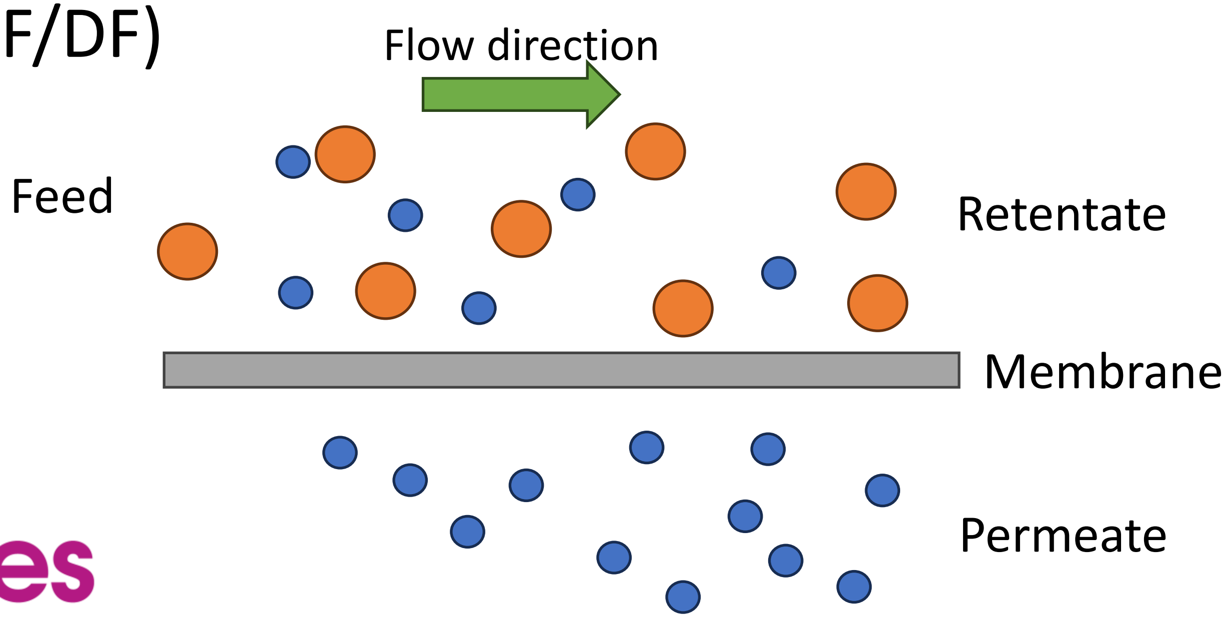
Using Machine Learning to Control Single-Pass Tangential Flow Filtration in Biopharmaceutical Processing

Bastian Oetomo, Michele Discepola, Saumya Karunadhika, Buddy Heydon, Sandra E. Kentish, Sally L. Gras, Ling Luo

Presenter: Bastian Oetomo (bastian.oetomo@unimelb.edu.au)

Tangential Flow Filtration

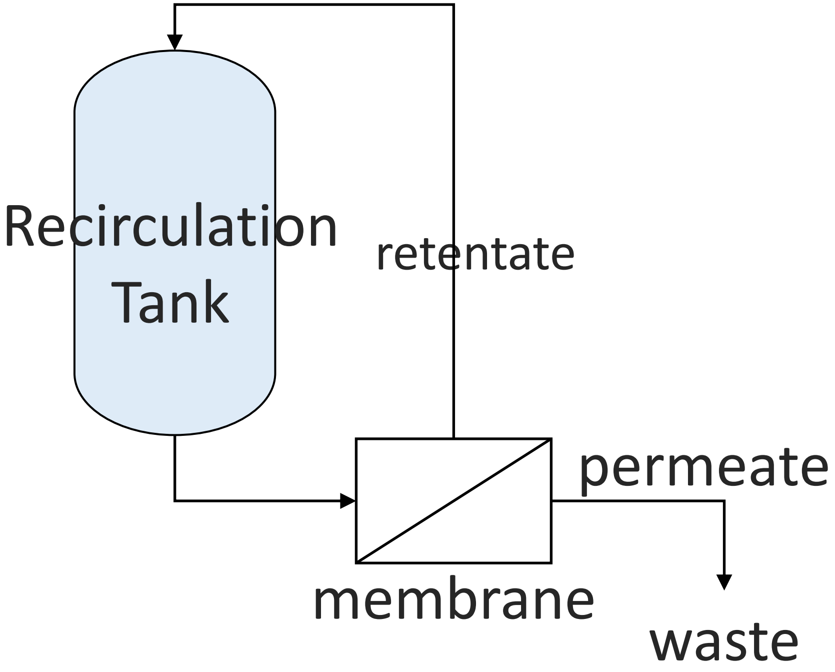
- **What it is:** A membrane separation by size, where the small particles pass as permeate and larger particles are retained as retentate.
- **How it flows:** tangentially (parallel) to the membrane surface
- **Used in biopharmaceutical processing:** for example, Ultrafiltration/ Diafiltration (UF/DF)



Motivation

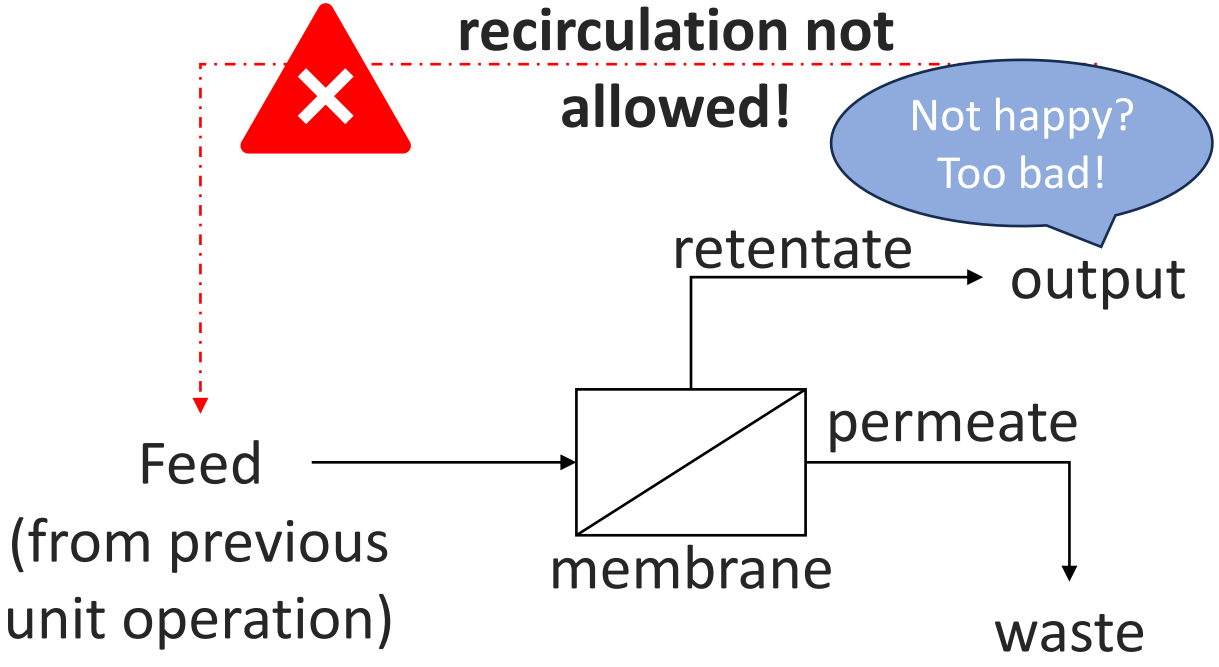
ARC **Digital Bioprocess Development** Hub

Batch Tangential Flow Filtration



× **does not support continuous bioprocessing**

Single-Pass Tangential Flow Filtration



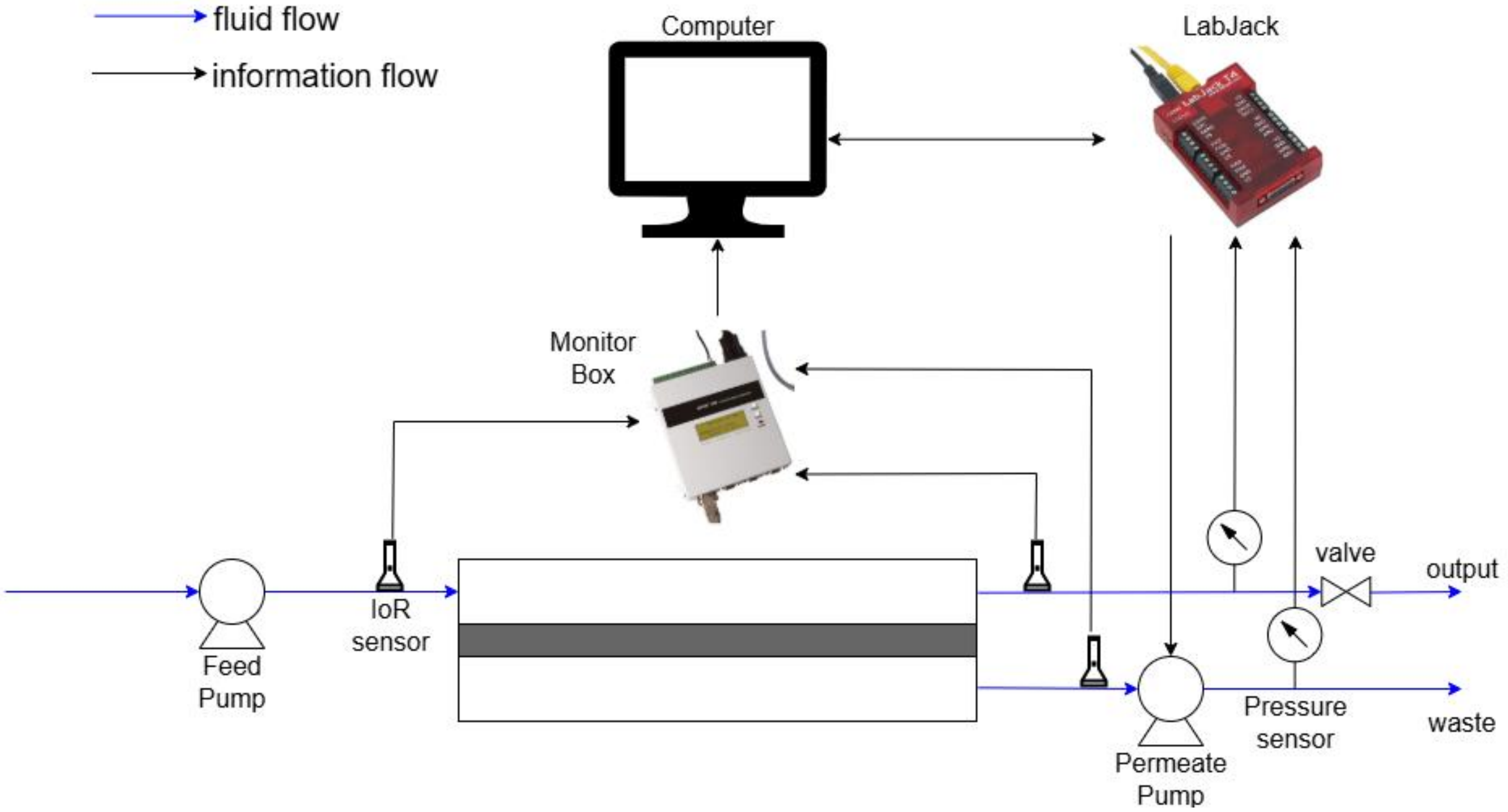
✓ **supports continuous bioprocessing**

Advances

IChemE

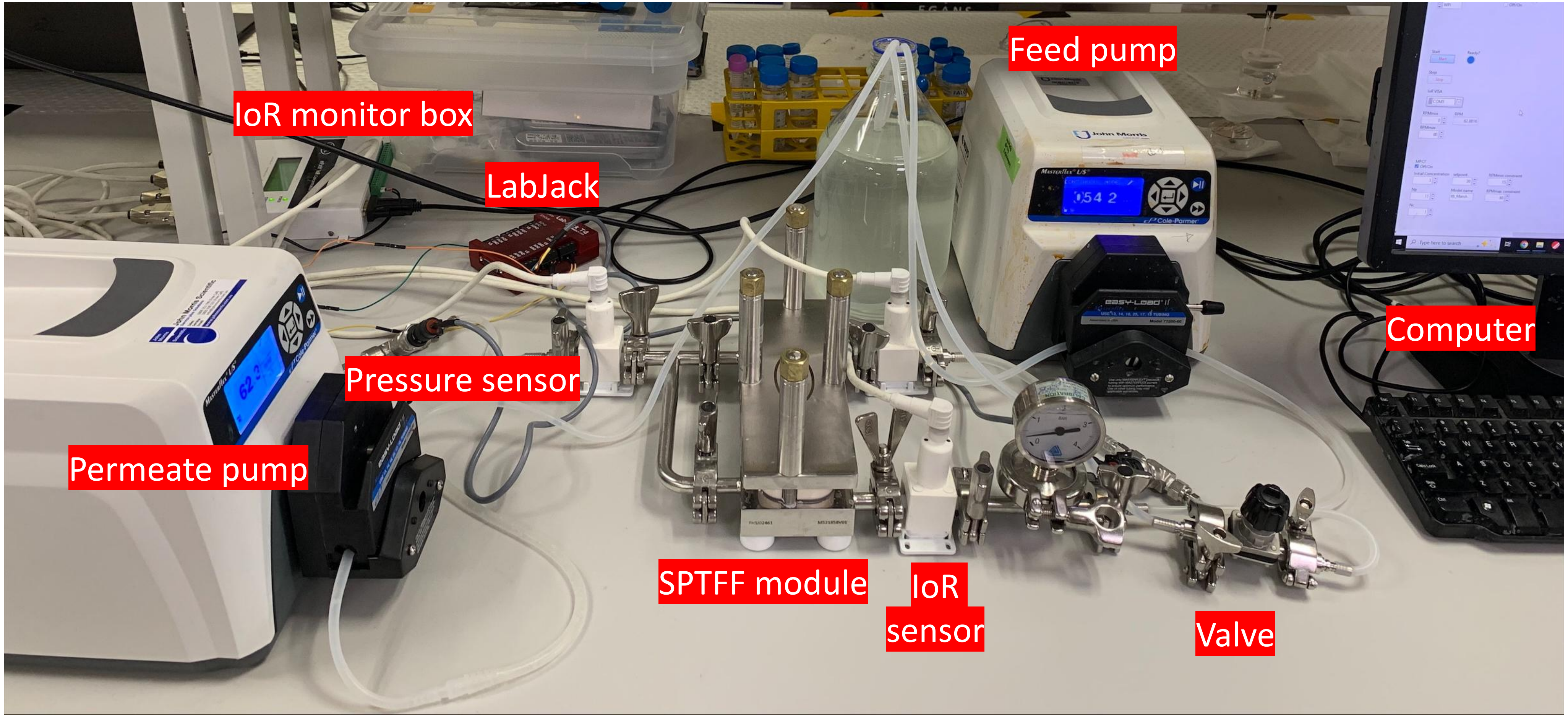
Control Architecture

ARC **Digital Bioprocess Development** Hub



Laboratory Setup

ARC **Digital Bioprocess**
Development Hub

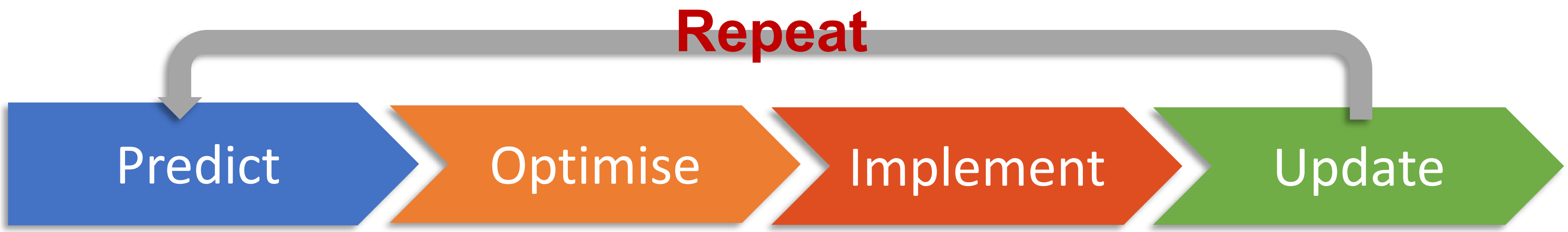


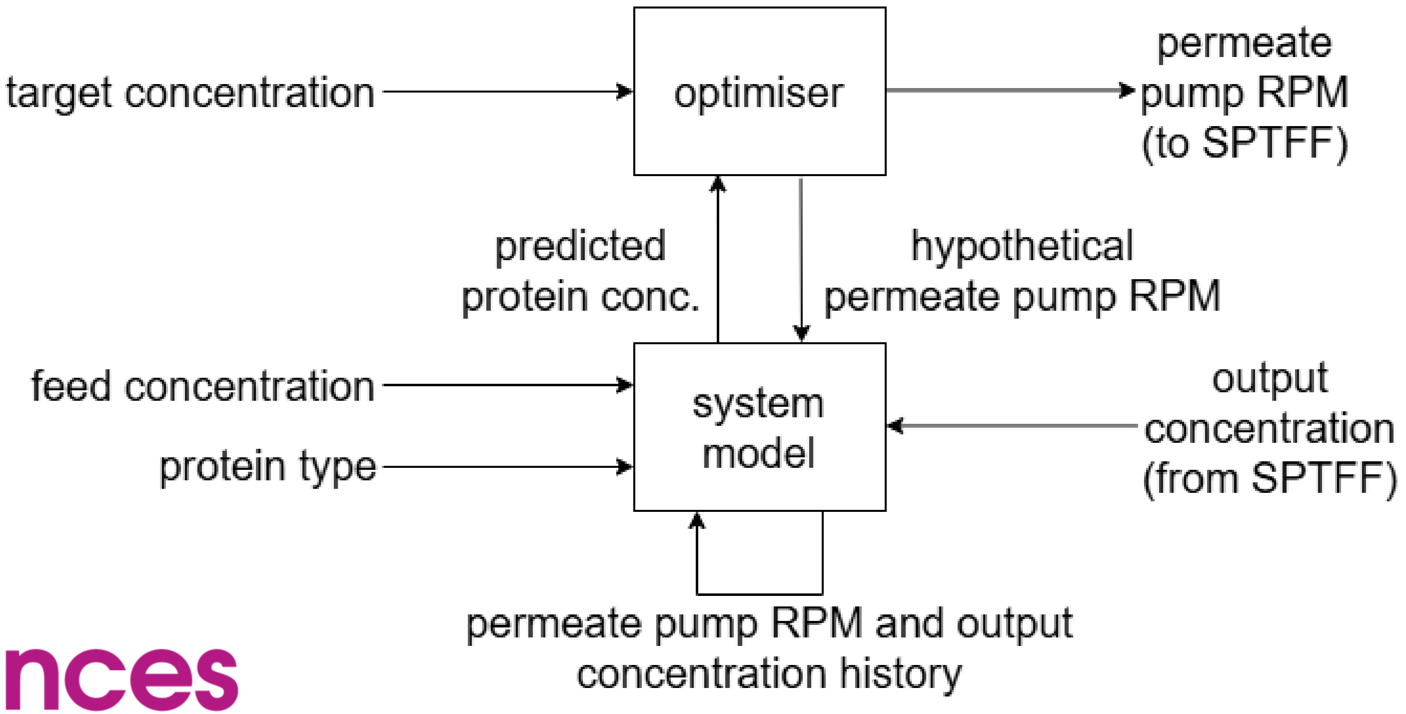
Process Requirements

- Protein concentration needs to get to the target range as soon as possible and be maintained within 5% error
- Absolute permeate pressure needs to be above 0.6 bar
- (Diafiltration) Buffer exchange rate above 99.9%

Model Predictive Control

ARC **Digital Bioprocess Development** Hub





Advances

IChemE

Challenges

ARC Digital Bioprocess Development Hub

Data-driven approach, no system expertise required

Relevant ML models: Nonlinear Autoregressive Model with Exogeneous Signal, Nonlinear Output Error, Transformers

Smarter controller optimisation method

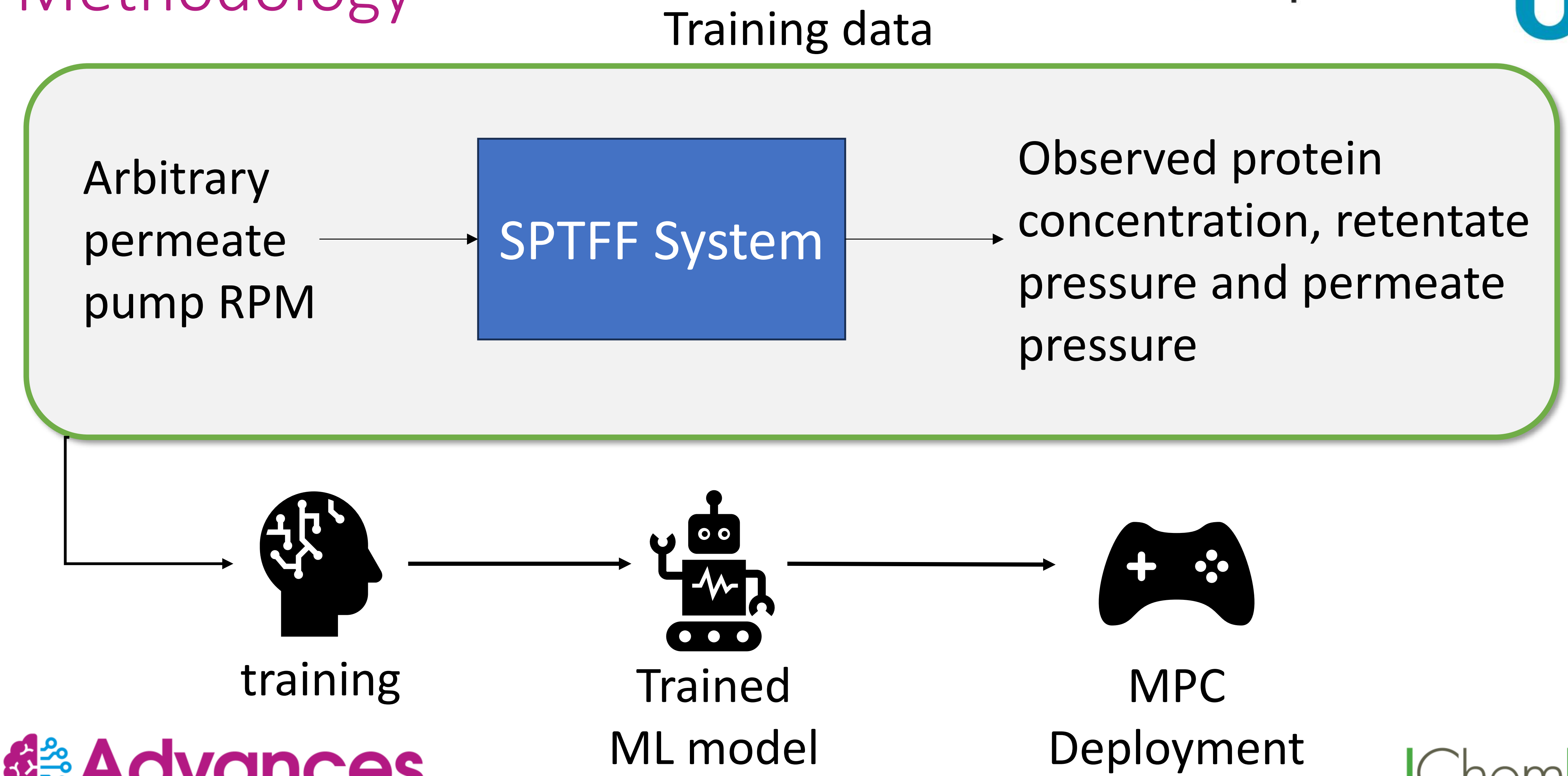
Relevant ML model: Bayesian Optimisation

Approximate the optimal solution

Relevant ML model: Artificial Neural Networks

ARC Digital Bioprocess Development Hub

Methodology

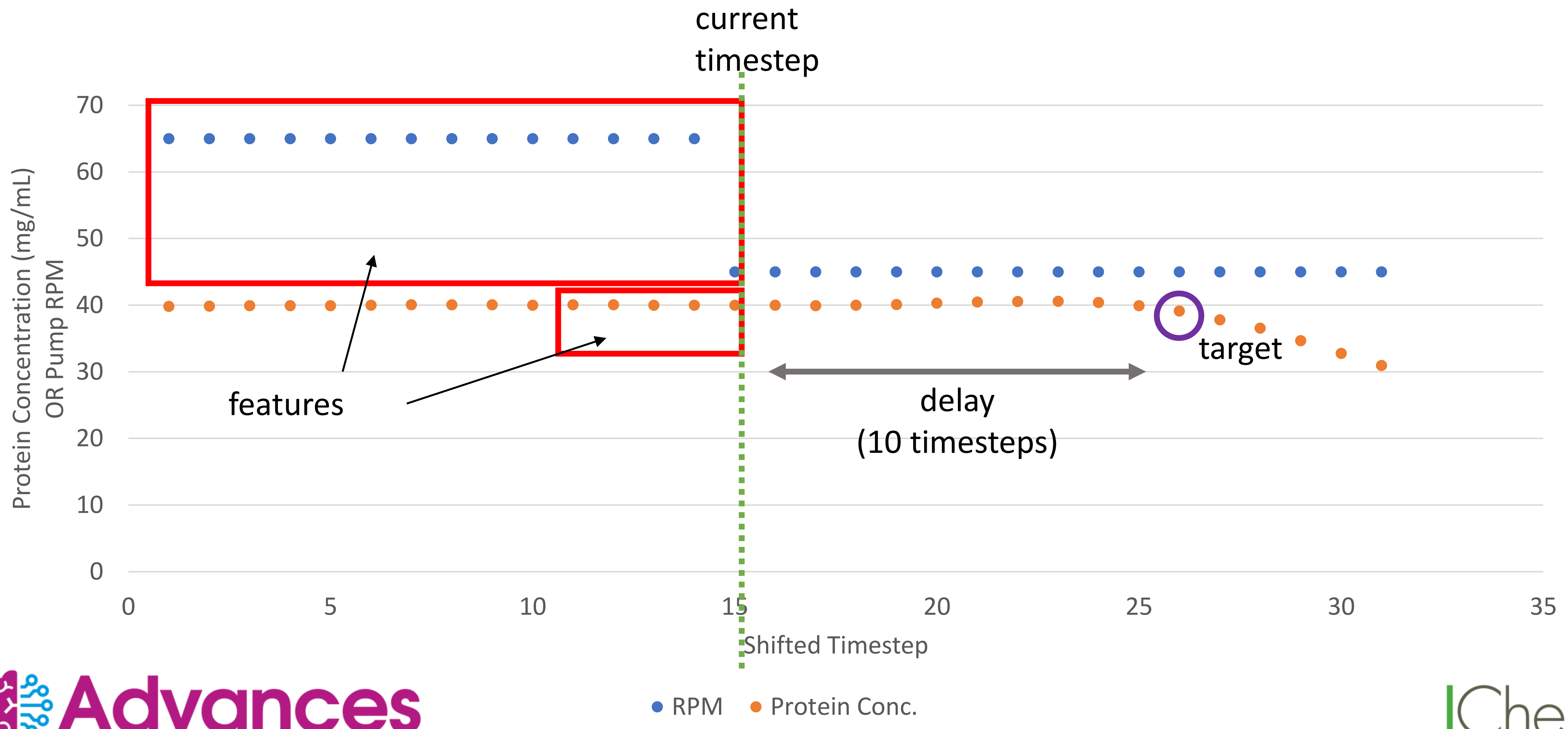


Advances

IChemE

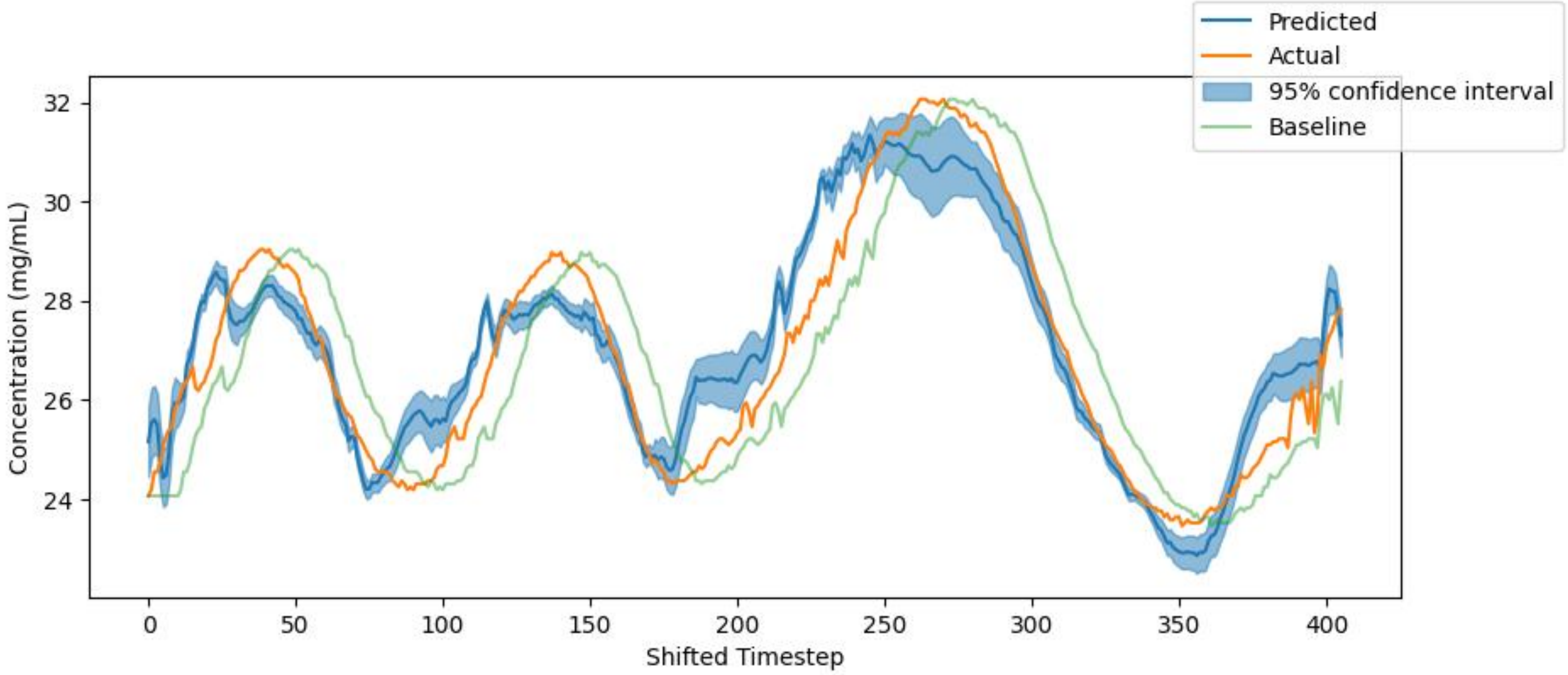
NARX Model

(Nonlinear AutoRegressive model with eXogenous input)



Predicting 11 Steps Ahead

ARC **Digital Bioprocess Development** Hub

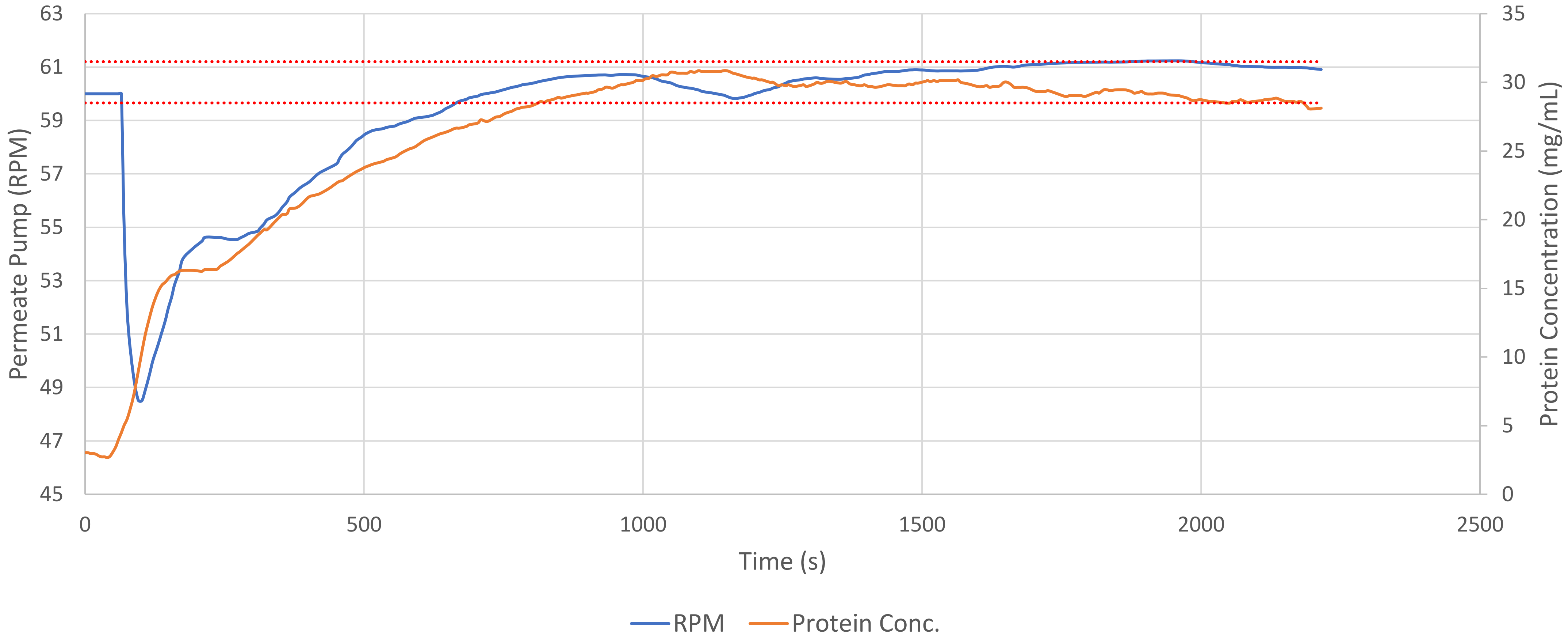


RMSE: 0.8864
MAE: 0.7398

Advances

IChemE

Prototype MPC Deployment I



ARC **Digital Bioprocess Development** Hub

Advances

IChemE

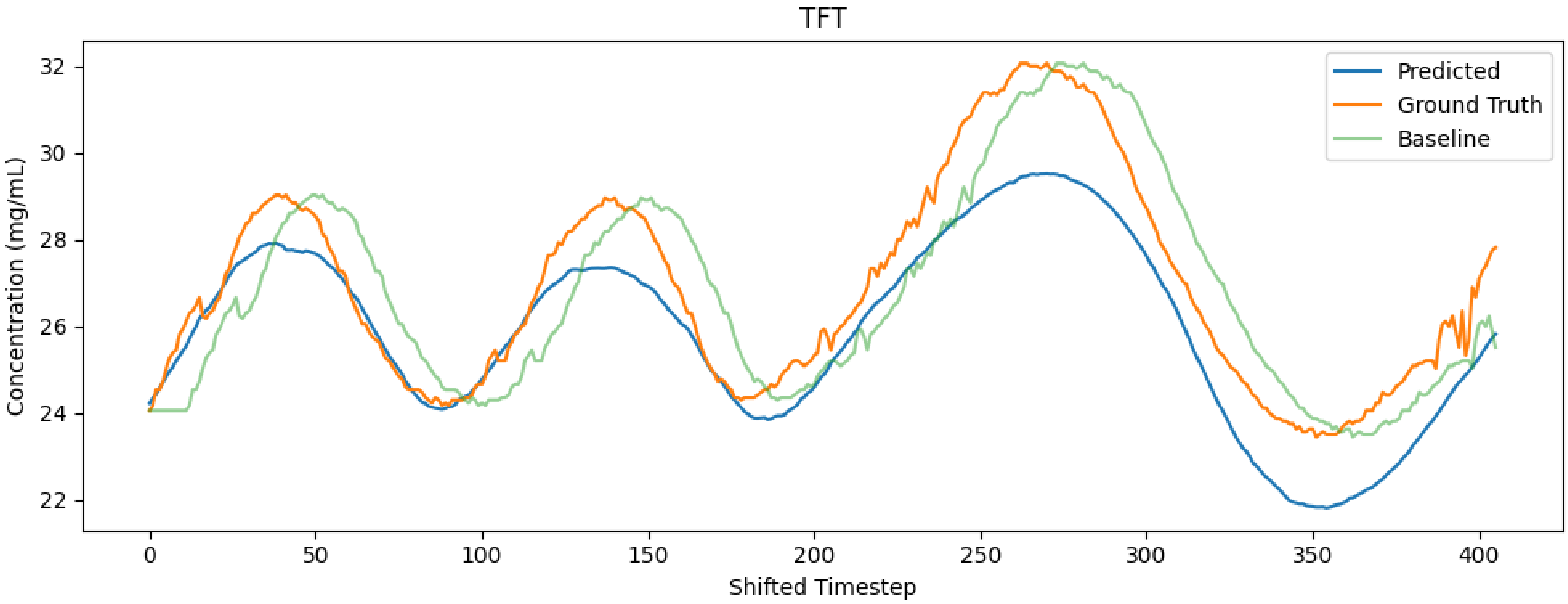
Transformers

ARC Digital Bioprocess Development Hub

- Initially developed for translation (Language A → Language B)
- We are interested in sequence-to-sequence forecasting of concentration given history + planned control signal.

Temporal Fusion Transformer (TFT)

ARC **Digital Bioprocess Development** Hub



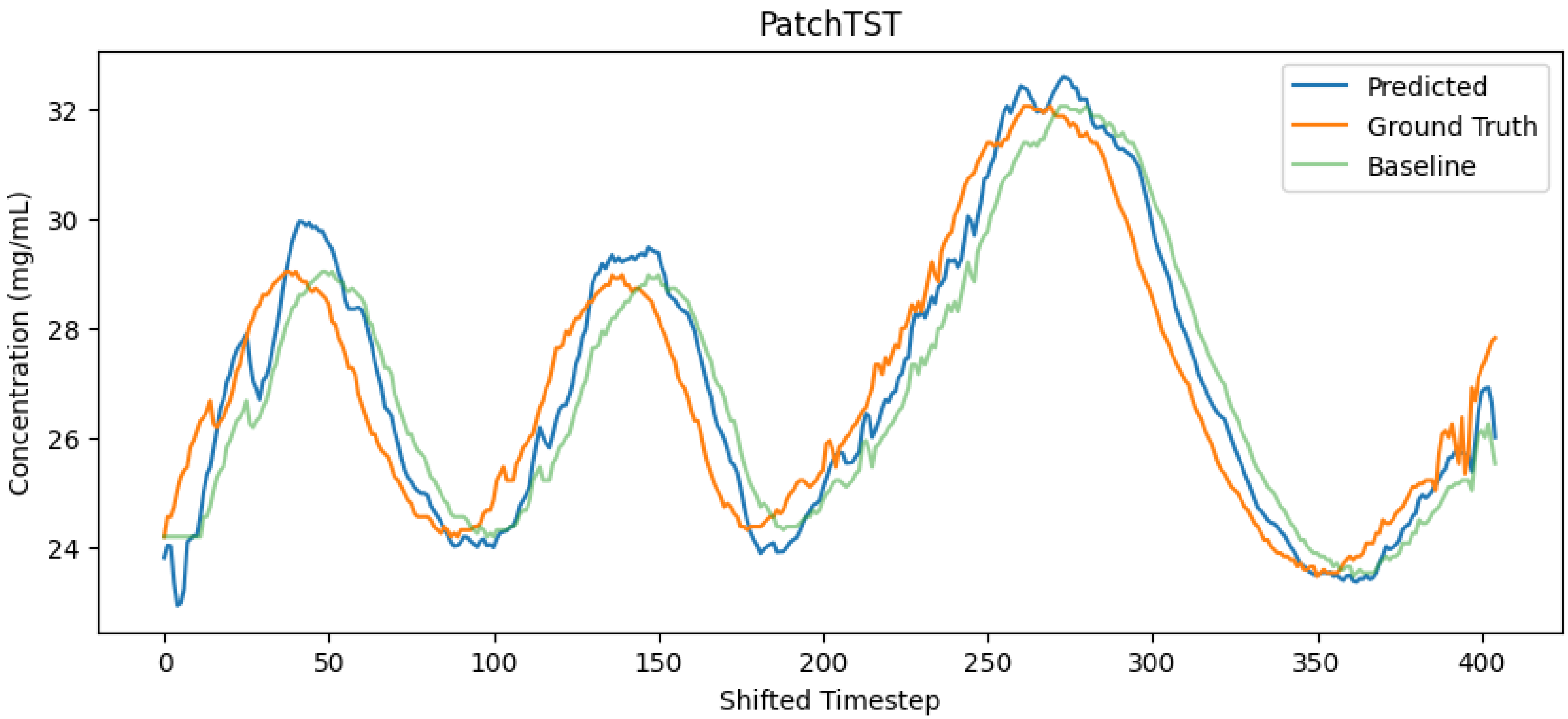
RMSE: 1.6594
MAE: 1.0631

Advances

IChemE

PatchTST

ARC **Digital Bioprocess Development** Hub

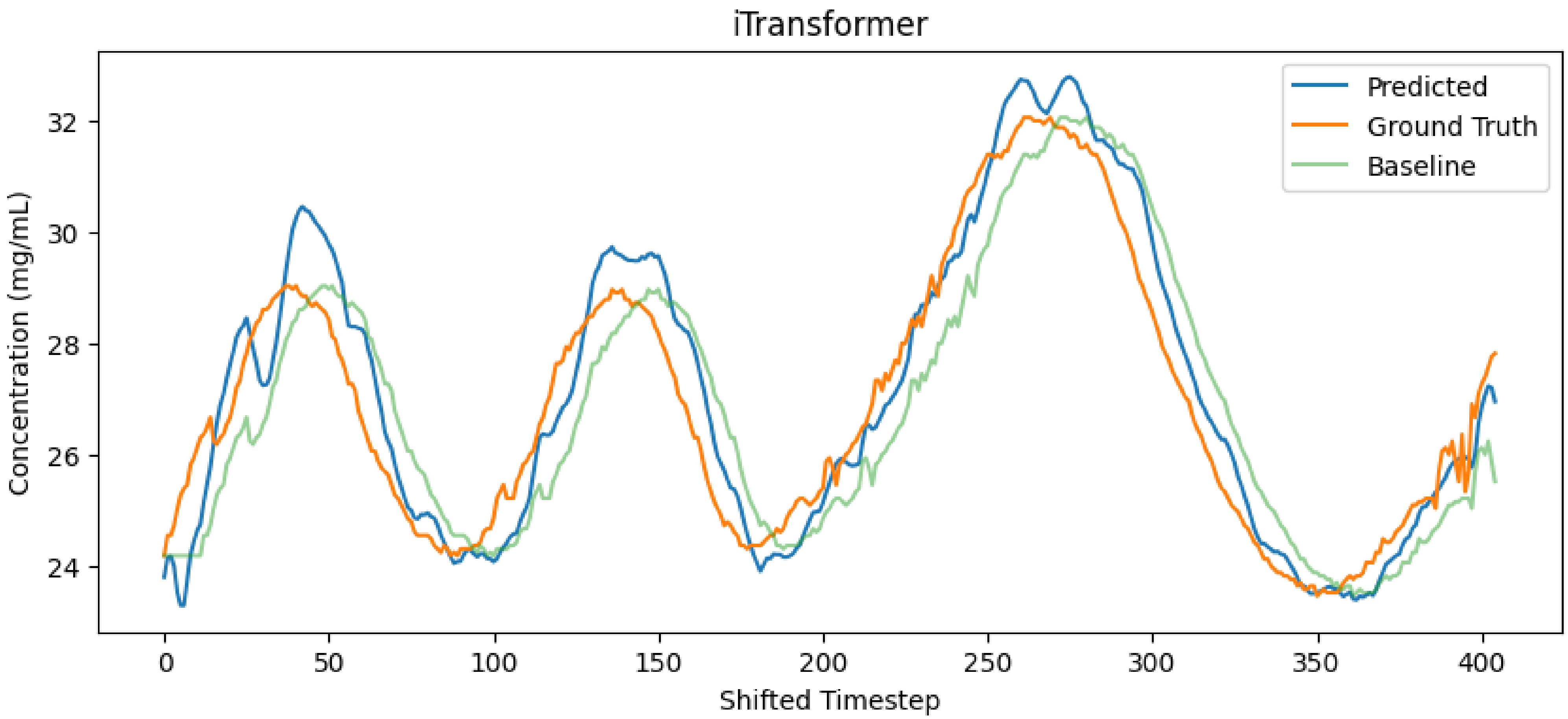


RMSE: 0.8387
MAE: 0.7080

Advances

IChemE

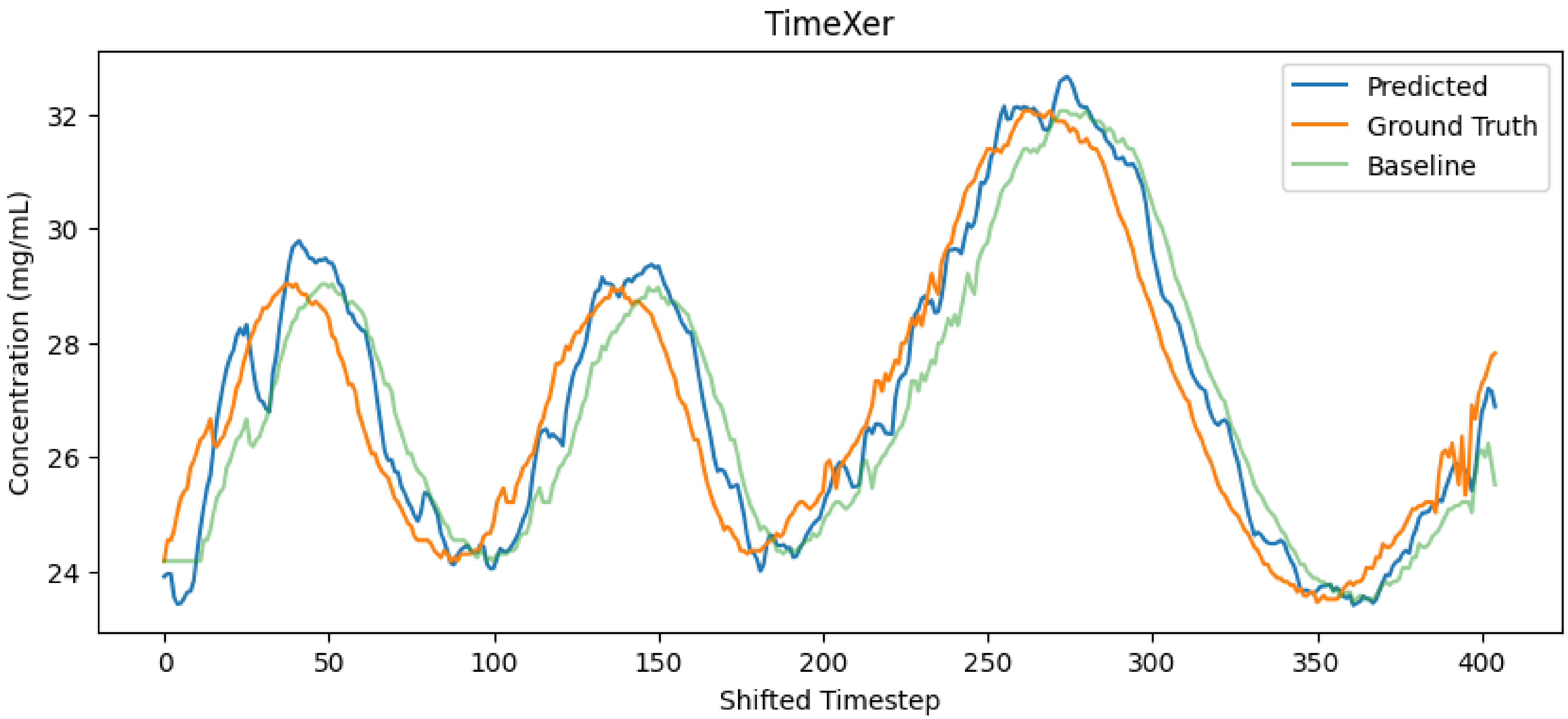
iTransformer



RMSE: 0.7986
MAE: 0.6663

TimeXer

ARC **Digital Bioprocess Development** Hub



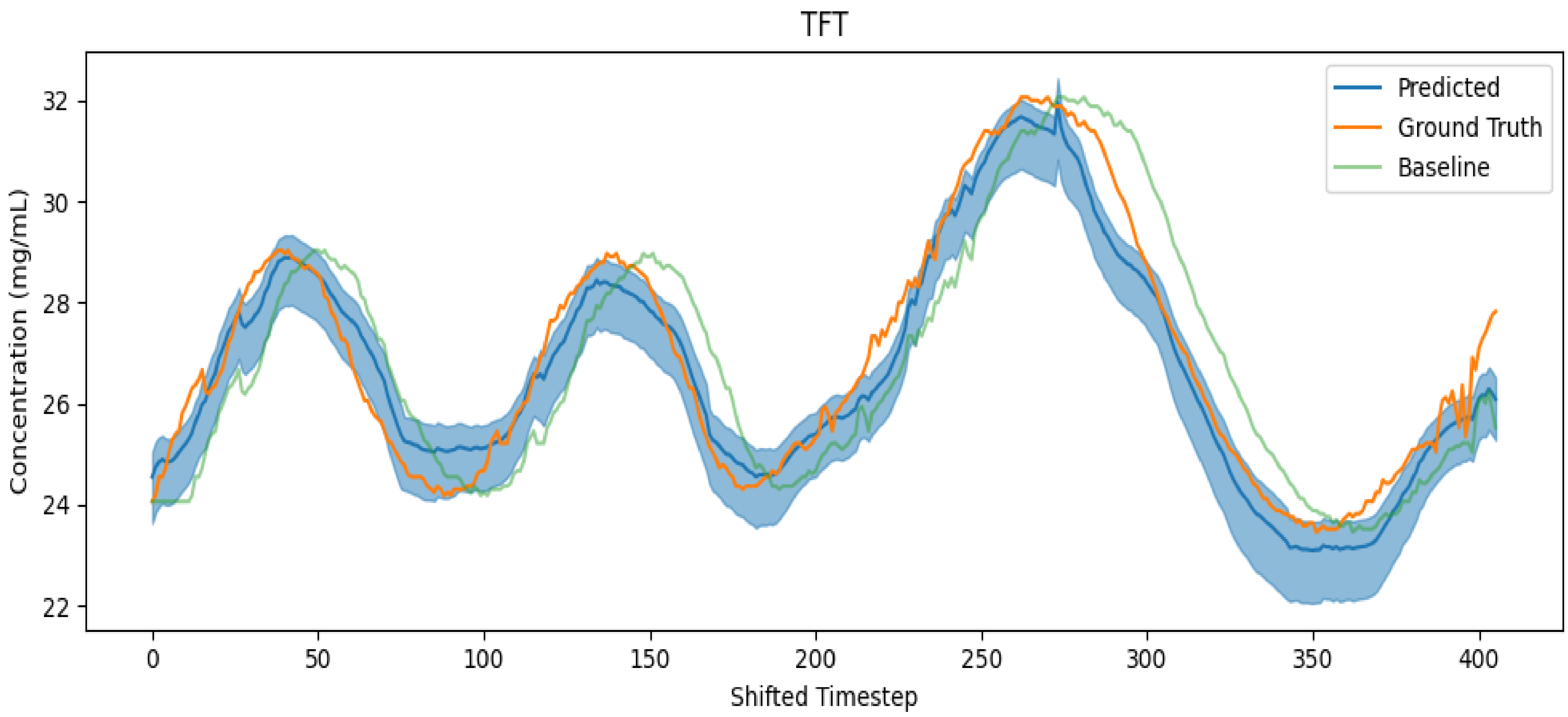
RMSE: 0.7914
MAE: 0.6531

Advances

IChemE

TFT (Optimised)

ARC **Digital Bioprocess Development** Hub



RMSE: 0.3457
MAE: 0.4865

Advances

IChemE

Next Steps

- Predict retentate pressure and permeate pressure, and use the predictions as constraints during optimisation.
- Use transformer-based methods for prediction in the controller.
- Incorporate online learning and improve adaptability
- Tune the controller's settings

Conclusion

ARC Digital Bioprocess Development Hub

- SPTFF eliminates the recirculation step, enabling continuous bioprocessing.
- Process control needs to be implemented in SPTFF.
- MPC is used to meet the process requirement of UF/DF in biopharmaceutical processing
- ML/AI can be used as a method for system identification, acting as the predictor in MPC

Advances

IChemE

ACKNOWLEDGEMENTS

ARC Digital Bioprocess Development Hub

Australian Government
Australian Research Council

THE UNIVERSITY OF MELBOURNE

UTS

RMIT UNIVERSITY

CSL™

cytiva

patheon
by Thermo Fisher Scientific

Advances

IChemE