Application Note # 179

MP-SPR and QCMD Characterization of Viral Spike Capture on Virus-Mimicking Supported Lipid Bilayers on SiO_2

This application note describes the combined use of MP-SPR and QCMD to validate supported lipid bilayer (SLB) formation on SiO_2 and to quantify immobilization and surface coverage of His-tagged SARS-CoV-2 spike proteins. QCMD confirms bilayer formation, integrity, and binding specificity, while MP-SPR provides quantitative spike surface coverage. Together, these complementary techniques enable robust structural and quantitative characterization of biomimetic membrane platforms.

Introduction

Viral attachment to host cells is an early and essential step in infection. Attachment can involve specific receptors and/or broader contributions from cell-surface components that facilitate initial contact. Traditional binding assays often rely on purified receptors or isolated viral proteins, which may not fully capture multivalent interactions occurring at membrane interfaces.

Orthogonal, label-free biophysical techniques such as Multi-Parametric Surface Plasmon Resonance (MP-SPR) and Quartz Crystal Microbalance with Dissipation (QCMD) enable quantitative characterization of supported lipid bilayers (SLBs) and subsequent protein capture on SiO_2 surfaces. SiO_2 surfaces are widely used in SLB research due to their hydrophilic nature, which promotes vesicle rupture and bilayer formation. On SiO_2, SLBs are separated from the solid support by a thin interstitial water layer of approximately 10-20 Å, which reduces substrate coupling and preserves lateral lipid mobility and diffusivity (1).

In Conca *et al.*, NTA-containing SLBs were used to immobilize His-tagged SARS-CoV-2 spike proteins via Ni-NTA/Histidine coordination, providing a controlled platform to verify specific immobilization, confirm tuneable spike loading, and estimate spike surface densities comparable to virion-like values. The validation of SLB formation and quantitative characterization of the protein capture and surface functionalization was achieved by the synergistic use of QCMD and MP-SPR.

Materials and Methods

Both MP-SPR and QCMD experiments used SiO2-coated sensors. Supported lipid bilayers (SLBs) were formed from small unilamellar vesicles (SUVs) composed of POPC:DGS-NTA in the presence of $NiCl_2$, which rupture on SiO_2 *in situ* to form a SLB. After rinsing with buffer, His-tagged spike protein was injected to enable Ni-NTA/His-tag-mediated capture. The MP-SPR measurements were performed using an MP-SPR Navi™ 220A NAALI with 670, 785, and 980 nm lasers in both channels. The multi-wavelength MP-SPR approach enables modelling of the SLB layer and can be used to estimate layer thickness (using LayerSolver), in addition to monitoring adsorption in real time (2). QCMD measurements were performed using BioNavis 4-cell station QCMD instrument.

Results and discussion

In MP-SPR and QCMD measurements, Conca et al. used QCMD to confirm that spike proteins were immobilized on NTA-containing SLBs in a stable and specific manner. Specificity was demonstrated by imidazole-mediated release of bound spike and by inhibition of binding through anti-His-tag antibody blocking, consistent with Ni-NTA/His-tag-mediated capture. Spike loading was tuneable by the molar fraction of NTA lipids in the SLB, with QCMD confirming increased capture at higher NTA content. Using MP-SPR sensograms and an optical mass model, they reported a spike surface coverage of 62 ng/cm² on 0.25% NTA SLBs, corresponding to approximately 920 trimers/µm² and approximately 45 trimers per 125 nm liposome (virion-like density estimate). Surface coverage (Γ) was estimated from the MP-SPR angular shift (Δθ) using

$$\Gamma = \frac{\Delta\theta\ \delta}{S_0\ b}$$

where δ is the evanescent field decay length, S_0 is the bulk sensitivity, and b is the refractive index increment (dn/dC). In addition, QCMD measurements using spike from multiple SARS-CoV-2 variants showed comparable immobilization on NTA-supported lipid bilayers, with equilibrium responses differing by <5% between variants (data not shown).

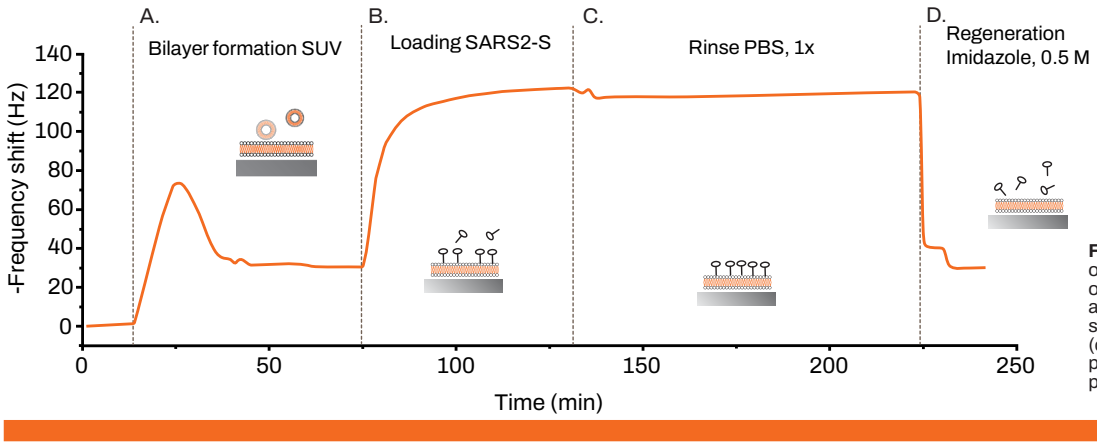

Figure 1. Schematic representation of the QCMD experiment: (a) Injection of SUVs onto the SiO_2 surface to form a SLB; (b) attachment of His-tagged spike protein via Ni–NTA coordination; (c) rinsing with PBS to remove unbound protein; (d) Imidazole-mediated spike protein removal from the lipid bilayer.

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Conclusions

MP-SPR and QCMD provide complementary information during SLB formation on SiO_2. MP-SPR quantifies the optical (dry) lipid mass and confirms bilayer surface coverage, whereas QCMD measures the total acoustically coupled mass, including trapped water, and reports on viscoelastic properties. During vesicle fusion, the divergence between MP-SPR and QCMD signals reflects the transition from water-rich intact vesicles to a rigid planar bilayer, as water is released upon rupture (3). Together, MP-SPR verifies quantitative bilayer formation, while QCMD confirms structural integrity and successful vesicle-to-bilayer conversion.

Building on this validated SLB platform, Conca et al. demonstrate controlled spike immobilization at virion-like densities and quantitative analysis of membrane interactions, highlighting how the combined use of MP-SPR and QCMD enables robust characterization of complex biomimetic membrane systems.

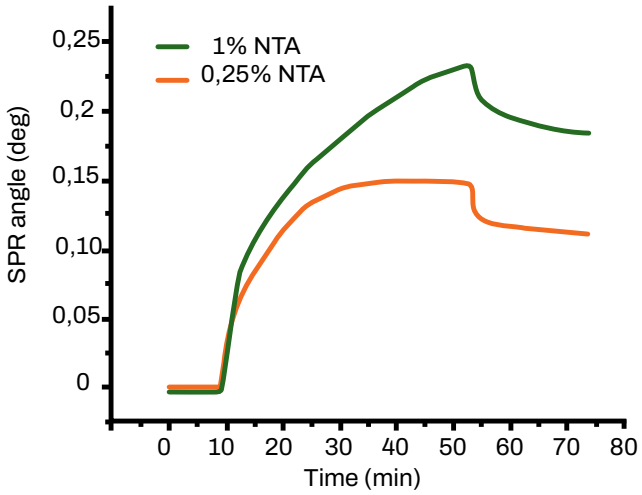

Figure 2. MP-SPR sensograms showing increased His-tagged spike surface coverage with increasing mol% DGS-NTA in the SLB.

Original publication:

Conca *et al.*, Analytical Chemistry, 97, 2025, 4318-4328.

References

1. Ulmefors *et al.*, Langmuir, 37, 2021, 5494-5505
2. Soler *et al.*, ACS Sensors, 3, 2018, 2286-2295
3. Keller *et al.*, Phys. Rev. Lett. 84, 2000, 5443-5446

Recommended instrumentation for reference assay experiments

MP-SPR Navi™ 220A NAALI, 210A VASA & BioNavis QCMD 400, QCMD 110

Sensor surface: SiO_2

Software: MP-SPR Navi™ Control, DataViewer, and LayerSolver™ for MP-SPR Navi™ & BioNavis Control

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