Electronic Supplementary Material (ESI) for Lab on a Chip

Supplementary information for "Nanomechanical identification of liquid reagents in a microfluidic channel"

M. Faheem Khan, Seonghwan Kim, Dongkyu Lee, Silvan Schmid, Anja Boisen &

Thomas Thundat

Device fabrication

A bimetallic microchannel cantilever is fabricated using silicon rich silicon nitride (SRN) which produces a transparent microchannel (refractive index 2.02) on the visible spectrum[1]. On four inch wafers, 10mm x 5mm BMC chips are fabricated at Danchip (a nanofabrication facility in Denmark) at the Technical University of Denmark. A 500 nm SRN film is deposited on a 350 µm thick substrate. This creates the bottom of the microchannel on a cantilever and is followed by adding a 3 µm thick layer of polysilicon as a sacrificial material. The patterned sacrificial layer is then covered by another 500 nm thick SRN film in order to create the walls and top of the microchannel. All of the deposition is performed using a low pressure chemical vapor deposition (LPCVD) technique. Later, the sacrificial material is wet etched using potassium hydroxide (KOH) at 80 ^{o}C. Up to 18 hours may be required in order to completely etch the sacrificial material depending on the length of the microchannel. Etching of the SRN layers is almost negligible in KOH. Additionally, the low stress nature of the silicon nitride assists in keeping the microchannel free of cracks. A 350 µm thick substrate is used specifically in order to keep the inlet on the back side of the chip 550 µm wide. This creates an opening of 100 µm on the top using KOH etching while following the anisotropic Si etch along 111 plane. On a 44 µm wide and 500 µm long cantilever, a U-shaped microfluidic channel (16 µm wide, 1050 µm long and 3 µm high) is fabricated. The height to width ratio is appropriate for the passage of small biological cells, while the U-shape of the microchannel allows for smooth flow inside the channel. Using an e-beam evaporator on the bottom side of the cantilever, a 500 nm thick layer of aluminum is deposited in order to make the cantilever a bimorph structure. This makes the cantilever to deflect on a change in the local heat on the cantilever. The chip has two openings (at the bottom) in order to provide fluidic interfaces between the chip and the macro sized Teflon tubes. The BMC has straight sample delivery channels (SDC) which are 3 µm high, 150 µm wide and 900 µm long. The SDC's are supported by micropillars (5 µm in diameter) in order to avoid collapse when a vacuum is created in the channels to load a sample.

Experimental setup

The details of the experimental setup are available under "methods" in the main article.

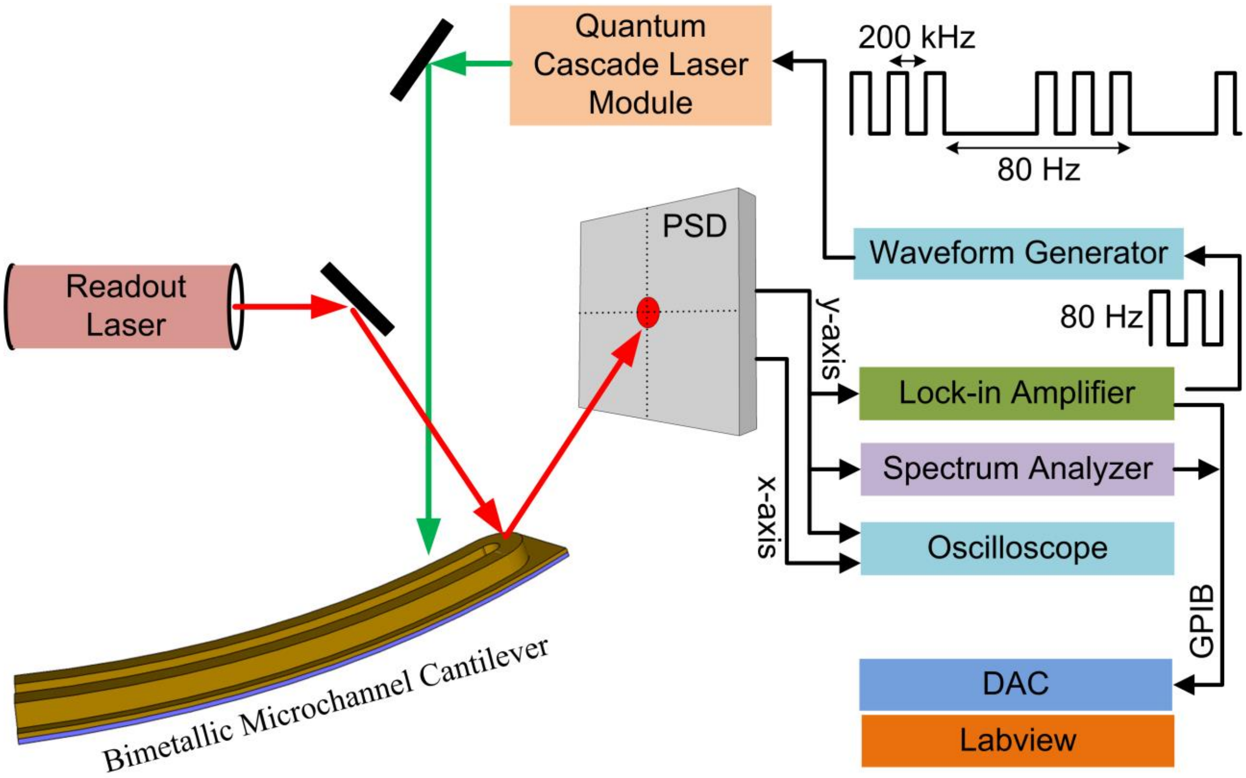

Fig. S1. Experimental setup of measurement of nanomechanical IR spectra of liquids

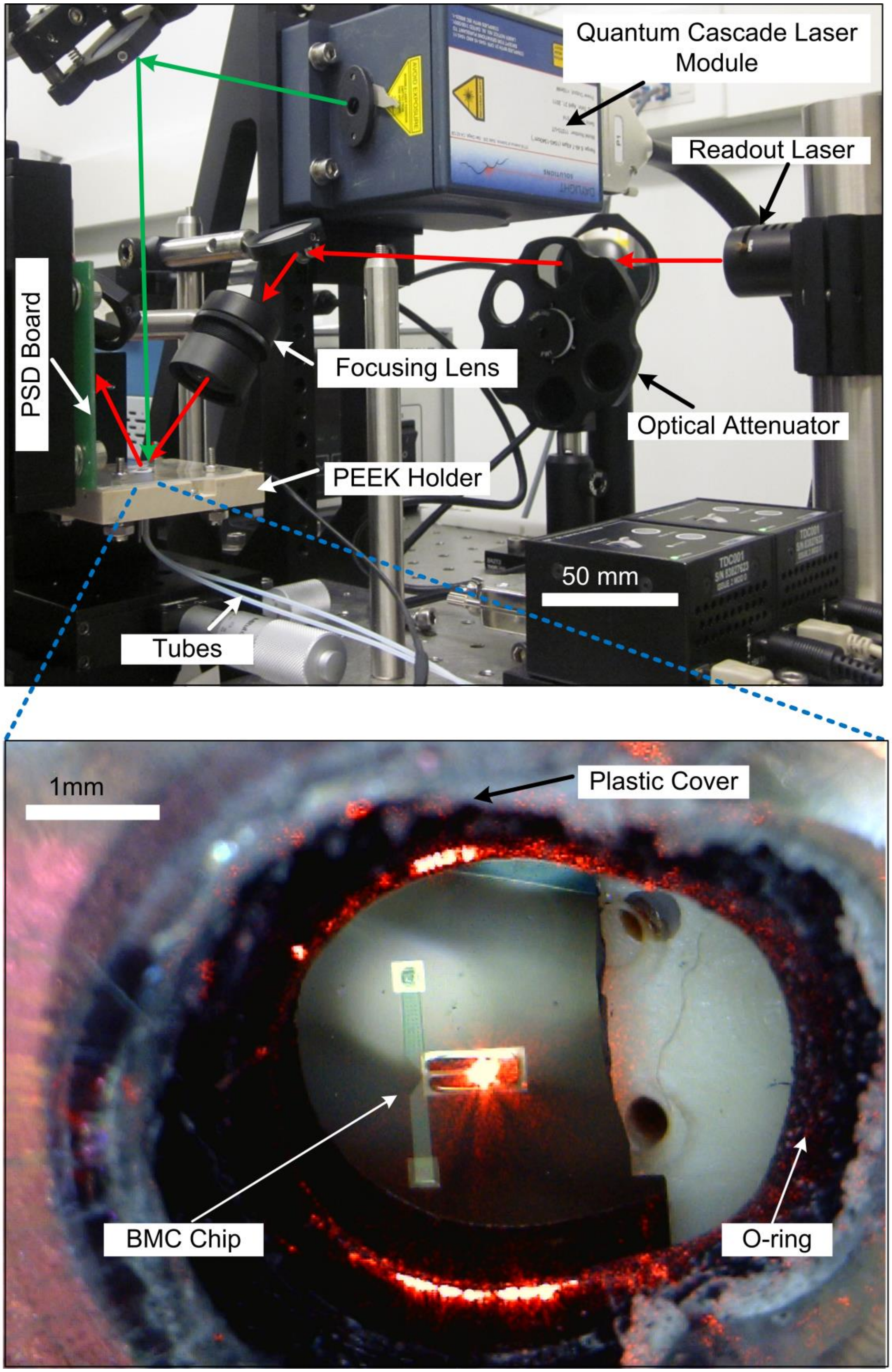

Fig. S2. Photograph of the experimental setup showing a QCL module, chip packaging, and readout laser. The zoom-in shows the top view of a chip with the readout laser focused at the tip of the BMC.

Loading liquid samples

In order to load a sample inside the BMC, a vacuum pump is connected at the outlet tube, creating a pressure difference of 1000 mbar which pulls the liquid sample into the microchannel. Due to the hydrophilic nature of the SRN, the sample immediately fills the microchannel. The presence of the sample inside the cantilever is visually verified through the transparent SRN channel as well as the by change in the BMC's resonance frequency. A 50 pL liquid sample from inside the microchannel is used to collect the nanomechanical IR spectrum. The packaging is well-sealed, allowing for precise measurement of the nanomechanical IR spectrum of volatile liquid samples. Once the spectrum is measured, the sample is unloaded by applying negative pressure to the outlet of the chip. The chip is flushed with ethanol and water to remove sample residues.

Loading solid/viscous polymeric samples

The BMC can be used not only for liquid samples; it also has a capability to measure IR spectra of solid or viscous polymeric samples. In order to take measurement such as these, the microchannel should be completely filled with the sample. In our experiments, a small quantity of these samples is placed on the backside of the BMC chip, as shown in Fig. S3a. The chip is then heated to the sample's melting temperature. The molten sample flows into the channel as a result of strong capillary forces, as shown in Fig. S3b. Once the microchannel is filled with the sample, the cantilever as well as the sample inside the microchannel, is cooled to room temperature in order to measure its nanomechanical IR spectrum. Fig. S3c shows a cantilever filled with a solid sample. One disadvantage of using this method is that after the measurement, the sample cannot be completely removed rendering the whole chip unusable.

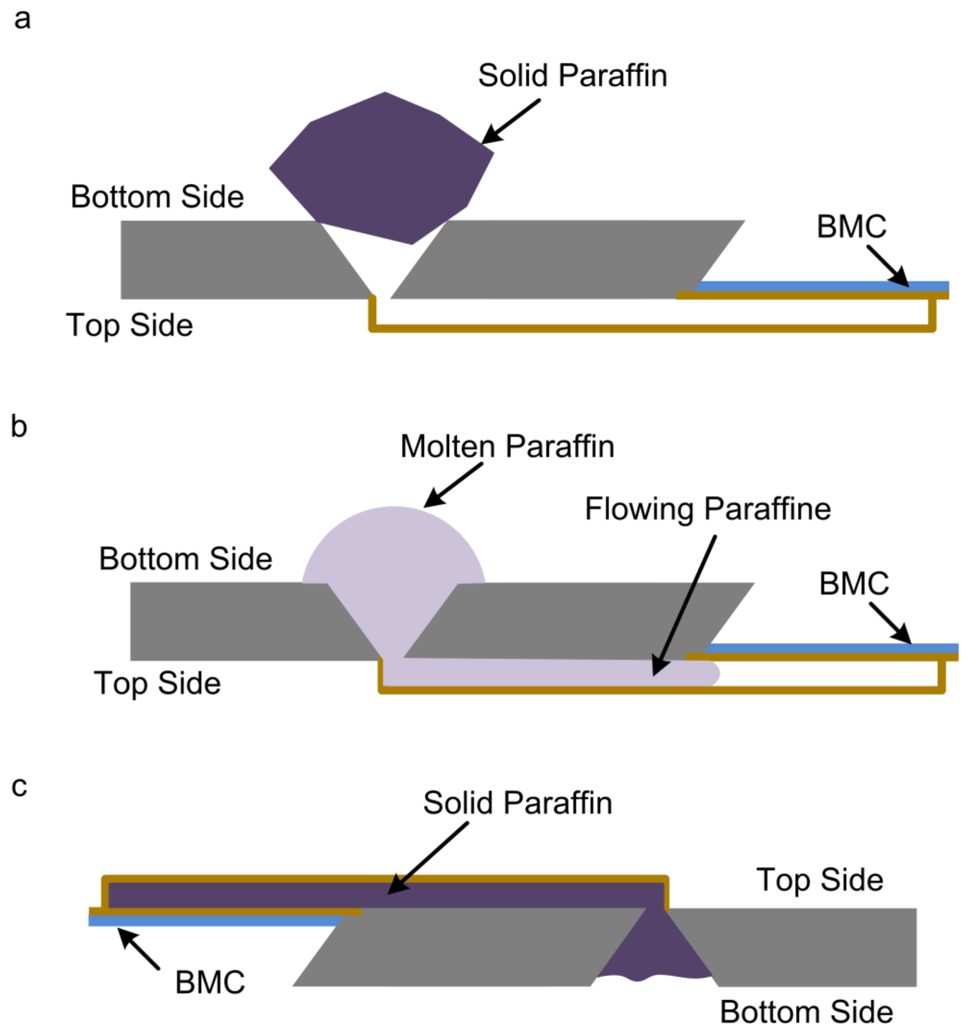

Fig. S3. Loading a solid sample **(a)** A small amount of solid paraffin is placed on the bottom side of a BMC chip **(b)** The chip is heated up to melting point of the sample. The molten paraffin flows inside the microchannel **(c)** To take a measurement the chip is cooled to room temperature.

Baseline IR spectra

Before loading a liquid sample, a baseline IR spectrum is measured with the empty BMC. Fig. S4 shows an example of baseline spectra (from 1540 cm^{-1} to 1145 cm^{-1}) which are measured for the results of different liquid samples reported in Fig. S6. In this particular example, the baseline spectra are measured with the empty BMC while using ÜT-7 and ÜT-8. The IR intensity (of both QCLs) is not uniform throughout the bandwidth. The ÜT-7 and ÜT-8 have maximum energy approximately at 1430 cm^{-1} and 1304 cm^{-1} respectively, and minimum energy at 1340 cm^{-1} and 1145 cm^{-1}, respectively. As a baseline, the spectrum shows the cantilever defection as broad upward peaks.

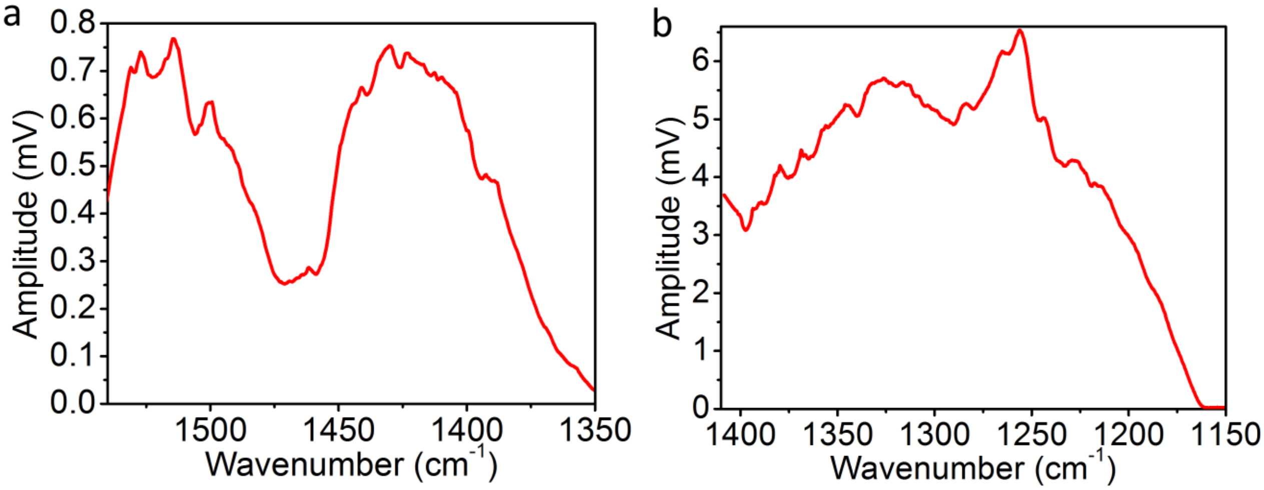

Fig. S4. Baseline spectra of the BMC for the results reported in Fig. S6 (a) The spectrum is measured with ÜT-7. The BMC deflects at 1520 cm^{-1} and 1420 cm^{-1} (b) The spectrum is measured with ÜT-8. The BMC deflects at 1325 cm^{-1}, and 1250 cm^{-1}. The cantilever deflections, in both cases, may be caused by IR absorption of SRN and air (present inside the empty BMC).

Nanomechanical IR spectra of ampicillin sodium salt

The BMC is used to measure IR spectra of 1, 2.5, 5 and 10 wt% of ampicillin sodium salt (Fig. S5). The results are compared with standard FTIR spectra in ATR mode. For the concentration of 10 wt% a clear match at 1400 cm^{-1} and 1456 cm^{-1} are found between the results by both techniques.

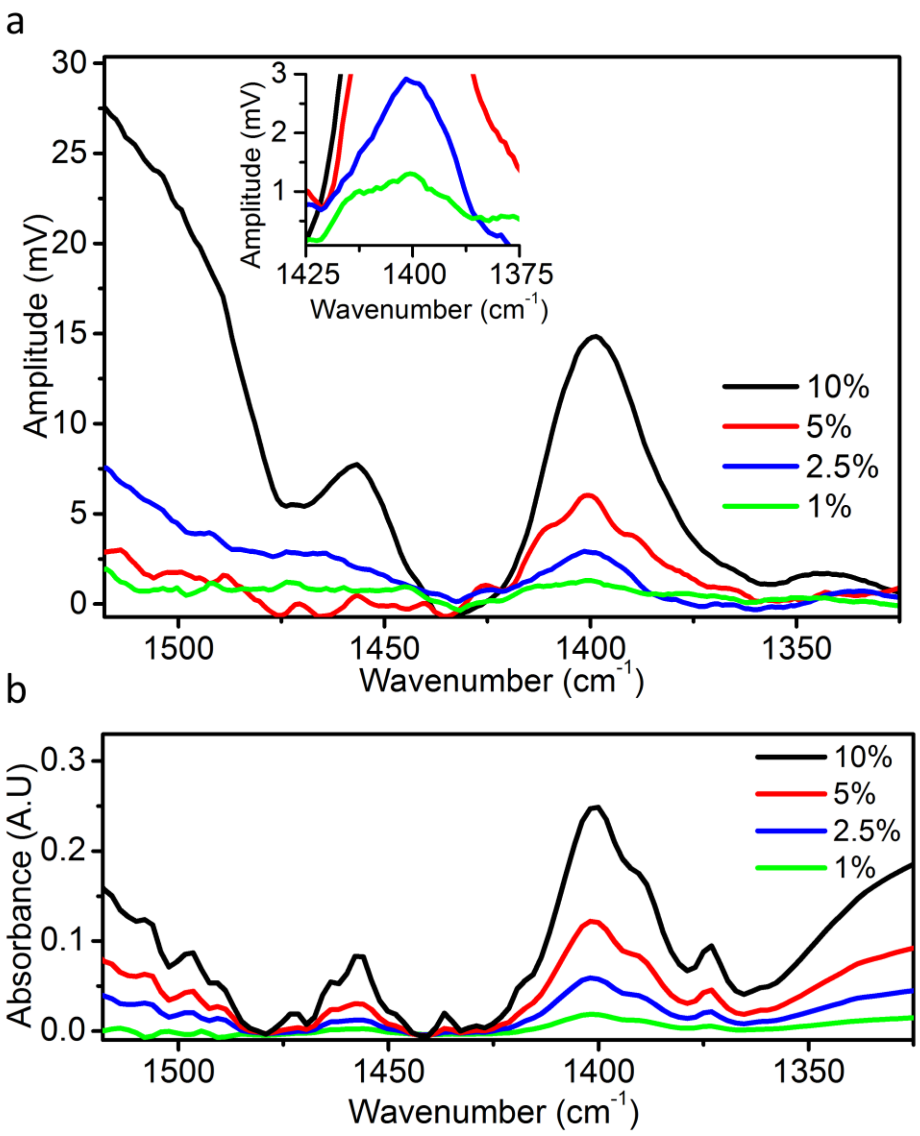

Fig. S5. (a) Nanomechanical IR spectra of ampicillin sodium salt. The inset shows zoomed in data at 1400 cm^{-1} for 1% ampicillin sodium salt. (b) FTIR-ATR spectra of ampicillin sodium salt.

Nanomechanical IR spectra of multiple analytes

Using the BMC, we measured nanomechanical IR spectra of multiple organic analytes, including n-hexadecane, isopropanol, naphtha, and paraffin, as shown in Fig. S6. The spectra are separately measured from 1540 cm^{-1} to 1350 cm^{-1} and from 1410 cm^{-1} to 1150 cm^{-1} by using ÜT-7 and ÜT-8 respectively.

As all chemicals have some common part in their molecular structure therefore the BMC also deflected at similar wavenumber. The green shaded area indicates an example of common peaks at 1385 cm^{-1} – 1370 cm^{-1} which is caused by CH_3 symmetric scissoring in the aliphatic molecules. It is noted that for same chemicals but different QCLs, the peaks in horizontal rows (under green shaded area in Fig. S6) matched quite well with a maximum variation of three wavenumber, in case of naphtha. Under grey shaded area, the peaks in the range of 1475 cm^{-1} – 1450 cm^{-1} are caused by CH_3 anti-symmetric and CH_2 scissoring. In addition, isopropanol shows C-OH bending at 1250 cm^{-1} and CC-H in-plane bending at 1345 cm^{-1}. Naphtha has a broad peak at 1263 cm^{-1} which is probably caused by complex hydrocarbons. Paraffin and isopropanol exhibit CH_2 twisting at 1308 cm^{-1} while paraffin has CH_2 bending at 1467 cm^{-1}. The data is plotted after smoothing using a Savitzky–Golay filter.

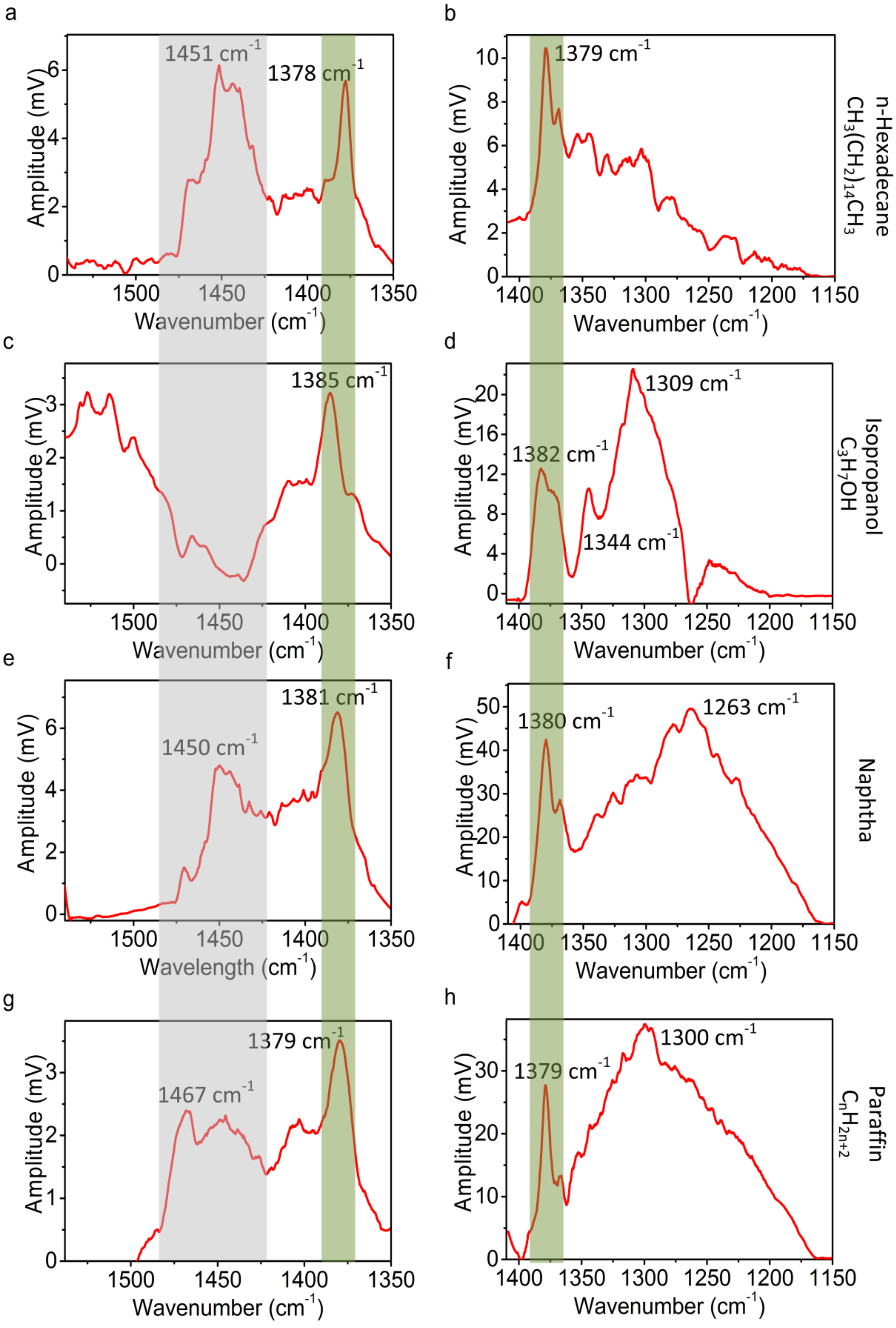

Fig. S6. Nanomechanical IR spectra of multiple organic compounds (a,b) n-Hexadecane, (c,d) isopropanol, (e,f) naphtha, (g,h) paraffin. ÜT-7 and ÜT-8 are used to measure these results in the range of 1540 cm^{-1} to 1350 cm^{-1} and from 1410 cm^{-1} to 1150 cm^{-1} respectively. In the green shaded area, the spectra show IR absorption peaks at about 1380 cm^{-1} which is caused by CH_3 symmetric scissoring. Additionally at 1380 cm^{-1}, the peaks measured by ÜT-7 and ÜT-8 well overlap on each other. The grey shaded area covers the peaks from 1475 cm^{-1} – 1450 cm^{-1} which are caused by CH_3 anti-symmetric and CH_2 scissoring. The spectra match well with standard FTIR spectra from literature.

Measuring mass density of a solution

The capability of the BMC to perform chemical characterization of liquids (by measuring nanomechanical IR spectra) is complemented by quantitative measurement of the physical properties of liquids. To measure the mass density of ethanol-water binary solutions, the BMC is calibrated with ethanol and de-ionized water at room temperature. The fundamental resonance frequency of a BMC, f_0, can be modeled as that of a solid cantilever with a changing density[1]. With the assumption that the fluid in the microchannel does not change the effective Young's modulus of the BMC, f_0 can be written as:

$$f_0 = \frac{A}{\sqrt{B + \rho_f}} \tag{S1}$$

where A and B are constants which can be determined from the resonance frequency measurements of two different fluids with well-known mass densities, such as ethanol and de-ionized water. Knowing A and B of the BMC, the mass density of the fluid in the microchannel can be determined by:

$$\rho_f = \left(\frac{A}{f_0}\right)^2 - B \tag{S2}$$

In the case of ethanol-water binary solutions (main Fig. 3b), fundamental resonance frequencies of the BMC are measured using three ethanol-water binary mixtures containing 5, 10, and 20 wt% of ethanol. The mass densities of these three solutions are calculated using Eq. S2. As the ethanol content decreases, the density of the binary solutions increases, and therefore the resonance frequency of the BMC decreases. In Fig. 3b, a fit function (Eq. S2) can help to determine the mass density of an ethanol-water binary mixture with an unknown ethanol concentration.

Reference

1. M.F. Khan, S. Schmid, Z.J. Davis and A. Boisen. *Microelectron. Eng*, 2011, **8**, 2300-2303