Developing Modelling Workflows for Cultivated Meat Yield Prediction

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Intent

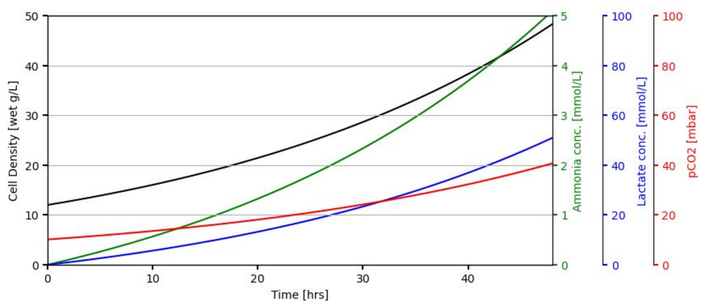
This project will build on existing technical modelling practices for the prediction of bioprocessing yield to facilitate more widespread use and to improve the accuracy of the models used.

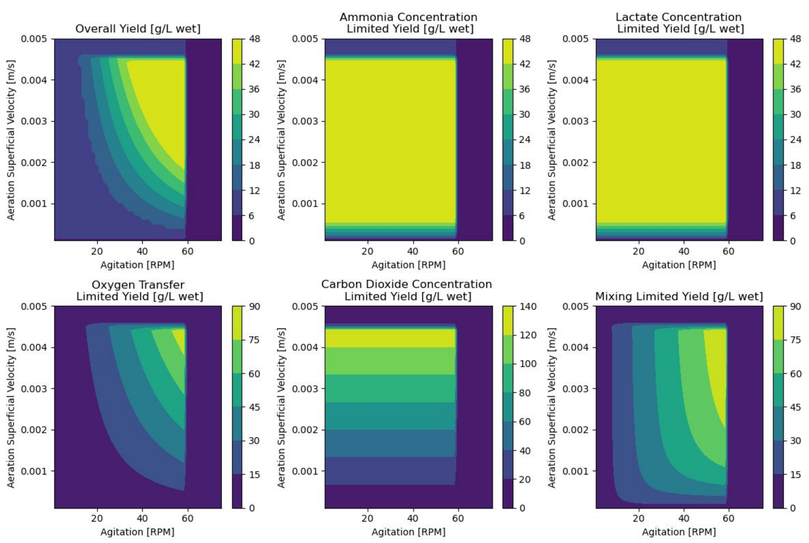
Existing Techno-Economic Analysis (TEA) Approaches

Existing technical models of bioreactor or production line performance (yield - grams / litre wet) broadly apply empirical equations that describe key performance characteristics, such as the rate of oxygen mass transfer in to the media.

Such an approach allows a wide range of bioreactor scales and architectures to be modelled in the same framework, allowing for yield predictions over various production and operational scenarios.

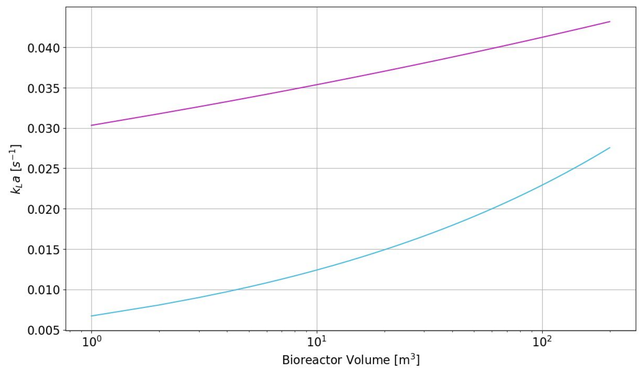
The technical approach of a recent TEA is used as a foundation for development, and is openly provided as a Python module. This module can be used to generate yield predictions for specific operating conditions, as in the graph below, and to show the optimum operating condition, both for overall yield and for the yield limited by specific constraints, bottom graph.



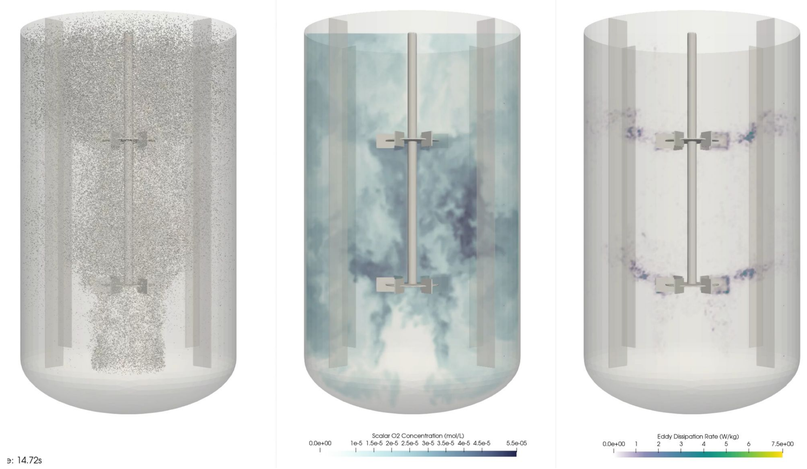


Using Computational Fluid Dynamics and Optimisation to Improve Models and Increase Yield

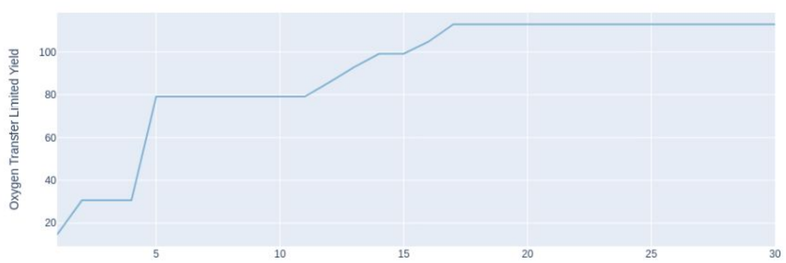
The broad use of empirical models of performance enables a variety of implementations which exist across the literature, which result in very different performance predictions. An example is the model used for the mass transfer coefficient of oxygen into the media, where published implementations result in very different values across the range of stirred tank bioreactor volumes, as shown below.



Computational fluid dynamics (CFD) can be used to predict performance characteristics in place of empirical equations, allowing performance evaluation of specific architectures and operation.



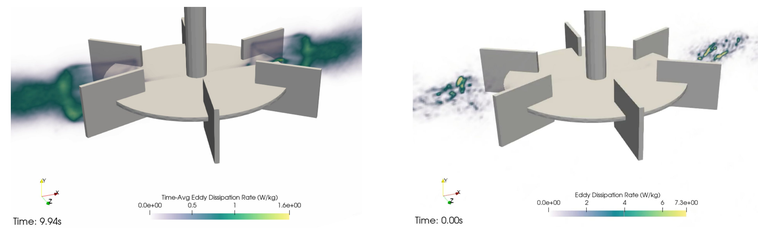
Combining CFD with optimisation techniques (here Bayesian optimisation) provides yield performance prediction through variation of impeller geometry, RPM and gas flow rate.



Improving Cell Stress Modelling

One of the constraints limiting yield is reduced cell growth in response to the hydrodynamic stress imposed by the bioreactor as it operates in a way to provide a well mixed, sufficiently oxygenated media. The rate at which energy is dissipated in the media is often used to characterize stress, with high levels stressing cells and reducing growth.

An average value is often used as depicted in the image below left, showing values in proximity to the impeller. Cells, however, will experience the instantaneous value as they pass through the impeller region, and these values are significantly higher, as shown below right.



Computational fluid dynamics (CFD) can be used to link the cell stress experience in bioreactors to that in microscale experiments in which cell viability is also measured. This offers the possibility of significantly improving predictions of the effects of stress on cell growth and yield.