ΛPOHΛ

Case study

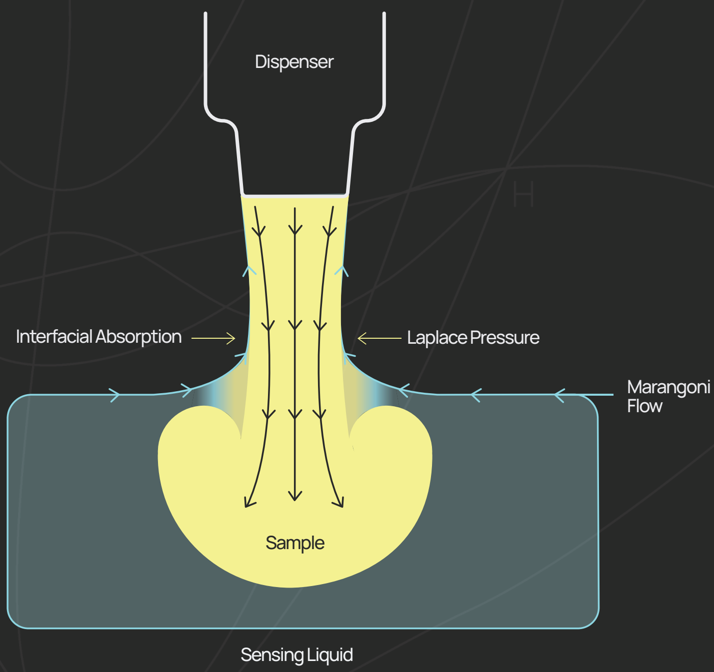
Decoding the physical events behind state data

At a glance

State data captures how molecules behave — not just what they are. It reflects dynamic transitions in complex liquid environments that conventional measurements cannot resolve.

But what physical events actually drive this signal?
In this study, we show that Apoha's liquid state machine drive antibodies into close contact from dilute samples, revealing **delayed viscoelastic coalescence and occasional gelation**. These high-concentration behaviors remain inaccessible to the low-concentration proxy assays used across developability today.

These transitions form the basis of high-resolution state data — enabling a fundamentally new way to understand and screen therapeutic candidates.



1) Why developability risk is invisible at the stage decisions are made.

Early-stage discovery lacks visibility into how candidates behave in complex environments. Standard measurements isolate properties, but fail to capture emergent behaviours that drive downstream risk.

2) Probing high-concentration phenomena with microgram-scale material.

We use a liquid state machine to probe high concentration phenomena using low concentration samples. We force antibody molecules to an air-water interface and record their dynamic response as they concentrate. Surface activity is not governed by any single property: hydrophobic patches drive adsorption, charged residues control orientation, and flexibility shapes the resulting film. The interface integrates these attributes simultaneously.

By tracking droplet formation, coalescence dynamics, and post-pinch-off evolution, we generate high-resolution state data that reflects collective molecular behaviour, not isolated properties.

Thermodynamic state machine's fluidics and detection layout

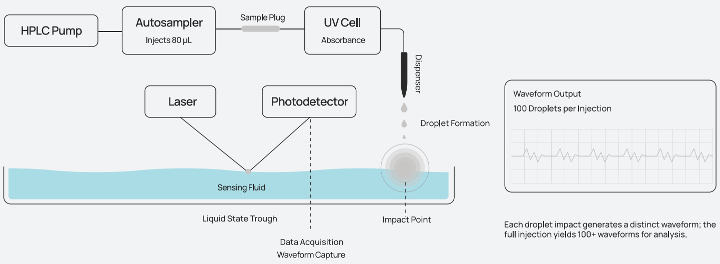


Figure 1: Our liquid state machine's fluidics and detection layout. Each droplet impact generates a distinct waveform; a full injection yields ~100 wavexsforms for analysis.

3) Three physical events distinguish good candidates from poor ones.

The system captures a sequence of physical events:

- Delayed coalescence driven by viscoelastic effects
- Non-linear droplet relaxation dynamics
- Stochastic gel formation after pinch-off

These phenomena are not directly observable in conventional assays — yet they encode critical information about molecular interactions, stability, and aggregation propensity.

To uncover the physical origin of state data, we captured coalescence events inside a liquid state machine measurement at 10,000 frames per second.

Coalescence at 10,000 fps reveals viscoelastic pinch-off in problematic antibodies

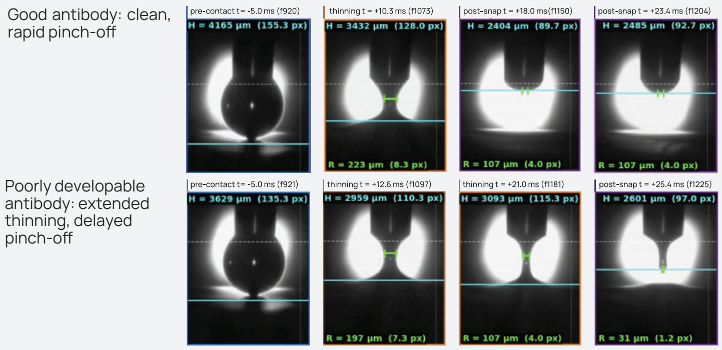


Figure 2: Four stages of a droplet coalescence event — pre-contact, thinning, post-snap (early), and post-snap (later) — captured at 10,000 fps. The well-behaved antibody (top) shows the clean snap-off of a simple Newtonian liquid. The poorly developable antibody (bottom) shows a thinning neck that persists tens of milliseconds longer before pinch-off, with a viscoelastic gel-like residue at the neck. H, droplet height; R, neck radius.

- In well-behaved antibodies, droplets coalesce with the clean, rapid snap-off expected of a simple Newtonian liquid.
- In poorly developable antibodies, pinch-off is delayed: the thinning neck between merging droplets persists for tens of milliseconds before snapping.
- Antibodies are forced into transient close contact during pinch-off. The system therefore probes a high-concentration crowding event using a low-concentration sample.
- After pinch-off, problematic antibodies stochastically leave behind a gel-like residue at the neck. This gel formation does not occur in every coalescence event, but when it does it is a striking secondary signature of the high-concentration aggregation behavior driving the signal.

Across conditions, we observe distinct and reproducible state signatures driven by these physical transitions.

- Coalescence delay correlates with interfacial viscoelasticity
- Post-pinch-off behaviour reveals aggregation pathway of a low concentration sample
- Emergent gel states differentiate otherwise similar candidates

Together, these signals form a multi-dimensional behavioural fingerprint.

A single measurement probes interfacial, mechanical, and chemical stress simultaneously.

These results confirm that state data is directly grounded in physical events that govern molecular behaviour in real environments.

This provides a mechanistic bridge between measurement and behaviour.

Each stress maps onto a different axis of developability risk. The viscoelastic response observed at pinch-off is most naturally interpreted as the antibody's combined response to these common stresses acting at once.

A single liquid state measurement therefore probes an antibody's combined response to interfacial, mechanical, and chemical stress simultaneously: the breadth that explains why state data correlates with assays spanning hydrophobicity, conformational stability, and polyreactivity.

This capability enables early identification of developability risks that are invisible to standard assays.

Teams can:
- Differentiate candidates based on real behavioural signatures
- Detect aggregation and instability pathways earlier
- Prioritise molecules with favourable interaction profiles

All from a single, integrated measurement.

In early screening, where hundreds of candidates cannot be deeply characterised, state data provides a scalable way to rank and triage molecules based on behaviour, not proxy measurements.

This enables better decisions earlier in the pipeline, reducing downstream failure risk.

About Apoha

Apoha has invented the world's first technology platform to resolve States - a new fundamental data class of molecular science, alongside Sequences and Structures.

Sequences told us what a molecule is. Structures showed us what it looks like. But molecular behaviour - the layer that determines whether a drug works, a formulation holds, or a material performs - has remained elusive. Until now.

We call this new paradigm Liquid State Intelligence: unlocking complex molecular behaviour under real-world conditions, generating data no simulation or model can reproduce. As this data layer grows, it gives humanity a new ability - not just to analyse the physical world, but to redesign it.