

Grabbing the 'flu' by the tail: Characterization of the replication dynamics of Influenza A virus at single molecule level

IMDEA - Nanociencia Institute

www.nanociencia.imdea.org

CENTRE DESCRIPTION

IMDEA Nanociencia is a young interdisciplinary research centre dedicated to the exploration of basic nanoscience and the development of applications of nanotechnology in connection with innovative industries.

Our purpose-built building was inaugurated in 2014 and features state-of-the-art facilities for 21st century science, where the frontiers between fields disappear and Physics, Chemistry, Biology, Engineering, and Medicine merge. It features more than 30 operative laboratories with over € 16 M worth of equipment -including the Centre for Micro and Nanofabrication. We are located at the UAM Campus, with access to all the facilities of one of Spain's largest and most prestigious Universities. The UAM Campus is just a few minutes away from Madrid's lively city centre, connected by "cercanías" trains and several bus lines.

We are over 150 scientists, with different professional and personal backgrounds. Approximately 40% of our PhD and postdocs come from outside Spain, representing every corner of the world, from Germany to China, from the USA to Singapore –a true international environment in which to develop your scientific career. Women make up 36% of our scientific and 62% of our management staff. No matter who you are or where you come from, you will feel welcome from the very first minute.

We take science seriously and value quality over quantity. Our scientists enjoy tackling complex multidisciplinary problems, often within in-house collaborations, so all of our students receive truly interdisciplinary training. We also enjoy publishing in the very best journals, with >200 publications a year, and an institutional h index of 79. Check out our webpage <http://nanociencia.imdea.org/>, facebook @IMDEANanociencia or twitter @IMDEA_Nano for more information.

So if you are a talented, hard-working individual with a real interest in Science, IMDEA Nanociencia is the right place for you! Come work with us!

ADDRESS

Faraday 9, 28049 Madrid, Madrid

AREA OF KNOWLEDGE

Life Sciences

GROUP OF DISCIPLINES

LIFE SCIENCES: Human Biology, Microbiology, Molecular Biology, Genetics, Cellular Biology, Genomics and Proteomics, Biochemistry.

GROUP LEADER

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Research project/ Research Group description

Influenza viruses are the causative agents of influenza (flu), which causes substantial morbidity and mortality in humans and a considerable financial burden worldwide. Because of their high mutation rate, Influenza viruses are difficult to target with vaccines. In this project we aim to develop a novel single-molecule manipulation approach to determine the operational dynamics of the viral RNA polymerase, which is the main source of mutations.

Using Optical Tweezers we will study the activity in real time of individual, biologically active genomes of Influenza A. In addition, we will use Optical Tweezers to apply mechanical force to the viral RNA polymerase, in order to characterize the mechano-chemical processes that govern its operation. The ability to manipulate mechanically biological systems one molecule at a time opens avenues of investigation that are not possible using classical ensemble methods. The expected results will be of therapeutic and fundamental importance, and will provide a new tool to understand the molecular effect of drugs on viral replication.

Given the novelty of the proposed research and the influence of Influenza virus in our society, we anticipate a high impact of our results. For instance, our previous works in the field were published in high impact journals such as, EMBO J (2009), PNAS (2012), NAR (2015, 2017), Chemical Science (2017), Nature Communications (2018).

Our laboratory uses state-of-the-art biophysical techniques to answer biological questions from a new perspective. The project will give the opportunity to a graduate student to be trained in the highly interdisciplinary research area of single-molecule biophysics. Our group is integrated by physicists, chemist and biologists, and has established a net of international collaborators, constituting a stimulating and highly interdisciplinary environment training place for a graduate student with a background in Biology, Chemistry or Physics seeking to start a Ph.D. in Biophysics.

Job position description

The proposed research project fits into the category of Single-Molecule Biophysics. This is a new, highly interdisciplinary field aimed to define and quantify the molecular mechanisms that govern the operation of biological systems. Spanning the distance between the complexity of life and the simplicity of physical laws is the challenge of biophysics. Therefore, a graduate student with a background in Biology, Chemistry or Physics, looking forward to decipher the mechanisms of life will definitely enjoy and will carry out successfully the proposed research.

The candidate will combine nano-technological tools (optical tweezers), molecular biology techniques and statistical physics approaches to tackle from a completely new perspective the study of one the most common infectious respiratory diseases in humans, 'the flu'. The development of an *in singulo*

method to study the real-time dynamics of biologically active viral genomes will provide a unique tool to identify new potential therapeutic targets and to understand the molecular effects of antiviral drugs.

The candidate training plan and activities will include:

- Biochemical and Molecular Biology Techniques for the preparation of biological systems under study.
- Use of force spectroscopy techniques, Optical Tweezers, for the study of biological systems at the level of individual molecules.
- Programming: MatLab and C++, for data analysis and software update.
- Use of Statistical Mechanics tools for the analysis and modeling of results.
- Attendance and participation in courses and congresses.
- The candidate will benefit from the network of national and international collaborations already established to carry out this project: Molecular Genetics of RNA Viruses Lab at Pasteur Institute, Paris (PI: Prof. Nadia Naffakh) and the Structural Virology Lab at CNB-CSIC, Madrid (PI: Jaime Martin-Benito).

OTHER RELEVANT WEBSITES

Group Homepage

<http://nanociencia.imdea.org/molecular-motors-manipulations-lab/group-home>