Supplementary Material

SERS optical accumulators as unified nanoplatforms for tear sampling and sensing in soft contact lenses

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Materials

Poly(allylamine hydrochloride) (PAH, MW=17,500), poly(diallyldimethylammonium chloride) solution (PDDA, MW=400,000–500,000, 20 wt% in water), sodium chloride (NaCl, 99.9%), sodium hydroxide (NaOH, >97%), tetrakis(hydroxymethyl)phosphonium chloride solution (THPC, 80% in water), tetrachloroauric(III) acid trihydrate ($HAuCl_4 \cdot 3H_2O$, 99.9%), ammonium hydroxide solution (NH_4OH, 28–30%), tetraethyl orthosilicate (TEOS, 98%), potassium carbonate (K_2CO_3, >99%), formaldehyde solution (HCOOH, 37 wt% in water), 2-hydroxyethyl methacrylate (HEMA, 99%), ethylene glycol dimethacrylate (EGMA, 98%), methacrylic acid (MAA, 99%), Irgacure® 295 (98%), dichloromethylsilane (DCMS, 98%), and xanthine oxidase (XOD, Grade IV, ammonium sulfate suspension) were purchased from Sigma-Aldrich. Cetyltrimethylammonium bromide (CTAB, 99%) was acquired from Acros. Polystyrene (PS) beads (500 nm in diameter) were obtained from Ikerlat Polymers. Ethanol absolute (EtOH, ≥99.9%) was purchased from Scharlab. All chemicals were of analytical grade and used without further purification. Milli-Q water (18.2 $M\Omega cm^{-1}$) was used in all the preparations. Glassware was cleaned with freshly prepared aqua regia before every procedure.

Methods

Fabrication of soft contact lenses: a mold consisting of two 15×15 mm^2 glass plates sandwiching a 0.5 mm thick silicon spacer was produced. With this aim, a first glass plate was immersed for 2 h in a PDDA solution prepared beforehand by adding PDDA (20 wt% in water) in a 0.5 M NaCl solution with a final polymer concentration of 2 mg/mL followed by a 15 min sonication. The resulting positively charged plate was washed with water and left to dry. After that, a gold-containing silica-shelled nanocapsule solution

(200 μL, 0.938 mg/mL) was deposited onto the glass and left to dry overnight. Plasmonic nanocapsules were previously prepared as described elsewhere.[1] At this point, a second glass plate was siliconized with a thin layer of dichloromethylsilane (preventing glass-polymer adhesion forces), left to dry and washed with water. In order to create the matrix of the contact lens, 2-hydroxyethyl methacrylate (HEMA, 97.64 wt%) as a monomer, ethylene glycol dimethacrylate (EGDMA, 1.44 wt%) as a cross-linker, and methacrylic acid (MAA, 0.77 wt%) as a wetting agent were mixed in a flask. Then, the radical photoinitiator Irgacure® 295 (0.15 wt%) was added and the solution was magnetically stirred until complete dissolution. At this time, the mixture was injected into the mold and placed in a photoreactor where it was subjected to UV irradiation (350 nm) for 20 min. After that, the polymerized hydrogel was removed from the mold, immersed in water and heated to boiling for 15 min so as to remove the unreacted compounds. Finally, the obtained hydrogel was sculpted into a circular shape (25 mm in diameter) using a die cutting tool and immersed in water for 2 weeks. The solvent was withdrawn at regular intervals (12 h) and replaced by the same volume of water after each extraction in order to remove the residual amount of unreacted species.

Preparation of simulated tear fluids (STF): as widely described in the literature, the simulated tear fluid was prepared by dissolving sodium chloride (0.67 g), sodium bicarbonate (0.20 g), and calcium chloride dihydrate (0.008 g) in 100 mL of Milli-Q water.

Tear mimicking experiments: adenine-containing STF solutions (1×10^{-3} M, 1×10^{-5} M, and 1×10^{-7} M) were added dropwise on soft contact lenses aiming at mimicking basal rate of tear secretion (average flow rate of 1.2 μL/min). Concomitantly, SERS measurements were periodically carried out in order to observe the accumulation of the analyte signal over time.

Tests of enzymatic activity: 50 µL of xanthine oxidase (1.0 U) were added over adenine-loaded nanocapsules embedded on a soft contact lens. These biomarker-containing nanostructures were prepared beforehand by overnight immersion of these architectures in an adenine STF solution (5×10^{-5} M). Then, SERS spectra were acquired over time in order to gain insights into the stability of the nucleobase under these conditions. As a control, 50 µL of xanthine oxidase (1.0 U) were added to an adenine-containing STF solution (5×10^{-5} M) in the absence of silica-shelled nanocapsules. UV-visible spectra were acquired over time in order to verify the formation of oxidation products, thus ensuring the proper functioning of the enzyme under the simulated tear physiological conditions.

Characterization

UV-visible spectra were recorded on an Agilent Cary 8454 spectrophotometer. Polymerization was carried out in a Luzchem ICH-2 photoreactor equipped with an 8-watt 350 nm UV lamp. SEM images were obtained with a JEOL JSM-6700F field emission scanning electron microscope. AFM measurements were performed using a ScanAsyst-Fluid (tip ROC<20nm, silicon nitride cantilever coated with Au, K=0.7 N/m, frequency=150 kHz) for liquid measurements. SERS spectra were acquired using an inVia confocal Raman microspectroscopy system (Renishaw) equipped with a 785 nm laser and a high-resolution grating (1,200-line/mm). Laser light (2.47 mW laser power at the sample) was focused through a 50× objective (Leica) on the soft contact lens with acquisition time of 10 s.

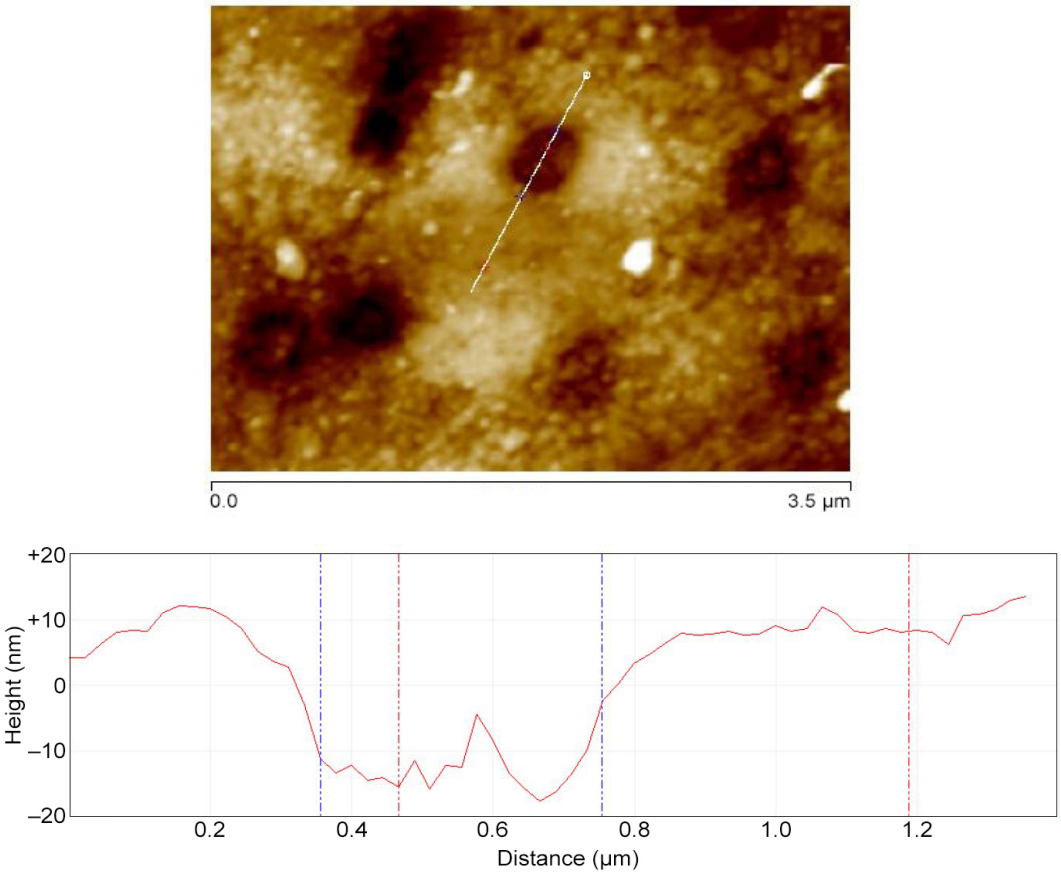

Figure S1. Typical AFM image (top) and cross-section profile (down) for a soft contact lens loaded with plasmonic nanocapsules where the embedment of the silica-shelled nanostructures onto the surface of the hydrogel film can be clearly discerned.

References

1 A. Mariño-Lopez, A. Sousa-Castillo, M. Blanco-Formoso, L. N. Furini, L. Rodríguez-Lorenzo, N. Pazos-Perez, L. Guerrini, M. Pérez-Lorenzo, M. A. Correa-Duarte and R. A. Alvarez-Puebla, *ChemNanoMat*, 2019, **5**, 46–50.