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## Nanomechanical properties of synthetic and natural lipid bilayers through Atomic Force Microscopy (AFM): from Supported Lipid Bilayers (SLBs) to vesicles

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Lipid bilayers are self-assembling structures constituting the membranes of every animal cell and many others cell-derived nanoparticles like Extracellular vesicles (EVs). EVs are vesicles with dimensions ranging from 50 to 500nm produced and released by cells to act as cargoes for biological material (proteins, nucleic acids) which play a pivotal role in intercellular communication and in other relevant biological processes. The mechanical properties of EVs regulate fundamental cellular mechanisms like membrane fusion and budding. Their characterization is not trivial, especially due to the many different components that are anchored to or embedded in the lipid matrix, such as proteins, carbohydrates and glycans. Liposomes represent ideal biomembrane models, mimicking their mechanical behavior but featuring a simpler composition. AFM-Force Spectroscopy (AFM-FS) can be exploited for studying the indentation mechanics of intact individual vesicles and determining their stiffness. Many models in literature relate this parameter to the bending modulus [1,2]; however, none of them seems to work properly for all the phases assumed by lipid bilayers, leaving open the issue. A possible strategy to tackle the problem could be to confine these lipid bilayers on surfaces, realizing SLBs that pattern native lipid membranes in a bidimensional space and still preserve most of their intrinsic mechanical parameters. Moreover, effects like curvature and luminal pressure, which are relevant in vesicles [1], are totally absent in SLBs. In an attempt to rationalize the observed discrepancies, we performed AFM-FS on SLBs obtained from liposomes and EVs and compared these results with the ones on vesicles of similar lipid composition. This parallel approach could provide an experimental strategy for a more robust estimation of the bending modulus of both synthetic and cell-derived lipid vesicles, contributing to address the role of membrane elasticity in biological interactions.

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1.D.V. et al.,ACS Nano,vol.11(2017),pp.2628–2636. 2.A.C. et al.,Nanoscale,vol.6(2014),pp.2275-2285.

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