

Polymer and Colloid Highlights

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Continuous Synthesis of Gold Nanoparticles Using the Segmented Flow Tubular Reactor (SFTR)

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Nanomaterials are nowadays produced in many laboratories worldwide at the mg scale *via* bottom-up approaches. The up-scaling from mg to g quantities by increasing the reactor volume, maintaining a well-defined particle size distribution (PSD), morphology, stoichiometry and polymorphic phase, is generally problematic because of the lack of fine control over mass and heat transport in large batches. In fact, the relative contribution of elementary processes which control the solid formation from solution, such as nucleation, growth and agglomeration, are extremely sensitive to the local environment of each particle.

In the last 20 years, a reliable concept for high quality nanoparticles (NPs) production in relatively large quantities was developed: the Segmented Flow Tubular Reactor (SFTR).^[1–7] The SFTR concept is as elegant as it is simple: instead of increasing the batch size, the number of small reactors, in form of droplets, is multiplied. The physicochemical transformation occurs in droplets confined in a tubular reactor and segmented by a secondary immiscible fluid. The solid formation could occur in water^[2–4] or in organic solvent,^[5,6] expanding the portfolio of the possible chemical reactions. This methodology was applied for the preparation of metals, simple and complex metal oxides, and salts. Here we present an additional SFTR product, gold NPs for biomedical application. The synthesis is realized by the citrate route, *i.e.* by reducing the gold precursors (HAuCl₄) with sodium citrate in water. Using the SFTR, the concentration of the chemicals, their ratio, the aging temperature and time can be accurately controlled and reset to different values within minutes, allowing a rapid screening of several experimental conditions. Fig. 1 shows an example of Au NPs prepared at 95 °C, with an aging time of 5 min, at the flow rate 1 L h⁻¹ and at the concentration of about 0.2 g L⁻¹. As demonstrated by several systems, the material properties, such as the PSD, are maintained over time thanks to the prevention of fouling action of the segmenting fluid. The daily throughput of such gold NPs can easily reach 5 g per reaction tube. The NP suspension can be concentrated by ultrafiltration and purified by dialysis.

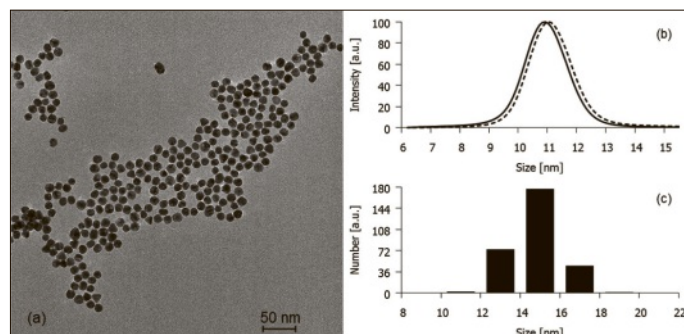


Fig. 1. (a) Low magnification TEM micrograph of Au NPs; (b) particle size distribution in number (–) and volume (–) by differential sedimentation methods, CPS Instruments, Inc. and (c) in number from TEM micrographs.

The SFTR technology is able to provide NPs with a narrow PSD, in a reproducible manner, at a limited cost, and in relatively high amount. The colloidal suspensions were produced to assess the interaction between NPs and biological systems by *in vitro* testing; they will be applied as long-term reference materials for toxicology, traceability, reliability, and measurement uncertainty testing by interlaboratory comparison that involves different Swiss research institutes and industrial partners with a direct link to regulatory European and American medical institutions.^[8]

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