INSTITUTO DE TECNOLOGIA QUÍMICA E BIOLÓGICA /UNL
Knowledge Creation

MSc Thesis

Dissertation Project – 2nd Cycle

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TITLE: Structural and dynamic properties of the Dengue fusion peptide in a membrane bilayer: A computational approach

BACKGROUND

Dengue virus is responsible for dengue fever, a mosquito-born tropical disease that affects more than 100 million people every year. Like all enveloped viruses, the dengue virus is encapsulated by a lipid membrane (envelope) and in order to infect host cells the virus must fuse its membrane with the host membrane. The fusion process is promoted by the glycoprotein E, a class II fusion protein. This protein is responsible for receptor binding, membrane fusion, and is also the target of protective antibodies.

Unlike class I fusion proteins (like influenza hemagglutinin), which have an N-terminal fusion peptide, in class II proteins, the region responsible for binding and perturbing the membrane is an internal fusion peptide (FP). [1]This region is believed to play a crucial role in the fusion process. However, the mechanism by which the dengue fusion peptide promotes fusion remains elusive.

Our group has a large experience in the analysis of the interaction of fusion peptides with model membranes. In two recent works, we have used non-standard simulation techniques (self-assembly and bias-exchange metadynamics) to study the influenza fusion peptide.[2,3] The use of these techniques was paramount and allowed us to provide interesting new insights into the structure and activity of this peptide. In the current project, we intend to use similar methodologies to analyse the dengue fusion peptide.

1. Allison S. L., et al., 2**001**, *Journal of Virology*, **75**, p. 4268–4275
2. Victor B. L., et al., **2015**, *Journal of Chemical Information and Modeling*, **55**, 795-805
3. Lousa D., et al., submitted

OBJECTIVES

The main goal of this project is to characterize the interaction of the dengue fusion peptide with model membranes, using a molecular simulation approcah. We want to address the following questions:

1- What structure and arrangement does the dengue FP adopt in the membrane?

2- How does the peptide affect the membrane properties and promote fusion?

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PROJECT DESCRIPTION

In order to provide molecular insights into the interaction of the dengue fusion peptide with a model membrane, we will use a computational approach. The student will learn and apply molecular simulation techniques to address the questions described in the objectives. Below we describe the main tasks of the project.

Task 1. Bibliographic research

The student will search and read the most relevant papers focusing on the subject addressed by this project.

Task 2. Learning the basics of molecular simulation

The student will get familiarized with the basic concepts of molecular simulation and learn how to use the techniques that will be applied during the project

Task 3. Simulations of the dengue fusion peptide

The student will perform simulations of the FP in the presence of a membrane bilayer. Several techniques and protocols will be tested, such as standard MD and metadynamics. Metadynamics is a state of the art molecular simulation method which can be applied to many different problems that require an efficient sampling of the system.

Task 4. Analysis of the results

TIMELINE (use fill tool for the cells)

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10
Task 1										
Task 2										
Task 3										
Task 4										
Thesis										