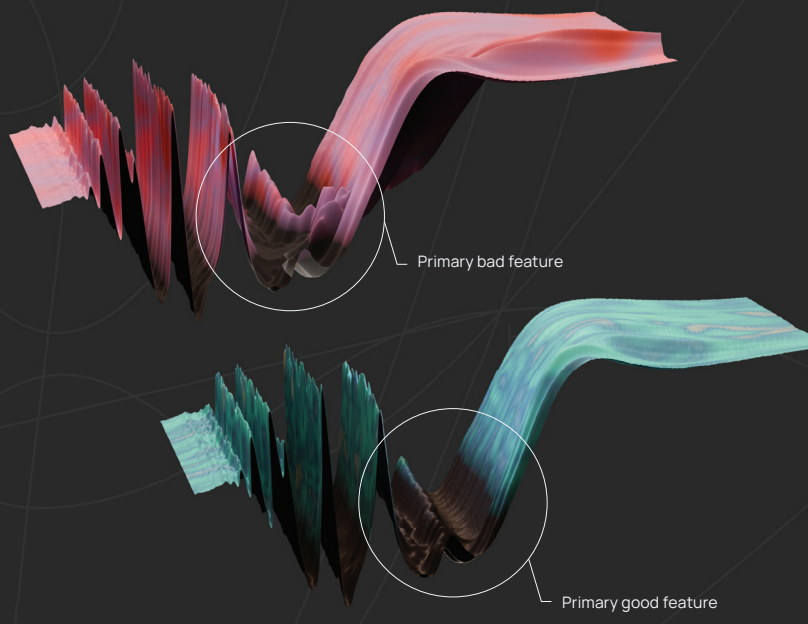
ΛPOHΛ

Case study

Antibody Developability Risk



At a glance

Whether an antibody actually becomes a drug is decided by how it behaves. But behaviour only becomes directly measurable late, once enough material exists for a full developability panel. By that point, the candidate pool has already collapsed from ~10,000 hits to ~50 leads — on the basis of indirect, static proxies. **The information arrives after the decision it should inform.**

A single measurement with Apoha's liquid state platform uses as little as 8 ug and captures the full behavioural state of an antibody – the kind of quantity available at hit ID.

So can a single behavioural measurement actually flag the candidates a multi-assay panel would later reject?

In a blind study of 71 clinical-stage antibodies from Boehringer Ingelheim, a single feature of our signal — VIBE1 — flagged high-risk candidates with 100% precision. Every flagged antibody had ≥2 developability liabilities measured by a standard panel of 5 assays.

The implication: developability calls that today wait for scale-up can be moved up the funnel — onto microgram-scale material, before commitment.

> "Apoha's technology works with practically no material, the biggest limitation at early stages, and it not only lets us detect liabilities earlier but also gives us additional insights beyond everything else we already have. That makes it incredibly easy to adopt into our workflow."
>
> - Boehringer Ingelheim

1) The behaviour that determines developability is currently invisible.

The properties that decide whether an antibody becomes a drug – viscosity at high concentration, aggregation under shear, conformational stability through freeze-thaw – are properties of behaviour, not static structure. And behaviour only becomes directly measurable once there is enough expressed, purified material to run a full assay panel.

By that point, candidates have already been advanced or dropped based on binding affinity or other indirect proxies. Conventional developability assays: HIC, Tm, AC-SINS, PSR, each probe a single biophysical axis, are often material-intensive, and are designed for late-stage characterisation. **No single assay covers more than one biophysical axis.**

2) 71 clinical-stage antibodies, screened blind, on 8 µg each.

Each antibody was m.easured in triplicate using 8 µg per injection, with no prior knowledge of BI's assay panel outcomes. From the resulting signal we extracted a single feature – VIBE1 – and classified each candidate against a threshold calibrated from a large clinical dataset of 235 antibodies.

3) 6 flagged. 6 confirmed. Zero false positives.

VIBE1 flagged 6 antibodies as high developability risk. All 6 were independently confirmed by BI's established panel (≥2 assay flags). Across the remaining 53 candidates VIBE1 classified as low risk, the false positive rate was zero.

12 antibodies that BI's panel flagged were not picked up by VIBE1 alone. That is expected – and informative. VIBE1 is a single extracted dimension of a much richer multi-feature signal; the candidates it doesn't pick up map directly onto the orthogonal axes we are bringing online next (*see Figure 2*).

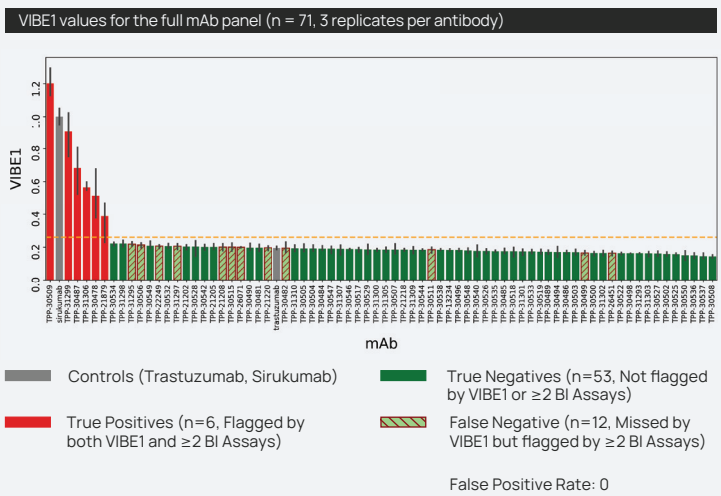


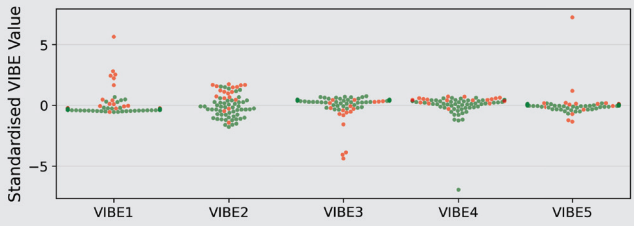
Figure 1: VIBE1 values for the full mAb panel (n = 71, 3 replicates per antibody). The orange dashed line is the VIBE1 risk threshold, calibrated from reference controls trastuzumab (low risk) and sirukumab (high risk), shown in grey. Red bars (n = 6): true positives – flagged by both VIBE1 and ≥2 BI assays. Solid green bars (n = 53): true negatives. Hatched green bars with red dashed outline (n = 12): flagged by ≥2 BI assays but not by VIBE1. False positive rate: 0.

4) VIBE1 is one dimension of a much richer signal.

A single 8 µg measurement encodes far more than what a single feature can extract. VIBE2-5 are in active validation, each targeting an orthogonal axis of developability risk. The data below previews what is already present in the signal: VIBE1's outliers (in red) recover cleanly within the multi-dimensional fingerprint, alongside additional behaviourally distinct clusters that VIBE1 alone would not surface – including a strong candidate cluster in VIBE2 that maps to several of the 12 antibodies VIBE1 missed.

5) The 12 antibodies VIBE1 doesn't catch are not noise. They are the development roadmap.

(a) VIBE1-5 strip plot



(b) Hierarchical clustermap of 5-dimensional VIBE distance across the panel

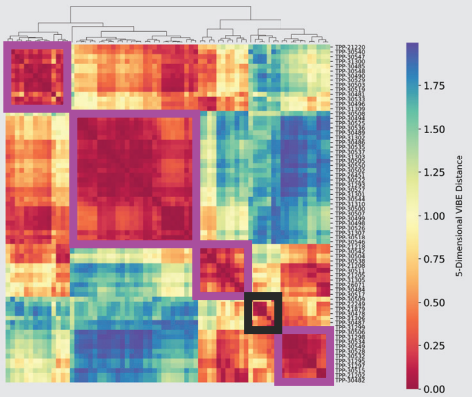


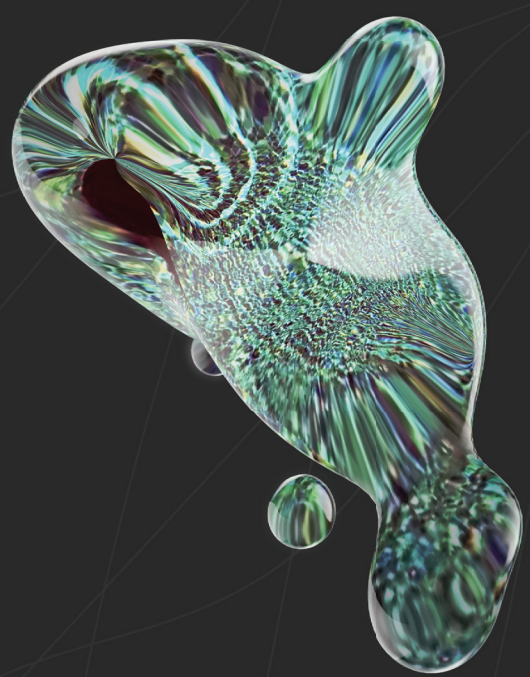
Figure 2: Preliminary multi-feature VIBE data across the mAb panel. (a) VIBE1-5 strip plot. While VIBE1 is a strong predictor of developability risk, higher VIBE dimensions identify outliers VIBE1 alone does not capture. Antibodies flagged by ≥2 BI assays are shown in red; cleared candidates in green. (b) Hierarchical clustermap of 5-dimensional VIBE distance across the panel. Pairwise distances followed by hierarchical clustering reveal multiple clusters of behaviourally similar antibodies (purple squares); the black square highlights the cluster of VIBE1 outliers – already recovered, plus more.

Using state data in early screening

A single behavioural measurement, on the material a discovery team already has at hit ID, changes three things at once:

1. Triage moves up the funnel. Developability calls today made on ~50 leads can be made at ~1,000 hits — before commitment to scale-up, expression, and a full assay panel.
2. Multi-liability molecules are caught by a single readout. Every VIBE1 flag in this study was a candidate that multiple conventional assays independently rejected — exactly the candidates a single-axis screen would miss.
3. The data layer compounds. Every measurement will add to a behavioural dataset that becomes more predictive with scale, accumulating into a reference library no single assay panel can produce.

The multi-dimensional developability picture — currently delayed until late characterisation — becomes available at the moment the candidate pool is being shaped.



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.