IMPRS on Multiscale Biosystems

Title: Message in a vesicle: Intercellular communication through extracellular vesicles

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Project description: Cells constantly release extracellular vesicles (EVs) of different origin and size (50 nm to 5 µm) that contain lipids, proteins, and various nucleic acid species of the source cell. EVs are attracting considerable interest in the scientific community due to their role in intercellular communication. Cancer cells have been shown to exploit EVs in tumor growth as well as preparing the pre-metastatic niche; neuronal survival and myelin formation have been proposed to involve EVs as well. Thus, EVs are increasingly employed as therapeutic agents in cancer, immune modulation and tissue regeneration. However, much remains unknown about the origin, secretion and fate of these vesicles.
Here, we intend to employ a bottom-up synthetic biology approach and build a biomimetic system allowing the study of EV generation and progression in an extracellular environment. For this, we will employ cell-sized giant unilamellar vesicles (GUVs, 10-100 µm) embedded in hydrogels mimicking the extracellular matrix, such as alginate, agarose or Matrigel, see Figure. Mechanical stress, pH and osmotic shocks will be used as triggers for GUV deformation and EV-like secretion. The diffusion of EV-like extruded liposomes (50-100 nm) in the matrix will be monitored with state-of-the-art techniques including confocal and super-resolution (STED) microscopy. Such biomimetic system will be compared with the secretion and diffusion of EVs of highly metastatic and weakly metastatic breast cancer cells.

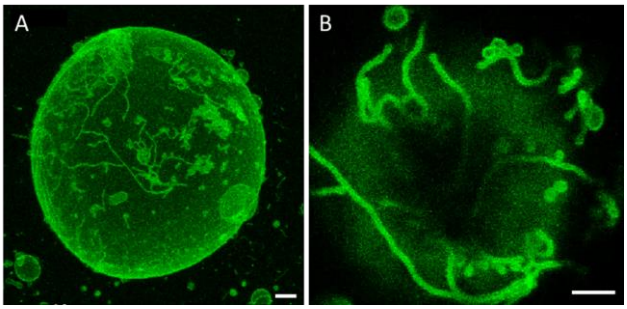

Figure: (A) Three-dimensional reconstruction of a GUV immobilized in an agarose gel. Note that the vesicle is non-spherical and slightly deformed by the gel and exhibits protrusions. (B) Magnified image of the upper surface of a GUV showing formed tubes protruding outwards and into the gel. Scale bars: 5 µm

Required background: MSc in biophysics, physics, chemistry or engineering; interest in physics of biological systems; interest in interdisciplinary work; basic knowledge of membranes and microscopy experience will be advantageous

Paper to read before the interview: van Niel et al., *Nat Rev Mol Cell Biol*. 19:213 (2018) doi:10.1038/nrm.2017.125; Wiklander et al, *Science Transl Med* 11:eaav8521 (2019) doi:10.1126/scitranslmed.aav8521; Lira et al., *Sci Rep* 6:25254 (2016) doi:10.1038/srep25254

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