Process and product understanding is at the root of manufacturers’ efforts to produce safe and effective medicines. The 2009 ICH and FDA Guidance for Industry Q8(R2) Pharmaceutical Development describes a quality by design (QbD) approach that emphasizes product and process understanding and process control, based on sound science and quality risk management. Here we present approaches for the cultivation of this understanding via advanced process modeling and control with specific applications in the continuous manufacturing for monoclonal antibodies (mAbs) being shown.

First-Principles Dynamic Simulation of an Integrated Continuous Biomanufacturing Platform
- Moo Sun Hong

This presentation describes a software tool for carrying out high-fidelity dynamic simulations of integrated continuous mAb manufacturing plants. The simulations include first-principles models of individual biomanufacturing unit operations, including bioreactors, chromatography columns, and viral inactivation units. Thoroughly validated models were not available for the quantitative prediction of some relationships. The lack of validated models was addressed by using the best models available in the literature and then validating them using experimental data collected for the individual unit operations from an automated integrated continuous manufacturing platform at MIT. These validated individual units are then combined into a plant-wide dynamic model that includes the effects of model parameter uncertainties and disturbances, which is then used to validate the integration of the individual models and to map the raw materials and operations to the critical quality attributes and other variables of interest anywhere in the system.

Process Control Strategy Development for an Integrated Continuous Platform for Monoclonal Antibody Manufacturing
- Andrew J. Maloney

This presentation describes advances in control, data storage, data acquisition, and process modeling. Implementation of lower level control strategies are discussed and methodologies for the integration and storage of various data streams are demonstrated. Modeling of N-linked glycosylation profile, a key quality attribute, is reviewed and reproduced. The process model is used for understanding parameter sensitivity and development of an integrated control strategy for eventual validation on the manufacturing testbed.
Many new data analytic tools for a variety of objectives such as model prediction, supervised and unsupervised classification and fault detection have been introduced in recent years. The increasing multitude of these powerful tools has motivated the development of smart data analytics approaches, i.e., a decision tree that automatically selects the most suitable method based on metadata and a systematic interrogation of the dataset. This presentation introduces a smart data analytics approach for the objective of supervised classification, which arises in fault diagnosis in chemical and biological manufacturing processes. The approach is applied to a biomanufacturing case study for the production of rotavirus subunit vaccines.