Seeding Distribution in the Channel of a Cell Culture Vessel

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Abstract

Introduction: Conventional cell culture (CC) techniques are advancing significantly with trend towards a mass production. The induced pluripotent cells (iPSC) strategy and studies are aimed to learn how to reprogram cells to repair damaged tissues in the human body. Plating density (number of cells per volume of culture medium) plays a critical role for some cell types. The cells transport at various process steps will have impact on the cells position inside growth zone. During uploading and growth process it is important to provide and sustain "in-situ" and "after seeding" distribution of the cells inside macro-channels of the CC vessel. As cells generally continue to divide in culture, they generally grow to fill the available area or volume. The initial distribution will depend on actual geometry in which cells are introduced, uploading procedure into seeding positions, impact of the nutrition media exchange, etc. This work is focused on analysis of cell distribution during seeding into a long macro-channel of CC vessel designated for mass-production of the cells.

Use of COMSOL Multiphysics: In this work we used Laminar flow and Particle Tracing for Fluid Flow that couples Fluid-Particle Interaction under COMSOL Multiphysics® software. The transit domain of CC plate was formed by serpentine macro-channel in the 3D space. Cells were exposed to drag force, buoyancy and gravitation force during transport in the liquid medium. We assumed free flow - that is the "air-plug" was not considered in this simulation. Post-processing of the computed data extensively utilized the animation tools and particle tracing capabilities of the software and further processing of exported data into Excel helped to analyze the actual distributions of the cells.

Results: The primary question is what is "in-situ" and "after seeding" distribution of the cells inside macro-channels of the CC vessel? To provide answer to this question we modeled a single release of the cells envelope (contained 1000 cells) to have an idea about the cells transit through the channel. The simulation of the continuous release of cells, e.g. a full dose (totaling up to 10,000 cells within modeled transit domain) during uploading, provided the downstream and across channel distribution profiles inside macro-channel. The residence time and population during transit through the seeding domain were determined. The experimental results were

assessed in various locations through the CC vessel and compared with model outputs. The agreement between experimental and simulation distributions was observed.

Conclusion: Discussion of the simulation model and obtained results extends the limited space within a short abstract. However, we can conclude that with a help of the COMSOL simulation tool we were able to analyze detailed transition of the many cells through the CC vessel and to determine a final distribution inside the macro-channel. More details on model and computational conditions will be reported during conference event. These results led to the new ideas on further improvement and are currently driving towards the next generation designs of the CC vessel.

Figures used in the abstract

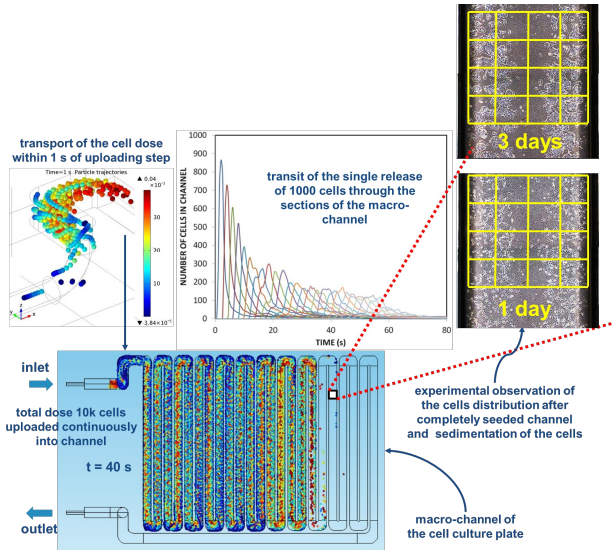

Figure 1: The illustration of the transport of the cell dose in a serpentine macro-channel (simulation output shown at instant time t = 40 s) with detailed propagation of the cell inside inlet section (top-left) and experimental observation of the cells within specific location inside channel after 1 and 3 days (top-right). Graph in the middle shows a transition of the cell envelope through the channel.

Figure 2

Figure 3

Figure 4