Simulation of charge transfer in DNA using QM/MM methods

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DFG: SP 1243

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Conduction and charge transfer in DNA

Physical experiments:

- DNA contacted by gold leads
- Current measurements

Chemical experiments:

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

- Conduction?
- Transport mechanism?

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

Theoretical Physics:

• tight binding Hamiltonian + Landauer theory

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

\[ G_D(E) = \left( E - H_D^{KS} - \Sigma_L - \Sigma_R \right)^{-1} \]

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

\[ I(V) = \frac{2e}{\hbar} \int_{\mu_2(V)}^{\mu_1(V)} T(E, V) dE \]

Theoretical Chemistry:

• superexchange: coherent tunneling

• thermal induced hopping

\[ k = \frac{2\pi}{\hbar} |T_{ij}|^2 \times FC \]
\( \varepsilon_i = \) ionisation potential

\( T_{ij} \) -> charge transfer matrix elements

Marcus theory:

\( \Delta G = \varepsilon_i - \varepsilon_j \)

\( H_{DA} = T_{ij} \)

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

Parameters: $\epsilon_i$ and $T_{ij}$

$\epsilon_i$: HOMO energy (Ip) of DNA base

$T_{ij}$: calculated from dimer

$\Rightarrow$ static picture

what about dynamics and solvent effects?

$\epsilon_A$, 0.4 eV

$\epsilon_G$

$A_n$-bridges:

$n=1-4$: superexchange

$n>4$: thermal induced hopping
Effect of solvent and dynamics

- Calculate parameters ‘on the fly’ along classical MD trajectories
- Include the interaction with DNA backbone, counterions, and water using a QM/MM scheme
- For sufficient sampling, use a fast QM method: SCC-DFTB
CT parameters from DFT

\[ \varepsilon_i = \langle \phi_i | H | \phi_i \rangle \]

\[ T_{ij} = \langle \phi_i | H | \phi_j \rangle \]

- \( \varepsilon_i \): energy of electron/hole on site i
- \( T_{ij} \): transfer integral from site i to j

Calculate \( \phi_i \) and H from DFT/DFTB along classical MD trajectories include:

- dynamical changes in parameters
- solvent effects

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

\[ \varepsilon_i = \langle \varphi_i | H | \varphi_i \rangle \]

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

- site i
- site j

\( \varepsilon_i \): energy of electron/hole on site i

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

Calculate \( \varphi_i \) and H from DFT/DFTB along classical MD trajectories

- dynamical changes in parameters
- solvent effects

Fragment Orbitals

Senthilkumar et al., JACS 127, 14894

Fragment orbitals (FO) in LCAO ansatz:

\[ \phi_i = \sum_{\mu} c^i_{\mu} \eta_{\mu} \]
\[ \phi_j = \sum_{v} c^j_{v} \eta_{v} \]

\[ T_{ij} = \sum_{\mu v} c^i_{\mu} c^j_{v} \left\langle \eta_{\mu} \right| H \left| \eta_{v} \right\rangle \]

\[ = \sum_{\mu v} c^i_{\mu} c^j_{v} H_{\mu v} \]
Couple to solvent degrees of freedom:

SCC-DFTB QM/MM Hamiltonian

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

interaction between
QM atoms

\[ T_{ij} = \sum_{ij} c^i_\mu c^i_\nu H_{\mu \nu} \]

includes the effect of environment

Q\(_A\): MM charges polarizing QM region:
backbone, waters, counterions
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

CT parameters along a QM/MM MD simulation

Coarse grained Hamiltonian

Time dependent parameters $\epsilon_i(t)$ and $T_{ij}(t)$ contain dynamical and solvation effects
Empirical Force Fields: **Molecular Mechanics** (MM)
\[
V_B = \sum_{\text{Bindungen}} \frac{1}{2} K_b (b - b_0)^2
\]

\[
V_a = \sum_{\text{Winkel}} \frac{1}{2} K_\theta (\theta - \theta_0)^2
\]

\[
V_{\text{imp}} = \sum_{\text{Extraplanarwinkel}} \frac{1}{2} K_\zeta (\zeta - \zeta_0)^2
\]

\[
V_D = \sum_{\text{Dihedralwinkel}} K_\varphi [1 + \cos(n\varphi - \delta)]
\]

\[
V_q = \sum_{\text{Paare}(i,j)} \frac{q_i q_j}{(4\pi \varepsilon_0 \varepsilon_r r_{ij})}
\]

\[
V_{\text{vdW}} = \sum_{\text{Paare}(i,j)} C_{12}(i,j)/r_{ij}^{12} - C_6(i,j)/r_{ij}^6
\]
Fluctuations of $I_p$

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

- 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

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: 1 ps
- ...
Strong correlation of electrostatic potentials with IPs:

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

Electrostatic potential of MM atoms at a Guanine

1ps
Electrostatic potential at a guanine by the molecules in action

10ns
Electrostatic potential at a guanine by the molecules in action

=> 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

**1 ps**

Electrostatic potential at a guanine
by the molecules in action

<table>
<thead>
<tr>
<th>Time (ns)</th>
<th>ESP (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-100</td>
<td>Na+</td>
</tr>
<tr>
<td>100-500</td>
<td>H2O</td>
</tr>
<tr>
<td>500-1000</td>
<td>total</td>
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**10 ns**

Electrostatic potential at a guanine
by the molecules in action

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

<table>
<thead>
<tr>
<th></th>
<th>water</th>
<th>ions</th>
<th>water + ions</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA</td>
<td>-0.08</td>
<td>-0.16</td>
<td>-0.44</td>
<td>0.18</td>
</tr>
<tr>
<td>water</td>
<td></td>
<td>-0.85</td>
<td>0.33</td>
<td>0.26</td>
</tr>
<tr>
<td>ions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>water + ions</td>
<td></td>
<td></td>
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</tr>
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Is there a correlation between the components?
Results: Ip of neighboring sites correlated

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

concentrated motion of neighboring sites (3-4) may have important implications or CT and transport

and this is due to solvent environment

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

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

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

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

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

\[ i\hbar \dot{\Psi} = H \Psi \]

- conductivity experiments
- coherent transport?
- 'chemical experiments'
- hole hopping: charge transfer

solve TDKS

hole WF
hole propagation

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

\[ i\hbar \frac{\partial}{\partial t} \Psi = H_{KS} \Psi \]
CT in DNA: A-bridges

Giese et al. Nature 2002

- exponential decay for short bridges
- algebraic for long A-tracks
Tunneling through A bridges

Experiments by Giese et al.,
superexchange tunneling for
$G(A)_n GGG$
for $n=1-4$

always static calculations!

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

- 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

only tunneling!

Kubar et al. submitted
CT in DNA: GAGGG

Energy difference between A and G populations is transferred when:
- energy difference is small
- couplings do not vanish

ε_A - ε_G

‘water modes’ drive the CT!
CT in GAGGG: role of solvent

\[ \varepsilon_A, \varepsilon_G \]

energy difference between A and G

black: with solvent
red: without solvent

'water modes' drive the CT!
CT in $\text{GA}_n\text{GGG}$: bridge occupation

bridge occupation in $\text{GAGGG}$:
- $\varepsilon_i$ kept fixed
- dynamic model

bridge occupation in $\text{GA}_n\text{GGG}$:
CT in DNA: GA\textsubscript{14}GGG

‘complete’ dynamics

correlated motion of neighboring sites

fluctuating onsite, but taken from onsite pdf

Kubar et al. submitted
CT in GA$_n$GGG: 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

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

=> still missing: proper account of solvation

Kubar et al. submitted
CT in DNA: solvation

Reorganization energy in Marcus theory

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

- put hole-charge on base \( \alpha \), equilibrate the system with MD: ensemble \( \alpha \)
- put hole-charge on base \( \beta \), equilibrate the system with MD: ensemble \( \beta \)

compute average energy of hole on \( \alpha \), using the ensemble \( \beta \)

Kubar& Elstner JPCB 2009 113 5653
CT in DNA: solvation

Reorganization energy in Marcus theory

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

E

\[ \varepsilon_A \]

0.4 eV

\[ \varepsilon_G \]

G1

A2

A3

A5

G4

Kubar & Elstner JPCB 2009 113 5653
CT in DNA: solvation delocalization???

Energy to delocalize hole between 2 bases: 0.6 eV

Reorganization energy to relocate delocalized hole:

$\approx 0.8$ eV less than for localized hole

Kubar& Elstner JPCB 2009 113 5653
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!

\[ \Rightarrow \text{coarse grained SCC-DFTB model} \]

Kubar et al. submitted
Charge transport in Physics and Chemistry

conductivity experiments 'chemical experiments'

hole hopping: charge transfer

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

Green functions

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

Landauer theory

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

Observables

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

Woiczikowski et al., JCP accepted

Gutierrez 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

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

\[ G_D(E) = \left( E - H_D^{KS} - \Sigma_L - \Sigma_R \right)^{-1} \]

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

for: pG, pA, p(AT), p(GA) ... for every time-step,

and then do what? average?
the reference: ideal B-DNA structures

transmission

\[ \epsilon_A \] 0.4 eV

\[ \epsilon_G \]

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

\[ \varepsilon_A, \varepsilon_G \]

\[ 0.4 \text{ eV} \]

\[ G1, G2, G3, G4, G5, G6 \]

pG: ‘good’ (conducting) sequence

pG: ‘bad’ (conducting) sequence
\( \varepsilon = \text{const} \) (B-DNA)

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

- the transmission is dominated by the fluctuation of the onsite \( \varepsilon(t) \):

\[ \Rightarrow \text{it is all about the solvent} \]
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 \(1600\text{ cm}^{-1}\)
- 'water modes': 40 fs \(800\text{ cm}^{-1}\)
- water+counterions: 1ps

cf. Yuri Berlin’s talk: \(\tau_{\text{elec}}\) and \(\tau_{\text{ionic}}\)

\(\tau_{\text{elec}} \ll \tau_{\text{ionic}}\): statistical analysis (as above)
\(\tau_{\text{ionic}} \ll \tau_{\text{elec}}\): 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!
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