MARIE SKŁODOWSKA-CURIE INDIVIDUAL FELLOWSHIPS 2019

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

NOVA Institute of Chemical and Biological Technology António Xavier | MOSTMICRO – Molecular, Structural and Cellular Microbiology Unit

RESEARCH GROUP AND URL

Multiscale Modeling Lab
https://www.itqb.unl.pt/labs/multiscale-modeling/

SUPERVISOR (NAME AND E-MAIL)

Manuel N. Melo
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SHORT CV OF THE SUPERVISOR

Manuel is the head of the Multiscale Modeling lab within the MOSTMICRO unit of ITQB NOVA.

Work at the Multiscale Modeling lab is centered on elucidating the molecular-level details of lipid–lipid, lipid–protein, and protein–protein interactions, using coarse-grained, atomistic, and hybrid molecular dynamic simulations. Recent collaborations also focus on modeling the Gram-positive peptidoglycan and other bacterial-specific structures. The spirit of the lab is to connect biophysics to microbiology, bridging these two sometimes far-apart fields. Additionally, the lab actively develops simulation and analysis software, with emphasis on large-scale parallelization of analysis.

Manuel carried out postdoctoral work at the Marrink lab, at the University of Groningen, where he was involved in the development and application of the widely-used Martini coarse-grain model. This followed a Ph.D. at the University of Lisbon studying the molecular-level interactions of antimicrobial peptides with cellular membranes, using spectroscopic techniques coupled to mathematical modeling.

5 SELECTED PUBLICATIONS

- M. N. Melo, R. Ferre and M. A. R. B. Castanho, Antimicrobial peptides: linking partition, activity and high membrane-bound concentrations; Nature Reviews Microbiology, 2009, 7:245-50;

- H. I. Ingólfsson, M. N. Melo, F. J. van Eerden, C. Arnarez, C. A. Lopez, T. A. Wassenaar, X. Periole, A. H. De Vries, D. P. Tieleman and S. J. Marrink, Lipid organization of the plasma membrane; Journal of the American Chemical Society 2014, 136(41):14554-59;

- M. N. Melo, H. I. Ingólfsson, S. J. Marrink, Parameters for Martini sterols and hopanoids based on a virtual-site description; The Journal of Chemical Physics 2015, 143(24):243152;

- S. Khalid, T. J. Piggot and F. Samsudin, Atomistic and Coarse Grain Simulations of the Cell Envelope of Gram-Negative Bacteria: What Have We Learned?, Accounts of Chemical Research 2019, 52(1):180-8;

- J. S. Hub, N. Awasthi, Probing a Continuous Polar Defect: A Reaction Coordinate for Pore Formation in Lipid Membranes; Journal of Chemical Theory and Computation 2017, 13(5):2352-66

PROJECT TITLE AND SHORT DESCRIPTION

Small-Scale, Large-Complexity Simulations of Antimicrobial Peptide Action

The antimicrobial peptide (AMP) class often acts by porating or otherwise disrupting bacterial membranes[1]. Although many advances have been made in their characterization, precise mechanisms and determinant factors remain elusive. Molecular dynamics simulations can provide important insight into the molecular-level processes by which AMPs perform their action. Notably, coarse-grain methods can reach the micro to millisecond timescales needed for the observation of these events.

In this project the Martini Coarse-Grain model will be used to simulate different AMPs in a membrane setting and infer mechanisms and promoting/inhibiting conditions. It will innovate relative to other approaches by i) employing realistically complex membrane compositions — made possible by recent advances in the modeling of different kinds of lipids[2,3,4] — and ii) developing and adapting simulation methods to force pore formation and measure energies therefrom[5].

This project can be further expanded by taking advantage of the lab's collaborative network in experimental biophysics to validate results, namely with UV/Vis/NMR spectroscopies, and with confocal/single-molecule fluorescence microscopy.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST

Chemistry (CHE)