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Supplementary Information for

"A Surface Acoustic Wave Biosensor for Interrogation of Single Tumour Cells in Microcavities"

Apparent viscosity of the cell can be obtained using frequency dependent attenuation constant. Derived from the Navier-Stokes equation, the wave equation based with the independent variable of pressure can be given as:

$$\frac{\partial^2 \delta\rho}{\partial t^2} = v_0^2 \nabla^2 \delta\rho + \frac{\eta_B + \frac{4}{3}\eta}{\rho_0} \nabla^2 \frac{\partial \delta\rho}{\partial t} \tag{1}$$

where the $\delta\rho$ is the pressure field, v_0 is the ultrasound velocity, ρ_0 is the density, η_B is the bulk viscosity and η is viscosity. The attenuation for propagation of such a wave is given by an extinction coefficient, α, defined as:

$$\alpha = \frac{\omega^2}{2\,\rho_0 v_0^3}\left(\eta_B + \frac{4}{3}\eta\right) \tag{2}$$

The loss associated with this loss factor is given by

$$\mathrm{A(x)} = A_0 \exp(-\alpha \mathrm{x}) \tag{3}$$

and can be used to obtain the viscosity figures if the distance related with the attenuation is known and if Newtonian fluids are in question. These equations are plugged into studies in[1, 2] to obtain the order of magnitude for the values shown in Fig. S1.

For the Maxwell model detailed in the manuscript, a single time constant is assumed, and attenuations are mainly governed by viscosity with the values obtained as explained above. In such materials, scaling of viscosity with the frequency is important to determine the region of operation. The low frequency region is described as the Newtonian region where the material acts as a liquid. At very high frequencies, the material acts as a solid as it cannot react fast enough to periodic changes in stress. The effective viscosity or apparent viscosity value shows how the low frequency viscosity, η_0, scales with frequency and is given by

$$\eta_{effective} = \frac{\eta}{\eta_0} = \frac{1}{1 + \omega^2 \left(\frac{\eta}{E}\right)^2} \tag{4}$$

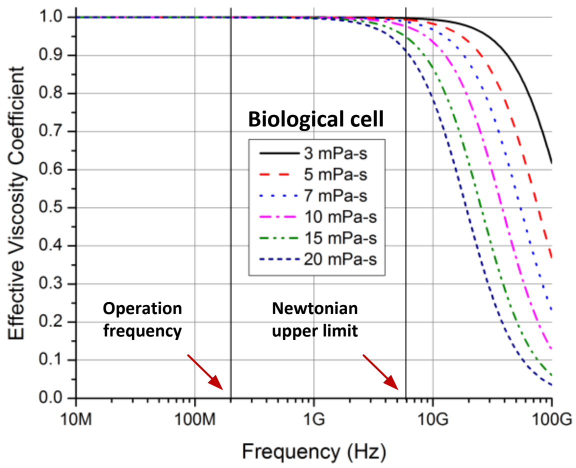

Fig. S1 Effective viscosity coefficient for acoustic modeling of cells. For a wide range of viscosity values, the cells exhibit liquid-like characteristics around 200 MHz in the Newtonian region. The transition to a complex material or solid-like material models is made at much higher frequencies in the order of GHz's.

Supplementary information about fabrication of the samples:

The process flow for the sensors is depicted in Fig. S2(a). Fabrication starts with cleaning of ST-cut quartz substrates with 4” diameter in acetone for 20 minutes using a 20 kHz ultrasonic buzzer. After dehydration at 150˚C in a nitrogen oven, samples were sputtered with a 1.1 μm layer of aluminium which serves as a hard mask for the reactive ion etching (RIE) process for forming the microcavities. The hard mask was patterned using AZ5214E type photoresist in positive mode and chemically etched using commercially available aluminium etchant at 50ºC. Formation of the microcavities was carried out with RIE using a CF_4/O_2 recipe at 200 W RF power under 180 mT of pressure. In order to reduce the surface roughness at the bottom of microcavities after etching, diluted BHF etchant was applied. The roughness was measured to be much smaller than the wavelength, approximately 350 nm, using atomic force microscopy.

On the other hand, no damage was observed on the substrate surface due to aluminium etching for hard mask patterning or due to removal of the hard mask layer. The depths of the microcavities on quartz were measured as 4.0±0.2 μm, corresponding to quarter wavelength. The IDT fingers were then formed using a lift-off process with nLOF 2020 type negative photoresist. The substrate etching was carried out before the finger formation step since aluminium is used for both layers, and since care was taken not to compromise the IDT structures.

Microfabrication of the soft microprobes are shown in Fig. S2(b). Omnicoat serves as an easy releasing layer on a handle wafer and underneath SU-8 as SU-8 photoresist is very difficult to remove reliably without additional sacrificial layers. After lithography, the probes were collected from the handle wafer with the application of remover-pg solution. Collected probes were placed on 3D printed pieces for accurate manipulation using micromanipulators.

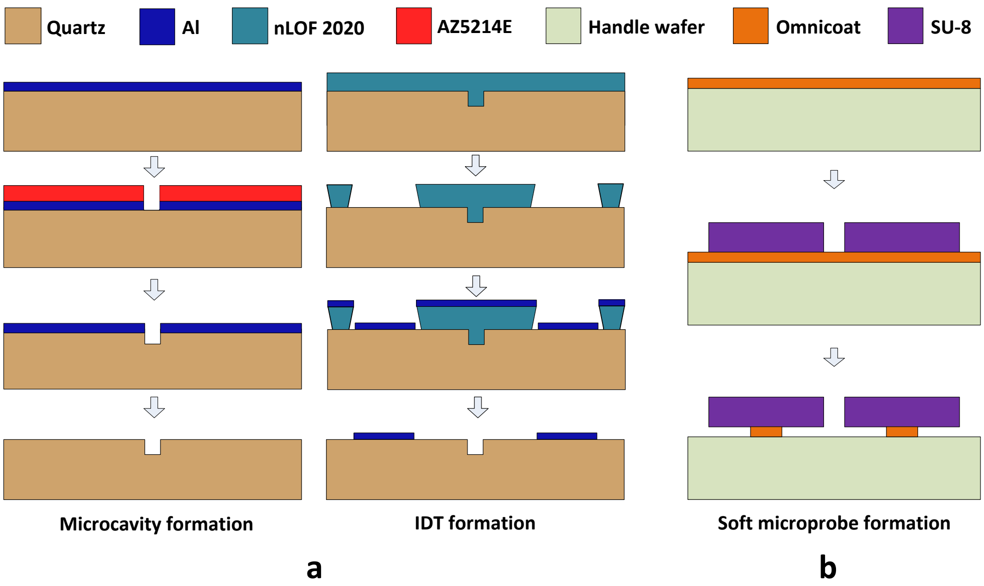

Fig. S2 Microfabrication flow for (a) the SAW devices with microcavities and (b) SU-8 microprobes.

REFERENCES

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