Simulation of charge transfer in DNA using QM/MM methods

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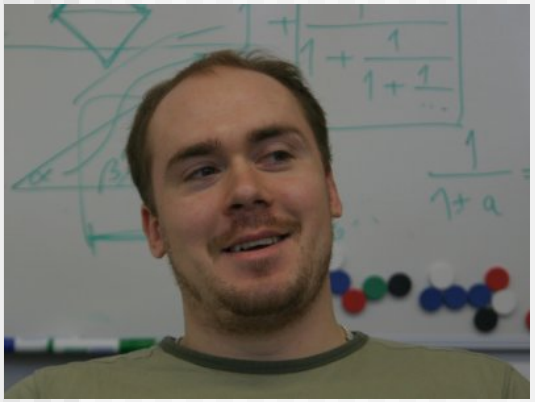
Acknowledgements

TU Braunschweig:



B. Woiczikowski

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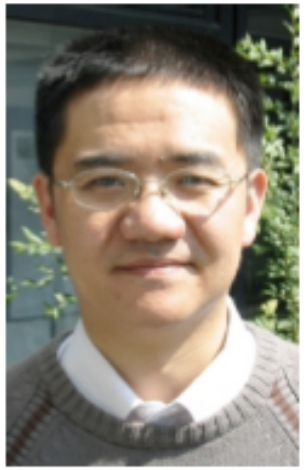
DFG: SP 1243

Dresden group

G.Cuniberti

R.Gutiérrez



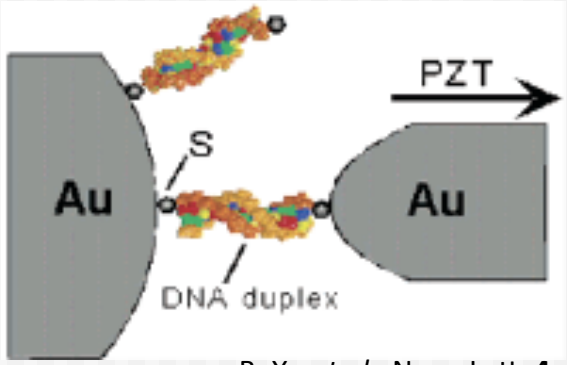
B.Song

R.Caetano

Conduction and charge transfer in DNA

Physical experiments:

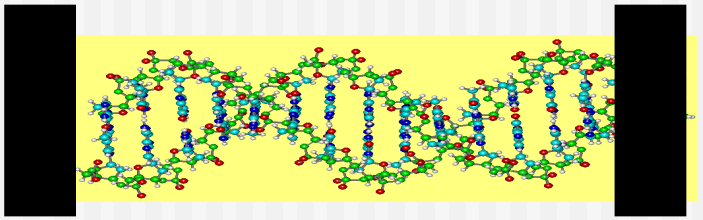
- DNA contacted by gold leads
- Current measurements



B. Xu *et al.*, Nano Lett. **4**, 1105 (2004)

Chemical experiments:

- Charge carrier injection
- long range transfer over several 100 nm



- conduction?
- Transport mechanism?

Theoretical description

Theoretical Physics:

- tight binding Hamiltonian+ Landauer theory

$$H = \sum_i \varepsilon_i c_i^+ c_i + \frac{1}{2}\sum_{ij} T_{ij}\left(c_i^+ c_j + c_j^+ c_i\right)$$

$$G_D(E) = (E - H_D^{KS} - \Sigma_L - \Sigma_R)^{-1}$$

$$T(E,V) = tr[\Gamma_L G_D^r \Gamma_R G_D^a]$$

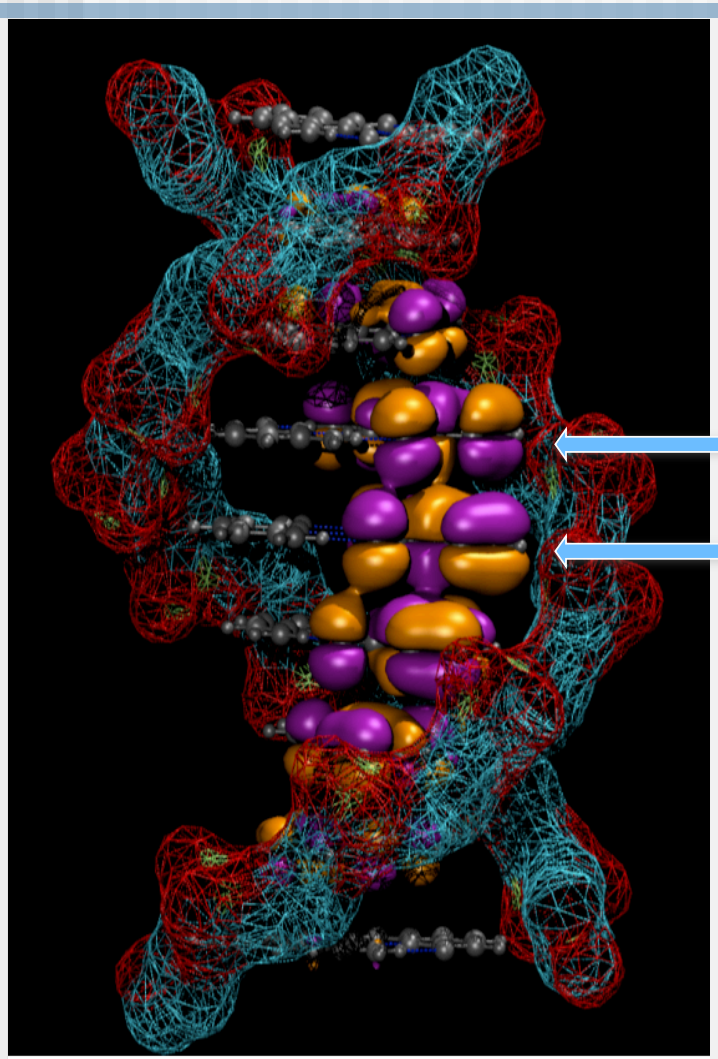
$$I(V) = \frac{2e}{h}\int_{\mu_1(V)}^{\mu_2(V)} T(E,V)dE$$

Theoretical Chemistry:

- superexchange: coherent tunneling
- thermal induced hopping

$$k = \frac{2\pi}{h}|T_{ij}|^2 \times \mathrm{FC}$$

Model



Base i

Base j

ε_i = ionisation potential

T_{ij} -> charge transfer matrix elements

Marcus theory:

$\Delta G = \varepsilon_i - \varepsilon_j$

$H_{DA} = T_{ij}$

$$k_{DA} = \frac{2\pi}{\hbar}|H_{DA}|^2 \frac{1}{\sqrt{4\pi\lambda k_B T}} \exp\left[-\frac{(\Delta G^0 + \lambda)^2}{4\lambda k_B T}\right]$$

Parameter determination

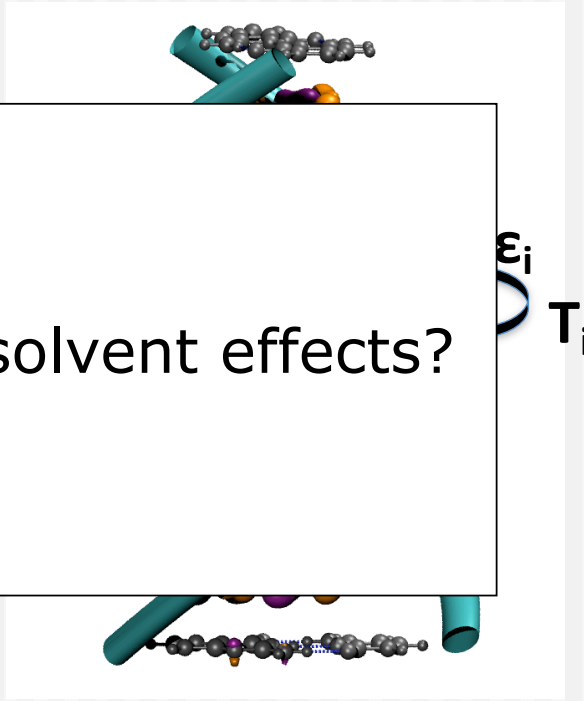
Parameters: ε_i **and** T_{ij}

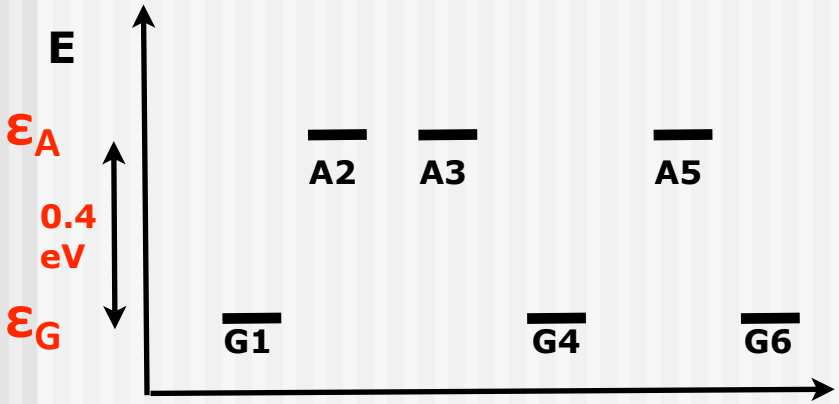
calculat
DNA ba

ε_i : HO
T_{ij}: calc

=> sta

what about dynamics and solvent effects?

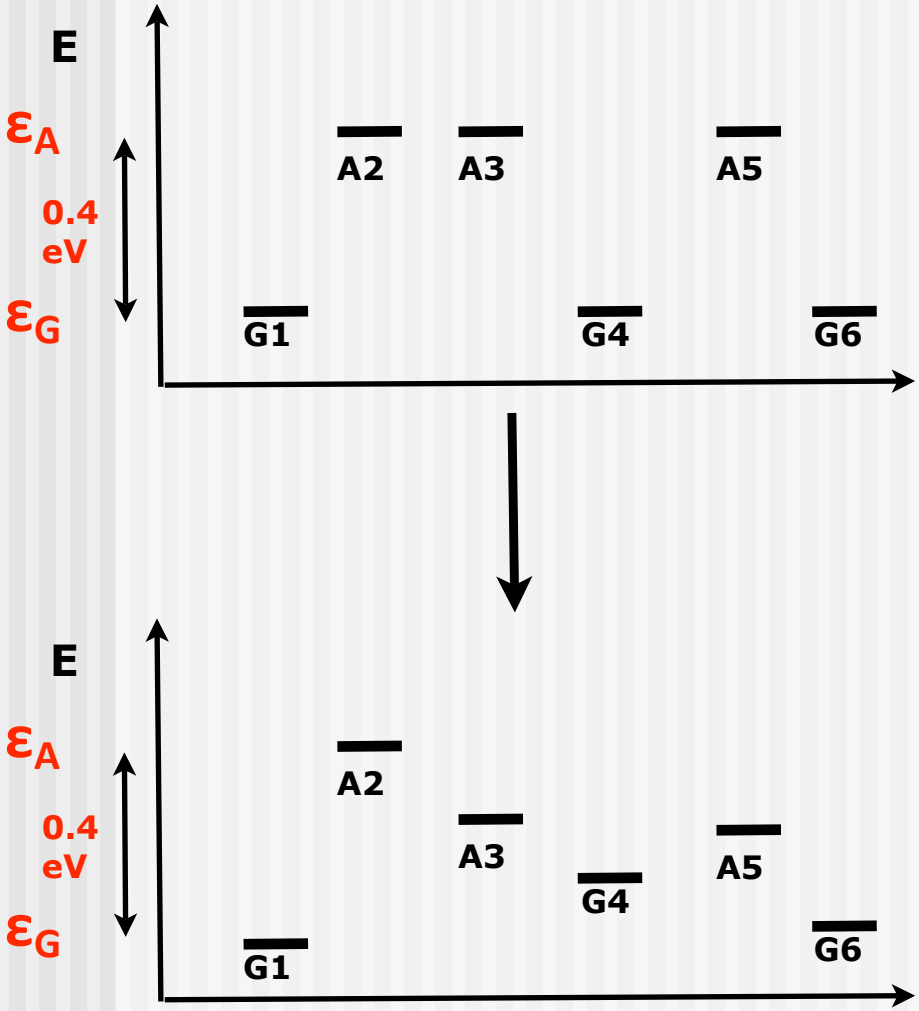




A_n-bridges:

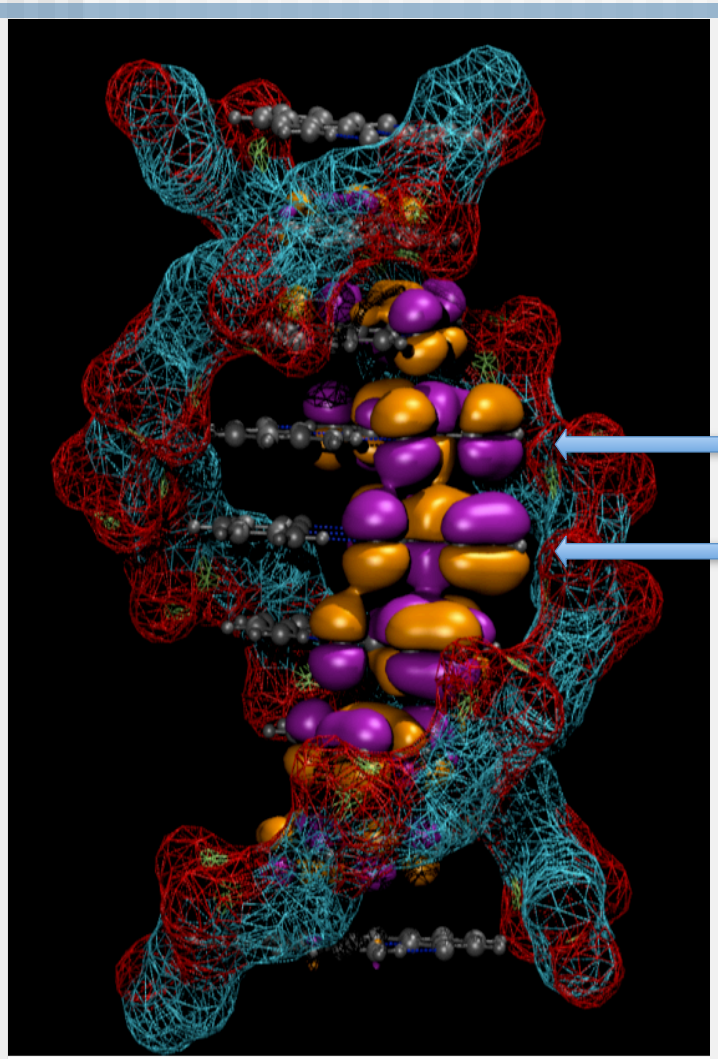
n= 1-4: superexchange
n>4 : thermal induced hopping

Effect of solvent and dynamics



- calculate parameters 'on the fly' along classical MD trajetories
- include the interaction with DNA backbone, couterions and water using a QM/MM scheme
- for sufficient sampling, use a fast QM method: SCC-DFTB

CT parameters from DFT



site i

site j

$\varepsilon_i = \langle \varphi_i | H | \varphi_i \rangle$

$T_{ij} = \langle \varphi_i | H | \varphi_j \rangle$

ε_i: energy of electron/hole on site i

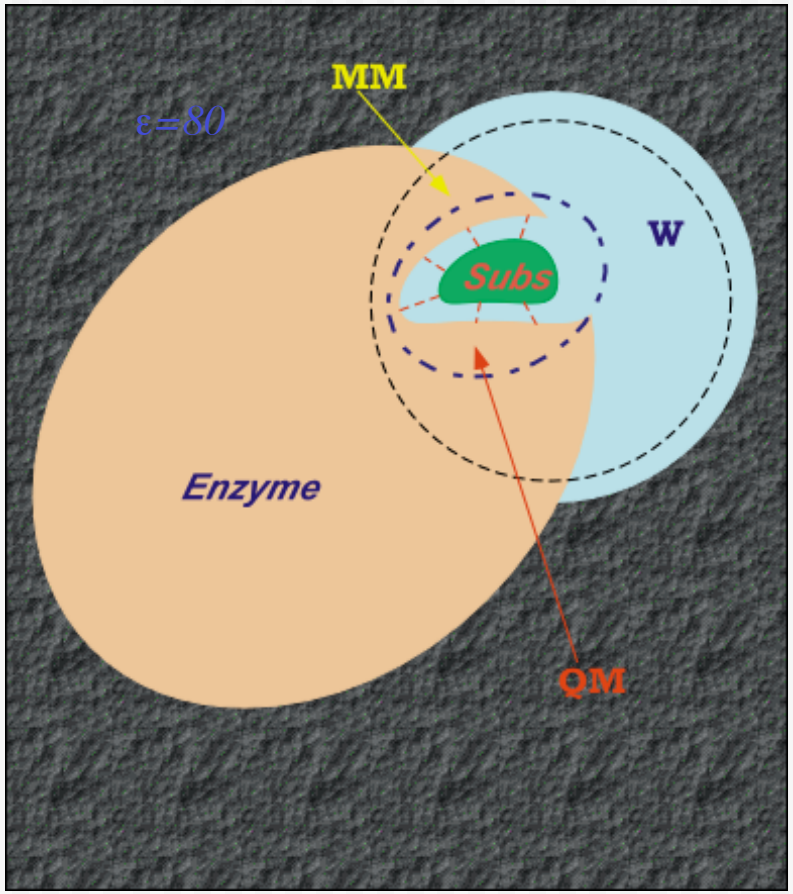
T_{ij}: transfer integral from site i to j

Calculate φ_i and H from DFT/DFTB
along classical MD trajectories➔ include:

- **dynamical changes in parameters**
- **solvent effects**

Kubar et al., *J. Phys. Chem. B* **2008,** *112*, 7937
Kubar & Elstner, *J. Phys. Chem. B* **2008,** *112*, 8788

Combined QM-MM Methods



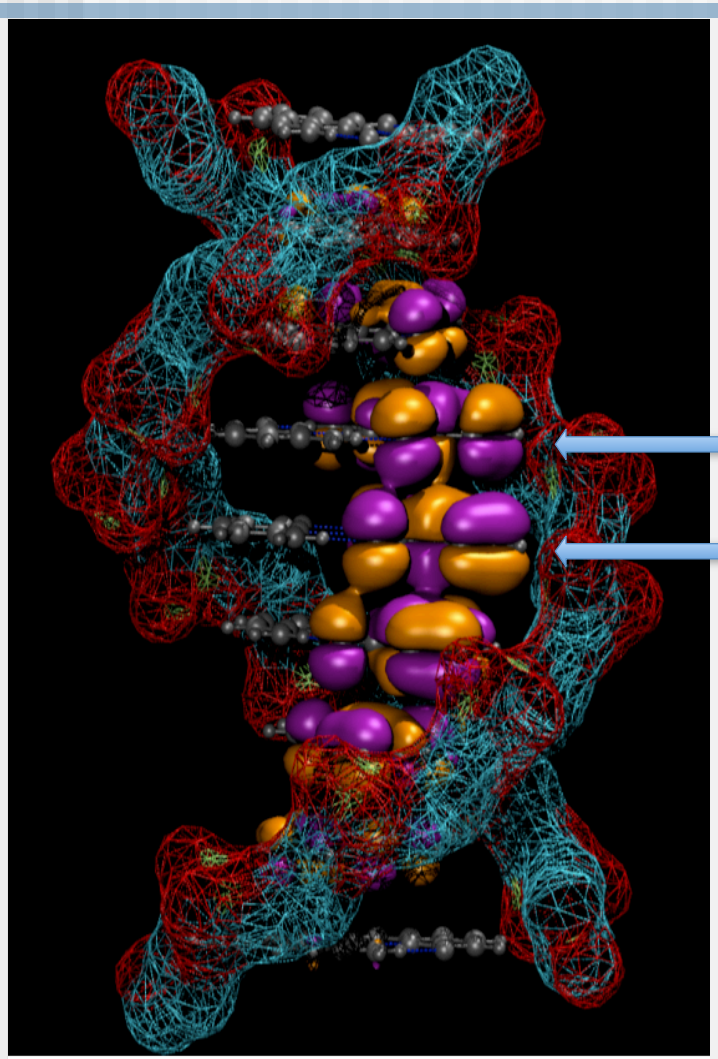
Quantum Mechanics (QM)

Molecular Mechanics (MM)

Polarization of the QM region through MM point charges

$$E = \langle \Psi | \hat{H}^{QM} + \hat{H}_{el}^{QM/MM} | \Psi \rangle + E_{van}^{QM/MM} + E^{MM}$$

CT parameters from DFT



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Calculate φ_i and H from DFT/DFTB
along classical MD trajectories➔ include:

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Kubar et al., *J. Phys. Chem. B* **2008,** *112*, 7937
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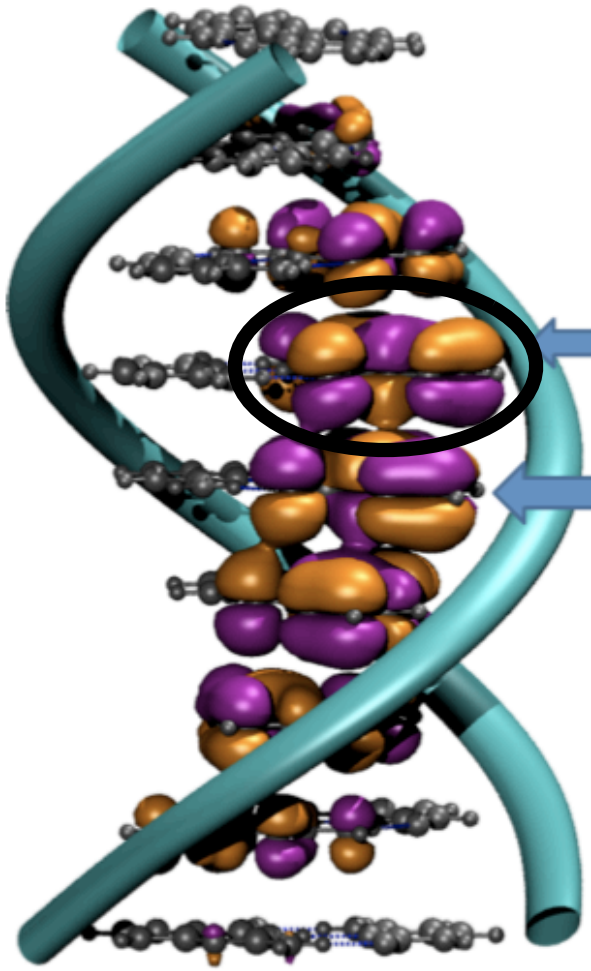
Fragment Orbitals

Senthilkumar et al., JACS 127, 14894



Fragment orbitals (FO) in LCAO ansatz:

$$\phi_i = \sum_\mu c_\mu^i \eta_\mu$$

$$\phi_j = \sum_\nu c_\nu^j \eta_\nu$$

T_{ij} , S_{ij}

$$T_{ij} = \sum_{\mu\nu} c_\mu^i c_\nu^j \langle \eta_\mu | H | \eta_\nu \rangle$$

$$= \sum_{\mu\nu} c_\mu^i c_\nu^j H_{\mu\nu}$$

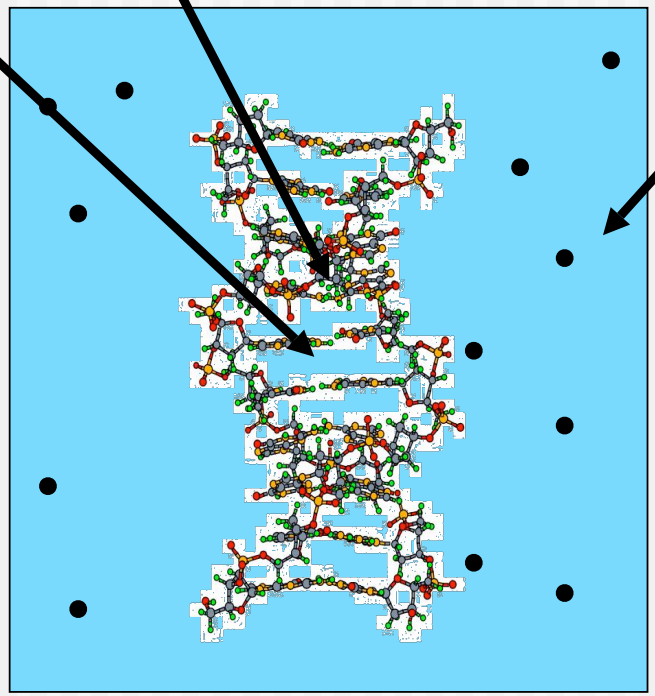
Couple to solvent degrees of freedom:

SCC-DFTB QM/MM Hamiltonian

$$H_{\mu\nu} = H^0_{\mu\upsilon} + \frac{1}{2} S_{\mu\upsilon} \sum_{\gamma} \Delta q_{\gamma} (\gamma_{\alpha\gamma} + \gamma_{\beta\gamma}) + \frac{1}{2} S^{\alpha\beta}_{\mu\upsilon} \sum_{A} Q_A (1/R_{\alpha A} + 1/R_{\beta A})$$

interaction between

QM atoms



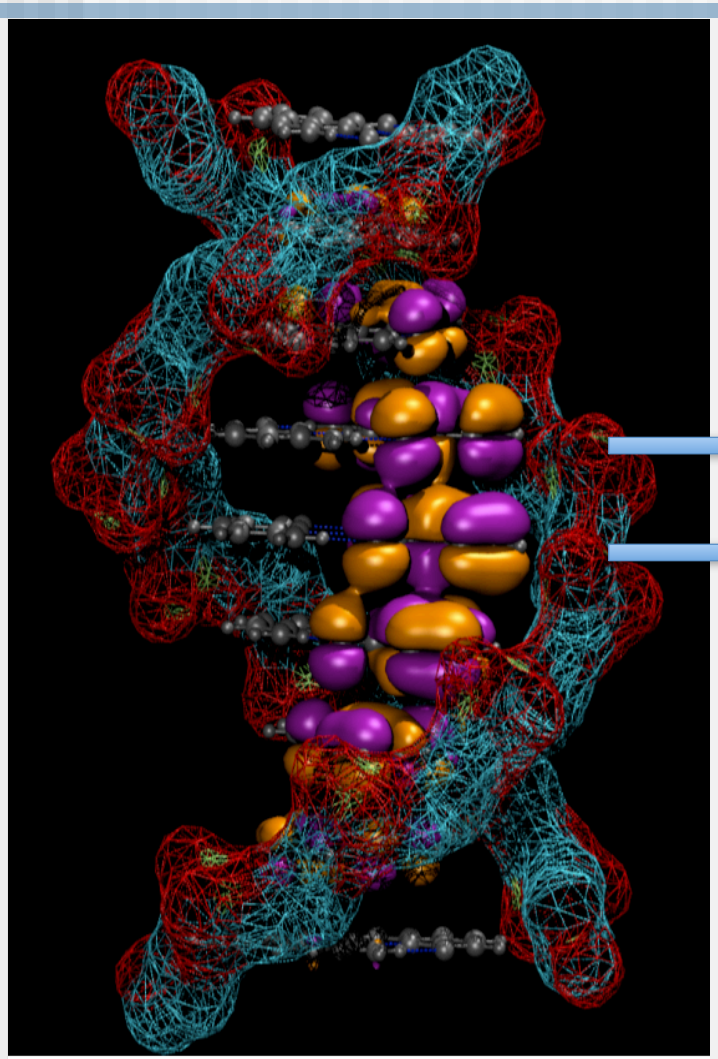
Q_A: MM charges polarizing QM region:

backbone, waters, counterions

$$T_{ij} = \sum_{ij} c^i_{\mu} c^i_{\upsilon} H_{\mu\upsilon}$$

includes the effect of environment

Coarse grained Hamiltonian

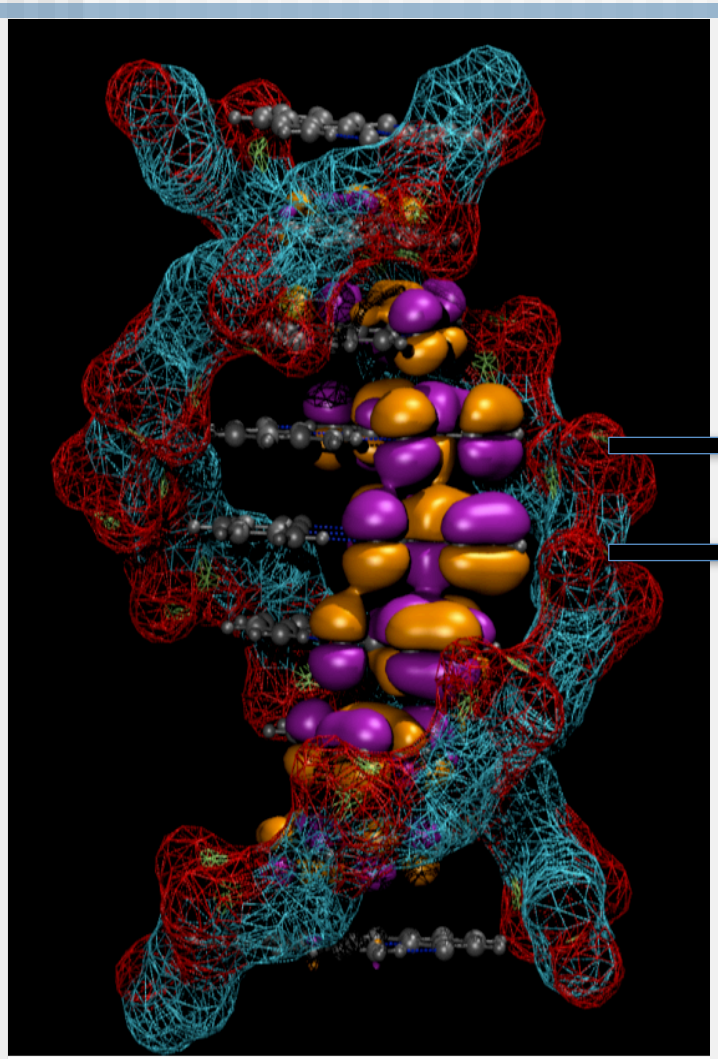


$$H = \sum_i \varepsilon_i a_i^+ a_i + \sum_{ij} T_{ij} a_i^+ a_j$$

Time dependent parameters $\varepsilon_i(t)$ and $T_{ij}(t)$ contain dynamical and solvation effects

Kubar et al., *J. Phys. Chem. B* **2008,** *112*, 7937
Kubar & Elstner, *J. Phys. Chem. B* **2008,** *112*, 8788

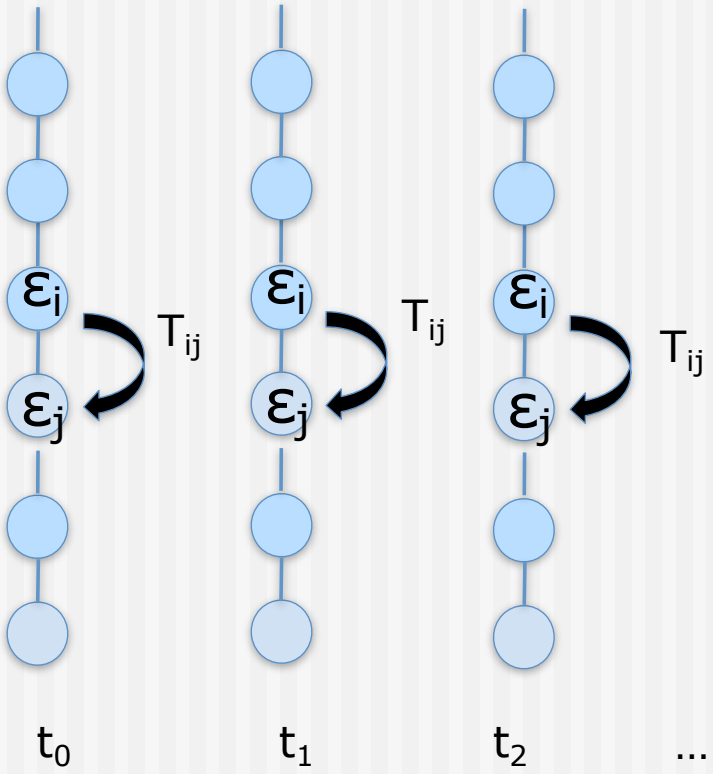
CT parameters along a QM/MM MD simulation



Coarse grained
Hamiltonian

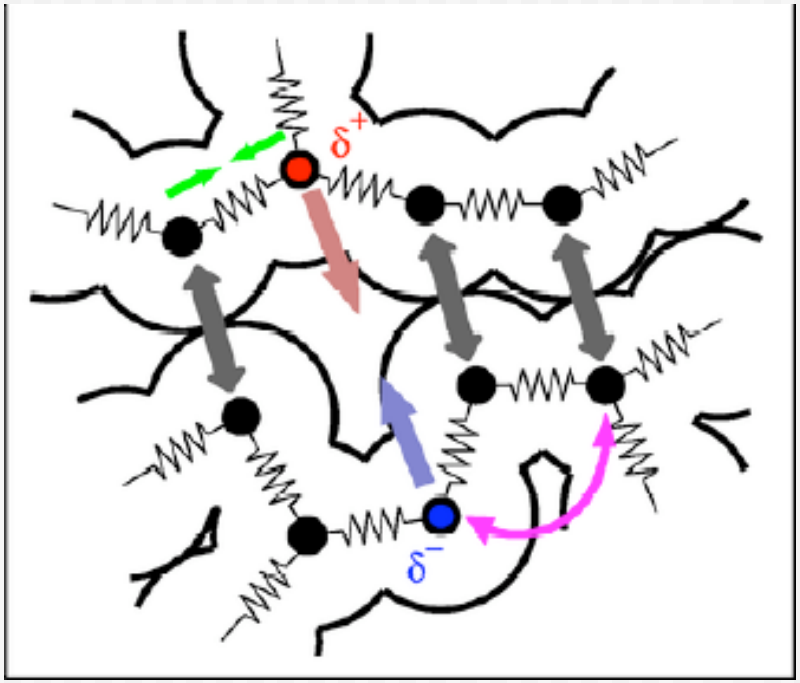
site i

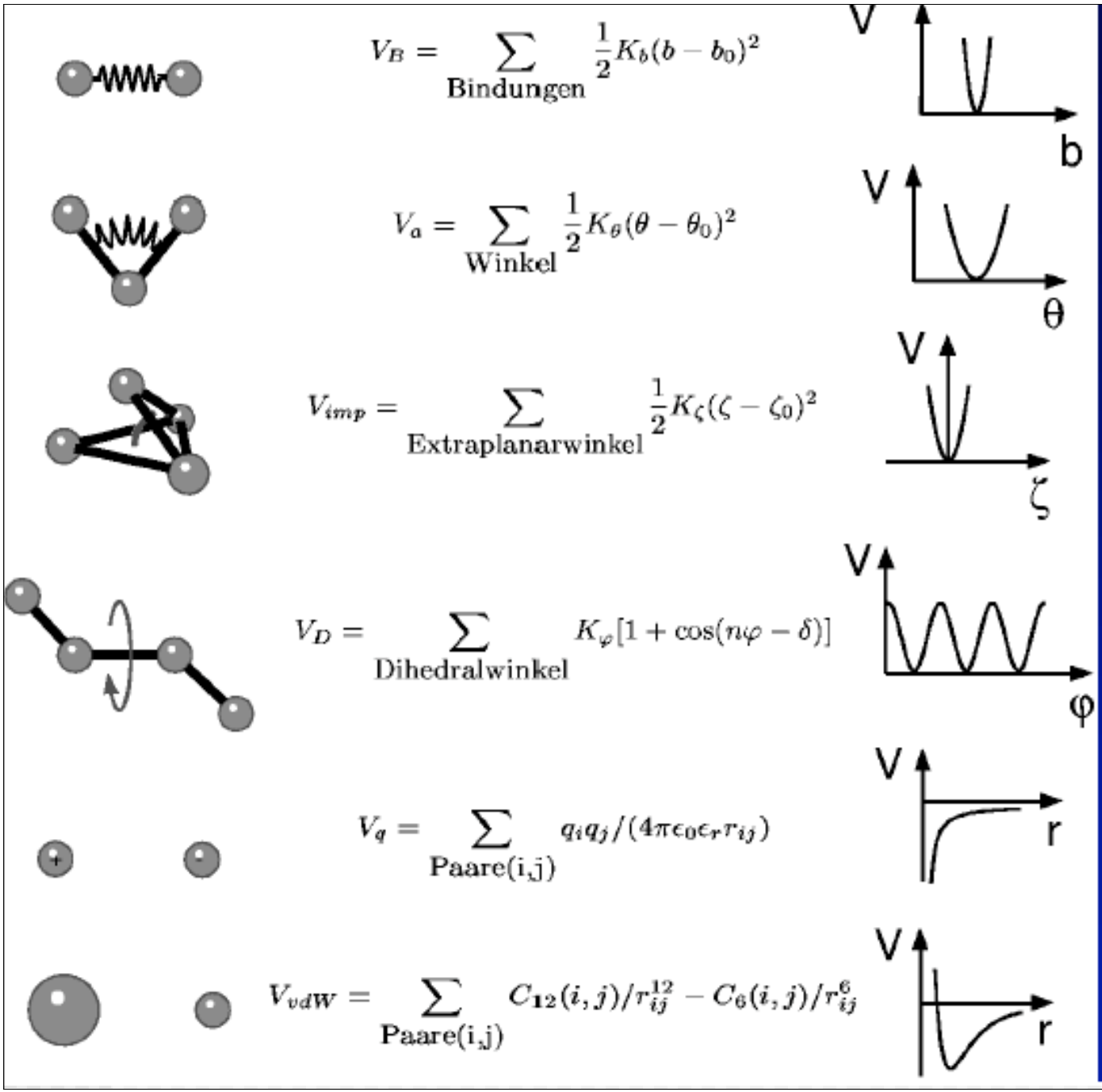
site j



Time dependent parameters
$\varepsilon_i(t)$ and $T_{ij}(t)$ contain dynamical and solvation effects

Empirical Force Fields: Molecular Mechanics (MM)

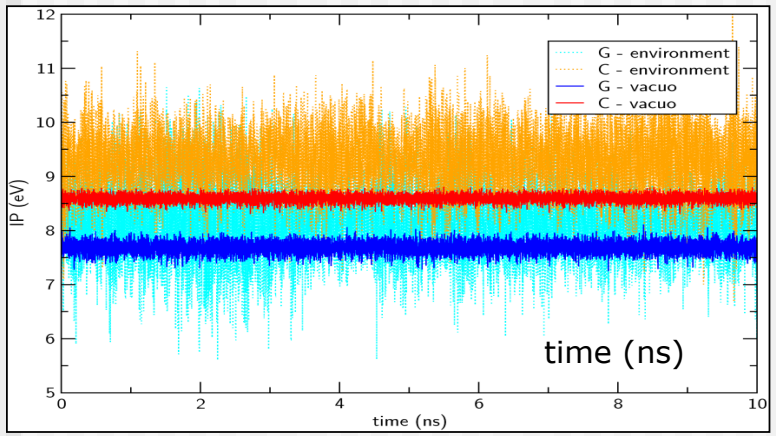




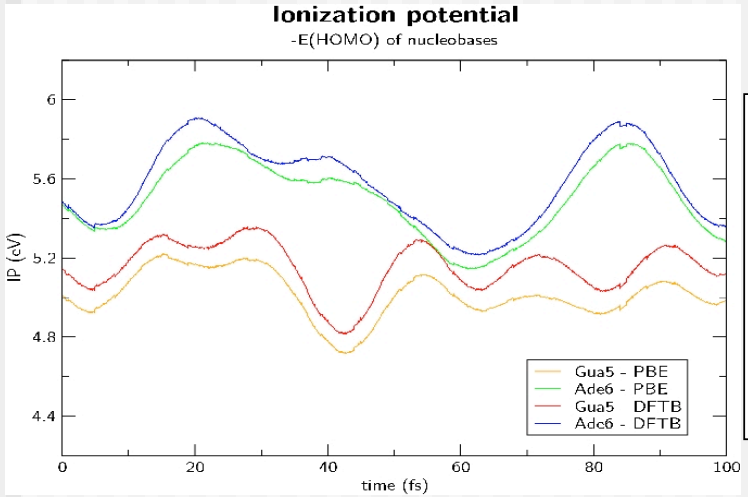
Quelle: Grubmüller
MPI Göttingen

Fluctuations of Ip

$$H_{\mu\nu} = H^0_{\mu\nu} + \frac{1}{2} S_{\mu\nu} \sum_{\gamma} \Delta q_{\gamma} (\gamma_{\alpha\gamma} + \gamma_{\beta\gamma}) + \frac{1}{2} S^{\alpha\beta}_{\mu\nu} \sum_{A} Q_A (1/R_{\alpha A} + 1/R_{\beta A})$$



- due to solvent: 0.4 eV
- 'gas phase' : 0.1 eV
(QM/MM term switched off)



- large fluctuations
- A and G states can have same energy

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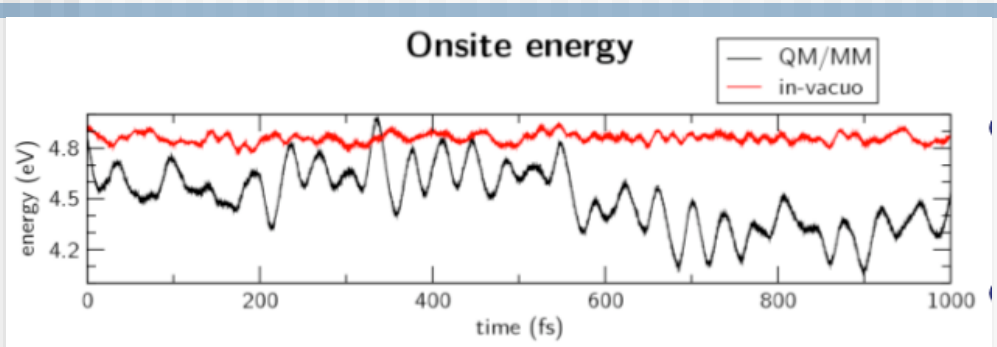
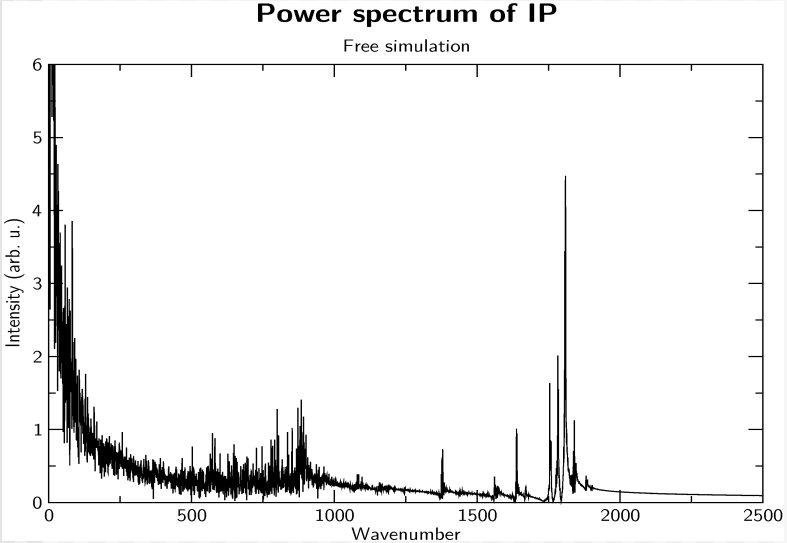
Characteristic modes



characteristic modes
- water: 40 fs
- bases: 20 fs



- internal base modes: 20 fs 1600 cm^{-1}
- 'water modes': 40 fs 800 cm^{-1}
- water+counterions: 1ps
- ...

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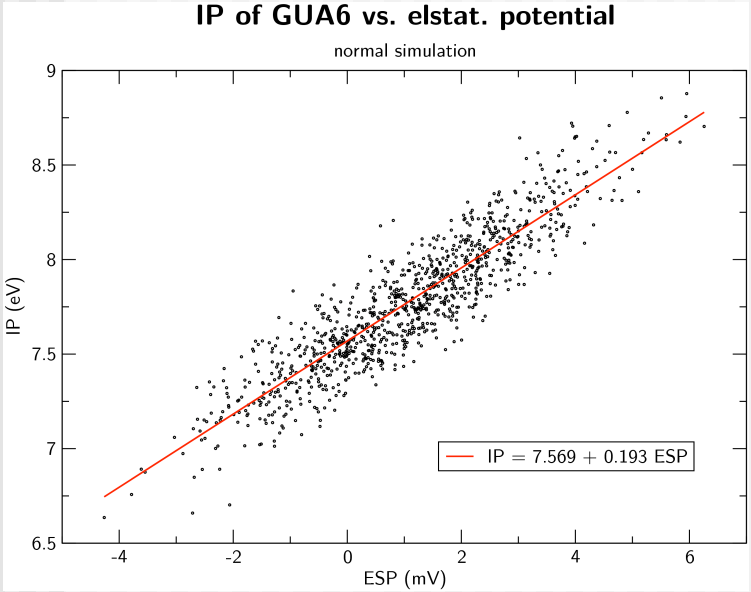
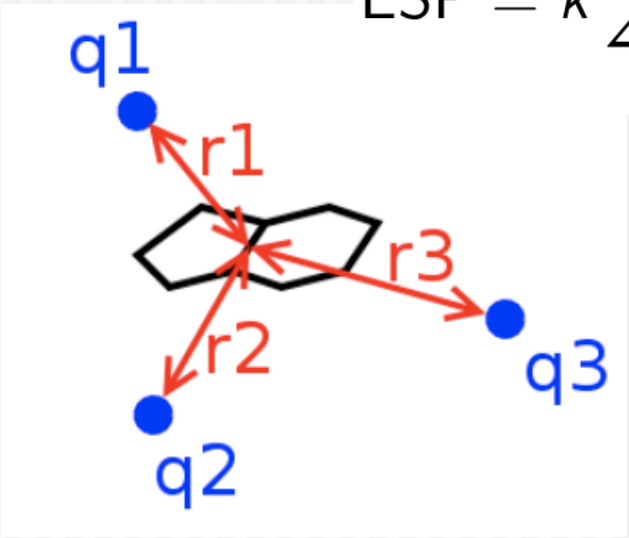
Correlation of Ip with MM electrostatic potential



$$\mathrm{ESP} = k \sum_i \frac{q_i}{r_i}$$



Strong correlation of electrostatic potentials with IPs:

➔we can decompose the potential to analyze the components from backbone, waters and ions

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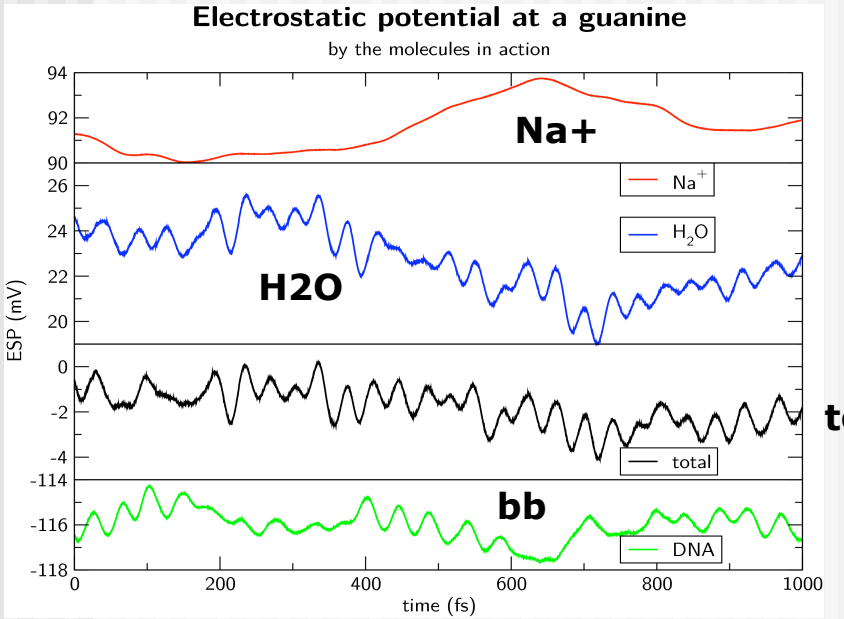
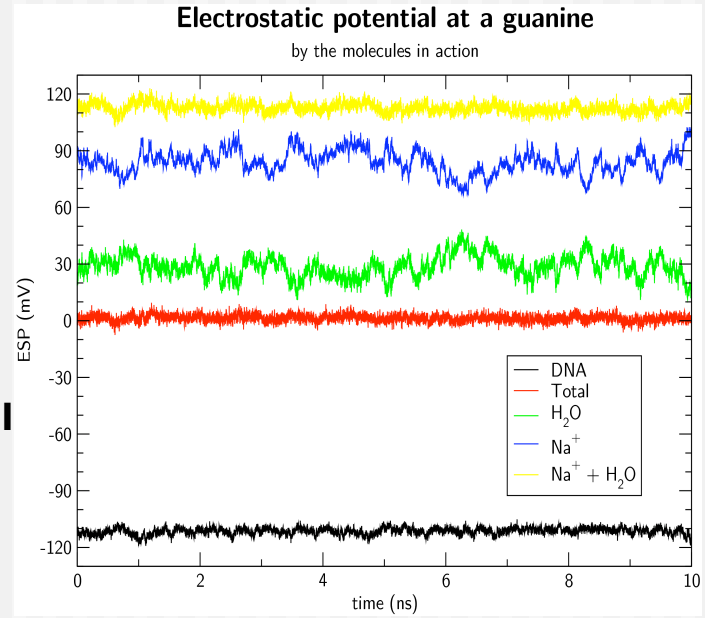
Electrostatic potential of MM atoms at a Guanine

1ps **10ns**



total



Na+

H2O

bb

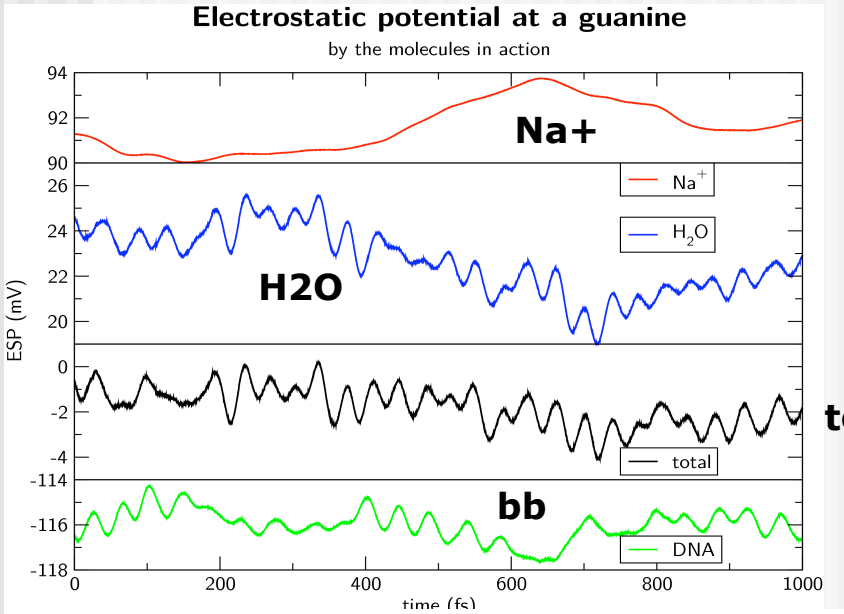
=> fluctuations of the solvent introduce 40 fs mode,

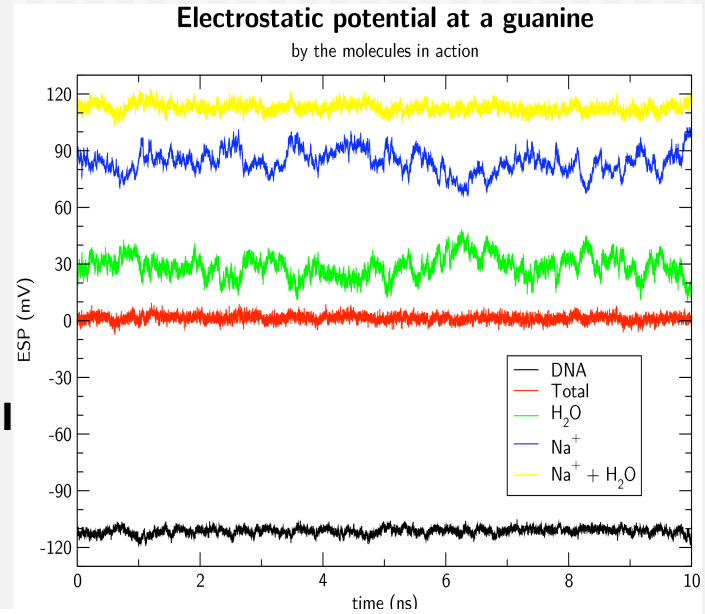
i.e. solvent introduces the fluctuations of the IP in the order of 0.4 eV

ion motion on ps-time-scale

Electrostatic potential of MM atoms at a Guanine

1ps **10ns**





Na+

H2O

bb

TABLE 3: Correlation Coefficient of the Individual Components of Electrostatic Potential

$\rho_{x,y}$	water	ions	water + ions	total
DNA	−0.08	−0.16	−0.44	0.18
water		−0.85	0.22	0.19
ions			0.33	0.26
water + ions				0.81

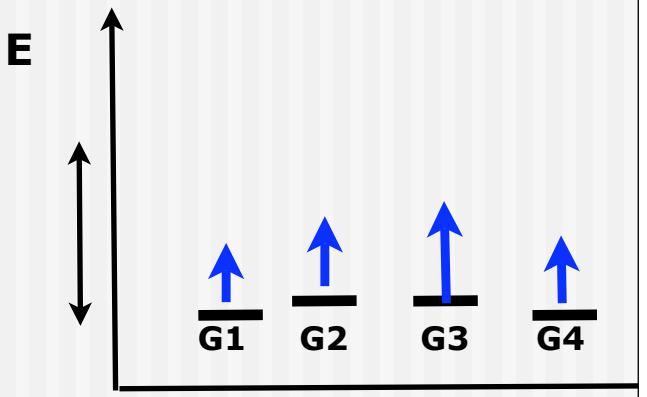
s?

Results: Ip of neighboring sites correlated

=> motion of water and ions determine Ip fluctuation to large degree

correlation of fluctuation of neighboring sites

$\rho_{\varepsilon_i,\varepsilon_j}$	G3	G4	G5	G6	G7	G8	G9
G3	1	0.66	0.33	−0.03	−0.22	−0.33	−0.37
G4		1	0.65	0.26	0.00	−0.17	−0.30
G5			1	0.60	0.29	0.07	−0.11
G6				1	0.67	0.43	0.20
G7					1	0.71	0.45
G8						1	0.72
G9							1



- **concerted motion of neighboring sites (3-4) may have important implications or CT and transport**
- **and this is due to solvent environment**

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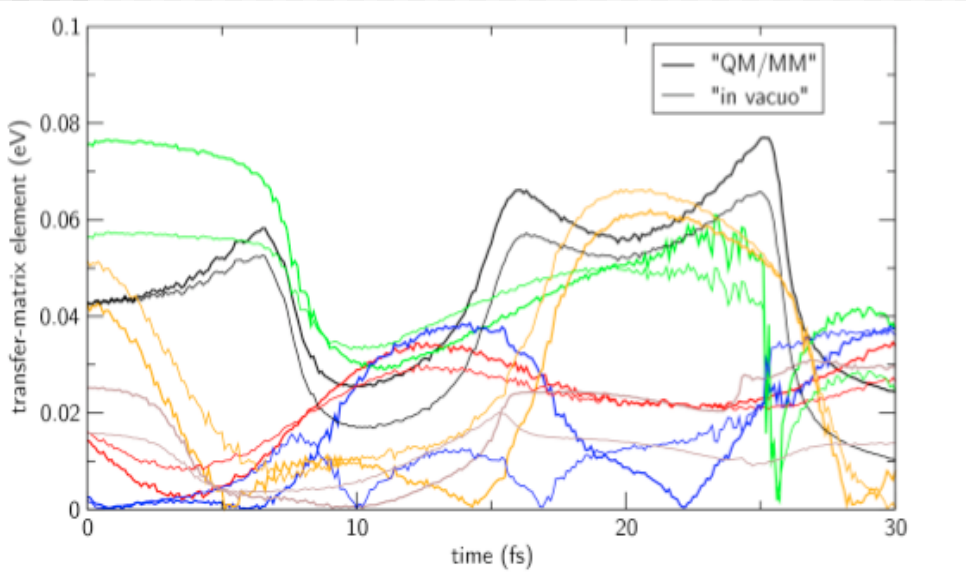
Fluctuations of T_{ij}

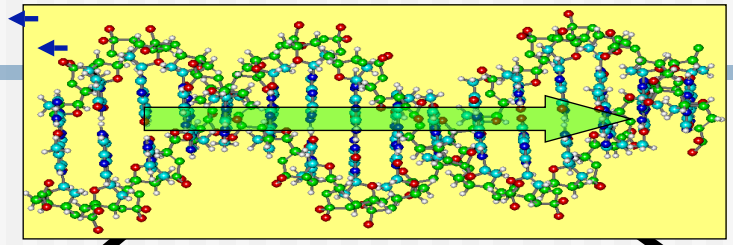


- large fluctuations
- small impact of environment on T_{ij}

- vanishing correlation between T_{ij}!

➔ no ‘collective modes’?

Charge transport in Physics and Chemistry



conductivity experiments

coherent tranport?

'chemical experiments'

hole hopping: charge transfer

$$H = \sum_i \varepsilon_i a_i^+ a_i + \sum_{ij} T_{ij} a_i^+ a_j$$

$$G_{\mathrm{D}}(E) = (E - H_{\mathrm{D}}^{\mathrm{KS}} - \Sigma_{\mathrm{L}} - \Sigma_{\mathrm{R}})^{-1}$$

$$T(E,V) = tr[\Gamma_{\mathrm{L}} G_{\mathrm{D}}^{\mathrm{r}} \Gamma_{\mathrm{R}} G_{\mathrm{D}}^{\mathrm{a}}]$$

$$I(V) = \frac{2e}{h} \int_{\mu_1(V)}^{\mu_2(V)} T(E,V) dE$$

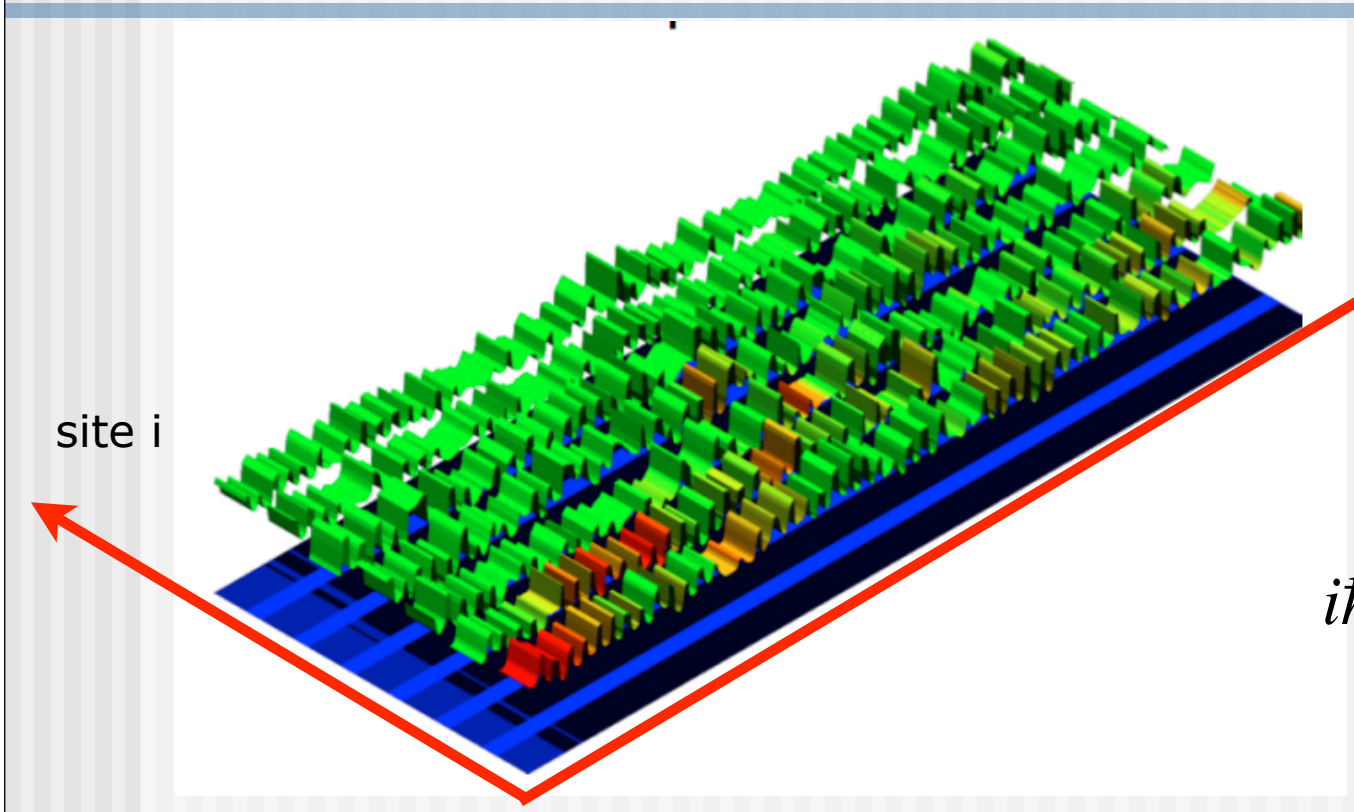
$$\Psi = \sum_i c_i \phi_i$$

hole WF

$$i\hbar\dot{\mathbf{c}} = \mathbf{H}\mathbf{c}$$

solve TDKS

hole propagation

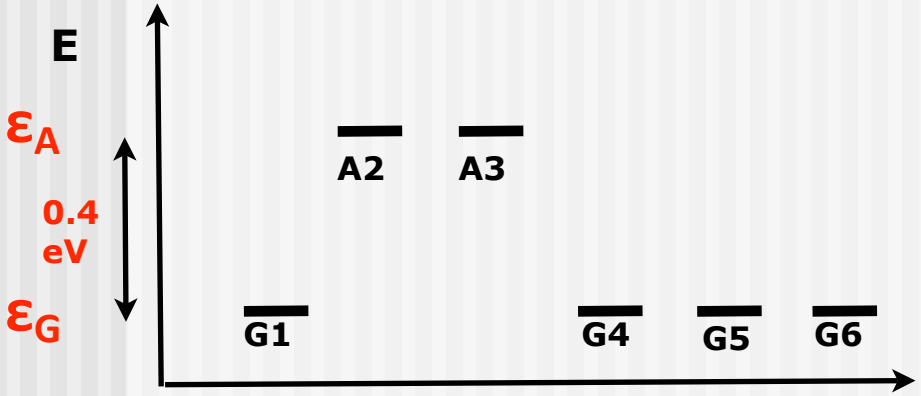


$$i\hbar \frac{\partial}{\partial t} \Psi = H_{KS} \Psi$$

coupled eq. of motion for hole and atoms:
classical MD for atoms
TDKS for hole wavefunction

CT in DNA: A-bridges

Giese et al. Nature 2002



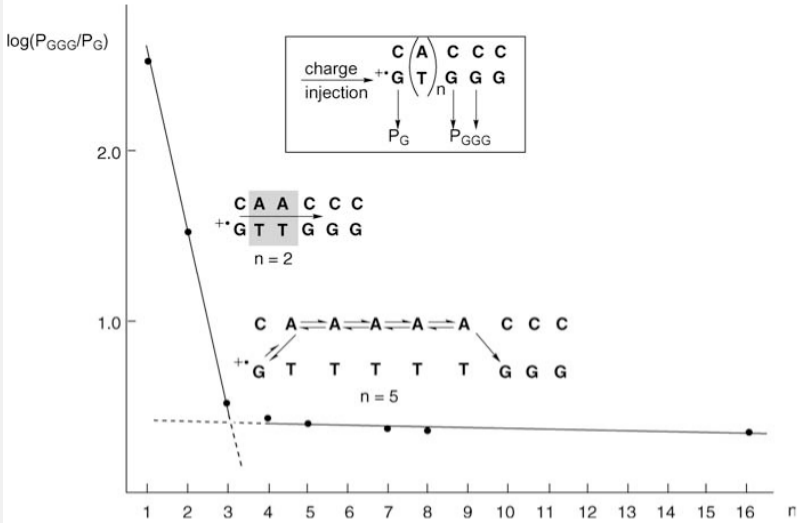
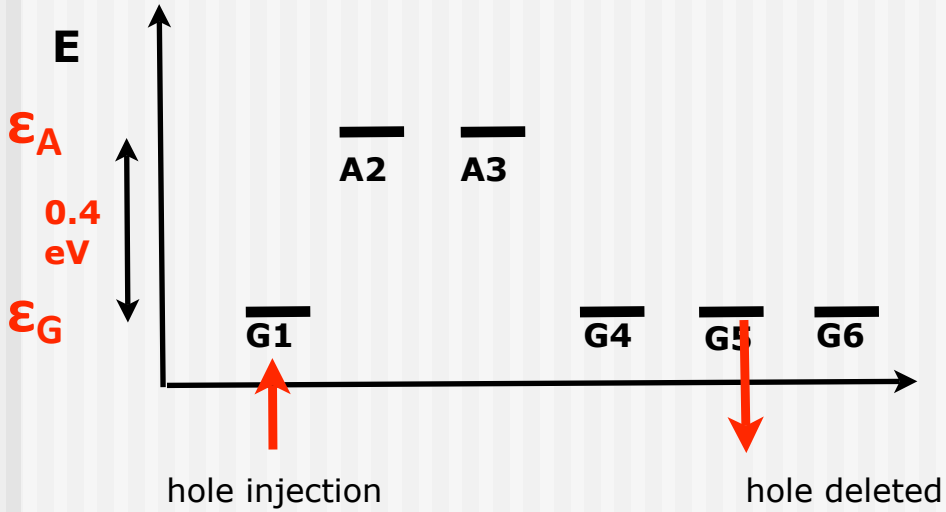


Fig. 13 Influence of the $(A:T)_n$ sequence on the hole transfer between a guanine radical cation G^{+} and a GGG triplet

- exponential decay for short bridges
- algebraic for long A-trackts

Tunneling through A bridges



Experiments by Giese et al.,

superexchange tunneling for $G(A)_nGGG$ for n=1-4

always static calculations!

MD simulations for $G(A)_nGGG$ (n=1-4)

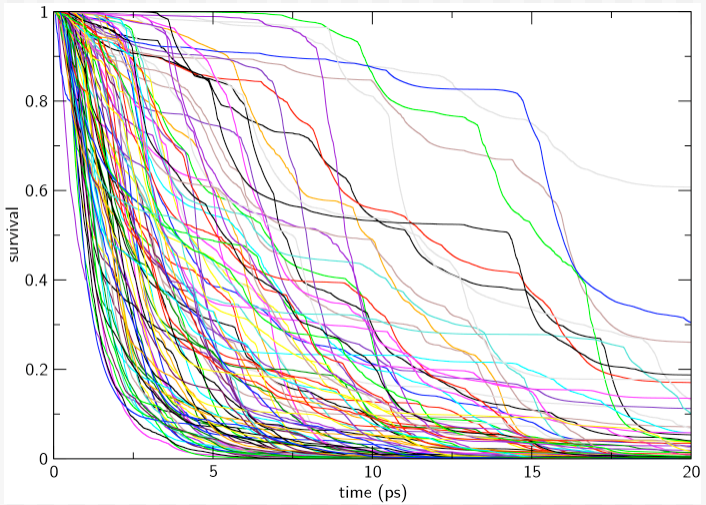
- sampling: average several trajectories over 20 ps hole motion
- calculate survival probability (eliminate hole at G6)

=> very different picture, since barriers not constant

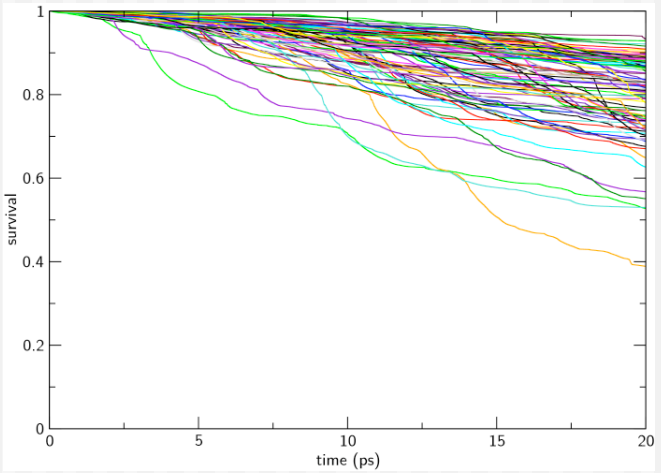
CT in GAGGG: 100 trajectories

population

'complete' dynamics

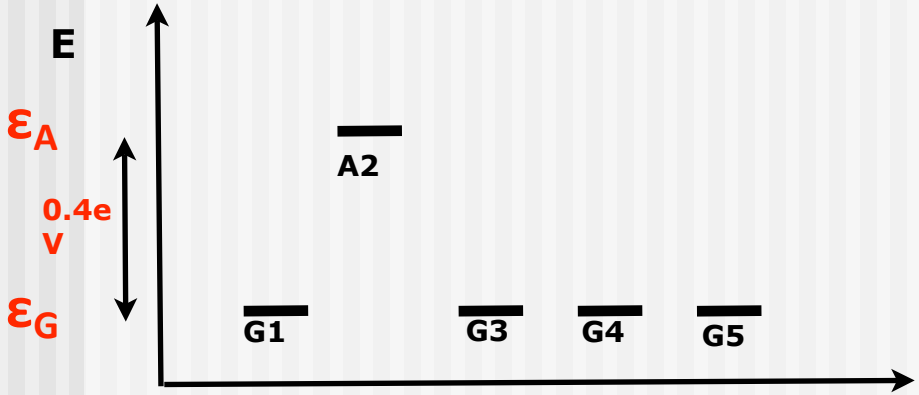


static onsite



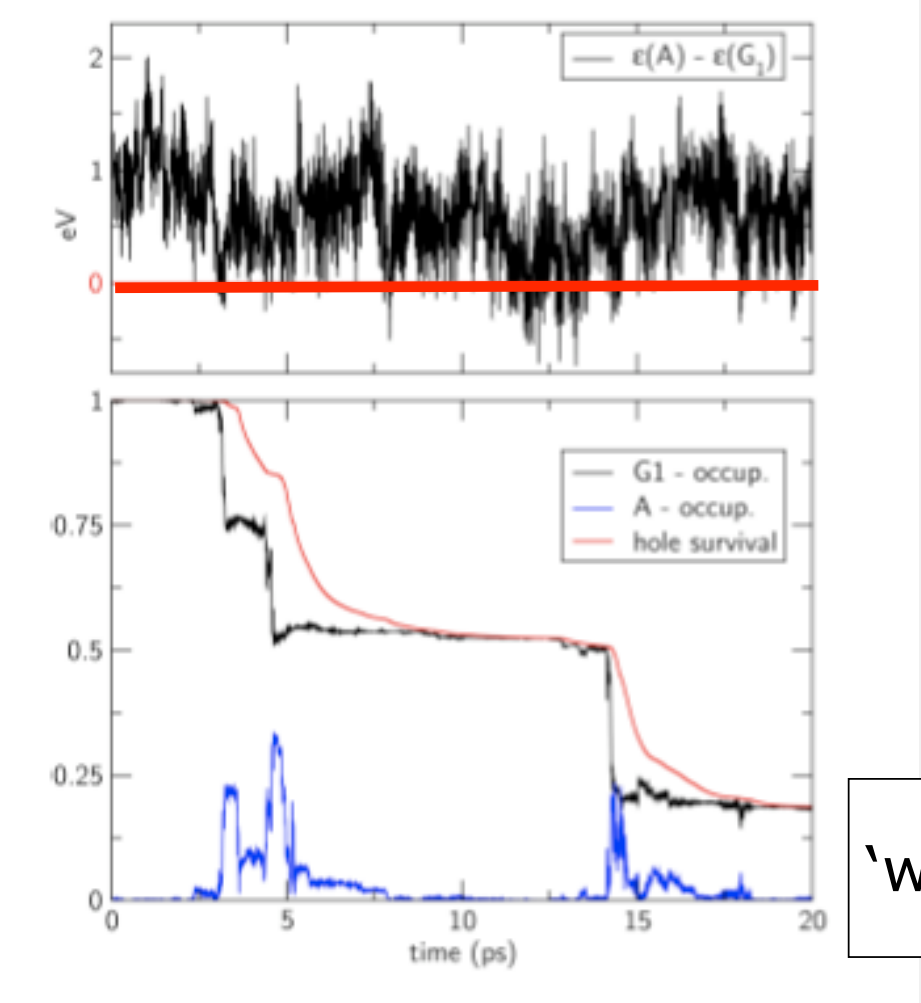
time: 20 ps

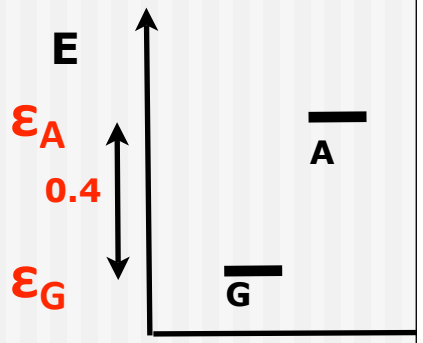
only tunneling!



Kubar et al. submitted

CT in DNA: GAGGG





ε_A-ε_G

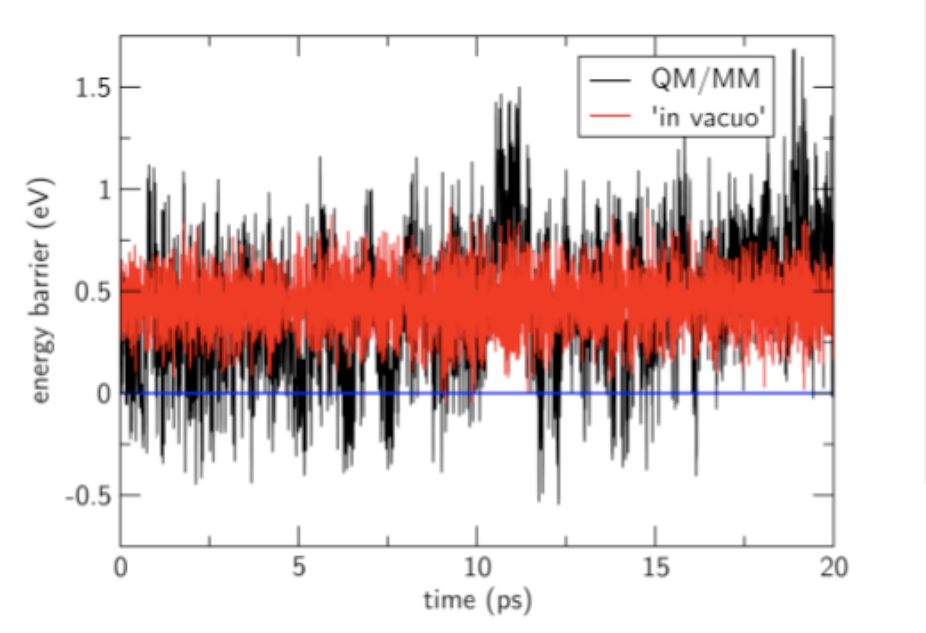
Energy difference between A and G

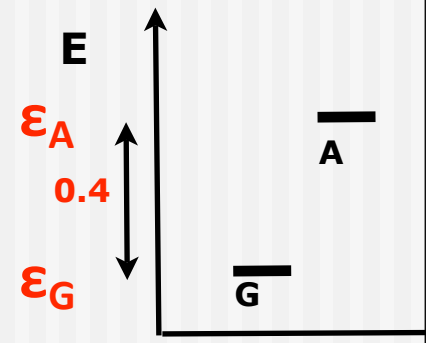
populations is transferred when:

- energy difference is small
- couplings do not vanish

'water modes' drive the CT!

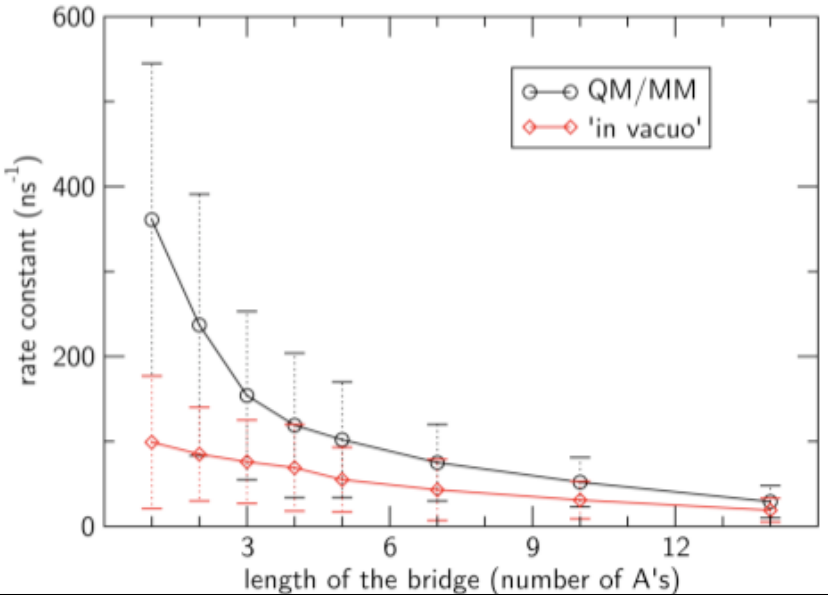
CT in GAGGG: role of solvent





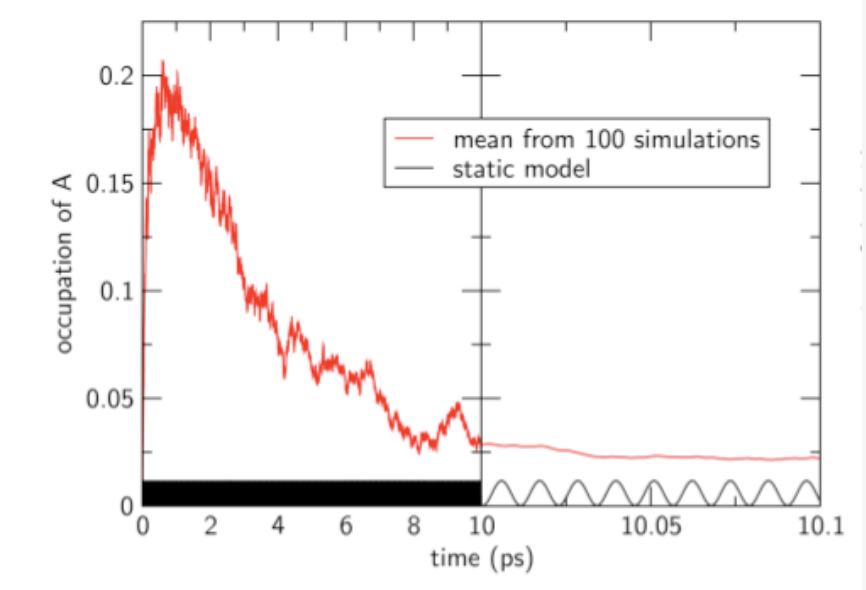
ε_A-ε_G
energy difference between A and G

black: with solvent
red: withot solvent



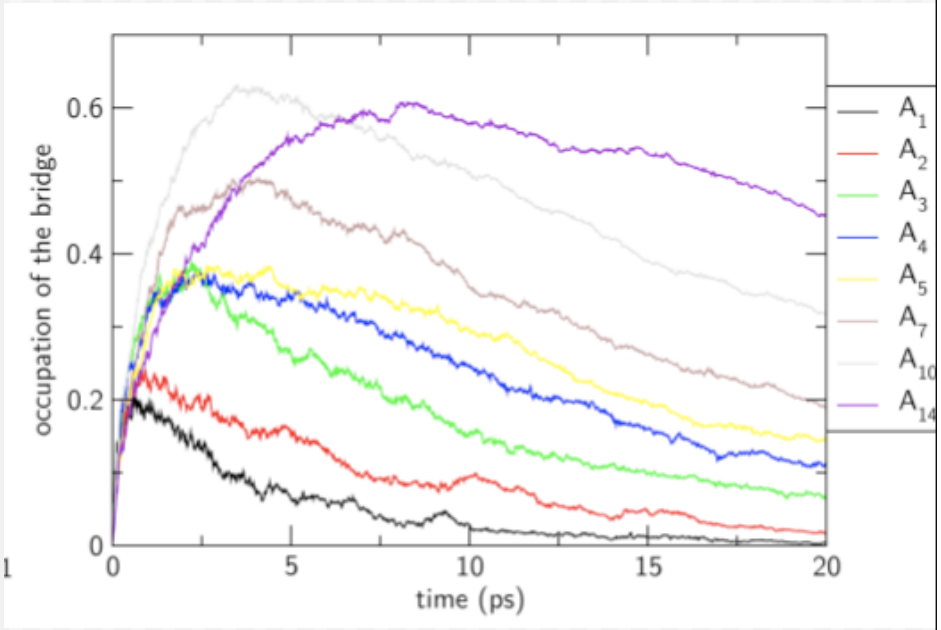
'water modes' drive the CT!

CT in GA_nGGG: bridge occupation



bridge occupation
in **GAGGG**:

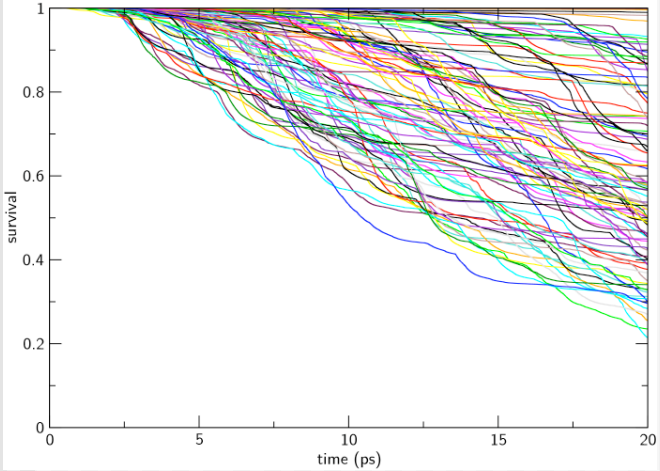
- ε_i kept fixed
- dynamic model



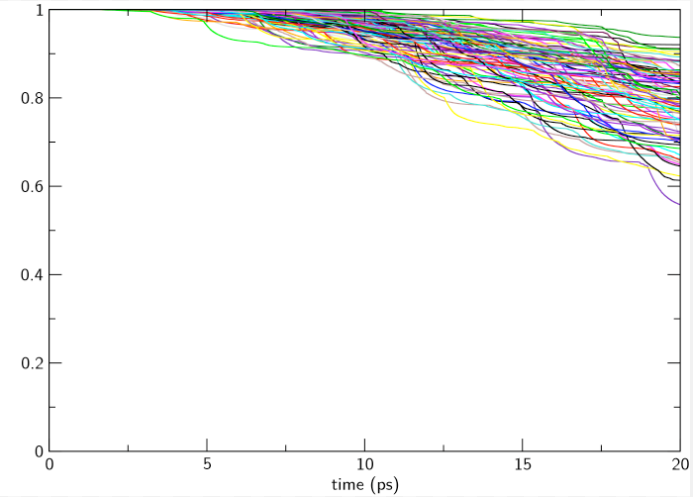
bridge occupation
in **GA_nGGG**:

CT in DNA: $GA_{14}GGG$

'complete' dynamics



fluctuating onsite, but taken from onsite pdf



correlated motion of neighboring sites

$\rho_{\varepsilon_i,\varepsilon_j}$	G3	G4	G5	G6	G7	G8	G9
G3	1	0.66	0.33	−0.03	−0.22	−0.33	−0.37
G4		1	0.65	0.26	0.00	−0.17	−0.30
G5			1	0.60	0.29	0.07	−0.11
G6				1	0.67	0.43	0.20
G7					1	0.71	0.45
G8						1	0.72
G9							1

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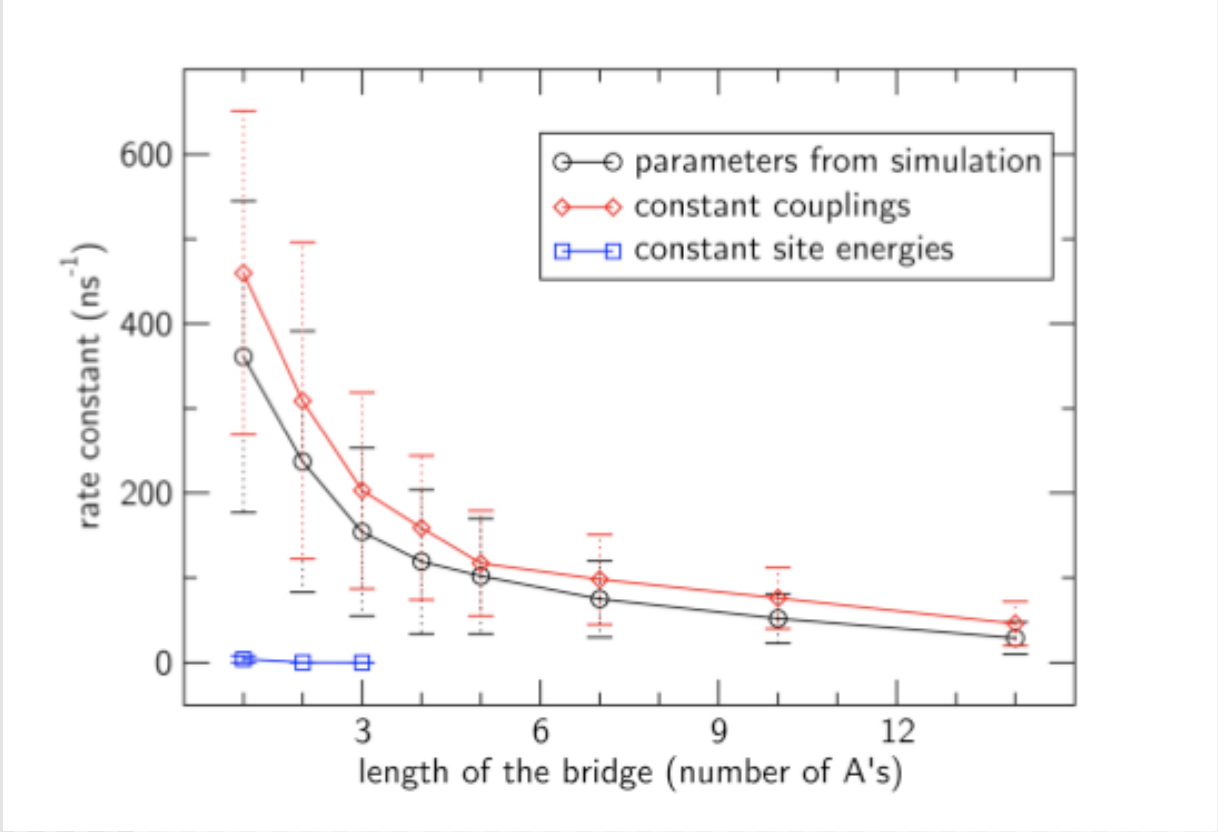
CT in GA_nGGG: role of couplings



time course of couplings can be substituted by their 'averages':

no special CT promoting modes?

CT in DNA: A-bridges

Giese et al

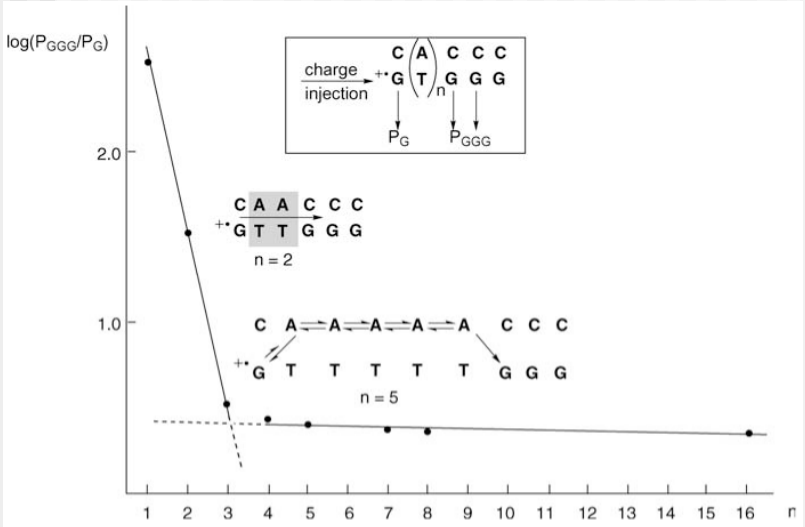
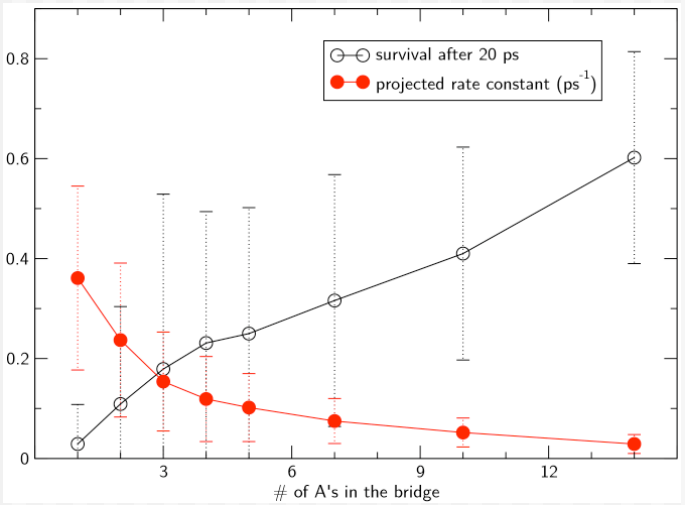


Fig. 13 Influence of the $(A:T)_n$ sequence on the hole transfer between a guanine radical cation G^+ and a GGG triplet

calc.



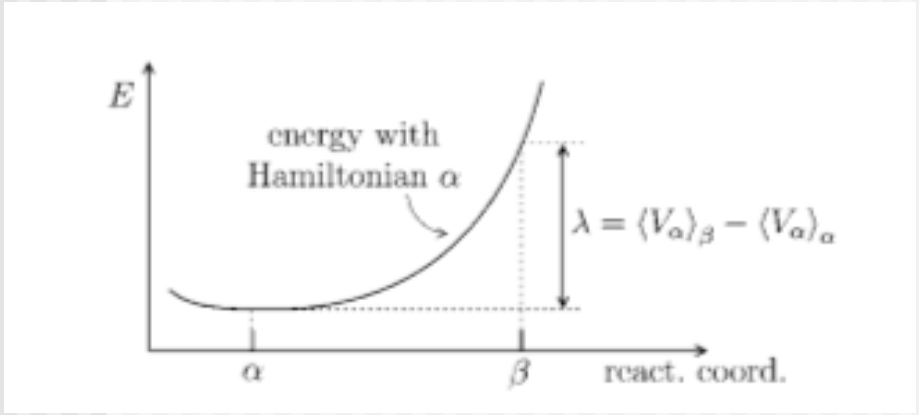
- exponential decay for short bridges
- algebraic for long A-trackts

=> still missing: proper account of solvation

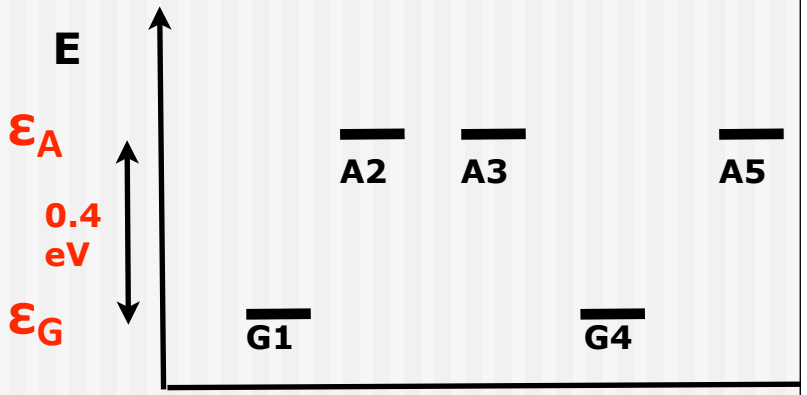
Kubar et al. submitted

CT in DNA: solvation

$$k = \frac{2\pi}{\hbar}|H_{DA}|^2 \frac{1}{\sqrt{4\pi\lambda k_B T}} \exp\left[-\frac{(\Delta G_0 + \lambda)^2}{4\lambda k_B T}\right]$$



Reorganization energy in Marcus theory



- put hole-charge on base α, equilibrate the system with MD: ensemble α
- put hole-charge on base β, equilibrate the system with MD: ensemble β

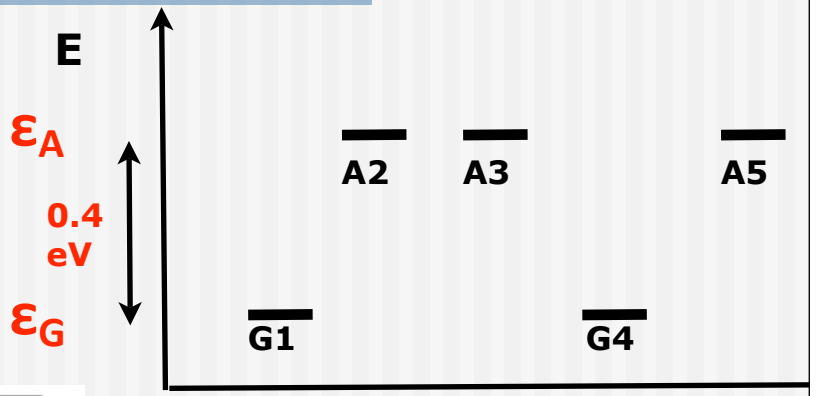
compute average energy of hole on α, using the ensemble β

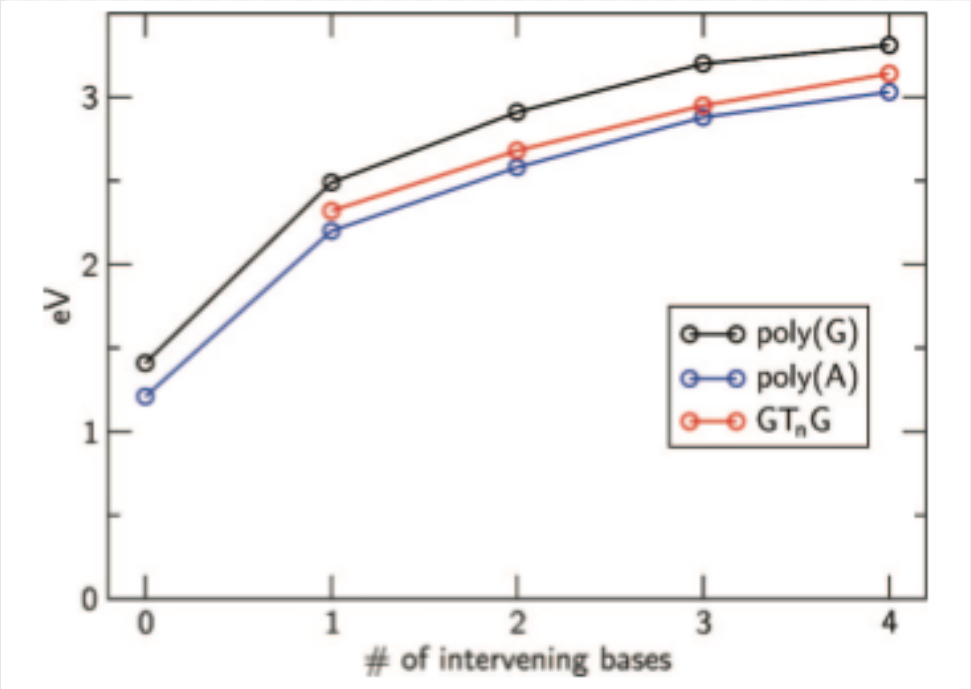
Kubar& Elstner JPCB 2009 113 5653

CT in DNA: solvation

Reorganization energy in Marcus theory

$$k = \frac{2\pi}{\hbar}|H_{DA}|^2 \frac{1}{\sqrt{4\pi\lambda k_B T}} \exp\left[-\frac{(\Delta G_0 + \lambda)^2}{4\lambda k_B T}\right]$$





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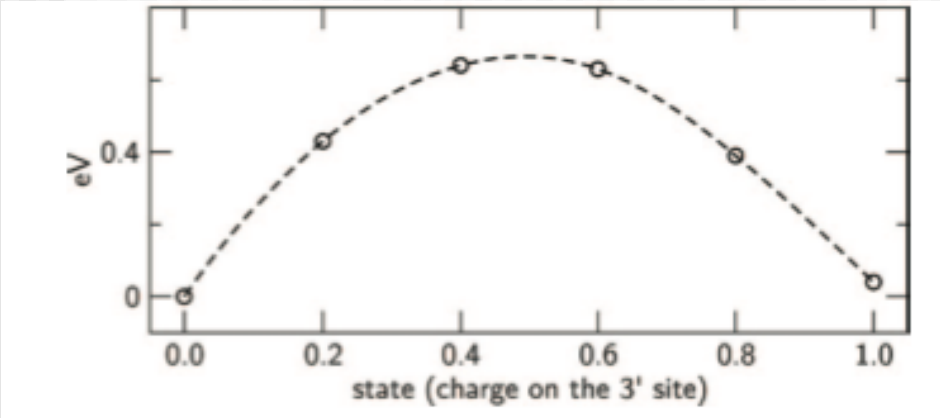
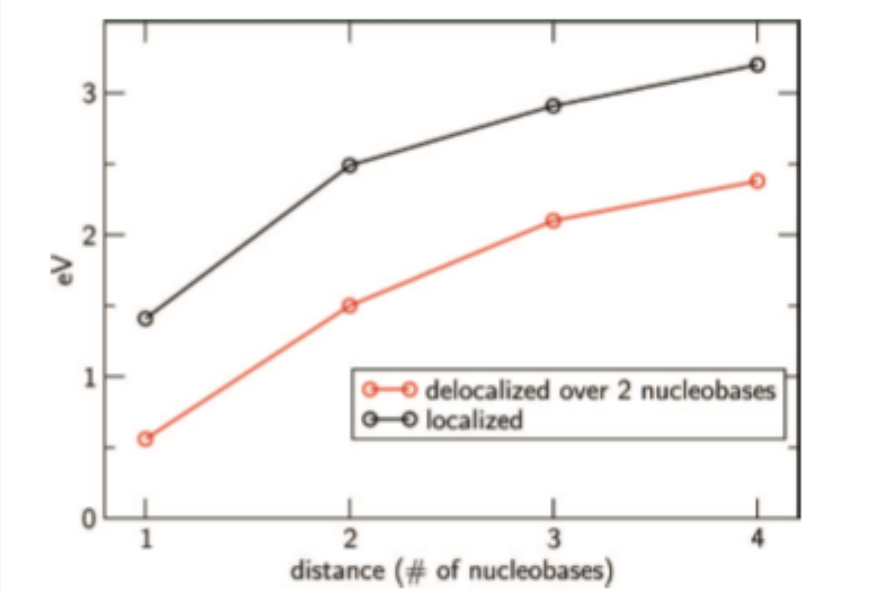
CT in DNA: solvation

delocalization????



energy to delocalize hole between 2 bases: 0.6 eV



reorganization energy to relocate delocalized hole:

≈0.8 eV less than for localized hole

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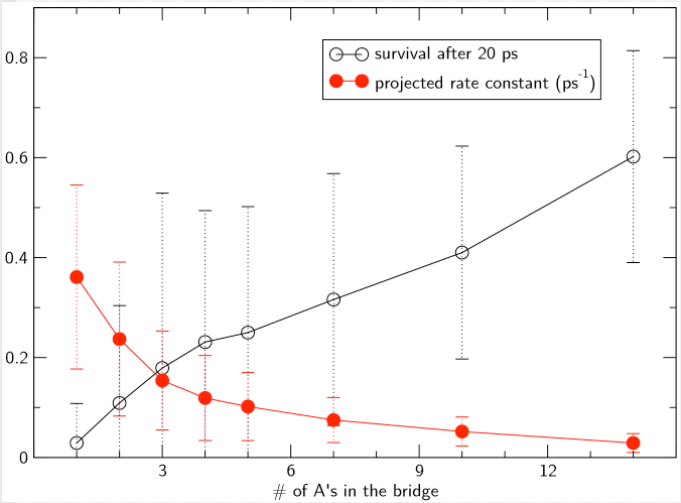
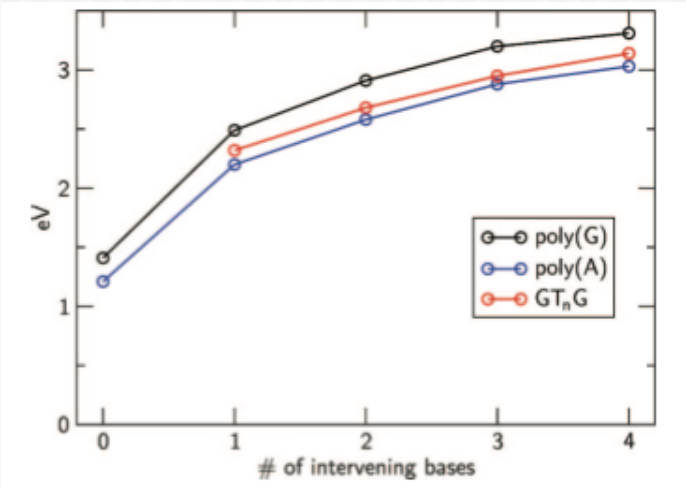
CT in DNA: A-bridges



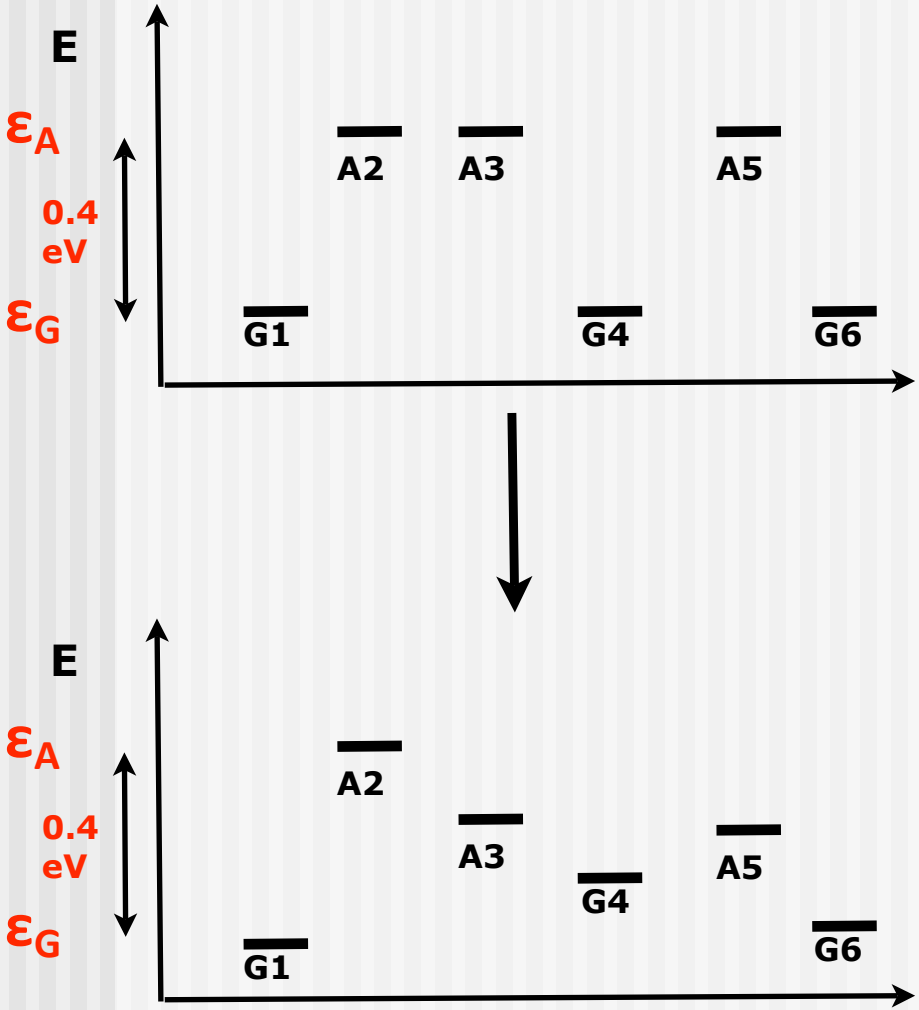


- exponential decay for short bridges
- distance dependent reorganization energy causes exponential dependence

=> still missing: proper account of solvation

Kubar et al. submitted

Effect of solvent and dynamics: new mechanistic picture

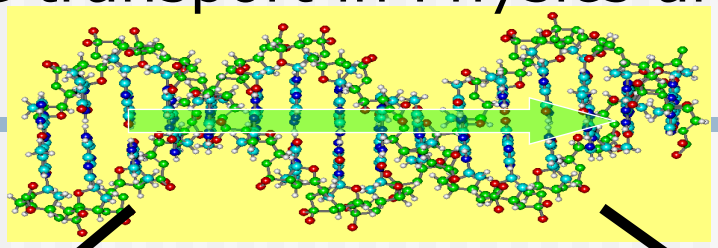


- static picture not really meaningful
- onsite fluctuations drive the CT
- correlation between sites important
- fluctuations of T_{ij} less important, contrary to the many proposals!
- New model: 'conformal gating'
- 'water modes' drive CT!
- solvent neglected so far, but important factor to determine absolute rates!

=> coarse grained SCC-DFTB model

Kubar et al. submitted

Charge transport in Physics and Chemistry



conductivity experiments

'chemical experiments'

hole hopping; charge transfer

$$H = \sum_i \varepsilon_i a_i^+ a_i + \sum_{ij} T_{ij} a_i^+ a_j$$

$$G_{\mathrm{D}}(E) = (E - H_{\mathrm{D}}^{\mathrm{KS}} - \Sigma_{\mathrm{L}} - \Sigma_{\mathrm{R}})^{-1}$$ **Green functions**

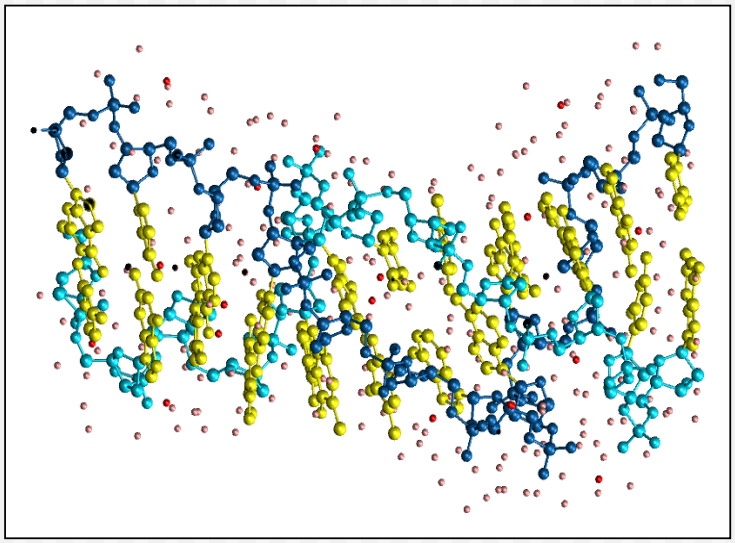
$$T(E,V) = tr[\Gamma_{\mathrm{L}} G_{\mathrm{D}}^{\mathrm{r}} \Gamma_{\mathrm{R}} G_{\mathrm{D}}^{\mathrm{a}}]$$ **Landauer theory**

$$I(V) = \frac{2e}{h} \int_{\mu_1(V)}^{\mu_2(V)} T(E,V) dE$$ **Observables**

Woiczikowski et al., JCP accepted

Guttierez et al., PRL accepted

The basis: classical MD simulation of DNA in water



- 50 ns MD
- AMBER 9
- Parm99+BSC0
- DNA fully solvated, TIP3P
- Periodic boundary cond.
- Ewald summation

compute $H = \sum_i \varepsilon_i a_i^+ a_i + \sum_{ij} T_{ij} a_i^+ a_j$

for: pG, pA, p(AT),p(GA) ...

$$G_{\mathrm{D}}(E) = (E - H_{\mathrm{D}}^{\mathrm{KS}} - \Sigma_{\mathrm{L}} - \Sigma_{\mathrm{R}})^{-1}$$

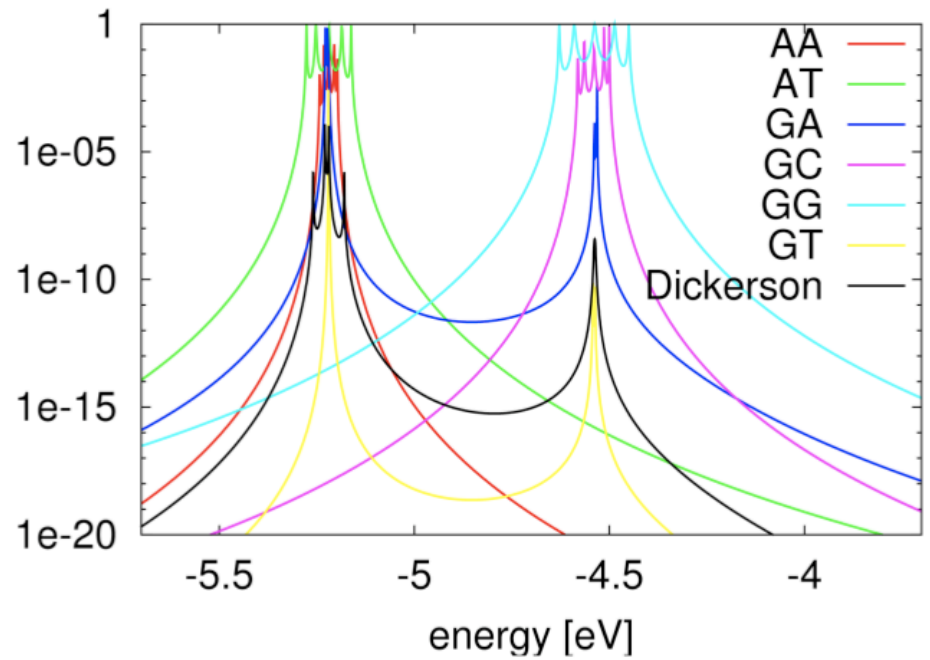
$$T(E,V) = tr[\Gamma_{\mathrm{L}} G_{\mathrm{D}}^{\mathrm{r}} \Gamma_{\mathrm{R}} G_{\mathrm{D}}^{\mathrm{a}}]$$

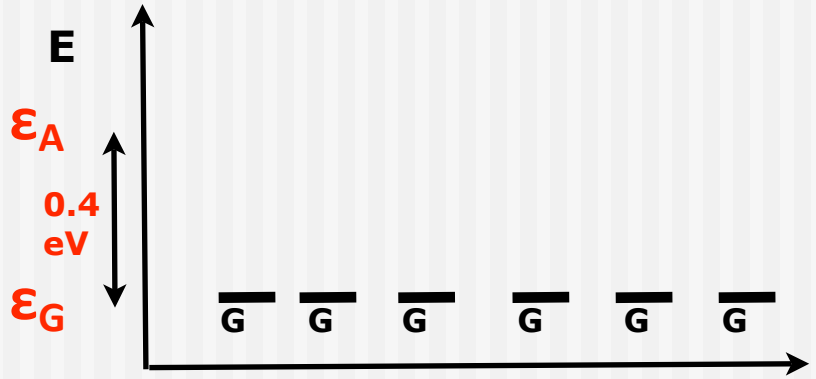
for every time-step,

and then do what? average?

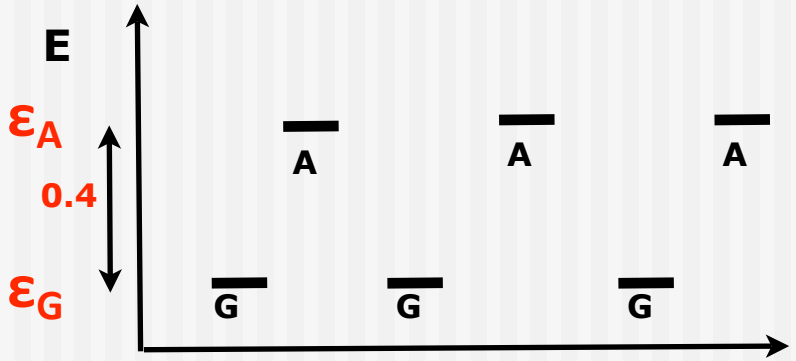
the reference: ideal B-DNA structures

transmission



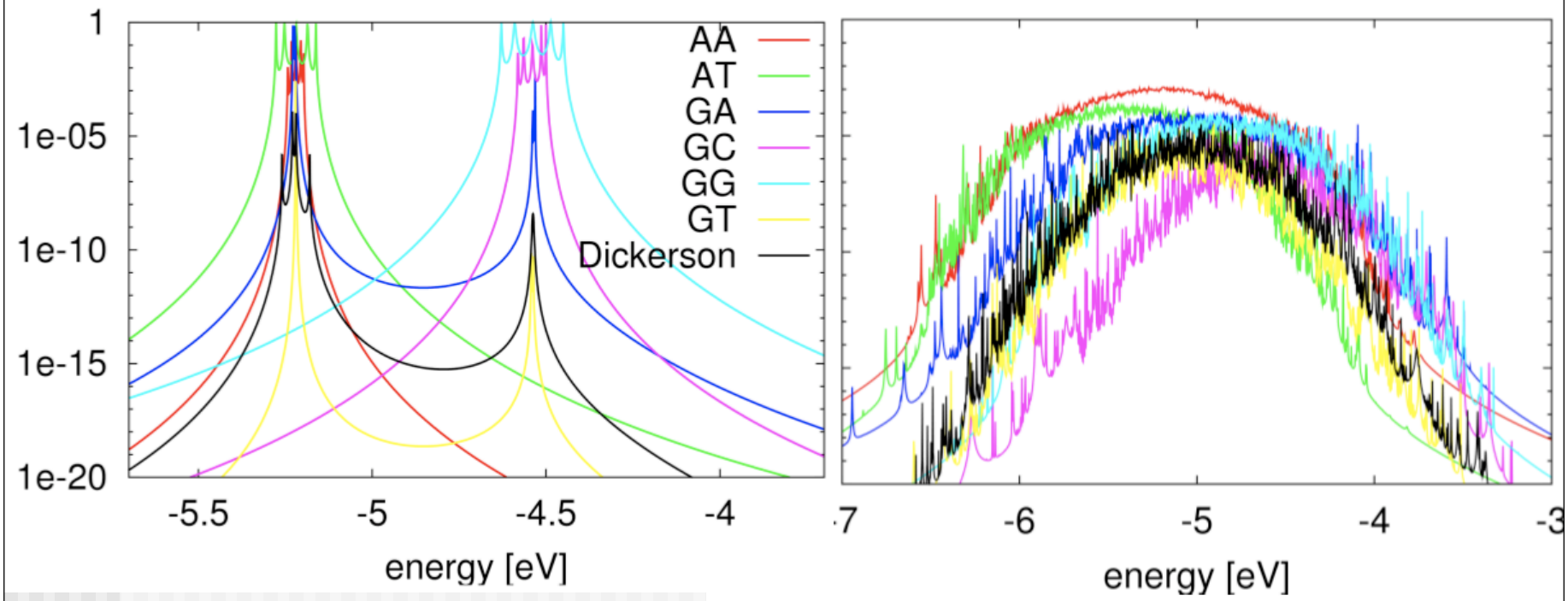


pG: '**good**' (conducting) **sequence**



pGA: '**bad**' (conducting) **sequence**

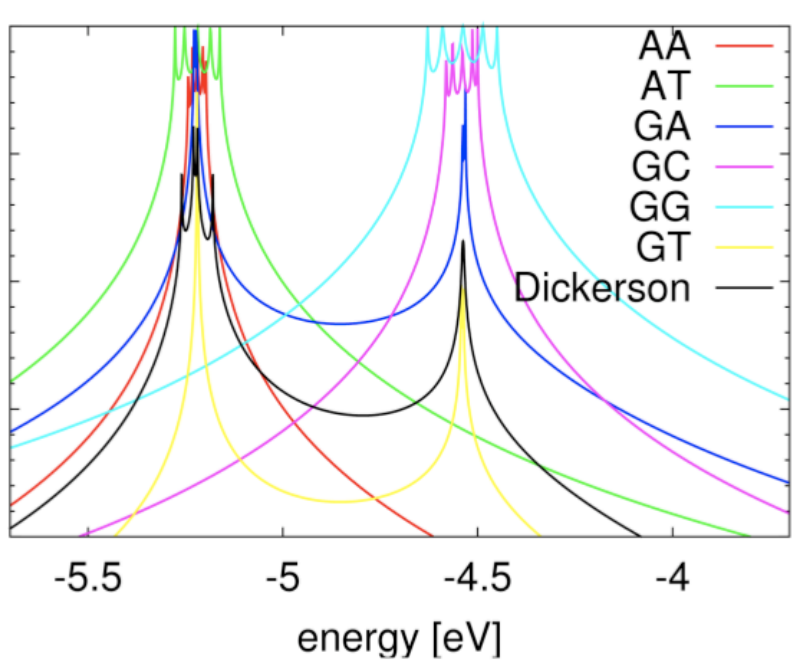
and in water

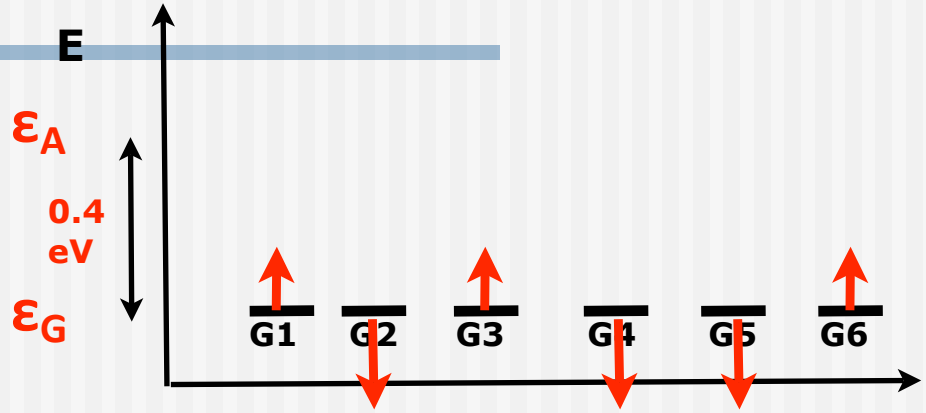


- transmission of 'good sequences' **reduced** by 5 orders of magnitude:
dynamical disorder

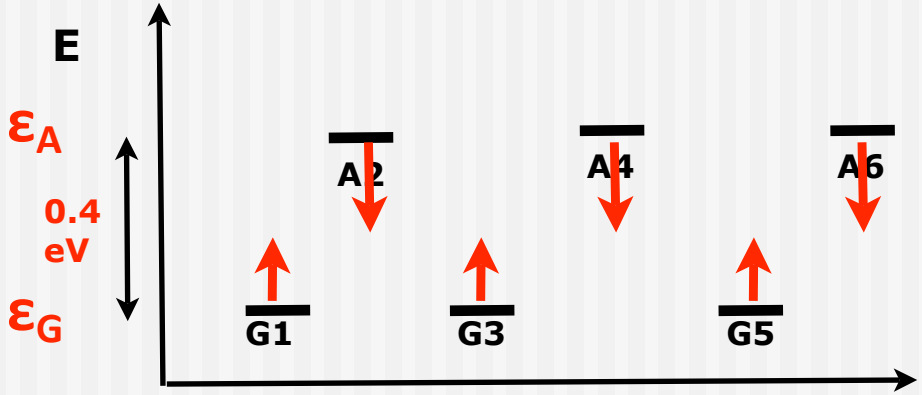
- transmission of 'bad sequences' **increased** by 5 orders of magnitude
dynamics introduces CT active conformations

effect of fluctuations

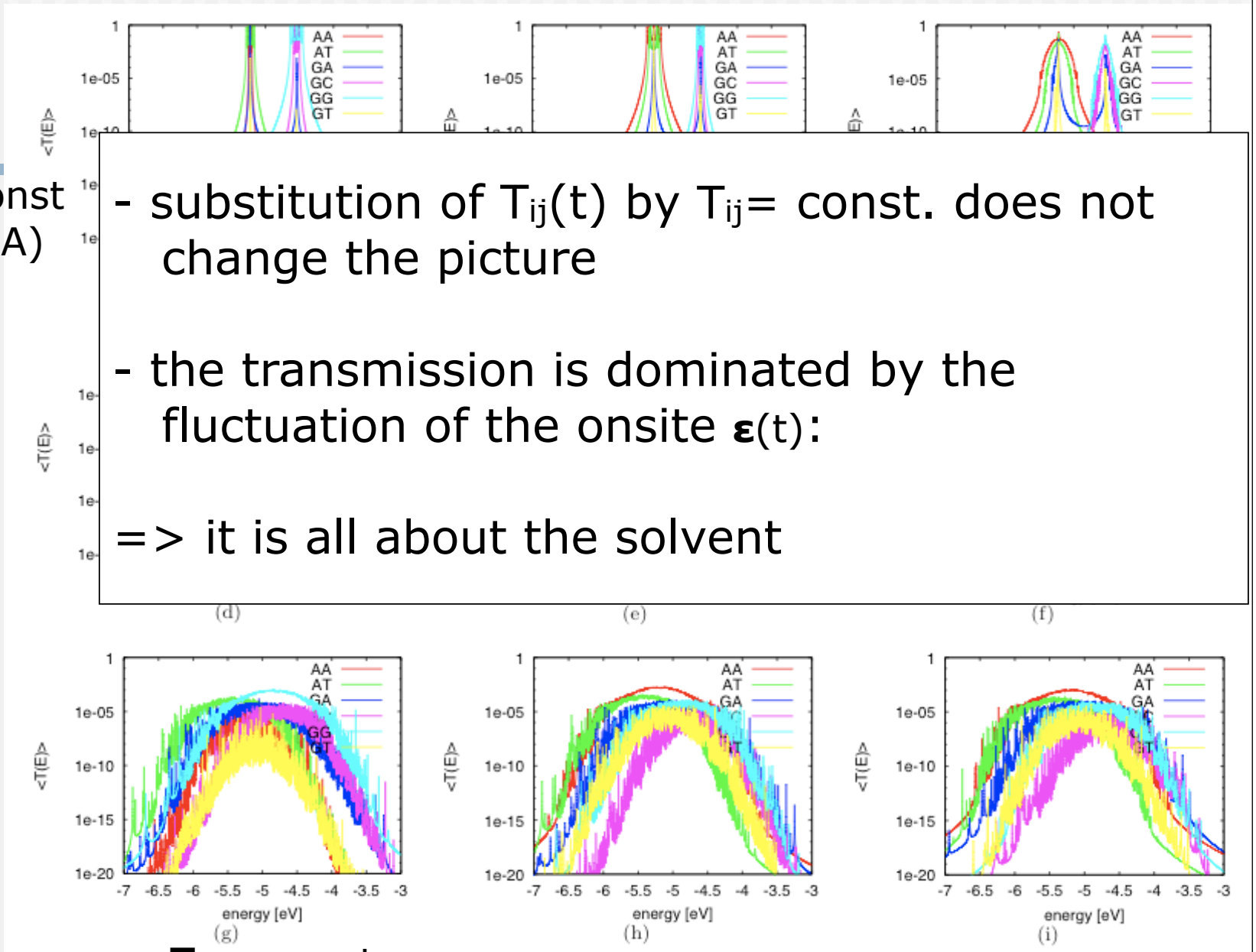




pG: '**good**' (conducting) **sequence**



pG: '**bad**' (conducting) **sequence**



ε = const (B-DNA)

<ε>

ε(t)

- substitution of $T_{ij}(t)$ by T_{ij}= const. does not change the picture

- the transmission is dominated by the fluctuation of the onsite **ε**(t):

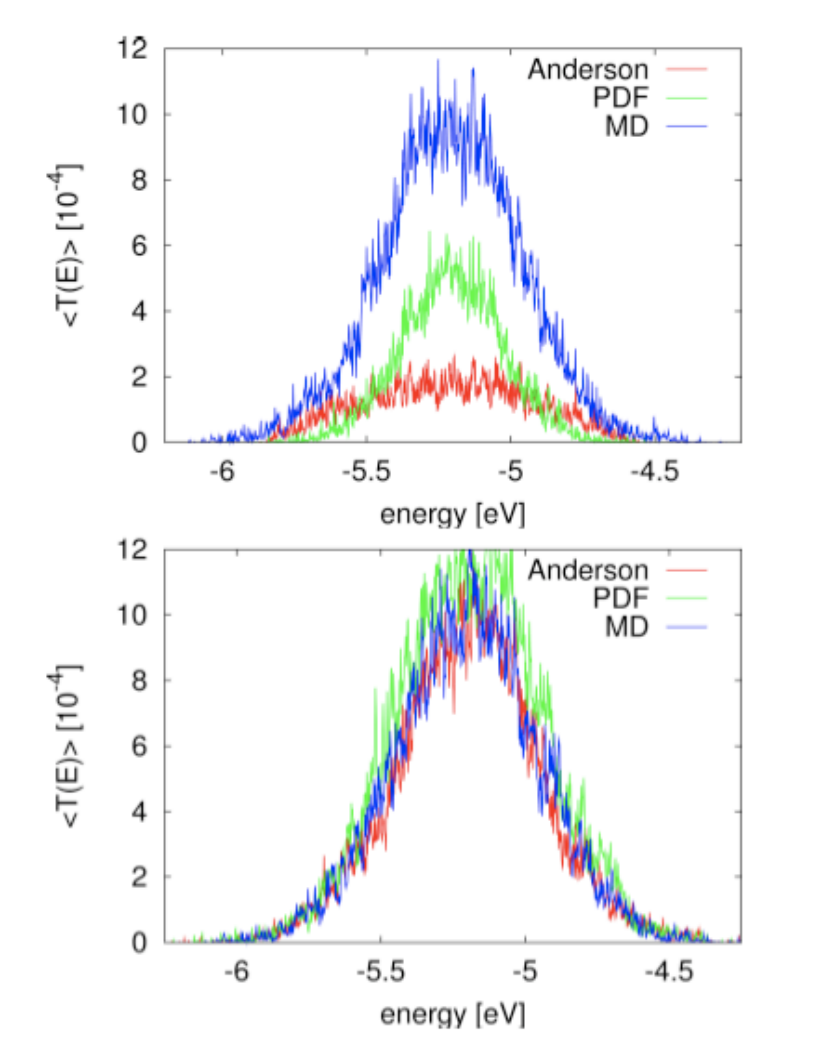
=> it is all about the solvent

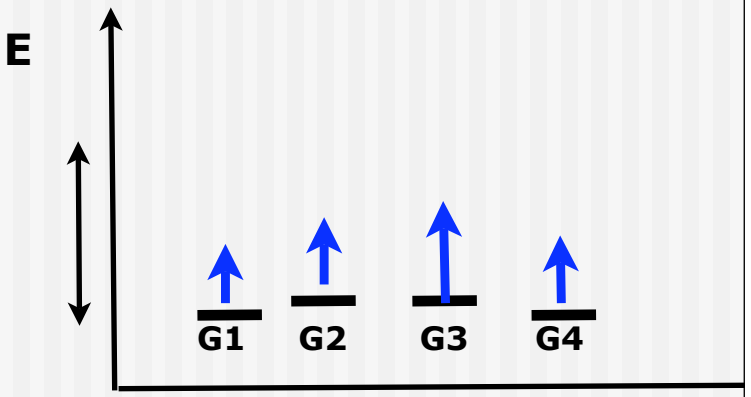
T_{ij} = const (B-DNA)

<T_{ij}> = const

T_{ij} (t)

How important is the correlation between the sites?



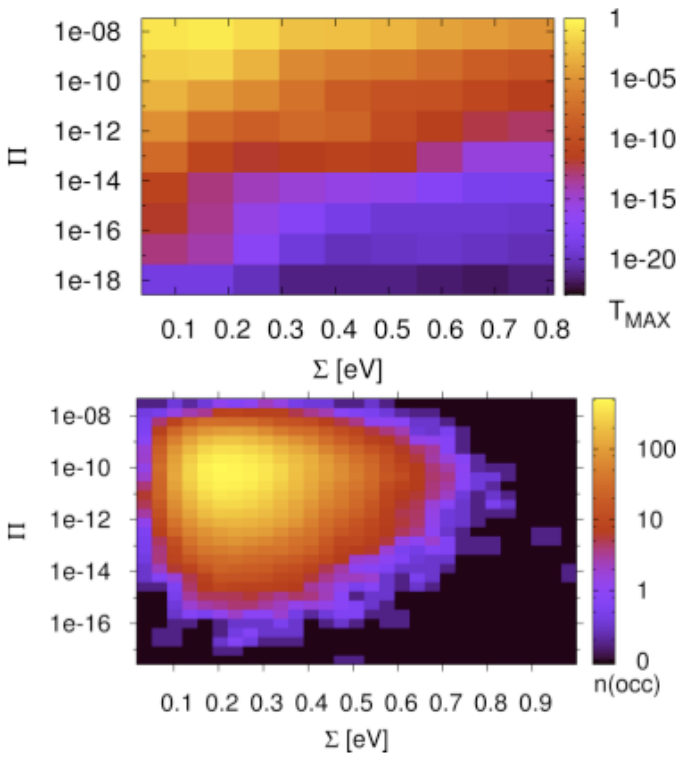


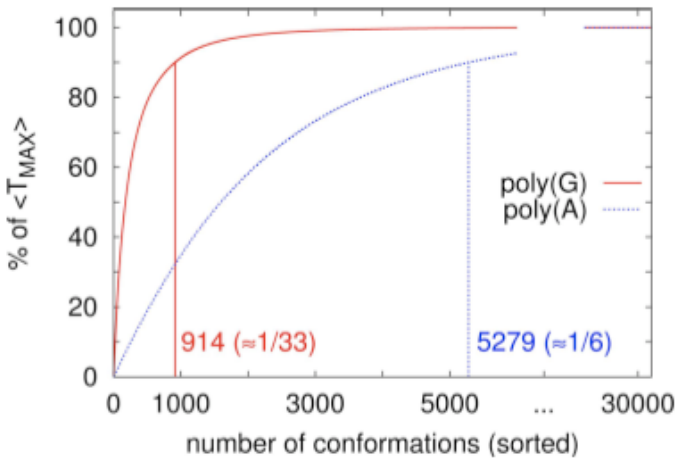
1) MD
2) draw the parameters from the distribution as generated by MD
3) statistical model

CT active conformations

$$\Sigma = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(\epsilon_i - \langle\epsilon\rangle_N)^2} = \sqrt{\langle\epsilon^2\rangle_N - \langle\epsilon\rangle_N^2}$$

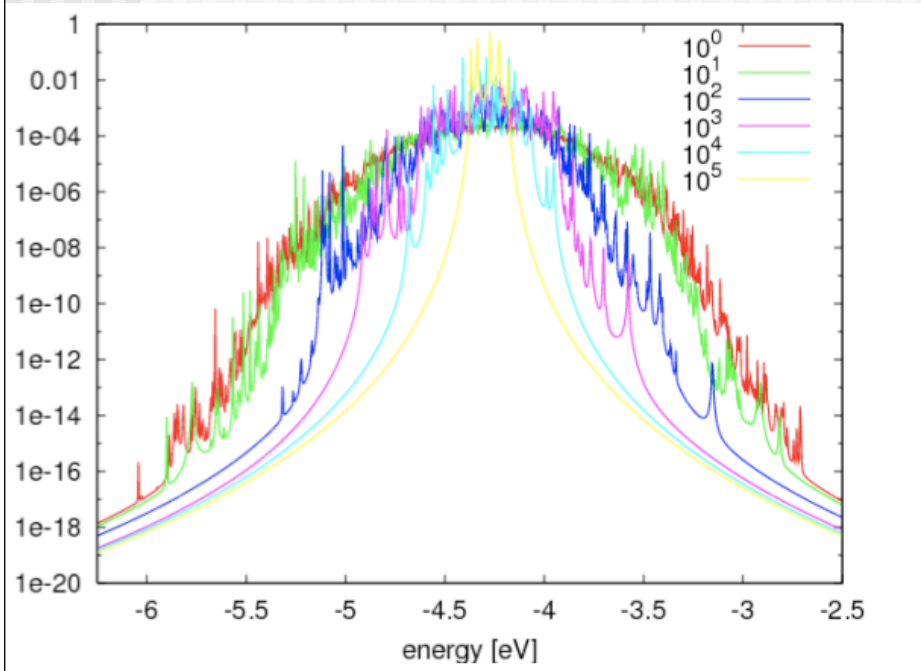
$$\Pi = \prod_{i=1}^{N-1} T_{i,i+1}$$

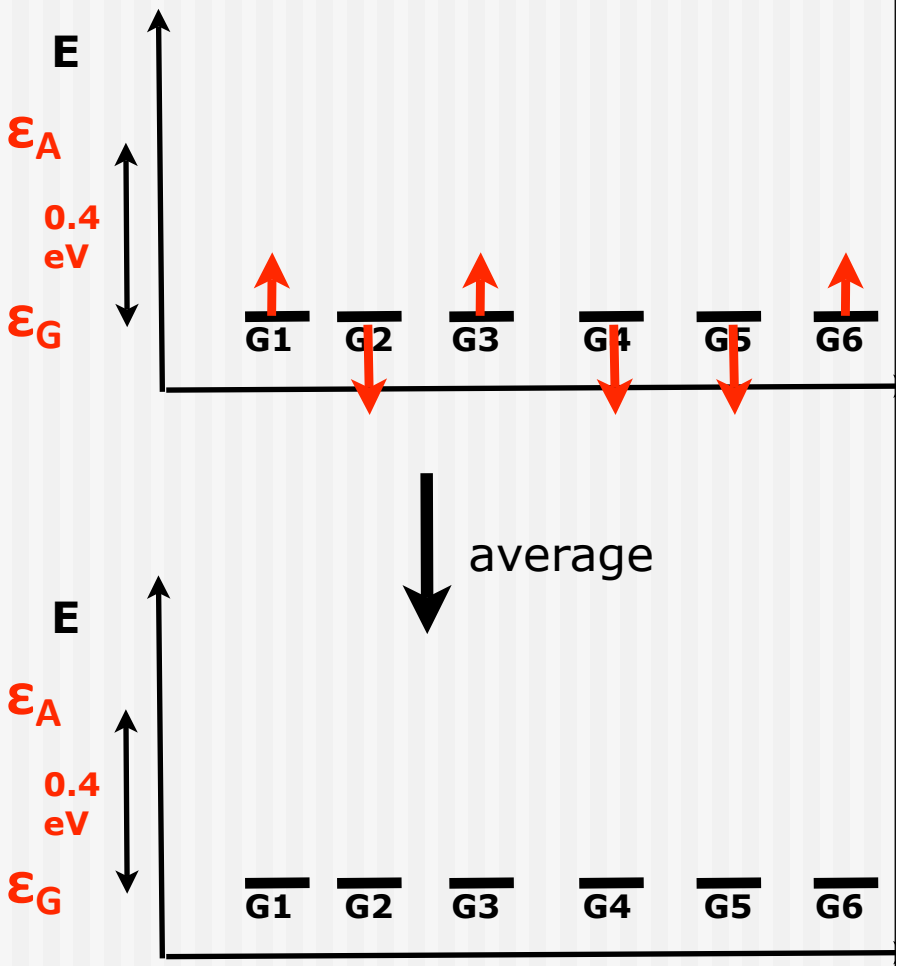




how to average the CT parameters?

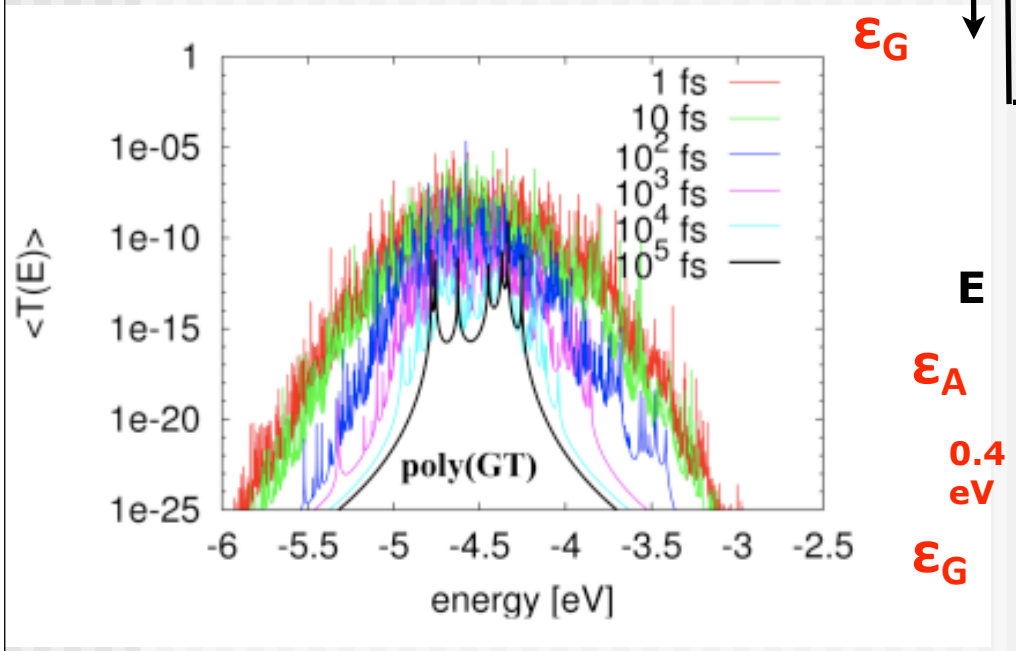
pA:
transmission **increases**
with averaging time

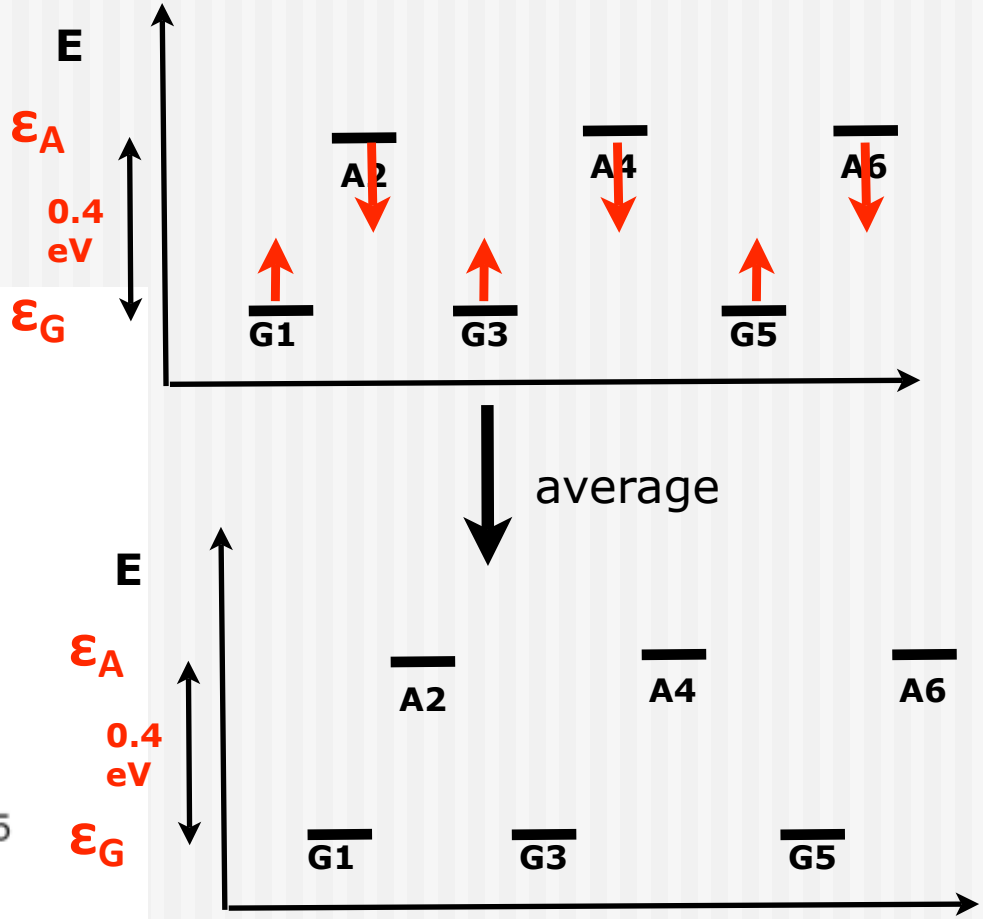




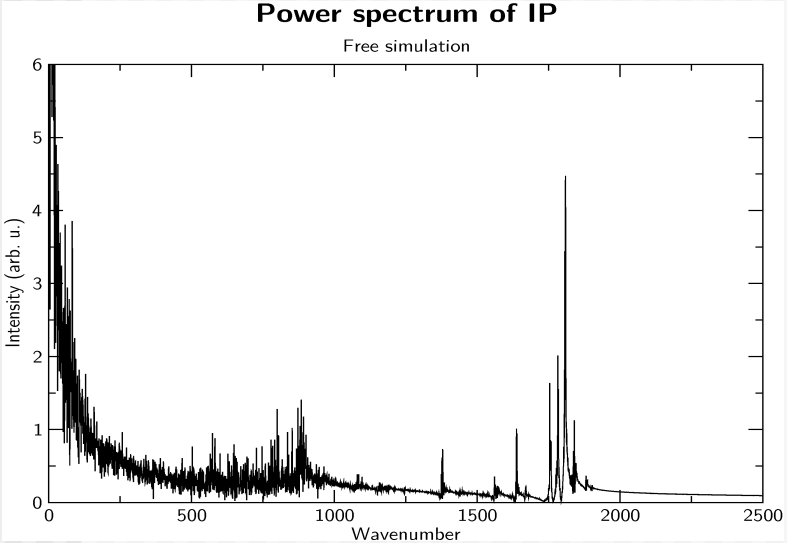
how to average the CT parameters?

pGT:
transmission **decreases**
with averaging time





so, what are the relevant time-scales?



- internal base modes: 20 fs 1600 cm^{-1}
- 'water modes': 40 fs 800 cm^{-1}
- water+counterions: 1ps
- ...

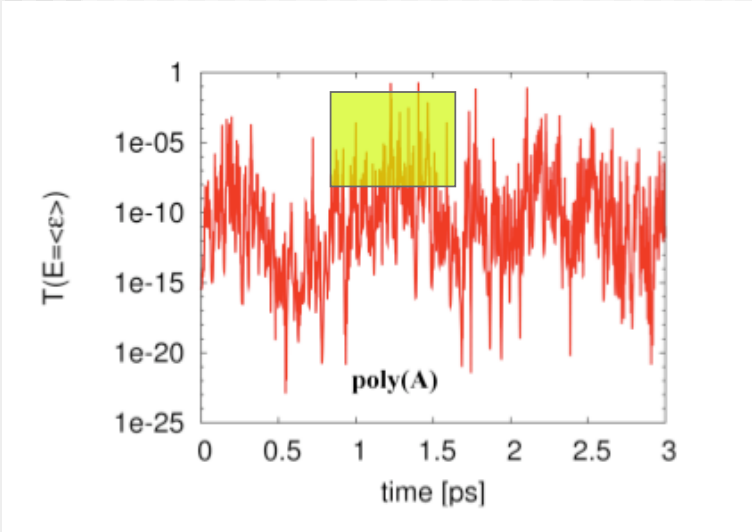
cf. Yuri Berlin's talk: T_{elec} and T_{ionic}

$T_{elec} << T_{ionic}$: statistical analysis (as above)

$T_{ionic} << T_{elec}$: self-averaging of CT parameters

Landauer and Büttiger 1982

so, what are the relevant time-scales?

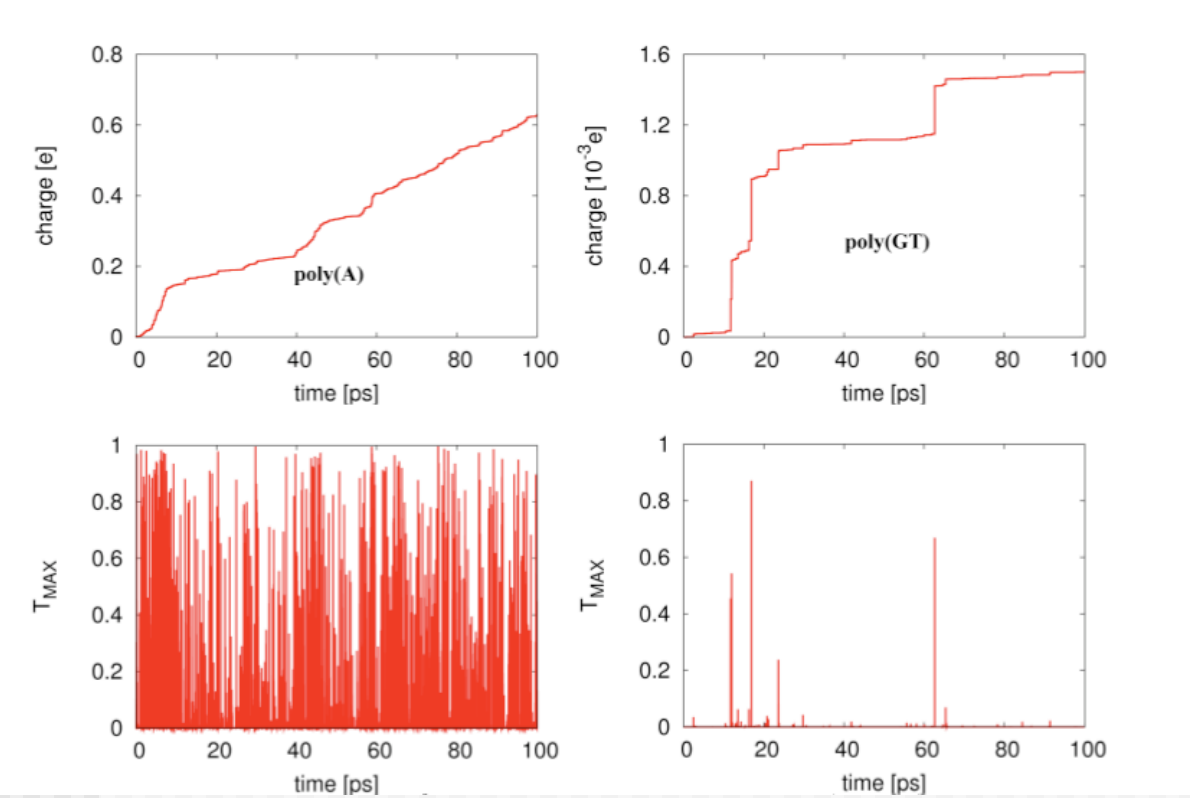


ps time-scale suggests:

CT active conformations persistent for several 100fs

average over fluctuations only in CT-active windows?

Integration of Landauer-current...



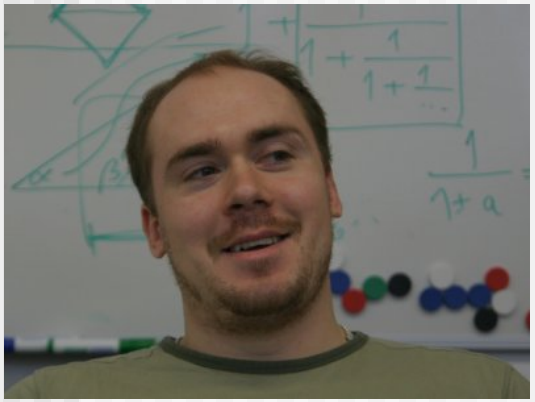
CT-active conformations in ps-time-scale

- 'fraction of electron' is transferred on ps-time-scale

=> probability, that an electron is transferred during an CT-active state with ps-persistance is about 0.1!

Acknowledgements

TU BS:



B. Woiczikowski

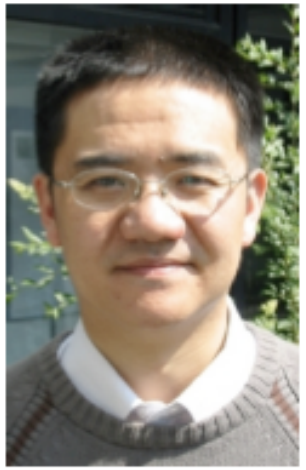
T. Kubar

DFG: SP 1243

Dresden group

G.Cuniberti

R.Gutiérrez



B.Song

R.Caetano