Material characterization of biological condensates using micropipette aspiration

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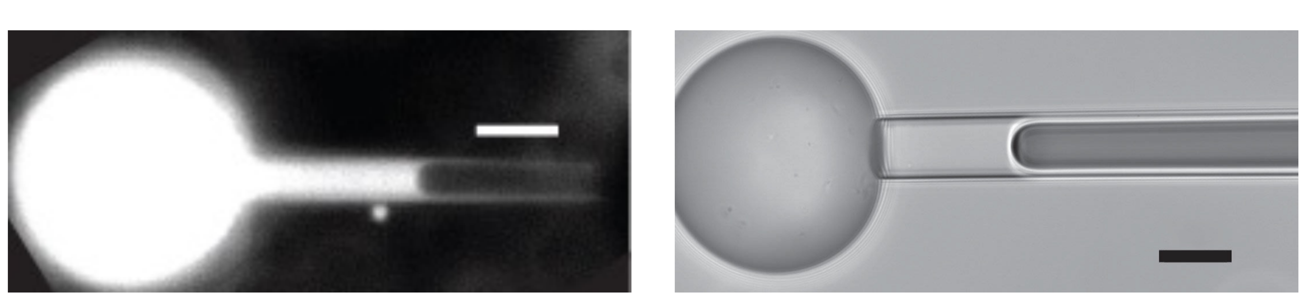
Research Aim

We propose a new model of micropipette aspiration (MPA), used by [1] to measure surface tension and viscosity of condensates, which is hydrodynamically consistent and includes no calibration parameters.

Motivation

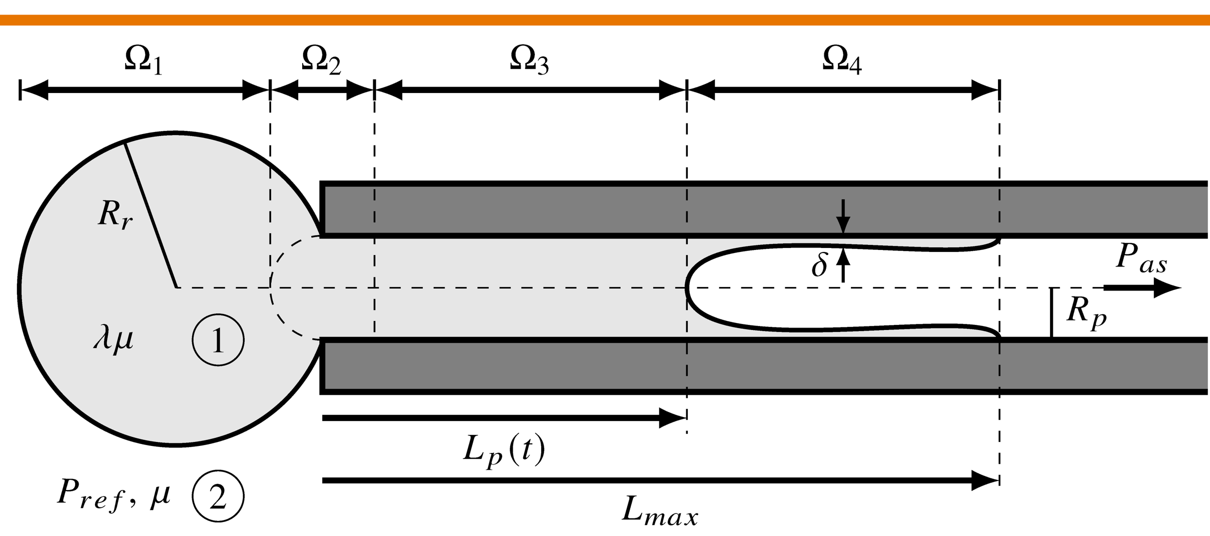
Popular methods of determining condensate material properties present several challenges, e.g. [2-3]

Viscosity	
FRAP	Dimensionality and lack of boundary condition limits its accuracy
Single molecule tracking	Protein molecules are not perfectly spherical
Single particle tracking	Challenging to get particles into condensate
Surface tension	
Fusion assay	Need another technique to know viscosity of protein condensates



MPA images of LAF-1 RGG condensate (left) and oil (right). Low pressure is applied to draw the fluid into the pipette. The curvature of the interface indicates that both fluids are wetting the glass of the pipette. Scale bars denote 10 μm.

Model



Schematic. The pressure drop ΔP is controlled by the dissipation in the pipette, leading to a scaling for penetration length $L_p \sim \sqrt{t}$. We assume $\lambda \gg 1$, but one can propose a similar model that includes the effect of fluid 2 [4].

Using assumptions of a Newtonian low-Reynolds number flow and lubrication approximation, the length of fluid in the pipette:

$$\frac{L_p(t)}{R_p} = \sqrt{\frac{1}{4\lambda\mu}\left(\Delta P + \frac{2\gamma}{R_p}\right)(t - t_0) + \left(\frac{L_0}{R_p}\right)^2}$$

Experimentally, we measure $L_p(t)$ for different ΔP and fit A:

$$\frac{L_p(t)}{R_p} = \sqrt{A(t - t_0) + \left(\frac{L_0}{R_p}\right)^2}$$

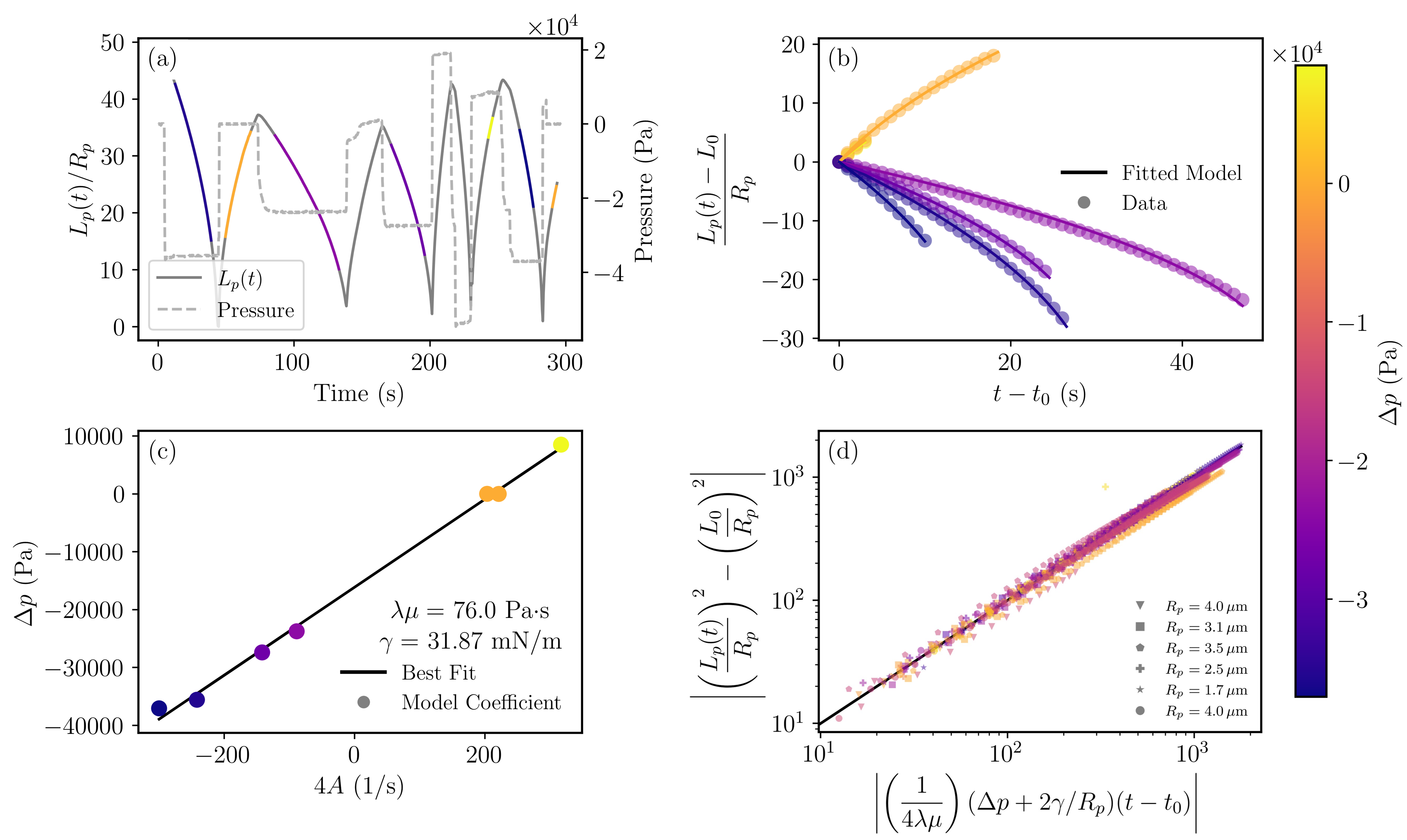
The material properties follow from:

$$A = \frac{1}{4\lambda\mu}\left(\Delta P + \frac{2\gamma}{R_p}\right) \text{ or alternatively } \lambda\mu(4A) - \frac{2\gamma}{R_p} = \Delta P$$

The slope of this relationship corresponds to the viscosity while the intercept gives a simple relation for the surface tension

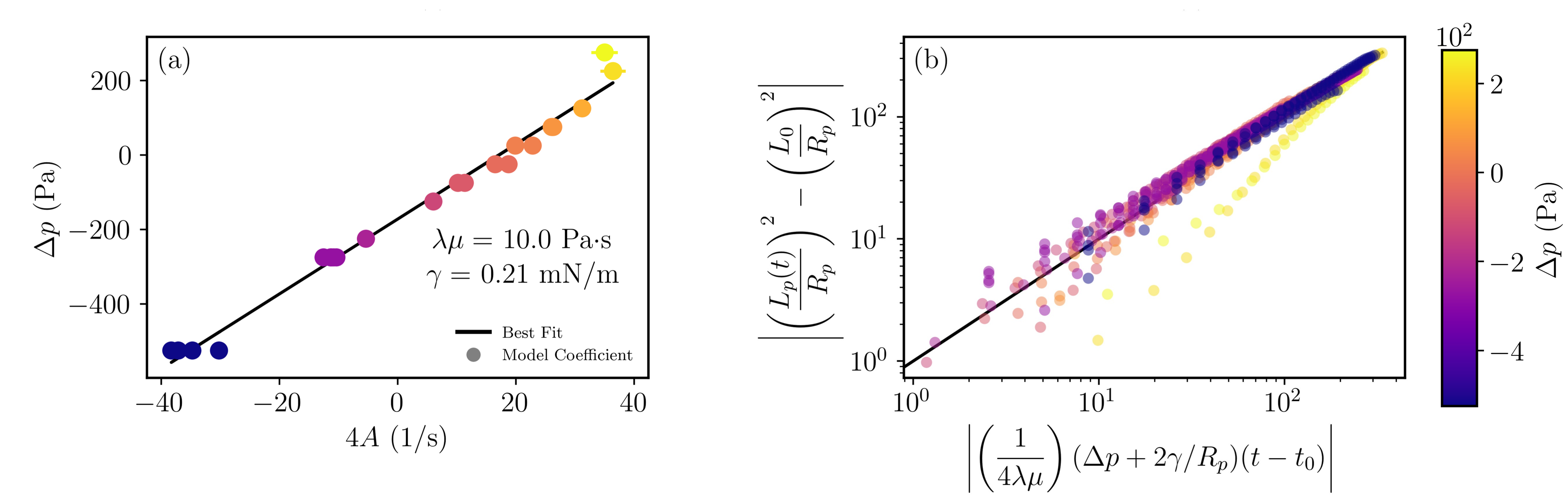
Experimental Results

Oil validation



(a) Typical data for one MPA experiment showing normalized penetration length $L_p(t)/R_p$, as well as the applied pressure (dotted line). The colored segments are regions of approximately uniform pressure, which are shown in (b), along with the fitted theoretical model. (c) plots the fitting coefficient with the applied pressure, which gives the viscosity and surface tension from the slope and intercept. (d) plots experimental data from many pipette radii rescaled to collapse to the model. We find a viscosity of $78.3 \pm 5.6\ \mathrm{Pa \cdot s}$ and a surface tension of $31.9 \pm 1.7\ \mathrm{mN/m}$, compared to $82.6\ \mathrm{Pa \cdot s}$ and $36.0\ \mathrm{mN/m}$ obtained with a shear viscometer and pendant drop tensiometer, respectively.

LAF-1 RGG domains (condensate)



(a) Fitting coefficient versus pressure for MPA of LAF-1 RGG domains presented in [1]. Using the new model, we find a viscosity of $11.1 \pm 1.12\ \mathrm{Pa \cdot s}$ and a surface tension of $0.17 \pm 0.02\ \mathrm{mN/m}$ across all experimental segments, a factor of five increase in the viscosity and roughly similar surface tension compared to [1]. (b) Experimental data rescaled according to model.

Key points

The improved model **removes the need for calibration parameters** and reduces error in fitted model by 97% compared to linear model used in [1].

This technique is a **simple** experimental protocol for determination of two Newtonian material parameters in a **single experiment** that can be applied to small volumes of fluid.

The estimation can be improved by reducing noise in measurements of the applied pressure.

Future work

- Modeling viscoelastic MPA
- Extending model to cover cases where the fluid does not wet the pipette

References & links

[1] Wang et al., Biophysical Reports, 2021.
[2] Bracha et al., Nature Biotech, 2019.
[3] Taylor et al., Biophysical Journal, 2019
[4] Roggeveen et al., Biophysical Journal, *in press*.

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