ΛPOHΛ

Case study

Tracking the antibody, not just the bioreactor

A daily behavioural readout of the product across the 14-day cycle, with Somru BioScience Inc.

At a glance

Every batch of an antibody spends ~14 days in cell culture, and its quality attributes are characterised only once the run is over, on harvested material. In-line and at-line sensors track the culture – pH, dissolved oxygen, viable cell density, glucose, lactate – not the antibody. Glycosylation can drift, aggregate levels can rise and charge variants can shift without ever showing up in those readings. The attributes that decide whether a batch passes belong to the product, and the product is what you cannot see during the run.

In collaboration with Somru BioScience Inc. and its proprietary Intelli.b™ technology, Apoha's platform tracks the product itself, daily, across the full cycle – a single behavioural measurement on ~8 µg of clarified in-process sample, the kind of volume a daily draw can spare.

So, can a daily behavioural readout see a batch converging – or going wrong – before end-of-cycle testing would?

Across four antibody batches and three biosimilar batches, a single daily measurement resolved a reproducible three-phase trajectory to a stable plateau, a persistent daily gap between biosimilar and reference product, and a day-3 reading already directional about the day-14 endpoint.

The implication: batch monitoring stops being a post-mortem. The product-quality information you currently wait 14 days to receive can be made visible from the first few.

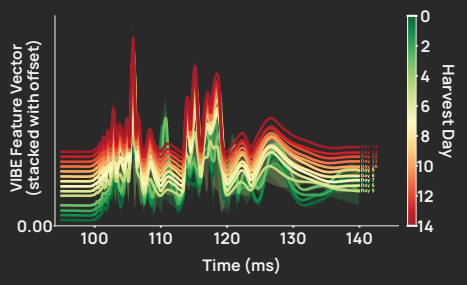


Figure 1: VIBE waveforms of rituximab sampled daily across the 14-day cycle (n = 3 per day), offset on the y-axis for clarity.

"If on Day 3 we saw the trajectory was clearly off, and knew that wouldn't change whatever we did, we'd scrap it. You're potentially saving up to a month – all the supporting reagents – and for a 500-litre bioreactor, that adds up to millions of dollars per batch."

- Jessi Rix, Somru BioScience Inc.

Bioreactor sensors track cells, not the product

Bioprocess monitoring is well-instrumented. Temperature, pH and dissolved oxygen are measured in-line; glucose, lactate and viable cell density are tracked by daily sampling. All of it tells you a great deal about whether the cells are alive and producing, and very little about the antibody. The attributes that decide whether a batch passes – glycosylation profile, aggregate (HMW) species, charge-variant distribution, host cell protein – are properties of the product, not the culture. End-of-cycle methods such as SEC, icIEF, released N-glycan analysis and HCP ELISA exist for this, but they need Protein A–purified material and turnaround measured in hours to days. None is practical to run daily. A healthy cell is a prerequisite for a good batch, not a guarantee of one.

A direct measurement of the product, on µg of material

Each daily sample is clarified to remove cells and normalised to a fixed antibody concentration (~80 µL at 0.1 mg/mL, about 8 µg). It is placed at a controlled liquid interface, perturbed, and its relaxation captured as a time-resolved waveform – a VIBE check (Variations in Interfacial Behaviour and their Evolution). Read against matched buffer and spent-media controls and collapsed to a single VIBE score, the waveform reports the behavioural state of that day's clarified in-process sample.

Three production phases, including a plateau

Somru sampled four production runs – two omalizumab, one palivizumab, one rituximab – daily across the cycle, each clarified, normalised to 0.1 mg/mL and measured in triplicate. A full 14-day trajectory consumed under 0.5 mg of antibody. Collapsed to a daily VIBE score, every run resolved the same three phases: an early, variable phase (culture days 0–3), a sharp transition (days 4–6), and a stable plateau (days 7–14). By day 8 the product has reached a stable behavioural state – six days before harvest, while continue-or-terminate is still a live decision.

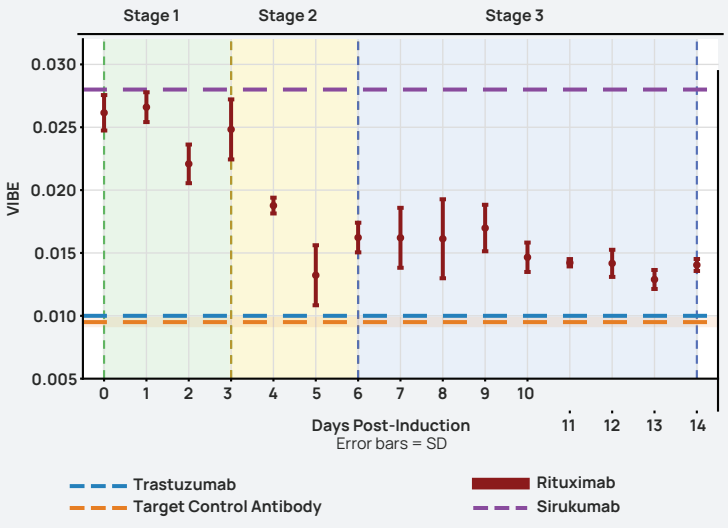


Figure 2: VIBE (seconds) versus culture day (days post-inoculation), rituximab (error bars = SD). The sirukumab (high VIBE) and trastuzumab (low VIBE) reference antibodies and the Xolair reference product, measured in the same run, are shown as horizontal dashed bands. Stages I, II and III mark the early, transition and plateau phases. The same three-phase structure reproduced across all four batches; the timing of the inflection varies by molecule and run, but the qualitative shape is consistent.

Process differences, resolved in real time

The same daily readout turns biosimilarity from an end-of-cycle verdict into a real-time trajectory. Across three omalizumab biosimilar batches, two cultured under identical process conditions tracked almost perfectly, while a third, run under a different process, separated by day 3 and stayed furthest from the reference product through day 14. A persistent daily gap to the Xolair VIBE, confirmed independently by Somru's release characterisation, was visible from day 5.

Feed strategy leaves its own early fingerprint. The runs above used fixed-schedule bolus feeds; a further set was fed dynamically – glucose-controlled, replenished whenever glucose fell below a setpoint – which produced a more consistent VIBE trajectory across the cycle. Galactose-supplemented feeds tracked more reproducibly than glucose alone, though on limited numbers. The same readout that flags a drifting batch can therefore guide media and feed development, not just monitor it.

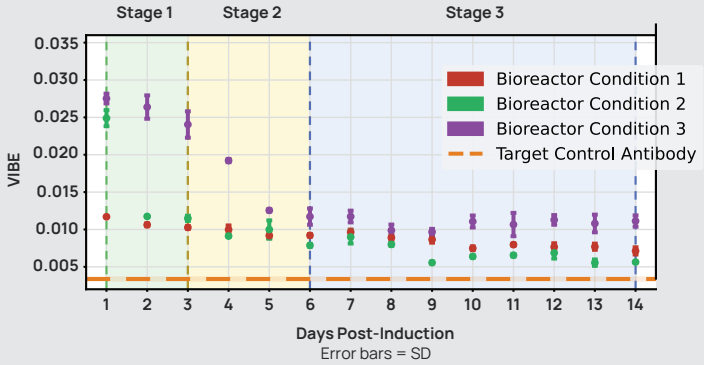
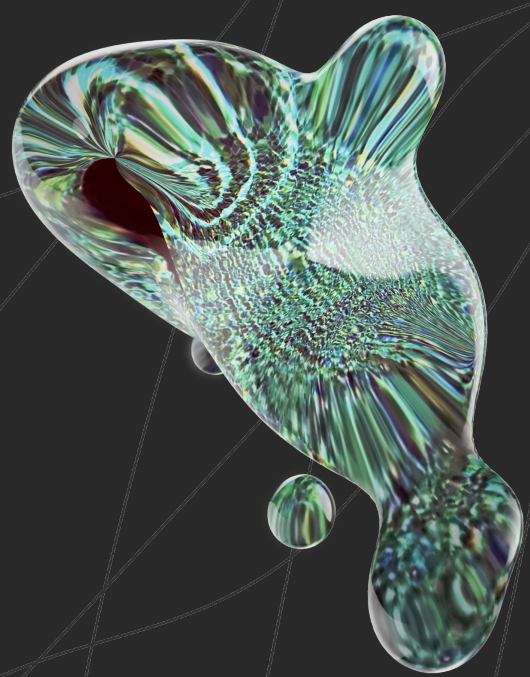


Figure 3: VIBE (seconds) versus culture day across three omalizumab biosimilar batches cultured under different process conditions, compared with the Xolair reference product (orange dashed band); error bars = SD. Batches 1 and 2 (identical conditions) follow near-identical trajectories; Batch 3 (different conditions) separates by day 3 and ends furthest from the reference. None converges to the Xolair VIBE – a stable gap runs from day 5 to day 14, consistent with Somru's independent release characterisation.

Using behavioural data in-process

1. A daily behavioural readout of the product, on the material a culture can already spare, changes three things at once:
2. **Deviations are caught early.** Once a reference VIBE trajectory is established from process-development batches, a run that drifts off it can be flagged days before release testing would catch it – six days of run time still on the clock, when the decision to continue or terminate is still meaningful.
3. **Process variants are compared in real time.** Different process conditions and feed strategies produce different VIBE trajectories, resolvable within days rather than weeks, accelerating process development and biosimilar matching.
4. **Monitoring moves toward in-process control.** Bioreactor integration and method qualification are the development path from an at-line daily measurement toward a PAT-style in-process control (IPC) – turning the daily readout into an actionable control, not a retrospective report.



About Apoha

Apoha has invented the world's first technology platform to understand the behaviour of molecules. It does so by resolving 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 — is determined by a molecule's thermodynamic state and has remained elusive. Until now.

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