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Quantum and classical simulations of DNA derivatives

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Outline

- Biomolecules in molecular electronics
 - Towards DNA derivatives

Quantum and classical simulations of G4-wires

- DFT ground-state electronic structure
- Wide bandgap, small bandwidths, wave functions
- Rigidity and flexibility
- Motion and relative stability of ionic species

Current activities: A4-tetrads and xDNA

- A4/G4 intercalation: electronic structure
- xDNA (aromatic expansion): optics and transfer rates





• Other...



Is DNA a viable electrical material?

D. Porath, G. Cuniberti, R. Di Felice, Topics in Current Chemistry 237, 183 (2004)

 Experiments on native-DNA charge mobility show poor conductivity for molecules deposited on substrates





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- Improve molecule-substrate coupling: quenching the surface field
 - Stiffer molecules (G4-DNA?)
 - Softer surfaces (alkanethiol monolayers?)
 - Avoiding non-specific DNAsubstrate interaction & controlling DNA-electrode covalent binding









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- Pt SiN SiO₂ Si

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- Alternative DNA-based candidates
 - Helical conformation
 - Base modification
 - Metal insertion



Modified DNA-based structures



Guanine Quadruplexes: **G4-wires**

Guanine quadruplexes stiffer than Watson-Crick duplexes

- AFM measurements \Rightarrow diameter(G4)~2×diameter(dsDNA)
- X-ray data \Rightarrow diameter(G4)~diameter(dsDNA)
- Larger persistence length

Improved conductivity?

- Uniform sequence, only guanine
- Smaller twist angle
- Alignment of metal ions at the core of the quadruple helix



A. B. Kotlyar et al., Adv.



Numb





Aromatically-expanded based: xDNA

Synthesis and characterization

- Expanded base-pairs feasible (e.g., T-xA)
- Double helices feasible
- Higher thermal stability if not mixed with natural pairs
- Suggestion: enhanced π -stacking







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Improved electronic coupling?

- π - π overlap: transfer integrals
- Optical signal of aromatic rings







G4-wires DFT electronic structure Classical MD simulations

- A. Calzolari, R. Di Felice, E. Molinari, A. Garbesi, *Appl. Phys. Lett.* **80**, 3331 (2002)
- R. Di Felice, A. Calzolari, A. Garbesi, S.S. Alexandre, J.M. Soler, J. Phys. Chem. B 109, 22301 (2005)
- M. Cavallari, A. Calzolari, A. Garbesi, R. Di Felice, J. Phys. Chem. B 110, 26337 (2006)





Structural Optimization

- <u>http://www.quantum-espresso.org</u>
- DFT-GGA (PW91, PBE), ultrasoft pseudopotentials, plane wave basis, periodically repeated supercells, BZ sampling
 - · Atomic displacement until forces vanish (within 0.05 eV/Å)
 - \cdot Particularly suitable to describe structures with long-range order
- Large supercells: up to ~200 atoms, thick vacuum layer (~10 Å)
- Tests on isolated G molecules and H-bonded ribbons
- (Relative formation energies \rightarrow stability)

Electronic properties

- Bandstructure
- Density of States
- Isosurface plots of Bloch orbitals



Guanine quadruple helices (G4-DNA molecules)



Guanine quadruple helices (G4-DNA molecules)





Novel long guanine quadruplexesA. B. Kotlyar et al., Adv.
Mater. 17, 1901 (2005)(G4-DNA wires)





Bandstructure calculations



Inspiration

- D. Porath et al., Nature 403, 635 (2000)
- "Semiconductor" behavior due to the bands of the material
- Semiconductor
 - Bandgap
 - Finite bandwidth: E(k) dispersion relation





K(I)-G4 Electronic Structure

A. Calzolari et al., Appl. Phys. Lett. 80, 3331 (2002); J. Phys. Chem. B 108, 2509 & 13058 (2004)



Bandstructure

- Flat bands gathered in manifolds
- No dispersion along wire axis (ΓA)
- No backbone effects
- Manifolds \rightarrow effective semiconductor

Contour plots

- Channels for charge motion through the bases
- Poor potassium-guanine coupling



Length measurements

<u>AFM: 1/5</u> of parent G-strand

A. B. Kotlyar et al., *Adv. Mater.* **17**, 1901 (2005)





G4-wires under axial strain



- •Only *d* is changed
- •All other degrees of freedom are frozen
- •No ions in the channel
- •C, N, O

How and to which extent **structural fluctuations** affect the electronic coupling along the stack?

Well known and relevant in carbon nanotubes



Electronic structure parameters





"Electromechanical" properties



- Saturation above ~2.8 Å
- Coherent bandwith (δ_{HOMO}) up to 100 meV at 20% strain
- *Incoherent* bandwidth (Δ_{HOMO}) up to 800 meV at 20% strain; vanishing gaps
- Structural relaxation partially compensates trends



Molecular Dynamics simulations of G4-wires





Schematic Initial Structures

 4-plane quadruplexes unfold in the absence of ions 				
 First objective: do enhanced 				
stacking interactions affect this				
behavior?				
		\bigcirc	<u> </u>	
Internal cations	Li+	Na⁺	K+	
ionic radius	0.68 Å	0.98 Å	1.33 Å	
vdW radius	1.137 Å	1.868 Å	2.658 Å	
Cation position	<i>intra</i> -plane	<i>inter</i> -plane	<i>inter</i> -plane	
External cations	Li+	Na ⁺	K+	Na ⁺









- Confirmed "stability" trend K+ > Na+ > Li+
- Empty quadruplexes are less deformed than shorter molecules → stability is likely to improve with increasing length



- G4-wire initially empty
- Li⁺ ions as counterions

A longer simulation (20 ns) of a longer helix (24 planes)

 A Li⁺ ion enters the channel from one side



 From the other side water enters and fills the channel

 Another Li⁺ ion enters the channel from the grooves



Average structure of the 24-plane quadruplex



Tetrad stacking and base co-planarity are almost precisely preserved

M. Cavallari, A. Calzolari, A. Garbesi, R. Di Felice, *J. Phys. Chem. B* **110**, 26337 (2006)

Increasing the number of stacked tetrads helps to preserve the G4-wire structure against unfolding in the absence of cation coordination



A4/G4 alternation

DFT electronic structure

• D. Varsano, A. Garbesi, R. Di Felice, in fieri







Non-linear electrical elements into G4-wires



■ Sequence interruption → quantum dot?

- Electronic structure of A4
- Comparison of A4 and G4 states
- A4 intercalated in a G4-wire d(GGTGG)₄ [M.S. Searle et al., *Org. Biomol. Chem.* **2**, 810 (2004)]





Choice of A4 structure

H-bonding pattern

- Amino-H with neighboring N1 or N7? N1
- Planar or non-planar? Planar
- On the basis of theoretical⁺ and experimental[§] considerations
- Hartree-Fock relaxation with BSSE and planar constraint



[†]J. Gu, J. Leszczynsky, *Chem. Phys. Lett.* **335**, 465 (2001)

§ M.S. Searle et al., Org. Biomol. Chem. 2, 810 (2004)
 M.K. Patel et al., Nucl. Acids Res. 27, 3836 (1999)



Electronic properties of relaxed structure

Various methods to test DFT xc functionals

- Hartree-Fock (Gausian; 6-311G**)
- DFT (Gaussian; 6-311G**, 6-311++G**): B3LYP, PBE0
- DFT (plane waves, ultrasoft pseudopotentials): PBE



Comments

- Occupied levels: regular 4-plets (base multiplicity)
- Unoccupied levels: 4-plets but... exception!





D. Varsano, R. Di Felice, M.A.L. Marques, A. Rubio, *J. Phys. Chem. B* 110, 129 (2006)
D. Varsano, A. Garbesi, R. Di Felice, in fieri



Optical properties by TDDFT

Optical absorption and CD

- Tools for structural characterization of biomolecules
- UV radiation-induced DNA damage

Calculation of linear absortpion spectra using OCTOPUS

www.tddft.org/programs/octopus

- Real-space uniform-grid implementation
- Ground state calculated within DFT
- Kohn-Sham equations are propagated in real time

 $ilde{\phi}_j(\mathbf{r})$: ground state

$$v(\mathbf{r},t)=-k_0x_
u\delta(t)$$
 $x_
u=x,y,z$

Time Evolution

$$i\frac{\partial}{\partial t}\phi_i(\mathbf{r},t) = \left[\frac{-\nabla^2}{2} + v_{KS}(\mathbf{r},t)\right]\phi_i(\mathbf{r},t)$$

Polarizability:

$$lpha_
u(\omega) = -rac{1}{k}\int d^3r x_
u \delta n{f r}, \omega)$$

photo-absorption cross-section:

$$\sigma(\omega) = -rac{4\pi\omega}{c}\Im\sum_n lpha_
u(\omega)$$



H-bonded GC_h pair





- Small shift of lowest frequency peaks
 - •Hypochromicity (~30%)

•Blue shift of out-of-plane spectrum (~0.48 eV)

Effect of GC_h stacking



53 C

Optical absorption of x-bases

Recent DFT studies of electronic properties

- Role of π -ring
- M. Fuentes-Cabrera & coworkers, *J. Phys. Chem. B* 109, 21135 (2005); *J. Phys. Chem. B* 110, 6379 (2006); *J. Phys. Chem. A* 110, 12249 (2006)

Consequenses on optics

Relation to natural bases

Shifts and hypochromism





Stacked xG-C pairs structures proposed by E.T. Kool and coworkers



T-xA pairs; flat pairs

eal: from *JACS* 2006; all 8 x-pairs; buckled pairs



To be done...

Optical absorption of H-bonded xG-C pair



Red-shift of lowest-energy peak

- •Stronger than in natural DNA Hbonded GC pair
- Identified in terms of singleparticle level shifts (predominance of π - π * character, HOMO \rightarrow LUMO+1)

Double-peak for real stack

•Charge-transfer transition HOMO-2,HOMO-3 \rightarrow LUMO (σ xG, π - π * C)



Other...

 G4-EFM simulations by electrostatic modeling

•H. Cohen et al., Nano Letters, May 2007





pGpC-STS interpretation by ab-initio DFT DOS calculation

•E. Shapir et al., preprint 2007

