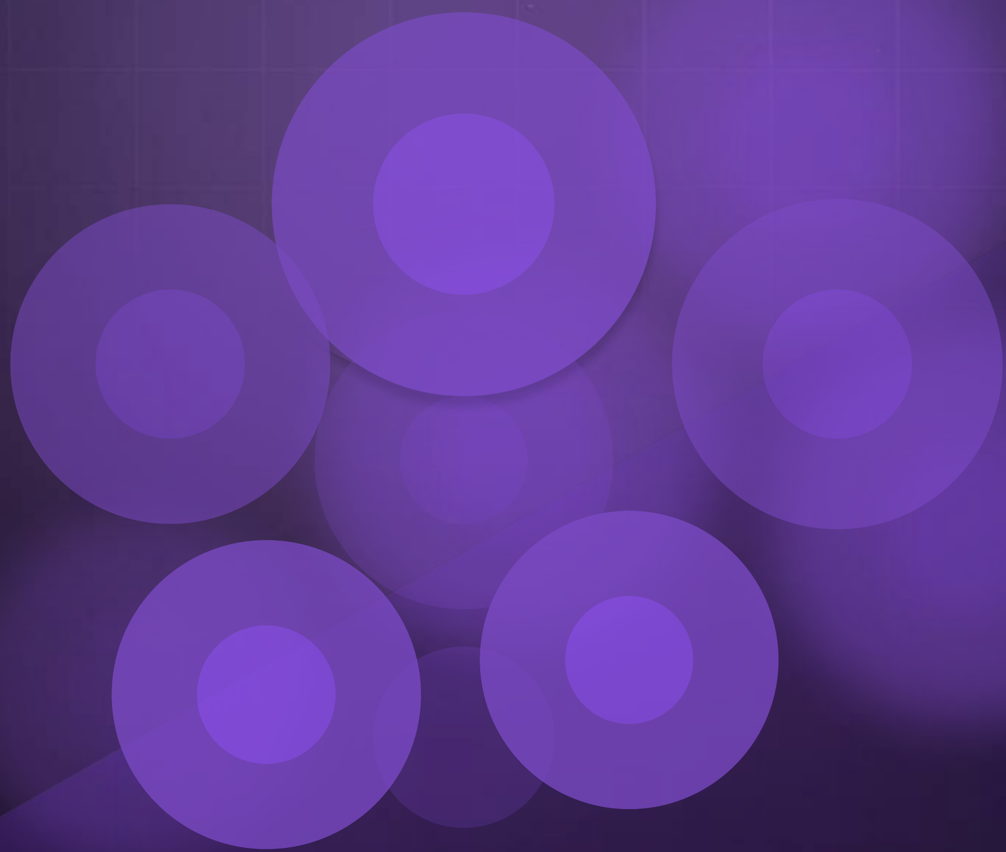
Optimized Clone Selection and Tech Transfer Using Basetwo's AI Platform

A hybrid modeling approach to support tech transfer from fed-batch to perfusion bioreactors.



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Problem

As demand for biologics grows and pressure mounts to reduce costs while increasing manufacturing agility, innovative companies are turning to perfusion bioreactors as a next-generation alternative to traditional fed-batch processes.

Unlike fed-batch systems (FBR), which operate in discrete production cycles, perfusion bioreactors enable continuous cell culture, where fresh medium is continuously supplied while waste is removed. This allows cells to remain in a productive growth phase for longer periods, leading to:

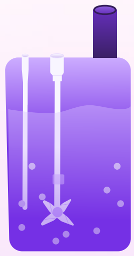
- Higher product yields within smaller bioreactors
- Reduced media and facility costs
- Greater process flexibility and scalability
- Improved consistency in product quality attributes (CQAs)

However, this transition introduces a major challenge: clone performance is highly context-dependent. A clone that performs optimally under fed-batch conditions may behave very differently under perfusion due to changes in nutrient dynamics, shear stress, and metabolic steady-state.

Historically, identifying suitable clones for perfusion required dozens of labor-intensive bioreactor experiments, making process development slow, costly, and data-heavy with limited predictive insight.

Fed-Batch Bioreactor (Ambr15):

Bioreactor system that operates in batch cycles designed for high-throughput process development.



Perfusion Bioreactor (3L):

Operates continuously, allowing cells to remain in a productive growth phase for longer.

Objective

The Basetwo customer aimed to develop a predictive digital twin capable of forecasting clone performance and CQAs during the transition from fed-batch to perfusion. The goal was to enable in-silico clone selection, allowing researchers to identify top candidates virtually, before committing to costly lab-scale validation and thereby reducing timelines, risk, and cost in upstream development.

Solution on Basetwo

Data Integration & Transformation

Basetwo's digital twin platform integrated the pharmaceutical manufacturer's historical fed-batch (Ambr15) and perfusion (3L) process data from process historians, ELNs, and LIMS systems. Key datasets included:

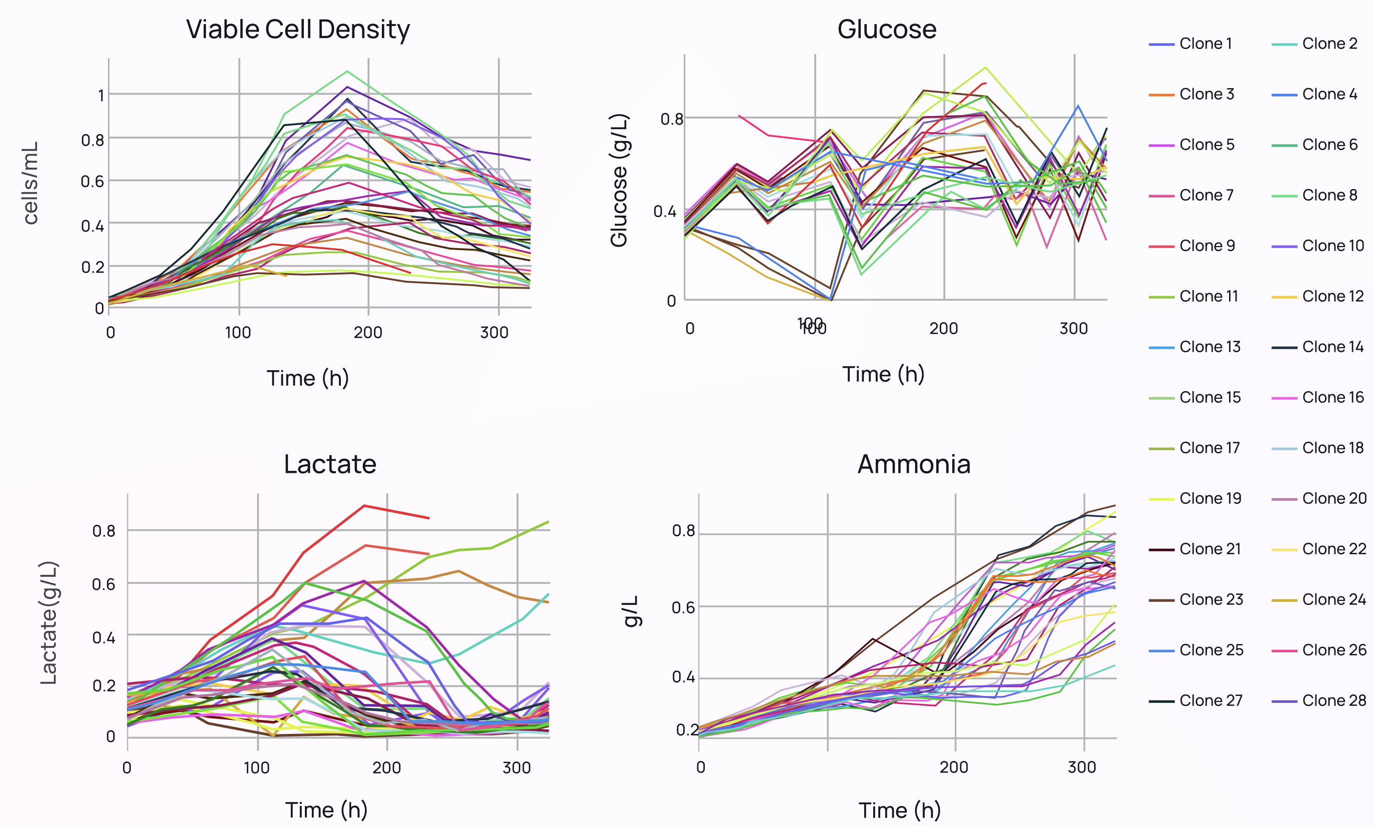
Process parameters:
pH, DO, temperature, perfusion rate

Cell properties & Metabolites:
viable cell density, glucose, lactate, ammonia

Performance metrics:
productivity (titer) and CQAs

Using Basetwo, the team automated the data preprocessing and cleaning, transforming heterogeneous datasets into a unified structure suitable for model training and cross-mode prediction. This enabled a repeatable data transformation pipeline for any new unstructured data.

Clone Profiles Visualized on Basetwo



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Model Development

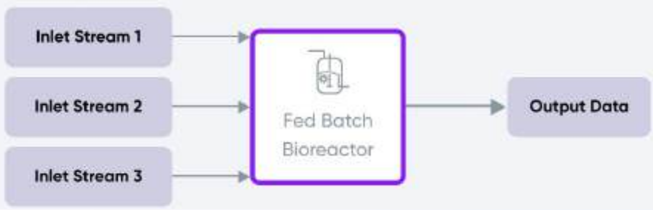
A hybrid modeling framework, combining mechanistic process models with machine learning algorithms, was implemented to bridge the gap between fed-batch (FBR) and perfusion behavior and support the following applications:

Model-Based Clone Performance

Basetwo's AI-driven digital twin replicated the bioreactor process, allowing the pharmaceutical manufacturer to simulate clone performance across feeding and perfusion strategies using only existing fed-batch data.

The model accurately predicted growth, productivity, metabolite trends, and CQAs, revealing clone-specific differences in nutrient use and metabolic flexibility.

Basetwo Mechanistic Digital Twin Template



Predicting Performance Across Scales

Basetwo's digital twin bridged fed-batch and perfusion processes by simulating key physical and biological shifts, like oxygen transfer and shear stress, allowing the engineers to anticipate clone performance changes and optimize feeding and bleed strategies in advance.

Hybrid Modeling on Basetwo

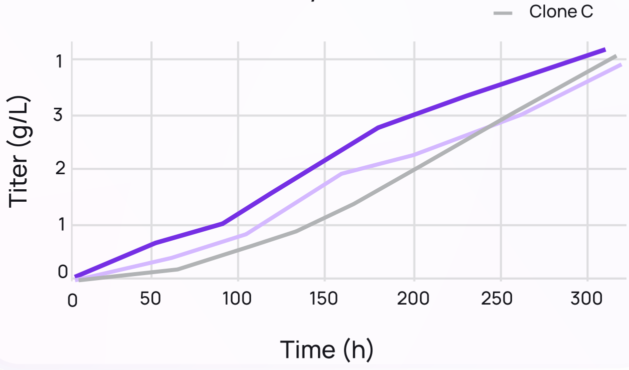
Basetwo's hybrid modeling approach integrates physics-based and machine learning models to create accurate, interpretable process simulations.

It enables reliable modeling even with sparse data, unknown kinetics, or complex nonlinear behavior, allowing engineers to develop physically consistent, data-driven digital twins for their processes.

In Silico Process Optimization

With the digital twin, they ran hundreds of virtual experiments to identify optimal conditions and rank clones by predicted perfusion performance. This cut weeks from development by reducing lab runs while aligning with the QbD framework.

Perfusion Bioreactor: Optimal Titer Performance by Clone



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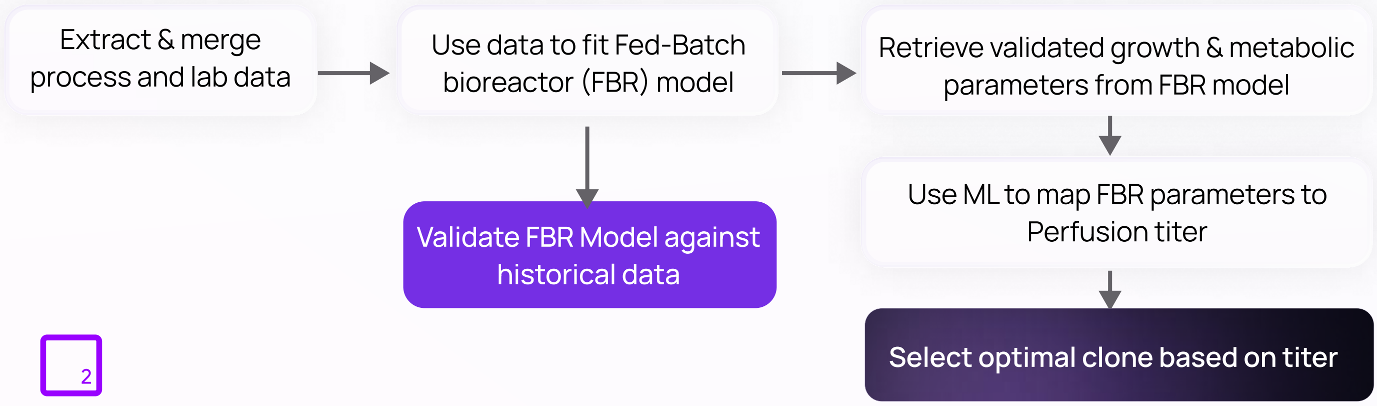
Workflow Overview

By combining process science and data intelligence, this global pharmaceutical manufacturer gained a predictive model that could both explain and forecast clone performance across scales.

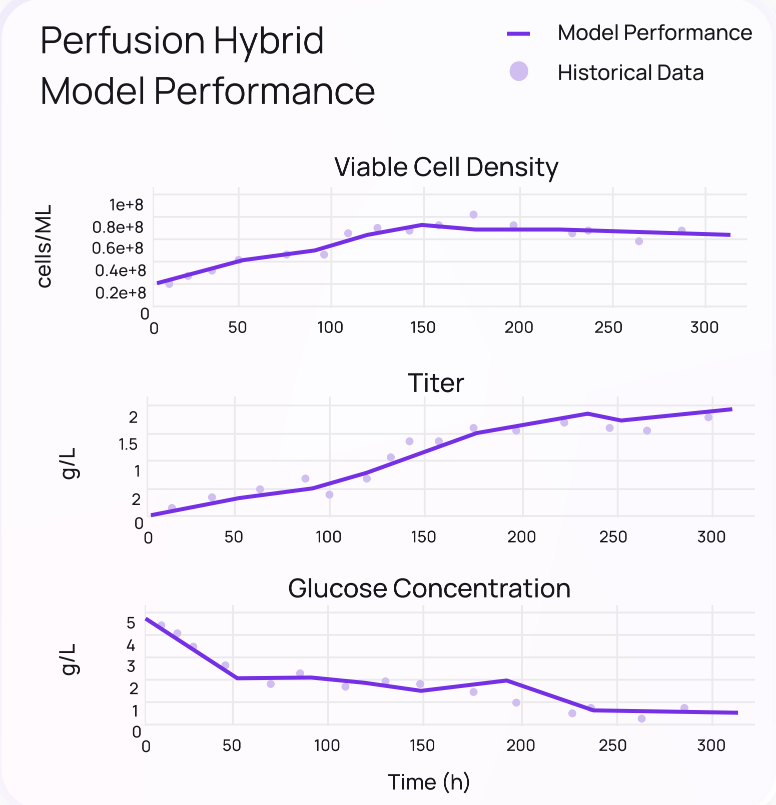
Clone Selection Digital Twin Workflow



Modeling Results

Model validation confirmed a high degree of accuracy and scalability, with predictions closely mirroring real-world process outcomes. The digital twin achieved over a 95% accuracy in predicting cumulative permeate titers and accurately capturing clone-specific cell growth and metabolic behavior.

These results demonstrated robust and accurate scalability from small-scale Ambr15 systems to 3L perfusion bioreactors, validating the model's reliability for process transfer and optimization.



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Impact of Optimized Clone Selection

With the implementation of hybrid modeling, the customer was able to scale up from a fed-batch to perfusion system, selecting a clone that maintains a balance of high cell viability, steady-state productivity, and stable metabolite levels across the culture duration.

20%
increase in titer through optimized clone selection

40%
reduction in number of experiments

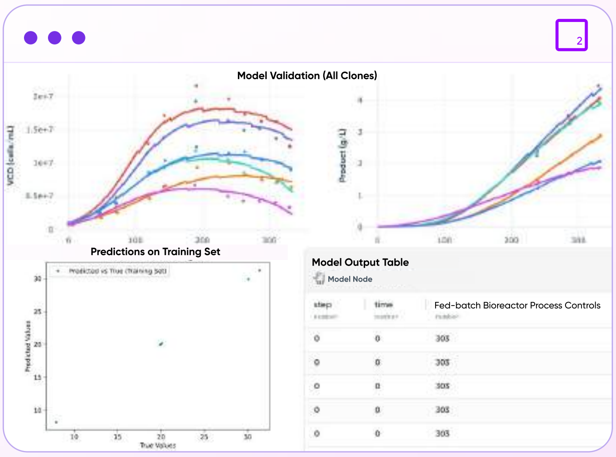
- Shortened timelines for upstream development
- Reduced experimental burden, cost, and resource load from perfusion testing
- Improved success rates during scale up and tech transfer

A Platform Built by Engineers for Engineers

> "We lacked a high-throughput way to screen clones under intensified conditions, with Basetwo we were able to test whether early fed-batch data could predict titer uplift."

— Senior Scientist
Top 5 Pharmaceutical Company

- Rapid cloud-based deployment in weeks.
- Intuitive, drag-and-drop interface; for simplified simulation, monitoring, and optimization.
- Live process models deployed as reusable, scalable workflows



Learn how Basetwo can help accelerate your clone selection and tech transfer workflows

Reach out today →

www. basetwo.ai