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Inertial-based Filtration Method for Scale Up Applications in Bioprocessing

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14 January 2019, Monday
10.00am

BTI Boardroom
Level 6, Centros

Hosted by Dr Steve Oh

Seminar Abstract

Emerging inertial focusing technique as an alternative method to microfiltration enables continuous and clog-free separations with lower maintenance costs. These features along with its relative ease of scalability to reach a relevant industrial scale will facilitate its potential adoption in various industries such as bioprocessing and waste water treatment. Of particular interest is the separation of particle sizes up to one order of magnitude larger than cell sizes (a > 50 µm) in bioprocessing in scaled-up channels while avoiding clogging. However, Dean-coupled inertial focusing has not been studied in detail when the channel hydraulic diameter is greater than $D_H \approx 0.3$ mm.

The mechanism of Dean-coupled inertial focusing inside scaled-up rectangular and trapezoidal spiral channels (i.e., 5-10x bigger than conventional microchannels) is studied with an aim to develop a continuous and clog-free microfiltration system for bioprocessing. Scaling up channel hydraulic diameter one order of magnitude from ~0.1 mm (micron scale) to ~1 mm (millimeter scale) quenches the inertia of flow for a given channel Re number (Re≤500), resulting in deterioration of Dean-coupled inertial focusing (D_H > ~1 mm). Accordingly, different scaled-up trapezoidal spirals have been developed to (i) filter cell-microcarrier complexes (retention device) and (ii) separate microcarriers from cell suspensions at high volumetric flow rate of 30 mL/min (Re~300) with cell yield of ~94%.

Moreover, in cell-based therapeutic products, particulates matter contamination is of great concern, as it adversely affects patient safety and product quality. In contrast to protein-based biologics, manufactured cell products are relatively large (above submicron) and this makes the use of membrane filtration impossible. Thus, a broad range of visible and sub visible particulates cannot be filtered out from the final product. A hybrid method is proposed to remove particulates from the final cell therapy product. In addition to the standard sieving process that excludes presumably a diverse range of particulates; inertial-based filtration is performed after sieving to alleviate the particulates count. A high-throughput spiral inertial microfluidic channel is demonstrated to filter a broad range of particulates from 75 µm down to 25 µm from mesenchymal stem cell (MSC) suspensions with an efficiency of greater than 95% at volumetric flow rate of 6 mL/min (Re~100). Simultaneously, the proposed method fractionated the MSC population to harvest the medium- to small-sized subpopulations (a ≤ 20 µm) that are the most multipotent and least senescence-associated subpopulations. Further biological experimentation validates the applicability of the developed devices.

About the Speaker

Reza Moloudi received his bachelor and master's degree in Mechanical Engineering-Thermofluids from Ferdowsi University of Mashhad (Iran). He is a recipient of prestigious Singapore International Graduate Award (SINGA)-A*STAR in 2015 and pursuing his PhD research at A*STAR-SIMTech in collaboration with A*STAR-BTI and WhirlCell Pte Ltd. He is currently completing his Ph.D. on large scale cell separation from manufactured cell products by exploiting Inertial Microfluidic techniques under the supervision of Dr. May Win Naing (SIMTech), Prof. Chun Yang (NTU), Dr. Warkiani (UTS) and Dr. Steve Oh (BTI).