Supplementary Information

Materials and Method

All reagents were procured from Sigma and were of AR grade (if not otherwise stated). Chloroauric acid ($HAuCl_4$) and L-Tryptophan were used without any pre-treatment. The heroin sample (white crystalline powder) was obtained from Lipomed: heroin HCl monohydrate, product ref. number M-29-HC, HPLC purity >98.5%, water content <10%, calculated hydrochloride content 8.6%. The cocaine sample was obtained internally. Ultrapure water (18.2 MΩ cm) produced with a Milli-Q RG system was used in all experiments. Naloxone hydrochloride was purchased from Sigma.

Well-mixed gold cation stock solution (0.25 M) and Trp aqueous stock solution (0.5 M) was prepared and drop-casted over a parafilm substrate in the volumetric ration of 1:1 (50 µl each). Si-nanopillar (Si NP) substrate was placed face-down over the reaction mixture for 30 minutes. This cycle was repeated again for another 30 min with fresh reaction mixture to support crystal growth phase. It should be noted that the size of the resulting Au nanostructure can be tuned by controlling the time and concentrations at this stage (seeding) stage. After 60 minutes, the Si NP substrate was picked along the edges and dried face-down at 40°C. Care should be take here as higher temperatures will cause faster drying, and in turn, uneven nanoparticle generation owing to coffee-ring effects.

5µL THF was added to 5 µL of Trp solution (0.5 M) together with 2.5 mg of Naloxone and was placed over the Au-NP chip. The chip was then gently heated at 60C under protonating conditions until the solvent evaporated. This resulted in poly-Trp formation with drug particles enmeshed into the matrix.

Fabrication of Si-nanopillar substrate

For silicon nanostructuring reactive ion etching (RIE) of undoped polished (100) silicon wafers was used. Silicon nanopillar (Si NP) structures were produced via maskless Si RIE process as previously described [Adv. Mater. 2012, 24, OP11–OP18]. The process yields vertically standing Si NP structures with radius ~20 nm, height ~500 nm, and the Si NP density ~18 pillars/μm^2 over a 4 inch Si wafer. The 4-inch wafer was diced into 4x4 mm chips using a laser micromachining tool (3D-Micromac AG, D-09126 Chemnitz, Germany).

SERS measurements

All Raman scattering and SERS measurements were performed using a Raman microscope (Thermo Scientific DXRxi, Waltham, MA, USA) equipped with a 780 nm laser. The microscope was coupled to a single grating spectrometer with a 5 cm^{-1} fwhm spectral resolution and a ±2 wavenumber accuracy. All spectra were collected using a 10x objective lens. The SERS signal collection time was 20s, averaged 3 times (Figure 3). 1 µl droplets of heroin and cocaine solutions (1 mg/ml) were deposited on Au nanocactus surfaces and let to dry prior to acquiring the spectra.

In the naloxone release study (Figure 4), the Raman signal collection time was 3s, averaged 3 times. The Raman scattering spectra were measured at t = 0-20 min time intervals after 30 µl of PBS were pipetted on the Au nanocactus surface. The same measurements were performed using three Au Nanocatus surfaces (3 chips). The results were then averaged and are shown in Figure 4 (b,c), In order to estimate

the final naloxone concentration in PBS, the naloxone calibration curve was obtained. The naloxone calibration study (Figure 4c, inset) was performed by recording naloxone Raman spectra from solutions with varying naloxone concentrations (0-60 mg/ml) and monitoring the intensity change of the characteristic naloxone Raman mode (637 cm^{-1}). The naloxone solutions were pipetted into a stainless steel cavity, and the laser focus was positioned approximately in the middle of the liquid volume. The recorded Raman spectra in Figure 4b and c were background corrected prior to extracting the 637 cm^{-1} Raman mode intensity values. Finally, optical images of naloxone crystals on the Au nanocactus surface exposed to the 30 µl PBS medium were taken at t ≈ 0, 10, 15 and 20 min time intervals.

Characterization

Scanning electron microscopic pictures were taken with JEOL JSM 5500LV scanning electron microscope. Attenuated Total Reflectance Fourier transform infrared spectra (ATR-FTIR) were recorded by a Perkin Elmer Spectrum (30 scans each). Optical microscope coupled with Raman and how the image/ were recorded or analyzed.

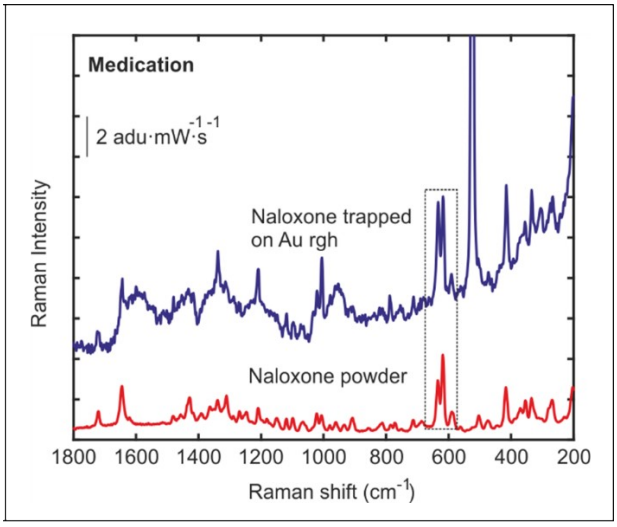

Figure **S1**. SERS spectra of Naloxone in free state vs. trapped on poly-Trp-Au interface (rough). Note the characteristic peak of Naloxone (633 cm^{-1} and 617 cm^{-1}) was identified in its native state and was also confirmed when bound to the polymeric-Trp.