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Cell-surface mimics to study virus-membrane interactions

Virus entry is a complex dynamic multistep process requiring a series of fine-tuned events mediating virus diffusion through the glycocalyx, its attachment to the cell membrane and lateral diffusion to the point of entry. This is followed by entry, involving membrane fusion or membrane deformation into an endocytic vesicle.

The aim of our research is elucidate the mechanisms by which viral pathogens interact with the cell's membrane to cross it and penetrate into the cell. We focus on the interplay between the membrane's physico-chemical properties and the virus attachment process and study how cellular and viral molecules act in concert to modulate the processes through multivalency. Our research strategy widely relies of the use of artificial lipid bilayers to mimic *in vitro* the basic molecular architecture of the cell membrane. We further, take advantage of total internal fluorescence microscopy and single particle tracking to study, on a single particle level, virus attachment to and diffusion on the cell surface.

To illustrate the potential of such a biophysical approach, I will, in my presentation, first focus on the interaction between norovirus and glycolipid-containing membranes and investigate the role of ligands mobility and ligand clustering in modulating the affinity of the virus particle to the membrane.^[1] In a second example, I concentrate on the role of Influenza's matrix protein in virus budding and search for mechanisms by which the protein can induce membrane deformations. ^[2] In a last example, we use model membranes carrying glycosaminoglycans, to elucidate the molecular mechanisms modulating attachment and release of the herpes simplex virus. ^[3, 4]

Taken together, these examples illustrate the potential of artificial cell membrane mimics in the study of processes occurring at the surface of a cell and demonstrate how such biophysical data can complement more classical cell-biology experiments.

1. Bally, M., et al., Norovirus GII.4 virus-like particles recognize galactosylceramides in domains of planar supported lipid bilayers. *Angew Chem Int Ed Engl*, 2012. 51(48): p. 12020-4.
2. Saletti, D., et al., M1 from influenza C virus induces tubular membrane invaginations *in vitro*. *in preparation* 2015.
3. Peerboom, N., et al., Binding Kinetics and Lateral Mobility of HSV-1 on End-Grafted Sulfated Glycosaminoglycans. *Biophys J*, 2017.
4. Peerboom, N., et al., Cell Membrane Derived Platform To Study Virus Binding Kinetics and Diffusion with Single Particle Sensitivity. *Acsl Infect Dis*, 2018. 4(6): p. 944-953.

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