CASE STUDIES: TECHNOLOGY IN ACTION

Mabxience & HP

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HP AI Lab & Solutions × mAbxience

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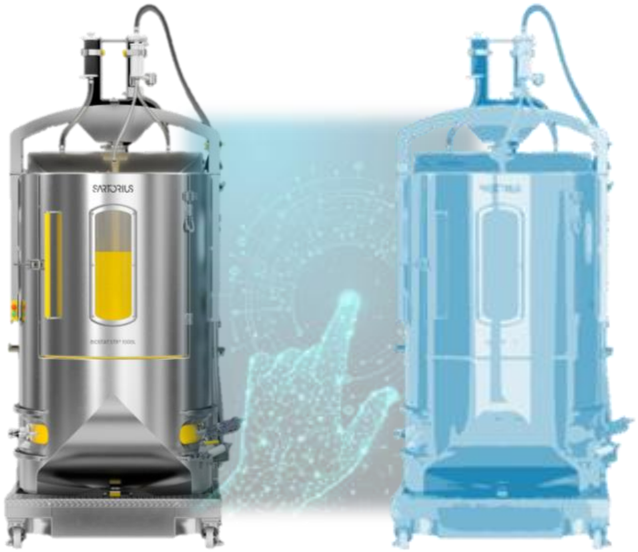


What is a Digital Twin?

A data-connected virtual copy of a real process, equipment or facility that stays synchronized with the plant.

In other words:

A "flight simulator" for the bioreactor: test changes virtually before touching the real batch.

The point: move from reactive troubleshooting to predictive, model-driven manufacturing.

How the twin works

Plant data sensors • MES • PAT → **Virtual model** biology + process physics → **Predictions** CQA • yield • deviations → **Actions** optimize • control • learn

Continuous data loop: the model learns from the plant, then informs better decisions back in the plant.

Why it matters for biosimilar production

Potential uses / benefits

1. **Connect CPPs to CQAs**
   Improve process understanding for quality-by-design and comparability.
2. **Predict batch performance**
   Use live + historical data to anticipate titer, quality drift and deviations.
3. **Accelerate scale-up & transfer**
   Run "what-if" scenarios before engineering runs or site transfer.
4. **Reduce waste, downtime and COGs**
   Fewer failed batches, smarter maintenance and faster troubleshooting.

Sources: Digital Twin Consortium definition; NIST Digital Twins; ISPE Pharma 4.0; Shahab et al., 2025 review on biopharmaceutical digital twins.

Our History

- Our company was born with the desire to bring high quality medicines to all parts of the world, making people's lives better. **Accessible. Affordable. Across the globe.**
- Since then, many things have happened that make us proud of and that serve us to imagine an even better future.

GMP: Good Manufacturing Practices
EMA: European Medicines Agency
FDA: US Food Drug Administration
GGBA: Global Generics & Biosimilar Awards

Founded by
Dr. Hugo Sigman

2010 - 2012

Munro: Argentina R&D & biomanufacturing center

2014 - 2015

Genhelix: Spain R&D center

- **First launch of MB01 rituximab** (Novex®, Argentina)

2016 - 2017

- **First launch of MB02 bevacizumab** (Bevax®, Argentina)
- **EMA GMP certification** granted to mAbxience Spain

2018 - 2019

- Partnered worldwide with **MB02 bevacizumab** biosimilar

Garin: mAbxience Argentina state-of-the-art biomanufacturing facility

2020 - 2021

- **EMA approval** for MB02 bevacizumab biosimilar
- Manufacture of **AstraZeneca/Oxford Covid19 Vaccine**
- Launch of **CDMO services**

2022 - 2024

- **FDA & PMDA approval** for MB02 bevacizumab
- **Fresenius Kabi acquires a majority stake in mAbxience**, joining Insud Pharma as shareholders

2025 - Present

- FDA & EMA approval for MB09 denosumab biosimilar

Upstream yield (titer) is driving COGs

The higher the titer, the lower the COGs and vice versa

- 4000 L single-use bioreactor containing **CHO** cells that **express** a **mAb**[1)] used as **medicine** in cancer treatment.

- The “**titer**” (amount of mAb) in cell culture fluid is a **major contributor** of the final COGs.

[1)] mAb: Monoclonal antibody
[2)] COGs: Cost of Goods (sold)

Partnership Overview

Advancing AI in Biopharmaceutical Manufacturing

Motivation

- Enhance the **efficiency and accuracy** of biopharmaceutical compound production using advanced artificial intelligence (AI) and cloud technologies.

- Use AI/cloud as a **practical lever** for improving how biosimilar products are produced and monitored.

Collaboration scope

- HP and mAbxience aim to jointly develop AI-field projects.

- Assess suitability and feasibility of **selected AI technologies**.

- **Conduct pilots** and proof-of-concept (PoC) tests in this area.

Desired project outcomes

- Enable **better management and monitoring** of the production chain through the digital twin (DT).

- **Foster innovation and technological advancement** in biopharmaceutical manufacturing.

- **Optimize** mAbxience production, **focus upstream yield**, while contributing to broader AI applications in healthcare.

What & how

Optimize biosimilar manufacturing outcomes through multivariate time-series modeling

Objective

Predict the temporal evolution of key manufacturing process variables for the biopharmaceutical compound MB02, with a **primary focus on optimize the protein titer at the end of the process**.

Problem Formulation

- Framed as a multivariate time-series prediction problem with temporally ordered input sequences
- Clear dependencies between consecutive observations drive the need for sequence-aware models
- Sufficient data volume (variable count and sequence length) supports expressive models designed for sequential information
- Captures complex temporal patterns across short, medium, and long-term horizons

The challenge

A multivariate time-series prediction problem requiring specialized neural architectures

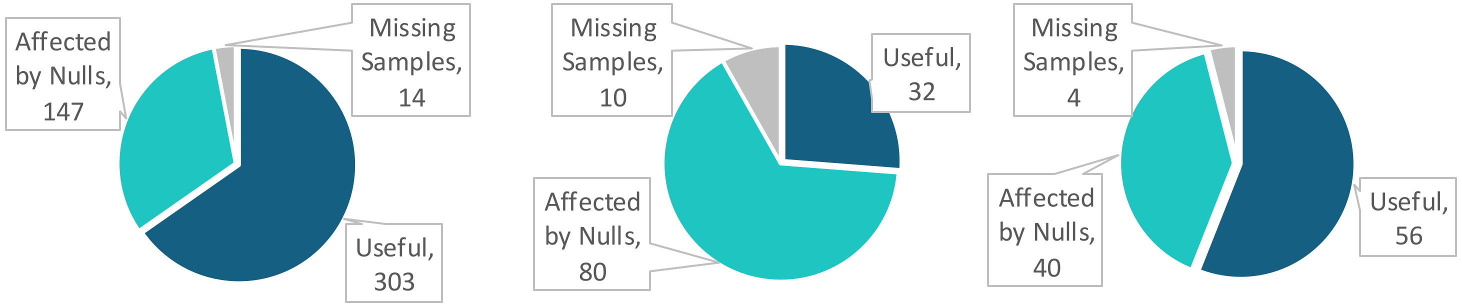
Temporal complexity

- Predicting protein titer requires capturing short-, medium-, and long-term dependencies across ordered time-series data.

Multi-step prediction

- The model must estimate future process evolution across multiple time steps, not just a single output.

Data from 3 different process generations analyzed



Fragmented data landscape

- Critical information is distributed across different repositories.

Mixed variable horizons

- Some input variables are known across the full timeline, while others are only available up to a certain point.

The AI solution

Autoregressive LSTM neural network selected after rigorous architecture evaluation

Architectures Evaluated

Feedforward NN

- Baseline reference.
- No temporal modeling.
- Discarded for final use.

CNN-LSTM hybrid

- Added complexity without consistent metric improvement.
- Kept as an experimental reference.

Autoregressive LSTM ✓

- Selected architecture.
- Stacked LSTM layers with warmup + iterative prediction and residual connections.

Autoregressive LSTM – Key Capabilities

1. Multi-step predictions across the fed-batch phase.
2. Handles both known and unknown variables across the prediction horizon.
3. Estimates protein titer on day 14.
4. Optimization possible by playing with additives.
5. Validated using Pearson correlation and an extensive metric set.

Autoregressive LSTM

How the selected model forecasts process evolution

Model behavior

• Models learn sequence patterns and dependencies and retain long-term dependencies in sequential data effectively.

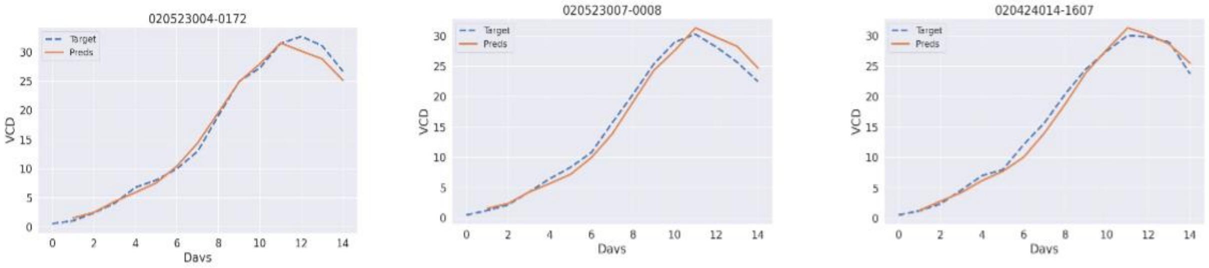
• LSTMs are applied in time-series forecasting, natural language processing, and speech recognition tasks.

• Autoregressive LSTMs use previous outputs as inputs for future sequence elements.

• Predictions are fed back recursively; small early errors can compound.

• Warm-up initializes and stabilizes internal states by feeding real observed data, reducing error accumulation.

VCD
R^2*=0.97



*R^2: Coefficient of determination. Predict how well a model fits data, and how well it can predict future outcomes

Demonstration of value within constraints

Understanding the context is critical to interpreting the results

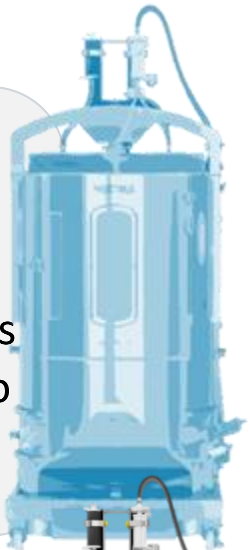
Constraints during this AI use case

- Model operated as an offline analysis (no real-time integration)
- Focus on titer optimization only (process was already robust)
- Approved medicinal product; regulatory frameworks dictate whether changes can be implemented immediately or require formal variation filings

Successfully simulated next process generation

Output result
In-silico

The upstream manufacturing process yield was **predicted** to **increase by 15-20%.**



Output result
Wet-lab confirmation

17% yield (titer) increase%!

Input
Output

OUTPUT

Status	Completed
Execution Date	2026-03-12T12:19:00.492106Z
Execution Time	132.9735 s
Exit Status	0
Exit Message	Success
AI-Service Version	v3.7
Optimizer Version	predictor:v3.7.2
Predictor Version	v3.7.2
Model Version	v3.7
Highest Final Protein Titer	[redacted]
Optimal Solution	

	MC-27 addition (%)	MC-72 addition (%)	MC-73 addition (%)
D03	0.76	2.27	0.565
D04	N/A	4.1	N/A
D05	0.074999996	3.0049999	0.69
D06	N/A	3.6299999	N/A

Input
Output

Results Table
for Optional Solution

	D03	D04	D05	D06	D07	D08	D09	D10	D11	D12	D13	D14
Time (h)	70.04	93.65	117.76	141.74	165.84	189.59	213.12	237.06	261.21	284.98	309.02	330.60
Protein titer (µg/mL)	[redacted]											
Ammonium (mmol/L)	4.87	6.68	7.52	7.84	8.72	9.45	8.02	8.02	7.30	9.14	9.13	36.47
Dissolved oxygen (%)	49.54	49.19	49.24	49.45	49.66	49.83	49.82	49.48	49.18	48.48	49.30	6.06
Glucose (g/L)	3.56	4.36	4.84	5.09	5.05	4.80	3.83	2.88	2.04	2.61	2.23	-13.62
Glutamate (g/L)	0.52	0.81	1.04	1.24	1.45	1.66	1.78	1.84	1.80	1.78	1.76	5.82
Glutamine (mmol/L)	0.64	0.81	0.65	0.27	0.22	0.27	0.14	0.17	0.22	0.43	0.45	-9.63
Lactate (mmol/L)	19.99	19.83	18.35	16.33	14.10	11.38	5.85	3.88	2.28	1.10	1.39	-51.15
MC-27 addition (%)	0.76	0.00	0.07	0.00	0.77	0.00	0.20	0.00	0.91	0.00	0.33	0.00
MC-72 addition (%)	2.27	4.10	3.00	3.63	4.99	1.99	2.43	1.64	4.87	4.75	0.33	0.00
MC-73 addition (%)	0.56	0.00	0.69	0.00	0.40	0.00	0.59	0.00	0.99	0.00	0.06	0.00
Mass ratio	1.00	1.03	1.05	1.07	1.10	1.13	1.16	1.20	1.23	1.27	1.30	1.34
VCD (Mcell/mL)	3.67	8.22	10.58	11.70	17.76	24.92	27.71	31.29	34.13	35.79	35.04	341.40
Viability (%)	97.31	97.72	97.26	96.36	96.33	96.56	96.32	96.14	95.41	93.66	89.37	170.63
pH	6.79	6.89	6.90	6.87	6.94	7.02	6.95	6.98	7.01	7.21	7.13	8.59

Digital Twin delivers measurable business value

Digital Twins amplify - not replace - experimental process optimization

Wins

- Simulation-driven optimization translated into measurable wet-lab gains
- +17% increase in product titer confirmed experimentally
- Efficient execution: delivery on timeline with strong cross-functional alignment

Conclusions

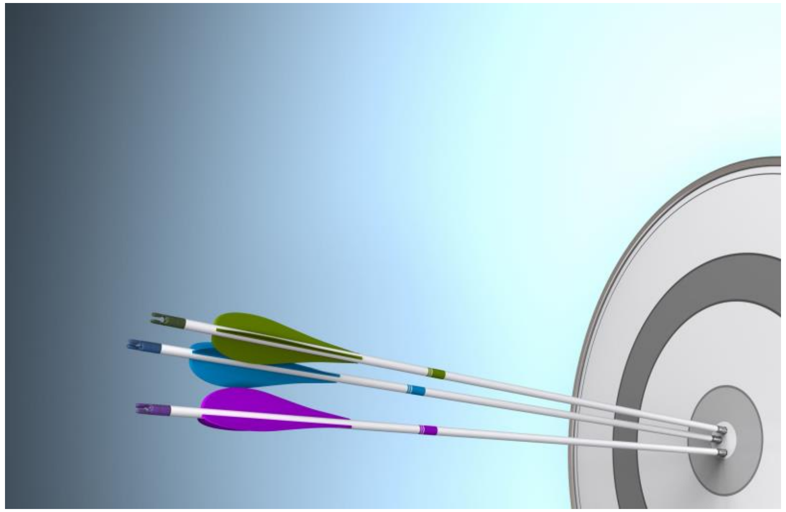
- Digital Twin alone is not a silver bullet - value comes from integration into PD workflows
- Hybrid optimization (in silico + in vitro) outperforms either approach alone
- Future state: self-learning Digital Twins embedded into manufacturing and R&D operations

Digital Twin impact was demonstrated - but under constrained, non-integrated conditions

Key takeaways

What it takes to translate Digital Twin into real process value

Digital Twins **accelerate** development and **save costs**
- when **embedded** in experimental workflows!


Q&A

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