DATAHOW

Wheeler Bio

Accelerating Scale up with Transfer Learning and DataHowLab

Bioprocess scale-up is complex, as biological systems often respond unpredictably to the changes in volume, mixing, and transfer rates etc. Despite existing knowledge at small scale, scientists still rely on extensive experimentation during scale up - adding cost and time to projects. AI-based transfer learning from small to large scale offers a new approach.

Transferring small scale process knowledge to large scale remains a challenge

Scaling up bioprocesses presents significant challenges due to the complexity of biological systems and the nonlinear nature of scale transitions. Maintaining consistent conditions for parameters like mixing, oxygen transfer, and temperature is often also difficult across bioreactor sizes.

Equipment design differences (such as sensors), limited early-stage process knowledge, and sensitivity of critical quality attributes further complicate scale-up, often forcing extensive large-scale experiments, leading to extended development timelines and additional cost.

Learn and predict large scale 10L runs from Ambr15 data via transfer learning

Faced with these complexities and operational challenges, Wheeler Bio, a US based CDMO, asked DataHow to support it with cross-scale modeling, with the objective to learn larger scale behaviour with as few large scale runs as possible as part of the calibration of the downscale process.

The assessment was run with DataHowLab, deploying its **transfer learning** capabilities via its advanced hybrid models.

DataHow was provided a standard historic process development data set, where **11 ambr15 runs** were initially conducted as part of a clone selection test and an additional **4 10L runs** were collected during a scale-up bulk-pool experiment.

OBJ 1: Demonstrate the ability of DataHowLab's hybrid models to transfer knowledge across scales - specifically, to predict 10 liter behaviour from Ambr15 data.

OBJ 2: Benchmark DataHowLab's hybrid models against multiple linear regression models (MLR) - the industry standard - for the scale-up challenge.

OBJ 3: Assess how DataHowLab support operational excellence by reducing the impact of issues or deviations

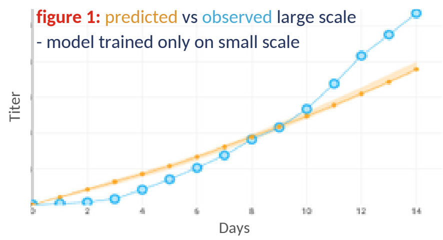
What is Transfer Learning?

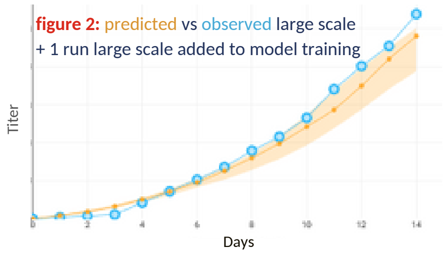
Transfer learning is a machine learning method that leverages data from historical processes to transfer knowledge horizontally to new projects.

This machine learning capability can be applied across molecules (historical insights applied to a new project) and across scales (transfering insight from small to large scale within a project).

This approach accelerates clone selection and transforms historical development data into a central development asset that delivers increasing benefits over time.

Insight 1 - Predict large scale behaviour from primarily small scale run to drive efficiency



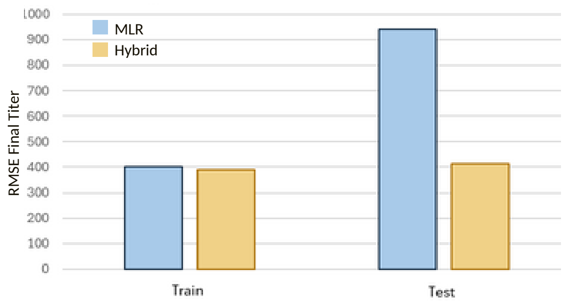


Scale-up often requires many additional large-scale experiments, adding time and development cost.

However, DataHowLab's transfer learning capability reduces the need for large-scale experiments by leveraging insights gained from small-scale data. An initial model trained on **only small-scale data (ambr 15)** was used to **predict large scale (10L)** with moderate success (figure 1). However, including **just one large-scale run** (10L) in training (figure 2) improved prediction accuracy by 50%.

- Only one 10L run was needed to accurately predict all other 10L runs
- Knowledge from small scale can now be leveraged as a development asset during scale up with DataHowLabs transfer learning
- A radical reduction in large-scale experiments is achievable, resulting in substantial cost savings and accelerated scale-up timelines

Insight 2 - Hybrid models outperform linear models when faced with scarce data



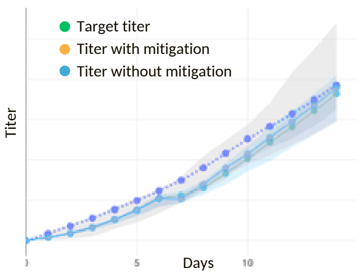
The hybrid modeling approach was benchmarked against multiple linear regression (MLR) models - an industry standard.

The hybrid and MLR models performed similarly on the training set (11 small scale + 1 large scale run), but on unseen large-scale runs, the **MLR's error more than doubled** while the hybrid model remained stable. The hybrid models' mechanistic core enables them to efficiently and effectively extrapolate from data at different scales.

- Hybrid models outperform MLR, especially when the data is limited and varied in scale
- To be effective, MLR models need a large volume of same-scale data.

Insight 3 - Hybrid models enable process simulations to support proactive deviation management

A feed mitigation strategy (yellow) to return final titer to target was recommended to offset a feed failure for days 1-5



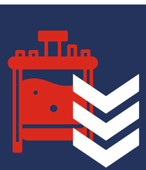
The adjusted feeding strategy restored the final titer to target levels, maintaining overall process productivity

Errors or deviations at commercial scale can lead to significant operational and financial consequences, as well as trigger time-consuming investigations. Proactive management of issues is hugely valuable.

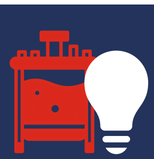
A case of an unnoticed feed failure (days 1-5) at commercial scale was simulated using the trained hybrid model highlighted above. As final titer was impacted, DataHowLab proposed a proactive mitigation strategy.

- The extrapolation capabilities of hybrid models enable the simulation of complex process dynamics
- Mitigation strategies can be generated and simulated to prevent the negative impact of errors and maintain operational excellence

Small Scale Data an Asset for Scale-up



Radical Reduction of Experiments at Large Scale



Increase Understanding at Large Scale

Proactive Deviation Management

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