PhD Project:

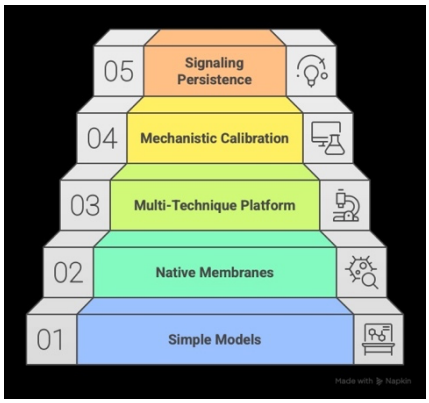
Correlation between cholesterol and the biophysical properties of lipid nanodomains in biomimetic models of cellular membranes: implications for HER2-positive breast cancer.

(ITA: Correlazione tra colesterolo e proprietà biofisiche dei nanodomini lipidici in modelli biomimetici di membrane cellulari: implicazioni per il carcinoma mammario HER2-positivo.)

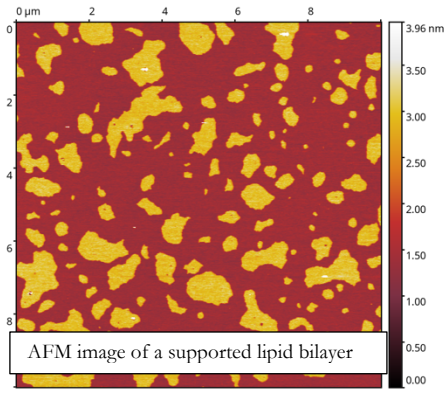
Supervisore: Dr. Loredana Casalis (Elettra Sincrotrone Trieste)

Co-Tutors: Dr. Pietro Parisse (CNR-IOM), Prof. Valeria Rondelli (Università di Milano)

The context of the present project is to introduce novel biophysical models to rationalize the resistance to HER2-targeting therapies in HER2+ breast cancer. The guiding hypothesis of this research is that cholesterol plays a pivotal role in regulating lipid nanodomains physical properties and stabilization within the plasma membrane. As a consequence, it constitutes an actionable upstream determinant of signaling persistence activated by HER2 dimerization in these nanodomains, and can be used as a target for adjuvant chemotherapies.



The candidate will study the cholesterol-driven structural and functional organization of nanodomains (lipid rafts) in plasma membranes, starting from simple models (supported lipid bilayers/liposomes) to native membranes (as Giant Plasma Membrane Vesicles from HER2+ breast cancer cells), to establish a causal and quantitative relationship between membrane cholesterol content, nanodomain stability, and HER2 nanoscale organization. Such data, collected through a multi-technique platform (AFM, Fluorescence Microsc opy, FTIR and Nano-IR, QCM, Neutron and X-ray scattering) will provide a mechanistic calibration step to be matched with cellular findings, in particular the sustained activation of the specific cellular pathways (as PI3K/AKT), w/wo therapeutic pressure. So far, the mechanistic link between membrane lipid remodeling, HER2 spatial organization, and signaling persistence has not been causally defined.



AFM image of a supported lipid bilayer

The PhD position is intended for a candidate with a background in biophysics, condensed matter physics, nanotechnology, biotechnology, chemistry, or related disciplines, and with a strong interest in membrane biophysics and quantitative analysis of macromolecular systems. The ideal candidate should have basic experience in macromolecular assembly and biophysical techniques operating in physiological environment, and an interest in interdisciplinary approaches combining complementary physical methods and biological models. Experience or familiarity with Atomic Force Microscopy, Fluorescence Microscopy, membrane model systems, data analysis of biophysical measurements will be considered an advantage. The candidate is expected to work within a multidisciplinary environment and to interact closely with researchers involved in membrane biophysics, cancer biology, and signaling studies.