Seeding Distribution in the Channel of a Cell Culture Vessel

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Introduction

Conventional cell culture (CC) techniques are advancing significantly with a trend towards mass production. Cell plating density (the number of cells per volume of culture medium) is a key factor in this process. Moreover, cell initial distribution depends on the actual size and shape of the space in which cells are introduced. This work focuses on analyzing cell distribution during seeding in a serpentine channel of CC vessel.

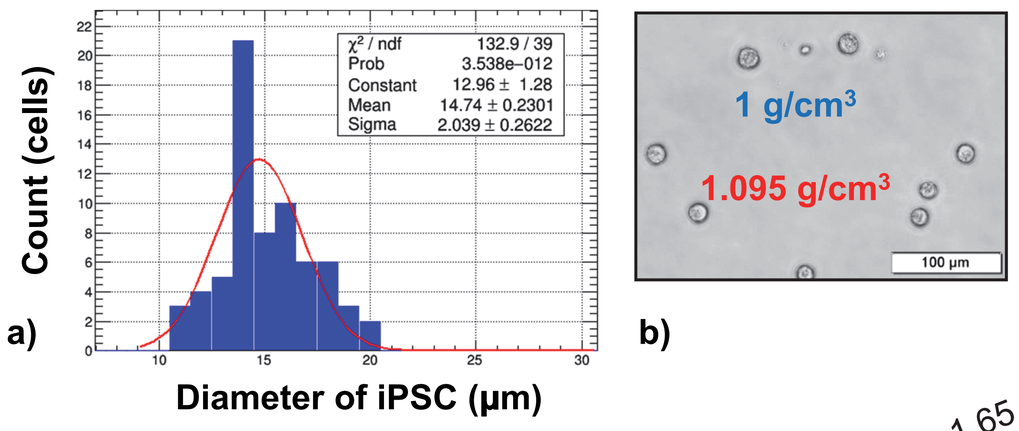

Figure 2. Typical size (a) and image (b) of the cells introduced into transporting suspension; (c) Poincaré plot in the center of the selected channels

Computational Methods

In this work we used physics interfaces Laminar flow and Particle Tracing for Fluid Flow. The transit domain of CC vessel had the shape of a serpentine fluidic channel with a 12 mm^2 square cross section. In the model a single pulse and continuous cell release mode were formulated. The free flow (no "air-plug") was considered in this simulation.

The incompressible fluid flow in the channel is governed by Navier-Stokes equations (Eqs. 1 and 2). During the seeding process, cells are exposed to a drag force, buoyancy and gravitation force and their position is tracked by Eq. 3. Post-processing of the computed data extensively utilized the animation tools and particle tracing capabilities and the actual distributions of the cells were analyzed using Excel with exported data from COMSOL.

$$\rho(\boldsymbol{u}\cdot\boldsymbol{\nabla})\boldsymbol{u} = \boldsymbol{\nabla}\cdot[-p\boldsymbol{I} + \mu(\boldsymbol{\nabla u} + (\nabla \boldsymbol{u})^T)] + \boldsymbol{F} \quad (1)$$

$$\rho\nabla\cdot(\boldsymbol{u}) = 0 \quad (2)$$

$$\frac{d(m_{cell}\boldsymbol{v}_{cell})}{dt} = \boldsymbol{F}_d + \boldsymbol{F}_g + \boldsymbol{F}_b \quad (3)$$

Here variables m_{cell}, $\mathbf{v}_{cell}$, $\mathbf{F}_d$, $\mathbf{F}_g$ and $\mathbf{F}_b$ are cell mass, velocity, drag force, gravitation and buoyancy, respectively.

Results

The highest velocity of liquid media was found to be around 4 cm/s in all sections of the serpentine channel. To seek an answer to the question *"what is in-situ and after seeding distribution of the cells inside cell culture vessel?,"* downstream cell distribution was determined from cell sediment in two cases. Case with a single instant pulse release and continuous release of the cells. A cross section distribution was estimated from cumulative densities in individual bins. Sections close to the inlet exhibited edge heavy seeding, while sections close to the outlet exhibited distribution that resemble a typical flow suspension profile. Increased uniformity was established by using air-plug.

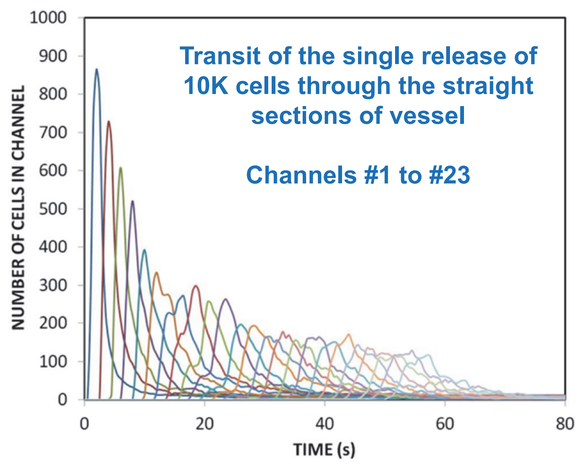

Figure 3. Downstream distribution of the single release of the cells

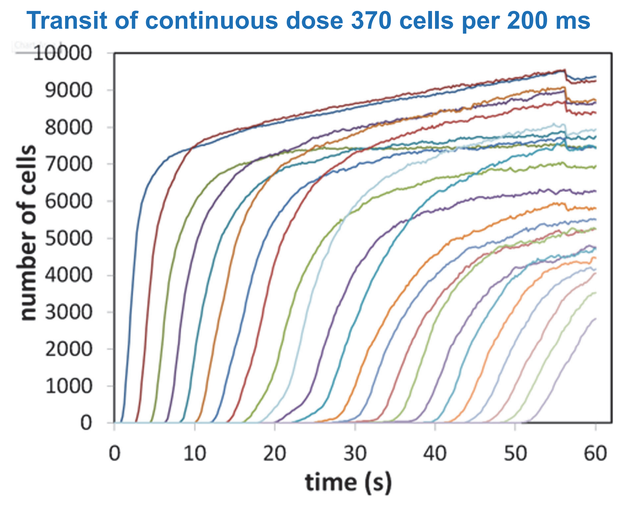

Figure 4. Downstream distribution of the continuous release of cells

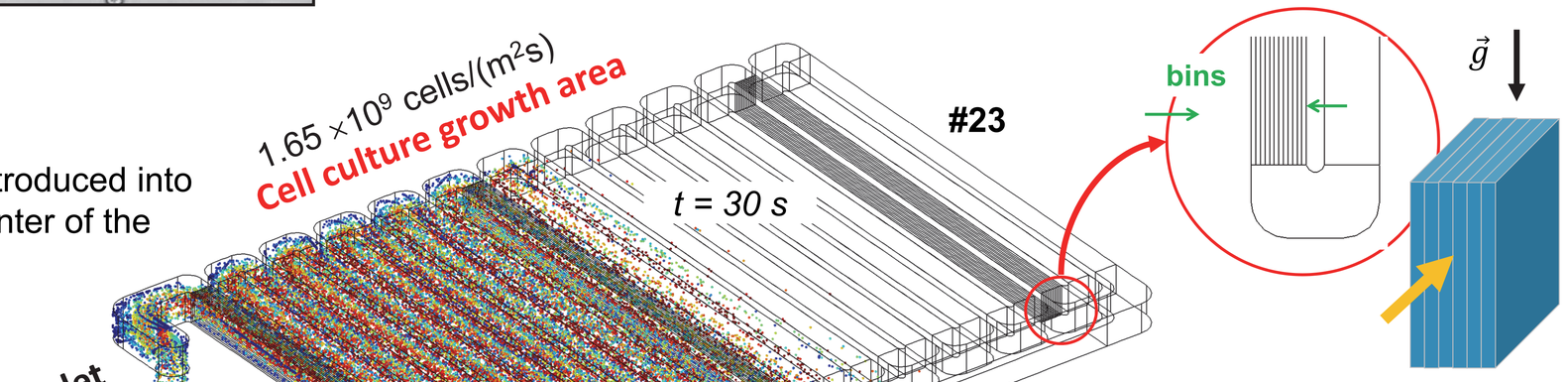

Figure 1. Cell culture vessel with serpentine channel. Some channels were split into several bins to track cross-channel distribution. Cell size is scaled 10x to visualize transition trough, the color corresponds to velocity of cells

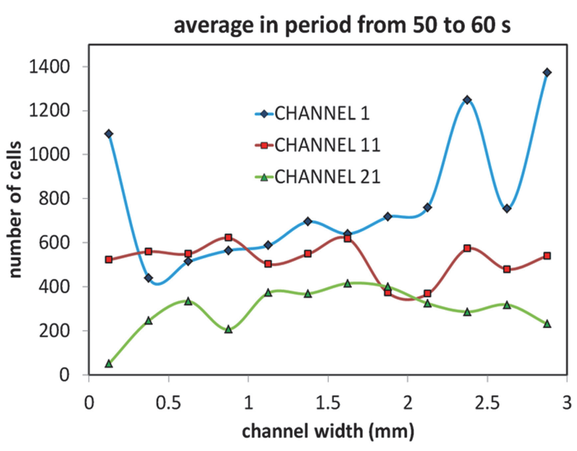

Figure 5. Cross-channel integral distribution is improved by downstream

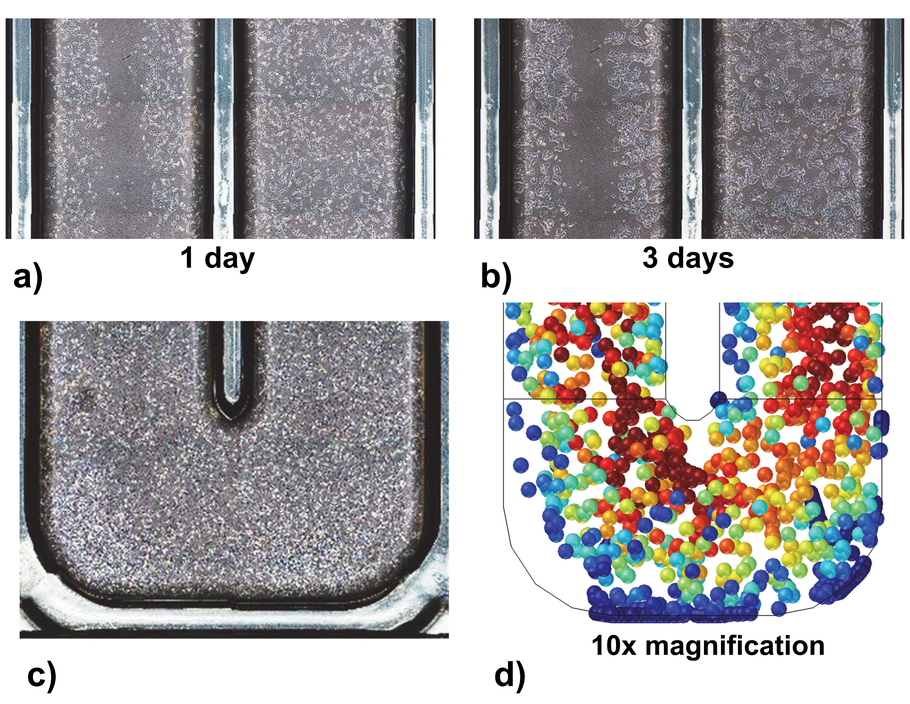

Figure 6. Experimental distribution of the cells in straight (a) and (b) and curved sections (c); (d) simulation

Conclusions

Simulation of the cell seeding distribution showed increased plating density due to boundary layer conditions in off-centerline and loop locations. Transit and sedimentation times estimated from the simulation correlated well with experimental observations. Slight compression of cells (~9%) was determined by matching a buoyance force to sedimentation time. Simulation indicated possibility towards higher yield performance of the cell culture vessel.