CBST Seminar

366 Colburn Lab
Friday, January 18, 2019
Time changed to 1:30 p.m.

"Engineering the Cold Side of Biotherapeutics"

Decreasing temperature is generally expected to decrease degradation kinetics, however, the complexity of biological products (as proteins or cells), associated to multiple intricate phenomena that are triggered by cooling, often brings unanticipated results. For example, when a solution is freezing, the growth of the ice crystals causes all the solutes concentrate, typically by one or two orders of magnitude, potentiating interactions, crystallization, aggregation, pH shifts, osmotic pressure and ionic force increase, protein unfolding by cold or extensive ice interfacial area, also oxygen and other gases saturate forming air interfaces (bubbles) and dehydration is generalized. The mechanistic contribution of each of these variables cannot be clearly deconvoluted and it is also not easily correlated with product quality because of the stochastic nature of nucleation, the spatial anisotropy that is generated by freezing (and thawing or drying) and the amplification of the previous factors by limited (or deficient) process control. Experimental and modelling approaches were developed to understand and anticipate some of these mechanisms within the ice structure. Computational Fluid Dynamics was used to access the microscale and virtually display local transient stresses, which was complemented by kinetic aggregation studies under ice-growth inhibition under isochoric cooling. This strategy has already contributed to clarify important mechanisms for biotherapeutic's degradation induced by freezing and used to assist the development of more rational formulations and optimized systems.

Miguel A. Rodrigues

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Dr. Rodrigues is Assistant Professor in Chemical Engineering Sciences at the Instituto Superior Técnico (IST) of the University of Lisbon. He graduated in Biological Engineering and received his Ph.D in Chemical Engineering (U. Lisbon) in 2006 on "Production of particles for controlled release of pharmaceutical substances using supercritical fluids". Before joining IST in 2009 he was an invited scientist at the University of Texas at Austin, where he developed "Controlled Freezing Processes for Producing Stable Protein Particles" sponsored by Pfizer. Since then his work has explored these two fields of Chemical Technology, namely, supercritical systems to improve stability and delivery of pharmaceutical products and new methods for cryopreservation (or cryoprocessing) of proteins and cells to enable emerging therapies. His research has motivated several collaborations in Europe and overseas, with colleagues from academia and industry. He has been invited to give seminars in R&D centres of pharmaceutical companies and in international conferences. He is also a co-founder of Smartfreez a Start-up that is shaping cryopreservation methods in biopharma industry.

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