DOCTORAL THESIS PROJECT OFFER. “AYUDAS PARA LA FORMACIÓN DE PROFESORADO UNIVERSITARIO (FPU) 2018”

Director

David Rodriguez Larrea

PhD thesis title

Sequencing single protein molecules

Scientific area

Biotechnology

Center

Instituto Biofisika

Place

Basque Country. Barrio Sarriena. 48940 Leioa. Vizcaya.

Website of the Research group or Center

Biofisika.org

Contact: Applicants are encouraged to send their CV through the Biofisika website contact page (http://biofisika.org/contact/), adding the following subject: [Job Application: FPUDRL]

DOCTORAL THESIS PROJECT

Currently tools exist for sequencing DNA at high speed and accuracy. While the human genome contains approximately 20.000 genes, the number of different proteins can exceed this by a factor of ten (>200.000 different proteins). This is caused by alternative splicing, RNA editing and posttranslational modifications. An added layer of complexity is the levels of each of these variants. While in general all cells in an organism contain the same genes, they differ greatly in the expressed protein variants and the levels of each (i.e. in their proteome).

Today the state-of-the-art technology for analyzing the proteome is mass spectrometry. While enormously powerful, it lags behind in the analysis of low abundance proteins, shows bias

towards some species and is hardly quantitative. New technologies are needed for a better characterization of the proteome.

Nanopore technology is one such technology. It works by measuring the ionic current flowing through a single hole (1-2 nm in diameter) made in a membrane. Due to its small size, when a molecule gets inside the pore it occupies a significant space which causes a decrease in the ionic current. Different bases have different sizes, and by measuring how the ionic current is modulated by the pass of a single strand of DNA the sequence can be deduced. This has been used for next-generation DNA sequencing (visit www.nanoporetech.com) and we propose to use it now for sequencing proteins.

The PI has pioneered the analysis of proteins with nanopores (see Nature Nanotechnology 2013, 8 (4) 288-295 and Nature Biotechnology 2014, 32 (2) 179-181) and is now a Ramon y Cajal researcher at Biofisika Institute (CSIC-Universidad del Pais Vasco) where he has set up his lab. This proposal will involve collaborations with Oxford University (Professor Hagan Bayley) and Oxford Nanopore Technologies; the PhD candidate is expected to spend times on these places and to attend national and international meetings.

This PhD proposal requires:

- Develop methods for the controlled translocation of proteins through nanopores.

- Develop methods for the analysis of the data. In particular through the use of Deep Learning approaches.

The PhD candidate is therefore expected to end up with knowledge in artificial intelligence, genetic and protein engineering. This multidisciplinary approach therefore requires a strong personal drive for science.