

Synthesis of thiol functionalized gold nanoparticles using a continuous flow microfluidic reactor

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Abstract

Microfluidic devices show much promise for the controlled synthesis of materials on the nanoscale. In this work the first report of a synthetic method for the preparation of nanoparticles of gold stabilized by an adsorbed monolayer of a thiol (monolayer protected clusters) using a microfluidic device is described. Improvements in monodispersity are observed relative to bulk synthetic methods.

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1. Introduction

Since the early work by Schmid [1], Giersig and Mulvaney [2] and Brust et al. [3] there has been much interest in the synthesis and application of thiol-passivated gold nanoparticles, often called monolayer protected clusters (MPCs). This interest derives from the versatility conferred on them through the protecting thiol monolayer. A typical thiol, $\text{HS}(\text{CH}_2)_n\text{X}$, allows properties such as chain length (denoted by n) and the chemical identity of the terminal functionality (denoted by X) to be modified either through the choice of the thiol, through ligand exchange (where one thiol replaces another either partly or completely) or through chemical modification by reaction with an appropriate terminal group on the thiol [4]. The thiol layer also confers the significant benefit of making the particles stable and isolable and allowing them to be re-suspended if desired. However, many suggested applications of these clusters, such as the construction of organized superlattices [5], require the preparation of particles

or clusters exhibiting narrow size distributions [6]. In some cases this can be achieved by fractional crystallization [7] or gel electrophoresis [8] of a polydisperse particle population. Alternative proposals towards reducing polydispersity include exploitation of size-dependent solubility of thiol derivatised gold nanoparticles in supercritical ethane [9] and digestive ripening [6]. The standard synthetic method [3] for the production of MPCs involves extraction of tetrachloroaurate (III) ($[\text{AuCl}_4]^-$) from an aqueous solution into toluene followed by the addition of a thiol. The mechanism is thought to follow a nucleation-growth-passivation process [4] and it seems that the first step produces a gold (I) thiolate oligomer or polymer $(-\text{AuS(R)}-)_n$ through sacrificial reduction by the thiol (represented by RSH). The polymer is then reduced by the addition of aqueous NaBH_4 , resulting in gold clusters that are surrounded by a monolayer of thiol. The influence of factors such as $\text{RSH}:[\text{AuCl}_4]^-$ mole ratio, temperature and the rate of reductant addition on particle size has been investigated [4,10]. Small particles are favoured by a large thiol:gold mole ratio, by swift addition of reductant and by lower temperatures. Crucially however, such studies have been performed in macroscopic reaction vessels. Recent work has shown that microfluidic devices are promising alternative tools in the synthesis of compound semiconductor nanoparticles such as CdS [11] and CdSe [12,13] and metal nanoparticles [14,15]. Such devices have the advantage of eliminating local variations in

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reaction conditions such as concentration and temperature and of allowing rapid, reproducible changes in these conditions should they be desired. In addition, microfluidic devices can be used to achieve rapid and controllable mixing via diffusion-mediated transport, and therefore aid in the control of both nucleation and particle growth [11]. We therefore reasoned that such systems have the potential for the controlled production of thiol functionalized nanoparticles or MPCs and report here the first synthesis of MPCs within a microfluidic device.

2. Experimental

2.1. Synthetic methods

The synthesis of MPCs followed the well-established literature method [3] with the pre-preparation of the gold thiolate polymer through the phase transfer of tetrachloroaurate (III) (0.155 g dissolved in 12.5 mL of pure water) into 40 mL of toluene using tetra-octylammonium bromide (0.75 g). As the phase transfer proceeds, the yellow aqueous phase turns clear and the toluene turns orange-red. After isolation of the organic phase using a separating funnel, 1-dodecanethiol was added (to achieve different mole ratios of $\text{RSH}:[\text{AuCl}_4]^-$, 0.19 mL of dodecanethiol provides a ratio of 2:1). The resulting solution containing the gold

thiolate polymer was then employed as one reactant stream in the microfluidic device with aqueous NaBH_4 (sodium borohydride) as the other. More details of the borohydride solution are provided below. Two different microfluidic devices were employed, and for each the mole ratio of $\text{RSH}:[\text{AuCl}_4]^-$ was varied. All experiments were performed at room temperature and the particles were analysed by ^1H NMR, UV–Visible absorption spectroscopy and transmission electron microscopy. In contrast to the experiments with CdS [11] and CdSe [12], where fluorescence or absorption spectra may be employed to monitor particles as they form within the microfluidic system, the MPCs produced here were collected and washed with ethanol and acetone prior to off-chip characterization.

2.2. Microfluidic device fabrication

Fluidic channel patterns were designed using AutoCad 2002 and fabricated using standard photolithographic, wet chemical etching and bonding procedures. In brief, the channel design was transferred to a positive photoresist coated chrome/glass substrate (Nanofilm, Westlake Village, CA, USA) using a direct write laser lithography system (DWL 2.0; Heidelberg Instruments, Heidelberg, Germany). The exposed regions of the photoresist were removed using a resist developer (Microposit 351, Shipley Europe

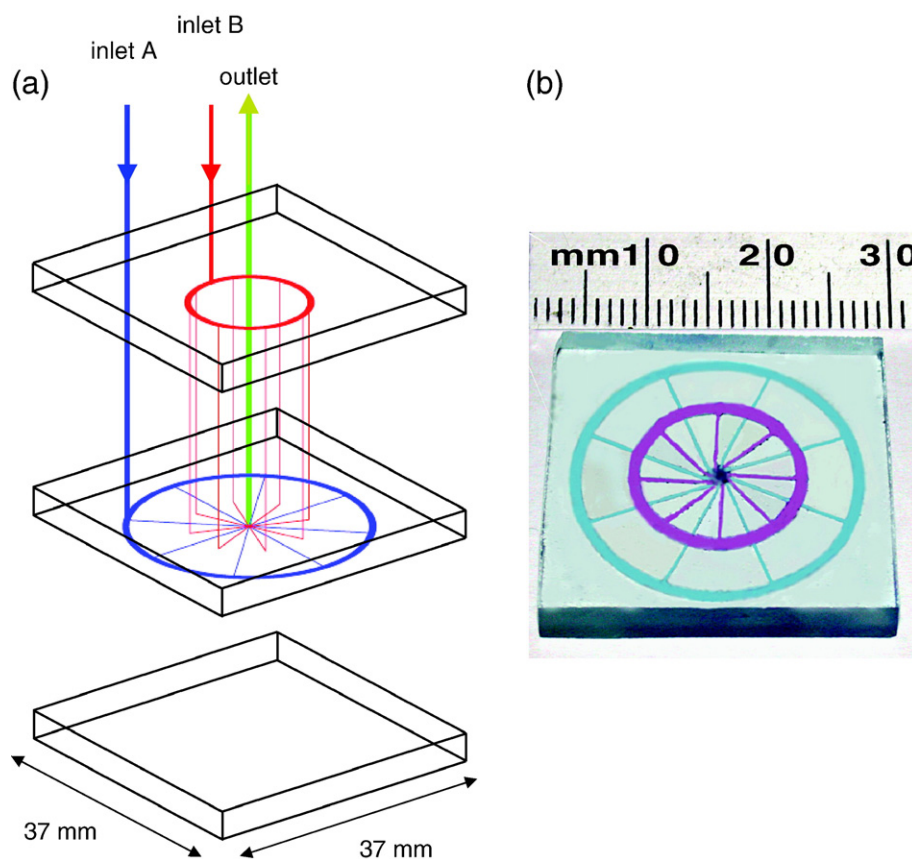


Fig. 1. (a) Three dimensional schematic of a radial interdigitated mixer. Each mixer is fabricated in 3-layers. In the first two layers input flows are directed to two circular bus channels which, in turn, split the flow into 8 identical fluid laminae and deliver reagent streams towards a central mixing chamber. The final layer acts as a cap to enclose channels and as a guide for input and output capillaries. The output is from the centre of the uppermost layer. (b) Photograph of the fabricated mixer. Microchannels are filled with dye solutions to show different shadings for the different channels.

Table 1
Particle size data (as measured from TEM analysis) for conventional bulk syntheses and for syntheses carried out with the radial interdigitated mixer

Thiol–gold ratio	Flow rate (mL/min)	Average particle diameter (nm)	Number of particles analysed
2:1	400	3.7±0.9	229
2:1	600	3.0±0.6	83
2:1	800	2.9±0.6	88
2:1	Bulk	4.9±2.1	62
3:1	400	3.5±0.7	148
3:1	Bulk	4.0±1.3	43

Ltd, Coventry, UK). The chromium layer was then removed using a chrome etchant (Lyodine, Microchem Systems Ltd, Coventry, UK). Channels were then etched into the substrate using a buffered oxide etching solution (HF–NH₄F) at ambient temperature. The remaining photoresist was then removed using dimethylformamide (DMF) and the chrome layer was removed using chrome etchant. Once complete, the etched substrate was washed sequentially in methanol and DMF and then immersed in H₂SO₄ for 1 h. The substrate was washed with ultra-pure water at ambient temperature, and dried with N₂ gas. Finally, a cover plate was thermally bonded to the substrate by heating the assembly at 550 °C for 1 h, 580 °C for 5 h and 555 °C for 1 h. The complete device was then allowed to cool for at least 8 h. Holes drilled in the top plate allow access to the fluidic network below. The structured microchannels exhibited an average depth of 60 µm and width of 150 µm.

2.3. Microfluidic system operation

Due to rapid particle formation and the high surface-to-volume ratios typical of microfluidic reactors, particle aggregation on channel surfaces is a common occurrence within simple T-mixer geometries. Accordingly, continuous flow reactors were designed to allow rapid and efficient mixing of reactants whilst allowing operation at relatively high flow rates ($\sim 1 \text{ mL min}^{-1}$). Devices were based on a radial interdigitated mixer design (Fig. 1) and function by diffusive mixing between 16 input laminae streams. Each mixing structure consists of 3 substrate layers. In the first two layers input flows are directed to two circular bus channels which split the flow into 8 identical fluid laminae and deliver reagent streams towards a central mixing chamber. The final layer acts as a cover to enclose channels and as a guide for input and output capillaries. During mixing, flow streams are brought together alternately in a radial sense and mixing is achieved via diffusion. The 16 convergent channels have a width of 150 µm and a depth of 50 µm. Fourier number calculations for monophasic flows in the fabricated structures indicate that complete mixing ($\tau=1$) occurs in the outlet capillary at volumetric flow rates of 900 µL min^{-1} or less and adequate mixing ($\tau>0.1$) occurs at flow rates lower than 4500 µL min^{-1} . Reynolds numbers remain lower than 20 for all flow rates employed. For the biphasic systems employed in the experiments described herein well-ordered bubble flow was observed in all cases, leading to maximized interfacial surface areas.

To further discourage particle aggregation silanisation of channel surfaces was performed using a 10% solution of trichloro (1H,1H,2H,2H — perfluoro-octylsilane) in tetrahydrofuran and injection of a distinct plug (rather than a continuous flow) of the gold thiolate polymer. This was achieved using a 50 µL, 6 port Rheodyne injection valve mounted between the syringe pump and chip inlet. Finally, it was observed that the use of aqueous sodium borohydride generated gas bubbles within the microchannels. This is due to the well-documented decomposition of borohydride reagents in aqueous conditions. To minimize gas bubble formation and disruption of hydrodynamic flow, iso-propanol was used as a co-solvent with water. A stock solution was prepared by adding 0.038 g of NaBH₄ to 30 mL of 1 M NaOH and 70 mL of pure water. 3 mL of this stock solution was then mixed with a solution containing 0.1 g of NaBH₄ in 30 mL of iso-propanol. This solution was then used as the reductant solution in the microfluidic syntheses.

3. Results and discussion

MPCs were synthesized as described earlier in both macroscale (batch) and microfluidic (continuous flow) formats with two different gold:thiol ratios. In addition, microfluidic syntheses were performed using a range of volumetric flow rates. Table 1 reports the average particle sizes and associated size distributions (extracted from the analysis of transmission electron micrographs) for all experiments. In addition, a TEM image of typical nanoparticles synthesized within the microfluidic reaction system is shown in Fig. 2.

Several conclusions emerge from these data. First, for the same gold–thiol ratio, the microfluidic reactor generates particles that are significantly smaller than a standard bulk synthesis. Second, all microfluidic syntheses produce particle populations with improved monodispersity with respect to the bulk syntheses. The standard deviations of particle size range between 0.6 and 0.9 nm for the micromixer experiments but are 1.3 and 2.1 nm for the bulk syntheses. This conclusion is also borne out by the size histograms shown in Fig. 3 which compare the particle sizes for a 2:1 thiol–gold ratio synthesized at

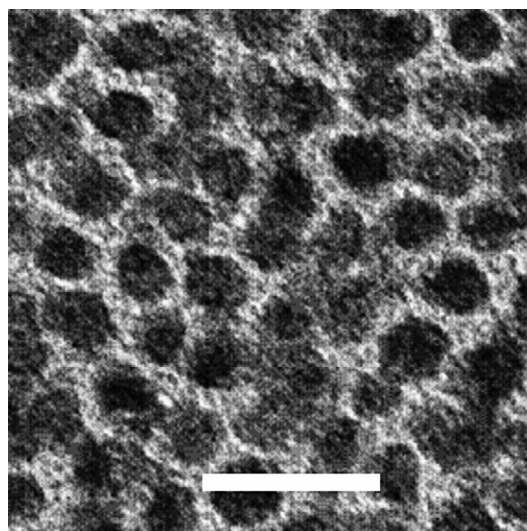


Fig. 2. A transmission electron micrograph showing MPCs prepared using the radial interdigitated mixer with a 2:1 thiol–gold ratio and a flow rate of 400 µL min^{-1} . The scale bar is equal to 10 nm.

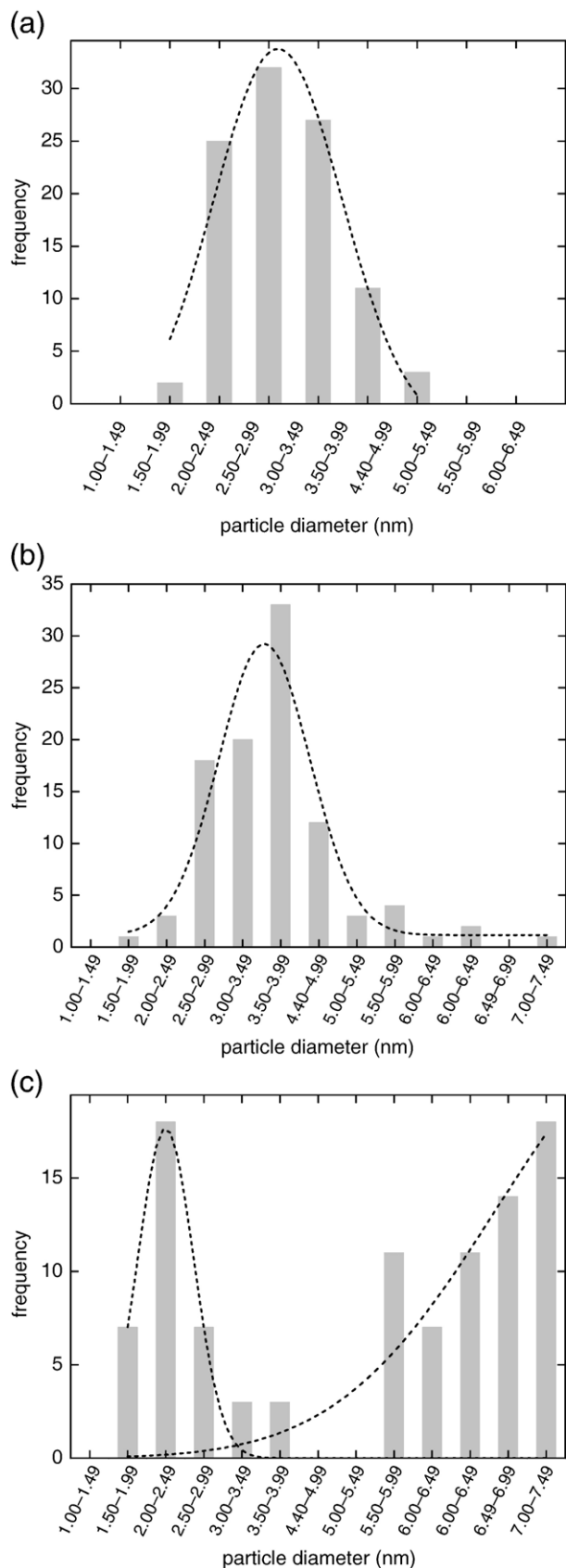


Fig. 3. Size histograms for particles made with a 2:1 thiol–gold ratio at 800 $\mu\text{L min}^{-1}$, (a) 400 $\mu\text{L min}^{-1}$ (b) and the comparable bulk synthesis (c).

800 $\mu\text{L min}^{-1}$ (Fig. 3a), the particle sizes for the same gold–thiol ratio but synthesized at 400 $\mu\text{L min}^{-1}$ (Fig. 3b) and the corresponding bulk synthesis (Fig. 3c). When considering these figures it should be noted that they have differing scales on the x axis. It is important to note that multimodal distributions are often seen in the synthesis of MPCs because of the documented preference for cluster “magic numbers” [10]. The effect of the rate of reductant addition has been reported previously [10] and the fact that smaller particles and improved monodispersity result from more rapid addition of reductant was suggested [10] to arise from the fact that when reductant addition is slow, small particles are formed but these particles are exposed to an excess of thiol. As the reaction proceeds the thiol concentration is decreased and this allows the cores nucleated later to grow to a larger size, thus creating a less monodisperse product overall. When the borohydride is added rapidly, fast nucleation occurs generating more particles early in the process but these cores then grow in a reaction mixture where the gold–thiol ratio is more uniform and the result is a more monodisperse product. In addition, under applied hydrodynamic pressure a parabolic velocity profile is established over the channel’s cross-section with fluid velocity zero at the channel walls and maximum at the centre. This means that a reaction mixture sampled after initiation of mixing is formed from an ensemble of volume elements that have spent varying times on chip [13]. This yields a residence time distribution which plays an important role in defining ultimate product size distributions. Since the residence time distribution is linearly proportional to the average residence time, and inversely proportional to the flow rate, a reduction in particle size distribution is expected as volumetric flow rates are increased.

Finally for the same thiol–gold ratio, particle size is seen to decrease with increasing flow rate, although the difference between the results obtained at 600 and 800 $\mu\text{L min}^{-1}$ is relatively small. This behaviour simply reflects the fact that the average residence time (and thus reaction time) is inversely proportional to flow rate, and thus higher flow rates define shorter average residence times.

4. Conclusions

Monolayer protected gold nanoparticles have been successfully synthesized using microfluidic reactor technology. Initial results show that the control of the rate of addition of reductant (through variation of flow rates) allows fine control of mean particle size. Moreover total reaction times for the syntheses are of the order of 4–40 s. Results also indicate that lowering the RSH: Au ratio leads to the generation of particles with larger average diameters. Since the average residence times (which define the reaction times) are controlled by both the microchannel dimensions and the volumetric flow rate, larger MPCs can be fabricated by a simple variation (increase) in either parameter.

The experiments reported herein represent the first step towards a more controlled synthesis of MPCs. Current studies are focusing on refining experimental conditions (with regard to reagent concentration and temperature) and optimizing microfluidic circuit architectures. The use of lithium triethylborohydride in THF as a reductant is also under exploration, since a single-phase system should offer the benefits of simpler fluidic control and higher product conversions, as a phase transfer reagent is no longer required [16]. In the longer term it might be envisaged that microfluidic systems could be used for the generation of MPCs derivatised with sensing species followed by analysis, all carried out on the microfluidic device.

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