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A microscale pulsatile flow device for dynamic cross-slot rheometry

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A B S T R A C T
The design of micropumps received full attention since micromanufacturing and microfluidics techniques have become part of the engineering toolbox. The focus of most studies has been on the efficiency of these pumps: maximal net (mean) flow at minimal input power.

We introduce a pulsatile micropump system, that is designed to dynamically perfuse a cross-slot micro-rheometer. To characterize complex materials dynamically, unsteady (oscillating and pulsating) flows with a frequency range of 0.1–20Hz at amplitudes of 10–100 nl/s are required. Hence, in our study the priority concerning micropumps shifts from efficiency to the ability to produce well-defined flow pulses.

For this purpose, an oscillatory micropump, based on a deflecting diaphragm, is designed and tested. By periodically deflecting a steel plate into a rigid fluidic chamber using a voice coil, an oscillatory flow is produced. Plate deflection is governed by bending, such that the stroke volume is proportional to the current through the voice coil. The oscillatory flow is superimposed to the steady flow of a syringe pump. The pump system obtained is characterized by micro particle image velocimetry (μ-PIV) measurements using fluorescence microscopy.

The results show that the superposition of the mean flow of the syringe pump and an oscillatory flow of the diaphragm pump, is valid. A linear scaling of flow amplitude with frequency and driving voltage is found for frequencies up to 4 Hz, after which excessive damping takes place. The causes for this behavior are identified and explain the results well. With this information, amplitude scaling for sinusoidal flow waves of different frequencies can be performed. In conclusion, with the present system, pulsatile flow with a well-defined waveform and a dynamic range up to 16 Hz, can be created in an open-loop driven fashion.

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1. Introduction
The last 30 years, various micromachining techniques were introduced, which opened the field of MEMS and microfluidics. The need to displace fluids at small scale followed, which resulted in the design and evaluation of dozens of microscale pumps (for extensive reviews, see [1–7]). In displacement micropumps, a moving boundary or liquid displacement exerts a pressure force, while dynamic micropumps rely on a direct energy transfer to the fluid to be pumped. The former usually generate pulsatile flow, the latter drive the fluid in a continuous, constant manner [3]. The focus here is on diaphragm displacement micropumps, where a solid diaphragm is deflected into a valve chamber to push fluid forward.

These pumps can be equipped with passive check valves with moving parts (flaps [8] or balls [9,10]), or non-moving valves (e.g. Tesla microvalve [11]), or be valveless (nozzle-diffuser design [12,13], vortex areas [14]).

Actuation is performed in several ways, among which piezoelectric [15–18] and electromagnetic or voice coil actuators [9,12,15,19] are most popular. Often, the pump is integrated with a fluidic system, ranging from lab-on-a-chip [20] or micro-total-analysis systems (μ-FACS, -ELISA or -mass-spectrometer [21]) to miniaturized fossil fuel cell batteries [22].

During characterization of these pumps, the focus has been on the efficiency and absolute net flow: how can a maximal net flow be produced with a minimal amount of power input. However, for some applications, such as the culturing of endothelial cells in a microfluidic channel, the periodic pulsatility is of interest, whereas efficiency is of secondary importance. Another application

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is experimental characterization of dispersion-induced boundary layer mixing, demanding two well-controlled pulsatile flows in counter-phase [23].

In this work, the device is designed to be applied to the dynamical probing of red blood cell mechanics. To extend the cross-slot principle towards a micro-rheometry setup, the inflow of the device should be made pulsatile (non-zero mean flow) with well-controlled period and amplitude, such that frequency-dependent behavior of the red blood cell under investigation can be characterized. Concerning the red blood cell membrane, which has (relaxation) time constants of 0.15–0.5 s, a pump that drives pulsatile flows with a frequency of about 20 Hz, and amplitudes down to 10 nL/s, is required. It is also essential that the waveform of the flow is purely sinusoidal, such that the cell can be probed at a single frequency. Although literature concerning micropumps is abundant, to our knowledge no data of instantaneous flows (i.e. waveforms) at these scales have been published.

State-of-the-art syringe pumps could not deliver sinusoidal pulsatile flows via the programming function (Harvard PHD 2000, Harvard Apparatus) or the command line option (Nexus 3000, Che- myx). Hence, a pulsatile micropump system is needed, with which the flow waveform is well-controlled and easily tunable. To our knowledge, such a device is neither commercially available, nor reported about in literature.

Altogether, our goal is to design a pump system, which produces pulsatile flows that are well-controlled in terms of amplitude, frequency, and pulse shape. In the rest of this paper, a motivation for the specific design is given, in which the flow is produced in an open-loop driven way. During the design phase, aspects concerning geometry, system dynamics, and fluid actuation, are taken into account.

Next, to assess the quality of the waveforms the microscale flows are measured with high temporal resolution, using micro particle image velocimetry (μ-PIV). Third, the results of steady, oscillatory, and pulsatile flow are presented, as well as passive and active noise responses. This should demonstrate the behavior of the pump system, as well as its capabilities. The dynamic behavior of the system can be explained by discussing different physical phenomena. These insights can be used to gain full control over the flow waveform.

### 2. Materials and methods

#### 2.1. Pump system design

The exact computation of impedance in oscillatory microflow is not straightforward [28]. However, we assumed that our system is linear and time invariant (LTI system), such that a pulsatile flow can be generated using a syringe pump and a reciprocal diaphragm pump in series: according to the superposition principle the constant and oscillating flow are summed [29]. This has successfully been applied in larger linear hydraulic systems [30].

The produced pulsatile flow of the pump system equals the stroke volume per unit of time: \( Q_{\text{pulse}} = Q_{\text{syringe}} + \lim_{\Delta t \to 0} \Delta V_{\text{stroke}} / \Delta t \). The required flows impose restrictions to the geometry and dimensions of the pump (Fig. 2a). The maximum flow amplitude is dependent on the pulse frequency. When the mean flow \( \bar{Q} = 100 \text{ nL}/\text{s} \), and the minimum in the pulse lies at zero, the necessary stroke volume \( V_{\text{stroke}} = \bar{Q} = 1/2 \pi f \). This implies that a frequency of 0.1 Hz demands a volume displacement of 159 nL. On the other hand, at higher frequencies and low amplitudes, the necessary stroke volume is reduced and noise suppression becomes more important.

To be in the right range of frequencies and flows, an axisymmetric valve chamber (radius \( a = 6.5 \text{ mm} \), height \( H_e = 2 \text{ mm} \)) holds a circular plate with a thickness of \( h = 200 \mu\text{m} \). An O-ring between the diaphragm and the lid of the pump, which is fully compressed to make steel-to-steel contract, ensures sealing of the chamber.

<table>
<thead>
<tr>
<th>symbol</th>
<th>description, unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>( A )</td>
<td>transfer function gain, ( - )</td>
</tr>
<tr>
<td>( a )</td>
<td>diaphragm radius, m</td>
</tr>
<tr>
<td>( a_t )</td>
<td>connecting tube radius, m</td>
</tr>
<tr>
<td>( C )</td>
<td>compliance, ( \text{m}^4 \text{s}^2 \text{kg}^{-1} )</td>
</tr>
<tr>
<td>( C_{\text{sat}} )</td>
<td>compl. saturated fluid, ( \text{m}^4 \text{s}^2 \text{kg}^{-1} )</td>
</tr>
<tr>
<td>( D )</td>
<td>plate constant, m</td>
</tr>
<tr>
<td>( D_H )</td>
<td>hydraulic diameter, m</td>
</tr>
<tr>
<td>( E )</td>
<td>Young’s modulus, ( \text{Pa} )</td>
</tr>
<tr>
<td>( F_L )</td>
<td>Lorentz force, N</td>
</tr>
<tr>
<td>( f )</td>
<td>flow frequency, Hz</td>
</tr>
<tr>
<td>( f_0 )</td>
<td>natural frequency, Hz</td>
</tr>
<tr>
<td>( f_c )</td>
<td>cutoff frequency, Hz</td>
</tr>
<tr>
<td>( f_{\text{res}} )</td>
<td>resonance frequency, Hz</td>
</tr>
<tr>
<td>( H )</td>
<td>channel height, m</td>
</tr>
<tr>
<td>( H_e )</td>
<td>height pump chamber, m</td>
</tr>
<tr>
<td>( h )</td>
<td>diaphragm thickness, m</td>
</tr>
<tr>
<td>( I )</td>
<td>inerter, kg m (^{-2})</td>
</tr>
<tr>
<td>( I_e )</td>
<td>inerter, kg m (^{-4})</td>
</tr>
<tr>
<td>( k )</td>
<td>diaphr. spring constant, N m (^{-1})</td>
</tr>
<tr>
<td>( L )</td>
<td>tube length, m</td>
</tr>
<tr>
<td>( L_t )</td>
<td>tube length, m</td>
</tr>
<tr>
<td>( M )</td>
<td>equivalent mass, kg</td>
</tr>
<tr>
<td>( p_{1,2} )</td>
<td>transfer function poles, ( - )</td>
</tr>
<tr>
<td>( Q )</td>
<td>mean flow, ( \text{m}^3 \text{s}^{-1} )</td>
</tr>
<tr>
<td>( Q_{1,2} )</td>
<td>outflow of cross-slot, ( \text{m}^3 \text{s}^{-1} )</td>
</tr>
<tr>
<td>( Q_{\text{out}} )</td>
<td>systemic outflow, ( \text{m}^3 \text{s}^{-1} )</td>
</tr>
<tr>
<td>( Q_{\text{pulse}} )</td>
<td>pulsatile flow, ( \text{m}^3 \text{s}^{-1} )</td>
</tr>
<tr>
<td>( Q_{\text{syringe}} )</td>
<td>syringe pump flow, ( \text{m}^3 \text{s}^{-1} )</td>
</tr>
<tr>
<td>( R_{(1,2)} )</td>
<td>radial coordinate diaphr., m</td>
</tr>
<tr>
<td>( R_{\text{max}} )</td>
<td>(max.) Reynolds number, ( - )</td>
</tr>
<tr>
<td>( r )</td>
<td>piston radius, m</td>
</tr>
<tr>
<td>( s )</td>
<td>Laplace parameter, ( - )</td>
</tr>
<tr>
<td>( V_{\text{max}} )</td>
<td>maximum velocity, ( \text{ms}^{-1} )</td>
</tr>
<tr>
<td>( W )</td>
<td>channel width, m</td>
</tr>
<tr>
<td>( y(r) )</td>
<td>diaphragm deflection, m</td>
</tr>
<tr>
<td>( \alpha )</td>
<td>Womersley number, ( - )</td>
</tr>
<tr>
<td>( \Delta V_{\text{stroke}} )</td>
<td>stroke volume, ( \text{m}^3 )</td>
</tr>
<tr>
<td>( \zeta )</td>
<td>damping constant, ( - )</td>
</tr>
<tr>
<td>( \nu )</td>
<td>kinematic viscosity, ( \text{m}^2 \text{s}^{-1} )</td>
</tr>
<tr>
<td>( \nu_p )</td>
<td>Poisson ratio, ( - )</td>
</tr>
<tr>
<td>( \rho )</td>
<td>fluid density, ( \text{kg} \text{m}^{-3} )</td>
</tr>
<tr>
<td>( \omega )</td>
<td>angular velocity, rad s (^{-1})</td>
</tr>
<tr>
<td>( \omega_n )</td>
<td>natural frequency, rad s (^{-1})</td>
</tr>
</tbody>
</table>
Moreover, by using a bending elastic plate in combination with the O-ring seal, hysteresis, stick-slip, and compliance are largely avoided, whereas accurate plate position control is straightforward (see Section 2.1.2).

2.1.1. Dynamics

Concerning pulsatile flow, frequency-dependent behavior is crucial for creating well-defined flow pulses. Any compliance in the system in combination with the large hydraulic resistances of the narrow channels downstream of the pump, will act as a low-pass filter such that higher frequencies are damped more. To avoid compliance, setup components are made rigid by fabricating them out of stainless steel: a circular stainless steel plate is periodically deflected into a rigid fluidic chamber, where plate deformation is fully elastic.

The impedance of the diaphragm pump, including tubing, is schematically given in Fig. 2c. The inertia forces on the fluid play a significant role at higher frequencies in these microfluidic circuits [31]. As the Reynolds number, Re, that is the ratio between steady inertia and viscous forces, is small (Re = ρaxVmax/ν = 0.05, with Vmax, the maximum mean velocity, ax the tube radius, and ν the kinematic viscosity), steady inertia forces can be neglected. However, the Womersley number α, that relates the unsteady inertia forces to the viscous forces, is larger than 1: α = ax · ν/2π = 3.5, where ω is the radial velocity. Consequently, unsteady inertia is significant. The inerterance I, which can be seen as the pressure difference that is required to change the flow in time [32], is highest in the connector tubing, and is given by

\[ I = \frac{\rho L}{\pi a_x^2} = 7.9 \times 10^4 \text{ kg m}^{-4} \text{ s} \]  

(1)

Here ρ is the fluid density and L the tube length.

The main contributor to the hydraulic resistance, R, is the resistance of the rectangular glass duct of width W and height H, where the velocity measurements are performed, see Section 2.2.1. The value of R is given by [33]

\[ R = \frac{12 \mu L}{WH^2} \left[ 1 - \frac{H}{W} \left( \frac{192}{\pi^5} \sum_{n=1}^{\infty} \frac{1}{n^5} \tanh \left( \frac{n\pi W}{2H} \right) \right) \right]^{-1} \]

(2)

where μ is the dynamic viscosity and L is the channel length.

2.1.2. Liquid actuation

A choice for closed-loop flow control can be made, such that a difference between the reference flow (desired flow) and the actual flow is corrected for by a sensor-actuator system. However, flow control on a microscale level is not trivial, as sensors and actuators need to be more sensitive than in macroscopic systems. On the scale of nl/s, it is not straightforward to measure the flow with sufficient sensitivity without influencing the flow itself. Moreover,
corrections demand for a fast and accurate actuator (ms and <nl/s, respectively).

A simpler approach is taken here, where an open-loop system is designed, built, and calibrated. Plate deflection is always governed by pure bending mechanics when the following criteria are met [34]: the plate is flat in the non-deflected state, deflection is less than half the plate thickness h, and the thickness is less than a quarter of radius a. Furthermore, all forces on the plate must work on it in normal direction, resulting in deformations that are within the linear elastic limit. The design of the present diaphragm pump fulfills these demands as the maximal deflection \( y_{\text{max}} = 0.62 \mu\text{m} \) at 0.9 N (current of 1.3 A). Hence, the deflection and stroke volume are proportional to the force exerted on the plate. Considering that the plate is fully clamped at its circumference and the force is exerted on a small concentric disk with radius \( r_0 \) (Fig. 2b), the deflection \( y \) over the radius \( r \) is given by [34]

\[
y(r) = F_l \frac{a^2}{16TD} \left( 1 - \left( \frac{r}{a} \right)^2 \left( 1 - \ln \left( \frac{r}{a} \right)^2 \right) \right)
\]

in which \( F_l \) the total force to the plate and \( D \) the plate constant given by

\[
D = \frac{Eh^3}{12(1 - \nu^2)}
\]

where \( E \) is the Young’s modulus and \( \nu \) the Poisson’s ratio. The stroke volume can simply be found by computing the integral of revolution of Eq. (3).

A linear voice coil actuator is used (LVCM013-013-02, Moticon), exerting a force proportional to the current through the coil. When using a current source, pump actuation is run in open-loop: coil self-induction is canceled. Moreover, the counter-electromotive force is negligible, as the displacements are in the order of a micron. In that way, a linear scaling between driving signal (voltage) and fluid displacement is achieved.

2.2. Measurement setup

A model, built with the real-time workshop of Matlab Simulink, runs at 10 kHz on a quad core desktop computer to drive the actuator and log electronic data. The pulsating signal for the pump is sent over Ethernet to an Ethercat D/A converter (Beckhoff EL3102). This signal passes a 1st order low-pass filter (cut-off frequency, \( f_c = 36 \) Hz) to filter out electronic background noise, before it goes to the current driver (TU/e DACS, inhouse manufactured). The filtered signal, as well as the camera trigger signal, which is used to synchronize flow and driving signal, are logged (A/D converter, Beckhoff EL4132).

2.2.1. Flow visualization

A steady flow is produced by a syringe pump (Harvard PHD2000, USA), using a 250 \( \mu \text{l} \) gas-tight glass syringe (Hamilton). The diaphragm pump is connected with PE tubing (1.6 mm OD, 0.7 mm ID), where a stainless steel narrowing is placed near the entrance to create extra impedance. From the exit of the diaphragm pump, the fluid flows towards a rectangular glass tube (inner dimensions: 2 mm \( \times \) 0.1 mm), in which the flow measurements take place. The fluid is seeded with 1.0 \( \mu \text{m} \) diameter fluorescent polystyrene beads (FluoSpheres 505/515, Invitrogen). Bead patterns are assessed using a fluorescence microscope (Zeiss M200, 63 x NA 0.75 LD objective), equipped with a high speed video camera (Phantom V9, vision-research). This combination ensures a high enough spatial and temporal resolution (setting of 512 Hz is used here), and sufficient light sensitivity (exposure time of 300 \( \mu \text{s} \)). The maximal depth for imaging using fluorescence microscopy is limited, such that the camera focus is set just above the plane of symmetry of the glass tube, at 33 \( \mu \text{m} \) depth. From the bead patterns velocity fields are determined using particle image velocimetry (PIV), as described below.

2.2.2. Micro-PIV analysis

Before the PIV analysis can be performed, the recorded out-of-plane fluorescence signal, that lowers the image contrast, must be removed. Out-of-focus particles appear as blurred, larger disks, that move slower or faster, caused by the velocity gradient in the channel. High-pass filtering in the frequency domain (FFT-algorithm in ImageJ, cutoff of 10 pixels) partly removes out-of-focus bead images, which are further suppressed by thresholding. Filtered images are divided into smaller interrogation areas of 128 \( \times \) 128 pixels (75% overlap), which are cross-correlated over consecutive time steps with GIPVtools [35]; for PIV fundamentals, see [36,37].

As numerous outliers are present in the velocity fields, especially because of the poor lighting conditions, a spatial data validation procedure has to be performed. First, extreme outliers are removed by thresholding with the maximum measurable velocity. Next, peaks lying outside one standard deviation from the mean velocity of the vector field are removed. Last, the velocity fields are subjected to the normalized local median test [38], with a radius of 3 pixels and a threshold of 0.2. Eventually, assuming uniformity of the measured velocity field, the vectors per time step are averaged and scaled to a flow using the syringe pump flow settings.

2.3. Pump characterization

Steady and oscillatory velocity measurements are performed to calibrate the open-loop response. The steady flows, that are known a priori as they are set by the syringe pump, can be used to convert the uniform velocity fields to a flow. Subsequently, these results are used to create pulsatile flows, in which the minimum is near zero. During both oscillatory and pulsatile flow experiments, measurements at different amplitudes (\( V_{\text{pp,m}} = 0.25–1.00 \) V) and frequencies (1–16 Hz) have been performed. The quality of the measured flow is determined by a signal-to-noise ratio (SNR), which is defined as the signal magnitude (amplitude of the main frequency component) divided by the sum of the other significant frequency peaks in the spectrum. By registering the trigger and filtered electronic signal, magnitude and phase shift information has been obtained, which can be visualized in Bode diagrams. Passive and active noise measurements are performed to evaluate background noise and the open-loop frequency response function. Furthermore, extra insights into the systems behavior are obtained by performing frequency-dependent deflection measurements on the bare plate with a laser triangulation distance meter (LK-H1W, Keyence). Last, results of some special cases, being non-sinusoidal flows, are given to demonstrate the versatility of this pump system.

3. Results

3.1. Steady flow

Table 1 displays the fluid velocities, measured with PIV, of 3 different steady flows, which make up a total of 22 measurements. 257 images are shot during 1 s, from which 256 velocity fields are determined, which are proportional to the flow set on the

<table>
<thead>
<tr>
<th>Syringe pump flow</th>
<th>Mean velocity</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.3 nl/s (n = 10)</td>
<td>47.7 ( \mu \text{m/s} )</td>
<td>4.7 ( \mu \text{m/s} )</td>
</tr>
<tr>
<td>50.0 nl/s (n = 4)</td>
<td>70.4 ( \mu \text{m/s} )</td>
<td>10.7 ( \mu \text{m/s} )</td>
</tr>
<tr>
<td>66.7 nl/s (n = 8)</td>
<td>97.8 ( \mu \text{m/s} )</td>
<td>8.6 ( \mu \text{m/s} )</td>
</tr>
</tbody>
</table>
3.2. Oscillatory flow

In Fig. 3a and c, two oscillatory flow measurements of 2 and 16 Hz, respectively, are shown. Their frequency spectra in Fig. 3b and d show, next to the ground frequency peak, concentrations of energy around specific frequencies: higher harmonics are clearly present in most cases. The velocity amplitude in the oscillatory flow experiments shows a linear scaling with the applied voltage, as shown in Fig. 3e. On the contrary, the relation between amplitude and frequency is linear only up to 4 Hz, after which leveling occurs (Fig. 3f). The error bars represent the spread where the number of measurements \( n = 3 \). The mean amplitude and the mean SNR are given in Table 2. The flows of the measurements at the lowest voltage amplitude and lowest frequency have the lowest flow amplitude and the lowest SNR (\( \approx 12 \)). On the other hand, the higher flow amplitude measurements are less troubled by noise (SNR \( \approx 20 \)).

3.3. Pulsatile flow

The fluid velocity, and corresponding frequency spectrum of two pulsatile flow experiments are shown in Fig. 4a and b, respectively. Here, also the syringe pump is switched on, which contributes to a more noisy flow than in case of the oscillatory experiments. Higher harmonics are again distinguishable from the noisy spectrum.

3.4. Noise measurements

The result of a velocity background noise measurement, in which the fluid should be at rest, is shown in Fig. 5. Looking at the frequency magnitude spectrum, some significant concentrations of noise are found at certain frequencies (112, 81, 186, 10 Hz, from highest to lowest magnitude). However, magnitudes are low enough to have insignificant influence on the flows under consideration, which typically have a velocity magnitude of 50–200 \( \mu \text{m/s} \).

The fluid velocity response on the applied band-limited white noise (0–5 kHz) is represented by the gray graphs in Fig. 6. The black dots in Fig. 6b are the results from all oscillatory experiments, which lie on top of the noise plot. Error bars are included,
but are hardly visible because of their small value. All voltages per frequency tested are normalized and subsequently averaged, permitted by the linear scaling of fluid velocities with driving voltage, observed in Fig. 3e. The frequency-dependent relationship between the measured fluid velocity and the applied actuator input voltage is given by the following transfer function, clarified in Section 4:

\[
\frac{v_{\text{fluid}}(s)}{V_{\text{act}}(s)} = \frac{A s^2}{s^2 + 2\xi \omega_n s + \omega_n^2} \frac{1}{s + p_1} \frac{1}{s + p_2},
\]

where \(A\) is the amplitude scaling and \(-p_2\) is the location of the stable pole of the electronic filter.

The first order subsystem with pole \(-p_2\) comes from a hydrodynamic effect (see Section 4). \(\omega_n\) and \(\xi\) are the natural frequency and damping constant of the system, respectively, which are typically present in a linear 2nd order system as in Fig. 2c. The transfer function is represented by the black curve in Fig. 6b and fits the experimental data up to a frequency of about 500 rad/s (80 Hz).

### 3.5 More complex flow cases

The results of flow experiments that have a more complex frequency spectrum, are shown in Fig. 7b–d. To compare, a sinusoidal oscillatory flow is shown in Fig. 7a. In case of the square wave flow (Fig. 7b), a relatively long rise time and an overdamped response is observed. Also shown are the time derivatives of the driving signals, synchronized with the measurements, which stand for the velocity of the pump diaphragm (proportional to the stroke volume). The phase shifts between fluid velocity and driving voltage are clearly visible.

### 4. Discussion

We introduced a pump system design for dynamic cross-slot rheometry, based on a diaphragm reciprocal pump, which is capable of producing microscale pulsatile flows with well-defined flow waves. Pulses with nonzero mean flow with frequencies of 0.1–20 Hz and amplitudes of 10–100 nl/s can be obtained, where the pulse shape is controllable. Linearity and time-invariance of the pump system is confirmed from the a fit of the oscillatory flow and frequency sweep measurements with a linear transfer function. This implies that the superposition principle is valid here and, hence, pulsatile flows can be produced by adding the oscillatory flows of the diaphragm pump to steady flows of the syringe pump. The pulsatile flow measurements confirm this.

Furthermore, particle image velocimetry appears to be a suitable method for microfluidic flow assessment. By making use of a high speed video camera and a continuous light source in combination with fluorescent beads, sufficient temporal resolution is obtained to characterize the present microfluidic pulsatile pump system.

The measured velocities in stationary flow experiments are proportional to the applied flow, as expected. Concerning the cases of oscillatory flow, a linear scaling of the amplitude with frequency was expected over the entire frequency range, which was rather low in this research. However, at flow frequencies of 8 and 16 Hz...

---

**Table 2**

Summary of the mean amplitudes and SNRs of the oscillatory flow experiments, averaged over 3 measurements (n = 3).

<table>
<thead>
<tr>
<th>Voltage (V)</th>
<th>0.25 V</th>
<th>0.50 V</th>
<th>0.75 V</th>
<th>1.00 V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency (Hz)</td>
<td>Mean ampl.</td>
<td>SNR</td>
<td>Mean ampl.</td>
<td>SNR</td>
</tr>
<tr>
<td>1 Hz</td>
<td>15.0 µm/s</td>
<td>11.4</td>
<td>30.7 µm/s</td>
<td>20.2</td>
</tr>
<tr>
<td>2 Hz</td>
<td>25.6 µm/s</td>
<td>13.2</td>
<td>57.1 µm/s</td>
<td>20.3</td>
</tr>
<tr>
<td>4 Hz</td>
<td>44.6 µm/s</td>
<td>27.6</td>
<td>100.9 µm/s</td>
<td>16.7</td>
</tr>
<tr>
<td>8 Hz</td>
<td>53.4 µm/s</td>
<td>28.5</td>
<td>123.8 µm/s</td>
<td>23.7</td>
</tr>
<tr>
<td>16 Hz</td>
<td>51.6 µm/s</td>
<td>13.2</td>
<td>112.1 µm/s</td>
<td>22.6</td>
</tr>
</tbody>
</table>

**Fig. 4.** In (a), the time domain results of two pulsatile flow experiments with a pulse frequency of 4 Hz, and a mean flow of 33 (black curve) and 67 nl/s (gray dashed curve) are shown. The minimum velocity in the pulses is almost zero when actuation voltages of 0.25 and 0.50 V are used for the 33 and 67 nl/s mean flow, respectively. In (b), the frequency spectra of both measurements are shown.

**Fig. 5.** Passive noise measurement with the diaphragm under a light prestress (0.2 V). Flow is oscillating around zero, with most important frequency component at 112 Hz. Additionally, a significant amount of energy is focused between 81 and 186 Hz, and some around 101 Hz. These components are also present when the actuator is offline, from which can be concluded that these are mechanical vibrations always present in the system.
(Fig. 3f) damping is observed. This behavior is consistent with the active noise response plot of Fig. 6a, which is found to resemble flow graphs in literature, e.g. Fig. 10 in [10]. Physical phenomena concerning this damping in these kind of microfluidic devices have been identified. First, the dominant effect is the system impedance of the hydraulics (pump chamber, tubing, and other channels), that can be described as the lumped parameter model of Fig. 2c. Second, hydrodynamic effects involved in oscillatory flow, like Womersley velocity profiles, influence local velocity measurements, when the unsteady inertia forces become comparable to the viscous forces, which is the case at 8 Hz and higher.

Below, these phenomena are considered one by one: the contribution of each effect on the frequency response function (see Eq. (5)) is determined by modeling the phenomenon under consideration and quantifying the model parameters. Hence, a priori known physics concerning this problem lead to the eventual fit of the model to the oscillatory flow data and the active white noise response in Fig. 6b. The transfer function zero (first term of Eq. (5)) is caused by the fact that the flow scales with the velocity of the diaphragm, implying \( Q = \frac{dV_{\text{stroke}}}{dt} = A \cdot \frac{dV_{\text{input}}}{dt} \). This derivative gives a transfer function zero at \( s = 0 \), multiplied by gain \( A \).

When the influence of the fluid is neglected, the diaphragm dynamics are described by a mass-spring system: \( \ddot{y} = k/M \), where \( y \) is the central deflection of the plate. The spring constant, \( k \), of the plate is high \( (k = Eh^2/0.217a^2 = 1.66 \times 10^5 \text{ N/m} [16]) \), and the equivalent mass, \( M \), would be the mass of the membrane and actuator body \( (7.8 \text{ g in total}) \). The expected natural frequency would be \( f_0 = \sqrt{k/M/(2\pi)} = 734 \text{ Hz} \). In accordance, the 'dry' deflection measurement in air using a laser triangulation meter gives a resonance frequency \( f_{\text{res}} = 714 \text{ Hz} \). However, from literature it is well known that the unsteady inertia forces greatly reduce the natural frequency of the pump [16,31].

The impedance of the pump system, which to a large extent determine its frequency response, can be modeled by the resistance–inertance–capacitance (RIC) circuit from Fig. 2c [11].

The RIC circuit translates into a second order transfer function in the Laplace domain with two complex poles [39], which forms the second term in Eq. (5). The natural frequency \( \omega_n \) is \( \frac{1}{\sqrt{RC}} \), and the damping constant \( \zeta \) is \( \frac{2}{\sqrt{RC}} \). As the dimensions of the channels, that play a significant role, are known, the values for \( I \) and \( R \) are calculated using Eqs. (1) and (2), respectively. The compliance component has two contributors, namely the membrane and the air present in the pump chamber’s fluid [11]. As the pump chamber and the membrane are thick components of stainless steel, the pumps compliance is negligible. However, the air present in the

![Fig. 6](image)

**Fig. 6.** (a) The frequency spectrum of the active noise measurement. In (b), a Bode diagram of the same data is displayed in gray. The black dots are the data points taken from the oscillatory flow experiments, which are per frequency averaged over all voltages. The black curve is the fitted transfer function of Eq. (5).

![Fig. 7](image)

**Fig. 7.** Plots of four different fluid velocity waves: (a) oscillatory sinusoidal flow, (b) square wave flow, (c) triangular flow, (d) flow as a result of a physiological blood pressure curve as input. The time derivative of the input signals are shown in gray.
Fig. 8. The midline velocity of the velocity profile, normalized to the viscosity dominated case (Poiseuille flow), for two different imaging depths (50 μm, which is the plane of symmetry of the channel, and 33 μm where the measurements are performed). The Womersley number is defined as \( \alpha = \omega H / \nu \), in which \( \nu \) is the kinematic viscosity and \( H \) represents the channel hydraulic diameter, defined by \( H = \frac{4W}{\pi} \). The increase in amplitude damping as well as the phase lag is observed for higher Womersley numbers when (a) and (b) are compared, where the Womersley number is 1 (6 Hz) and 2 (64 Hz), respectively.

fluid turned out to be determinant in the systemic compliance. The exact value for \( C \) is unknown, and therefore, \( C \) is one of the fitting parameters in Eq. (5), together with the magnitude gain, \( A \). The fitted compliance is \( 7.1 \times 10^{-14} \text{kg}^{-1} \text{m}^4 \text{s}^{-2} \), which is of the same order of magnitude as the estimated compliance of a pump chamber volume of water fully saturated with air: \( C_{\text{sys}} = 4.3 \times 10^{-13} \text{kg}^{-1} \text{m}^4 \text{s}^{-2} \) (see Eq. 8 in [11]).

The pole of the 3rd term of Eq. (5) is determined by the passive low-pass filter in the electronics. The Laplace representation of this first order subsystem contains a stable pole, which lies at \(-p_1 = -72\pi \) \((f_c = 36 \text{ Hz})\), whereas the filter DC gain, obtained by measurements, is 0.68 and is part of the total magnitude gain, \( A \), from above.

A phenomenon that partly explains the dynamic behavior at higher frequencies, is the presence of inertia induced alterations of the assumed Poiseuille profile (Womersley profiles). In these high aspect ratio channels (\( W/H = 20 \)), a parabolic velocity profile only exists in the height direction, while the profile is plug-like on the long side of the slit (for the equations of the slit velocity profiles in 3D, see [41]). By taking the hydraulic diameter, which is defined as \( WH(1 + H) \), a first order approximation for the velocity gradients near the walls at \(-1/2W\) and \(1/2W\) is obtained. Dependent on the Womersley number, the velocity profile changes [41]: the core of the flow will be more dominated by unsteady inertia forces, causing a lower maximal velocity and a phase lag in the measurement volume. In the case of a flow oscillating at 16 Hz, the Womersley number in the measurement channel, \( \alpha \), is about 1, such that the velocity profile has undergone a significant change, displayed by the centerline velocity shown in Fig. 8. This behavior can quite well be represented by a first order damped system in the frequency range investigated here resulting in a stable pole located at \(-p_2 = -134\) in Eq. (5).

The transfer function Eq. (5) fits the experimental oscillatory measurements, including the phase shift between driving signal and the measured flows, and explains the sudden damping of the measurements at 8 and 16 Hz (Fig. 6b). It also follows the active noise response quite well to about 500 rad/s (80 Hz). Now that this relation between velocity magnitude and frequency is known, one can compensate for the non-proportionalities in the input–output scaling, provided that the system is linear. Pulsatile flow experiments, where the oscillatory flow is added to a steady flow, show validity of the superposition principle, which indicates that the system is indeed linear. Under this condition, amplitude corrections at different frequencies of sinusoidal flows can be performed. To extend the linear relation of the sinusoidal flow amplitude and frequency to higher frequencies than tested here, more attention should be given to the design of the complete system. As discussed, the system impedance is determined by inertia, resistance, and compliance, which are all non-negligible in this range of oscillatory flows [11]. Therefore, for better performance, diffuser/nozzle configurations, pump chamber, and connection channels should be redesigned, using correct modeling of the impedance [28]. Concerning the compliance, all hydraulic parts should be as stiff as possible, but more importantly, thorough degassing of the working fluid should be performed in a vacuum oven. Taken together, this should result in a higher natural frequency and lower damping constant, implying a larger bandwidth in which the pump system can operate.

5. Conclusion

A pump system, connecting a syringe pump and reciprocal diaphragm pump in series, is designed to produce well-controlled pulsed flows, in terms of amplitude, frequency, and pulse shape. This is achieved by constructing an open-loop driven diaphragm pump, actuated by a voice coil. Diaphragm deflection is governed purely by bending mechanics, such that the displaced fluid volume is proportional to the current through the voice coil. With \( \mu \)-PIV analyses of bead image patterns, captured in a fluorescence microscope, the generated fluid velocity fields in time are determined. By scaling the velocity values with the velocity magnitude, obtained during steady flow experiments, in which the flow is known, the instantaneous flow is determined. Pulsatile flows, obtained by adding an oscillatory flow to a steady flow of a syringe pump, show the validity of the superposition principle for this system. Oscillatory flow measurements, together with the frequency response on a white noise input measurement, show substantial damping. To a larger extent this damping can be described by including physical phenomena occurring in the system, the main ones being the correct impedance with inertance and compliance, a first order low-pass behavior for the electronic filter, and the occurrence of Womersley velocity profiles in the measurement volume. Assuming the system is linear and time invariant, this enables scaling of the input signal, such that sinusoidal flow pulses with a well-controlled amplitude can be achieved accurately in an open-loop sense. The dynamic range can be increased by taking the total systemic impedance into account in the design phase when the pump is integrated into microfluidic devices. The device tested here is suitable to perfuse the cross-slot microrheometer with pulsatile flows.

References

at the Aeronautics department. He experimentally investigated the influence of different gas flows on the breakup of a supersonic liquid jet. During his Master Thesis, René conducted experimental and numerical work, serving risk-of-rupture assessment of intracranial aneurysms, using particle image velocimetry in phantoms and videodensitometry on angiograms.

In 2009 he started his Ph.D. in the group of Cardiovascular Biomechanics under Prof. Frans van de Vosse. He has worked on a miniaturized cross-slot rheometer, aiming at the characterization of the dynamics of the red blood cell. The pump presented here is built to perfuse this microfluidic rheometer.

Currently, René van der Burgt is working as a technical project leader at SolarTec BV, a developer and producer of ultrafast spatial atomic layer deposition machinery for the photovoltaic wafer industry. There, his interests in microfluidics, (thermo-)fluid mechanics, dynamics control systems, and mechatronics are met by new challenges.

Patrick Anderson is professor in structure and rheology of complex fluids. He studied Applied Mathematics at the Eindhoven University of Technology with Prof. Dr. Arnold A. Beukers as his advisor. In 1999 he received his Ph.D. degree from the Department of Mechanical Engineering at the same university with Prof. dr. ir. Han E.H. Meijer as his advisor. Following a year break at Océ Technologies he joined the Polymer Technology group.

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In 2008 he received the International Polymer Processing society Morand Lamba award.

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In 1995, he joined Philips Research Laboratories in Eindhoven, The Netherlands. He worked on a wide variety of applications such as optical storage systems, RF MEMS, biomedical devices, polymer MEMS, immersion lithography and microfluidics. In 2008, he became Chief Technologist, leading the R&D programs on (micro-)fluidics and materials science and engineering. Next to his main job at Philips, he was a part-time professor of Microfluidics Technology at Eindhoven University of Technology between 2004 and 2013. In 2013, Jaap den Toonder was appointed full-time professor and chair of Microsystems in the Department of Mechanical Engineering at Eindhoven University of Technology (TU/e).

His current main research interests are microfluidics, out-of-cleanroom microfabrication technologies, mechanical properties of biological cells and tissues, nature-inspired micro-actuators, and organs on chips.

Frans van de Vosse is professor of Cardiovascular Biomechanics. From 1976 to 1982 he studied Applied Physics at Eindhoven University of Technology (TU/e). He earned his Ph.D. degree from the same university in 1987. His Ph.D. research was focused on the numerical analysis of carotid artery flow. From 1987 to 2001 he was lecturer in fluid mechanics with the Materials Technology group in the department of Mechanical Engineering (W, TU/e). In 2001 he was appointed at the department of Biomedical engineering (BMT, TU/e). His current research interests are related to the computational and experimental biomechanical analysis of the cardiovascular system and its application to clinical diagnosis and intervention, cardiovascular prostheses, extra corporeal systems and medical devices.