Theoretical investigation of the ultra-fast dissociation of ionized biomolecules immersed in water: direct vs indirect effects

Rodolphe Vuilleumier

Theoretical Chemical Physics sector
Département de chimie de l’Ecole normale supérieure, Paris
Theoretical work

• Marie-Pierre Gaigeot, Université d’Evry
• Marie-Françoise Politis, Alain Touati and Marie-Anne Hervé du Penhoat, Université Pierre et Marie Curie
• Ivano Tavernelli – Lausanne
• Fernando Martin, Manuel Alcamí - Madrid (see Poster 2)
• Pablo Lopez-Tarifa – PhD Madrid/Paris + CUPSFEL Short term visit

Experimental work

• Groupe de P. Moretto-Cappelle - Toulouse, France
• Groupe de L. Adoui, B. Gervais - Caen, France
• Groupe de T. Douki - Grenoble, France
• Groupe de C. Miron - Paris, France
Introduction

• High ionization density in swift heavy ion tracks (Ar$^{18+}$, C$^{6+}$; v=1/3c)

• K-shell ionization

• Multiple ionization (M$^{2+}$, M$^{3+}$, …) represent about 10% of collision events but most lethal events

• Long chain of events from irradiation to cell death or chromosomic aberration

• Liquid water: Important amount of HO$_2$ / O$_2^-$ radicals & O$_2$ molecules (very harmful for the cell)

• Direct or indirect mechanisms: are damages caused by water ionization that produces oxydative stress or by direct ionization of DNA?
Three stages description

1. Physical stage
   \[ t < 10^{-15} \text{ s} \]
   collision of swift ions with molecules in the path
   transport and interaction of secondary \( e^- \), Auger effect

2. Chemical-physics stage
   \[ t \approx 10^{-15} - 10^{-12} \text{ s} \]
   fragmentation, recombination with close partners

3. Chemical stage
   \[ t >> 10^{-12} \text{ s} \]
   diffusion of radicals, chemical reactions

And further: biological events…
Modelling of the chemical-physics stage: double ionisations

- Multiple ionization are not negligible at high LET (Linear Energy Transfer)

- Very damaging

- It was shown (A. Chetioui et al.) that cell death is correlated with K-shell ionization

  double ionisation after Auger effect

Simulation of the fragmentation induced by double ionization or core hole of water and biomolecules
Outline

• Methodology
  • Propagation: TD-DFT + Ehrenfest dynamics
  • Initial wavefunction (following double ionization)

• Coulomb explosion following double ionization
  • Water molecule in water and water clusters
  • Uracil in gas phase
  • Uracil in liquid water: direct and indirect effects

• Core hole excitation of water and uracil

• Conclusions
Propagation of electron density by TD-DFT

TDDFT equation:

\[ i \hbar \frac{\partial \phi_i}{\partial t} = -\frac{1}{2} \nabla^2 \phi_i + v_s(\vec{r}, t) \phi_i, \]

where the orbitals depend on positions and time.

The TD-KS potential is a functional of the time-dependent density

\[ v_s(\vec{r}, t) = v_{ext}(\vec{r}, t) + v_H(\vec{r}, t; [n(\tau)]) + v_{xc}(\vec{r}, t; [n(\tau)]) \]

- External potential term
- Hartree term \[ v_H(\vec{r}, t; [n(\tau)]) = \int d^3 \vec{r'} \frac{n(\vec{r'}, t)}{|\vec{r} - \vec{r'}|} \]
- Exchange-correlation term taken in the adiabatic approximation i.e. use of ground state xc potential (BLYP)
Nuclear motion: Ehrenfest approximation

- Atomic motion is classical and atoms follow Newton’s equations of motion
- Nuclear forces: calculated from the average instantaneous density as given by the TDDFT propagation
- The atoms evolve on an effective potential representing an average over the adiabatic electronic states weighted by their occupation probabilities
- Mean-field type approach
Numerical propagation scheme for solving the TD-KS equations

- Crank-Nicholson time-propagation

\[ |\varphi(t + dt)\rangle = \frac{1 - i\hat{H}(t)\frac{dt}{2}}{1 + i\hat{H}(t)\frac{dt}{2}} |\varphi(t + dt)\rangle \]

- Solved iteratively

- *Integration time-step of equations of motion*: 1 as

- BLYP functional

- Plane-waves & norm-conserving pseudopotentials (CPMD framework)

- Periodic boundary conditions (liquid phase representation)

- Cut-off 70 or 90 Ry
Attributing electrons to molecules

We want to prepare an initial state with two electrons taken away from one water molecule of the liquid sample.

Maximally localized Wannier orbitals find a unitary transformation of the orbitals so as to minimize the sum of spreads:

$$\langle \Omega \rangle = \sum_i \left( \langle \phi_i | r^2 | \phi_i \rangle - \langle \phi_i | r | \phi_i \rangle^2 \right)$$

Use of Berry phase for boundary conditions:

$$\Omega = \frac{-1}{(2\pi)^2} w_\alpha \ln |z_\alpha|^2 ; \quad z_\alpha = \langle \Psi | e^{i \frac{2\pi}{L} r_\alpha} | \Psi \rangle$$
Wannier orbitals and Wannier centers

Electron pairs can be attributed unambiguously to molecules
Effective molecular orbitals: Liquid water

Wannier orbitals attributed to individual molecules

One-electron Hamiltonian projected on that basis is rediagonalized

\[
\left( H^S \right)_{ij} = \langle w_i | \hat{H} | w_j \rangle
\]

\[
\sum_{ij} U^S_{ki} H^S_{ij} \left( U^S \right)^\dagger_{jl} = \alpha_k \delta_{kl}
\]

Four orbitals with character: 2A_1, 1B_1, 1B_2 et 3A_1

Effective orbitals from the same molecule are decoupled:

\[
\langle \phi_k | \hat{H} | \phi_l \rangle = \alpha_k \delta_{kl}
\]

P. Hunt et al. CPL 376,68 (2003)

Initial conditions: Slater determinant of effective MO
**H$_2$O$^{2+}$ coulomb explosion in liquid : TD-DFT in liquid water**

Evolution with time of the two O-H distances of the ionized H$_2$O$^{2+}$ water molecule

Fragmentation leads to one O and two H$^+$ atoms & recombination with the surrounding solvent: H$_2$O$^{2+}$ $\rightarrow$ 2H$_3$O$^+$ + O

Ionization from inner-shells: faster time-scale
$H_2O^{2+}$ coulomb explosion in liquid: TD-DFT in liquid water

Charge reorganization with time: a Bader analysis

1B$_1$

Total charge of the 32W sample

Ionized $H_2O^{2+}$ water molecule

4 surrounding W molecules

O atom produced
**H$_2$O$^{2+}$ coulomb explosion in liquid : TD-DFT in liquid water**

Charge reorganization with time : a Bader analysis

- Check that H$_2$O$^{2+}$
  - H$_2$O$^{2+}$ : O, H$^+$, H$^+$ (q$_{tot}$=+2)
  - other H$_2$O : O$^-$, H$^+$, H$^+$ (q$_{tot}$=0)

Total charge of the sampling is always +2
After 0.5 fs dynamics:
rapid charge transfer of ~ 1e from the surrounding  --> $\text{H}_2\text{O}^+$
O atom is negatively charged ~ -1e
$\text{H}_2\text{O}^{2+}$ coulomb explosion in liquid : TD-DFT in liquid water

Charge reorganization with time : a Bader analysis

1.0 - 3.5 fs dynamics:
the charge on the Oxygen is brought away by the 
2 hydrogens $\text{H}^+$ as they detach 
and O becomes neutral
H$_2$O$^{2+}$ coulomb explosion in liquid: TD-DFT in liquid water

**Charge reorganization with time: a Bader analysis**

3.5 - 4 fs dynamics:
the bare neutral oxygen becomes negatively charged (~ -0.37 e) by charge transfer from the surrounding water solvent

Solvent charge relaxation in the cage of the O atom
Formation of atomic oxygen

- Highly reactive
- Born-Oppenheimer MD leads quickly to the formation of $\text{H}_2\text{O}_2$
- In presence of OH radical leads to the superoxyde HO$_2$
For small clusters (3 molecules), only H\(^+\) production is observed.

At $t = 12$ fs

Fast successive proton transfers
Direct effects of ionization: gas phase Uracil$^{2+}$

Hypothesis: remove 2 electrons from the inner shell molecular orbitals of neutral Uracil (most violent events)

Initial ionisation is either localised on C=O groups or partially delocalised on the ring.
Ionisation from C=O
Follow-up with Born-Oppenheimer dynamics

up to 386 fs of dynamics
Ionisation from second C=O
Follow-up with Born-Oppenheimer dynamics up to 396 fs of dynamics
Comparison with experiment

Uracil in gas phase collision with protons in the 25 keV– 100 keV energy range

Coincidence diagram of charged fragments:

Our deepest orbital O.M.1: 43/41

The O.M.2: 53/43

P Moretto-Cappelle's Group - Toulouse, France
Direct effects of ionization: Uracil$^{2+}$ immersed in liquid water

Ionisation from the two C=O effective MO’s
Ionisation from C=O

- After 31.20 fs of TD-DFT dynamics
- Loss of an oxygen atom in the liquid
- Oxygen negatively charged, just like after the Coulomb explosion of H$_2$O$^{2+}$ in pure liquid water
Follow-up with Born-Oppenheimer dynamics

- The ring closes
- Loss of a proton accompanied by the formation of $\text{H}_3\text{O}^+$ in the liquid
- Oxygen (-0.5e) still in water
Ionisation from second C=O

- After 31 fs of TD-DFT dynamics
- Loss of two fragments
Follow-up with Born-Oppenheimer dynamics

After a short preliminary BO dynamics of 20 fs, the 2 fragments remain stable (charge transfers)
Indirect effects of ionization: \( \text{H}_2\text{O}^{2+} \) close to the Uracil

\( \text{H}_2\text{O} \) initially as \( \text{H}_2\text{W}...\text{O} = \text{C} = 2.0 \) Ang. sphere

After 17 fs of TD-DFT dynamics: \( \text{H}_2\text{O}^{2+} \) has Coulomb exploded into its 3 atoms

Again: Oxygen negatively charged released in liquid water
Core shell ionization

- Were shown experimentally to be correlated with DNA damages and cell death
- Lead to double ionization after Auger effect
- Is the damage induced by the localized charge or does it follow from the subsequent double ionization?
  - Pseudo-potential generated with core hole
  - Born-Oppenheimer propagation on the ground state for the valence electrons in presence of the core hole
Coulomb explosion following a K-shell ionization: liquid water

Specific atomic pseudo-potentials in order to mimic atomic core-holes
Car-Parrinello MD

O*: core-hole oxygen

Statistics on 96 dynamics:
OH + H 65%
explosion 35%

O*: core-hole oxygen

Statistics on 96 dynamics:
OH + H 65%
explosion 35%
Transfer of second H depends on number of H-bonds of the acceptor molecule.
Core shell ionization of Uracil in water

No disturbance of the ring. Energy dissipated by proton transfer
Conclusions

• Formation of atomic oxygen from double ionization of water molecule as was hypothesized from the production yields of HO$_2$ in water radiolysis

• Gas phase uracil double ionization: fragments in agreement with coincidence measurements (P. Moretto-Capelle)

• Uracil in water: both direct and indirect ionization can produce atomic oxygen

• Core hole in itself does not produces significant damage. Points to the role of the ensuing double ionization.