Title: Bacterial mimetic systems for the study of bacterial inactivation and infection

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Project description: Electric-field treatments are abundant in medicine but biotechnology applications are emerging only now (see Trends Biotechnol 33:480, 2015). Bacterial inactivation (e.g. in waste water treatment) and gene transfection, both based on cell electroporation, are just two examples. The Gram-negative bacterial cell wall represents a complex matrix of lipids, proteins and glycans that form a rigid protective layer against the environment. It is also the main access point for antibiotic therapy and bacterial viruses (phages). Major components are lipopolysaccharides (LPSs), which maintain the outer membrane stability (Nature Reviews Microbiology 11:467, 2013). In contrast to eukaryotic membranes, models for the Gram-negative outer membrane are lacking, mainly due to the high aggregation propensity of LPSs (Biophys. J. 100:978, 2011). Aim of the project is therefore the construction of an LPS-containing in vitro model for a Gram-negative outer membrane using giant vesicles (see Figure) and to explore the mechanisms for membrane poration under electric fields. In the Barbirz Lab, the candidate will use highly purified LPS to prepare vesicles that mimic the Gram-negative cell envelope; bacteriophages specific for the glycan moiety of LPS will then be employed to investigate the properties of these artificial outer membrane systems. Microfluidics-based approaches for the vesicle preparation and manipulation will be explored in collaboration with the Robinson Lab. The vesicles will be characterized using fluorescence microscopy and biophysical techniques developed in the Dimova Lab. Their response to electric fields will be assessed with ultra-high-speed digital imaging.

Required background: MSc in biophysics, (bio)chemistry, physics or physical chemistry. Strong motivation for quantitative biophysical work and interest in interdisciplinary approaches. Basic knowledge of membranes and microscopy experience will be advantageous.

Papers to read before the interview: https://doi.org/10.1016/B978-0-12-396534-9.00001-5, DOI: 10.1039/B901963D, DOI: 10.1111/mmi.13729

Figure: Confocal cross sections of a giant vesicle before (left) and during (right) exposure to an electric pulse (arrow indicates field direction, time stamps show the time of pulse application). The membrane is labeled with a fluorescent lipid (green) and the vesicle is loaded with a water-soluble dye (red) which is entrapped in the GUV and is used as an indicator for membrane leakiness.

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