PhD Thesis Proposal

Thesis title:

Sub-THz Excitation of Collective Protein Modes : Mechanisms and Dynamics

Department / Research team:

Département Nanosciences - Équipe Physique Appliquée aux Protéines

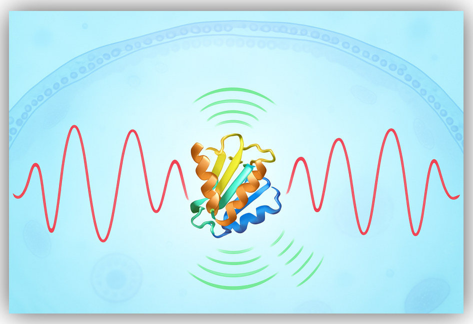
Thesis Supervision and, if applicable, co-supervision:

Patrick SENET (psenet@ube.fr)

Adrien NICOLAÏ (adrien.nicolai@ube.fr)

Experimental partner : Jérémie Margueritat (Institut Lumière Matière, Lyon)

Background – Description of the topic – Objectives:



Proteins are nano-scale biological objects whose characteristic dimensions (1–10 nm) allow them to sustain collective low-frequency vibrational modes in the sub-THz and near THz range (< 1.2 THz). Although their experimental detection under physiological conditions remains challenging, spectroscopic techniques such as Brillouin scattering, Far-Infrared and Raman spectroscopy have revealed low-frequency resonances in several proteins in the spectral region 0.6 – 0.9 THz [1]. Recent experimental approaches based on the interaction of proteins with oscillating electromagnetic fields at low frequency (< 300 GHz), notably Extraordinary Acoustic Raman (EAR) spectroscopy, have demonstrated the existence of collective vibrational modes at the single-molecule level at very low frequency (< 100 GHz ≅ 3 – 4 cm^{-1}). These extremely low-frequency vibrations described as acoustic modes by analogy with acoustical phonons, should involve coherent motions of large protein segments or domains.

Increasing theoretical evidence suggests that acoustic modes may facilitate conformational transitions between metastable states separated by free-energy barriers and may therefore be relevant to protein functions. In contrast to intramolecular vibrations, such excitations are primarily governed by the global size, shape and mechanical properties of the protein rather than by detailed chemical structure. They are thus particularly sensitive to conformational changes and environmental conditions.

The mechanism of excitation of the acoustic modes (< 300 GHz) by an electric field remains unclear, the role of solvent damping, the role of the protein physical chemical properties, anharmonicity and electrostriction unexplored and debated [2].

The objective of this PhD project is to elucidate the physical mechanisms enabling the excitation of acoustic modes of proteins by sub-THz electric fields in EAR and to determine the conditions required for resonant and selective excitation of specific low-frequency collective modes in solution (by EAR) and in protein crystals (by Brillouin scattering). Model proteins studied experimentally by our collaborators and in the literature (Conalbumin, Hsp70, Lysozyme) will be simulated in realistic conditions by Molecular Dynamics. Spectral responses will be computed using linear and nonlinear response theory and compare to experimental data.

References:

[1] Nicolaï, A., Delarue, P., Senet, P. (2014). Low-Frequency, Functional, Modes of Proteins: All-Atom and Coarse-Grained Normal Mode Analysis. In: Liwo, A. (eds) Computational Methods to Study the Structure and Dynamics of Biomolecules and Biomolecular Processes. Springer Series in Bio-/Neuroinformatics, vol 1. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-28554-7_15

[2] Nicolaï, A., Delarue, P., Senet, P. (2016). Theoretical Insights into Sub-Terahertz Acoustic Vibrations of Proteins Measured in Single-Molecule Experiments. *The Journal of Physical Chemistry Letters 7* (24), 5128-5136. https://doi.org/10.1021/acs.jpclett.6b01812

Keywords:

Protein dynamics ; Collective modes ; sub-THz spectroscopy ; Low-frequency vibrations ; Molecular dynamics simulations.

Candidate profile:

We are looking for a motivated Master student in Physics, Biophysics, Material Science, or a related field, with a strong foundation in at least one or two of the following areas:

- Biophysics and Bioinformatics
- Nanotechnology and Nanobiosciences
- Atomistic modeling and Molecular Dynamics
- Scientific programming and Data Analysis

Applications should be sent to the contact persons listed above and must include a detailed CV, a motivation letter, and one or more reference letters, including the Master supervisor's reference.