Mechanoresponsive Artificial Cells

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Artificial cells are highly functional forms of soft matter that mimic characteristics of biological cells. These artificial cells are constructed from the bottom-up by a wide range of molecular and particulate components that can be biological or synthetic in origin. This leads to the development of hybrid bio-/synthetic materials, often exhibiting additional novel properties that are not found in natural living systems. Reconstituting matter with life-like properties can provide new insights into biological systems, but also has broad potential for future industrial applications, including chemical manufacture, environmental sensing and remediation, and medical diagnostics and therapy.

In this project, we will develop mechanoresponsive artificial cells that reversibly change their permeability in response to mechanical stress. Microfluidic devices have been developed in the Evans group to investigate the deformation kinetics of living cells under hydrodynamic stresses (10.1016/j.bpj.2019.01.034). From these measurements, mechanical properties such as the Young's modulus and plasticity of the cell can be determined (**Figure 1**). Current hypotheses predict that the internal structure of a cell determines its response to inertial fluid forces, while surface properties of the cell's membrane determine its response to shear fluid forces. However, the high complexity of living cells makes these hypotheses challenging to test rigorously. Therefore, artificial cells provide an opportunity to systematically investigate how variations in the structure and composition of soft cell-like systems regulate their mechanical responses in fluid flow.

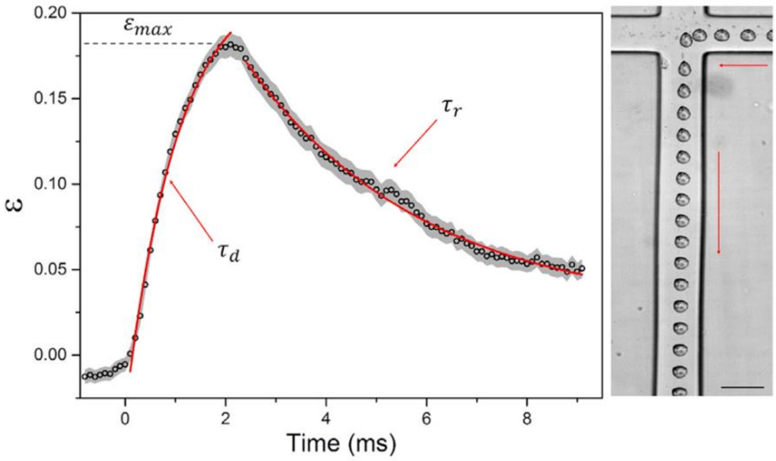

Figure 1. [*left*] Strain (ε) kinetics of HL60 cells under mechanical deformation induced by a microfluidic flow device [*right*]. The maximum strain (ε_{max}), deformation time (τ_d) and relaxation time (τ_r) of the cell can be determined. Cell plasticity can also be quantified by the non-zero strain that the cell initially relaxes to.

Artificial cells will be constructed using microfluidic assembly (10.1039/D0SM01684E). The structure and mechanics of the artificial cell membrane will be controlled using mixtures of lipids and block copolymers (e.g. 10.1039/D1SM01591E). Furthermore, cytoskeletal components can be encapsulated that scaffold the membrane. The internal structure of the artificial cells will additionally be varied by encapsulation of viscoelastic polymer solutions, nanoparticles and vesicle sub-compartments, mimicking the structure and granularity of eukaryotic cells. Phase separation within the membrane and/or the artificial cytoplasm can also provide structural heterogeneity to tune the mechanical response of these artificial cells.

The mechanical response of these artificial cells will be investigated using microfluidic flow-focusing devices similar to those previously developed to study living cells. The experiments will aim to: (i) provide new insight into the underlying biophysics of the mechanical deformation of living cells and (ii) create design rules for constructing bespoke mechanoresponsive artificial cells. Our findings will be used to create mechanosresponsive artificial cells that controllably and reversibly change their permeability in response to the forces of fluid flow. We will investigate the size and lifetime of pores that form within the artificial cell by investigating their transitory release properties under mechanical deformations.

Mechanoresponsive artificial cells with controllable changes in permeability will enable a range of technological applications that require the transfection of new reagents into the artificial cell or the controlled release of encapsulated cargo. The latter case would be particularly interesting for the design of novel cardiovascular therapies, e.g. artificial cells that mimic the release of ATP from red blood cells as a vasodilatory signal in response to shear stresses from constrictions in blood vessels (10.1073/pnas.0805779105).

In general, we aim to develop artificial cells where, by tuning their soft matter properties, mechanical cues from their environment can be used to trigger the release of a wide range of chemical signals from molecules to nanoparticles. The project will have a broad scope for the student to show initiative and creativity, co-creating new concepts and strategies with the supervisory team.