Using molecules to detune nanodrums

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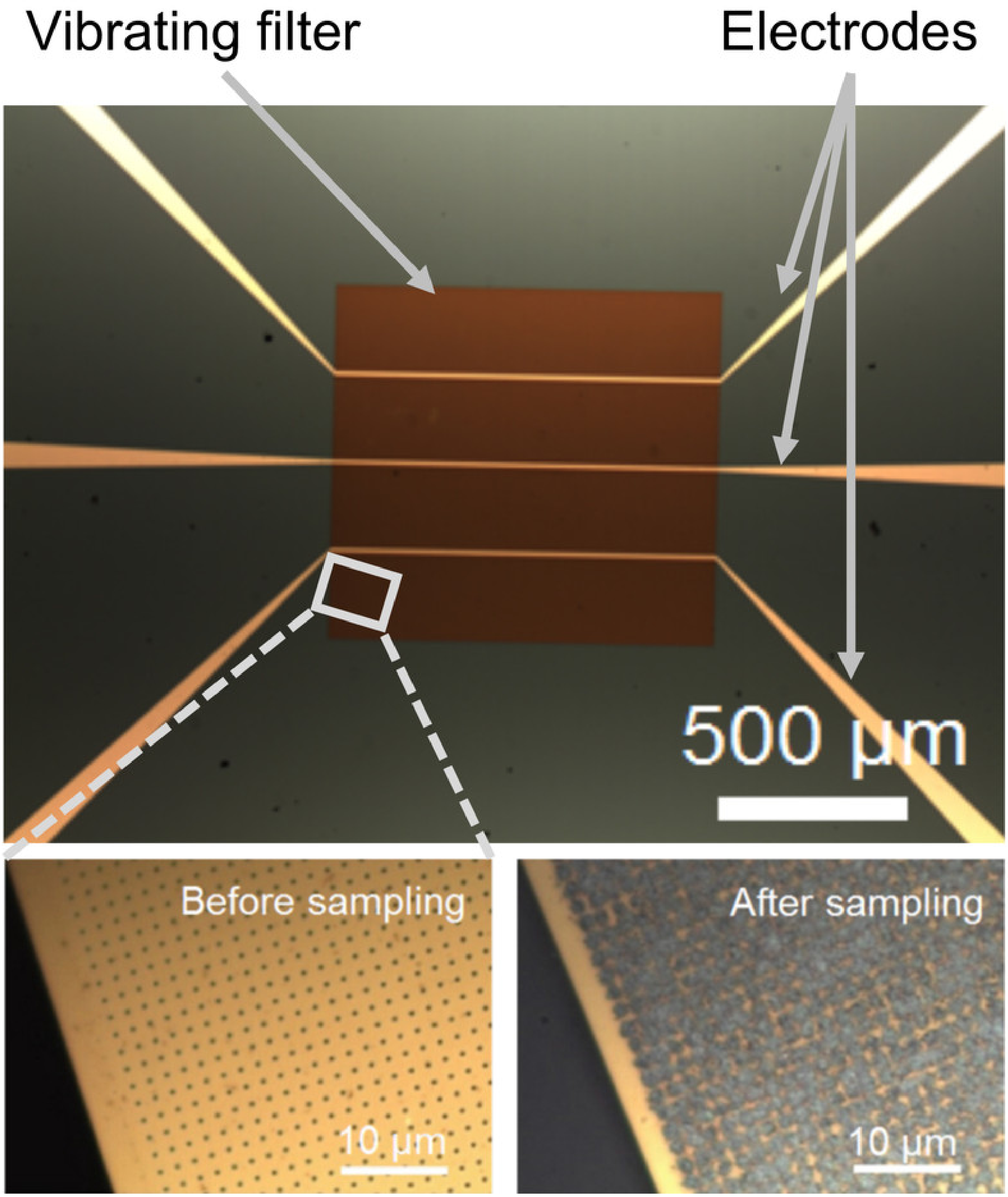

(above) Microscope image of a filter membrane with gold electrodes to detect the mechanical vibrations. (below) Microscope images of the filter membrane before and after the sampling of a chemical specimen. Credit: Technical University of Denmark

The analysis of the minutest quantities of pharmaceutical samples is of crucial importance for the research and synthesis of new medications. At the moment it represents a technical challenge, but a new infrared method of measurement developed by TU Wien in collaboration with two research groups from Copenhagen may remedy this.

Materials for pharmaceutical products are an expensive commodity, meaning appropriate caution is called for when it comes to synthesising new medications, for example. A precise measuring instrument is required in order to test or adapt the desired composition. A common measurement method to date has been infrared spectroscopy. However, the sample must first be prepared before it can be analysed. The pharmaceutical material can, for example, be dissolved in an aqueous solution. However, the high degree of light absorption exhibited by water makes accurate measurement difficult. Alternatives would be to freeze-dry the material, or to prepare it in powder form, but both options require approx. 1 mg of the material which, depending on what it is to be used for, is a relatively large quantity. Professor Silvan Schmid from the TU Wien Institute of Sensor and Actuator Systems, together with two research groups from the Technical University of Denmark and the University of Copenhagen, has developed a new method of measurement which is already delivering precise measurements from the smallest sample quantities.

Vibration of molecules

"A high source of errors in the measurement process can be attributed to the sample preparation, where the direct handling of the probe material encourages contamination," explains Professor Schmid. In the developed measurement method, sample material is added directly from a solution and is subsequently converted into an aerosol. The probe material is then transported together with the air in the aerosol and blown directly into the measuring instrument – without risk of contamination by handling. Inside the instrument, the aerosol is blown through a vibrating air filter, made from silicon nitride, and is captured there. "Our method is based on nanomechanical resonators. These can be compared to tiny perforated drums, which are also able to vibrate at specific resonance frequencies," explains Professor Schmid. These vibrating filters are around 1,000 times thinner than a strand of hair and around 500–1000 µm wide. In addition, the filters feature electrodes in order to measure the vibration of the filter drum. An infrared laser is then aligned with the filter. The light from the laser stimulates molecular vibration in the sample material adsorbed on the filter, which heats the drum, thereby creating a measurable detuning of the mechanical vibration. The molecular vibrations of the probe material can be obtained by tuning the wavelength of the infrared source and simultaneous monitoring of the filter frequency. "We have measured the molecular vibration peaks of pharmaceutical compounds, such as indomethacin, which agree with their expected absorption spectra. Furthermore, our method requires less than one millionth of the sample material needed for a standard infrared spectroscopy," explains Professor Schmid excitedly.

Next step: increased sensitivity and industrial application

Silvan Schmid continues to take further steps towards realistic industry applicability with his research. Amongst other things, his group is currently working on optimising the vibrating filter, in order to further increase the sensitivity. This would enable a further reduction in the amount of sample material required.

More information: Maksymilian Kurek et al. Nanomechanical Infrared Spectroscopy with Vibrating Filters for Pharmaceutical

Analysis, *Angewandte Chemie International Edition* (2017). DOI: 10.1002/anie.201700052

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