



## Wolfson Department of Chemical Engineering Special Seminar

Lecture Hall 6, Wolfson Department of Chemical Engineering,

**25<sup>th</sup> May, 2016, at 13:30**

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## **Dynamic Optimization of Continuous Manufacturing of Pharmaceuticals**

Continuous manufacturing (CM) of pharmaceuticals is being explored as an alternative to traditional batch-wise production. This shift holds a great promise to increase production efficiency, enable smaller production facilities, minimize waste, energy consumption, and raw material use and to enable drug quality monitoring on a continuous basis. However, implementing CM in the pharmaceuticals industry suggests short operational campaigns, with significant transient phases (start-up and shutdown), constituting up to 30% of the entire time horizon. This significantly hampers the plant's economic feasibility.

Efforts to optimize the overall production process involve mathematical modeling and solution of hybrid (discrete-continuous) systems embedding Differential-Algebraic-Equations (DAEs), along with the associated parametric sensitivity trajectories to be used in rigorous gradient-based optimization algorithms.

In this talk, these efforts will be described, emphasizing the numerical issues related to the hybrid and non-smooth nature of the mathematical model. In this context our in-house specialized code, DAEPACK, will be presented. A case-study pilot plant incorporating several synthesis and separation steps to produce final tablets is used as proof of feasibility. The dynamic optimization approach that is employed maximizes the accumulated on-spec production directly over the entire time horizon (so-called Economic-Optimization), while guarantying differentiability with respect to the controls. The intelligent choice of controls will be discussed and some preliminary results will be presented.