Computational fluid dynamics (CFD) studies of a miniaturized dissolution system

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Graphical abstract

Abstract

Dissolution testing is an important tool that has applications ranging from fundamental studies of drug-release mechanisms to quality control of the final product. The rate of release of the drug from the delivery system is known to be affected by hydrodynamics. In this study we used computational fluid dynamics to simulate and investigate the hydrodynamics in a novel miniaturized dissolution method for parenteral formulations. The dissolution method is based on a rotating disc system and uses a rotating sample reservoir which is separated from the remaining dissolution medium by a nylon screen. Sample reservoirs of two sizes were investigated (SR6 and SR8) and the hydrodynamic studies were performed at rotation rates of 100, 200 and 400 rpm.

The overall fluid flow was similar for all investigated cases, with a lateral upward spiraling motion and central downward motion in the form of a vortex through the screen. The simulations indicated that the exchange of dissolution medium between the sample reservoir and the remaining release medium was rapid for typical screens, for which almost complete
mixing would be expected to occur within less than one minute at 400 rpm. The local
hydrodynamic conditions in the sample reservoirs depended on their size; SR8 appeared to be
relatively more affected than SR6 by the resistance to liquid flow resulting from the screen.

**Keywords**

Computational fluid dynamics, miniaturized dissolution testing, drug-release mechanisms
1. Introduction

_In vitro_ dissolution testing is a crucial part of the biopharmaceutical toolkit used in the development and evaluation of drug-delivery systems (DDSs). There are various aspects to consider when applying a method that claims to be predictive of the _in vivo_ situation.

Compendial _in vitro_ dissolution methods such as the paddle and basket methods are generally used for solid oral DDSs (Kostewicz et al., 2014), whereas no standardized _in vitro_ methods exist for pharmaceutical products administered by the parenteral route (Shen and Burgess, 2015). Compendial tests use considerable amounts of release medium (500 – 1000 ml) and therefore require relatively large quantities of the DDS (Kostewicz et al., 2014). In early drug development, large quantities of the DDS are not always available; therefore, there is growing interest in miniaturized dissolution tests (Ahnfelt et al., 2015; Tsinman et al., 2009; Wang and Armenante, 2016). There is also interest in how the different components of an advanced modified-release (MR) formulation release the drug, especially when they are designed to have different release profiles for different therapeutic objectives.

Recently, two miniaturized _in vitro_ methods were compared to study the diffusion-based release of doxorubicin from microspheres: a free-flowing method and a sample reservoir method (Ahnfelt et al., 2016). In the free-flowing method, drug-releasing beads were added to a glass vial containing 20 ml of buffer solution that was agitated by a Teflon-coated magnet. The sample reservoir method was based on a rotating-disc system; the specially designed disc contained a sample reservoir that was separated from the remaining release medium by a nylon mesh filter. The disc also had two integrated wings or baffles in the lid to stir the release medium (Ahnfelt et al., 2016).

It has been suggested that hydrodynamics could affect the release rate from DDSs like the drug-releasing beads where diffusion is the rate-limiting step (McCarthy et al., 2004).
Therefore, it is essential to investigate the hydrodynamics of *in vitro* dissolution methods used for detailed study of drug release mechanisms (McCarthy et al., 2004). In recent years, hydrodynamic investigations have been conducted for both compendial methods (D’Arcy et al., 2006; Kostewicz et al., 2014; McCarthy et al., 2004) and non-compendial tests (Boetker et al., 2013; Kaunisto et al., 2009; Wang and Armenante, 2016).

The objective of this study was to use computational fluid dynamics (CFD) to simulate and investigate the fluid flow in the sample reservoir method. Specific secondary aims were to investigate the effects of the nylon mesh filter firstly on convective drug exchange between the sample reservoir and the release medium and secondly on the hydrodynamic conditions in the sample reservoir.

2. Methods

2.1 The sample reservoir method

The modified sample reservoir method described by Ahnfelt et al. (Ahnfelt et al., 2016) and simulated in this study is shown in Figure 1. The modified method used a μDiss profiler (pION, USA) with specially designed discs (diameter 22 mm), each containing an embedded magnet and a cylindrical cavity. There were two sizes of cylindrical cavity, henceforth referred to as the sample reservoirs: sample reservoir 6 (SR6) had a diameter of 6 mm, a depth of 2 mm, and a cavity volume of 57 μl; sample reservoir 8 (SR8) had a diameter of 8 mm, a depth of 1 mm and a cavity volume of 50 μl (Table 1). A nylon mesh filter (Merck Millipore Ltd, Germany), henceforth referred to as the screen, was used to retain the sample in the sample reservoir. The screen was kept in place by a plate and a lid with two integrated wings (5.5×1×2 mm). When transport across the screen is discussed, the sample reservoir will be referred to as the donor compartment and the remainder of the release medium as the acceptor.
compartment. In this study, the volume of release medium in the acceptor compartment was kept constant at 20 ml.

2.2 Simulation Model

The CFD model was set up in ANSYS Fluent (version 17.0). The realizable $k – \varepsilon$ turbulence model was adopted (Shih et al., 1995). This model provides scalar equations for $k$, the turbulence kinetic energy per unit mass, and $\varepsilon$, the rate of dissipation of turbulence kinetic energy per unit mass. These quantities are used to calculate the Reynolds stress that is needed to close the system of equations when turbulence modeling is based on the Reynolds-averaged Navier–Stokes (RANS) equations. Enhanced Wall Treatment was used (ANSYS, 2016a).

A stationary state was simulated, using a reference frame that co-rotated with the rotating disc. Hence, all walls on the rotating disc (the sample container and lid, including the wings) were stationary in this rotating reference frame. The lateral walls of the glass vial were stationary in an absolute reference frame and a symmetry boundary condition was used for the top face of the liquid (such that no axial liquid motion was possible). Since the rotating-disc system has two-fold rotational symmetry, only half the volume was simulated, using rotationally periodic boundary conditions on the remaining faces. The computational mesh consisted of about 2.2 million tetrahedral cells for SR8 (Figure 1) and about 2.1 million cells for SR6. For simplicity, the fluid was set to water-liquid at room temperature, implying that the fluid density $\rho = 0.9982 \times 10^3$ kg/m$^3$ and the dynamic viscosity $\mu = 1.003 \times 10^{-3}$ Pa·s. Simulations were performed three different rotation rates: 100, 200 and 400 rpm. Hence the rotational Reynolds number (Shevchuk, 2009),

$$Re_\omega = \frac{\rho \omega R^2}{\mu},$$

(1)
where $\omega$ is the angular velocity and $R$ is the radius of the rotating disc, ranged from about 1000 to 5000 (Table 2). These relatively high values indicated that the flow was turbulent, although turbulence was probably not fully developed.

The screen between the donor and acceptor compartments was modeled in a simplified manner by using a Porous Jump boundary condition (ANSYS, 2016b) in which the pressure drop across the screen was related to the specific fluid flux, as described in the next section.

### 2.3 Fluid permeability estimate

Convection through a porous medium, such as a screen, might generally be described by the Forchheimer equation (eq 2) (Nield and Bejan, 2013), which relates the magnitude of the pressure drop $\Delta p$ across a medium of thickness $L$ to the magnitude of the specific fluid flux (the volume of fluid that passes across the screen per unit area and unit time, also referred to as the Darcy velocity) $v$ as

$$\frac{\Delta p}{L} = \frac{\mu}{K} v + \frac{c_F}{\sqrt{K}} \rho v^2$$  \hspace{1cm} (2)

where $K$ is the permeability of the porous medium to fluid (SI unit: m$^2$) and $c_F$ is a dimensionless form-drag constant. The first term on the right-hand side of eq (2) (the Darcy term) is linear in the magnitude of the specific fluid flux $v$. The second term (the Forchheimer term) originates from inertia effects and is quadratic in $v$.

When the flow is sufficiently slow so that the Forchheimer term can be neglected in comparison with the Darcy term (this can be done for fiber Reynolds numbers up to about unity; see below), it is convenient to introduce the screen resistance $R_s$ (SI unit: m$^{-1}$) as
\[ R_s = \frac{\Delta p}{\mu v} = \frac{L}{K} \]  \hfill (3)

where the second equality follows from eq (2) when only the Darcy term is retained.

In this study, the magnitude of the pressure drop was estimated from the Brundrett (Brundrett, 1993) correlation, as summarized by Valli, et al. (Valli et al., 2009). The importance of inertia effects can be inferred from the fiber Reynolds number,

\[ Re_f = \frac{\rho v d_f}{\mu} \]  \hfill (4)

where \( d_f \) is the fiber diameter (Figure 2).

For the screens characterized and used in this study (Table 3), \( d_f \sim 10^{-4} \) m and simulations performed without any screen demonstrated that \( v \sim 10^{-2} \) m/s. Since \( \rho \sim 10^3 \) kg/m\(^3\) and \( \mu \sim 10^{-3} \) Pa \( \cdot \) s, one finds that \( Re_f \sim 1 \), indicating that the effects of inertia are not important (Valli et al., 2009). Keeping only the Darcy term in the correlation (Brundrett, 1993), the pressure drop can be expressed as (Valli et al., 2009)

\[ \Delta p = 3.5625 \times \frac{\mu v}{d_f} \times \frac{1 - \alpha^2}{\alpha^2}. \]  \hfill (5)

Hence the screen resistance becomes

\[ R_s = \frac{\Delta p}{\mu v} = \frac{3.5625}{d_f} \times \frac{1 - \alpha^2}{\alpha^2} \]  \hfill (6)

where \( \alpha \) is the screen porosity, defined as the ratio of the open area of the screen to its total area in the orthogonal projection. For a regular screen, the screen porosity can in turn be determined as

\[ \alpha = \frac{d_p^2}{(d_p + d_f)^2} \]  \hfill (7)

where \( d_p \) is the pore size (see Figure 2).
The permeability of the screen to fluids was estimated using a falling-head permeameter (see Appendix A). When a falling-head permeameter is used, the screen resistance can be expressed as (Head and Epps, 2011)

\[
\frac{1}{R_s} = \frac{K}{L} = \frac{\mu}{\rho g t} \times \frac{a}{A} \times \ln \left( \frac{h_1}{h_2} \right)
\]

where \( g \) is the acceleration due to gravity, \( t \) is the time taken for the head to decrease from \( h_1 \) to \( h_2 \) and \( A \) and \( a \) are the cross-sectional areas of the sample and the standpipe tube, respectively. The above equation assumes creeping flow, and is hence valid only when \( Re_f \) is smaller than about unity.

Table 3 summarizes values for common nylon meshes provided by Merck Millipore (Germany). For the NY11 filter, with a pore size of 11 \( \mu \)m, \( Re_f \sim 1 \) and the experimentally determined screen resistance is similar to, but somewhat larger than, the estimated resistance. No meaningful estimates were be obtained for the other pore sizes, because \( Re_f \) was significantly larger than unity.

3. Results

3.1 Qualitative description of flow

Meridional streamlines constructed from the in-plane components of the flow are depicted in Figures 3 and 4 for SR8 and SR6, respectively. The left half of each figure shows a section perpendicular to and the right half a section parallel to the wings integrated in the rotating lid. Despite variations in the geometry of the donor compartment, the rotation speed, and the resistance of the screen that separated the donor from the acceptor compartments, the overall intra-chamber flow pattern appeared similar in all cases. The in-plane components of the flow exhibited an overall circular motion with a lateral upward and a central downward fluid
direction. This behavior is consistent with that seen in prior simulations of axisymmetric flow for low to moderate values of $Re_\omega$ and/or high values of the aspect ratio $H/R$ and indicates that the flow is steady with meridional main circulation only (Iwatsu, 2005).

With increasing rotational speed, the velocity of the main meridional flow increases and the inertia of the liquid gives rise to increased curvature of the flow lines close to the corners, especially the top lateral corners. Moreover, increased screen resistance had considerable local effects on the flow pattern, leading to expulsion of flow lines from the donor compartment and, especially for SR6, recirculation in the donor compartment (see Figures 3 and 4).

Three-dimensional depictions of streamlines originating at the screen are displayed in Figures 5 and 6 for SR8 and SR6, respectively. Streamlines corresponding to an upward liquid motion are drawn in red and streamlines corresponding to a downward motion are drawn in blue to clarify the intra-chamber hydrodynamics. The qualitative flow pattern was similar for all investigated cases. The rotating disc and wings imparted a rotating motion to the liquid in the vicinity of the disc. As a result, the liquid moved radially outward from the rotating disc, resulting in an upward motion close to the cylindrical vessel boundary. Downward motion occurred in the form of a vortex that reached through the liquid down to and through the screen separating the donor compartment from the acceptor compartment (Figures 5 and 6).

As anticipated, the vortex became more developed with increasing flow rates (see Figures 5 and 6). There was a tendency for the vortex to narrow with increasing screen resistance. It should be emphasized, however, that the illustrated streamlines originated at the screen, implying that only that part of the fluid flow that reached through the screen contributed to the streamlines. In other words, with increasing screen resistance, only a relatively small part of
the downward liquid motion actually penetrated the screen. This conclusion is supported by comparison with Figures 3 and 4, which display the overall meridional flow pattern.

3.2 Quantitative description of flow

3.2.1 Fluid flux between compartments

The total fluid flux $\phi$ between compartments was calculated as

$$
\phi = \iint_{\text{screen}} v_{1\rightarrow2} \, ds = \iint_{\text{screen}} v_{2\rightarrow1} \, ds = \frac{1}{2} \iint_{\text{screen}} v \, ds,
$$

(9)

where $v_{1\rightarrow2}$ and $v_{2\rightarrow1}$ are the magnitudes of the specific fluid fluxes from compartment 1 to compartment 2 and from compartment 2 to compartment 1, respectively, and $v$ (as before) is the magnitude of the specific fluid flux, irrespective of direction. The second equality in eq (9) is a consequence of mass conservation and the factor $1/2$ is included in the last part in order to make sure that the flux is not counted twice. When the screen resistance was negligible, the fluid flux between compartments ranged from about 75 to about 225 $\mu l/s$ for SR8 and from about 45 to about 135 $\mu l/s$ for SR6 when the rotation rate increased from 100 to 400 rpm (Figure 7). As anticipated from the diameters of the sample reservoirs, $\phi$ was thus generally higher for SR8 than for SR6 (diameters of 8 and 6 mm). The effects of a finite screen resistance started to appear at a value of about $10^{-3} \mu m^{-1}$ irrespective of geometry and rotation rate. For screens with greater resistance, a considerable reduction in fluid flux between compartments was predicted.

Assuming that convective transport across the screen is the rate-limiting step of drug release, a well-stirred two-compartment model can be used to estimate the exchange of drug between the two compartments. For an initial condition corresponding to a concentration $C_0$ of drug in
the donor compartment and zero concentration in the acceptor compartment, such a model would suggest that deviations from the equilibrium drug concentration $C_\infty$ (obtained after a sufficient duration) decay exponentially with time $t$ (see Appendix B):

$$\frac{C_1(t) - C_\infty}{C_0 - C_\infty} = \frac{C_\infty - C_2(t)}{C_\infty} = e^{-t/\tau}$$

(10)

Here, $C_1(t)$ and $C_2(t)$ are the concentrations in the donor and acceptor compartments, respectively, at time $t$,

$$\tau = \frac{V_1 V_2}{V_1 + V_2} \times \frac{1}{\phi}$$

(11)

is a characteristic mixing time, such that deviations from the final drug concentration $C_\infty$ decrease by a factor $e^{-1} \approx 0.37$ (where $e$ is the base of the natural logarithm) over a time lapse of $\tau$. As seen, $\tau$ is inversely proportional to $\phi$ and also depends on the volumes of the donor and acceptor compartments ($V_1$ and $V_2$, respectively).

As seen in Figure 8, characteristic mixing times below 1 s were obtained for SR8 when the screen resistance was negligible. The mixing times were about 0.67, 0.37, and 0.22 s for rotation rates of 100, 200, and 400 rpm, respectively. For SR6, the corresponding mixing times were somewhat higher but remained relatively small. They were about 1.27, 0.70, and 0.42 s for rotation rates of 100, 200, and 400 rpm, respectively. The characteristic mixing time mirrored the flux and, thus, the effects of a finite screen resistance started to appear at a value of approximately $10^{-3}\mu m^{-1}$, irrespective of compartment geometry and rotation rate. For a screen resistance of 1 $\mu m^{-1}$, which appears to be a fairly realistic value, the characteristic mixing time ranged from 15 to 1.5 s for SR8 and from 49 to 5.7 s for SR6 when the rotation rate increased from 100 to 400 rpm. Using previously determined experimental data (Ahnfelt et al., 2016) obtained for an NY80 nylon mesh with an estimated screen resistance of about
0.4 \mu m^{-1} (Table 3), the characteristic mixing time was estimated as 7.0 ± 3.0 s (mean value ± standard deviation for three independent measurements) for SR6 at a rotation rate of 400 rpm. It can be noted that the characteristic mixing time extracted from the simulations (Fig. 8) compares favourably with the experimental results.

3.2.2 Hydrodynamic conditions in the sample reservoir

The magnitude of the volume-averaged velocity can be used as a measure of the local hydrodynamic conditions in the sample reservoir (donor compartment). Since all walls of the sample reservoir, including the screen, rotated with the same angular velocity, it made sense to calculate the volume-averaged velocity in a reference frame that rotated with the sample reservoir. The results of this calculation are displayed in Figure 9. As can clearly be seen, the movement was faster in SR8 than in SR6 for low screen resistances at any given rotation rate. The effects the hydrodynamic conditions in the sample reservoir of a finite screen resistance started to appear at a value of about $10^{-3}\mu m^{-1}$ irrespective of geometry and rotation rate, as for the fluid flux between compartments (and hence the characteristic mixing time).

Moreover, in relative terms, SR8 appeared to be more affected than SR6 by a finite screen resistance.

4. Discussion

In their study, Ahnfelt et al. (Ahnfelt et al., 2016) applied a one-phase association equation to describe the release kinetics of doxorubicin from drug-releasing beads, using both the free-flowing and the sample-reservoir methods. For the latter method, an NY80 nylon mesh with an estimated screen resistance of about 0.4 \mu m^{-1} was used (Table 3). It was found that the sample reservoir generated slower release rates than the free-flowing method, but that these correlated better with in vivo release data. Moreover, for small (70 – 150 \mu m) and
intermediate (100 – 300 µm) bead sizes, the release rate at 400 rpm was considerably slower for SR6 than for SR8, whereas the release rates were comparable for large beads (300 – 500 µm). Despite the differences in experimental setup, all the release rates $k_{rel}$ were in the order of 1 h$^{-1}$. Since $1/k_{rel} \gg \tau$ (remember that the predicted characteristic mixing time $\tau$ was less than 10 s at 400 rpm), these values indicate that the effects of a limited fluid flux between the donor and acceptor compartments should be negligible. This conclusion is corroborated by experimental results presented by Ahnfelt et al., (Ahnfelt et al., 2016) which also suggest that complete mixing between the compartments would occur within about one minute at 400 rpm, in good agreement with the theoretical predictions.

The simulations in this study indicated that differences in hydrodynamic conditions would be expected between SR8 and SR6, especially for low screen resistances (compare, for example, Figures 9A and B). This appears to be the most likely reason for the lower release rates observed for SR6 than for SR8 for the small (70 – 150 µm) and intermediate (100 – 300 µm) sized beads. It should be noted, however, that the simulations in this study were carried out with empty sample reservoirs and that the presence of drug-releasing beads would probably influence the intra-compartmental hydrodynamics somewhat. In addition, differing packing or confinement patterns of the beads would probably affect the drug release rate (Carugo et al., 2015). It is also worth noting that the balance between the inertia and drag forces on the beads will be size-dependent, which in the Stokes equation would result in a settling velocity that is proportional to the size squared (Harker et al., 2002). In general, large DDSs (e.g., large beads) would tend to be more aligned with the outer boundary of the sample reservoir, where they would follow the rotation at that point. Small DDSs (e.g., small beads) would be expected to follow the liquid flow to a greater extent, resulting accordingly in a more dynamic situation. However, the critical size for the transition is difficult to pinpoint, since it depends
not only on the local liquid flow around the DDS but also on the difference in density between the DDS and the dissolution medium (Harker et al., 2002). This could explain the differences in the release rate of doxorubicin between SR6 and SR8 for the small (release rate was 0.35 h\(^{-1}\) for SR6 and 0.88 h\(^{-1}\) for SR8) and intermediate-sized (release rate was 0.32 h\(^{-1}\) for SR6 and 1.3 h\(^{-1}\) for SR8) beads but not for the large beads (release rate was 0.87 h\(^{-1}\) for SR6 and 0.82 h\(^{-1}\) for SR8).

5. Conclusions

The simulated flow and hydrodynamics of liquids in equipment used in the sample reservoir method, a recently proposed miniaturized \textit{in vitro} method for assessing parenteral formulations, have been investigated using CFD. Based on the visual inspection of two- and three-dimensional flow lines, it can be concluded that flow is steady with meridional main circulation only. Parametric studies coupled with mathematical modeling revealed that the exchange of dissolution media between the sample reservoir and the acceptor compartment would be rapid for typical screens, and that almost complete mixing could be expected within less than one minute. Qualitative inspection of flow lines and quantitative estimation of the liquid velocity in the sample reservoir indicated that the hydrodynamic conditions differed between the differently sized sample reservoirs (SR8 and SR6). It is suggested that these differences in hydrodynamic conditions, when coupled with the effects of confinement of the drug-releasing beads and the size-dependent balance between the inertia and drag forces, give rise to the previously observed differences in the release rate of doxorubicin from the beads between the two sample reservoirs.

6. Acknowledgments
Financial support was provided by the Swedish Research Council, grant number 521-2011-373.
Appendix A: Falling-head permeameter

A custom-made falling-head permeameter was used to measure the permeability of the NY11 screen to liquids. The screen (the sample) was mounted on a 15-ml vial with the tip sawn off, which was connected to a graduated 50-ml measuring cylinder (the standpipe tube) as illustrated in Figure A1. The screen and the standpipe tube both had circular cross sections, with respective cross-sectional areas of $A = \pi D^2 / 4$ and $a = \pi d^2 / 4$. Here, $D$ and $d$ are the diameters of the screen and the standpipe tube, respectively.

![Figure A1: Schematic illustration of the custom-made falling-head permeameter.](image-url)
Appendix B: Well stirred two-compartment model

Assuming that convective transport across the screen is the rate-limiting step, a well stirred two-compartment model can be used to estimate the exchange of drug between the compartments. When the drug concentration is uniform in each compartment, conservation of mass requires that

\[ V_1 \frac{dC_1}{dt} = -\phi C_1 + \phi C_2 \]  \hspace{1cm} (B1)

\[ V_2 \frac{dC_2}{dt} = +\phi C_1 - \phi C_2 \]  \hspace{1cm} (B2)

where \( C_1 \) and \( C_2 \) are the concentrations in the donor and acceptor compartments, respectively, \( V_1 \) and \( V_2 \) are the corresponding volumes and \( \phi \) is the flux between the compartments defined by eq (9) in the main text. The initial conditions are

\[ C_1(0) = C_0 \]  \hspace{1cm} (B3)

\[ C_2(0) = 0 \]  \hspace{1cm} (B4)

When the characteristic mixing time \( \tau \) is defined according to eq (11) in the main text and the final concentration \( C_\infty \) is defined as follows:

\[ C_\infty = \frac{V_1}{V_1 + V_2} \times C_0 \]  \hspace{1cm} (B5)

the solution can be written

\[ C_1(t) = C_\infty + (C_0 - C_\infty) e^{-t/\tau} \]  \hspace{1cm} (B6)

\[ C_2(t) = C_\infty (1 - e^{-t/\tau}) \]  \hspace{1cm} (B7)

Eqs (B6) and (B7) can be rephrased as eq (10) in the main text which shows that the deviations from the final concentration \( C_\infty \) decay exponentially with a characteristic time \( \tau \).
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Figures

Figure 1. (Left) Dimensions of the disc and glass vial used. All dimensions in mm. (Middle) Illustration of the setup used for the sample reservoir method. (Right) The computational mesh used for the numerical simulations. All drawn for SR8.
**Figure 2.** An example of a nylon mesh microscopic picture (5x) (left) and a schematic illustration of the definition of the pore ($d_p$) and the fiber ($d_f$) sizes for regular screens (right).
Figure 3. Meridional streamlines obtained for SR8 at the indicated rotation rates and screen resistances. The left half of each picture shows a section perpendicular to and the right half a section parallel to the wings integrated in the rotating lid.
Figure 4. Meridional streamlines obtained for SR6 at the indicated rotation rates and screen resistances. The left half of each picture shows a section perpendicular to and the right half a section parallel to the wings integrated in the rotating lid.
**Figure 5.** Three-dimensional depiction of streamlines obtained for SR8, coloured according to their vertical velocity (red for upward and blue for downward motion) at the indicated rotation rates and screen resistances.
Figure 6. Three-dimensional depiction of streamlines obtained for SR6, coloured according to their vertical velocity (red for upward and blue for downward motion) at the indicated rotation rates and screen resistances.
Figure 7. Fluid flux between the donor and acceptor compartments as a function of screen resistance for SR8 (A) and SR6 (B) at the indicated rotation rates.
Figure 8. Characteristic mixing time as a function of screen resistance for SR8 (A) and SR6 (B) at the indicated rotation rates.
Figure 9. Volume-averaged velocity in the sample reservoir in a co-rotating reference frame for SR8 (A) and SR6 (B) at the indicated rotation rates.
Tables

Table 1. Characteristics of the modified sample reservoir method.

<table>
<thead>
<tr>
<th>Denomination</th>
<th>$V_1$ (ml)</th>
<th>$V_2$ (ml)</th>
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<tbody>
<tr>
<td>SR8</td>
<td>0.0503</td>
<td>20</td>
</tr>
<tr>
<td>SR6</td>
<td>0.0565</td>
<td>20</td>
</tr>
</tbody>
</table>

$V_1$, volume of sample reservoir, $V_2$, volume of release medium, SR8 and SR6, 8-mm and 6-mm sample reservoir.

Table 2. Reynolds numbers for the simulated rotation rates.

<table>
<thead>
<tr>
<th>Rotation rate (rpm)</th>
<th>$Re_\omega$ (–)</th>
</tr>
</thead>
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<tr>
<td>100</td>
<td>1260</td>
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<tr>
<td>200</td>
<td>2520</td>
</tr>
<tr>
<td>400</td>
<td>5040</td>
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$Re_\omega$, rotational Reynolds number

Table 3. Screen characteristics.

<table>
<thead>
<tr>
<th>Type</th>
<th>$d_p$ (μm) $^a$</th>
<th>$\alpha$ (%) $^a$</th>
<th>$d_f$ (μm) $^b$</th>
<th>$R_s$ (μm$^{-1}$) $^b$</th>
<th>$R_s$ (μm$^{-1}$) $^c$</th>
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</thead>
<tbody>
<tr>
<td>NY11</td>
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<td>34</td>
<td>29.08</td>
<td>38.6</td>
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<tr>
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<td>41</td>
<td>34</td>
<td>0.52</td>
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<tr>
<td>NY80</td>
<td>80</td>
<td>41</td>
<td>45</td>
<td>0.39</td>
<td>NA</td>
</tr>
</tbody>
</table>

$^a$ From specifications
$^b$ Calculated
$^c$ Measured
NA: Not applicable