Multiscale Modeling of Structural and Electronic Properties of DNA

- Motivation: sequencing, epigenetics, replication and repair, ...

- Coarse-grained potential: model, simulations, validation

- Translocation dynamics through nanopores

- Electronic properties

EMRS - May 14-17, 2012, Strasbourg
Symposium J: DNA Directed Programmable Self-Assembly of Nanoparticles into Meta Materials for Energy and other Applications
DNA sequencing: biochemical methods - cut pieces (ending at specific bases), measure by *gel electrophoresis*.

Instead, use **electronic signature** for sequencing - multiscale process
Multiple length/time scales:
DNA electronic sequencing
Structure of DNA on several scales: From NUCLEOSOME to CHROMOSOME

EPIGENETICS: passing genetic information NOT encoded in DNA base sequence
Tail of H3

Papamokos et al., Biophysical J. (2012)
Coarse-grained potential for DNA

W. Hsu, M. Fyta, G. Lakatos, S. Melchionna, EK (2012)
Goal: derive coarse-grained potential: **minimal** (but sufficient) model; all parameters from *ab-initio* calculations*.

Assumption: **separable** interactions

- Hydrogen bonding (distance; dihedral, flip angles)
- Stacking interactions (distance; twist angle)
- Backbone interactions (distance; 3’-5’ orientation)
- Electrostatic interactions

* To the extent possible

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Data points: DFT calculations, 
Lines: fits with simple curves
Coarse-grained potential – hydrogen bonding

Distance between bases, dihedral angle

- Distance between bases, dihedral angle
- \( r_{hb} \): distance between hydrogen bonding sites
- \( \phi_{hb} \): dihedral angle
- \( r_{cc} \): distance between carbon-carbon atoms
- \( r_{CN} \): distance between carbon-nitrogen atoms
- Graph showing the energy as a function of distance and dihedral angle

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[Harvard University logo]
Coarse-grained potential – hydrogen bonding II

Flip angle

$E_{\text{hb}, f}$ (eV)

$\Delta \phi_{\text{hb}}$ (deg)

(a)

(b)

base

sugar

$r_{\text{hb}}$

$r_{\text{cc}}$

$r_{\text{CN}}$

$r^{(1)}_{\text{CN}}$

$r^{(2)}_{\text{CN}}$

$\phi^{(1)}_{\text{hb}}$

$\phi^{(2)}_{\text{hb}}$

$\phi_{\text{hb}}$

H1

H9

N1

N9

T

A

Cl'

Cl'
Coarse-grained potential – stacking interactions

Distance between planes

Distance between planes

\[ \theta_{tw} \]

\[ E_{st,r} (\text{eV}) \]

\[ r_{st} (\text{Å}) \]

\[ \text{GC-TA} \]
\[ \text{GC-CG} \]
\[ \text{AT-TA} \]
\[ \text{GC-AT} \]
\[ \text{GC-GC} \]
\[ \text{AT-AT} \]
Coarse-grained potential – stacking interactions

Twist angle between pairs

(a) Coarse-grained potential – stacking interactions

(b) Twist angle between pairs
Coarse-grained potential – backbone interactions
Coarse-grained potential – electrostatic interactions

\[ E = \frac{1}{4\pi \varepsilon_0 \varepsilon(r) r} e^2 \]

\[ \varepsilon(r) = \varepsilon_{in} \quad r < r_0 \]

\[ \varepsilon(r) = \varepsilon_{in} e^{\alpha(r-r_0)} \quad r_0 < r < r_1 \]

\[ \varepsilon(r) = \varepsilon_{\infty} e^{-kr} \quad r > r_1 \]

\[ K^{-1} = \sqrt{\frac{\varepsilon_0 \varepsilon_{\infty} k_B T}{2N_A e^2 I}} \]

Three parameters!
Coarse-grained potential – validation

Two parallel strands coil to form double-helix
Coarse-grained potential – validation

Persistence length (~50 nm)

Persistance length (≈50 nm)
Force-extension simulations
Force-extension simulations

(a) Force (pN) vs. Rise per base-pair (Å)
(b) Force (pN) vs. Twist angle $\theta_{tw}$ (deg.)

- Black circles: pulling 3’ end
- Red diamonds: pulling 5’ end

Inset:
- "worm-like chain"
- "overstretcing transition"
- "enthalpic regime"
- "entropic regime"
Melting simulations

(a) Bond fraction vs. Time (ns)

(b) Bond fraction vs. Time (ns)
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