Microfluidics to fabricate and probe vesicles mimicking cells

Pierre Joseph, Marianne Elias, Fabien Mesnilgrente, Adrian Laborde, Debora Berti, Costanza Montis, Lucrezia Caselli, Barbara Lonetti, Chiara Magnani, Anne-Françoise Mingotaud

Joseph P, Elias M, Mesnilgrente F, Laborde A, [LAAS-CNRS, Université de Toulouse]
Berti D, Montis C, Caselli L [CSGI, Departement of Chemistry, Florence University]
Lonetti B, Magnani C, Mingotaud AF [Lab des IMRCP, Université Toulouse III PS]

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Being the base element of cell membranes, lipid bilayers are an essential ingredient of many biological processes. In order to understand mechanisms at play for example in molecule translocation through membrane proteins, or interaction of the cell with nanoparticles (NPs), artificial, biomimetic membranes have been developed: supported or suspended bilayers, Giant Unilamellar Vesicles (GUV) which are micron-sized compartments. They constitute simplified models to decompose the elementary events (biochemical, physical, and chemical) at stake in real biological situations[1]. Existing Methods to work with these artificial membranes do not permit reproducible properties or complex configurations (size, chemical composition of the membrane). Microfluidics, the handling of fluids in microfabricated chips, offers new and versatile tools, both to fabricate more elaborated "artificial cells"[2] and to manipulate and study them[3].
We propose to combine microfluidics (LAAS team, https://www.laas.fr/public/en/mile), physico-chemistry with biological relevance (Italian team), and polymeric self-assemblies for nanomedicine (IMRCP team) in order to decipher biological processes occurring at cell membranes, particularly as regards nanoparticles/membrane interaction. Two applications are targeted: nanoparticles toxicity and nanomedicine.

A few results (more or less preliminary) will be discussed: Chips designed to characterize vesicle mechanical properties, in the spirit of on-chip micropipettes[4], show significant stiffening of GUV after their incubation with gold NP. They also permit to test hybrid vesicles, composed of mixtures of lipids and copolymers, promising in particular for nanomedicine[5]. The effects of photoactive drugs included in polymeric nanocarriers are also characterized in real-time on vesicles sensitive to oxidation, thanks to a microfluidic architecture permitting to switch inlet solution. Droplet-based configurations to fabricate GUV are also implemented.

On-going work aims at extracting quantitative information: improving designs, understanding how intrinsic properties (membrane bending modulus) relate to measured properties (such as the critical pressure to release a vesicle), as function of nanoparticles surface chemistry, membrane composition, flow conditions.

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