Raman-enabled Bioreactor Monitoring

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Summary

Raman spectroscopy can monitor a wide range of process parameters including metabolite concentrations, cell density and cell viability online. It achieves this by monitoring the cell culture with a laser. Monitoring these parameters in real-time can significantly reduce batch failures and reduce the number of process development runs required for a new therapeutic. It enables automated feed control strategies and could enable real-time product release in the future. Despite its potential, Raman bioreactor monitoring has seen limited application to date, due to performance challenges.

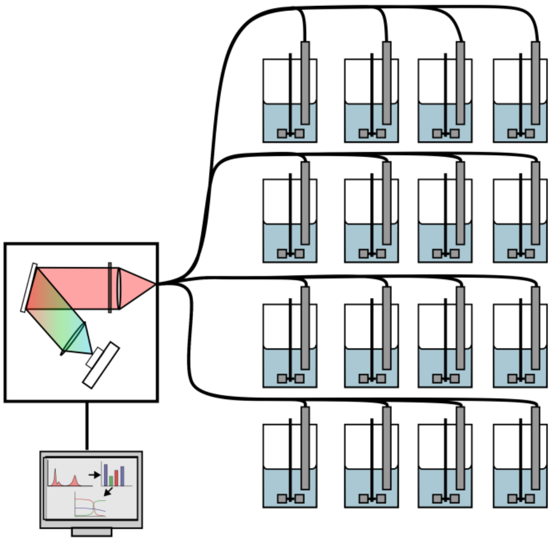
Background

Bioreactors are large cell culture vessels used for the production of many biological materials, including pharmaceuticals and alocholic drinks. Existing bioreactor systems measure very few parameters in real time (typically pH and oxygen content) and rely on offline assays to determine other parameters such as glucose, lactate and glutamine concentration and cell density. These offline assays require an operator's intervention into the process, taking time and therefore limiting the data collection rate. As a result, process development for new pharmaceuticals takes longer, and batch failures are detected more slowly.

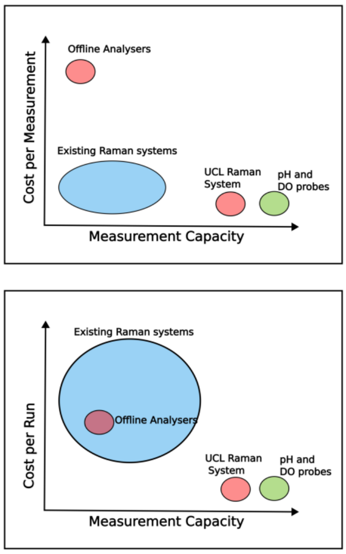
Many technologies have tried to fill the need. Spectroscopic techniques, particularly Raman spectroscopy, are front-runners since they require no chemical reagents and provide a data-dense signal. Existing Raman systems have failed to exploit this market due to failings in capacity (i.e., how many bioreactors can be measured at once, how many parameters can be analysed simultaneously, how frequently), performance (i.e., reproducibility between processes, process independent, and minimally invasive), and simplicity (i.e., the learning curve to setup the system, the safety requirements of the laser system, the compatibility with potential single-use requirements).

The technology

UCL has developed a Bioreactor monitoring system based on Raman spectroscopy that addresses the challenges found with other Raman systems. The system can run in a high throughput mode, where it can monitor up to 16 bioreactors simultaneously, which is sufficient for use in high throughput bioreactor setups. The probe design fully encloses the laser, ensuring that there is no risk of user exposure, allaying safety concerns. The simplified probe design means it is possible to create single use Raman probes and means that the cost per bioreactor run is comparable, if not cheaper, than offline monitoring. Finally, UCL is designing an analysis algorithm that leverages the improved physical properties of the probe design to enable turn-key measurement: no algorithm training will be required. This will also make Raman measurements process independent and therefore more attractive to regulatory agencies.



UCL's Raman system can monitor up to 16 bioreactors simultaneously.



Cost per measurement and cost per run provide different benefit profiles for Raman bioreactor monitoring.

Further Information

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