Penn Engineering
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Chemical and Biomolecular Engineering

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FRANCESCO DESTRO

"Systems Engineering for Addressing Critical Challenges in Viral Vector Manufacturing"

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Wu and Chen Auditorium
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ABSTRACT

The demand for viral vectors is poised to soon exceed current production capacities, driven by the surging number of clinical trials for gene and cell therapies. Unfortunately, current manufacturing processes for viral vectors have high costs and low titers. This talk will demonstrate how process systems engineering tools can be leveraged for addressing the most critical challenges in the manufacturing process for recombinant adeno-associated virus (rAAV), the most widely used viral vector in commercial gene therapies. FDA recently approved the first rAAV-based gene therapies manufactured in the Sf9/baculovirus expression vector system (BEVS). Within the BEVS, Sf9 cells produce rAAV as a result of infection with recombinant baculoviruses that carry the genetic blueprint for vector production. A mechanistic model is developed to identify the bottlenecks to full capsid formation in the intracellular pathway for rAAV production in Sf9 cells. The model indicates genetic modifications to the baculovirus vectors that can enhance the productivity of the platform. Further, the optimal process conditions to establish continuous rAAV manufacturing in the BEVS are identified through a novel numerical method for solving systems of partial differential equations. Finally, a powerful machine learning model is introduced for real-time prediction of rAAV titers based on single-cell biophysical signatures.

BIO

Dr. Francesco Destro is a Postdoctoral Associate at the Department of Chemical Engineering and at the Center for Biomedical Innovation at MIT, where he conducts research into process systems engineering and advanced biopharmaceutical manufacturing. He obtained a Ph.D. in Chemical Engineering from University of Padova in 2022, with a dissertation on the use of mechanistic modeling and machine learning for optimizing pharmaceutical systems. He is the first author of 11 peer-reviewed publications, and complemented his research training in systems engineering and (bio)pharmaceutical manufacturing as a Visiting Scholar at Siemens Process Systems Engineering (London, UK) in 2019 and at Purdue University in 2020 and 2022.