RESEARCH SUJECT TITLE :
Charge detection mass spectrometry coupled action spectroscopy in the mid-IR range for structural characterization of viruses.

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Doctoral School/Ecole doctorale : ED52 PHAST : Physics and Astrophysics
Lab Language: English
Abstract :

Viruses appear to constitute the most abundant and robust biological entities on earth. All viruses contain a nucleic acid genome and a protein capsid that covers the genome. The capsid is almost always made up of repeating structural subunits that are arranged in one of two symmetrical structures, a helix or an icosahedron. The final, mature capsid is a relatively robust protein complex able to protect the viral genome from physicochemical aggressions; however, it is also a metastable, dynamic structure poised to undergo controlled conformational transitions required to perform its biological activity. Studies aiming at evaluating the fragmentation of viruses are very scarce.
New electrostatic traps (based on charge detection mass spectrometry (CDMS)[1]) have recently been implemented to achieve fragmentation experiments on selected ions. The coupling with a CO_2 laser allows to perform infrared multiphoton dissociation of and to determine the unimolecular dissociation energy of activation of macro-polymers and whole DNAs. The trapped ions are then irradiated with CO_2 laser and fragmented by vibrational heating following a multiphoton IR activation.[2]
The project will be conducted following two key objectives:
(i) Perform native mass spectrometry on molecular self-assemblies of single viral particles and demonstrate that the CDMS technique is a viable experimental method for the detection and identification of viral particles
(ii) Adopt a multi-scale approach to obtain structural and energetic information on single viral particles using action spectroscopy, i.e. stability studies by photo-dissociation using wide spectral range available by compact laboratory lasers in mid-infrared (IR).
These studies would permit to apprehend mass distribution and dissociation pattern of viruses at the single molecule level. These measurements will be improved by the implementation of vibration selective photofragmentation using tunable mid-IR laser (5 to 9 µm range) to access their fine structures. Indeed, in this mid-IR range, vibrations are specific to the different components of viral particles and can be used as fingerprints. In particular one of the ultimate goal is to establish a link

between the photo-fragmentation observed in viruses and their structure and establish laws and mechanisms for energy dissipation in these objects.

Provisional schedule for achieving the objectives of the thesis:
First year: adaptation and modification of the experimental setup for optimal detection, mass measurement and trapping of virus. First experiments of photodissociation using CO2 lasers as excitation laser.
Second year: Establishment of the link between the photo-fragmentation observed in viruses and their structure and establishment of laws and mechanisms of energy dissipation in these objects (spherical and rods viruses).
Third year: These measurements will be improved by the implementation of vibration selective photofragmentation using tunable mid-IR laser (5 to 9 µm range) to access their fine structures.

The phD student will work on the upgrading of the experimental set-up as well as on the development of the experimental setup aiming at characterizing viruses and their photo-fragmentation. A big part of the phD work will be to perform and interpret photo-fragmentation induced by infrared laser irradiation on intact viruses. Also, the student will take part in statistical modeling development models polymers using heating/cooling stages to reproduce the observed dissociation dynamics.
The candidate should possess a master in chemistry or physical chemsitry and basic knowledge in molecular physics and spectroscopy, biochemistry and technical knowledge in mass spectrometry.

References:

[1] Doussineau T, Mathevon C, Altamura L, Vendrely C, Dugourd P, Forge V, et al. Mass Determination of Entire Amyloid Fibrils by Using Mass Spectrometry. Angewandte Chemie International Edition. 2016,55, 2340-4.
[2] Doussineau, T.; Antoine, R.; Santacreu, M.; Dugourd, P., Pushing the Limit of Infrared Multiphoton Dissociation to Megadalton-Size DNA Ions. Journal of Physical Chemistry Letters 2012, 3, 2141-2145.