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Cell inspired force and light responsive polymersome nanoreactors and polymerisation based diagnostics

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Cellular adaptation is the result of millions of years of evolution. Cells can adapt to chemical and macroscopic stimuli by generating changes in the permeability of their membranes. This is generated by the amplification of these stimuli into a variety of chemical pathways. This thesis focusses on the generation of polymersome membranes which could selectively and reversely adapt to macroscopic stimuli such as force or light by generating changes in permeability to small molecules. During this thesis, the mechanically induced melting properties of DNA were employed to achieve force labile membranes. Nucleobase pairs were used as mechanophores. Adenine and thymine functionalised complementary amphiphilic block copolymers were self-assembled into polymersomes. The nucleobases formed hydrogen bonds which were disrupted upon shearing. The exposure of the unpaired nucleobases to the hydrophobic matrix of the membranes leads to a change of permeability which permitted the exchange of water-soluble molecules throughout the polymer matrix. Moreover, the encapsulation of horseradish peroxidase enabled to achieve force responsive nanoreactors which could catalyse a variety of chemical reactions.

Donor-Acceptor Stenhouse Adducts (DASAs), with their ability to switch polarity upon irradiation with visible light, were employed to change the permeability of polymersome membranes. To this end, amphiphilic block copolymers were functionalised either with a DASA that is based on Meldrum's acid, or with a novel fast switching pyrazalone-based DASA. These polymers were self-assembled into vesicles. Release of hydrophilic payload could be triggered by light and stopped as soon as the light was turned off. The encapsulation of enzymes yielded photo-responsive nanoreactors that catalysed reactions only if they were irradiated with light. A mixture of polymersome nanoreactors, one that switches in green light, the other switching in red light, permitted to specifically control the individual reactions of a reaction cascade in one pot by irradiation with varied wavelengths, thus enabling light-controlled wavelength-selective catalysis.

Finally, cellular amplification systems were taken as the inspiration to generate a polymerisation-based amplification method for the detection of analytes which could catalyse Atom Transfer Radical Polymerisation (ATRP) reactions. In this thesis I report an ultrasensitive, yet low-resource chemical assay for the detection and quantification of hemozoin, a metabolic by-product and biomarker of all Plasmodium sp. Solubilised hemozoin catalysed the atom transfer radical polymerisation of N-isopropylacrylamide above the lower critical solution temperature of poly(N-isopropylacrylamide). The solution becomes turbid, which can be observed by naked eye and can be quantified by UV-visible spectroscopy. The rate of turbidity increase is proportional to the concentration of hemozoin, with a detection limit of 0.85 ng mL-1 (1.4 parasites µL-1 of blood). The assay was found to be 140-times more sensitive than other malaria rapid diagnostic tests and could be applied as a point-of-care test in the field. The signal-amplification of an analyte by biocatalytic precipitation polymerisation represents a powerful novel approach in biosensing. As haemoglobin is also known to catalyse ATRP reactions, the same approach could be used also to quantitatively detect minimal concentrations of haemoglobin in biological fluids, i.e. at concentrations or tissues were it is indicative of disease. The high sensitivity of the tests relied on the amplification on two levels: intrinsic catalytic turnover of the polymerisation reaction and radical chain growth.

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