



Department of Chemical Engineering Special Guest Seminar



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**“Modeling,
Simulation & Control
of Batch Protein
Crystallization
Processes”**

Thursday, March 20
315 Shillman Hall
11:45a – 1:00p

*Refreshments will be
served*

ABSTRACT Batch protein crystallization is used in pharmaceutical industries for the production of many types of pharmaceuticals, and also for the separation and purification of a drug from a solvent. Since the produced crystals must conform to desired specifications and since deviations from these specifications are often associated with high costs, a well-controlled crystallization is a crucial operation in pharmaceutical manufacturing. Crystallization is also used in protein structure determination. Although X-ray crystallography has proven to be a valuable technique in determining protein structure, the structures of many proteins are not known because they cannot crystallize easily, i.e., within a practical time frame. Motivated by these considerations, the present work focuses on the development of a computational framework to simulate, model and control a batch protein crystallizer in order to produce a substantial number of crystals of desired size and shape. The batch crystallizer model involves a kinetic Monte Carlo simulation method which describes protein crystal growth via adsorption, desorption, and migration mechanisms and mass and energy balances for the continuous phase. The required nucleation rates are obtained from available experimental data. The model is used in conjunction with a model predictive controller (MPC) to obtain protein crystals of desired size and shape at the end of the batch process. Simulation results for a batch crystallizer that produces tetragonal hen egg white lysozyme crystals demonstrate that the proposed MPC, which adjusts the

crystallizer temperature, is able to drive the crystal shape to a desired set-point value with a low polydispersity for crystal size. In the present work, a Monte Carlo simulation method to determine protein solubility is also developed. The method is based on a generalization of constrained cell model simulation techniques for fluid-solid equilibrium. In future work, this method will be used to describe crystal nucleation. Regarding crystal growth, future work will involve addition of aggregates of two or more protein molecules onto the crystal surfaces. This consideration can potentially produce more realistic crystal growth rates and can account for the phenomenon of cessation of growth which is sometimes observed in protein crystallization.

BIOGRAPHY Dr. Orkoulas received a BS in chemical engineering from the University of Patras, Greece, and PhD in chemical engineering from Cornell University. He held postdoc research positions at the University of Maryland, Pennsylvania State University, and Rensselaer Polytechnic Institute. He is Assistant Professor in chemical and biomolecular engineering at UCLA. His research interests are in the area of mathematical modeling, simulation, optimization and control of multiscale physico-chemical process systems and in the area of thermodynamic modeling and molecular simulation (Monte Carlo, Molecular Dynamics and kinetic Monte Carlo) of complex fluids.

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