The Model of Porous Media - Complete Description for Aggregation of Bead-Monolayers in Flat Microfluidic Chambers

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ABSTRACT

In this paper we for the first time adopt the model of porous media to simulate the complete course of the formation of monolayers from bead suspensions in a flat microfluidic chamber. The chambers are flat enough to enforce monolayer formation and the beads are confined by geometrical constrictions which sieve the beads from a pressure-driven flow through the chamber. The aggregation pattern of the beads impacts the trajectory of subsequently incoming beads.

By modelling the previously aggregated beads with zones of porous media, we can drastically reduce the degrees of freedom in a two-phase, multi-particle problem. This way, we are able to compute stationary hydrodynamic flow patterns in the chamber. In an iterative master routine, these stationary solutions are taken as initial conditions for the next step. At the end of each iteration step, the aggregation pattern is extended according to the points where the newly added beads have settled down.

keywords: bead aggregation, monolayer, microfluidics, porous media, 2-phase flow

1 INTRODUCTION

Microfluidic technologies are increasingly used to miniaturize analytical instruments to so-called „labs-on-a-chip“ [1, 2, 3, 4]. Striking advantages of these lab-on-a-chip concepts are the small volume of sample and reagents as well as the increased process integration and automation on behalf of the technological backend. Bead-based assays are already a well established analytical method for multi-parameter screening of a given sample. Beads are spherical particles made of polymers or glass with diameters between a few and several hundred micrometers.

In a bead-based assay, an ensemble of beads is exposed to a liquid sample. Prior to the assay, each bead is coated with a designated biosensitive layer to detect a specific target molecule in the sample. Bead-based analytical methods are favorable in terms of ease of preparation, enhanced reaction kinetics, and the reduction of „dead surface“ of the solid substrate which normally has to be blocked to avoid unspecific binding.

The complex problem of simulating the flow of multi-particle suspensions is subject of research with different approaches [5, 6, 7]. In this paper, the hydrodynamic interaction of liquid flow with a stationary monolayer of beads is modelled by the flow through porous media [8]. Here, the hydrodynamic penetration of liquid is described by the Navier-Stokes-Equation, the Stokes law of friction (two-phase flow simulation) and Darcy's law of flow through porous media. Darcy's law provides a linear relationship between the velocity of a liquid through a porous media and the pressure gradient at laminar conditions. The local distribution of the hydrodynamic resistance of the previously accumulated beads is taken into account by a taylor-made iterative master routine implemented in JAVA.

2 AGGREGATION OF BEAD-MONOLAYERS

We have recently proposed a concept to carry out immunochemical reactions and detection inside a flat chamber where the beads aggregate in form of a monolayer [9]. In our investigations, the beads are filled into the detection chamber prior to processing a diagnostic assay (Fig. 1).

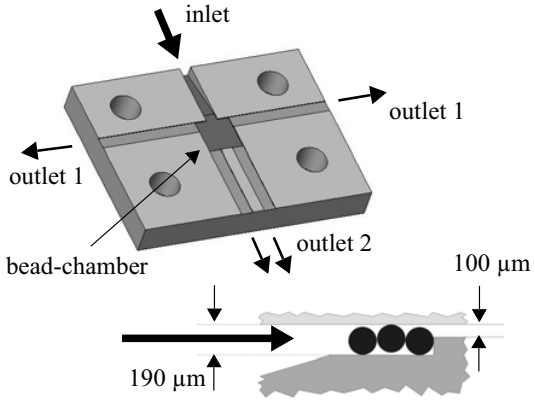

Figure 1: Schematic drawing of the microfluidic chip with the central bead aggregation chamber (dark gray) and four separate outlet channels. The cross-section shows the depth profile of the aggregation chamber and a subsequently connected outlet.

With 200 µm, the chamber depth is kept only slightly higher than the diameter of the beads (180 µm) in order to enforce the alignment into a monolayer. Since the outlets possess a depth of only 100 µm, the beads accumulate and successively fill the chamber.

3 SIMULATON OF BEAD-AGGREGATION

To our knowledge, no commercial CFD tool is currently available which is capable of simulating the hydrodynamic flow of a suspension containing numerous spatially expanded particles, taking into account all types of mechanical and hydrodynamic interaction between, particles, the walls and the liquid matrix. This way, the aggregation due to the geometrical barrier cannot be directly modeled.

All simulations were carried out with the two-phase-flow mode of FIDAP (Fluent Inc.) using the above-mentioned chamber geometry (Fig. 2). Though, the particles are implemented as point-like bodies as well, FIDAP was evaluated to be the most appropriate tool.

To simulate the movement of 40 beads in the carrier fluid, particles (e.g. beads) are generated at 40 positions which are linearly distributed throughout the entrance area of the common inlet. Generally, the simulations remain numerically stable up to an inlet pressure of typically 30 kPa. Exceeding this boundary leads to non-converging results.

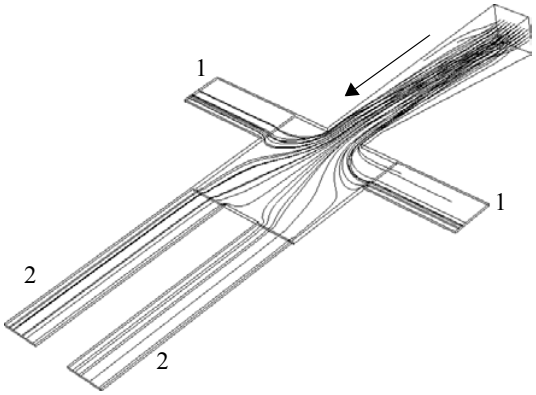

Figure 2: Simulation of the trajectories of 40 beads at an inlet pressure of 1 kPa.

4 THE MODEL OF POROUS MEDIA

Regions of previously accumulated beads elevate the local hydrodynamic resistance which must be overcome by the subsequent fluid. In the region of a porous medium, the „common“ Navier-Stokes-equation extends to

$$\rho\left[\frac{1}{\phi}\frac{\partial}{\partial t}\vec{v} + \frac{1}{\phi^2}(\vec{v}\nabla)\vec{v}\right] = -\nabla p + \eta_e\nabla^2\vec{v} + \rho\vec{g} - \left(\frac{\eta}{[K]}\vec{v} + a\rho|\vec{v}|\vec{v}\right) \quad (1)$$

whereas the additional parameters porosity ϕ, effective viscosity η_e, Forchheimer-coefficient a, and permeability $[K]$ have to be taken into account.

The porosity is defined as

$$\phi = \frac{V_{free}}{V_{total}} \quad (2)$$

and describes the fraction of the free remaining volume with respect to the total volume.

For porous media, Darcy adapted the linear relationship between a driving pressure gradient ∇p and the resulting fluid velocity $\vec{v}$ with the permeability $[K]$.

$$-\vec{F} = -\nabla p = \frac{\eta}{[K]}\vec{v} \quad (3)$$

The equation of Darcy is only valid in the laminar regime. Forchheimer extended the equation of Darcy with a term (ρv^2) in order to explain the non-linear behavior of porous media in the turbulent regime.

$$-\vec{F} = -\nabla p = \frac{\eta}{[K]}\vec{v} + a\rho|\vec{v}|\vec{v} \quad (4)$$

The Forchheimer-coefficient a is experimentally determined for different types of porous media [8]. An analytical derivation of a and $[K]$ leads to

$$a = \frac{1.75}{\sqrt{150\phi^3}} \quad \text{and} \quad K = \frac{\phi^3 d_p^2}{150(1-\phi)^2} \quad (5)\ (6)$$

For a periodical monolayer of beads with a diameter of 180 µm and quadratic aggregation pattern, the porosity and the permeability are set to $a = 0.476$ and $K = 8.5 \cdot 10^{-11}$ m².

5 EVALUATION OF THE POROUS MEDIA CONCEPT

To run CFD-simulations with porous media, FIDAP offers a model (POROUS ENTITY) where the Navier-Stokes-Equation is extended with the equations of Darcy and Forchheimer (1). However, to model monolayers of beads as porous media, we first had to evaluate the equivalent porosity of a locally aggregated monolayer of beads (2). To this end, a symmetric channel structure comprising one inlet and two outlet channels was fabricated in PMMA (Fig. 4, inset).

A series of experiments was performed involving different numbers of aggregated beads in the right-hand channel, ranging between 0 to nearly 4000, to record the ratio of the flow-rates. In this design, roughly 35 beads completely fill a row of beads.

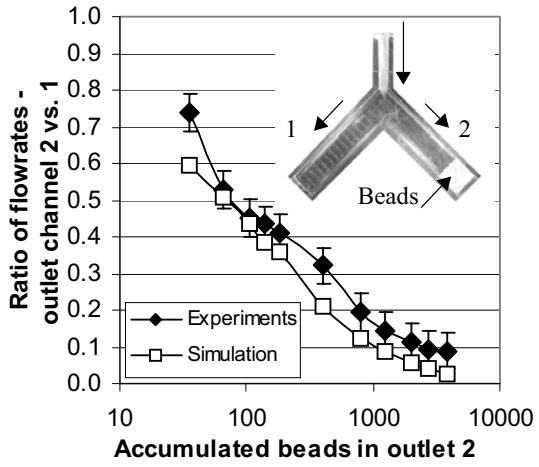

Figure 3: Impact of accumulated beads to the flow-rate: Comparison of experimental results with simulations. Inset: Symmetrical microfluidic structure, beads were accumulated in outlet channel 2 in front of the geometrical barrier.

Each experimentally detected ratio of flow-rates was subsequently fitted by simulations with the effective viscosity η_e and the internal FIDAP A-coefficient as free fit parameters. An extensive numerical fit determined the internal FIDAP A-coefficient ($A = 10^{-2}$) and the effective viscosity of the accumulated beads (η_e = 0.1 Pas) - which turns out to be roughly 100-fold higher than pure water.

6 ITERARTIVE SIMULATION OF THE FILLING

To investigate the complete filling of the aggregation chamber, the local distribution of the hydrodynamic resistance of the previously accumulated beads has to be taken into account by an iterative master routine which has been implemented in JAVA.

At the beginning of each iterative step, the spatial distribution of the porous media inside the aggregation chamber from the preceding step defines the new hydrodynamic boundary conditions (Fig. 4, a). Next, the set of particles is launched and the resulting trajectories are analyzed to pinpoint so-called „cells of observation“. These cells which are connected to the outlet or whose adjacent cells were previously switched to porous media.

In the next step, the geometrical coordinates of all bead trajectories are scanned for a point of intersection with one of the observed cells (Fig. 4, b). In case several candidates for a possible attachment are evaluated along the same trajectory, the cell of observation is chosen which represents the outermost point of the particle trajectory that is still inside the aggregation chamber. At the end of the multi-particle iteration step, all selected cells are turned into porous media.

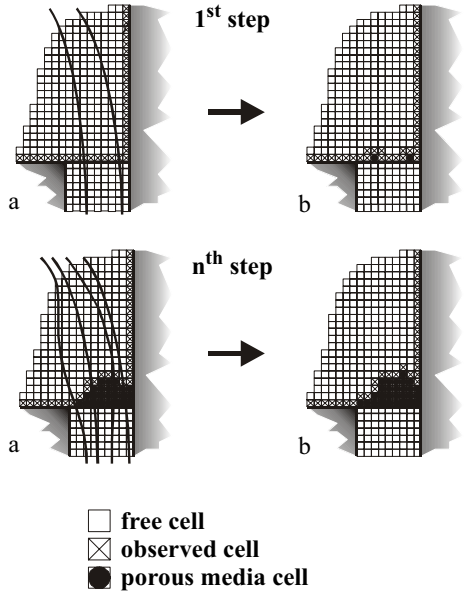

Figure 4: Concept of the master routine which analyzes the rest positions of the particles in each simulation step and, accordingly, activates porous cells as static boundary condition for the consecutive step.
a: For a given configuration of porous cells, the cells of observation are identified and activated. The points of intersection between the particle trajectory and the layer of observed cells are identified.
b: These cells are switched to porous media.

The width of the steps was typically set to 10 beads per iteration. The numerical mesh size of the aggregation chamber was set to $(200\,\mu m)^3$ which is adapted to the bead diameter of 180 µm and leads to 900 cubicles for the entire aggregation chamber.

Applying the master routine to the microfluidic design shown in Fig. 2, we found good agreement between experimental and numerical results (Fig. 5). During the initial phase of filling, the flow properties of the bead suspension are determined by the distribution of the (undisturbed) hydrodynamic resistances of the four outlets.

Ongoing, separate clusters of aggregated beads emerge. Their location and also the shape is in good qualitative agreement with the experimental observation.

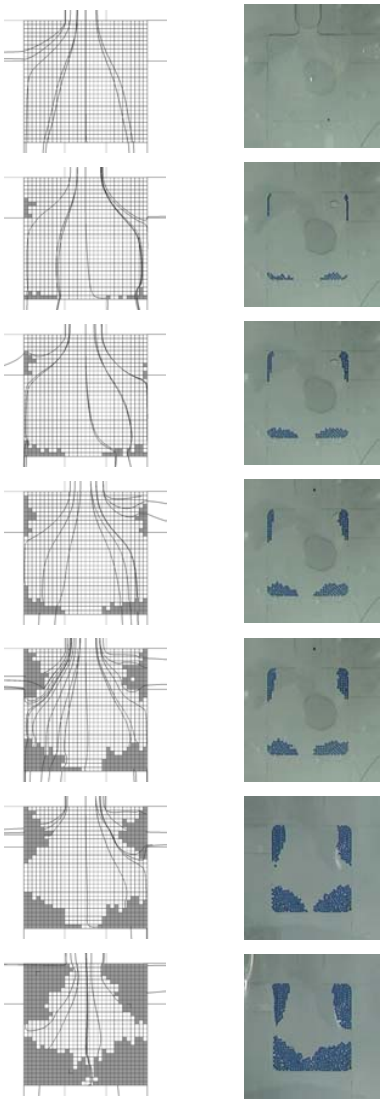

Figure 5:Complete course of filling:
Iterative two-phase-flow-simulation (left sequence). Video-frame sequence at an inlet pressure of 20 kPa (right sequence). Initially, four separate zones of aggregated beads emerge during filling. The spatial distribution of the aggregated beads is governed by the geometry of the aggregation chamber and the pattern of the previously aggregated beads.

7 CONCLUSION

Experimental and simulative investigations were carried out to demonstrate that the hydrodynamic properties of locally aggregated monolayers of beads can be modeled by porous media. The equivalent hydrodynamic resistance of aggregated beads was determined experimentally by flow rate measurements and compared to simulations of the flow through porous media.

The two phase flow simulation was used to investigate the flow properties of the beads in an aggregation chamber and to calculate their particle trajectories. The simulation results were successfully verified by experimental measurements. Initially, the spatial distribution of the aggregated beads is governed by the geometrical shape of the aggregation chamber and the local distribution of the hydrodynamic resistance. During the ongoing process of filling, the distribution of aggregated beads seeks to balance the flow rates through the upper and lower outlet channels.

Our model can be extended by an appropriate master routine to all problems involving the complex interaction between beads which are suspended in the flow and ensembles of beads which have aggregated at high particle densities at fixed positions in a microfluidic chamber. The iterative routine furthermore allows to visualize the full course of a dynamic aggregation process.

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