Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

One-step Continuous Synthesis of Biocompatible Gold Nanorods for Optical Coherence Tomography

Víctor Sebastián,[#,&]Seung-Kon Lee,[#], Chao Zhou[†] Martin F. Kraus,[†,‡]
James G. Fujimoto,*[†] and Klavs F. Jensen*'[#]

[#]Department of Chemical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA. [†]Department of Electrical Engineering and Computer Science and Research Laboratory of Electronics, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA

* jgfuji@mit.edu; kfjensen@mit.edu;

& Present address, Universidad de Zaragoza, Departamento de Ingenieria Quimica, Facultad de Ciencias, C/Pedro Cerbuna 12, 50009 Zaragoza (Spain)

[‡] Present address, Pattern Recognition Lab, Graduate School in Advanced Optical Technologies (SAOT), University Erlangen-Nuremberg, 91054 Erlangen, Germany

Experimental Details:

Chemicals:

Chloroauric acid ($HAuCl_4.3\ H_2O$, Aldrich), sodium borohydride ($NaBH_4$, Aldrich), Potassium carbonate (K_2CO_3, Aldrich), Lysine (Aldrich), Alanine (Aldrich), Adenosine (Aldrich) and Milli-Q water, were used as purchased.

Procedure (Batch reactor):

A 0.4 mM aqueous solution of chloroauric acid with a K_2CO_3/Au molar ratio of 5.5 was prepared. The solution was kept under stirring overnight in the dark to promote the hydrolysis of most of the Au–Cl bond and formation of the soluble gold hydroxide complex $[Au(OH)_4]^-$. The corresponding amount of amino acid was mixed at room temperature with the aged gold solution and a 9.7 mM $NaBH_4$ solution, keeping constant a $NaBH_4$/Au molar ratio of 5.5. The gold solution and reductant solution was mixed under ultrasonic radiation during 10 minutes. Afterwards, the gold colloid was centrifuged at 10,000 rpm and was redispersed in MIlli-Q water. The samples were analyzed using UV absorption (Agilent 8453 UV-Visible spectrophotometer), transmission electron microscopy (JEOL JEM 200CX and HRTEM JEOL 2010 microscopes at an accelerating voltage of 200 kV). XRD spectra were recorded from the dried Au nanorods mounted on the (100) silicon wafer using powder diffractometer (H3R Diffractometer, Rigaku).

Procedure (Continuous flow reactor):

All experiments were performed in a PTFE tubing reactor (id. 760 μm and od.1590 μm, proper length to get a residence time of 10 minutes). The tubing reactor was rolled in a coil and set down in an ultrasonic bath, see Figure S3. A 0.4 mM aqueous solution of chloroauric acid with a K_2CO_3/Au molar ratio of 5.5 was prepared. The solution was kept under stirring overnight in the dark to promote the hydrolysis of most of the Au–Cl bond and formation of the soluble gold hydroxide complex $[Au(OH)_4]^-$. The corresponding amount of amino acid was mixed at room temperature with the aged gold solution (oxidant stream). A 9.7 mM $NaBH_4$ solution (reductant stream) was kept cold using an ice bath. The oxidant and reductant streams were injected using a syringe pump, modifying the volume flow ratio. Afterwards, the gold colloid was centrifuged at 10,000 rpm and was redispersed in Milli-Q water.

Photothermal OCT Imaging:

Optical coherence tomography (OCT) is a high-resolution biomedical imaging modality that produces cross-sectional and three-dimensional images of tissue microstructure by interferometrically measuring the amplitude and echo time delay of backscattered light. OCT imaging can derive contrast from sources that are either endogenous or exogenous to the tissue being imaged.

We performed photothermal OCT imaging using gold nanorods prepared in the current study as the contrast agent. About 20 uL gold nanorods at ~3 pM concentration were injected into freshly excised human breast tissue to simulate local accumulation of the contrast agents.

The photothermal OCT system was improved upon a recent design reported by our group[1]. In the current system, a Fourier Domain Mode Locked (FDML) laser running at 240 kHz was used as the light source. The laser has a central wavelength of 1.3 um and a swept range of 170 nm. The full-width-at-half-maximum (FWHM) bandwidth of the sweep is 110 nm, which supports an axial imaging resolution of 5 um in tissue. The transverse resolution of the OCT system is ~20 um. A 830 nm laser was modulated with a 20 kHz square wave to generate photothermal modulation. A 50/50 fiber coupler was used to combine the 830 nm photothermal light source and the 1.3 um OCT imaging beam on the sample arm. The average power delivered to the sample is 11 mW and 19 mW for the photothermal and OCT beams, respectively.

The OCT imaging and photothermal modulation beams are continuously scanned over 2 mm on the sample at 12 frames per second. Each frame consisted of 20,000 A-lines and the corresponding scanning speed of the OCT beam on the sample was 24 mm/s. A high speed data acquisition card (400 MS/s) was used to stream the data to the hard drive. In post-processing, the amplitude of the phase change associated with the photothermal modulation was extracted from the frequency spectrum of the phase over 256 consecutive A-lines. A derivative was taken of the phase modulation amplitude along the depth dimension to extract the photothermal signal shown in Figure 5. A SNR threshold of 5 was used to select the regions of interest where the nanorods accumulated.

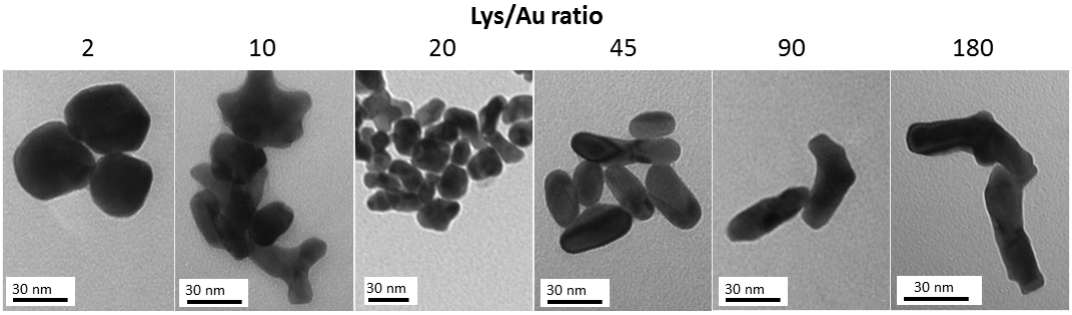

Figure S1. TEM images of Au nanostructures obtained at different Lys/Au molar ratios: 2, 10, 20, 45, 90 and 180, respectively.

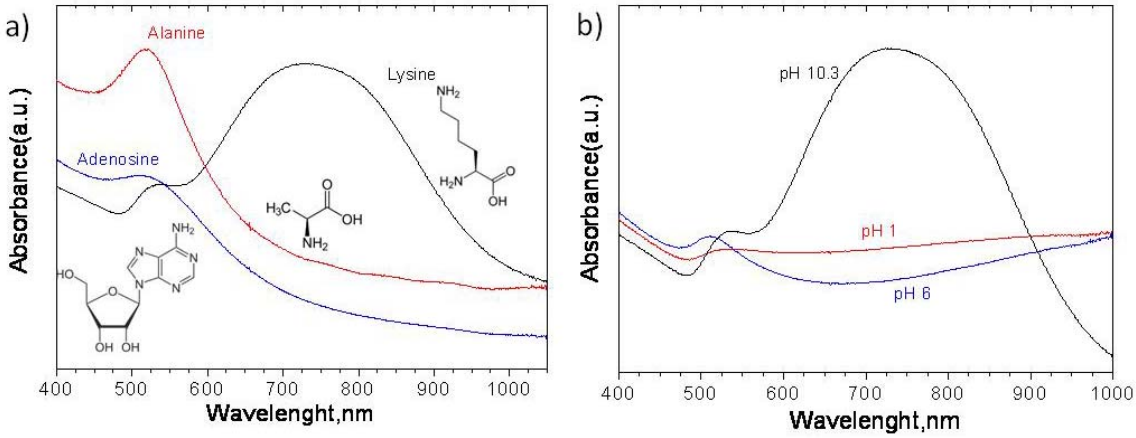

Figure S2. a) UV-VIS spectra of gold nanostructures obtained using different amino acids an ultrasonic irradiation at pH value of 10.3: Alanine, Adenosine and Lysine. b) UV-VIS spectra of gold nanostructures obtained at a Lys/Au = 180 and using ultrasonic irradiation at different pH values: 1, 6 and 10.3.

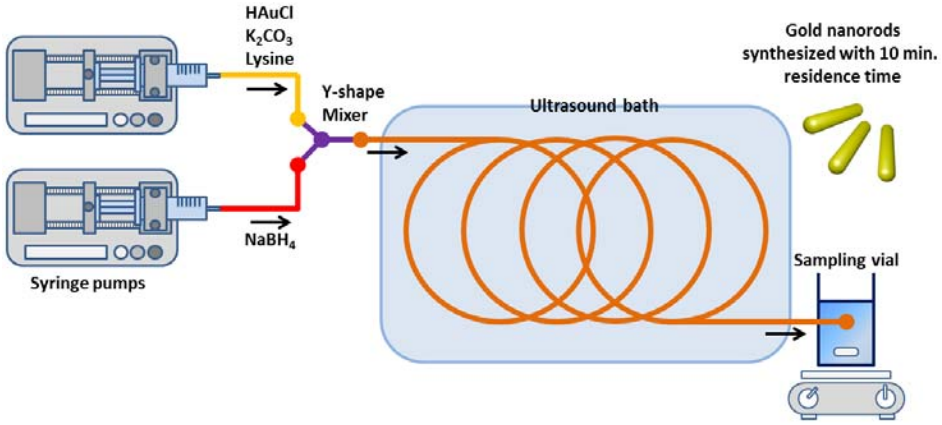

Figure S3. Schematic of continuous gold nanorods production setup with 10 min. residence time.

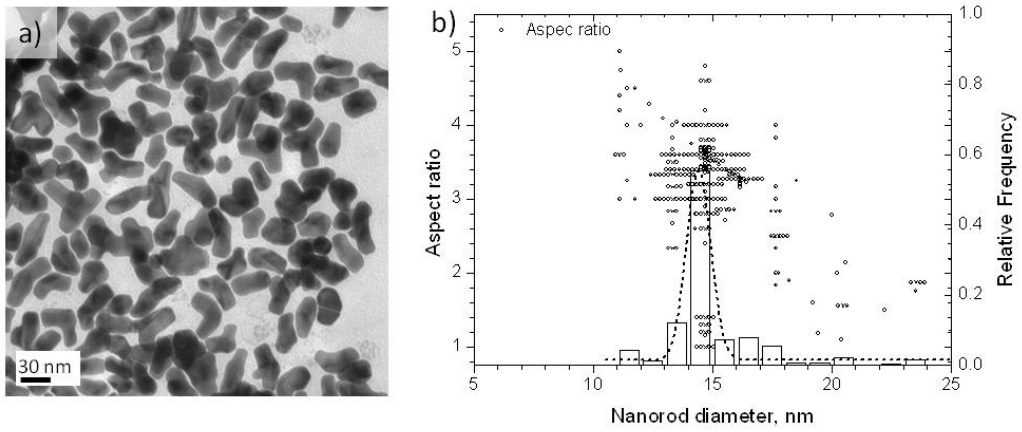

Figure S4. Gold nanorods grown in a continuous flow reactor a) TEM image . b) Statistical analysis (270 nanorods): relative frequency vs. diameter (bars) and aspect ratio vs. diameter (open circles)

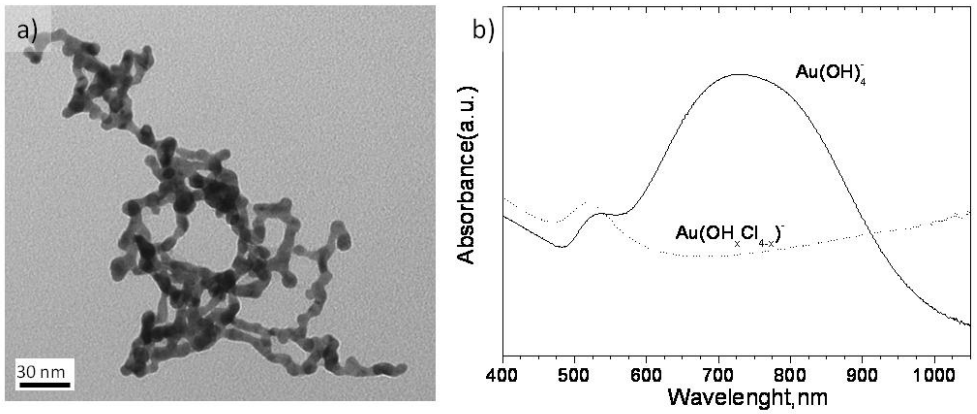

Figure S5. a) TEM image of gold nanostructures obtained using a fresh solution of $AuCl_4^-$ at pH value of 10.3. b) UV-VIS spectra of gold nanostructures obtained at pH value of 10.3, using fresh solution of $AuCl_4^-$ and an overnight aged solution of $AuCl_4^-$ to promote the hydrolysis of Au-Cl bonds.

[1] Zhou, C.; Tsai, T.-H.; Adler, D. C.; Lee, H.-C.; Cohen, D. W.; Mondelblatt, A.; Wang, Y. H.; Connolly, J. L.; Fujimoto, J. G. Optics Letters 2010, 35, 700- 702.