Magnetically actuated delivery vehicles

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Aim, motivation and hypotheses

Our aim is the creation of nanoparticle (NP) actuated vesicles, which can be used for spatial and temporal controlled release of substances such as peptides and assembled into scaffolds for tissue culture. To reach this aim multiple areas of expertise have to be combined to break new ground in the understanding of: design and assembly of polymersomes, nanoparticle assembly into amphiphilic vesicle membranes, local actuation and control of permeability of such membranes through incorporated nanoparticles and assembly of vesicles at high density in tissue engineering scaffolds. In order to do so we will combine complementary expertise from two groups in Vienna and Singapore in NP synthesis, block copolymer synthesis and the assembly of NPs into vesicular structures, and their characterization.

In a tissue culture platform, time and spatially programmed release would be highly desirable.[1, 2] A dose of e.g. growth factors often has to be given in concentrated dose a couple of days into a tissue culture, but not before.[3] The release profile is ideally programmable and not continuous. For tissues, where our model system will be the culture of embryonic bodies, the culture closes within 1-2 days and after that chemical stimuli cannot be delivered from the outside. Thus drug delivery vehicles that can be triggered to release at a given time point in response to an external trigger are especially useful for such cell cultures as the drug delivery vehicles can be incorporated on the inside of the cell culture at the start and then triggered to release later. We will primarily investigate triggered release vesicles with this application in mind.

In order to incorporate such delivery vehicles into scaffolds suitable for cell culture, and to allow for the simultaneous use of delivery vehicles for different substances and to protect them from cell induced degradation, we will further develop the concept of recently introduced so called capsosomes[4-6] with diverse and externally triggered actuated lipid and polymer vesicles incorporated in polyelectrolyte membrane films and capsules. Such PEMs have been shown useful as substrates for cell and tissue culture and will also protect its encapsulated interior from direct cell induced degradation.

Triggered release will be achieved primarily through ultra-stable, hydrophobically coated, core-shell superparamagnetic iron oxide NPs,[7, 8] which we have already shown can be incorporated into stable lipid vesicle membranes[9] and which we hypothesize can be incorporated in any fluid type of amphiphilic membrane of similar dimensions, including amphiphilic block copolymer membranes.

Embedded particles can actuate vesicle membranes through applied magnetic fields, which can localize (by static magnetic fields (SMF)), image (by magnetic resonance imaging) and trigger release (by local heating through alternating magnetic fields (AMF) or deformations (through SMF or AMF).[10] The major scientific challenge is to understand the relationship between the design parameters of NPs (used for actuation), responsive membranes (used to control permeability) and polymer scaffolds (used to integrate, order and protect delivery vehicles into substrates for e.g. tissue culture). The working hypothesis, supported by our preliminary work, is that with sufficient control and stability of interfacial properties of both NPs and vesicles, stable vesicular and other membranous superstructures can be assembled which directly couple energy induced through the NP transducer to responsive elements of the supramolecular (lipid or polymer) scaffold. By creating responsive structures with weak supramolecular interactions, sharp phase transitions can be designed to trigger release through such systems without major side effects on the local environment. Recent advances in NP functionalization and vesicle assembly have shown that indeed such levels of control and design are possible, but detailed investigations of membranes actuated by incorporated NPs or their further assembly into smart materials structures for biomedical applications are still lacking.

We will give particular focus to understanding and tailoring the properties of the vesicular membranes (e.g. hydrophobic core thickness, fluidity, molecular composition, hydrophilic shielding region and charge) and the properties of the NPs (size, hydrophobic coating, functionalization, charge and loading fraction). Our detailed hypothesis is that incorporation of magnetic NPs of high magnetic moment (requiring cores >10 nm in diameter) into an amphiphilic membrane will allow more powerful actuation of the permeability of the membrane both by high frequency AMFs (through heating leading to membrane phase transition) and by static or slowly varying magnetic fields (deformation of the membrane leading to pore formation). Preliminary results on liposomes have shown a direct experimental relationship between the thickness of the membrane hydrophobic core and the size of the incorporated NPs, and therefore we expect to find and investigate the optimal trade-off for polymersomes that allows maximum control over membrane permeability as well as an optimal NP design and membrane loading fraction to avoid aggregation and passive leakage but yielding efficient release.

References

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