Electroporation in oxidized lipid bilayers

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Model lipid bilayers are useful biomimetic objects for understanding fundamental properties of the intracellular and the plasma membranes. Over the last decades, many self-assembling, manipulation and observation techniques have been developed to probe and understand adhesion, permeation, mechanical bending or stretching of these natural barriers. Although membranes formed from a variety of lipid compositions have been explored, little is known about membranes containing oxidized lipids. Yet, lipid oxidation plays a central role in the life of the eukariotic cells, where it is a direct consequence of the reactive oxygen species generated by mitochondrial respiration, but also relevant to understand many other processes such as inflammation, virus phagocytosis, and the consequences of ultraviolet irradiation.

We have recently published precise data on structure modification of unsaturated lipids upon oxidation of their double bonds, and on mechanical properties of membranes made from these oxidized lipids (see figure). During this PhD, we intend to study the influence of lipid oxidation on the electroporation properties of membranes. Recent preliminary measurements made by us have already shown that pores with unexpected stability can form in oxidized membranes submitted to a low electric tension (compared to non-oxidized membranes).

This work is mainly experimental. The student will use an innovative electroporation microsystem to study the formation, the stability, and the breaking down of membrane pores as a function of the applied electric tension. We will address systematically the role of membrane complexity in pore formation. We will study first a simple mixture of a given lipid with various fractions of its oxidized counterpart, and then build more complex biomimetic membranes made from mixtures of unsaturated, saturated lipids, and cholesterol, with a fraction of oxidized lipids. The experimental parts of this work will be made in close collaboration with Pierre Muller and André Schroder.

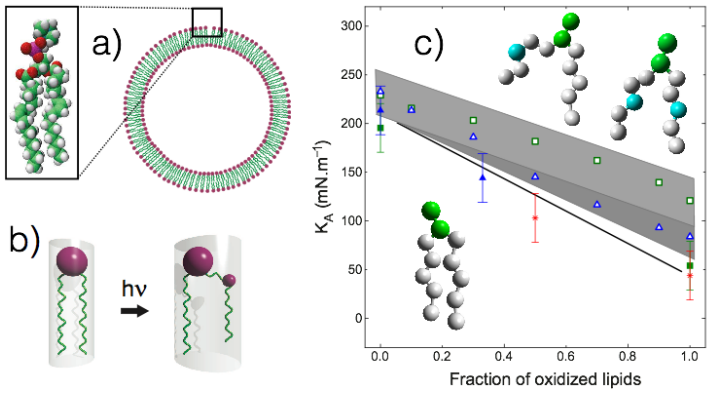

Figure 1 : a) phospholipids self assemble into bilayers, that close into capsules called liposomes or vesicles. b) when phospholipids are submitted to light irradiation in presence of a photosensible molecule, oxidation of a double bond of the lipid tail can occur, inserting an OOH group in the tail, and modifying the lipid structure and the membrane properties. c) decrease of the elastic modulus of a POPC membrane as a function of the fraction of oxidized lipids.