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Chemeca 2026 and Hazards Australasia
28 – 30 September, Melbourne, Australia

A Hybrid Neural Network–Mechanistic Framework for Predictive CHO Cell Culture Modelling

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ABSTRACT

Advanced biomanufacturing involves the use of mammalian cells such as Chinese Hamster Ovary (CHO) cells to produce biologics. These processes are inherently complex, nonlinear and sensitive to culture conditions and media formulations, making robust optimisation essential for improving the affordability and accessibility of biologics. Developing predictive models is of increasing interest to accelerate process development and improve process control and monitoring. Machine learning algorithms/data driven techniques can capture complexities associated with these biological systems without having to mathematically describe every intricate biological process. However, more robust and interpretable models can be built by combining machine learning with mechanistic equations informed by biology and process knowledge.

In this work, we develop a hybrid modelling framework that integrates a deep neural network with mechanistic mass balances and specific reaction rate relationships to dynamically predict the variation of cell culture profiles including cell density, titre, glucose and amino acid concentrations, as well as the concentrations of metabolic byproducts, including lactate and ammonia. The model was initially trained on 18 bioreactor runs, spanning 6 different feed media compositions with varying feed delivery. The model was capable of successfully predicting cell culture dynamics in unseen bioreactor runs with different feed media compositions and regimes. Where the cell culture process was different, retraining the model with an additional experiment, enabled rapid model adpatation and imporoved prediction fidelity.

This approach demonstrates hybrid models can leverage existing process knowledge while capturing complex biological behaviour, offering a scalable framework for accelerating media optimisation, reducing experimental burden, and supporting next-generation biologics production.

KEY WORDS

Hybrid modelling, Bioprocess optimisation

BIOGRAPHY

Dr. Bhagya Yatipanthalawa is a postdoctoral research fellow in the Department of Chemical Engineering, at the University of Melbourne. Her research focuses on advancing bioprocess engineering approaches for sustainable food, fuel and biopharmaceutical production. She is affiliated with the ARC Digital Bioprocess Development Hub, a collaboration between leading universities and biopharmaceutical manufacturing companies in Australia. In collaboration with CSL, one of the world's leading biopharmaceutical manufacturers, her research focuses on addressing industry relevant challenges through advanced modelling and data driven approaches

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