Master 2 Internship Proposal

Academic year: 2025–2026
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Title: *Numerical modeling of the fragmentation dynamics of DNA irradiated by protons in ionic aqueous media*
Nature of the work: Internship with a strong computational component (Python or C programming).
Keywords: radiation–matter interaction, DNA fragmentation, fluorescence microscopy, soft matter, image analysis

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Numerical modeling of the fragmentation dynamics of DNA irradiated by protons in ionic aqueous media

Context and motivation

Understanding the physical mechanisms involved in the irradiation of DNA by protons in aqueous environments is crucial in several fields:

- **Proton therapy,** to optimize treatment efficiency and safety [1].
- **Human space exploration,** since high-energy protons make up about 90% of cosmic radiation [2].

This context motivates the study of the **fragmentation dynamics of DNA in aqueous solution**, which helps elucidate how the energy deposited by protons dissipates in the medium [3], and how it destabilizes molecular systems leading to DNA double-strand breaks (DSBs). The approach developed in this project combines **single-molecule experiments** on irradiated DNA in solution with **numerical modeling**, providing both statistical and dynamical insight into the processes at play [4,5].

Experimental approach

At LP2I, we study the fragmentation of DNA in solution (bacteriophage T4, ~169,000 base pairs) after controlled irradiation with 3 MeV protons (Figure 1). This unique combination of a **spatially resolved proton microbeam** and **real-time single-molecule fluorescence microscopy** allows us to:

- Quantify **fragmentation cross sections** and **DSB occurrence probabilities** with ~10% accuracy;
- Monitor the **real-time fragmentation dynamics** with 100 ms temporal resolution.

This innovative setup yields a rich dataset, with over a thousand fragmentation events recorded so far. We have recently shown that **fragmentation rates depend on the depth within the irradiated target** [6]. Preliminary studies have also revealed that **the ionic charge of the solvent** strongly affects DNA fragmentation probabilities [5], and that **delayed fragmentation events** can occur (Figure 2) [7]. Further dependencies on **temperature** and **AT/CG sequence composition** are suspected and will be investigated.

Theoretical and numerical approach

The internship will focus on developing an integrated **numerical model** to describe the fragmentation dynamics of DNA and to interpret experimental data. The work will include:

1. **Local modeling of the double helix:**
   Implementing the *Peyrard–Bishop–Dauxois (PBD)* model to describe the stability of AT and CG base pairs and their associated energy barriers to denaturation [5,8].
2. **Stochastic dynamics:**
   Using Langevin-type equations to simulate the progressive strand separation following the creation of two nearby lesions spaced by a few base pairs [9].
3. **Parametric studies:**
   Exploring how temperature, AT/CG composition, and ionic concentration influence post-irradiation fragmentation kinetics.

This approach will connect **local molecular properties** to **global fragmentation dynamics**, providing a quantitative framework for interpreting single-molecule experimental data.

Participation in experiments

The student will also have the opportunity to participate in a **one-week experimental campaign**, tentatively planned for May, aimed at observing fragmentation processes or water radiolysis under **ultra-high dose rate proton irradiation** [11]. This hands-on experience will complement the modeling work and provide a broader understanding of the team's ongoing research activities.

. Figure 1 : AIFIRA / LP2I irradiation platform used for conducting DNA in solution irradiation experiments.

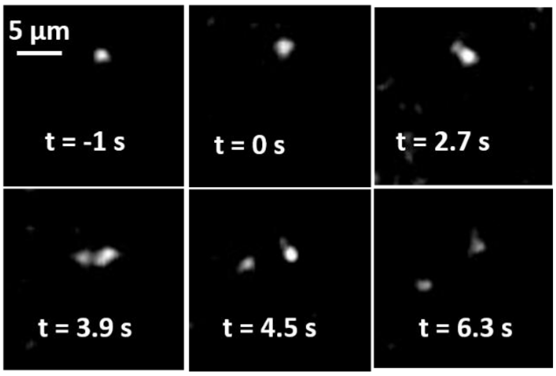

Figure 2 : *In situ* observation of the fragmentation dynamics of a T4 phage DNA molecule in aqueous solution following a proton impact at time t = 0.
In this case, the two fragments appear approximately 3s after irradiation, highlighting a delayed dissociation of the irradiated DNA strand

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References

1. Marco Durante et al., *Charged particles in radiation oncology*, Nature Reviews Clinical Oncology, 7(1):37–43, 2010.
2. Jeffery C. Chancellor et al., *Limitations in predicting the space radiation health risk for exploration astronauts*, npj Microgravity, 4(1):8, 2018.
3. Christopher Shepard et al., *Electronic excitation response of DNA to high-energy proton radiation in water,* Phys. Rev. Lett., 130:118401, 2023.
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11. Franck Gobet et al., *Electric fields in liquid water irradiated with protons at ultrahigh dose rates*, Phys. Rev. Lett., 131:178001, 2023.