Towards a novel microfluidic device for synthesis of gold nano-particles for drug delivery

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1.Motivation and challenges:

- Gold nanoparticles (AuNPs) are bio-compatible and exhibit unique size dependent optical, chemical, physical and electromagnetic properties [1]. As such, AuNPs are increasingly used in various industries and research areas, such as electronics, sensing, catalysis and drug/gene delivery [2].
- AuNPs are relatively easier and inexpensive to synthesise using chemical reduction between a suitable gold salt and a reducing agent.
- Unlike the most common batch processes, microfluidic approach provides improved control over the size and the polydispersity of the synthesised AuNPs and many more advantages such as possibility to use expensive/toxic materials in small volumes, integration of several unit operations in a single device [3] etc.
- Main limitation of synthesis of AuNPs in microfluidic devices is the reactor fouling which need to be addressed when considering scale-up processes.

2. Microfluidic device:

Co-flow glass capillary device was fabricated in the laboratory by coaxially centring a round capillary with specifically tapered injection orifice with a square capillary and fixed on a micro-scopic slide using epoxy glue. Specially prepared hypodermic needles were placed on delivery points as shown in the Figures 1 and 2.

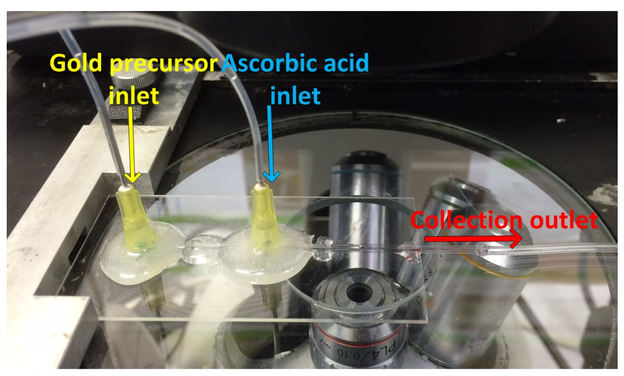


Figure 1: Photograph of the co-flow glass capillary microfluidic device on the inverted microscope

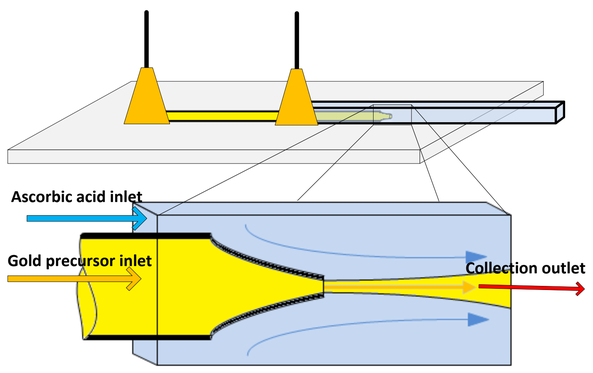


Figure 2: Co-flow glass capillary microfluidic device and the flow pattern inside the device

3. Experimental setup and the reaction:

Effect of injection orifice size (100 µm, 180 µm, 240 µm), ascorbic acid flow rate and the pH of ascorbic acid stream (pH 3.0±0.2 & pH 10.3±0.2) on particle size and the polydispersity of synthesised AuNPs were investigated to determine optimum conditions to synthesise smaller AuNPs.

Use of PVP and change of pH of ascorbic acid stream was investigated to minimise reactor fouling.

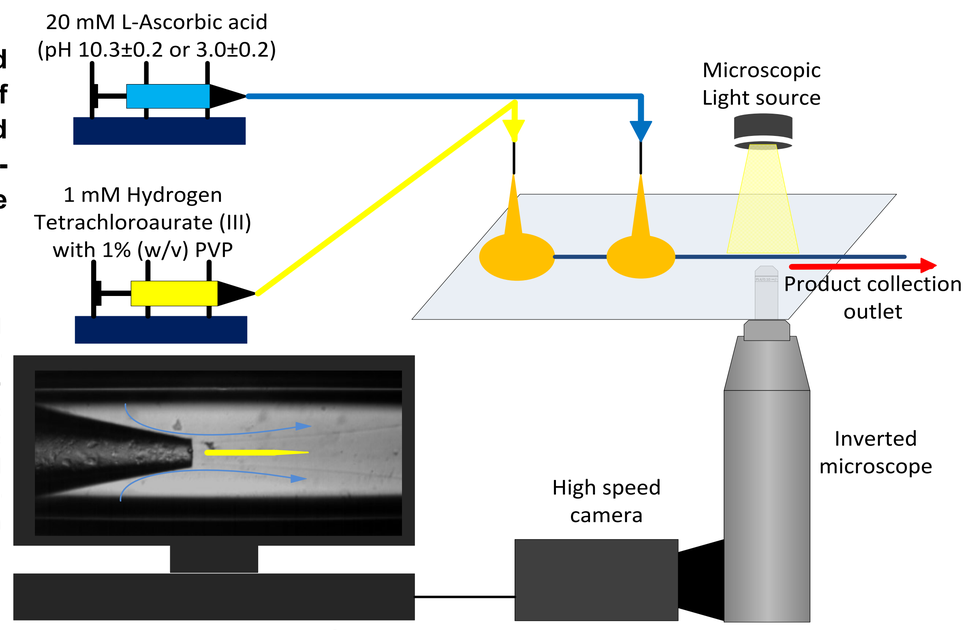


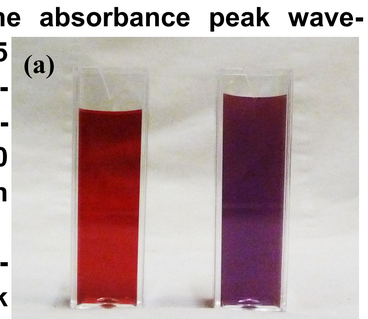
Figure 3: Experimental setup. Microfluidic device placed on the inverted microscope which is attached to the high speed camera and the computer to observe the flow pattern inside the device.

$$2AuCl_4^- + 3C_6H_8O_6 \rightarrow 2Au^0 + 3C_6H_6O_6 + 8Cl^- + 6H^+ \quad [4]$$

4. Characterisation of AuNPs suspensions:

Dynamic Light Scattering was used to determine the particle size and the polydispersity. UV-Vis spectroscopy was used to measure the absorbance spectra of AuNPs suspensions.

When the synthesised AuNPs were in the range of 40-80 nm , suspension appeared bright red confirming the absorbance peak wavelength around 525 nm while the suspension with particles of 120 - 160 nm appeared in bluish-purple which has an absorbance peak wavelength around 550 nm [5].



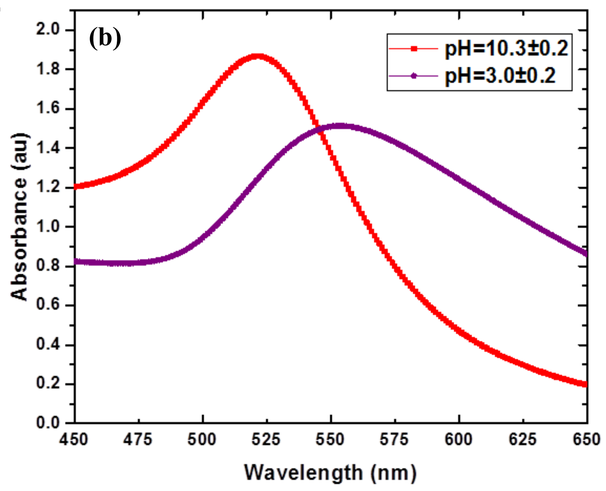


Figure 4: (a) Difference between the colour of the suspension with different size AuNPs (b) Absorbance spectra of above shown nanoparticle suspensions. (Injection orifice size 180µm, reactants flow rates were 156 ml/h, 1% (w/v) 40000 g/mol PVP in the gold precursor stream)

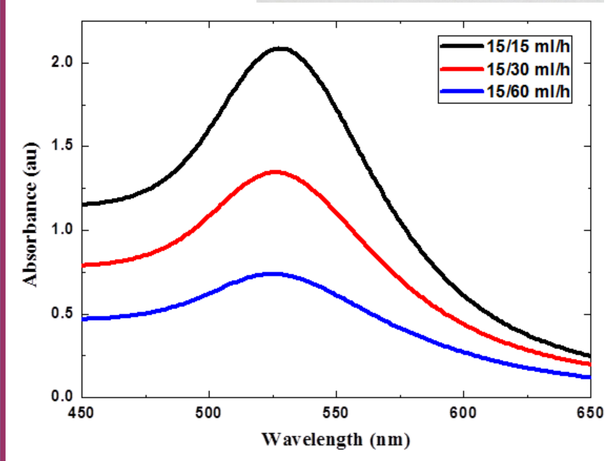


Figure 5: Absorbance spectra of synthesised gold nanoparticles with different ascorbic acid flow rates indicating decrease of absorbance (15/15 ml/h, 15/30 ml/h, 15/60 ml/h - gold precursor stream / ascorbic acid stream flow rates)

5. Experimental results:

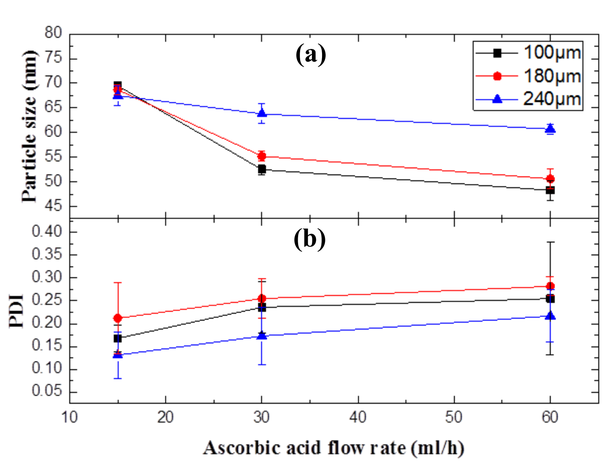


Figure 6: (a) Particle size Vs Ascorbic acid flow rate (b) Polydispersity Index Vs Ascorbic acid flow rate in different injection orifice sizes of 100, 180 and 240 µm when the gold precursor flow rate was 15 ml/hr and initial pH of ascorbic stream was 10.2

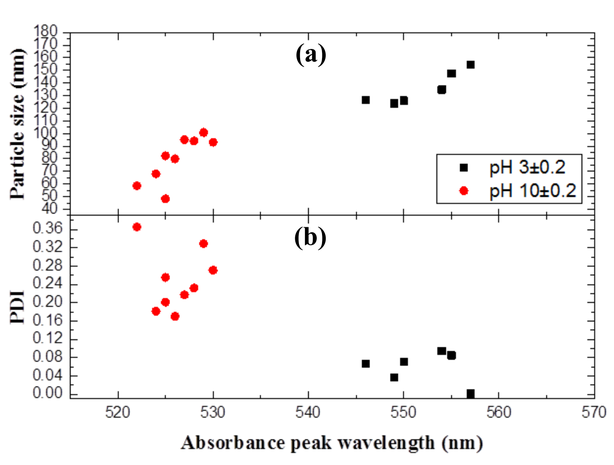


Figure 7: (a) Particle size Vs Absorbance peak wavelength (b) PDI Vs Absorbance peak wavelength of synthesised AuNPs with different pH of ascorbic acid stream

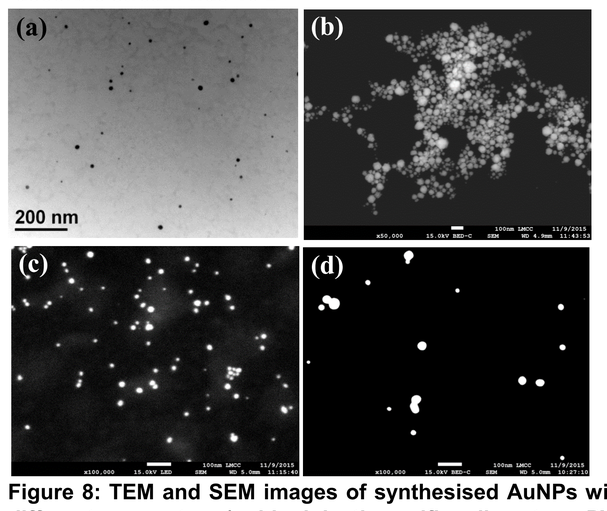


Figure 8: TEM and SEM images of synthesised AuNPs with different parameters (guide; injection orifice diameter – PVP status – initial pH of ascorbic acid) (a) TEM image 180µm–40K PVP-pH around 10 (b) 240µm-with40KPVP-pH around 3 (c) 240µm–40KPVP-pH around 10 (d) 180µm-40KPVP-pH around 3.

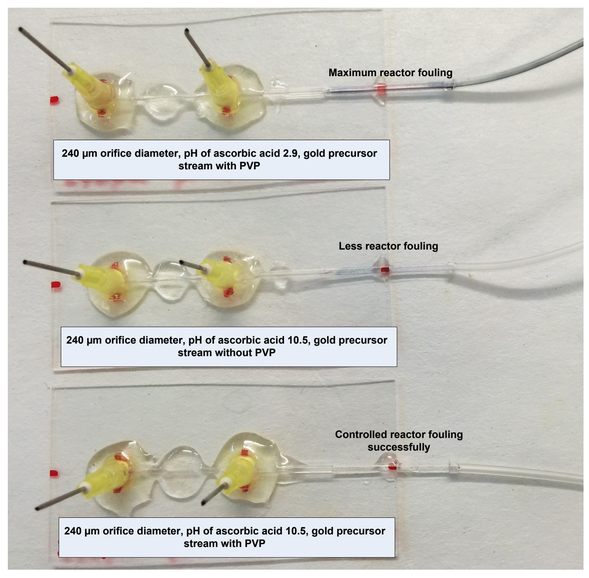


Figure 9: Observations done by the naked eye regarding the reactor fouling control. By using PVP in the gold precursor stream and elevating pH of ascorbic acid stream, reactor fouling was controlled successfully.

6. Conclusions:

- Successfully synthesised 40 - 80nm AuNPs with very low polydispersity using smaller injection orifice sizes, higher ascorbic acid flow rates and higher pH of ascorbic acid stream.
- Successfully minimise the reactor fouling by using PVP in the gold precursor stream and changing the pH of ascorbic acid stream to 10.3±0.2.

7. Future work:

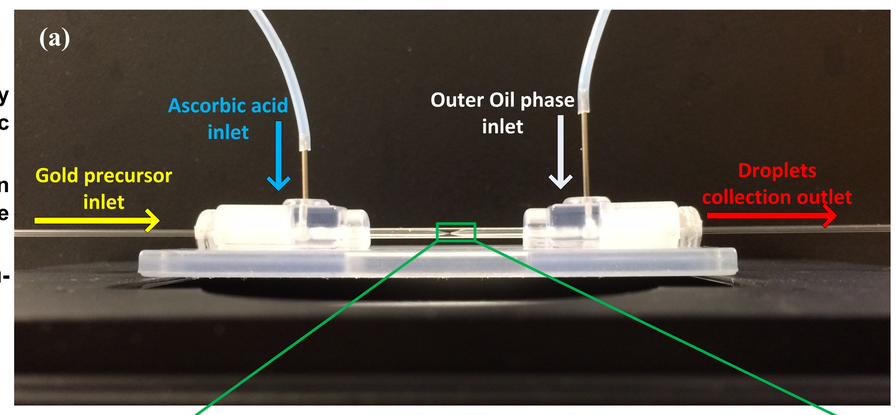
- Use of 3 phase droplet based microfluidic device to prevent reactor fouling as well as improve mixing of reactants to achieve better results on size and polydispersity of AuNPs.
- Investigations on new 3D printed microfluidic device design [6].
- Encapsulation of a drug using AuNPs and a polymer and investigations of drug administration using a gene gun [7].

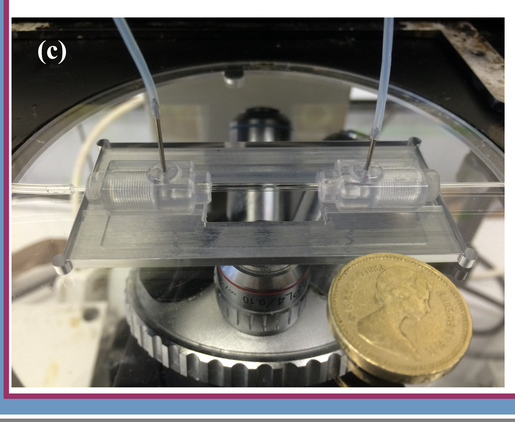
Figure 10:

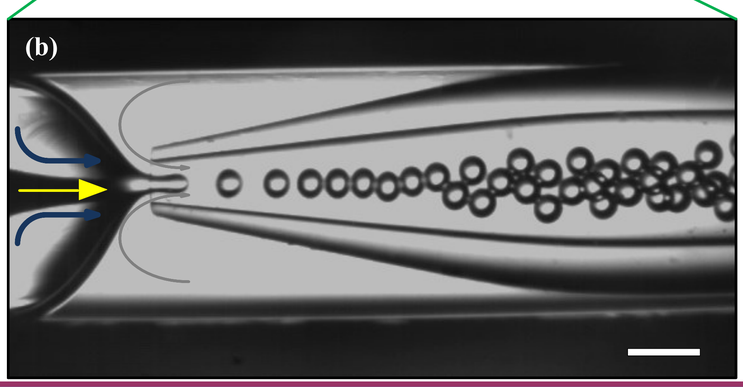
(a) 3D printed glass capillary droplet generation microfluidic device

(b) flow pattern and the reaction droplet generation inside the device (scale bar is 300 µm)

(c) size of the 3D printed microfluidic device







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