Single-Strand Breaks Induced by Low-Energy Electrons in DNA

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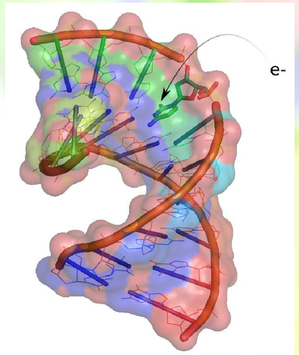
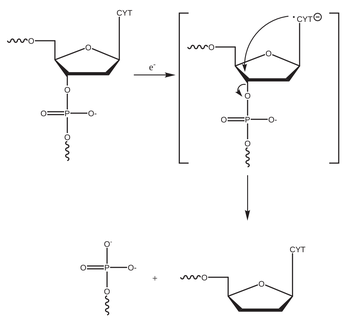
Introduction

Recent experiments have shown that low-energy electrons (0.1-2 eV) can induce single-strand breaks (SSBs) in DNA[1]. Understanding these mechanisms is of great importance for the developement of medicinal sciences. Previous studies on model systems demonstrate that low-energy electrons induce the covalent-bond cleavage in DNA according to a through-bond electron transfer process between the π^* orbitals of the nucleic base and a specific bond[2, 3, 4, 5, 6, 7]. It has been shown that the $C_{3'}$-$O_{3'}$ σ sugar bond rupture dominates the SSBs of DNA[6, 7].



Within the LSCF/MM method[8, 9], we examine the effect of including the neighboring nucleotides at the molecular mechanic (MM) level. Because of the spatially-extended behaviour of this phenomenon, the whole nucleotide where the bond cleavage occurred must be included in the quantum mechanic (QM) part.

Proposed Mechanism of the SSB



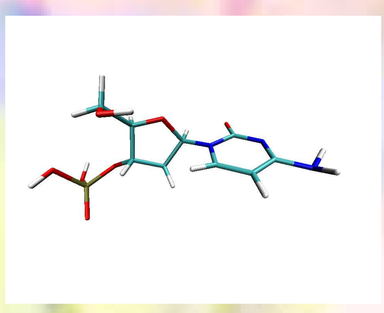
Computational details

- QM calculations : B3LYP/6-311+G(d) level of theory (Gaussian 03[10])
- MM calculations : Amber *ff99* force field for DNA and RNA (Tinker4.2[11])
- SCRF calculations : PCM solvation model ($\varepsilon = 4$)

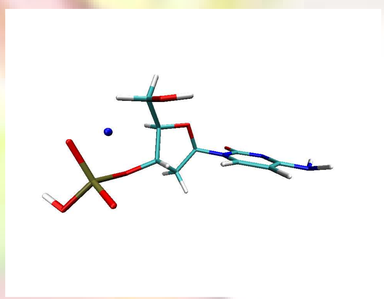
Model systems

Adiabatic Electron Affinities (PCM correction)

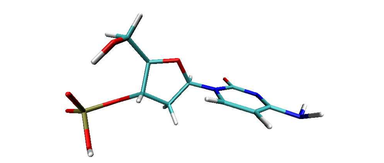
- Protonated Form: 0.15 (1.51) eV



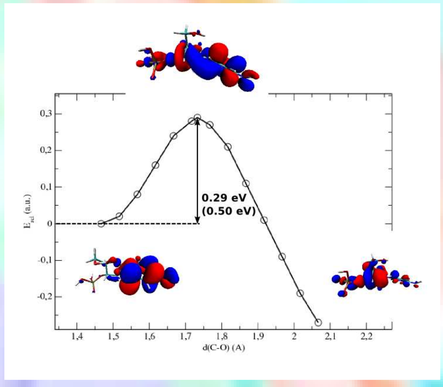
- Counterion (Na^+): 0.75 (1.50) eV



- Deprotonated Form: -2.18 (0.94) eV



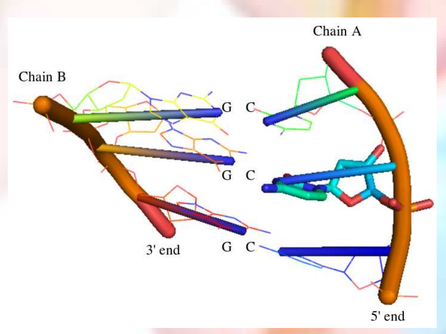
Scan of the $C_{3'}$-$O_{3'}$ distance



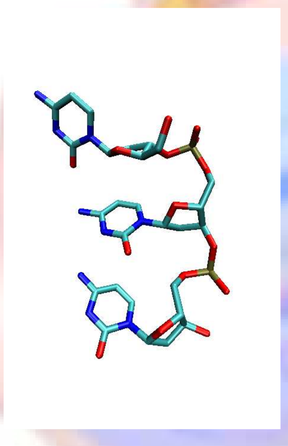
Transition state

d(C-O) = 1.733 Å (1.761 Å)
ν(TS) = -607 cm^{-1} (-827 cm^{-1})

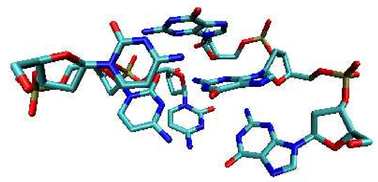
QM/MM models



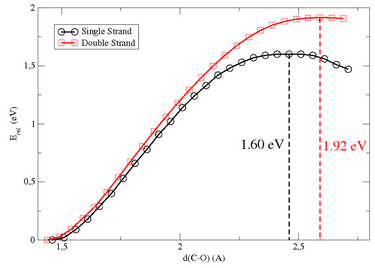
Single strand DNA



Double Strand DNA



Scan of the the $C_{3'}$-$O_{3'}$ bond for the Single Strand and Double Strand DNA



Stable conformations of Single Strand and Double Strand DNA

- SS: d(C-O) = 1.46 Å
- DS: d(C-O) = 1.44 Å

Transition state of Single Strand and Double Strand DNA

- SS:
  - d(C-O) $\simeq$ 2.46 Å
  - $\Delta E \simeq$ 1.60 eV
- DS:
  - d(C-O) $\simeq$ 2.59 Å
  - $\Delta E \simeq$ 1.92 eV

Conclusions

- Model systems:
  - SSB is independent of the phosphate protonation state
  - Surroundings effect must be taken into account
- QM/MM systems:
  - MM surroundings largely stabilize the anion (results not shown)
  - Strong effect of the complementary bases (H-bond)
  - MM surroundings increase the barrier of the $C_{3'}$-$O_{3'}$ bond breaking

Outlooks

- Scan of the $C_{3'}$-$O_{3'}$ bond for the A-DNA and B-DNA under progress
- Scan and barrier of the $C_{5'}$-$O_{5'}$ bond
- SSBs of GUA, ADE and THY bases

References

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