# Supporting Information

## How an ACE2 mimicking epitope-MIP nanofilm recognizes template-related peptides and the Receptor Binding Domain of SARS-CoV-2

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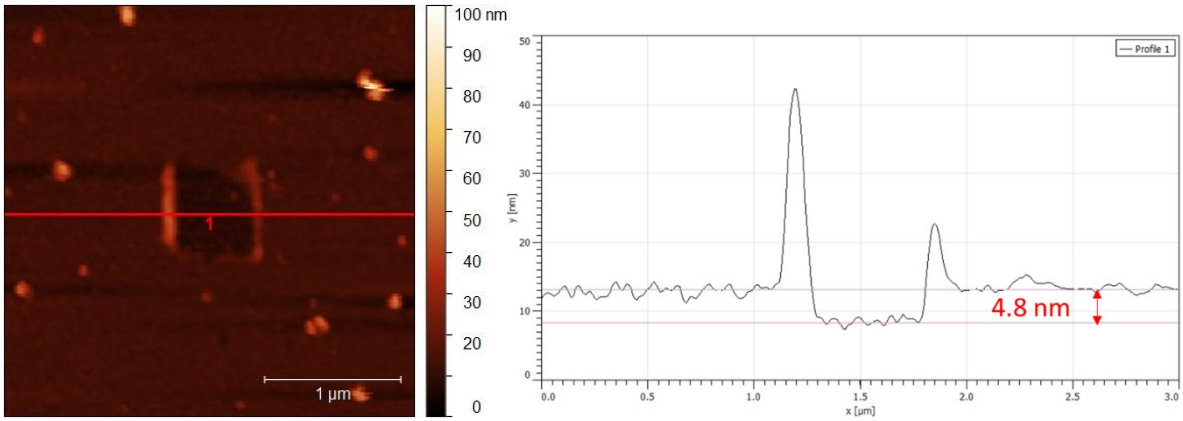


**Fig. S1** Determination of the polyscopoletin nanofilm thickness by local removal of the polymer from the gold surface in a rectangular area (left) to reveal the cross-section (right).

## S2. Electrochemical assesment of the binding site dentsity of MIPs

First, 6-(ferrocenyl)hexanethiol was immobilized on the surface of cleaned bare gold electrodes (Ø 2.0 mm) to deteremine the peak current corresponding to the full electrode area. Each electrode was incubated in 200 µL of 1 mM 6-(ferrocenyl)hexanethiol dissolved in ethanol for 1 hour, at 25 °C, 350 rpm. After rinsing the electrodes in water and dried with $N_2$, the modification was investigated with cyclic voltammetry (0.1-0.55 V, 10 mV/s) in Britton-Robinson buffer (0.04 M boric acid, 0.04 M phosphoric acid, 0.04 M acetic acid and 0.1 M $NaClO_4$) and the oxidation peak current was integrated to calculate the charge. The thiol was cleaved from the surface of the gold electrode with oxidative stripping to obtain a bare gold surface without changing the real surface area of the electrode. To prepare the epitope imprinted polyscopoletin nanofilm, the clean gold disk electrodes were first incubated in G-Peptide solution (GFNCYFP) in PBS followed by rinsing with DI water and drying under $N_2$ stream. The polyscopoletin layer was then deposited on the electrode by electropolymerizing a solution containing 0.5 mM scopoletin in 10 mM NaCl with 20 pulse cycles starting with 0 V for 5 s and followed by 0.7 V for 1 s. The NIP was prepared in the same way but without peptide. After synthesis of the polymer layer, the electrodes were carefully rinsed with water and dried gently under nitrogen stream. The surface was further blocked with 1 mM of 6-mercapto-1-hexanol in PBS for 1 hour, at 25 °C, 350 rpm and then the template was stripped by anodic oxidation. The surface density of the cavities in the polymer film was determined by immobilization of 1 mM 6-(ferrocenyl)hexanethiol in EtOH and cyclic voltammetry (0.1 - 0.55 V, 10 mV/s) was performed in Britton- Robinson buffer. The surface percentage of the cavities was determined by referencing the 6-(ferrocenyl)hexanethiol signal of the MIP to that of the bare gold electrode.

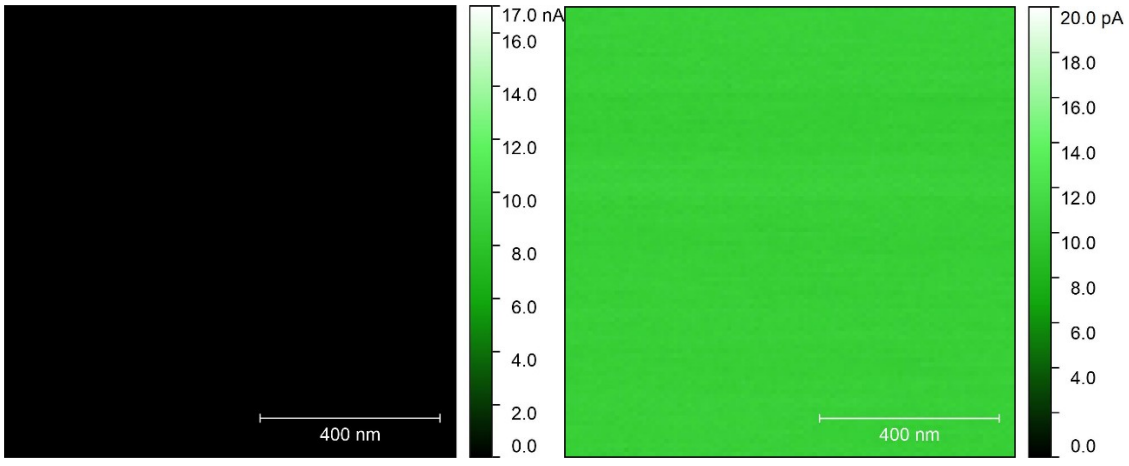


**Fig. S2** Current maps of the polyscopoletin film (NIP) by c-AFM in low (left) and high (right) current sensitivity mode that shows the excellent electrical insulating property of the film.

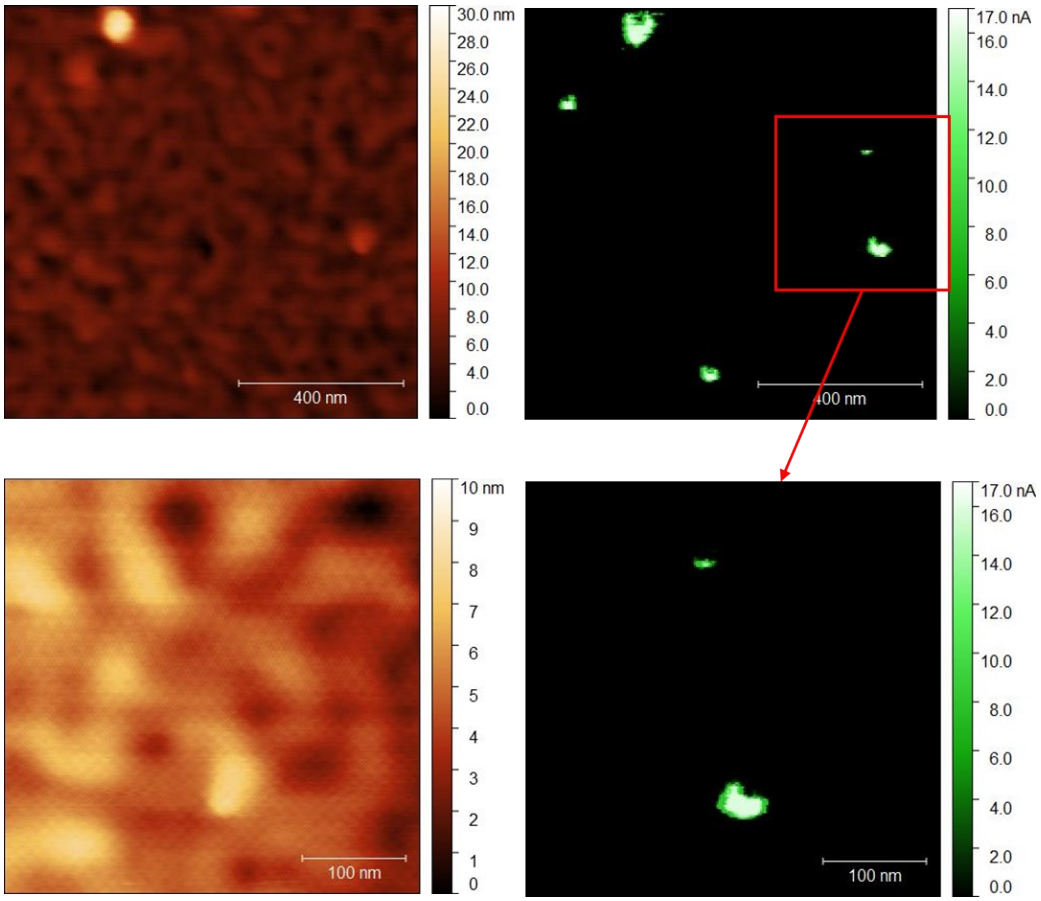


**Fig. S3** High resolution topographic and current maps of G-Peptide (5 µM) imprinted polyscopoletin nanofilms after template removal recorded by c-AFM.

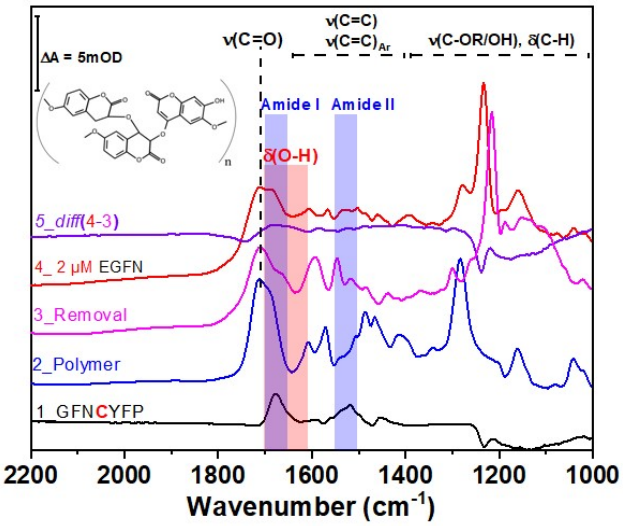


**Fig. S4** IR absorbance spectra of individual steps of the MIP formation on SEIRA gold surface. Trace 1 shows the adsorption of G-Peptide highlighted by the corresponding amide I and amide II bands at 1673 $cm^{-1}$ and 1517 $cm^{-1}$ (blue rectangle), respectively. The observed bands in trace 2 are attributed to the carbonyl ν(C=O) stretching vibration (1715 $cm^{-1}$), aromatic and vinyl ν(C=C) stretching modes (1600 – 1400 $cm^{-1}$), ν(C–O) stretching vibration

of the ester group (1280 $cm^{-1}$), the ν(C–O–C) stretching of alkyl ethers (1160 $cm^{-1}$) and δ(C–H) bending modes (1400 – 1000 $cm^{-1}$), all of these are characteristic of the polyscopoletin film. Electrochemical template removal (trace 3) is monitored through the appearance of a broad absorption band at ca. 1640 $cm^{-1}$ attributed to the δ(O–H) bending vibrations (red rectangle) of water molecules reaching the gold surface via the created MIP cavities (trace 4). Subsequent rebinding of the EGFN shows only the appearance of water molecules reaching the Au surface as highlighted by the δ(O–H) bending vibration mode.

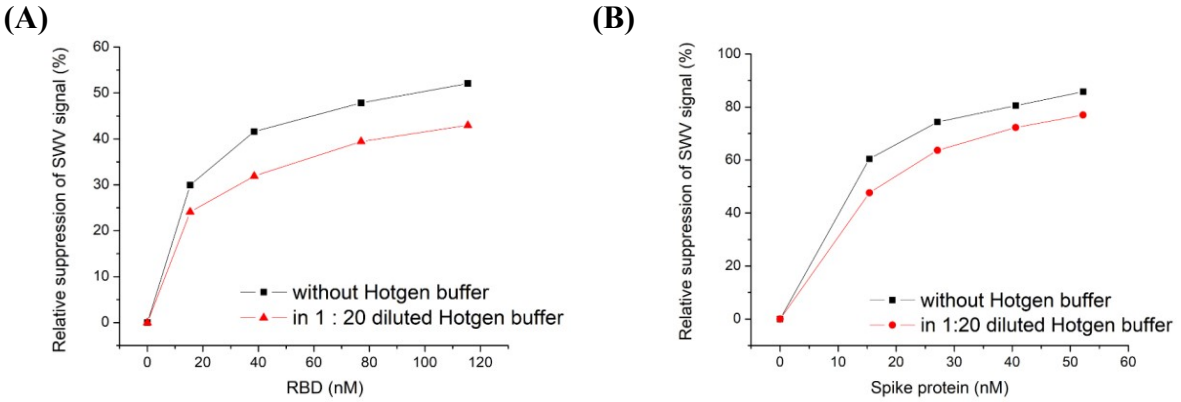


**Fig. S5** Comparison of binding of RBD (A) and spike protein (B) to the MIP measured in 5 mM $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$ in PBS or 1:20 diluted Hotgen buffer.

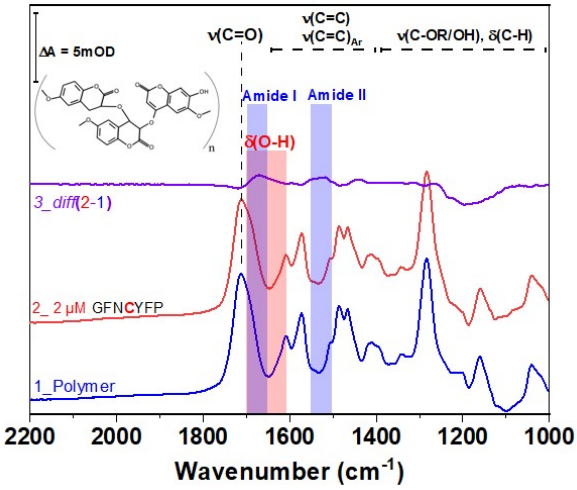


**Fig. S6** IR absorbance spectra of individual steps of the NIP formation on SEIRA gold surface. The observed bands in trace 1 are attributed to the carbonyl ν(C=O) stretching vibration (1715 $cm^{-1}$), aromatic and vinyl ν(C=C) stretching modes (1600 – 1400 $cm^{-1}$), ν(C–O) stretching vibration of the ester group (1280 $cm^{-1}$), the ν(C–O–C) stretching of alkyl ethers (1160 $cm^{-1}$) and δ(C–H) bending modes (1400 – 1000 $cm^{-1}$), all of these are characteristic of the polyscopoletin film. Subsequent binding of the G-Peptide leads to the appearance of amide I and II, detectable from the corresponding difference spectrum (trace 3) between trace 2 and trace 1.