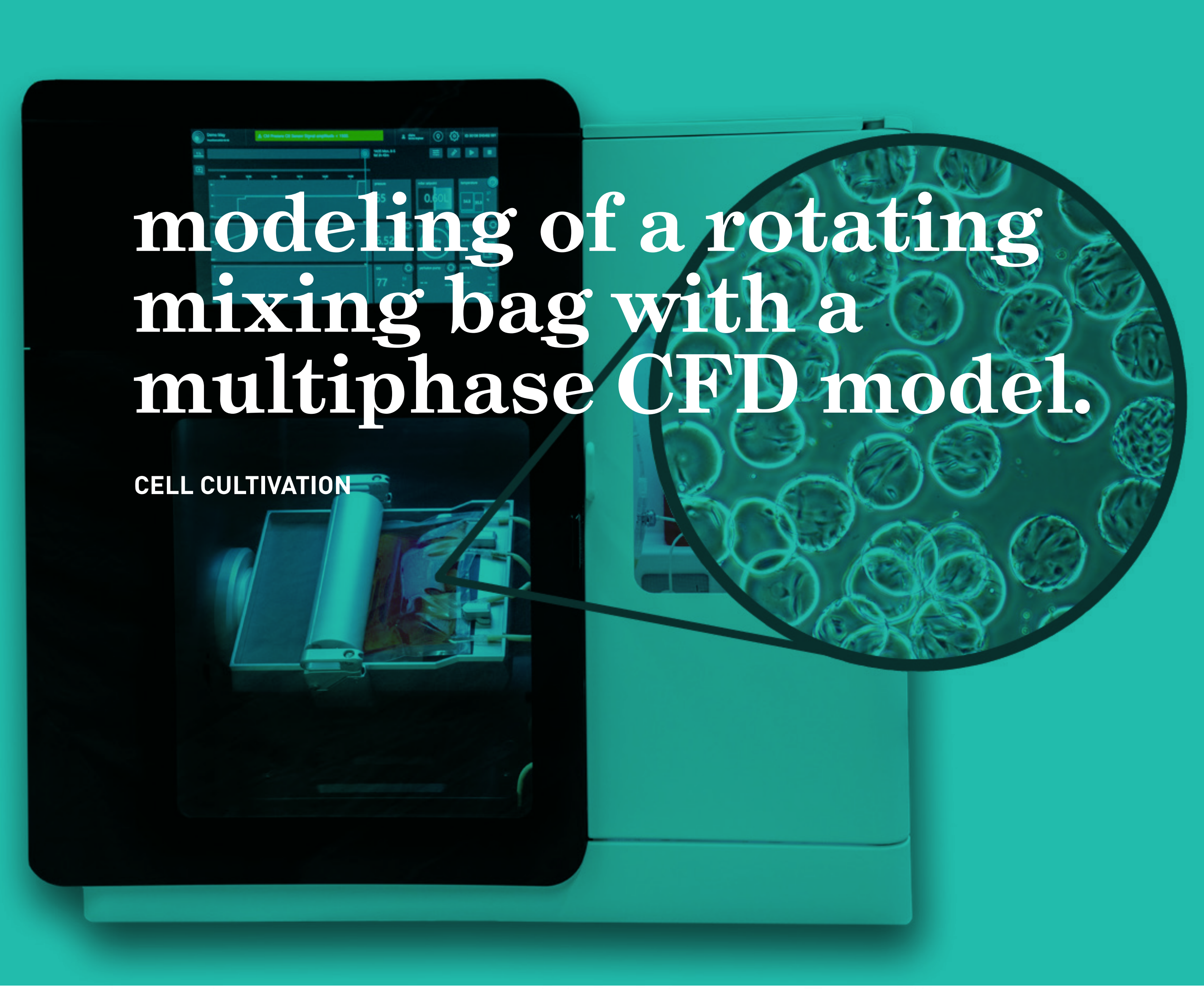

modeling of a rotating mixing bag with a multiphase CFD model.

CELL CULTIVATION

Goal

For the treatment of several diseases, different forms of cellular therapy are used. One way is to take cells from a patient's body, cultivate them and insert them back into the patient's body after sufficient growth. SCINUS Cell Expansion provides an innovative, controlled and cost-effective solution to automate cell culture processes. The SCINUS Cell Expansion system is a closed bioreactor system for the controlled cultivation of cells [1]. Inside the bioreactor, the cells are kept in suspension in a liquid solution of nutrients, allowing these cells to multiply.

As the initial amount of donor cells is limited, the efficiency of the cultivation process needs to be optimal. For optimal performance, sufficient mixing of the cells with nutrients is required. Hence, it should be prevented that the cells settle at the bottom of the bioreactor vessel. This is achieved by periodically rotating the reactor vessel which leads to circulating flow inside the vessel. The process continues until sufficient multiplication has taken place.

At Demcon multiphysics, we aided in the optimization of the mixing, by modeling the behavior of the suspension in the bioreactor and optimizing the rotating movement to achieve optimal mixing.

AUTHOR: HARMEN KREDIET
+31 (0)88 - 115 20 20
demcon.com/multiphysics

CONTACT US

DEMCON | MULTIPHYSICS

Approach

Accurate modeling of the behavior of the suspension in the bioreactor is required to optimize the cultivation process. The cells were modeled as small solid particles. The so-called mixture model [2] was selected as an appropriate multiphase model for this system. The rotation of the reactor was modeled with Ansys CFX's 'Rotating domain' option, which uses the rotational speed as function of time as input parameter.

Although the bag is 3D, the mixing behaves largely in a 2D manner, so a 2D approach was chosen. Using a sensitivity analysis, several rotational patterns were investigated to optimize the mixing behavior.

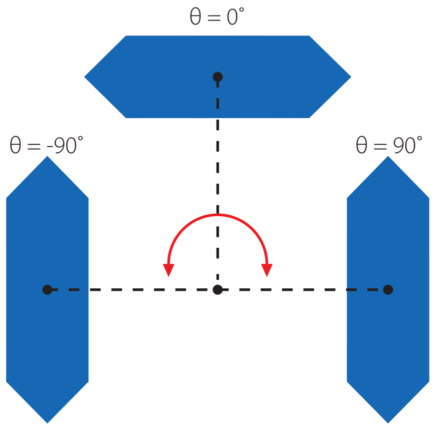

Figure 1. Rotation of the reactor vessel.

Results

Before the reactor starts rotating, there is a thin layer of cells at the bottom of the reactor. This initial solution can be considered an extreme case. When the rotation starts, gradually the cells mix more with the liquid nutrients solution (Figure 2). After a while, the mixture fraction becomes highly uniform, as seen in Figure 3.

With these simulations, we gained insight in the mixing behavior of the cells and microcarrier particles, for several rotational patterns of the bioreactor. We were able to optimize the rotational pattern such that the mixture fraction is highly uniform.

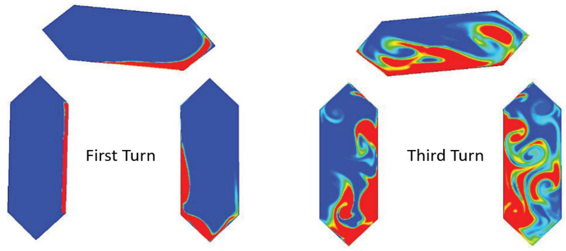

Figure 2. Volume fraction of cells (solid). Red indicates solid particles, blue indicates no particles (only liquid). After a while the volume fraction becomes more uniform, indicating that the cells are mixing with the nutrient solution.

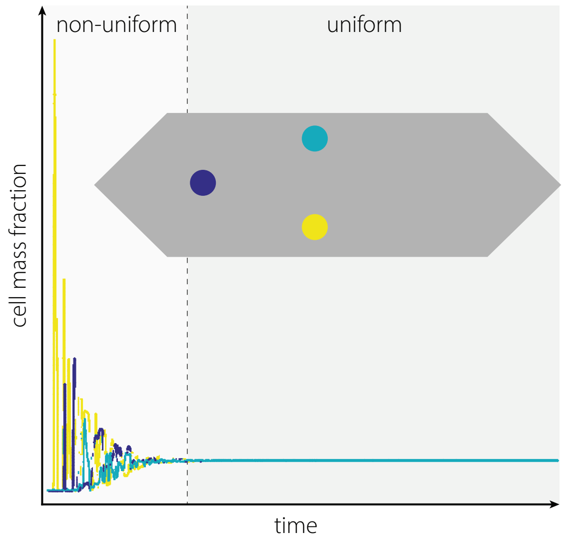

Figure 3. The cell mass fraction versus time, plotted for three different locations in the mixing bag. The cell mass fraction is the highest at the bottom of the bag (yellow) in the beginning, indicating that there is a layer of cells at the bottom of the reactor. After some time, the three lines overlap, meaning that the mixing fraction became uniform.

Bibliography

[1] SCINUS Cell Expansion System
<https://www.scinus.com/scinus-cell-expansion-technology>
[2] Manninen, M., Taivassalo, V., & Kallio, S. (1996). On the mixture model for multiphase flow. VTT Publications.