

L'attaque de l'électron masqué (de basse énergie)

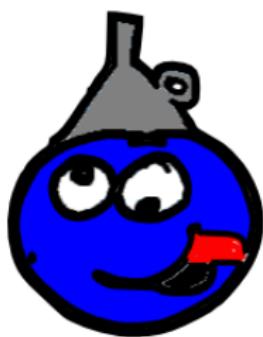
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Xavier Assfeld[‡]

[‡]Équipe de Chimie et Biochimie Théoriques,
UMR 7565 CNRS-UHP,
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Faculté des Sciences et Techniques,
Nancy-Université, France

* Laboratoire de Chimie, UMR 5182 CNRS
École Normale Supérieure de Lyon,
Lyon, France.

19th September 2008

The murderer: **the electron**

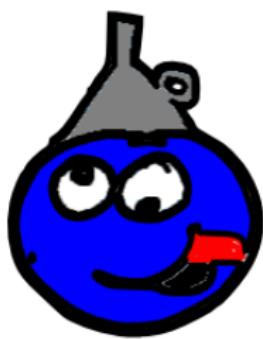


- Secondary electrons¹ of low-energy² (< 30 eV)

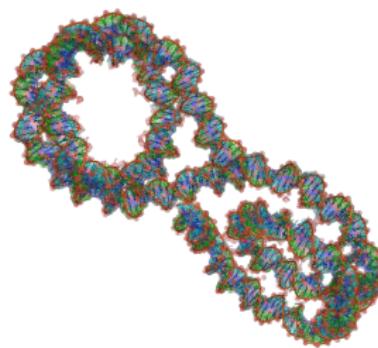
¹L. Sanche *Radiat. Phys. Chem.* **1989**, *34*, 15.

²L. Sanche *Eur. Phys. J. D* **2005**, *35*, 367.

The murderer: the electron



The victim: the supercoiled DNA

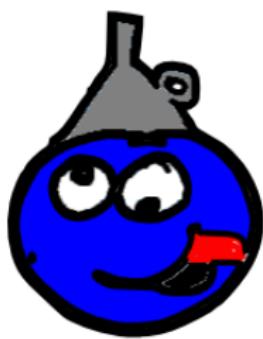


- Secondary electrons¹ of low-energy² (< 30 eV)
- Dry DNA (only structural H₂O and counterions)

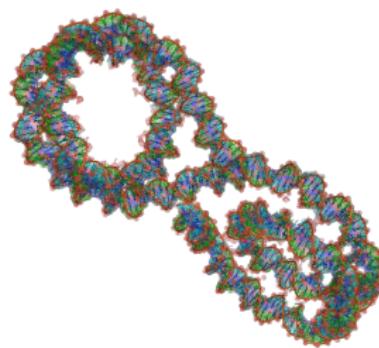
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The murderer: the electron



The victim: the supercoiled DNA



- Secondary electrons¹ of low-energy² (< 30 eV)
 - Dry DNA (only structural H₂O and counterions)
- ⇒ Single-strand breaks (SSB) and double-strand breaks (DSB)

¹L. Sanche *Radiat. Phys. Chem.* **1989**, *34*, 15.

²L. Sanche *Eur. Phys. J. D* **2005**, *35*, 367.

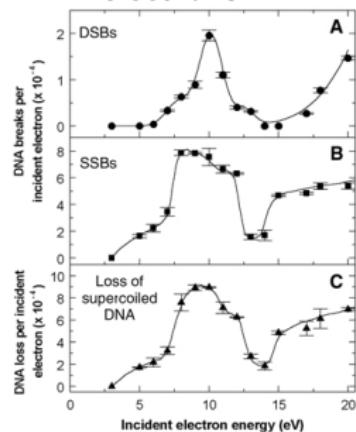
The pieces of evidence

³Boudaïffa et al. *Science* **2000**, 287, 1658.

⁴Martin et al. *PRL* **2004**, 93, 068101.

The pieces of evidence

"Resonant formation of DNA strand breaks by low-energy (**3-20 eV**) electrons"³

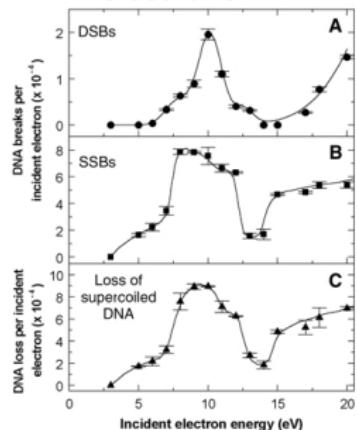


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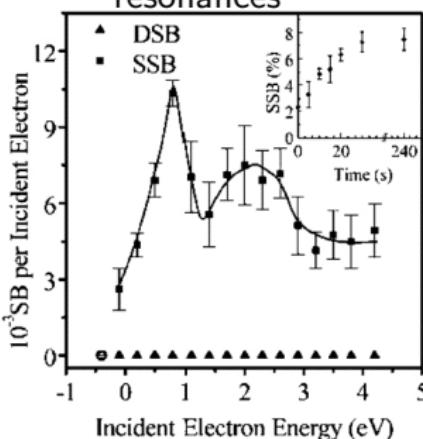
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The pieces of evidence

"Resonant formation of DNA strand breaks by low-energy (**3-20 eV**) electrons"³



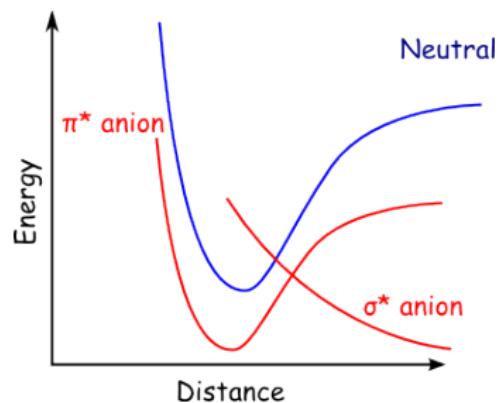
"DNA strand breaks induced by **0-4 eV** electrons: the role of shape resonances"⁴



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⁴Martin et al. *PRL* **2004**, 93, 068101.

A through-bond electron transfer process⁵



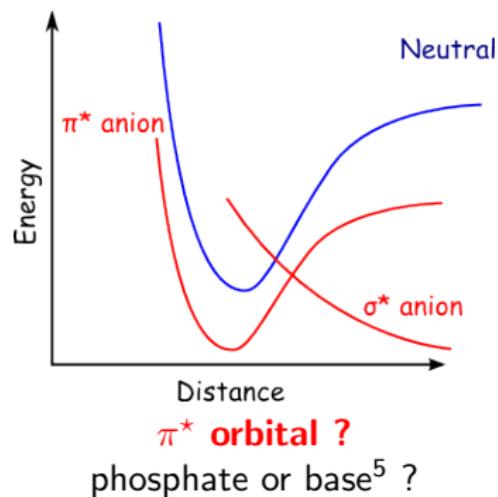
⁵ Barrios et al. *JPCB* **2002**, *106*, 7991; J. Simons *Acc. Chem. Res.* **2006**, *39*, 772.

⁶ Li et al. *JACS* **2003**, *125*, 13668; Gu et al. *JACS* **2006**, *128*, 9322.

⁷ Theodore et al. *Chem. Phys.* **2006**, *329*, 139; Gu et al. *Angewandte* **2007**, *46*, 1.

⁸ Liang et al. *JCC* **2008**, in press.

A through-bond electron transfer process⁵



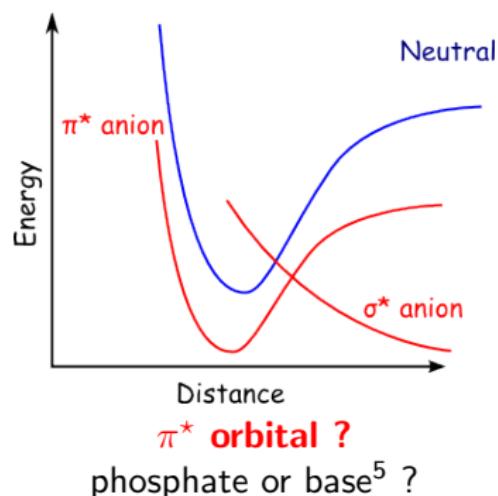
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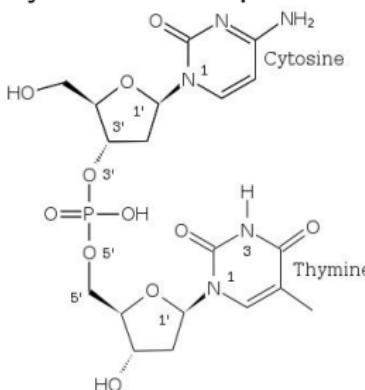
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A through-bond electron transfer process⁵



Pyrimidines or purines ?



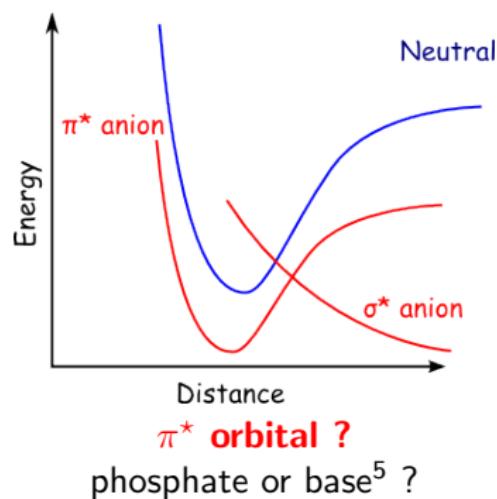
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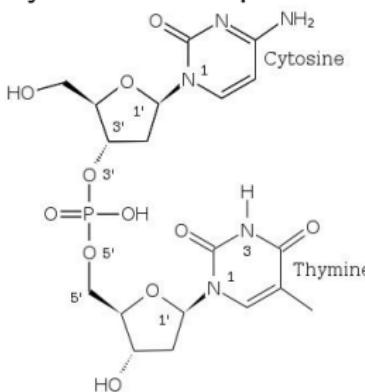
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A through-bond electron transfer process⁵



Pyrimidines or purines ?



σ bond ?

$C_{3'}-O_{3'}$ or $C_{5'}-O_{5'}$?⁶
 $C_{1'}-N_1$ or N_3-H ?⁷ Other⁸ ?

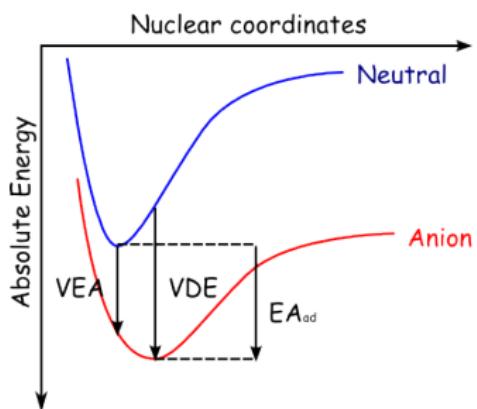
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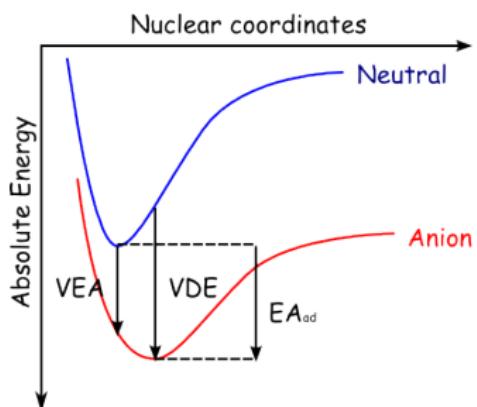
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Requirement for an electron capture

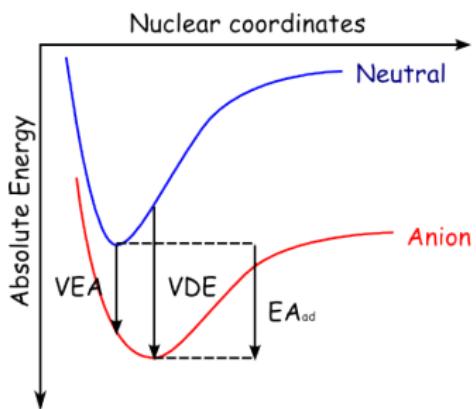


Requirement for an electron capture



- **VEA:** Vertical Electron Affinity
- **EA_{ad}:** adiabatic Electron Affinity
- **VDE:** Vertical Detachment Energy

Requirement for an electron capture



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- **EA_{ad}:** adiabatic Electron Affinity
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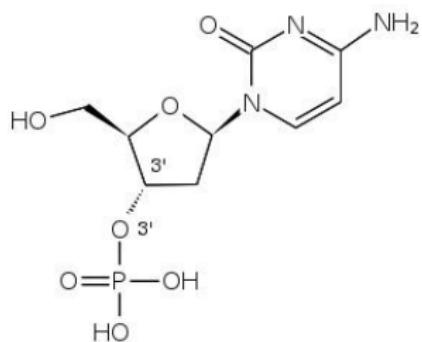
Electron capture \iff **VEA, EA_{ad} and VDE should be > 0**

Single nucleotide: 2'-deoxycytidine-3'-monophosphate (3'-dCMPH)

⁹Gu et al. JACS 2006, 128, 1250.
¹⁰Gu et al. JACS 2006, 128, 9322.

Single nucleotide: 2'-deoxycytidine-3'-monophosphate (3'-dCMPH)

■ Electron affinities⁹ (eV)



EA_{ad}	0.15
VEA	0.00
VDE	0.87

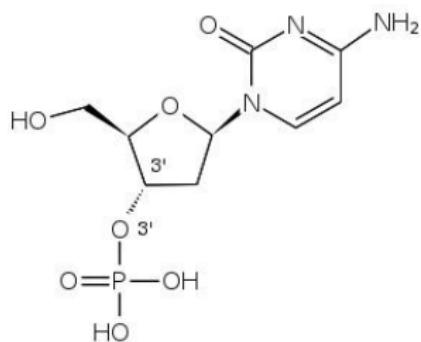
Level of theory: B3LYP/6-311+G*

⁹Gu et al. JACS 2006, 128, 1250.

¹⁰Gu et al. JACS 2006, 128, 9322.

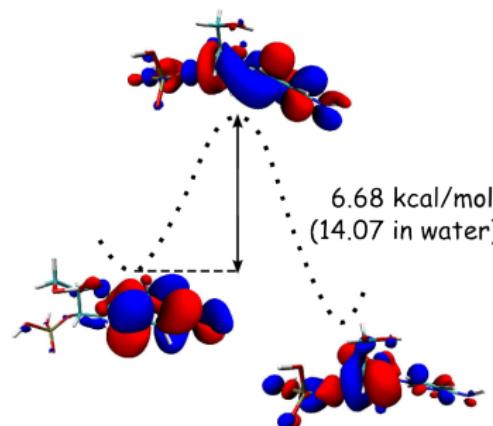
Single nucleotide: 2'-deoxycytidine-3'-monophosphate (3'-dCMPH)

- Electron affinities⁹ (eV)



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VEA	0.00
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- Energetic barrier of the C_{3'}-O_{3'} bond cleavage¹⁰ (kcal/mol)



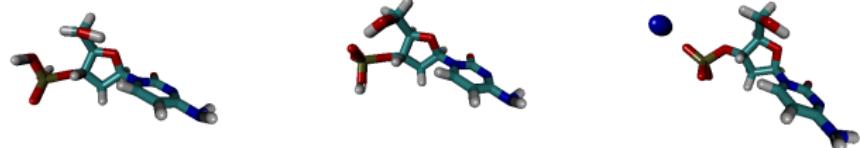
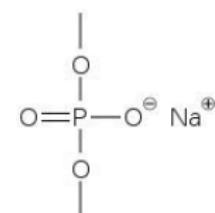
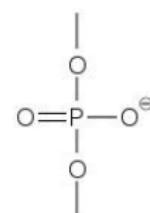
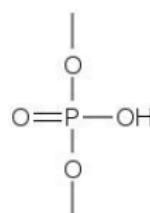
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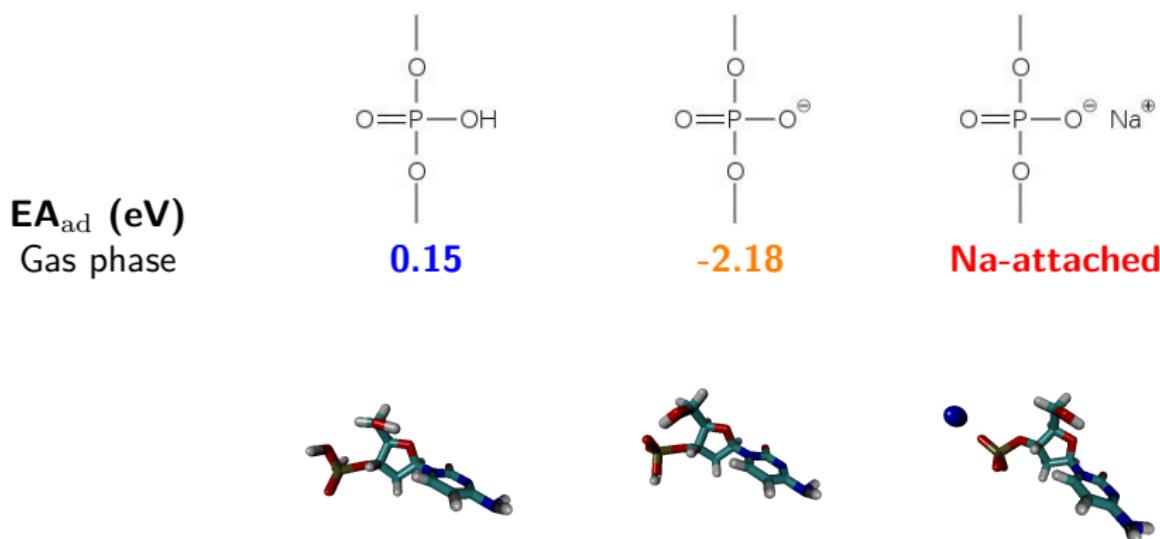
Adiabatic electron affinities wrt protonation state

EA_{ad} (eV)



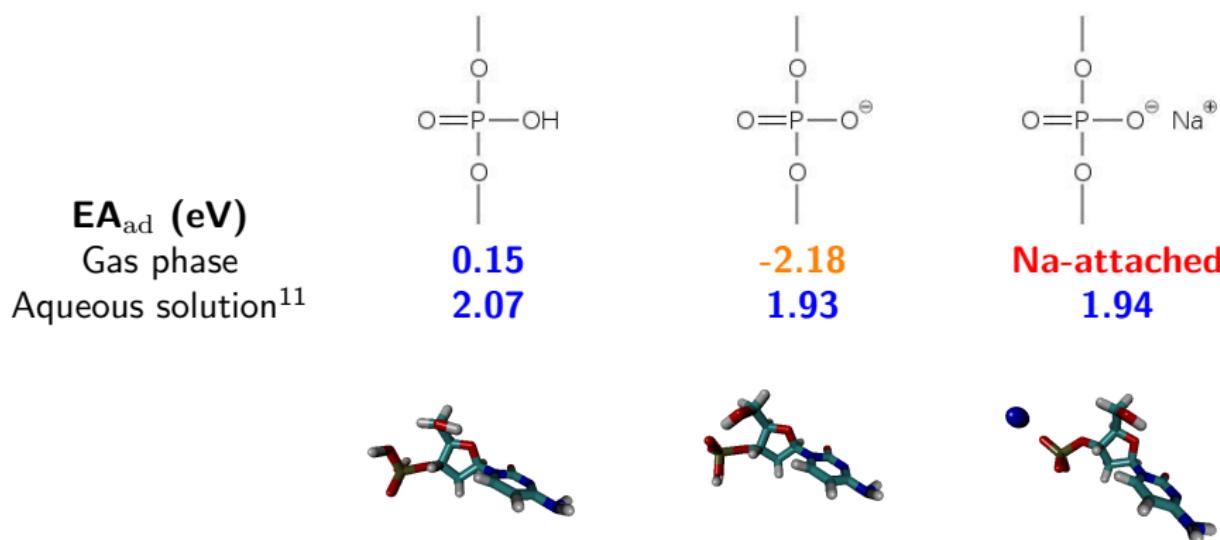
¹¹IEF-PCM model using water solvent and UA0 radii.

Adiabatic electron affinities wrt protonation state



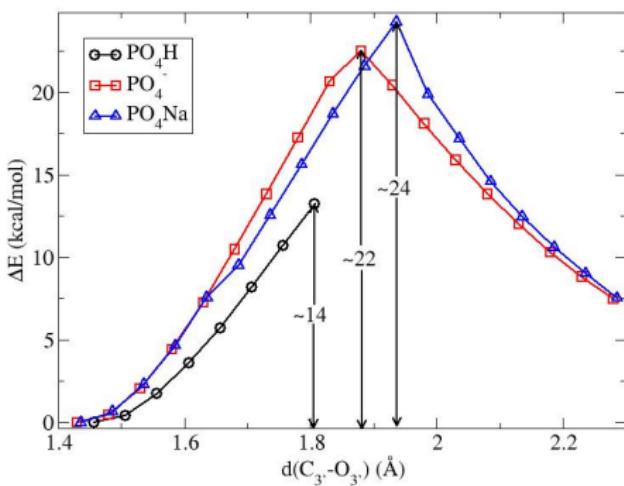
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Adiabatic electron affinities wrt protonation state

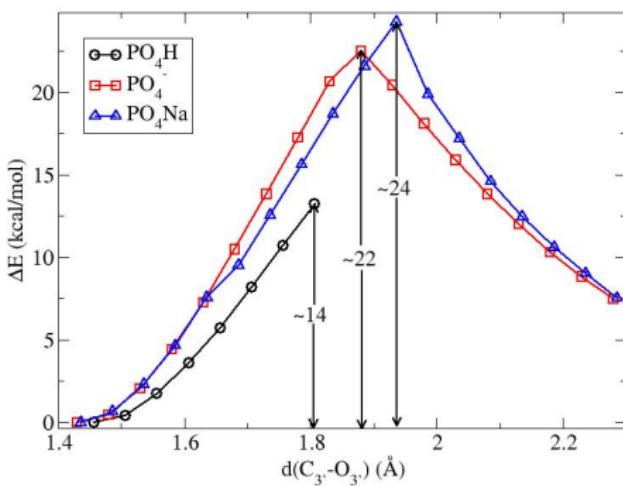


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Barrier of the C_{3'}-O_{3'} bond cleavage wrt protonation state in aqueous solution



Barrier of the C_{3'}-O_{3'} bond cleavage wrt protonation state in aqueous solution



A key question: modulation due to the environment ?

The Local Self-Consistent Field method

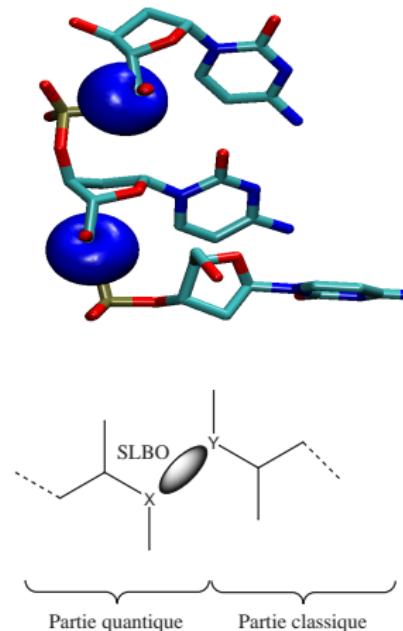
- Optimization of the WF under constraint¹²

$$\mathbf{F} \cdot \mathbf{C} = \underbrace{\mathbf{S} \cdot \mathbf{C} \cdot \mathbf{E}}_{\text{variational}} + \underbrace{\mathbf{S} \cdot \mathbf{L} \cdot \Lambda}_{\text{frozen}}$$

- QM/MM boundary¹³
Strictly Localized Bond Orbital (SLBO) \iff

$$|I_I\rangle = \sum_{\mu \in \{X, Y\}} I_{\mu I} |\mu\rangle$$

\implies Localization criteria
(transferability principle)



¹²Assfeld et al. *Chem. Phys. Lett.* **1996**, 263, 100.

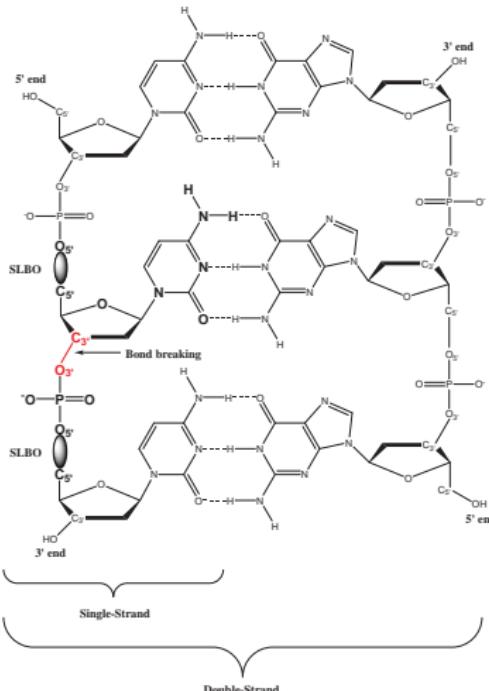
¹³Ferré et al. *J. Comput. Chem.*, **2002**, 23, 610.

LSCF/MM calculation

- Electrostatic Embedding:
polarization of the WF

$$\sum_{A \in \text{MM}} \sum_{\mu\nu} P_{\mu\nu}^T \left\langle \mu \left| \frac{q_A}{|\mathbf{r} - \mathbf{R}_A|} \right| \nu \right\rangle$$

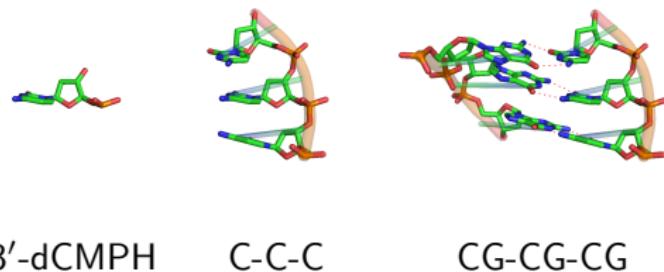
- Self-consistent core orbitals¹⁴:
 - any additional parameters for the QM/MM frontier¹⁵
 - proper treatment of the electronic attachment
 - No ponctual charges redistribution



¹⁴Loos et al. *Comput. Lett.* **2007**, *4*, 473.

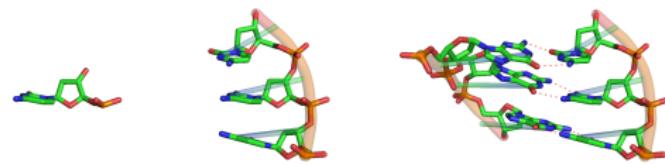
¹⁵Fornili et al. *CPL* **2006**, *427*, 236.

From single nucleotide to double-stranded DNA



Level of theory: B3LYP/6-311+G*/Amber ff99 for nucleic acids

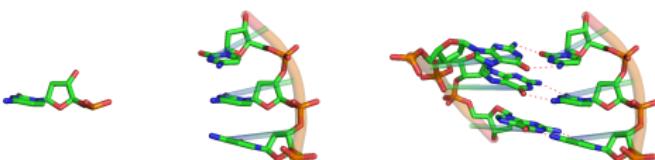
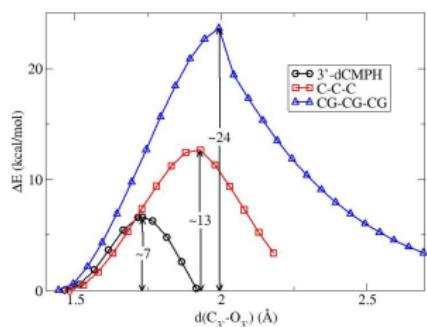
From single nucleotide to double-stranded DNA



EA_{ad} (eV)	3'-dCMPH	C-C-C	CG-CG-CG
	0.15	0.32	0.92

Level of theory: B3LYP/6-311+G*/Amber ff99 for nucleic acids

From single nucleotide to double-stranded DNA



	3'-dCMPH	C-C-C	CG-CG-CG
EA _{ad} (eV)	0.15	0.32	0.92
ΔE (kcal/mol)	6.69	≈ 13	≈ 24

Level of theory: B3LYP/6-311+G*/Amber *ff99* for nucleic acids

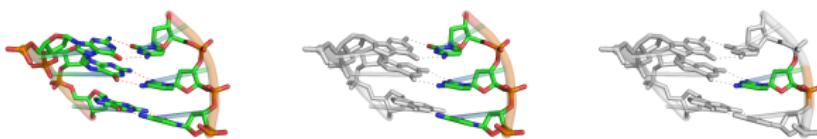
Switch off the electrostatic embedding¹⁶

Embedding

Full

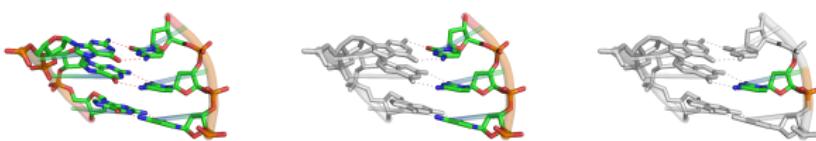
Only SS

None



¹⁶Loos et al. *JCTC* 2008, 4, 637; Dumont et al. *JCTC* 2008, 4, 1171.

Switch off the electrostatic embedding¹⁶



Embedding
 EA_{ad} (eV)

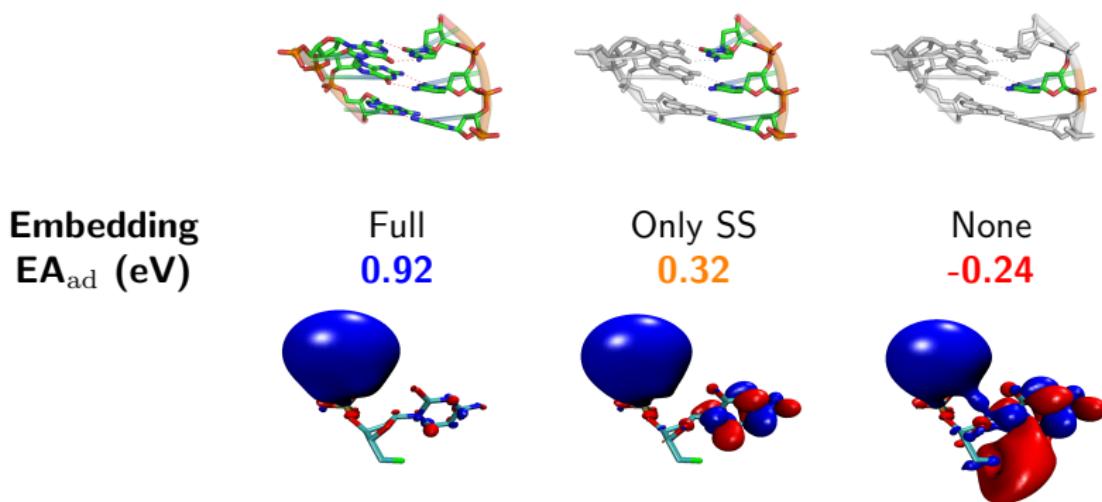
Full
0.92

Only SS
0.32

None
-0.24

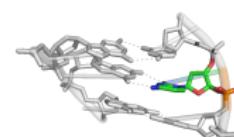
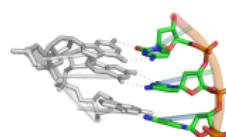
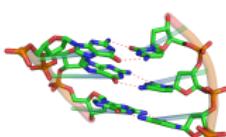
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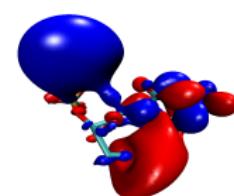
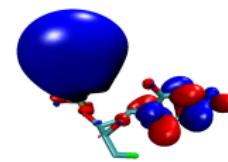
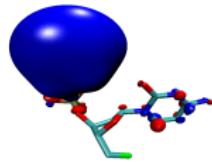


Embedding
 EA_{ad} (eV)

Full
0.92

Only SS
0.32

None
-0.24



Spin densities

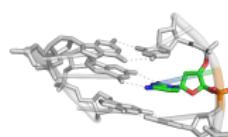
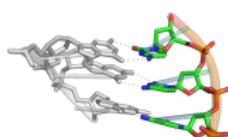
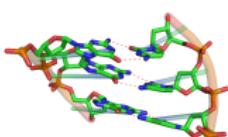
0.92; 0.02; 0.06

0.77; -0.02; 0.25

0.36; 0.27; 0.37

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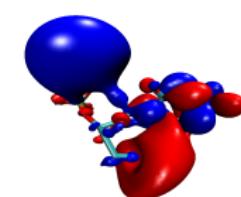
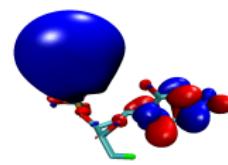
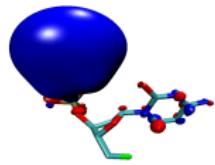


Embedding
 EA_{ad} (eV)

Full
0.92

Only SS
0.32

None
-0.24



Spin densities
 ΔE (kcal/mol)

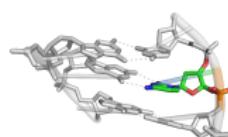
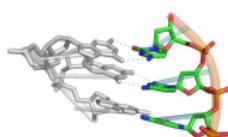
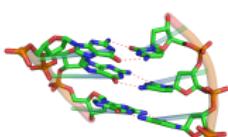
0.92; 0.02; 0.06
 $\simeq 24$

0.77; -0.02; 0.25
 $\simeq 19$

0.36; 0.27; 0.37
 $\simeq 8$

¹⁶Loos et al. *JCTC* 2008, 4, 637; Dumont et al. *JCTC* 2008, 4, 1171.

Switch off the electrostatic embedding¹⁶

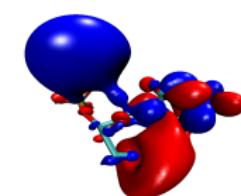
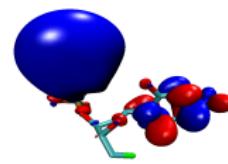
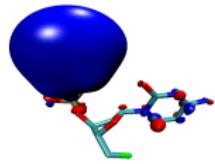


Embedding
 EA_{ad} (eV)

Full
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Only SS
0.32

None
-0.24



Spin densities
 ΔE (kcal/mol)

0.92; 0.02; 0.06
 $\simeq 24$

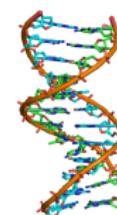
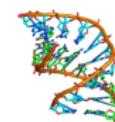
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Conclusions

- Huge modulation once the environment is taken into account:
 - Electron affinities increase (electrostatic effects)
 - and also the barriers of the 3' cleavage
- Other pathways may exist ...



Outlooks

- Other bonds¹⁷: C_{5'}-O_{5'}?
- Other nucleobases: Thymine and purines¹⁸
- Helical structures: A-DNA, B-DNA, Z-DNA

¹⁷Gu et al. *PNAS* **2008**, *105*, 12224.

¹⁸Schymanski et al. *JACS* **2008**, *130*, 12224.

Nancy

- Elise Dumont and Adèle Laurent



LSCF

- Yohann Moreau (Orsay) and Nicolas Ferré (Marseille)



Namur

- Denis Jacquemin, Julien Preat and Eric Perpète



Boss

- Jean-Louis Rivail and Xavier Assfeld

