Stabilization and Functionalization of Superparamagnetic Iron Oxide Nanoparticles (SPIONs)

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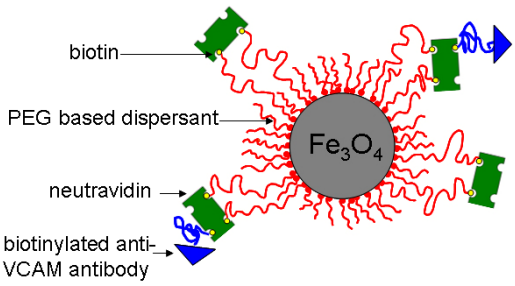

Figure 1: Layer-by-layer build-up of individually stabilized, functionalized SPIONs

Superparamagnetic iron oxide nanoparticles (SPIONs) are not only of scientific but also of commercial interest e.g. for contrast enhanced magnetic resonance imaging (MRI). Commercially available iron oxide based MR contrast agents are often stabilized with high molecular weight surfactants such as dextran or siloxanes. The comparably low binding affinity of these surfactants towards iron oxide leads to poor particle stability and limited control over the interfacial chemistry. The latter point is important for efficient targeting which is thought to lead to cellular or even molecular resolution in MRI. The stabilization of individual iron oxide cores with low molecular weight dispersants, which have one high affinity binding group per molecule, is an attractive alternative to the commercially used stabilization method. It not only leads to higher particle stability but also allows for a smaller hydrodynamic diameter and a controlled interfacial chemistry.

Superparamagnetic iron oxide nanoparticles have been synthesized by an aqueous precipitation route[1]. PEG-gallol, a low molecular weight, single chain, one foot, dispersant, was used to individually stabilize these SPIONs (fig. 1). Gallol shows a comparably high binding affinity towards iron oxide. It is a derivative of the amino acid DOPA, abundantly present in the mussel adhesive protein Mytilus edulis[2]. These PEG-gallol coated particles are stable under physiological conditions for more than 9 months. Furthermore, we could design the interfacial chemistry of these nanoparticles by adsorbing a mixture of methoxy terminated and biotinylated PEG-gallol on iron oxide nanoparticles. This allowed us to functionalize these nanoparticles with any biotinylated ligand using the neutravidin-biotin linkage. After having compared the size, size distribution and magnetic properties PEG-gallol stabilized SPIONs to Feridex, a commercially available dextran stabilized iron oxide based MR contrast agent, the amount of PEG-gallol and neutravidin adsorbed on one particle was quantified. Finally, biotinylated anti-human VCAM antibodies were bound to these individually stabilized neutravidin bearing SPIONs. VCAM is thought to be an early marker of atherosclerosis and a well suited receptor for targeted MR contrast agents[3]. Specific, fast and strong binding of so-functionalized particles was shown by *in vitro* quartz crystal microbalance with dissipation monitoring (QCM-D) measurements. The high particle stability, close control over the hydrodynamic diameter, narrow particle size distribution and high flexibility for further functionalization of these SPIONs opens up attractive possibilities for further studies mainly, but not exclusively, in the field of targeted MRI.

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2 Waite, J. H. and Tanzer, M. L., *Biochemical and Biophysical Research Communications* **96** (4), 1554 (1980).

3 Kelly, K. A., Allport, J. R., Tsourkas, A., Shinde-Patil, V. R., Josephson, L., and Weissleder, R., *Circulation Research* **96** (3), 327 (2005).