

# Label-free NEMS-based protein quantitation combining UV and IR spectroscopy with femtogram sensitivity

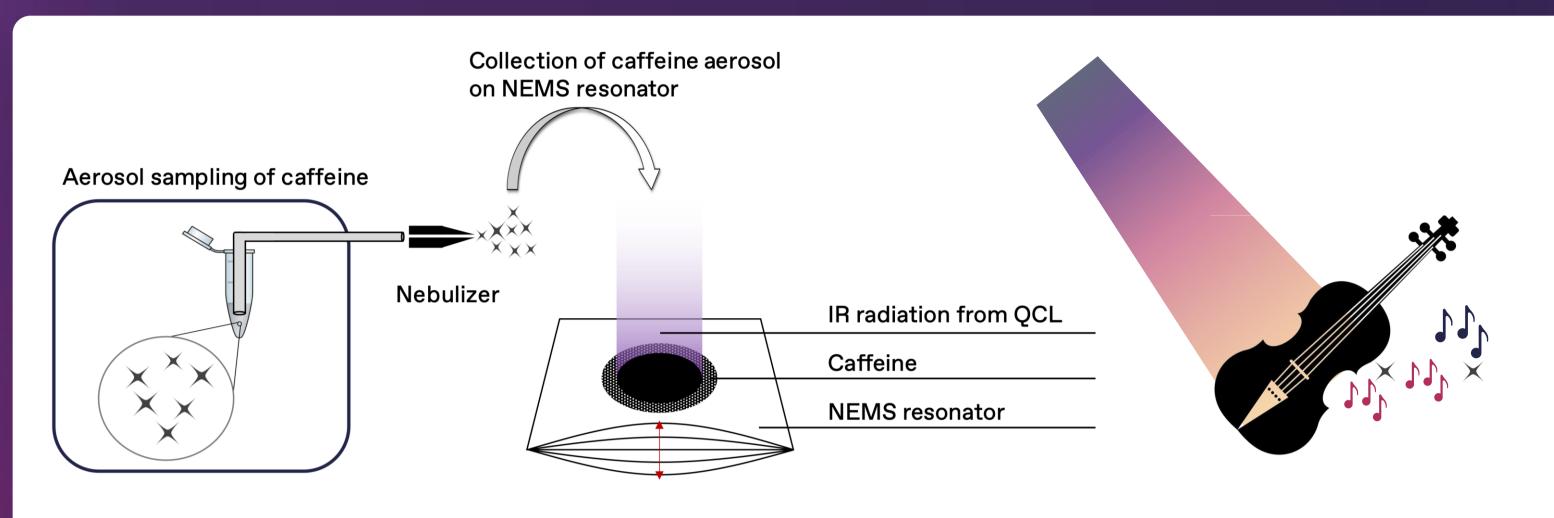


Niklas Luhmann<sup>1</sup>, Raphael Pliessnig<sup>1</sup>, Josiane P. Lafleur<sup>2</sup> and Silvan Schmid<sup>1</sup>

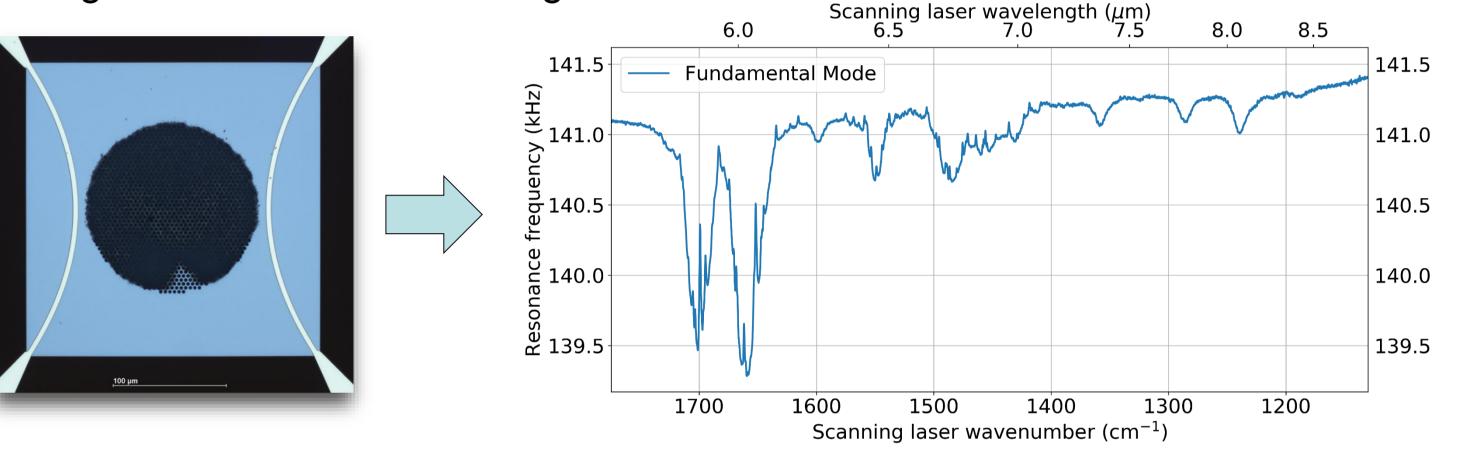
Dissertation project at the Institute of Sensor and Actuator Systems – MNS group, TU Wien

With focus on emerging tasks of infrared (IR) spectroscopy ranging from rapid detection of pathogens, such as viruses, to environmental analysis, the limited sensitivity of existing IR detectors calls for novel techniques. Employing thermal detectors in Fourier-transform IR spectroscopy allows for the detection of chemical compounds down to a few micrograms. However, to reach higher sensitivities IR detectors require expensive and impractical cryogenic cooling. During the past decade, nanoelectromechanical photothermal infrared spectroscopy (NEMS-IR) has shown exceptional sensitivities for the analysis of dispersed particles and dissolved compounds. To the current stage of this project, we demonstrate an advanced approach of NEMS-IR spectroscopy enabling label-free quantitative spectral analysis of volatile chemical compounds. The developed setup allows for rapid sampling and spectra acquisition within 10 min. Using this technique, we present high resolution infrared spectra of caffeine with a limit of detection of 20 pg and qualitative analysis of environmental airborne pollutants.

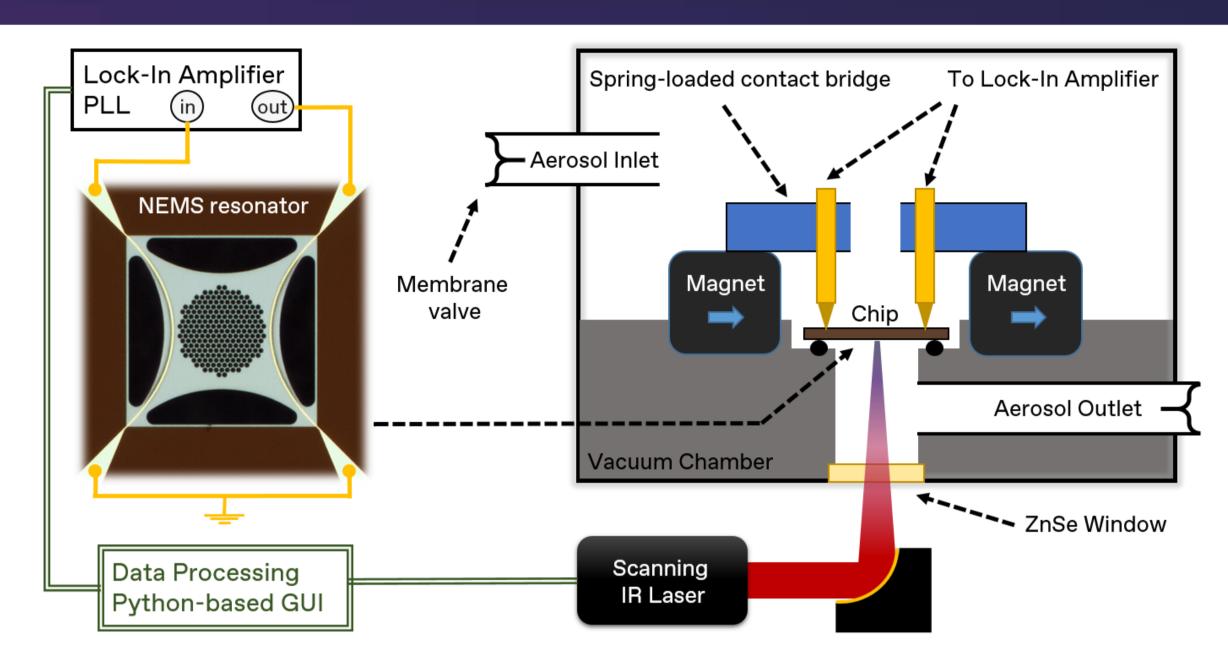
## Principle of NEMS-IR spectroscopy

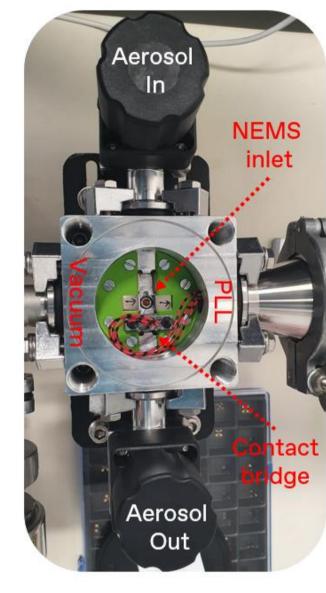


A chemical compound is deposited to a nanoelectromechanical resonator through aerosol sampling. Our technique is analog to the thermally-induced detuning of a guitar string. We exploit the thermal frequency detuning of the nanomechanical resonator due to the photothermal heating of the sample during irradiation with infrared light.



### Setup and Specs

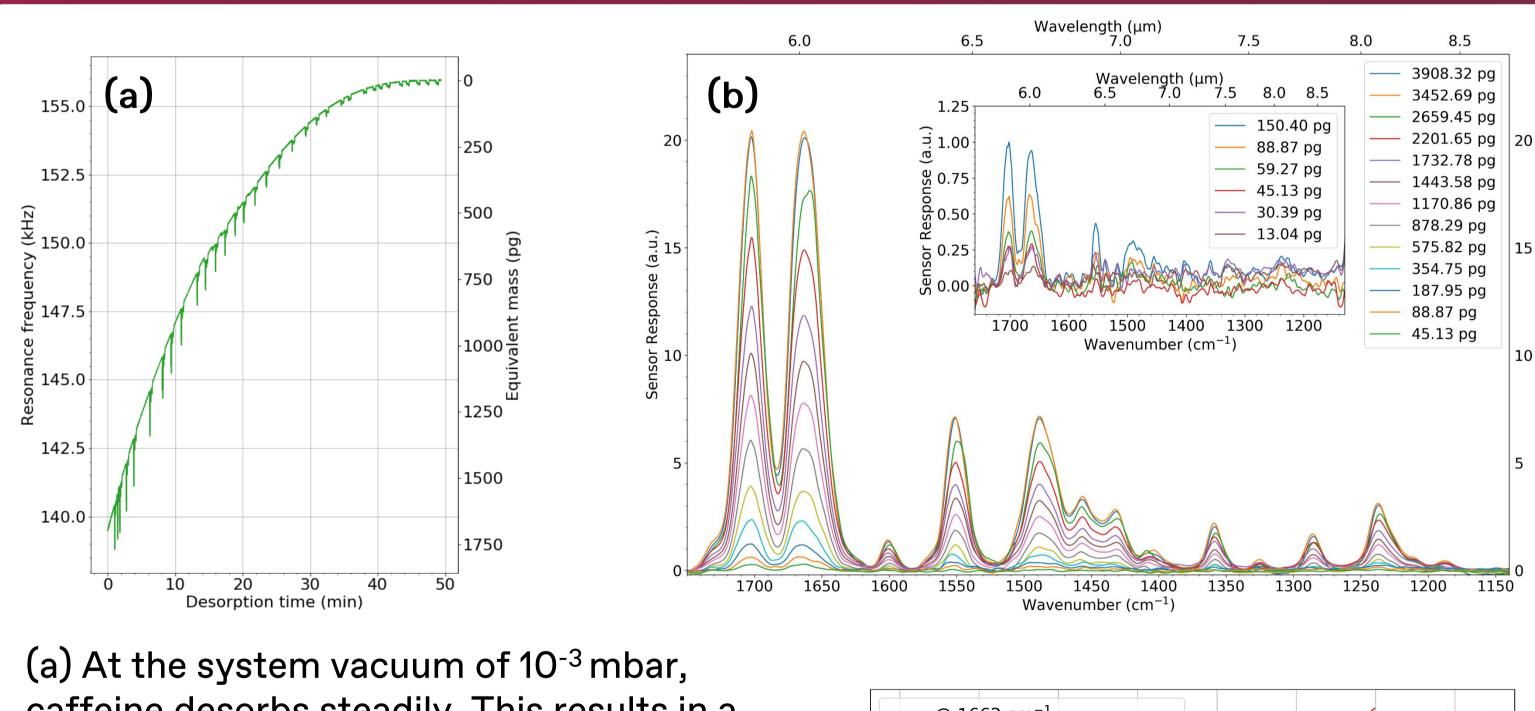




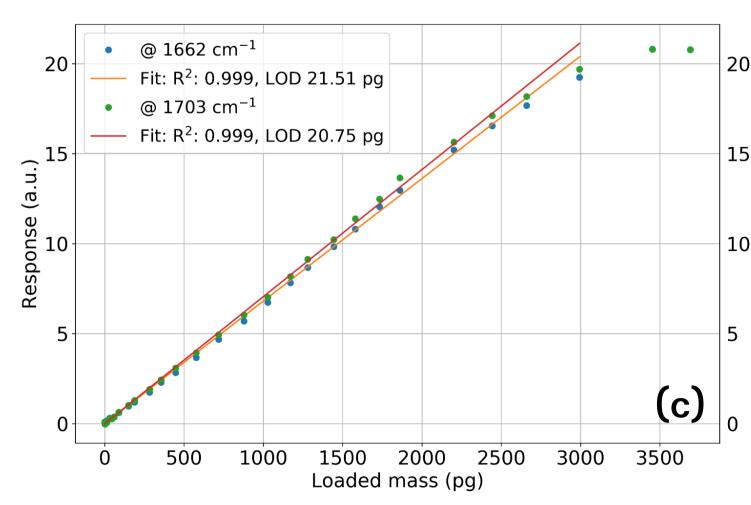
Spring-loaded connectors enable a rapid exchange of the resonator chip while providing electrical contact and sufficient pressure on the chip to seal it for aerosol sampling. The nanomechanical vibration is transduced through an inductive scheme by placing the chip in a static magnetic field. The nanoelectro-mechanical resonator is driven at its resonance frequency by means of a phase-locked loop, which allows the monitoring of the resonance frequency during the irradiation with IR light.

#### Evaluation of LOD by natural desorption

Micrograph of a resonator sampled with caffeine & corresponding frequency response.

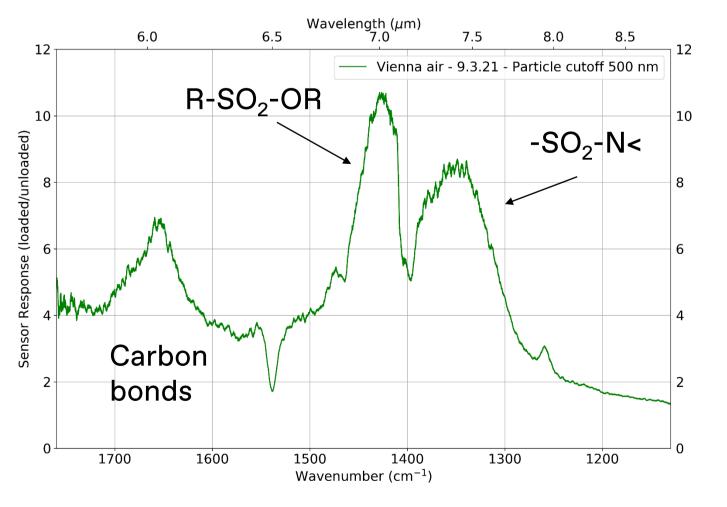


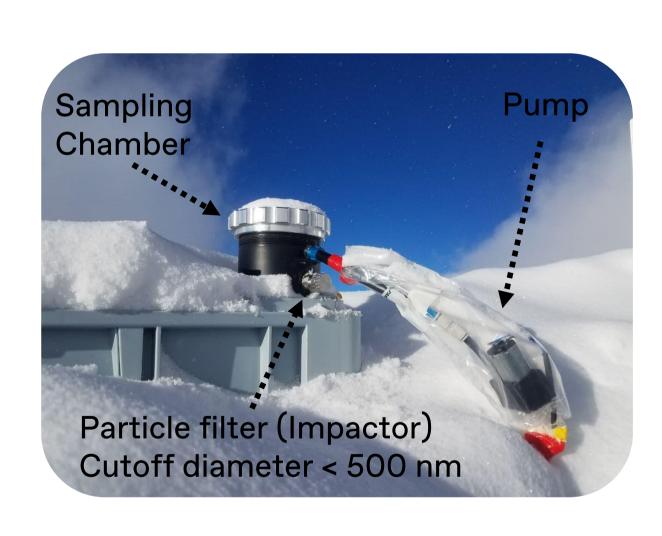
caffeine desorbs steadily. This results in a constant mass loss and change of the resonance frequency. (b) By recording IR spectra during the desorption process, it is possible to obtain the detector response for different mass loads of caffeine. (c) A calibration curve was extracted from the strongest peaks and a limit-of-detection (LOD) of ~ 20 pg was determined. The curve further shows a dynamical range of three orders of magnitude.



## Analysis of environmental pollutants

In the framework of this study, a portable aerosol sampling chamber was developed to enable the sampling of environmental airborne pollutants. A commercial impactor was mounted at the inlet, acting as a filter that limits the collection to particles below PM<sub>2.5</sub>. After a successful sampling, the loaded resonator chip was placed in the sensor setup and can be analyzed within a few minutes.





Airborne nanoparticles were sampled from the rooftop of the laboratory in Vienna. The measured IR spectra show spectral features of sulfur- and carbon related compounds. Based on the general frequency shift from before and after sampling, an equivalent mass of approximately 20 ng can be estimated.

#### Conclusion

In the framework of the ongoing project it was possible to enable rapid qualitative and quantitative analysis of volatile compounds and environmental airborne pollutants based on nanoelectromechanical infrared spectroscopy. Testing the developed setup with caffeine sampled with an aerosol-based technique, we currently obtain a limit-of-detection of 20 pg, which represents a million times higher sensitivity compared to standard FT-IR devices. With further optimizations of the resonator geometry and tensile stress, we predict to reach the femtogram regime. Due to buffer related issues during sampling, protein analysis was yet not possible. Currently, several other sampling methods and the implementation of UV optics is about to be tested.

