Supporting Information

for

Monitoring the Stimulated Uncapping Process of Gold-Capped Mesoporous Silica Nanoparticles

by

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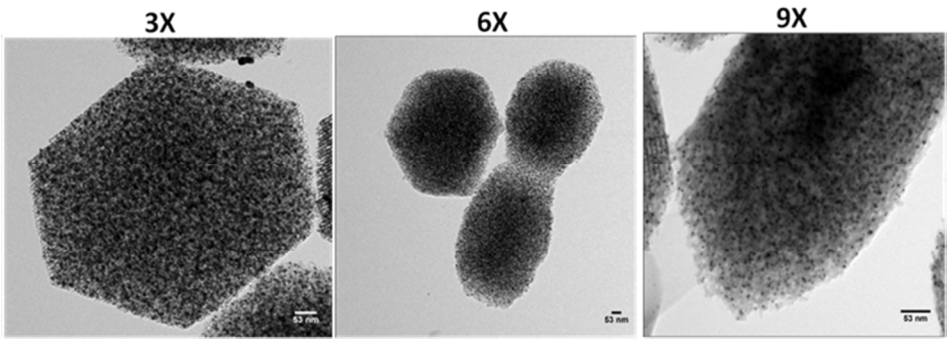

Figure S1: TEM images of gold-plated MSN

TEM images of MSN that were plated with gold nanoparticles inside the MSN channels. It is important to notice that the gold is well-dispersed but frequently larger agglomerated clusters of gold are seen. Scale bars represent 53 nm.

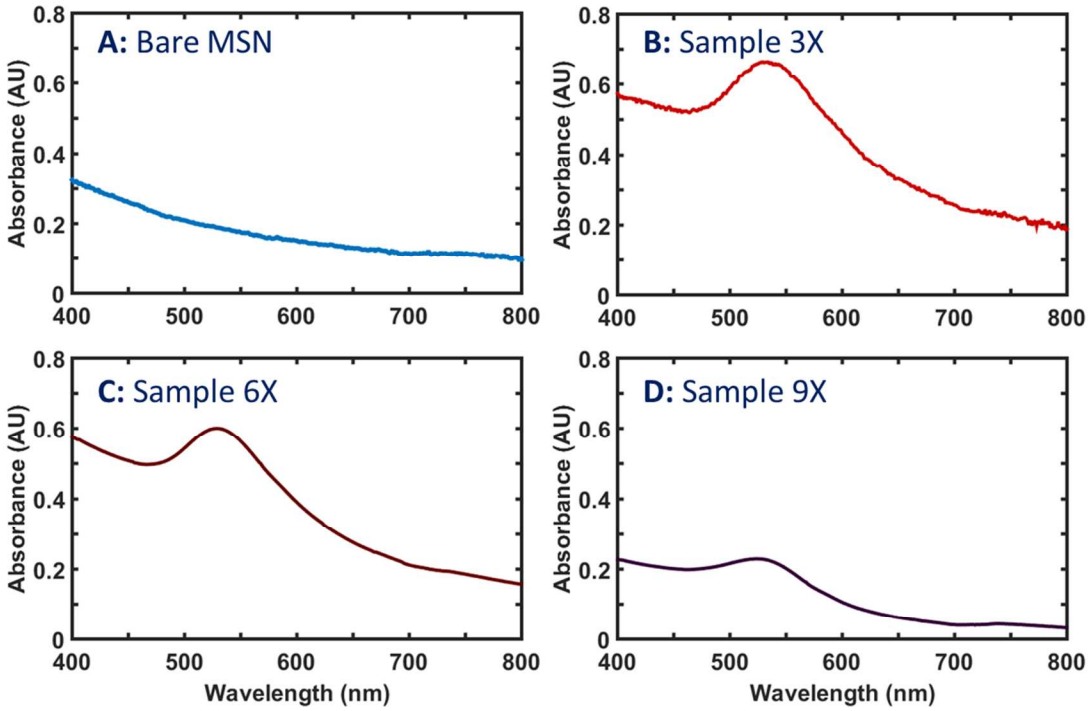

Figure S2: UV-Vis absorbance spectra of bare and gold-plated MSN

Absorbance spectra from the four samples discussed in Figure 2 of the main text. Each sample was suspended in water, and the data were collected using a Varian Cary 300 UV-Visible spectrophotometer.

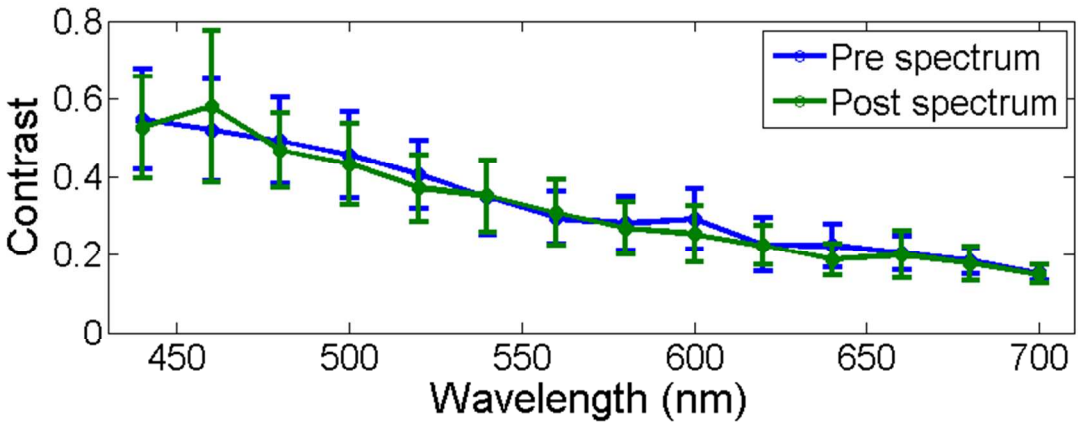

Figure S3: Control experiment with water

Spectra (440 nm – 700 nm) of 10 MSN were taken before and after water was flowed continuously through the microchannel for 3 hours, and the contrast data were averaged. There is no significant statistical change between the spectra. Thus the gold was not cleaved from the MSN.

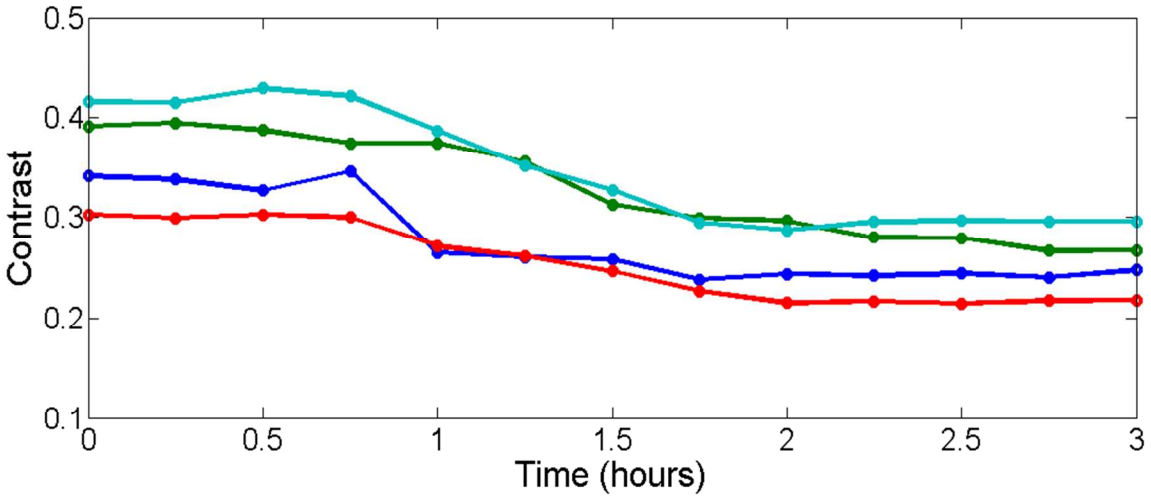

Figure S4: Cleaving gold nanoparticles from MSN with glutathione

The time series DIC contrast data at 540 nm of four single particles as AuNP are cleaved from the MSN using 5 mM GSH. The cleaving process was complete at the 2-hour mark.

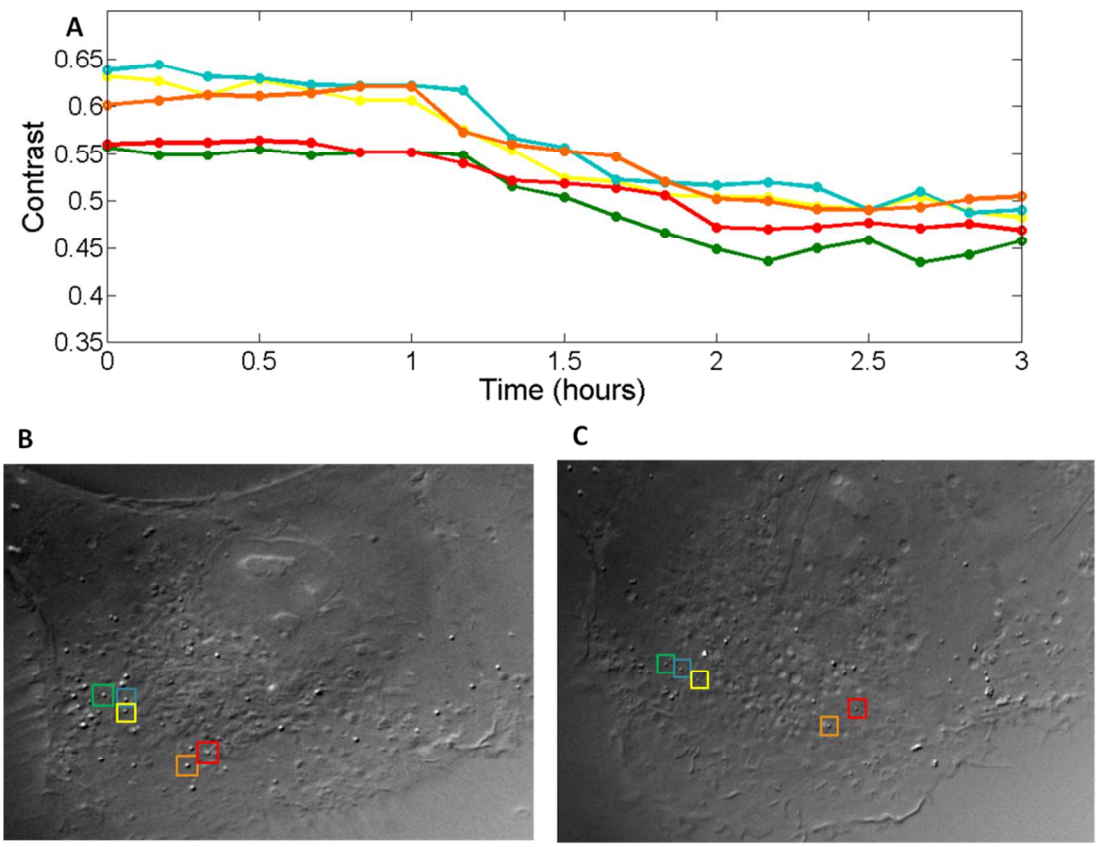

Figure S5: Cleaving of gold from MSN with intracellular glutathione

The colors in panels A, B, and C correspond to the same MSN and to the line colors in Figure 4. A) Time series data collected at 540 nm during the cleaving of AuNP from 5 MSN via intracellular GSH. Because the MSN entered the cells by way of endocytosis, the MSN first had to be released from endosomes before they could be exposed to the cytosol, where the GSH is located. For the initial 40 min, contrast remained relatively steady. After that time, contrast declined until the 2 h mark was reached. From that time onward, contrast again remained relatively steady for the last hour of imaging. DIC images of an A549 lung cancer cell with internalized gold-capped MSN B) at the initial imaging time, and C) at the last imaging time, after cleaving with internal GSH was completed. The particles moved during the experiment but were tracked throughout the three hours.

Computational data and discussion on optical behavior of gold incorporated MSN

Since silica is neither plasmonic nor absorbing over the optical range studied here, it provides a simple and convenient substrate for embedding gold nanoparticles.[1,2] Silica's spectral profile rises in intensity with decreasing wavelength, as expected for a purely scattering object. Gold nanoparticles both scatter and absorb light; however, plasmonic nanoparticles in the size regime used here (5 – 10 nm) are known to predominately absorb light.[3,4]

The efficiency at which an object responds to light is mathematically described in terms of optical cross sections, σ. For cases, such as the one described here, where the objects are much smaller than the wavelength of irradiation, the absorption cross-section is defined as[5,6]

$$\sigma_{abs} = -\frac{8\pi^2}{\lambda} r^3 \,\mathrm{Im}\left[\frac{m^2-1}{m^2+2}\right] \qquad (1)$$

whilst the scattering cross-section is[5,6]

$$\sigma_{sca} = \frac{128\pi^5}{3\lambda^4} r^6 \left[\frac{m^2-1}{m^2+2}\right]^2, \qquad (2)$$

where λ represents the illumination wavelength, r is the object's radius, and m is the ratio of the refractive index of the particle to that of the medium. As the refractive index of a particle approaches that of the medium, the cross sections approach zero. In general, as a particle increases in size, r is the key variable, and scattering efficiency increases more rapidly than absorption. As particles decrease in radius, λ becomes the critical variable, and absorption becomes the dominant effect.

These spectra are complex due to the two size regimes involved (>100 nm and 5 nm). Gold nanoparticles with a 5 nm diameter exhibit a distinct absorption peak near 520 nm, but once a gold particle surpasses 100 nm diameter and continues to grow, the absorption peak broadens, dampens, and takes on the appearance of a bulk gold film.[7] The present situation is further complicated due to the mesoporous silica scaffold and the seemingly arbitrary spacing between the individual gold nanoparticles, which was on display in Figures 1 (in the main text) and S1.

To understand the trend in the behavior of these complex spectra, a computational approach was taken. Since silica is non-absorbing, the optical effect of gold-loading is better understood by focusing on the absorption spectra. As shown in Figure S6 below, bare silica was compared against three different levels of gold loading onto MSN. For the modeling exercise, it was assumed that gold would distribute itself evenly and fill the channel space before forming external layers or clusters. The true situation is more complex, as the TEM images in Figure 1 suggest, but without further information about how the gold actually incorporate themselves onto MSN (such as in situ real time TEM images, or cross-sectional slices through the MSN), it is difficult to recreate spectra identical to those presented in Figure 2 of the paper.

In the computational exercise, at low concentrations of gold (3 and 11 wt%), a single absorption peak appears, centered at 544 nm. This agrees well with the 3X (12 wt%) profile in Figure 2 and suggests that at low concentrations of gold incorporation, the gold is well-dispersed within the MSN. Agglomeration of gold nanoparticles must be relatively low at these levels of gold incorporation. As a result, the spectra indeed resemble a gold colloid. Ordinarily for 5 nm diameter gold in an aqueous environment, the absorbance peak would be found near 520 nm, but

since the gold is embedded within a matrix of higher refractive index, the peak is accordingly red-shifted. Assuming that gold is forced to completely fill the MSN channels before filling up space on the MSN exterior, at 24 wt% loading, the channels would become completely filled. As this value is approached, the individual gold particles become packed closely enough for their plasmons to couple, resulting in a double-peaked spectrum. This was not observed in the experimental data, and by also taking the TEM images into consideration, it can be assumed that gold does not completely fill the channels before forming an external coating on the MSN. Due to the overall low contrast observed through the microscope at high gold incorporation, it seems reasonable to assume that the secondary peak is too weak to be observed.

The computational data do not explain the loss of contrast in the observational data. However, the addition of gold into the MSN results in a decreased refractive index for the MSN. The well-reported method of adjusting the refractive index of the medium has been previously used to enhance or diminish a sample's contrast relative to the background.[7] In this counter scenario, the particle's refractive index is gradually lowered to that of the medium (water, 1.33), and the imaging contrast is drastically reduced as a result.

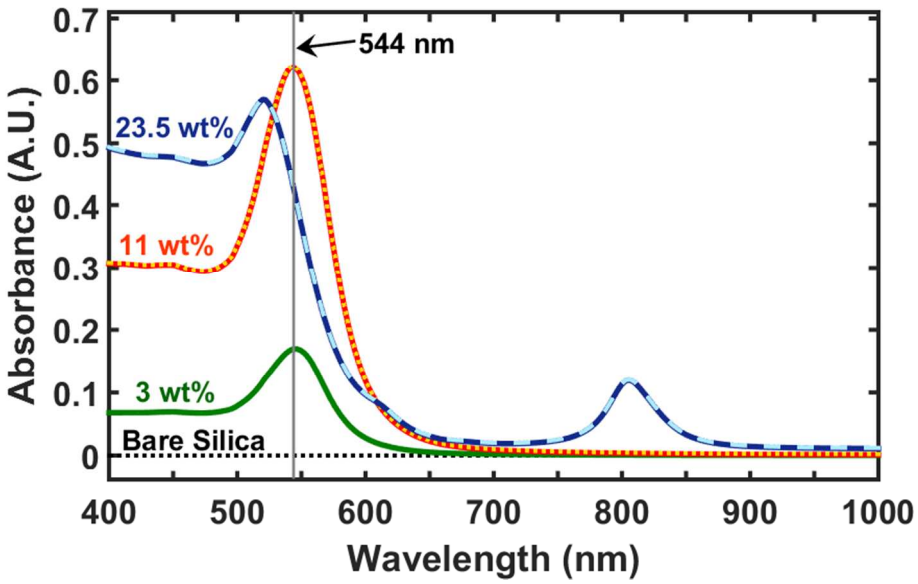

Figure S6: Computed absorption spectra of MSN and gold incorporated MSN

DDA-calculated absorption spectra for gold-plated MSN as well as their weight percentages of gold. Bare silica is essentially non-absorbing. Gold is assumed to be evenly dispersed within the MSN channels, resulting in an absorption peak centered at 544 nm for the 3 and 11 wt% samples. At 23.5 wt%, the channels are almost filled with gold, and plasmonic coupling results in a double-peak.

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