to the stresses of hypo-osmotic shock and isotonic recovery, and membrane integrity is quantitatively evaluated with or without the presence of block co-polymers. The cell protection required sufficient hydrophobicity of the block copolymers, controlled by either the hydrophobic PPO block or endgroup modification. At least 9 PPO units were needed for protection at 150 μM. Addition of hydrophobic tert-butyl endgroup enhanced the protection ability at reduced concentration. With fixed hydrophobicity, increasing hydrophilic PEO block length improved protection. In addition to the cellular integrity assay, we synthesized fluorophore-labeled block copolymers and performed confocal microscopy to image subcellular localization to further understand the membrane protection mechanism.

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Interactions of Lipid Multilayers in the Presence of ATP

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One interesting class of biomaterials are multilamellar stacks of phospholipid bilayers. Phospholipids (lipids in short) found in biological membranes are of significant interest in material research due to their distinctive mechanical and electrical properties. In water or buffer solutions, lipids spontaneously form membrane structures with thicknesses on the order of 4-5 nm. In addition, van der Waals attraction causes membranes to form regular stacks of many layers with repeat lattice spacings (D-spacings) on the order of tens to hundreds of nanometers. The D-spacing depends on both lipid type and on the composition of the buffer solution in which membranes are formed. Adenosine triphosphate (ATP) is a molecule involved in energy transfer in biological processes and is therefore of interest in bio-inspired material research. Using three complementary experimental methods, namely small-angle x-ray scattering (SAXS), NMR spectroscopy, and dynamic light scattering (DLS), as well as molecular dynamics simulations (MD), we show that ATP can be used to modify the material properties of lipid stacks. In particular, ATP induces an ubinding transition from multilamellar to single layers followed by reforming of multilayer structures as ATP concentration is increased. This effect is also seen with ADP and AMP at progressively higher concentrations. These findings can help design applications in which ATP and its hydrolysis products can control material properties of layered structures.

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Biomimetic Membrane Design Principles for Angstrom Scale Separation

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Functional biomimetic membranes are membrane protein-polymer based, or membrane protein-lipid based hybrid membranes. Biomimetic membranes can preserve membrane protein function and have been applied to areas such as DNA sequencing, drug delivery and water purification. Especially the discovery of Aquaporins has promoted studies into the development of biomimetic membranes as highly selective and permeable separation membranes. This presentation will describe our work on biomimetic membrane design principles, including both biomaterial selection for highly integrated biomimetic membranes with compatible protein-polymer combinations and robust membrane protein redesign targeting accurate small molecule separations.

For biomaterial selection, we studied a range of amphiphilic materials used for membrane protein incorporation, and investigated their influence on Aquaporin performances in biomimetic membranes. We found that average single protein activity remained unchanged while reconstitution density varied when using different biomimetic materials. Moreover, we found that minimizing chemical hydrophobicity mismatches between membrane materials and proteins lead to high protein reconstitution density. This provides a strategy to increase the overall permeability of biomimetic membranes.

In addition, we also developed a method to create a membrane protein ''library'' with different pore sizes. Using Outer Membrane Protein F (OmpF) as a ''scaffold'', we created variety OmpF mutant designs with pore sizes less than 4 Å by computational design procedures. Experimental results revealed these designs maintained protein water permeability exceeding classical AQPs by more than an order of magnitude at over 10 billion water molecules per second, while providing specific pore designs that exclude sucrose (342Da) and larger solutes, glucose (180Da) and larger solutes or salt (58Da) and larger solutes. This new protein redesign and testing workflow provides us the ability to design specified Å pore size to conduct Angstrom-scale aqueous separations by using the precisely designed membrane protein based biomimetic membranes.

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A Fluorescent Nanoprobe for the Detection of in Situ Temperature Changes during Hyperthermia Treatment of Tumors

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Magnetic hyperthermia is a promising new treatment, allowing to locally induce a temperature increase in cancer tumors that leads to a lethal effect. For this, magnetic nanoparticles are introduced in tumors and exposed to an alternative magnetic field which produces the wanted temperature rise. While the final biological effect can be assessed by many techniques, the in situ temperature changes are often difficult to evaluate otherwise than with a regular thermometer. This fairly crude procedure does not allow to finely report changes at the tissue or cell level. In this context, we report here an original method based on a chemical nanoprobe designed to follow temperatures changes during hyperthermia therapy. In our work, AMB-1 magnetotactic bacteria produce the magnetic nanoparticles (magnetosomes), since we have already shown that this type of nanoparticles had a much better magnetic activity than chemically synthesized particles (Alphandery et al. ACS Nano, 2011, 5:6279). Interestingly, by introducing rhodamine B in an optimized growth medium for these bacteria, we were able to extract fluorescent magnetosomes with new characteristics. Indeed, keeping their typical magnetic activity useful for cancer therapy, they would also display a temperature-dependence fluorescence allowing to perform local measurements at a microscopic level in biological tissues. The molecular mechanism would be discussed, as well as results obtained with different cell types (RG2, TC1-GFP, C57NL/6 peritoneal macrophages, U87-MG) and tissues (RG2-implanted rat brain).

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Biocompatible Coated Magnetosome Minerals for Application in the Magnetic Hyperthermia Treatment of Tumors

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Glioblastoma are aggressive brain cancer tumors with very poor prognosis; they often cannot be eradicated using conventional therapies, mainly because of their treatment resistance and ability to infiltrate the surrounding brain tissue. In this context, a promising technique leading to an increased patient life expectancy is currently assessed: magnetic hyperthermia. For this, magnetic nanoparticles are introduced into tumors and exposed to an alternating magnetic field, inducing a lethal and localized heat increase. These nanoparticles are either chemically synthesized (superparamagnetic iron oxide nanoparticles (SPION)), or obtained from bacteria that naturally produce such particles for their own biological activity. These "magnetosomes" attract much attention because of their specific characteristics. Indeed, compared with SPION, magnetosomes are better crystallized, yielding to improved magnetic properties. In this work, they were extracted from MSR-1 magnetotactic bacteria, purified to remove potentially toxic organic bacterial residues and replaced by various biocompatible coating agents. The coated magnetosomes that we obtained were characterized by transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FT-IR) and CHNS analysis. *In vitro* studies were carried out to evaluate biocompatibility on mouse fibroblast cells (3T3) and mouse glioblastoma cells (GL-261) cell line. The heating properties and cytotoxicity effect of magnetic hyperthermia on GL-261 cell line of the coated magnetosomes were also evaluated. References: 1) Y. Hamdous, et al. *J Nanobiotechnol* 2017. *In press* and 2) C. Mandawala et al. *J. Mater. Chem. B* 2017. *In press*.