

# Gold-Mediated Functionalization of NEMS-FTIR Resonators for Selective Molecular Detection

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## Summary:

NEMS-FTIR has recently demonstrated picogram-level limits of detection for both airborne and aqueous samples, with chemical specificity provided by the analyte's mid-IR fingerprint. However, the analysis of complex samples remains limited by overlapping molecular signatures and labor-intensive sample preparation. To address this, a gold-mediated functionalization strategy is introduced to enable selective analyte capture directly on the NEMS surface, demonstrated by the immobilization of a CD66e antibody and verified through the characteristic mid-IR fingerprint of the bound bioreceptor layer.

**Keywords:** NEMS-FTIR, molecular detection, photothermal sensing, functionalization, biosensing

## Introduction

Nanoelectromechanical Fourier-transform infrared spectroscopy (NEMS-FTIR) has recently demonstrated picogram-level chemical identification of nanoplastics in aqueous samples [1] and of submicrometer atmospheric aerosols [2]. This high sensitivity enables the analysis of minute sample quantities, such as nanolitre volumes in aqueous samples [1], and reduces the sampling time required for ultrafine aerosols from hours to minutes [2].

Although the NEMS-FTIR platform can provide spectroscopic fingerprints, interpreting complex matrices remains challenging. Therefore, this work introduces gold-mediated surface functionalization to create selective biorecognition layers on NEMS membranes via stable Au-S bond formation, as schematically depicted in Fig. 1. The strong affinity between thiol groups and gold enables robust attachment of thiol-containing crosslinkers, providing a stable interface for bioreceptor immobilization and subsequent specific detection of target analytes in complex biological samples.

## Methods

The central element of the NEMS-FTIR platform is a silicon nitride (SiN) membrane, which serves simultaneously as photothermal sensor and sample carrier. The chips consist of 5 mm × 5 mm, 380 µm thick silicon substrates supporting a 50 nm low-stress SiN membrane, patterned by UV lithography and released by backside KOH

etching. Electrical transduction is enabled by 10 µm lithographically defined gold electrodes [2].

After chip fabrication, an additional circular gold pad was deposited on the backside of the released membrane by physical vapor deposition (PVD) through a laser-cut stainless-steel shadow mask. The 600 µm diameter pad consisted of a 10 nm chromium adhesion layer, followed by a 50 nm gold layer. This configuration provided sufficient surface area for functionalization and high IR reflectance, while minimizing added mass and preserving the resonator's thermomechanical dynamics.

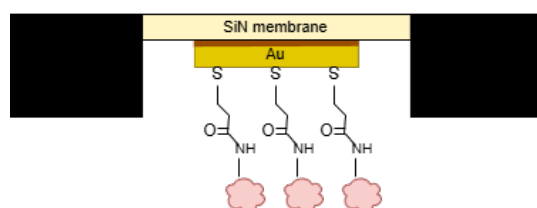


*Fig. 1. Schematic representation of the biofunctionalized NEMS chip, illustrating the silicon nitride membrane with a localized gold pad serving as the functional interface for immobilization of the biorecognition element, enabling selective capture of the target analyte through specific functional-group interactions.*

To demonstrate this concept, an antibody against the Carcinoembryonic Antigen (CEA), also known as CD66e, was immobilized on the gold-coated, oxygen plasma-treated NEMS surface using dithiobis(succinimidyl propionate) (DSP). DSP dissolved in dimethyl sulfoxide (DMSO) was first chemisorbed onto the gold

through its disulfide group by incubating the chip in a 10  $\mu\text{g}/\mu\text{L}$  solution for 30 min, leaving NHS-reactive groups exposed at the surface. These groups then reacted with the primary amines of the 1  $\mu\text{g}/\mu\text{L}$  CD66e antibody during incubation for 1 h. This facilitates covalent bonding between the protein and the surface of the resonator. The chip was then rinsed thoroughly with water to remove any unbound protein and by-products from the reaction.

The measurements were performed using a nanoelectromechanical IR analyzer (EMILIE, Invisible-Light Labs GmbH, Austria), coupled to a FTIR spectrometer (Vertex 70, Bruker Optics, MA, USA), that was operated under high-vacuum conditions ( $10^{-5}$  mbar) to reduce air damping and enable sensitive resonance-frequency tracking. The FTIR spectrometer served as a broadband mid-infrared light source over the range of 4000–400  $\text{cm}^{-1}$ . The resonator frequency shifts were recorded in closed-loop operation and correlated with the FTIR wavenumber scan to reconstruct nanomechanical infrared spectra. The final spectra were background-corrected and normalized to remove substrate and baseline contributions [2].

## Results

The NEMS-FTIR spectrum after DSP-mediated immobilization of the anti-CD66e antibody is shown in Fig. 2. The most pronounced DSP-related features are observed in the 2000–1750  $\text{cm}^{-1}$  region and are assigned to NHS ester/ester carbonyl stretching vibrations. Additional DSP contributions are observed at 1251  $\text{cm}^{-1}$  and 1112  $\text{cm}^{-1}$ , corresponding to characteristic succinimide/NHS ester vibrations, including C–N–C and N–C–O stretching modes [3]. The remaining bands in the 1700–1000  $\text{cm}^{-1}$  region are mainly attributed to fingerprint vibrations of the antibody. The bands at 1640  $\text{cm}^{-1}$  and 1537  $\text{cm}^{-1}$  correspond to amide I and amide II vibrations, respectively, which serve as key indicators of CD66e antibody immobilization [4]. These spectral features remained unchanged after multiple washing-measurement cycles, suggesting stable antibody immobilization rather than weak physical adsorption.

The predominance of DSP-related carbonyl bands is attributed to the strong spectral contribution of the linker layer, resulting from the relatively high DSP concentration, which could be addressed by optimizing the surface chemistry.

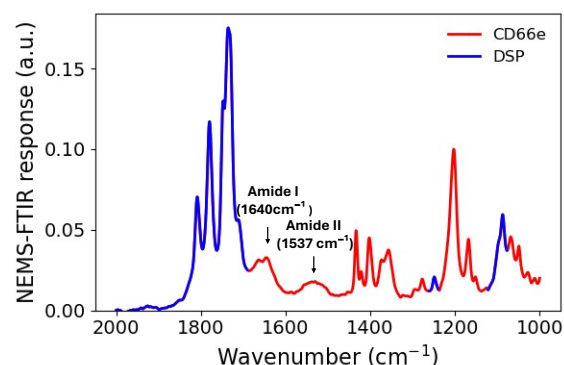


Fig. 2. NEMS-FTIR spectrum of a gold-coated resonator after DSP-CD66e immobilization, obtained following incubation with DSP cross-linker in DMSO at 10  $\mu\text{g}/\mu\text{L}$  for 30 min, subsequent incubation with CD66e at 1  $\mu\text{g}/\mu\text{L}$  for 1 h, and thorough washing with water.

## Conclusion

This work demonstrates successful functionalization of NEMS-FTIR resonators through gold-thiol chemistry, confirmed by characteristic DSP- and antibody-related spectral features and their stability after repeated washing-measurement cycles. These results demonstrate the potential of introducing molecular selectivity to NEMS membranes. With further optimization of chip design, transduction, and surface chemistry, this approach could broaden the application of NEMS-FTIR to complex biological samples and support the development of next-generation bio-sensing technologies.

## References

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