Production and application of polymeric nanoparticles for the optical determination of physiological parameters

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Keywords: polymeric nanoparticles, optical sensors, light harvesting, oxygen imaging

Recently, polymeric nanoparticles attracted interest in such different fields as drug delivery, nanotherapeutics, multi-modal imaging, catalysis and optical sensing. Especially for optical sensing, nano-structured materials can be highly advantageous compared to their bulk analogs. Response times are significantly lower and the spatial resolution in imaging applications is greatly improved. Moreover, nanoparticle sensors are more favorable than dissolved indicator dyes because of several reasons. Dyes are safely embedded in a matrix which inhibits signal distortion by interferents such as ionic species and also minimizes the dyes' leaching into the media which could have toxic effects on biological samples. Moreover, a fine-tuning of the sensor properties is easily possible by adjusting the composition of the matrix.

In our laboratory, we developed a range of different polymeric sensor particles, with functions even beyond optical sensing [1-3]. These particles are *e.g.* magnetically separable which greatly improves their functionality. They can be trapped in front of an optical fiber to produce a sensor spot for read-out or can be used to cover the surface of a biological sample for measuring the analyte concentration (figure 1). After the experiment, the particles might be released and recovered by magnetic separation.

Due to the small sizes of nanoparticles it is also possible to use confocal microscopy for 3D imaging of analytes. Nanoparticles can – depending on their size – either surround the cells and elucidate inter-cellular metabolite concentrations or even penetrate cells and allow to image intra-cellular metabolic parameters. Especially when the sensing layers are very thin it is important to have powerful dyes which ensure high signal intensities. This can be accomplished by a light-harvesting system [4,5]. Using such a combination of dyes, the energy of a broad light spectrum is transferred to a single sensor dye (figure 2a). Thereby, the signal intensity can be greatly enhanced (figure 2b). This concept can be extended for the development of two-photon sensor dyes.

To better understand the sensor and material properties of the here described nanosensors and to get an overview of the processes that occurred during the particle synthesis, we also investigated our samples by electron microscopy. We succeeded, for example, in imaging the swelling of PS-PVP nanoparticles from 122 to 152 nm *in situ* by ESEM with a Peltier cooling stage (figure 3). Moreover, porous structures of our particles could be proved by electron microscopy. It was also possible to understand why spray-dried particles behaved similarly to nanoparticles providing both extraordinary sensor properties.

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6. We gratefully acknowledge the technical assistance of S. Fladischer and DI C. Gspan.

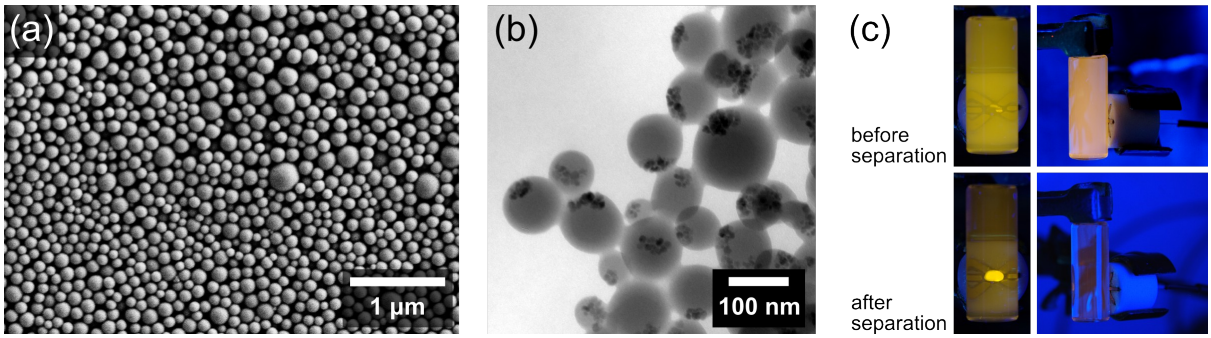

Figure 1. Magnetic Optical Sensor Particles (MOSePs). In (a) and (b) a SEM and TEM image of the polymeric particles with incorporated superparamagnetic iron oxide nanoparticles (darker particles in b) can be seen. The surface of these particles is hydrophilic which ensures stable dispersions in aqueous media, whereas the magnetic properties allow separation at a desired position (c).

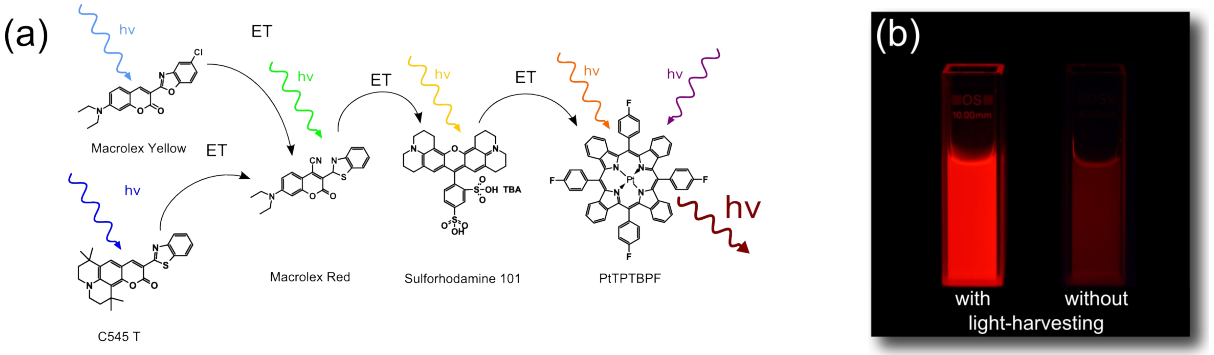

Figure 2. a) A light harvesting cascade collects light of different wavelength and transfers the energy to a final oxygen sensing dye. This significantly increases the brightness of such sensor particles (b).

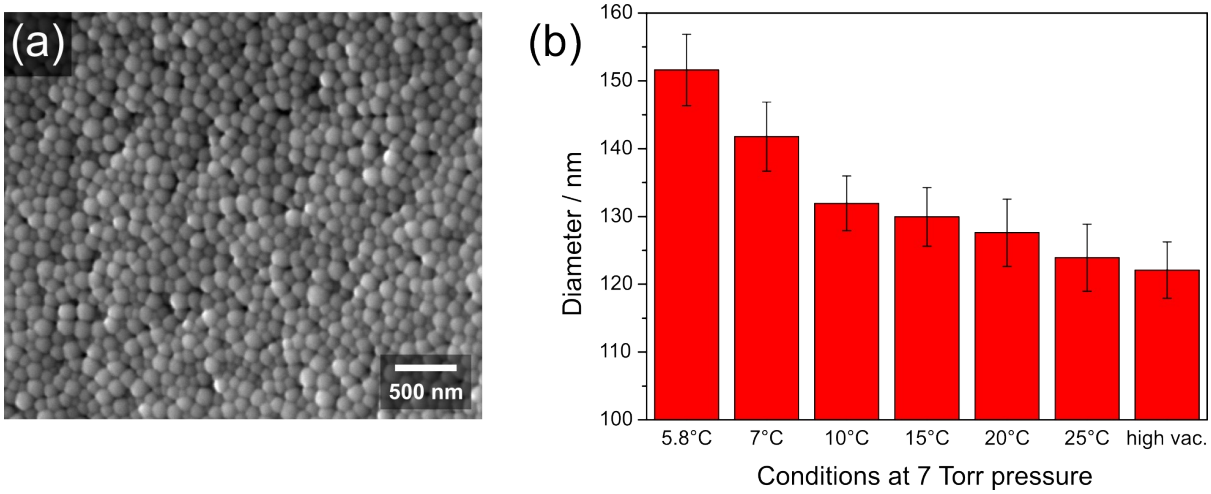

Figure 3. a) ESEM image of water dispersible, core-shell poly(1-vinylpyrrolidone-*co*-styrene) particles. In (b) the drying process of the particles from their swollen state at 5.8°C (7 Torr) to their dry state at 25°C and high vacuum was followed by in-situ environmental scanning electron microscopy.

DOI: 10.3217/978-3-85125-062-6-453 , © Verlag der TU Graz 2009