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Normally-closed peristaltic micropump with re-usable actuator and disposable fluidic chip

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ABSTRACT

We present a new peristaltic micropump offering three key features: (i) a disposable pump body and a re-useable actuator unit, (ii) an intrinsic normally-closed mechanism blocking unintended liquid flows up to a pressure of 100 kPa and (iii) a backpressure independent pump performance up to 40 kPa. The modular concept basing on a re-usable actuator unit and a low-cost disposable microfluidic chip enables an easy and cost-efficient exchange of all contaminated parts after use, which addresses especially the needs in the health care sector. The intrinsic normally-closed feature blocks liquid flow in both directions up to a pressure difference of 100 kPa when the electric power is off. The micropump is actuated in a peristaltic manner by three piezostack actuators. Up to a frequency of 15 Hz the pump rate increases linearly with operation frequency leading to a pump rate of 120 μL/min. This was proved for an operation voltage of 140 V by pumping water. In addition the pump rate is independent on backpressure up to 40 kPa and shows a linear decrease for higher pressure differences. The maximum achievable backpressure at zero flow rate was extrapolated to be 180 kPa. As for all peristaltic micropumps, the pump is bidirectional, e.g. the pump direction can be changed forward to reverse mode.

1. Introduction

Increasing cost pressure in aging societies is one of the biggest challenges in the health care industry. One trend to cut down costs is to reduce hospitalization time per patient. Consequently, more and more ambulant (i.e. "out of hospital") types of therapies are required. For drug delivery for example, ambulatory infusion pumps are used to medicate people in their every day surrounding.

For a high level of security and flexibility, these pumps should offer the following features: (i) *portability* (i.e. small size and energy consumption), (ii) *free flow prevention* ("normally-closed") when the electric power is off, (iii) *modular setup* (i.e. re-usable actuation unit and disposable microfluidic part for cost-efficient exchange of contaminated parts), (iv) *high precision*, (v) *robust* liquid propulsion (e.g. backpressure independent pump performance) and (vi) a *high flexibility* in terms of flow rates and flow rate profiles. Hardly any portable pumping system exists, that meets all the requirements listed above so far. The micropump presented in the following is designed to meet these challenges and should enable ambulant medication with a high level of precision and security in the future.

Although, many micropumps have been published, the aspect of normally-closed performance was barely considered, compared to the hundreds of different micropumps and actuation concepts published in the last two decades [1–3]. This is very astonishing, because the normally-closed feature itself was already recognized to be important by Esashi et al. [4] in the early days of micropump development in 1989. They presented a piezostack actuated normally-closed valve and demonstrated the possibility to use a serial connection of two of those valves with a pressure chamber in between, also driven by a piezostack actuator, as a normally-closed micropump. Another normally-closed micropump concept with active valves has been published by Shinohara et al. [5]. In that case a normally-closed valve is manufactured by filling up silicone rubber paste after bonding glass substrate and silicon substrate. This silicone rubber works as a "gate" for shutting off the flow when the pump is not actuated. The normally-closed function was shown up to 50 kPa. Cao et al. [6] showed a concept with a prestressed silicon membrane with a boss structure in the center pushing against in- and outlet of the micropump and keeping it normally-closed. The proper function of the pump could not be demonstrated in their paper. The company Debiotech [7] reported their commercial available micropump to be normally-closed for pressure differences of 5 kPa by a check valve mechanism, based on a prestressed silicon structure [8] but they did not show any experiments. Commercial available drug delivery systems that are in use in hospitals or in

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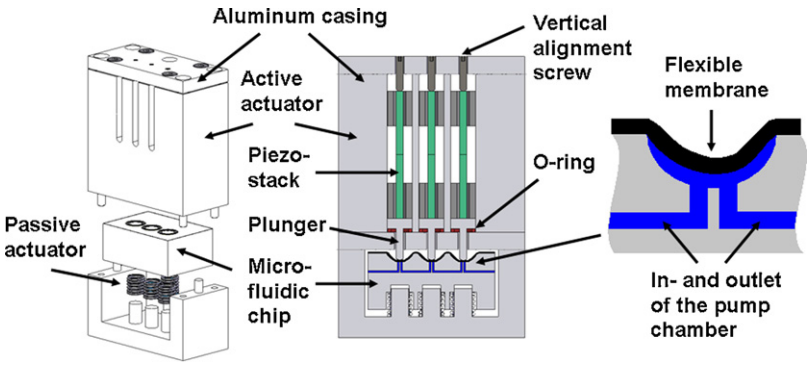

Fig. 1. Exploded view of the modular concept (left) and cross sectional view (middle) of the micropump with implemented normally-closed mechanism. A detailed view of one pump chamber is depicted on the right hand side.

the health care industry [9,10] often use passive free flow protections, which have to be manually activated. Therefore, in case of a voltage breakdown or other unexpected errors during the drug delivery process, the free flow protection does mostly not prevent an uncontrolled dosage in such a system.

Usually, the flow rate of a micropump decreases linearly with increasing backpressure [11–13]. Therefore, with varying backpressures a precise delivery of liquid is not possible any longer without additional flow sensing and feedback loop to the actuation mechanism. In contrast backpressure independent pump performance enables high precision liquid delivery independently on varying conditions in the environment. Recent works in the field of backpressure independent micropumps [14,15] have shown the possibility to pump against backpressures up to 30 kPa [15] without significant decrease in flow rate.

2. Micropump design and normally-closed principle

The modular concept of the micropump presented in this paper is based on a re-usable actuator unit and a disposable microfluidic chip. Fig. 1 (left) shows an exploded view of those building blocks. The actuator unit itself can be sub-classified in an active part featuring three piezostack actuators and a passive part. The piezostack actuators are assembled with adjustment parts (distance sleeves, o-rings for pre-tension, vertical alignment screws) in an aluminium casing. The passive actuator features four spring elements (or alternatively o-rings) and is arranged underneath the microfluidic chip. The microfluidic chip comprises three serially interconnected pump chambers which are confined by a flexible membrane on the top and two orifices (inlet and outlet) at the bottom of each chamber. The three membranes in combination with the orifices in the pump chambers form three serially interconnected microvalves. After insertion of the microfluidic chip it is pushed up by the springs towards the plungers and all three flexible membranes are displaced completely into the pump chambers even when the voltage is turned off. This way all three valves are closed during stand-by. The maximum pressure every valve can withstand is defined by the prestress of the springs and the stiffness of the membranes. This represents the normally-closed property of the micropump. In Fig. 2 the laboratory prototype of the disassembled micropump can be seen. The re-usable piezostack actuator, the disposable microfluidic chip and the bottom part with the passive actuators are shown.

3. Micropump working principle

In Fig. 3 the sequence of membrane displacements into the three pump chambers is depicted (left) together with the sequence of actuation voltages on all three piezostack actuators (right). A pump cycle can be separated into five states or phases respectively. State 1 is the stand-by mode. All piezostack actuators are in the relaxed off-state and all three membranes are displaced into the pump chambers due to the passive actuators underneath the chip. The pump is switched into state 2 by applying a voltage to all three piezostack actuators. The chip is slightly tilted but there is no change regarding the membrane displacements into the pump

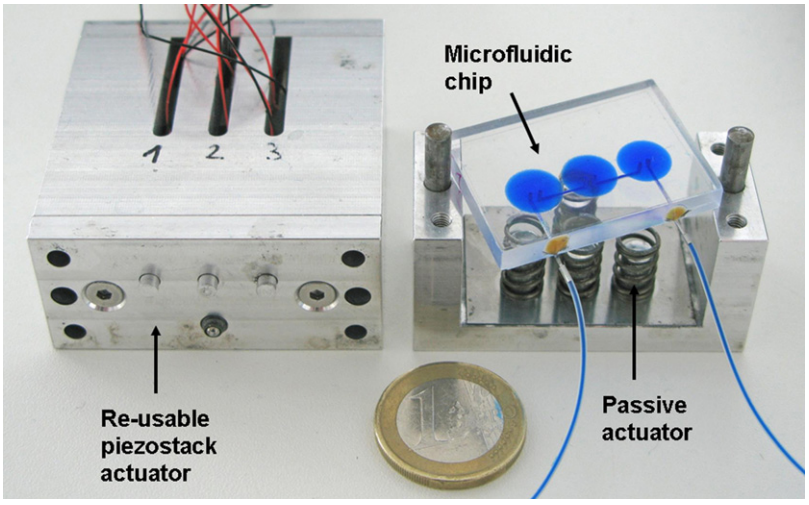

Fig. 2. Laboratory prototype of the micropump with disposable microfluidic chip and re-usable actuator unit.

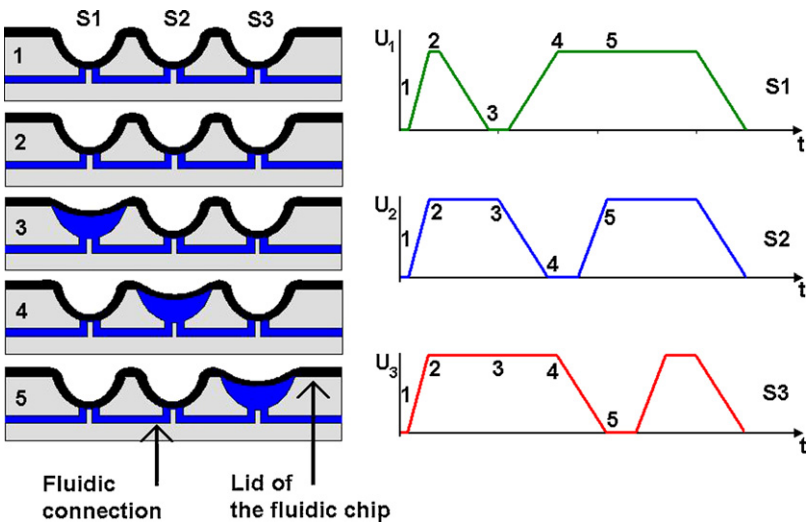

Fig. 3. Electric drive signals (right) and corresponding fluid motion in the microfluidic chip (left).

chambers because all pump chambers are aligned along a straight line. In the next phase the pump is switched from state 2 into state 3 by reducing the voltage at piezoactuator 1 controlling the membrane displacement at the inlet pump chamber S1. The membrane relaxes due to the intrinsic stress according to its initial displacement and with it liquid is sucked into the pump chamber 1 (Fig. 3, left, 3). During switching from state 3 to state 4, fluid is just displaced from the inlet chamber S1 to the neighbouring chamber S2. This is initiated by reducing the voltage at actuator S2 and increasing the voltage at actuator S1 which causes a low pressure in chamber S2 and a high pressure in chamber S1. Due to the fact that the valve in pump chamber S3 is completely blocked during that period and due to the fact that the flow resistance between chamber S1 and S2 is much smaller than the flow resistance between S1 and the inlet tubing, theoretically no liquid is pushed back to the inlet tubing during that liquid transfer phase. During switching from state 4 to state 5 the same happens and liquid is transferred from chamber S2 to S3. In a final phase the liquid is pushed out through the outlet side by displacing membrane S3 by the piezoactuator S3. This equals the switch from state 5 back to state 2 (state 3–5 in Fig. 4, left). It can easily be seen that during a pump cycle an open fluidic path between inlet and outlet port never exists. At least one of the three valves is closed during all phases and so the complete amount of liquid should be transferred from one chamber to the other without any backflow during switching between two states. This prevents any unintended flow and at the same time enables backpressure independent performance of the micropump.

The electric drive signals S1 to S3 shown in Fig. 3 (right) were defined, so that the transfer of fluid between the pump chambers is supported. For the liquid transfer phase between pump chamber S1 and S2 this means for example, that the membrane S2 opens the valve of pump chamber 2 by moving upwards 1 ms before the pump chamber S1 starts to close again. At the end of the transfer phase, the pump membrane of chamber S2 reaches its full deflection 1 ms before the pump membrane S1 closes the valve of pump chamber 1. For other frequencies than the defined base frequency of 28.57 Hz (35 ms/pump cycle) these times are scaled linearly.

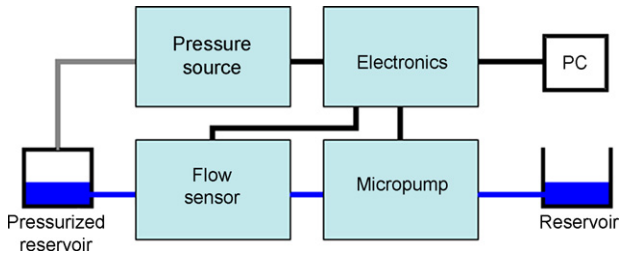

Fig. 4. Laboratory setup for characterizing the micropump (e.g. frequency behaviour).

4. Measurement setup

A schematic drawing of the measurement setup for the characterization of the micropump is shown in Fig. 4. A PC with a LabVIEW™ program is used to provide the drive signals over an analog output module. The signal is pre-amplified by a not inverting operational amplifier circuitry and finally amplified by a commercial available three-channel voltage amplifier (Physik Instrumente, P-863), generating voltages between −20 V and 120 V. The multilayer piezostack actuators (P882.51) were purchased from Physik Instrumente. The size of every actuator was 2.0 mm × 3.0 mm × 36.0 mm. The total length of 36 mm was achieved by stacking two individual actuators of the half length each. The actuator stroke was 40 μm (−20 V to +120 V), the blocking force is 210 N. For characterization of the flow rates, a flow sensor (LiquiFlow, Bronkhorst) is used to measure flow rates up to 180 μL/min. The outlet reservoir can be pressurized to perform tests of the normally-closed mechanism and to characterize the backpressure behaviour of the micropump.

5. Manufacturing of the fluidic chip

The bottom of the pump chamber should adapt the shape of a deflected membrane to enable a sufficient sealing at the in- and outlet of each pump chamber. So, the desired normally-closed mechanism can be realized efficiently. Additionally, the dead volume of a pump chamber can be reduced, if the bottom of the pump chamber forms the exact shape of the deflected membrane. For this, the pump chambers of the fluidic chip are casted in a mould as a negative of the deflected membrane using an epoxy resin (Struers/SpeciFix-20). To mould the pump chambers, the lid of the fluidic chip is mechanically clamped with an assembly tool onto an aluminium blank (shown in Fig. 5). The clamped lid above the milled edges are deflected by a certain spring force into the aluminium blank and build the negative shape of a pump chamber.

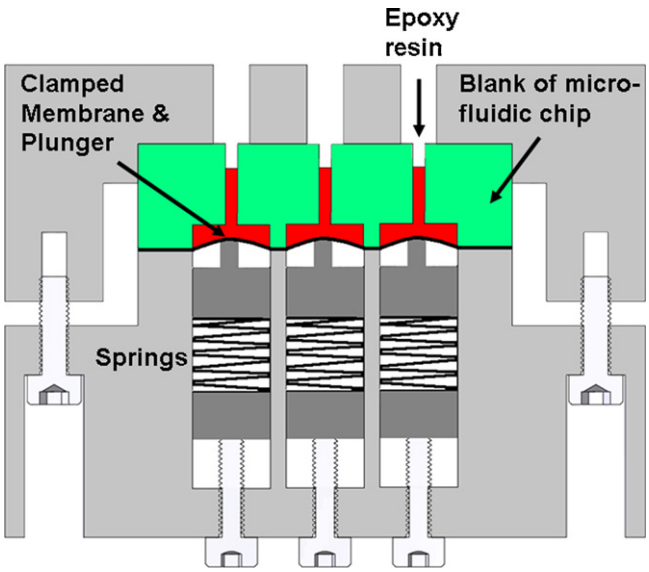

Fig. 5. Assembly tool for prototype version of the microfluidic chip with moulded pump chambers.

From the bottom side of the assembly tool, the aluminium blank is filled with epoxy resin. So, the cavities underneath the lid are filled out (Fig. 5) and form the pump chambers after curing for 12 h at room temperature. For a proper release after the curing process, the surface of the membrane was pretreated with car polish. In the first prototype version of the fluidic chip, this process was done for every individual microfluidic chip (Fig. 6, left). In the final version (Fig. 6, right) a master chip was casted in a mould and the data of a profilometer scan were used for micro-milling of the pump chambers directly into a polycarbonate block. Additionally, the fluidic interconnections between the pump chambers and holes for the in- and outlet are milled and drilled into the chip body. After gluing stainless steel tubes into the drilled in- and outlet holes as connectors for a flexible tube, the chip body is ready for the capping process of the lid. This is done in a heat bonding step with a laminator (Weiss & Soehne, Pilot Coater PCS-30) and a hot melt adhesive (Buehnen D 1544). The bottom side of the fluidic chip was sealed with an adhesive tape. Fig. 6 shows the two versions of the microfluidic chip. The aluminium prototype version with moulded pump chambers (left) and the miniaturized polycarbonate version of the fluidic chip (right) with micro-milled pump chambers.

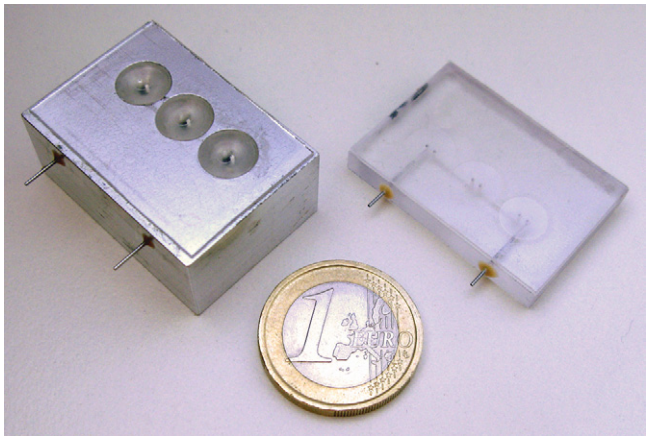

Fig. 6. Aluminium chip with moulded pump chambers (left) and polycarbonate chip with micro-milled pump chambers (right).

6. Experimental results

The micropump is designed for a precise dispensing of small volumes with flow rates up to 100 μL/min. The experiments have been performed with water. The characteristics of the normally-closed mechanism, is depicted in Fig. 7. It was measured by connecting the flow sensor to the inlet port of the pump and pressurizing the outlet reservoir connected to the outlet of the pump. Without energy consumption, the micropump is normally-closed up to a pressure difference between inlet and outlet port of 100 kPa (no fluid flow was measured). For higher pressure differences, a measurable flow rate can be observed. This proves a good sealing between the membrane and the inlet and outlet ports at the bottom of the pump chambers caused by the force of the passive actuators, up to a pressure of 100 kPa.

The flow rate versus frequency characteristics, for voltage amplitudes of 140 V (+120 V/−20 V), can be seen in Fig. 8. A linear increase in the frequency of the driving signal up to 15 Hz goes along with a linear increase in the flow rate (pointed out by the linear fit with $R^2 = 0.998$). A flow rate peak at 150 μL/min is achieved at frequencies between 20 and 25 Hz. The linear frequency range up to 15 Hz with flow rates increasing linearly with frequencies allows a precise dispensing of liquid up to 120 μL/min. The pumped liquid volume per cycle was about 130 nL according to these experimental results.

The backpressure behaviour of the micropump is shown in Fig. 9. A backpressure independent flow rate was obtained up to 40 kPa. The slight variations around the mean value of about 70 μL/min are below 10% and can be explained with the capacitance of the tubing that is charged for small backpressures by the micropump and slightly lowers the flow rate in this region. For a further increase of the backpressure above the critical value p_c (flow rate declined to 90% of the maximum value), a linear decrease ($R^2 = 1.00$) in flow rate versus backpressure can be observed. This is plotted for backpres-

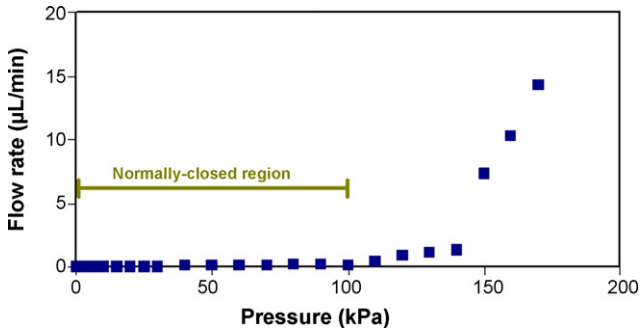

Fig. 7. Characteristics of the normally-closed mechanism. Up to a pressure of 100 kPa no fluid flow was measured (normally-closed region).

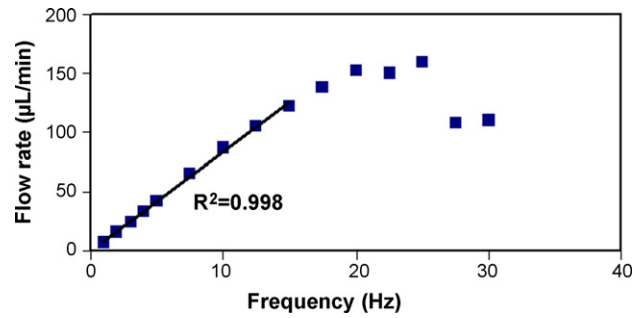

Fig. 8. Frequency characteristics of the micropump. A linear increase can be measured up to 15 Hz, which allows a precise dispensing with flow rates up to 120 μL/min.

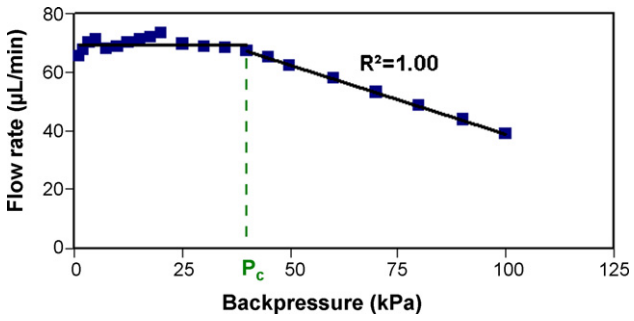

Fig. 9. Backpressure characteristics of the micropump. Backpressure independent pumping with a constant frequency of 7.5 Hz is shown up to 40 kPa (the mean flow rate is marked at 70 µL/min). For higher pressures a linear decrease occurs (zero flow rate can be extrapolated to be at a backpressure of 180 kPa).

sures up to 100 kPa in Fig. 9. The maximum achievable backpressure was estimated to be 180 kPa by extrapolating that linear decrease to the pressure of zero pump rate.

7. Conclusions and outlook

We presented a modular micropump with an integrated normally-closed mechanism. The pump is actuated in a peristaltic manner by three piezostacks and features several relevant characteristics for ambulatory infusion therapy. The normally-closed mechanism in the off-state is an important step towards increasing patient safety. The backpressure independent pump characteristics together with the linear increase of pump rate with operation frequency enables a very good controllability of infusion with programmable drug delivery rates. Precise dispensing of volumes from the sub-µL range up to several mL is possible and independent of a wide backpressure range. Additionally, the modular setup with a low-cost fluidic chip and a re-usable actuator unit perfectly fits the needs in the medical field and health care industry. The next step towards a prototype for field use is the development of a new demonstrator offering a smart mechanism for easy manual exchange of the microfluidic disposable. This portable and wearable demonstrator will have required electronics, display, touch panel and energy supply integrated.

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Biographies

Fabian Trenkle was born in 1981. He studied Microsystems Engineering at the University of Freiburg, Germany, and received his diploma in 2006. Since 2007 he works as a member of research staff at the Laboratory for MEMS Applications of Prof. Dr. Roland Zengerle. In parallel he works on his PhD in the field of micropumps.

Stefan Haeberle was born in 1977. He holds a PhD degree in Microsystems Engineering and worked for 5 years in the Microfluidic R&D group at HSG-IMIT and IMTEK, focusing on miniaturized drug delivery systems and lab-on-a-chip devices.

Roland Zengerle was born in 1965. He received his diploma in physics from the Technical University of Munich in 1990, the PhD from the "Universität der Bundeswehr München" based on the development of an electrostatically driven micropump in 1994. Since 1999 he is full professor at the Department of Microsystems Engineering (IMTEK) at the University of Freiburg, Germany. Today Dr. Zengerle in addition is a director at the Institut für Mikro- und Informationstechnik of the Hahn-Schickard-Gesellschaft (HSG-IMIT) and vice director on the centre for Biological Signalling Studies (bioss). The research of Dr. Zengerle is focused on microfluidics and nanofluidics.