Bilayers at the ILL

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Shedding light into membrane receptor functioning and lipid interactions by plasmon waveguide resonance

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G-protein coupled receptors (GPCRs) are a large receptor protein family that sense molecules outside the cell and activate intracellular signal transduction pathways and modulate cellular responses. Since they are activated by extracellular stimuli of varied size and nature such as light, odors, hormones, and neurotransmitters, these receptors are extremely important therapeutic targets. Over the last decades, the comprehension of their activation mechanism provided by the growing number of high resolution structures has allowed significant advances. However, key aspects in the functioning of these proteins remain obscure, especially with respect to the role of the membrane lipid environment in the activation and signaling events. This can be in part explained by the lack of approaches that allow to follow such processes in a very sensitive and direct manner. We have developed an innovative technique named plasmon waveguide resonance (PWR) that is ideal to study thin anisotropic films such as proteolipid membranes[1].
PWR can be applied both to the study of GPCRs in their native cell membrane (whose membrane lipid composition can be altered) and in reconstituted model lipid systems of controlled lipid composition. Recent studies on the chemokine receptors CCR5 and CXCR3 will be presented concerning: 1) direct monitoring of CCR5 reconstitution in lipid model membranes and the role of cholesterol in receptor/ligand interaction[2]; 2) the complexity of CXCR3 pharmacology in the context of cancer development[3].
Additionally the impact of polyunsaturated fatty acids in Dopamine D2 receptor activation, in the context of lipid dysfunctions observed in psychiatric disorders will be discussed.

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