



Insights into DNA lesions formation and structural outcome by simulation tools

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► To cite this version:

Elise Dumont, Chen-Hui Chan, Emmanuelle Bignon, François Dehez, Antonio Monari. Insights into DNA lesions formation and structural outcome by simulation tools. Fifteenth edition of the international Workshop on Radiation Damage to DNA, May 2018, Aussois, France. hal-02114267

HAL Id: hal-02114267

<https://hal.science/hal-02114267>

Submitted on 29 Apr 2019

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Insights into DNA lesions formation and structural outcome by simulation tools.

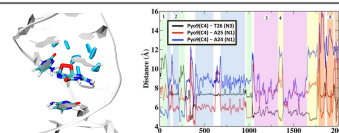
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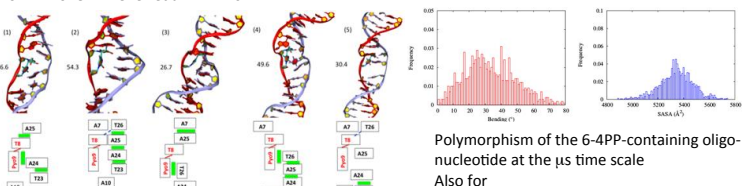
Context and our computational tools

Modelling can get insights and provide a **same-footing comparison**: compare reactivity ? $\Delta\Delta G^\ddagger$ ease of formation ? $\Delta\Delta G^{\text{destab}}$
Molecular dynamics MD (AMBER or NAMD GPU-accelerated) with accurate force field ; DFT calculations (eventually coupled to MD)
We can extract characteristic B-helix angles (coll. F. Lankas) and reveal non-covalent interactions that stabilize damaged duplexes.

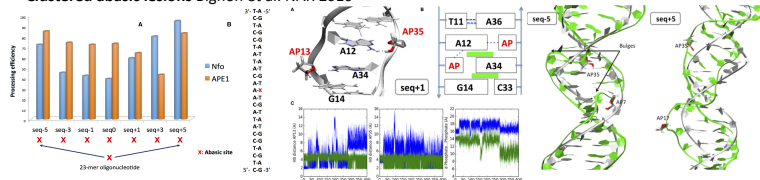


Structural insights into complex DNA lesions (and their proteins...)

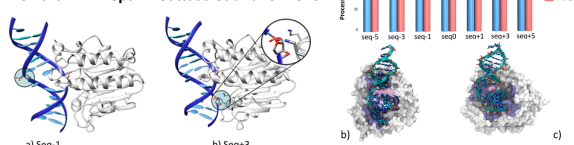
6-4PP vs. CPD Dehez et al. NAR 2017



Clustered abasic lesions Bignon et al. NAR 2016



Toward DNA repair Gattuso et al. JPCL 2016

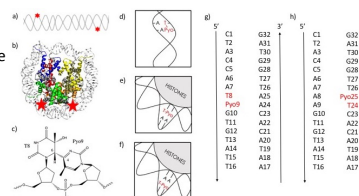


Damaged N-DNA (ongoing)

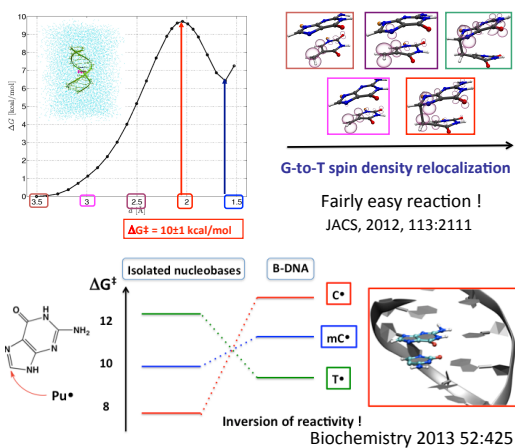
Several X-ray structures of damaged N-DNA have become available.

At the μs range, we probe contrasted mechanical properties (inward vs. outward).

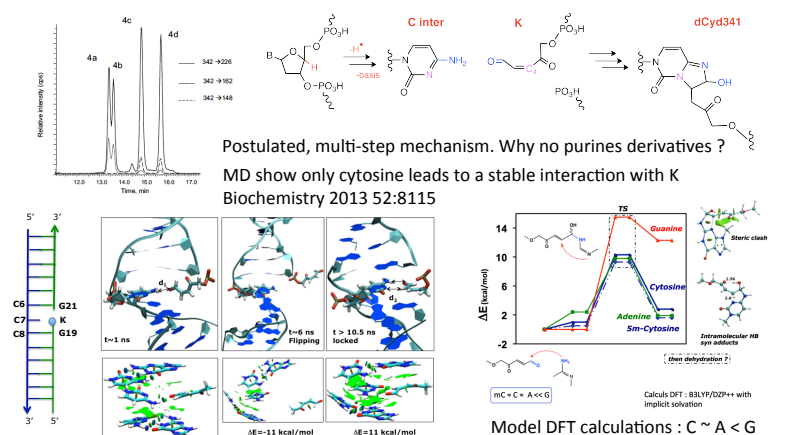
Methodological calibration is also needed...



Formation of intrastrand CLs



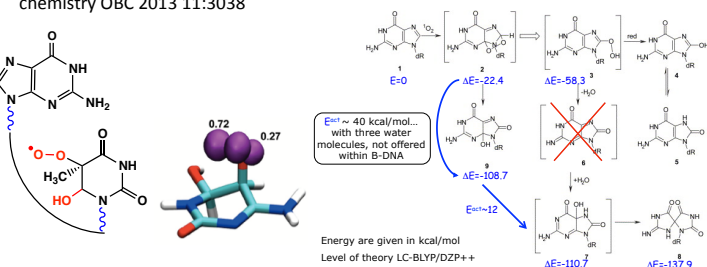
Interstrand lesions via C4'-oxidized abasic sites



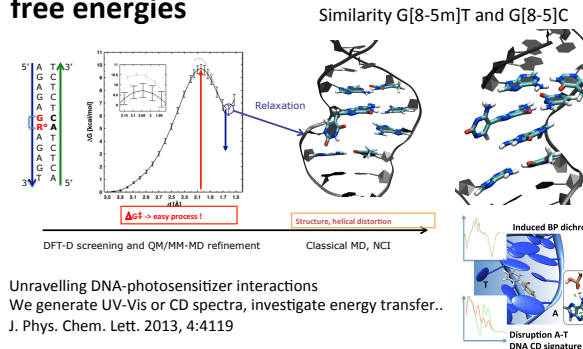
Mechanistic insights on radical and ROS reactivity

Peroxy-mediated, combinatorial chemistry OBC 2013 11:3038

Singlet oxygen NAR 2016, Chem. Eur. J. 2017



Structural predictions and destabilization free energies



Collaborators: F. Lankas (Prah), C. Fonseca-Guerra (Amsterdam)

This work was performed within the framework of the LABEX PRIMES (ANR-11-LABEX-0063) of Université de Lyon, within the program "Investissements d'Avenir" (ANR-11-IDEX-0007) operated by the French National Research Agency (ANR)