

Redox-active polymer microcapsules for DNA delivery

Presented by Alisa L. Becker – Structured Matter

Nucleic acid therapeutics such as siRNA and gene therapy are promising drug candidates for several disease states. However, progress in this field has been hindered by the difficulty of delivering intact drugs. Nucleic acids such as DNA and RNA are rapidly degraded in the blood stream, and so they require protection to reach the site of action. In addition, when they reach the cell they are unable to efficiently cross the cell membrane unaided, due to their high charge. To solve these problems, we have developed an encapsulation method that aims to protect the DNA in the blood stream, allow it to cross the cell membrane and selectively release the drugs when the vehicle has reached the cytoplasm of the cell. Hollow polymeric capsules in the size range of 300 nm to 5 μm can be formed using the layer-by-layer (LbL) technique for thin film formation. Thiol-functionalized poly(methacrylic acid) (PMA) and poly(vinylpyrrolidone) were deposited alternately on a sacrificial colloidal template using hydrogen bonding for thin film build-up. After cross-linking and core removal, hollow capsules are obtained. Using disulfide cross-links between PMA layers gives rise to redox-active deconstructable capsules. The reducing environment within a cell changes the disulfides to thiols, and the capsules are able to deconstruct and release their cargo. Variation of the thiolation degree and molecular weight of PMA can control the capsule properties and cargo release. DNA was encapsulated within semi permeable capsules by adsorption of DNA onto amine-functionalized silica (SiO_2^+) particles, followed by thin film formation using LbL, and removal of the sacrificial SiO_2^+ particles (Figure 1). DNA ranging from oligonucleotides to plasmids was encapsulated. DNA that was encapsulated and subsequently released was active in polymerase chain reactions and was also transcriptionally active in *E.coli*, indicating minimal functional loss.

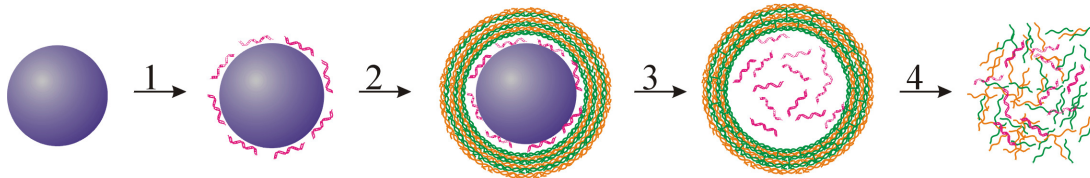


Fig. 1: Encapsulation of DNA within polymeric microcapsules. 1. Adsorption of DNA onto positively charged silica. 2. LbL thin film formation. 3. Cross linking and core removal. 4. Capsule deconstruction and DNA release

Email contact: a.becker@pgrad.unimelb.edu.au