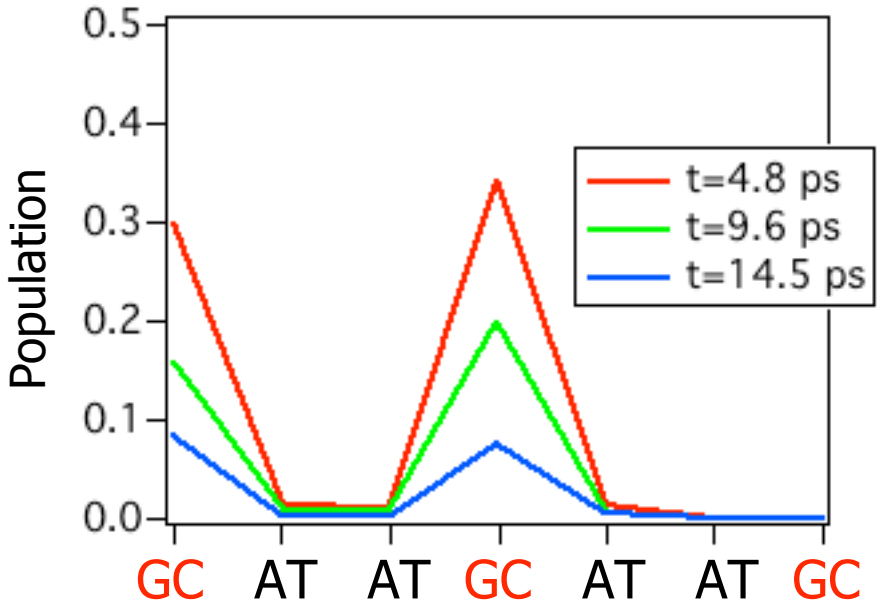
Population analysis

AT sequence interrupted by GC



Population at three different times



Population on AT is negligible

Charge tunnels through AT bridge to next GC

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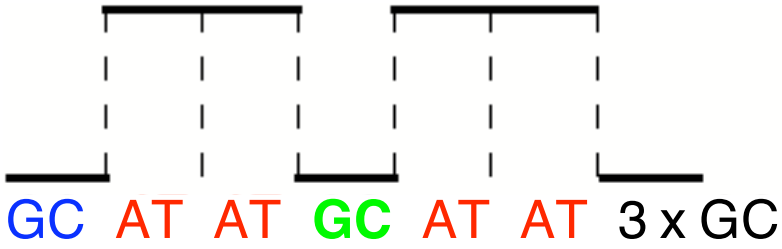
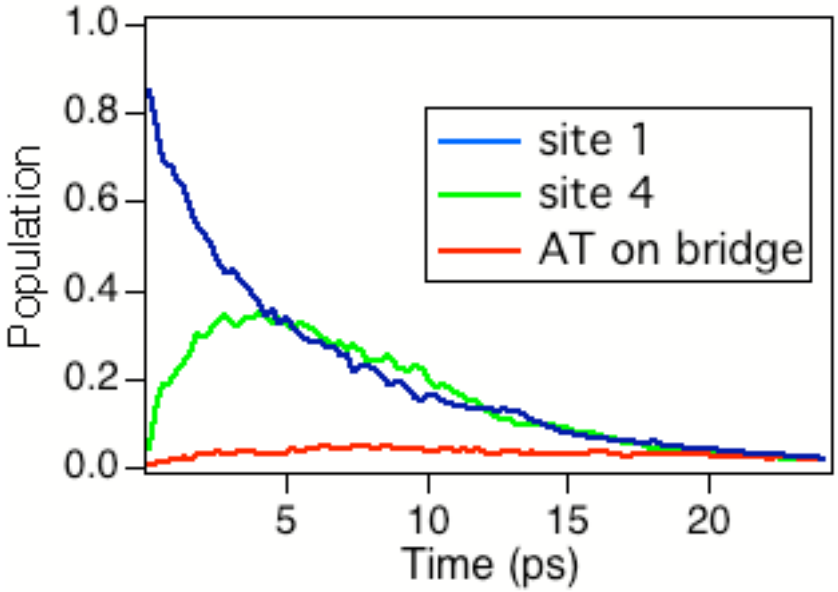
Population analysis



Charge effectively hops between GC base pairs

Population at GC sites as a function of time



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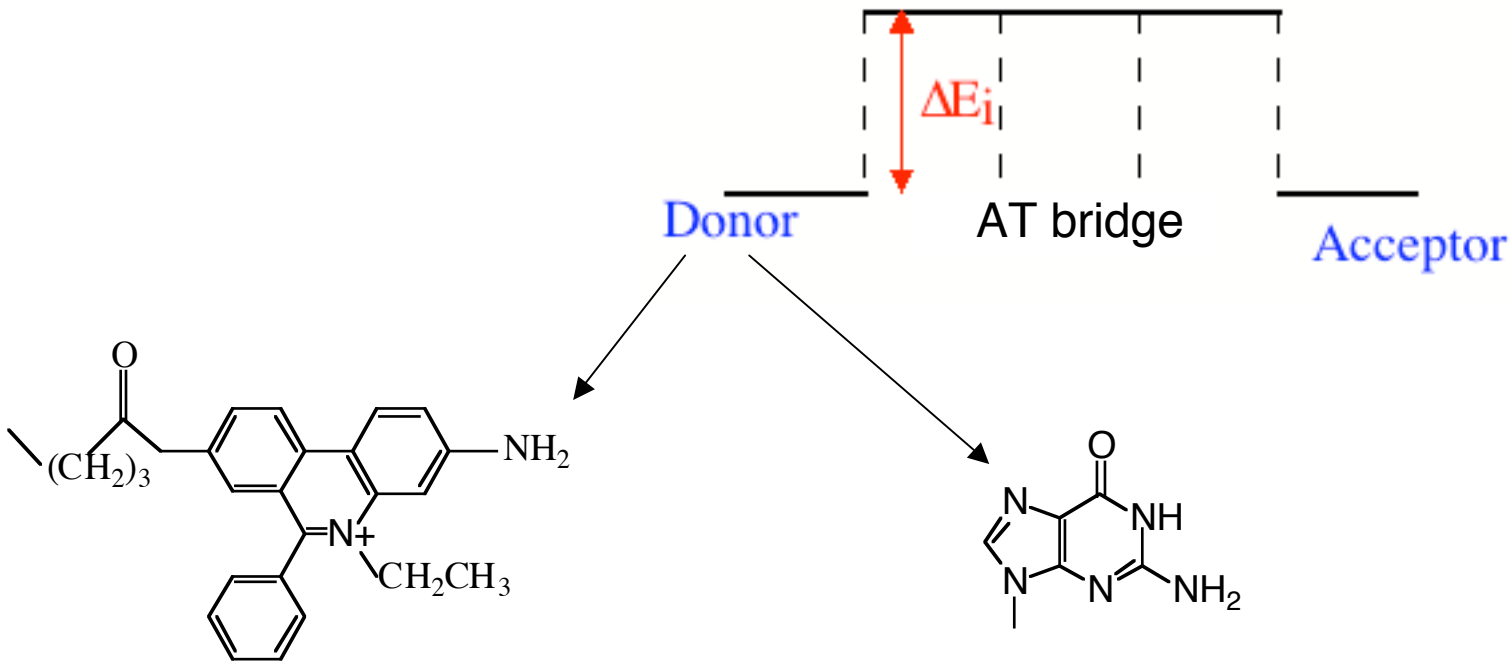
Distance dependence depends on donor



Donor used by Barton et al. is photoexcited ethidium: $\beta \sim 0.2$ Å^{-1}

Donor used by Meggers et al. is guanine cation: $\beta \sim 0.7$ Å^{-1}

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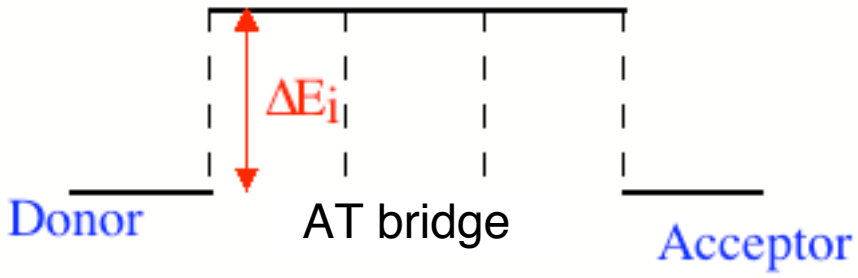
Effect of injection barrier

Ionization potential of donor determines injection barrier ΔE_i



ΔE_i eV	β Å^{-1}
0	0.09
0.14	0.13
0.27	0.34
0.41	0.53
0.55	0.85
0.70	≈ 1

Strong dependence of β on ΔE_i

Distance dependence is very small for vanishing ΔE_i

→ transition to molecular wire behaviour

→ may explain results of Barton group

Chem.Biol. 5 (1998) 413

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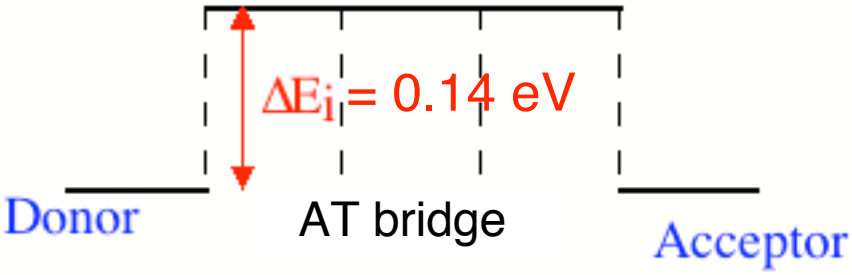
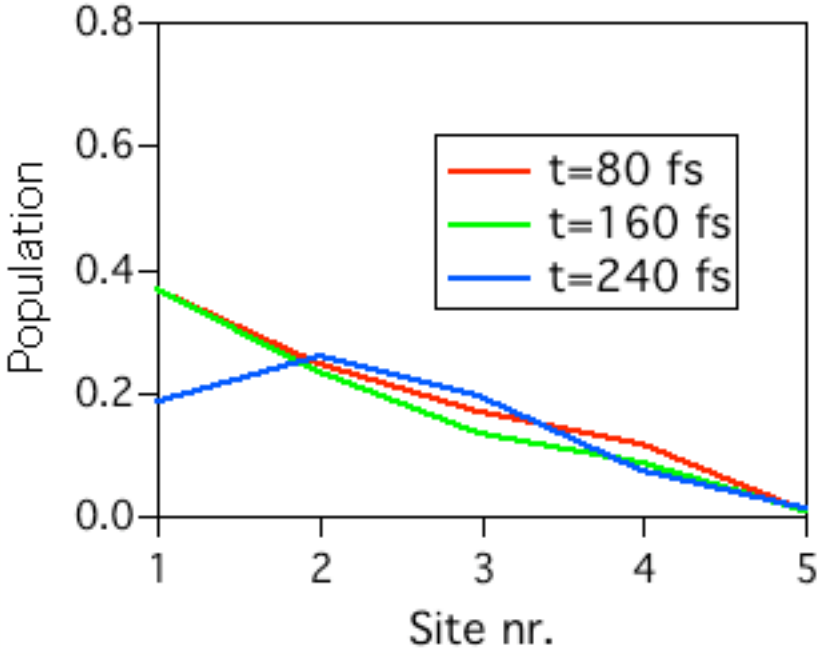
Charge distribution at three different times





Low injection barrier leads to molecular wire type charge transport

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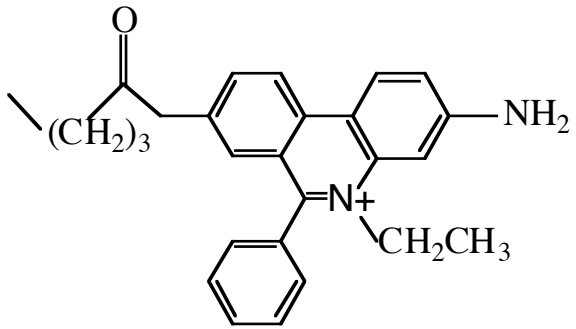
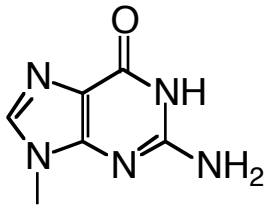
Effect of donor energy

Distance dependence determined by donor energy





Donor used by Barton et al. is photoexcited ethidium: $\beta \sim 0.2$ Å^{-1}

Donor used by Meggers et al. is guanine cation: $\beta \sim 0.7$ Å^{-1}

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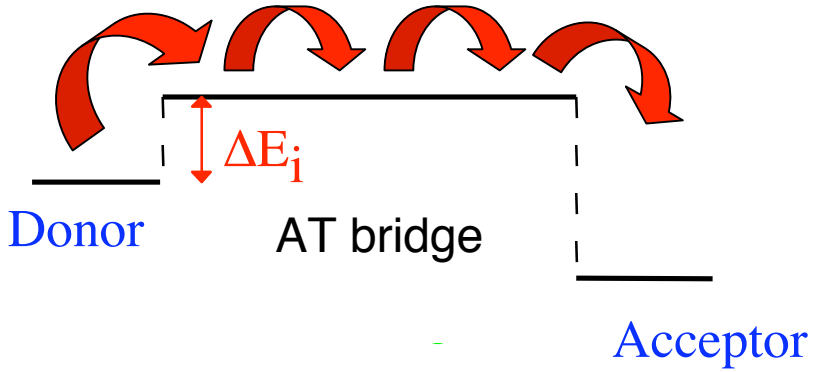
Molecular wire behaviour

Low β due to small injection energy from donor to bridge



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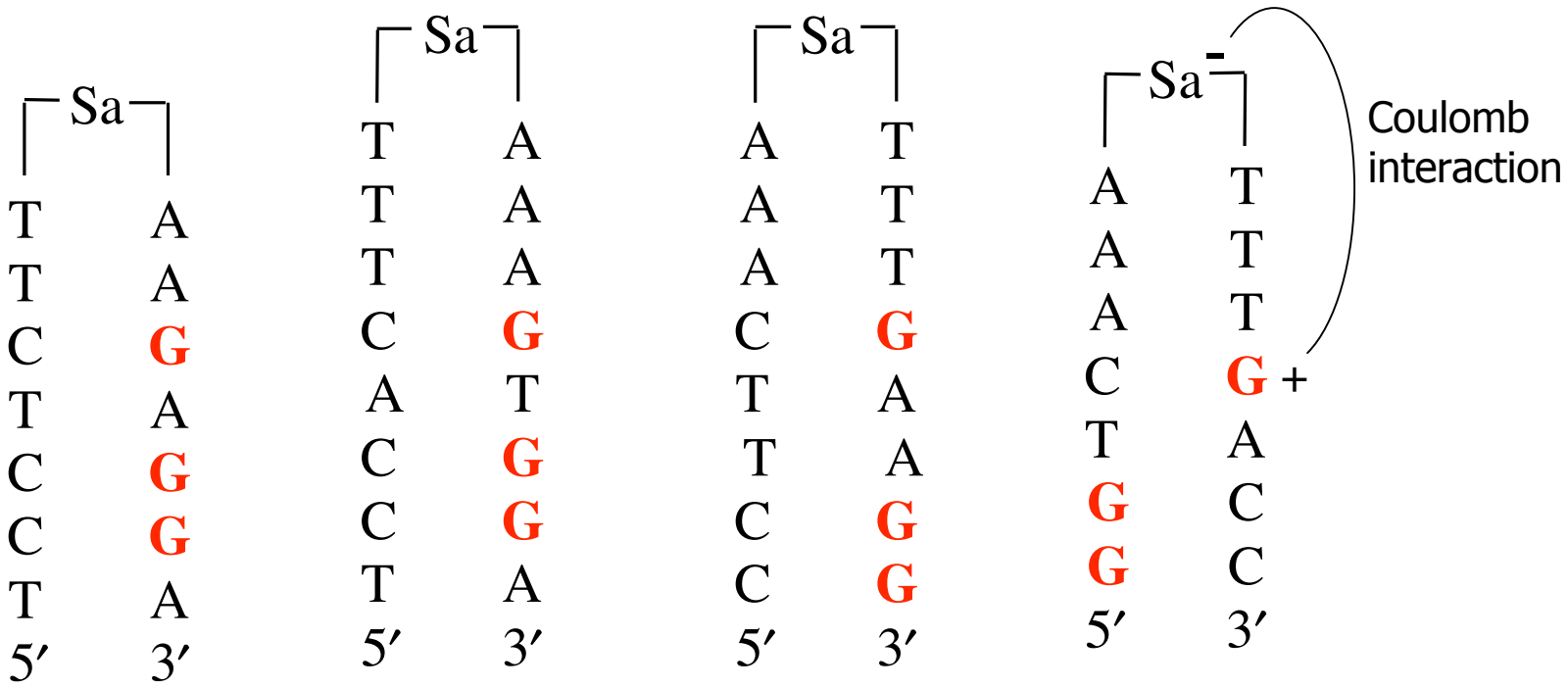
Absolute rates of charge transport from G to GG sites in DNA hairpins



	2b	*3b*	*4c*	*5b*	
Exptl. rate:	6.0	0.33	0.05	0.09	($10^7 s^{-1}$)
Exptl. time:	**17 ns**	**300 ns**	**2000 ns**	**1100 ns**	

Lewis et al. JACS 124 (2002) 4568 & JACS 125 (2003) 4850.

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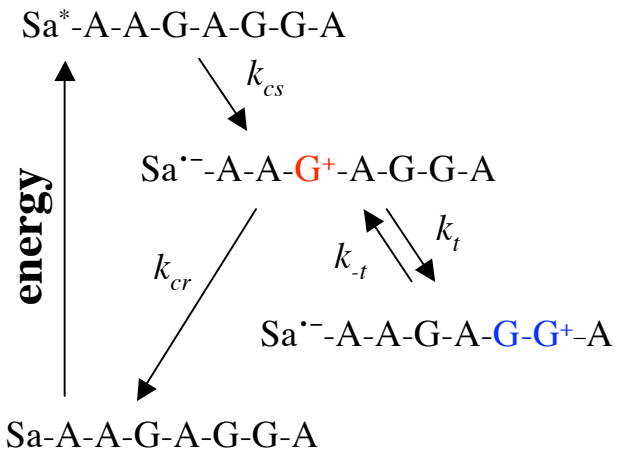
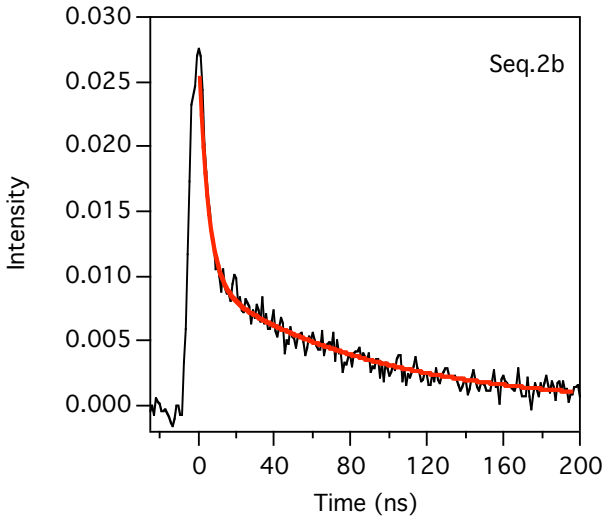
Kinetic analysis of transient absorption spectra

Kinetic scheme





$$\frac{dX}{dt} = -k_t X - k_{cr} X + k_{-t} Y$$

$$\frac{dY}{dt} = k_t X - k_{-t} Y$$

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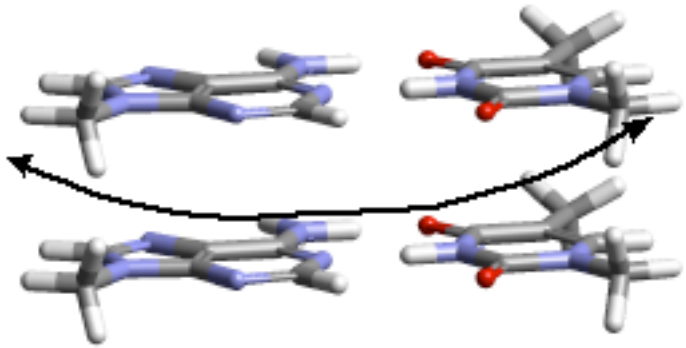
Theoretical model of charge transport via twisting base pairs



Twisting motion F_{rot}

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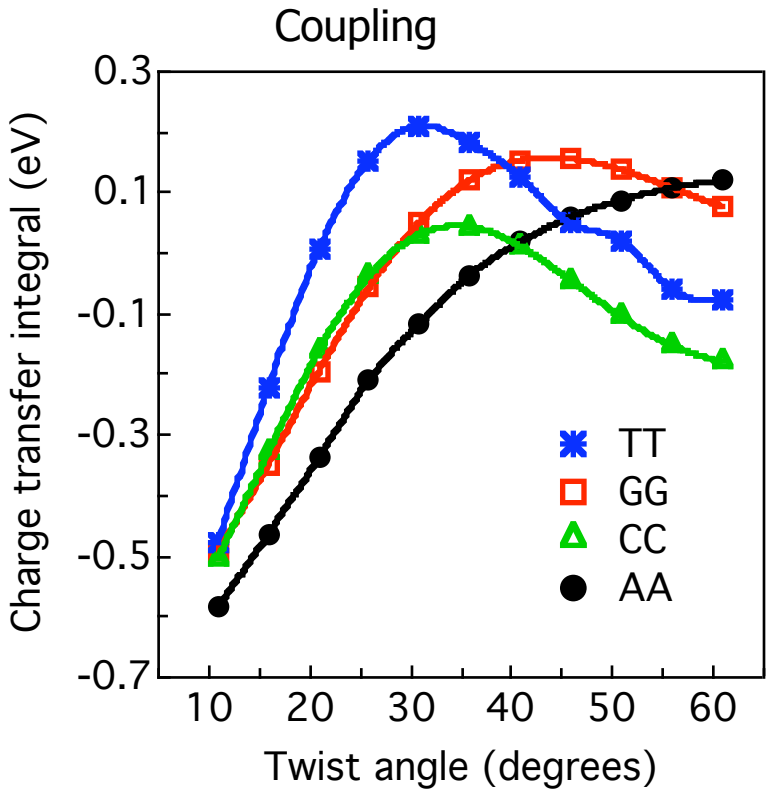
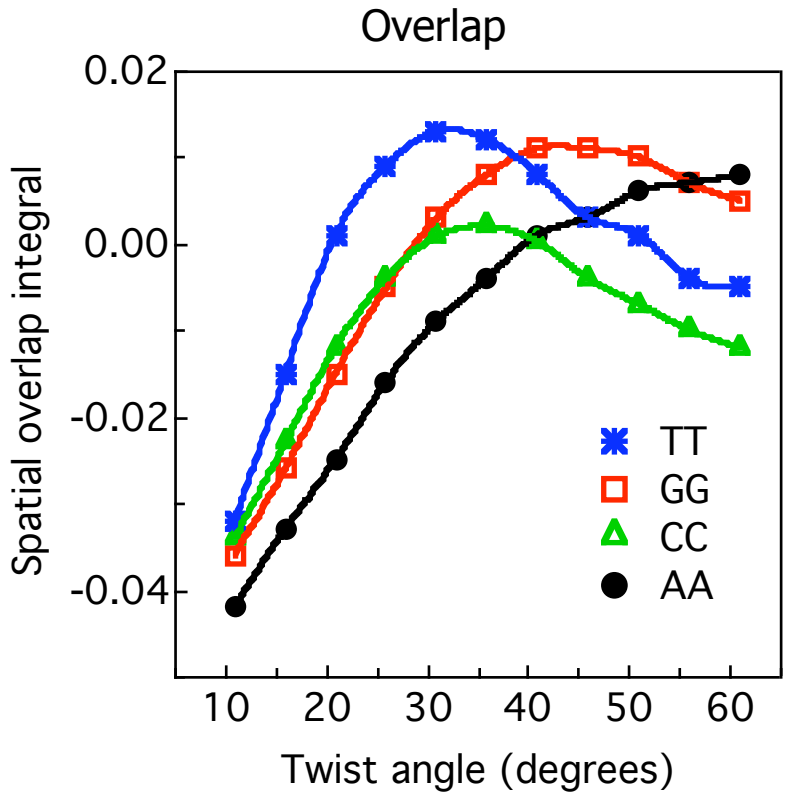
Effect of twisting on electronic coupling





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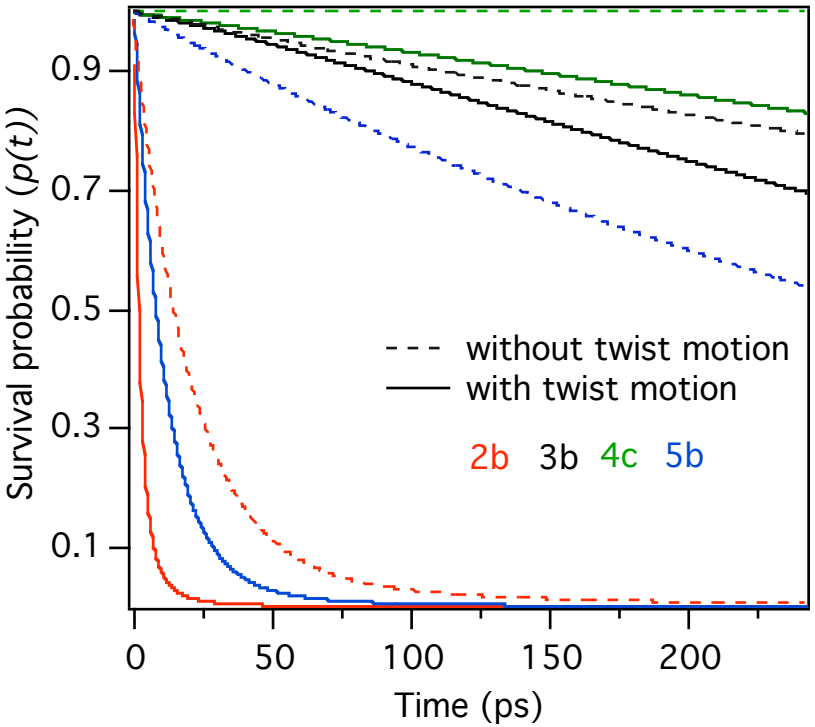
Twisting enhances charge transfer rate



No Coulomb interaction between Sa^- and hole on DNA in calculations

Calculated decay time for **3b** > **5b**!

Disagreement with expt.

3b: 300 ns **5b: 1100 ns**

5´-AGTGGA-
-TCACCT-

5´-TGACC-
-ACTGG-

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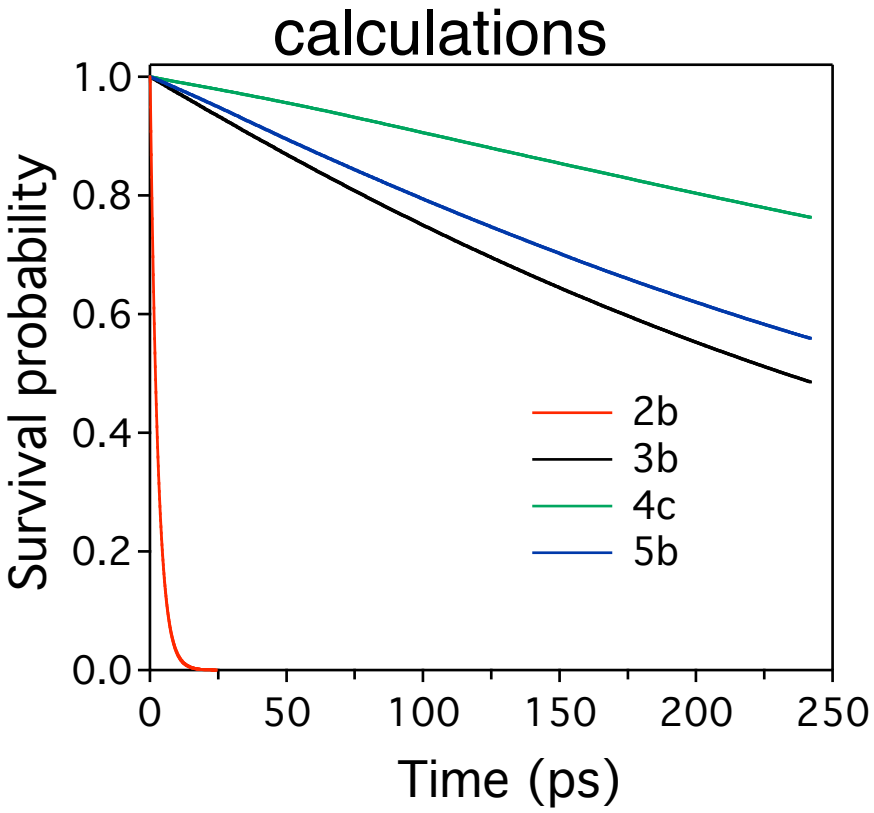
Relative rates reproduced by inclusion of Coulomb interaction in tight-binding calculations.

Absolute rates much too fast (~ factor 1000) !



		experiments
2b	5´-AGAGGA- -TCTCCT-	17 ns
3b	5´-AGTGGA- -TCACCT-	300 ns
4c	5´-TGAAGG- -ACTTCC-	2000 ns
5b	5´-TGACC- -ACTGG-	1100 ns

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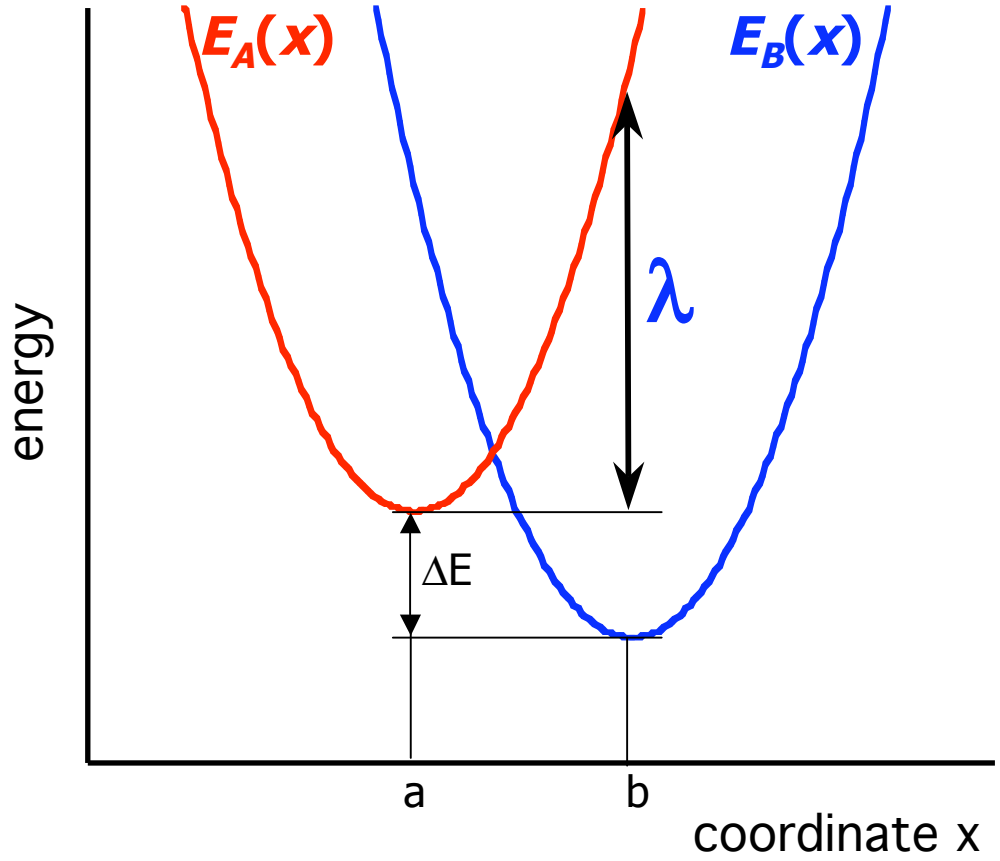
Charge induces lattice distortion of nucleobase and polarizes surrounding water: reorganization energy to be included

Marcus or Holstein theory for charge transfer rate



Initial and **final** state energies

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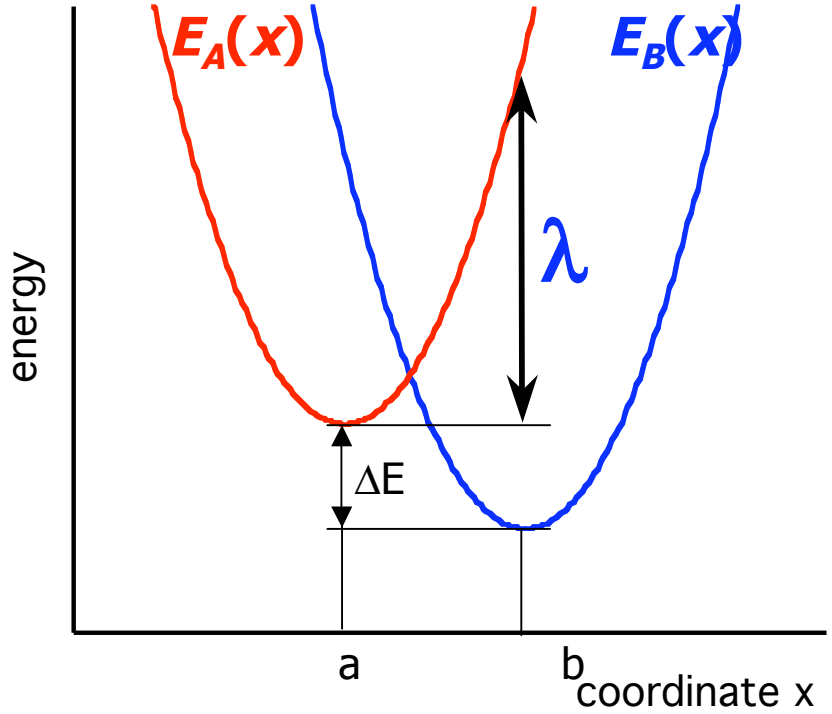
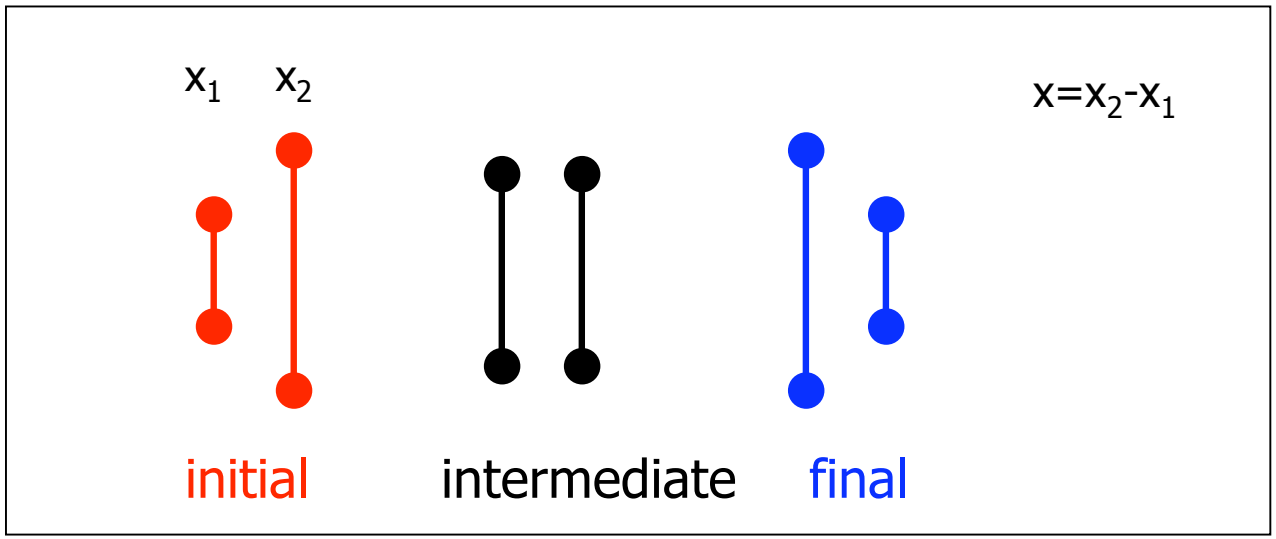
Initial and **final** states





Classical Marcus rate

- classical treatment of vibration $k_B T \gg \hbar\omega$
- start from Fermi Golden Rule

$$k(x) = \frac{2\pi}{\hbar} V^2 \delta\left(E_B(x) - E_A(x)\right)$$

$$E_A(x) = \bar{E}_A + \frac{1}{2} C x^2 \qquad E_B(x) = \bar{E}_B + \frac{1}{2} C (x-b)^2$$

$$E_B(x) - E_A(x) = \bar{E}_B - \bar{E}_A + \frac{1}{2} C b^2 - Cbx \qquad \Delta E = \bar{E}_B - \bar{E}_A$$

$$k_{CT} \equiv \langle k \rangle = \int k(x) f(x) dx$$

$$f(x) = \sqrt{\frac{C}{2\pi k_B T}} e^{-E_A(x)/k_B T}$$

Boltzmann distribution of distances *x*

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Classical Marcus rate

- classical treatment of vibration
- start from Fermi Golden Rule

$$k_{CT} = \frac{2\pi}{\hbar} V^2 \sqrt{\frac{C}{2\pi k_B T}} \int \exp\left[-Cx^2 / \left(2k_B T\right)\right] \delta\left(E_B(x) - E_A(x)\right) dx$$

$$y = Cbx$$

$$k_{CT} = \frac{2\pi}{\hbar} V^2 \sqrt{\frac{C}{2\pi k_B T}} \frac{1}{Cb} \int \exp\left[-y^2 / \left(2Cb^2 k_B T\right)\right] \delta\left(\Delta E + \frac{Cb^2}{2} - y\right) dy$$

$$k_{CT} = \frac{2\pi}{\hbar} V^2 \sqrt{\frac{1}{2\pi k_B T Cb^2}} \frac{1}{Cb} \exp\left[-\left(\Delta E + \frac{Cb^2}{2}\right)^2 \Big/ \left(2Cb^2 k_B T\right)\right]$$

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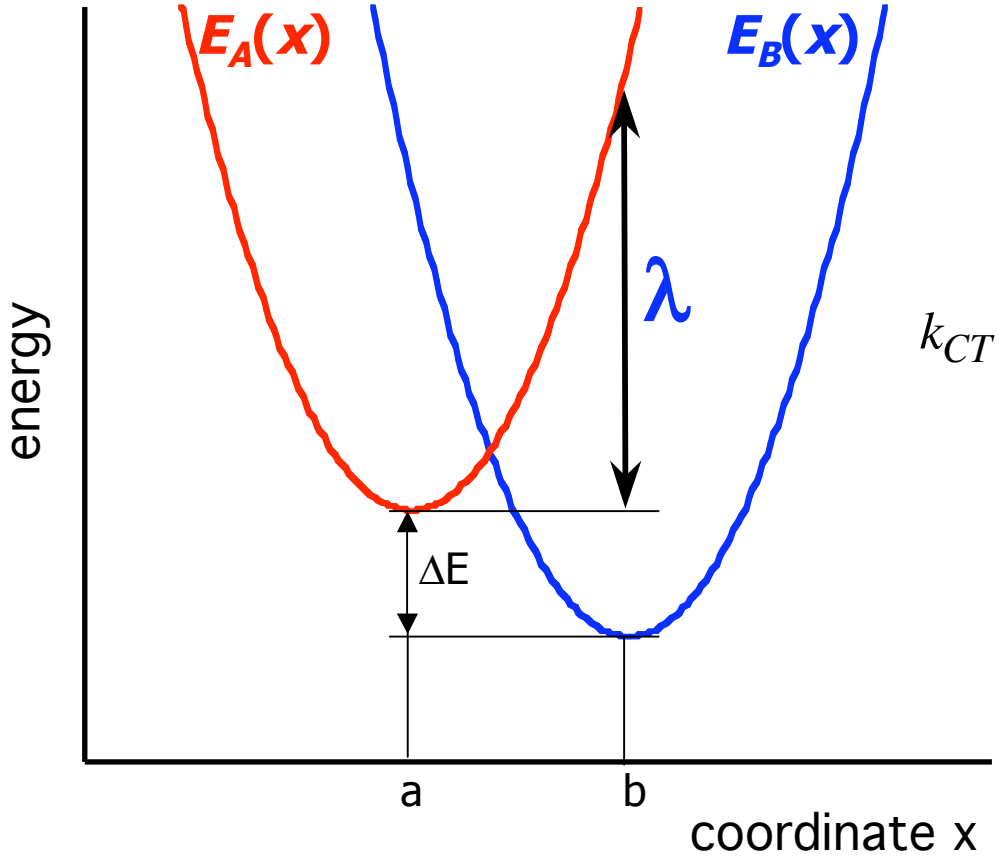
Classical Marcus rate for charge transfer



$$k_{CT} = \frac{2\pi}{\hbar} V^2 \sqrt{\frac{1}{4\pi\lambda k_B T}} \exp\left[-\frac{(\Delta E + \lambda)^2}{4\lambda k_B T}\right]$$

with the reorganization energy

$$\lambda = \frac{1}{2} C (b-a)^2 = \frac{1}{2} C b^2$$

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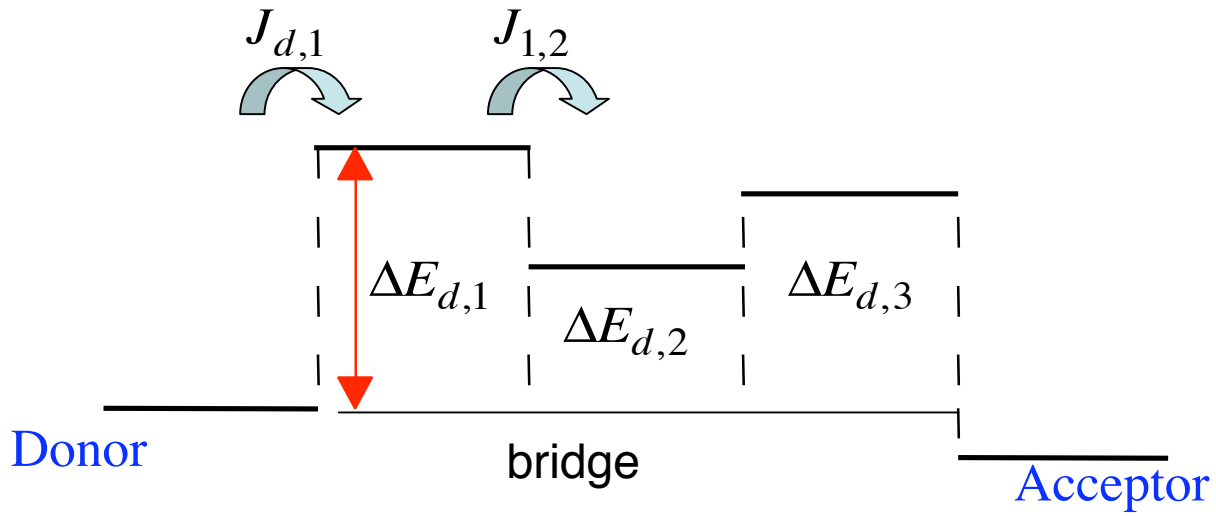
Superexchange coupling V for tunneling through bridge



Superexchange coupling depends on J and ΔE ($J \ll \Delta E$):

$$V = \frac{J_{d,1} J_{n,a}}{\Delta E_{d,1}} \prod_{k=1}^{n-1} \frac{J_{k,\,k+1}}{\Delta E_{d,\,k+1}}$$

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Exptl. rates reproduced with reorganization energy near 1 eV

Sequence		Exptl. rate K_{CT} (s^{-1})	Coupling V (meV)	Reorg. energy λ (eV)
2b	5´-AGAGGA- -TCTCCT-	6.0×10^7	8.68	1.00
3b	5´-AGTGGA- -TCACCT-	0.33×10^7	2.15	1.46
4c	5´-TGAAGG- -ACTTCC-	0.05×10^7	0.49	1.09
5b	5´-TGACC- -ACTGG-	0.09×10^7	0.42	1.00

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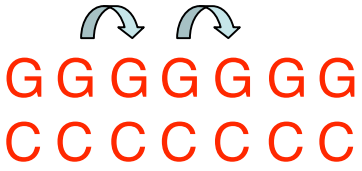
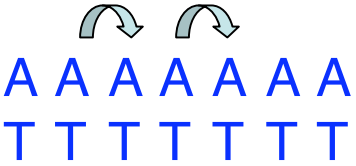
Polaronic hopping mobility with λ = 1 eV

For GC



$$\mu = \frac{e}{kT}\frac{2\pi}{\hbar}\frac{|V|^2}{\sqrt{4\pi\lambda kT}}\exp\left(-\frac{\lambda}{4kT}\right)\delta^2 = 10^{-4}\,cm^2V^{-1}s^{-1}$$

For AT



$$\mu = 2\cdot 10^{-5}\,cm^2V^{-1}s^{-1}$$

For λ = 0 mobility is few $cm^2V^{-1}s^{-1}$; comparable with pentacene

K. Senthilkumar et al., J. Am. Chem. Soc. **127** (2005) 14899

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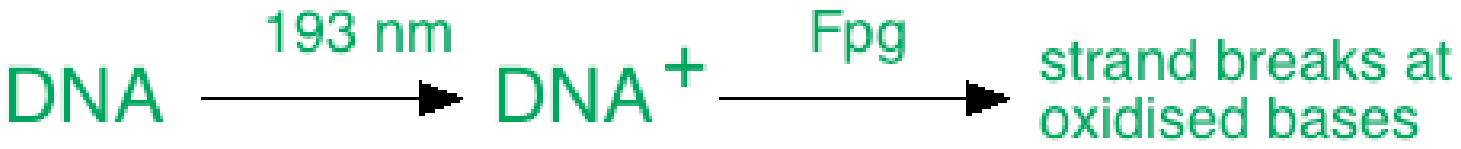
Charge distribution on photo-oxidized DNA



BASE	ε ($M^{-1}cm^{-1}$)	Φ	ION. PROB.	IP (VERT.)
G	25900	0.044	0.43	8.21 eV
C	19500	0.029	0.22	8.88 eV
A	18600	0.033	0.23	8.54 eV
T	5700	0.055	0.12	9.16 eV

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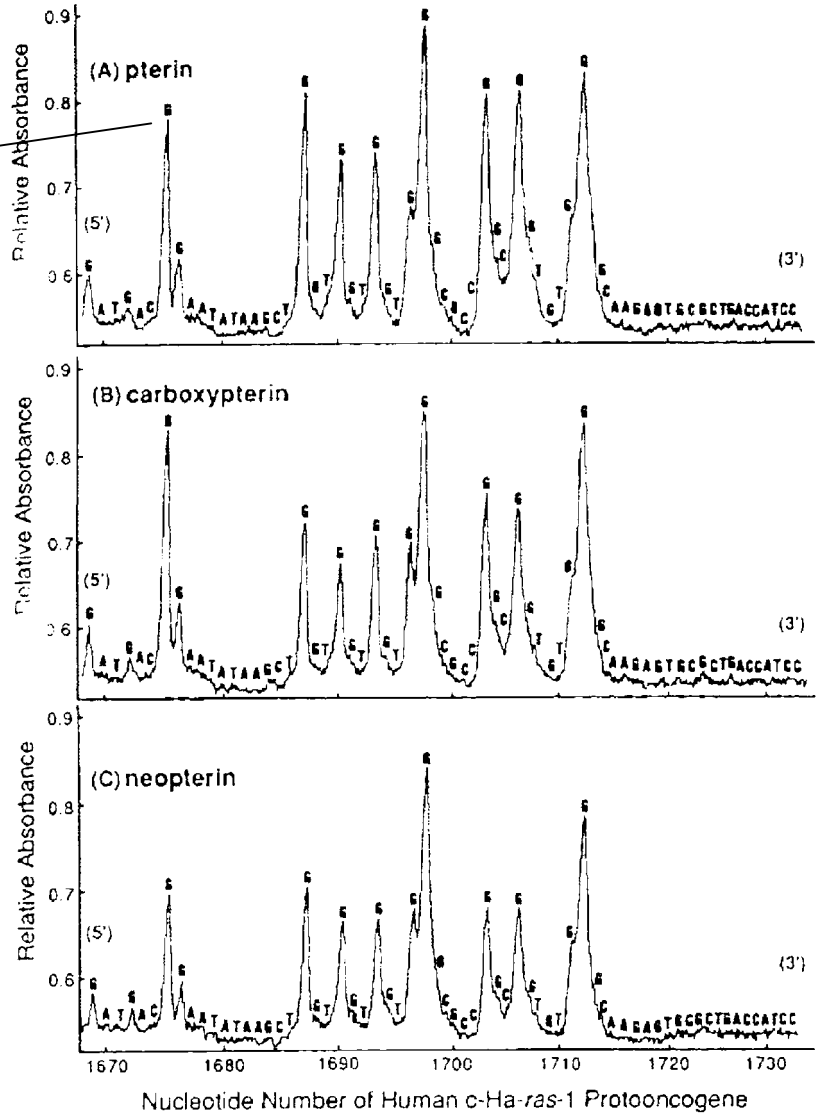
Photocleavage is site-selective

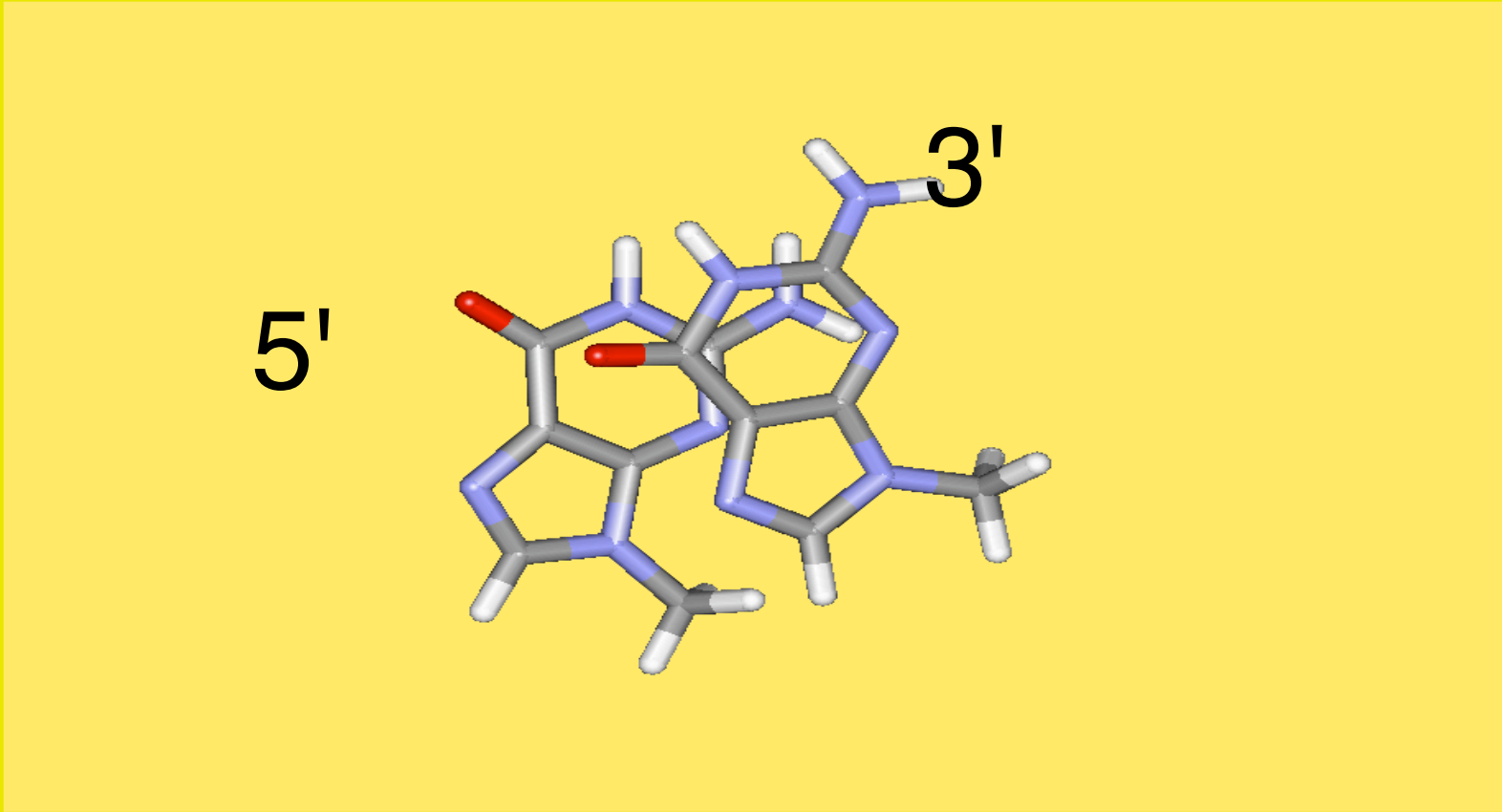
Ito *et al*. Bio. Chem. 36 (1997) 1774

5'-CGGA-3'

G oxidized most



Energy of charge at 5' G and 3' G are different: site-selective photo-oxidation



5' and 3' guanine are in different environment

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Site energy of 5' G lower than 3' G

$$E = \langle \Psi_{HOMO} | H | \Psi_{HOMO} \rangle$$

Charge

$$q_i = C_i^2 + C_i C_j S_{ij}$$

J_{GG} = 0.165 eV

S_{GG} = 0.012

G site-energies in eV

7.90 8.04 5'-A**GG**A-3' 3'-TCCT-5'	7.90 8.31 5'-A**G**GC-3' 3'-TCCG-5'	7.90 8.29 5'-A**G**GT-3' 3'-TCCA-5'
7.96 8.04 5'-C**GG**A-3' 3'-GCCT-5'	7.96 8.31 5'-C**G**GC-3' 3'-GCCG-5'	7.96 8.29 5'-C**G**GT-3' 3'-GCCA-5'
7.97 8.04 5'-T**GG**A-3' 3'-ACCT-5'	7.97 8.31 5'-T**G**GC-3' 3'-ACCG-5'	7.97 8.29 5'-T**G**GT-3' 3'-ACCA-5'

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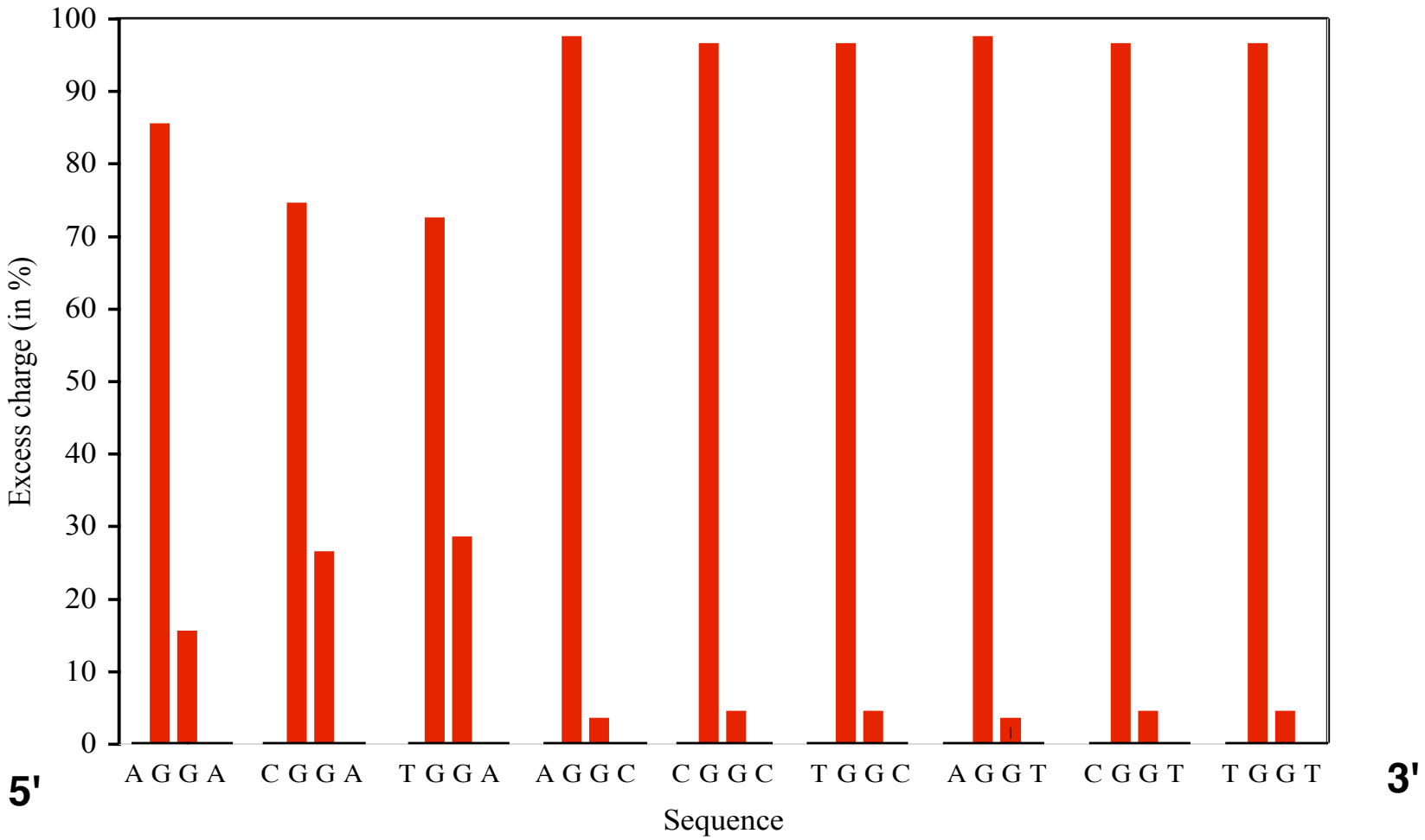
Charge distribution in 5'-XGGY-3' sequences



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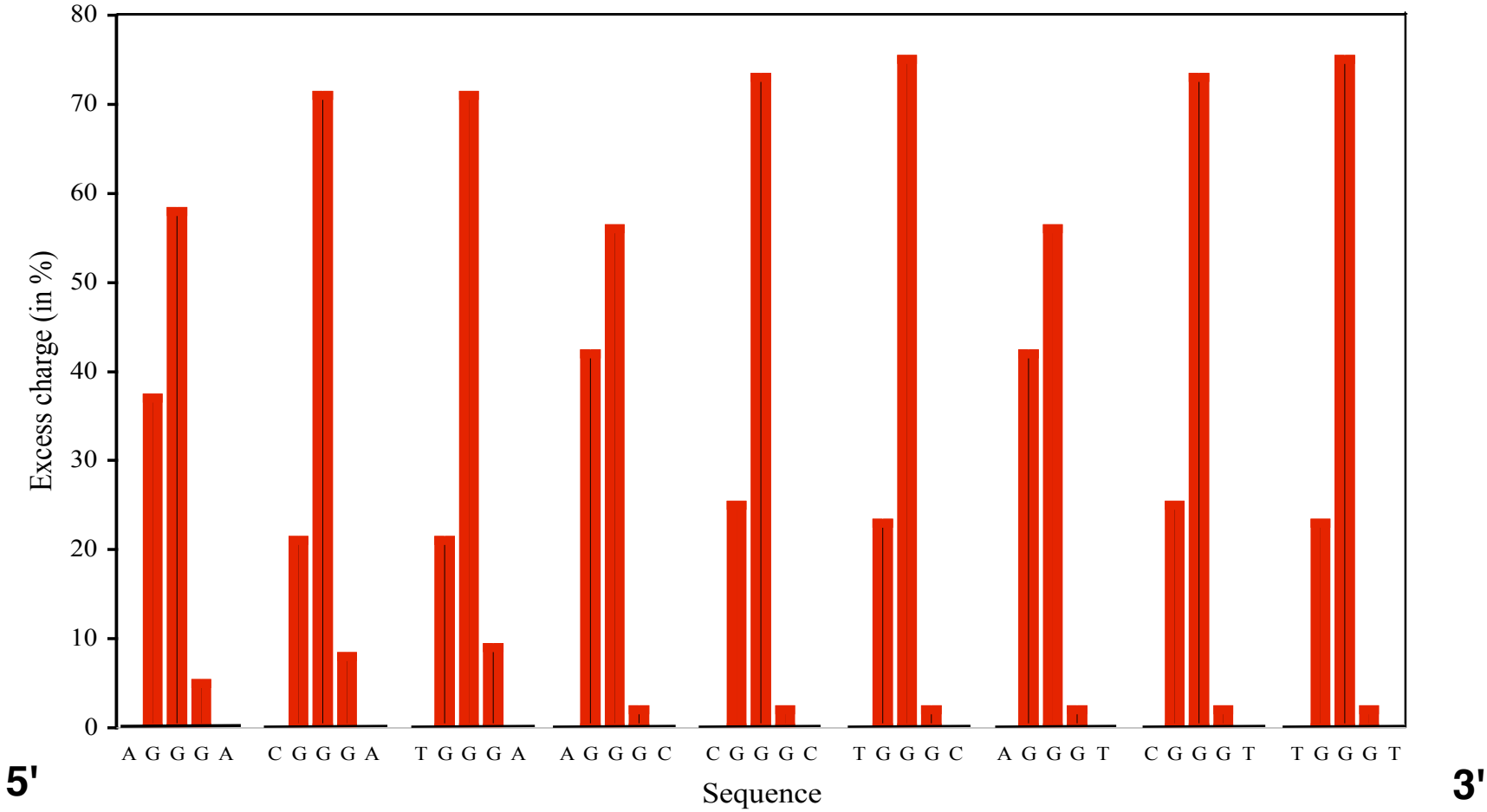
Charge distribution in 5'-XGGGY-3' sequences



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Conclusions

1. Distance and sequence dependence of charge transfer through donor-DNA-acceptor systems can be understood by tight-binding model

2. Experimental rate constants were reproduced with reorganization energy near 1 eV.

3. Mobility along GC (AT) stacks ~10^{-4} (~10^{-5}) cm^2/Vs

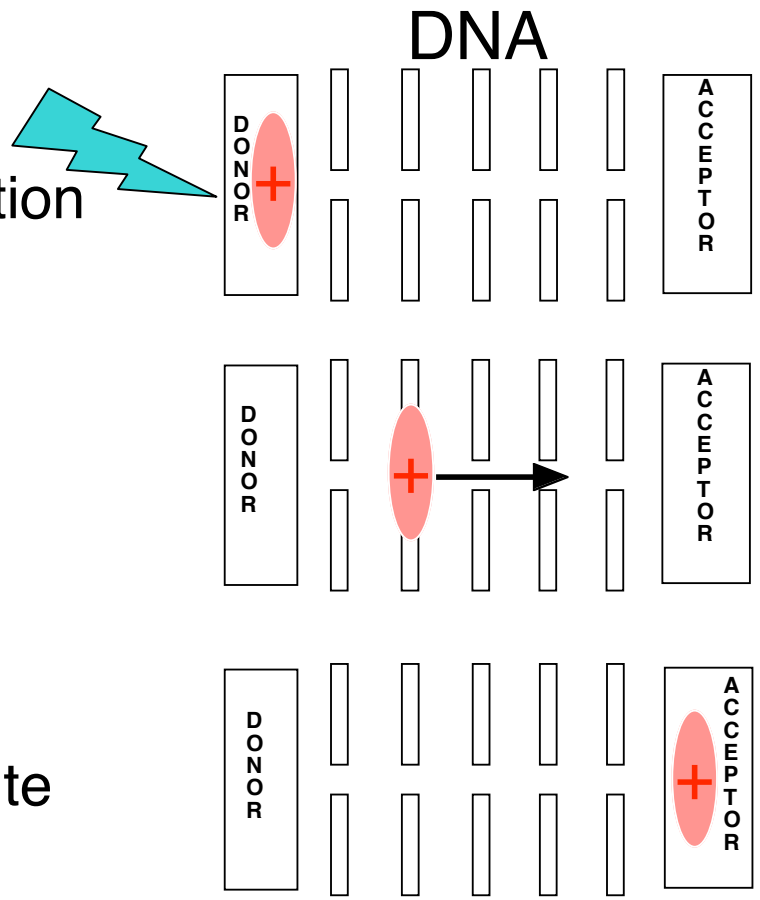
4. Selective photo-oxidation of specific G's due to different site-energies

Donor-DNA-Acceptor

charge creation by radiation

charge migration in DNA

charge at the acceptor site



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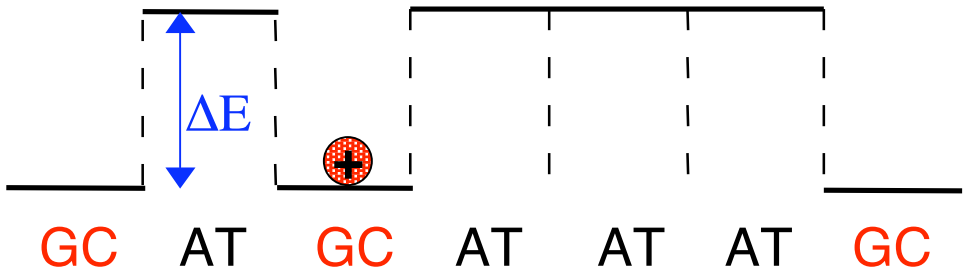
Positive charges reside on guanine

$\Delta E \sim 0.5$ eV



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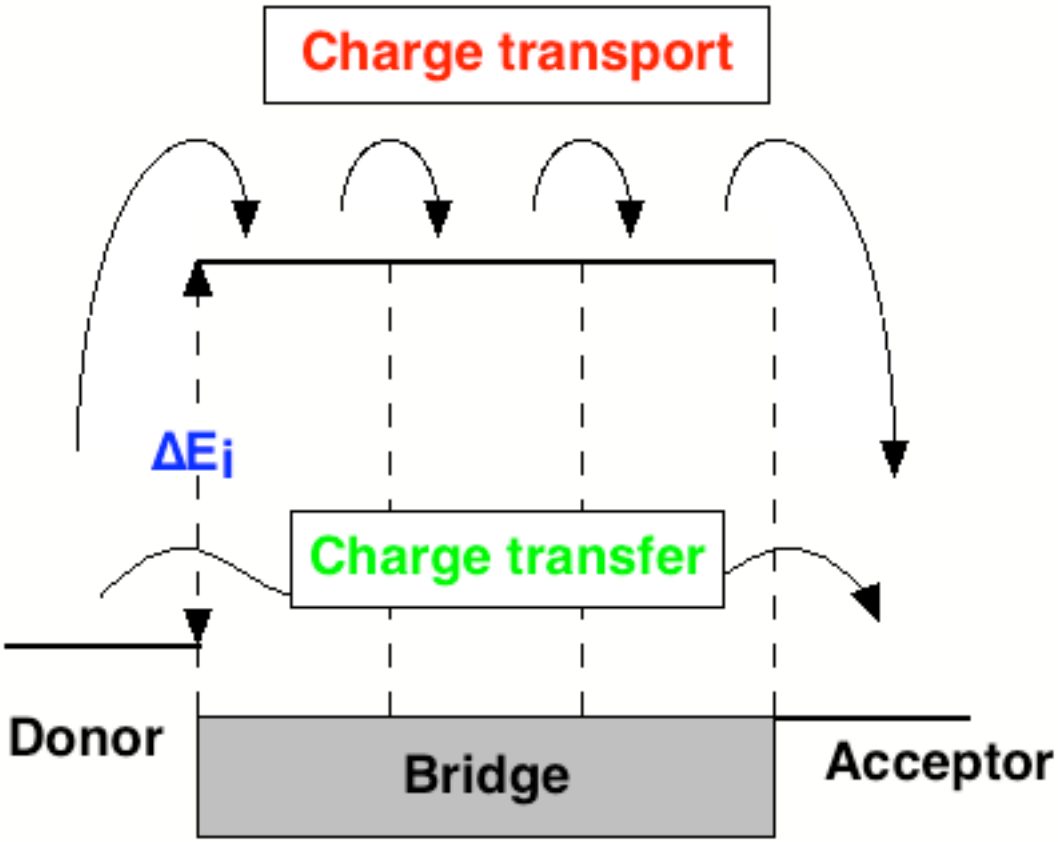
Tunneling vs. Hopping

- High β indicates single step tunneling transport
- Low β characteristic for hopping type transport



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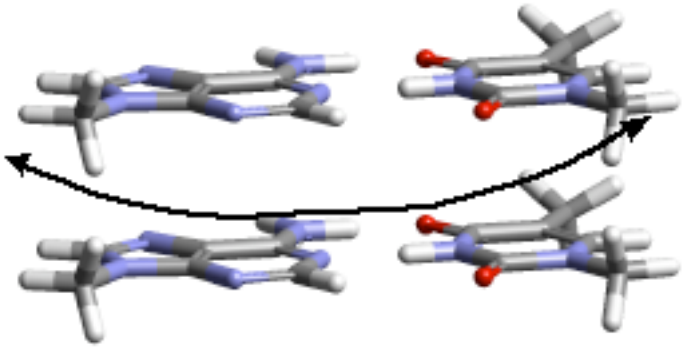
Theoretical model of charge transport via twisting base pairs



Twisting motion F_{rot}

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Site energy of a nucleobase B in 5´-XBY-3´ triplets (X, B, Y = G, A, C, T)

Y ⟶	G	A	C	T
GGY	7.890	8.040	8.310	8.290
AGY	7.900	8.060	8.341	8.320
CGY	7.957	8.115	8.383	8.361
TGY	7.965	8.124	8.407	8.380
GAY	8.343	8.487	8.716	8.712
AAY	8.376	8.558	8.763	8.799
CAY	8.438	8.584	8.800	8.793
TAY	8.434	8.630	8.810	8.858

Y ⟶	G	A	C	T
GCY	9.446	9.637	9.857	9.870
ACY	9.441	9.630	9.851	9.867
CCY	9.490	9.667	9.882	9.917
TCY	9.499	9.679	9.895	9.925
GTY	9.111	9.308	9.557	9.533
ATY	9.130	9.370	9.578	9.586
CTY	9.268	9.451	9.701	9.662
TTY	9.273	9.499	9.705	9.699

- *E* strongly depends on neighboring bases

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