Miniaturized peristaltic rotary pump for non-continuous drug dosing*

Izadyar Tamadon, Virginia Simoni, Veronica Iacovacci, *Member, IEEE,* Fabio Vistoli, Leonardo Ricotti, *Member, IEEE,* and Arianna Menciassi, *Senior Member, IEEE*

***Abstract*— Micro dosing pumps are the beating heart of infusion systems. Among many technologies to inject micro quantities of fluids, peristaltic pumps show high precision and the possibility to not alter the fluid properties. However, in real drug delivery applications, the continuous release behavior of typical peristaltic pumps is not favorable. In this paper, we investigate the intermittent performance of two prototypes of peristaltic pumps, based on four and five rollers, used to occlude the tube. The pump performances are reported for different rotation speeds and lag times between consecutive infusions. The proposed pumps showed a good volumetric precision (2.88 μL for the five rollers pump and 4.11 μL for the four rollers pump) without any dependency on rotation speed and lag time.**

I. Introduction

Infusion pumps are programmable medical devices that deliver controlled amounts of medication directly inside the body [1]. Among other applications, such devices - either implantable or wearable - have been proposed for chronic pain management [2], [3] and diabetes treatment, through insulin infusion [4], [5]. Thanks to the possibility to infuse drugs in the desired target location (where they are actually needed), infusion pumps technology shows higher efficacy and smaller side effects respect to systemic delivery strategies. High volumetric resolution (in the μL range) and accuracy must be pursued, when designing this kind of medical devices [6], [7].

Traditional infusion systems normally exploit pumps, valves, reservoirs and catheters to accomplish a precise and reliable circulation of fluids [8]. The pump is undoubtedly the core of an infusion system; pumping technology should be selected based on the specific application and on the need to minimize alterations of the infused drug [9]. For example, insulin infusion systems used to control glycemic levels in diabetic patients, mostly use syringe- or piston-based pumps to minimize possible changes in the insulin properties (*e.g.* hormone aggregation) and to favor refilling and injection by means of a single actuator. However, controlling the infusion of small doses with these pumps calls for very precise actuators and driving systems, featured by large dimensions or high driving voltages, thus making such kind of pumps hard to be integrated in fully implantable devices [10], [11]. Recently, innovative solutions have been proposed to minimize pump dimensions or to remove batteries, thus making them more suitable for implantable systems. Lee et al. designed a novel implantable insulin infusion system actuated by a magnetic pen [12]. However, the control loop was not closed through any digital sensors, thus limiting the potential autonomy of the device. Piezoelectric actuators [13] show a high potential in micro scale pumping, due to their miniature size and very accurate volumetric output. However, the operating voltage of piezoelectric pumps is typically well above the powering ranges supported by batteries suitable for implantable medical devices [14], [15]. Peristaltic rotary pumps can fill this gap by ensuring low voltage actuation, ease of sealing, low impact on fluid properties and precise delivery [16]. Although peristaltic rotary pumps have been widely used since the 1930's in medical applications as continuous delivering pumps [17], [18], their intermittent behavior and their ability to work as dosing systems have been not investigated and characterized, yet.

In this paper a small scale peristaltic rotary pump working as a dosing system and suitable for inclusion in implantable devices, *e.g.* in artificial pancreas, is proposed. Two pump designs, based on four and five rollers, were designed and fabricated. Both systems were characterized to assess their maximum dosing resolution. Both pumps were controlled in order to rotate the rollers by a specific angle and to perform precise intermittent injections. Pump performances were characterized when varying operating speed and operation timing. The remainder of the paper is organized as follows: Section II describes pump design, selection of driving and actuation system, and the experimental setup for pump characterization; Section III reports pump performances in different operating configurations; finally, Section IV draws the conclusion and highlights the possible impact of the proposed pump in the field of implantable and wearable devices for drug and hormone delivery.

II. Materials and Methods

A. Pump Design

Peristaltic pumps are positive displacement pumps used for a variety of fluids, including sterile and aggressive ones [19]. The fluid travels in a flexible tube that is fitted between a

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Izadyar Tamadon (corresponding author), Veronica Iacovacci, Leonardo Ricotti and Arianna Menciassi are with the BioRobotics Institute, Scuola Superiore Sant'Anna, Pisa, 56025, ITALY (E-mail: {i.tamadon and arianna.menciassi}@santannapisa.it).

Virginia Simoni and Fabio Vistoli are with the Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, 56126, ITALY

circular housing and a rotor including a certain number of rollers. The rollers normally compress the tube and occlude the flow [20]. As the rotor turns, *e.g.* by means of a rotational motor, the portion of fluid interposed between consecutive rollers advances through the tube producing dose ejection. Additionally, as the tube opens again when the roller moves on, the fluid is aspirated from a reservoir. Typically, depending on the application, the pump includes two or more rollers transporting the fluid towards the pump outlet. The rollers can be installed thus to have a constant occlusion, as in the simplest designs, or can be spring-loaded to maximize tube lifetime. Generally peristaltic pumps have simple designs without any valves, O-rings or seals that might limit the compatibility with fluids [12]. The tube is the only component entering in contact with the fluid and should be made of a material chemically compatible with the drug of interest. Furthermore, the tube should be featured by specific mechanical properties combining at the same time high elasticity (to favor occlusion by the rollers) and high resistance to mechanical stresses, to keep the circular cross section stable upon repeated pump cycles.

The performance of peristaltic pumps is mainly affected by the entity of tube compression between the rollers and the housing. A low compression can cause slip back or leakage to the output, whereas a high compression can lead to a reduced tube lifetime. Consequently, an optimal level of compression should be pursued. The term *occlusion* is used to define the minimum gap in the pump based on the flexibility of the tube. In order to properly design the pump, the gap can be calculated based on tube thickness (*t*) and expected tube occlusion, as follows:

$$\text{occlusion}=\left({}^{(2t-gap)}/_{2t}\right)*100\% \qquad (1)$$

The occlusion is typically 10-20%, with a higher value for softer tubes and lower for harder ones. Pursuing an optimal occlusion, thus selecting the proper carrying tube, is very important for both guaranteeing the correct operating principle and to avoid fluid leakage when the pump is stopped [21].

Peristaltic pumps may run continuously, or they may be rotated through partial revolutions to deliver small amounts of fluid in non-continuous (*i.e.* intermittent) mode. The flow rate during partial rotation is determined by tube internal diameter, housing dimensions and number of rollers. The fluid volume trapped between two adjacent rollers determines the volumetric output. Typically, in implantable devices, the dimension of the housing is constrained by the space available, so the other geometrical entities can be dimensioned consequently.

In this paper, we imposed a maximum volume of 12 cm^3 for the overall pump to guarantee an effective integration in an implantable device. We imposed a diameter of 18 mm for the external housing "Fig. 1". A relatively large thickness tube (external diameter: 3 mm, internal diameter: 1 mm - Primasil Silicones Ltd., UK), made of medical grade silicone (material ref: PR 410/40) with shore 40A hardness, was selected as the best compromise to extend tube lifetime. With reference to "Fig. 2", a 10 % tube occlusion, leading to a 1.8 mm gap, was pursued to guarantee the maximum tube lifetime and an optimal sealing [21]. The rollers were provided with gears (10 teeth, module 0.4) on the bottom side to be engaged with a pinion gear (12 teeth, module 0.4). All rollers were caged together by the rotor, to enable their engaging with the pinion and their rotation with the same speed. The proposed pump was actuated by a DC micromotor (Faulhaber 1512U003SR 324:1) provided with a high reduction gear ratio and with an embedded optical encoder.

As mentioned, in the intermittent mode, the dose delivered through a partial rotation corresponds to the fluid volume trapped between consecutive rollers. The pump output (*dose*) can be thus calculated as:

$$\text{dose}=AR(a-2s) \qquad (2)$$

Where *A* is the internal cross section of the tube (0.785 mm^2), *R* is the tube curvature inside the housing (6.9 mm), *a* is the angle between two adjacent rollers and *s* is the angle that a deformed tube will form around each roller ($2\pi/14.4$). By considering a uniform tube compression and a constant tube curvature around the rollers, theoretical pump doses can be calculated "Table I".

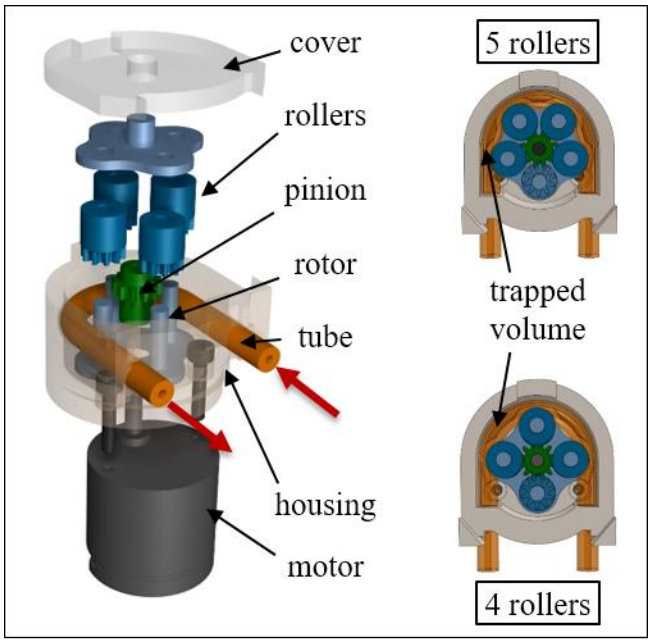

Figure 1. The proposed rotary peristaltic pump and its components. Red arrows indicate flow direction.

Both pumps were designed by keeping the same housing, the same tube, the same diameter of rotor and rollers, and by only varying the number of rollers that compress the tube. The pump housing, rotor, pinion gear and rollers were fabricated by 3D printing (ProJet MJP3600, 3D systems, USA, material: VisiJet M3 crystal) and the cover with laser cutting techniques (material: transparent Plexiglass, thickness: 2mm).

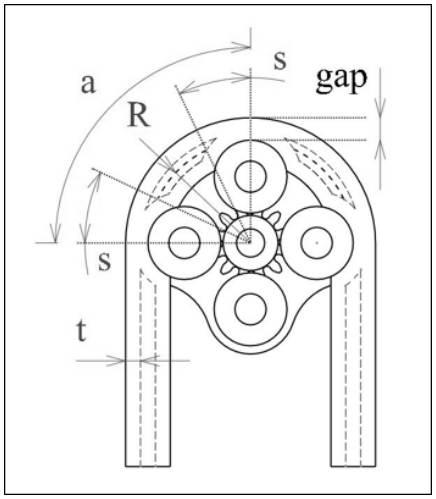

Figure 2. Geometrical parameters featuring the pump.

TABLE I. THEORETICAL DOSE VOLUME GUARANTEED BY THE TWO PUMP TYPES

Pump type	*a [rad]*	*Dose [µL]*
4 rollers	$\pi/2$	3.78
5 rollers	$2\pi/5$	2.08

B. Pump Driving and Bench Testing

To control the pump operation, the motor was connected to a low voltage driver IC (DRV8833, Texas Instrument) and Arduino Uno (Arduino, IT). The motor encoder was wired to Arduino's counter to precisely control the pump angular displacement. Also, for fully characterizing pump performances, the output was evaluated for both pumps designs when varying operating speed and dose delivery timing (*i.e.* by varying the delay between consecutive infusion periods). In order to modulate the pump speed, pump driving was performed through 100%, 50% and 25% duty cycle PWM signals. By this elaboration, the effects of different battery conditions (fully charged or depleted) were considered. For the four rollers pump, such an input variation corresponded to a pump speed of 15.8, 12.5 and 7.4 rpm, respectively. On the other hand, for the five rollers pump, the different battery conditions corresponded to 15.4, 11.3 and 6.5 rpm, respectively. This small difference can be ascribed to the higher resistance load on the motor produced by the five rollers pump.

The Arduino program provided different delays between consecutive releases. This aimed at characterizing the pump in a non-continuous operation mode, thus simulating real on-demand drug delivery working scenarios which require intermittent release (*i.e.* a certain amount of dose followed by a certain lag time). In particular, five intermittent release conditions were evaluated to assess the impact of the lag time on dosing precision: continuous rotation (without any lag time), 5, 10, 20 and 60 s of lag time between each release task. Lag time was introduced every 90° for the four rollers pump and every 72° for the five rollers pump, to let advance precisely the amount of volume comprised between consecutive rollers.

Experiments were performed for both pump designs by varying the driving parameters and by measuring correspondingly the fluid amount (water at 25 °C) transferred by the pumps from a 4 mm^3 cylinder reservoir to a Petri dish. To limit fluid pressure effects on the rollers, reservoir and pump were kept at the same geodetic height. The Petri dish was placed on a laboratory precision balance (Entris, Sartorius, DE) with 1 µL resolution. The laboratory scale was connected through a serial communication (rate 5 Hz) with a PC to receive the data recorded, as in "Fig. 3". Ten 90° rotations and ten 72° rotations were performed, by varying both rotation speed and lag time between each rotation, and by recording the volume of liquid released. The experiments were repeated three times with a new tube and data were processed by using the Matlab software (MathWorks, USA).

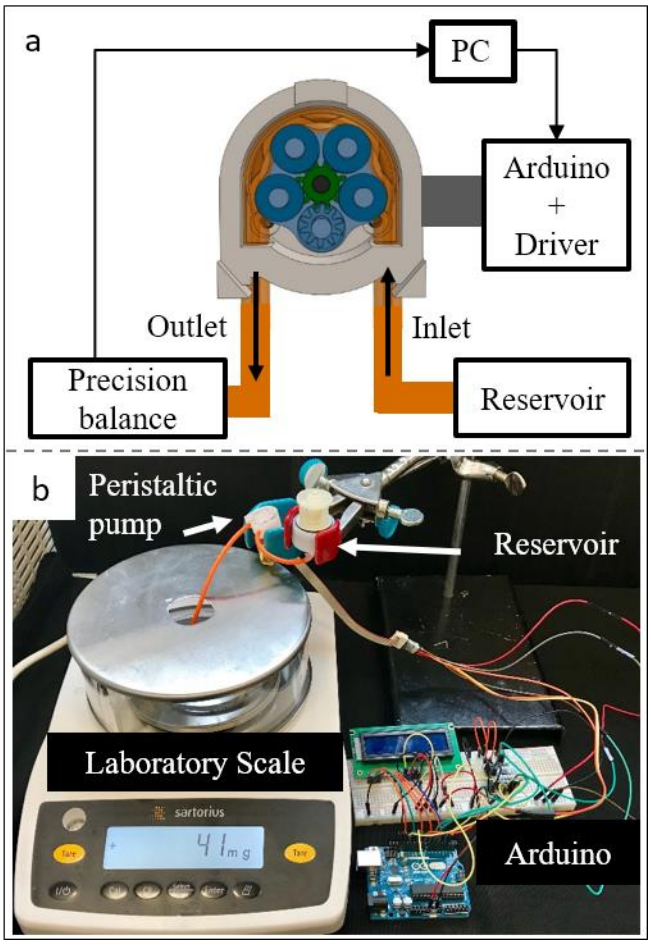

Figure 3. Experimental setup for testing the pumps (the five rollers pump is shown, as an example): schematic representation (a) and photo (b).

III. RESULTS

Pictures of the fabricated miniature peristaltic rotary pumps are reported in "Fig. 4." These prototypes were tested through the procedure described in section II.B. Cumulative pump release upon ten pump operation steps was evaluated by varying the lag time (driving input was 100% of duty cycle

PWM) and the rotation speed (with the pump running in continuous mode). “Fig. 5” shows the results in terms of volume released for the four rollers pump, while “Fig. 6” shows the correspondent results obtained for the five rollers pump.

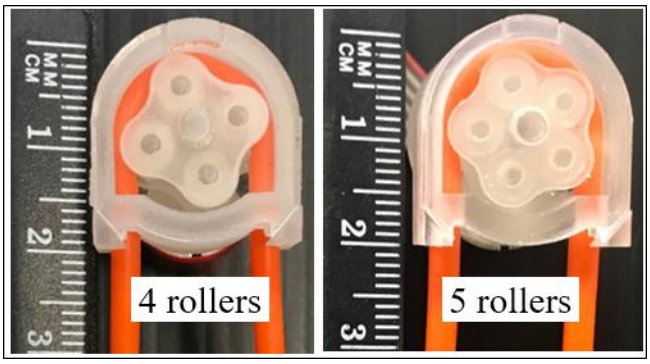

Figure 4. Prototypes of the proposed peristaltic rotary pumps with four rollers (left) and five rollers (right).

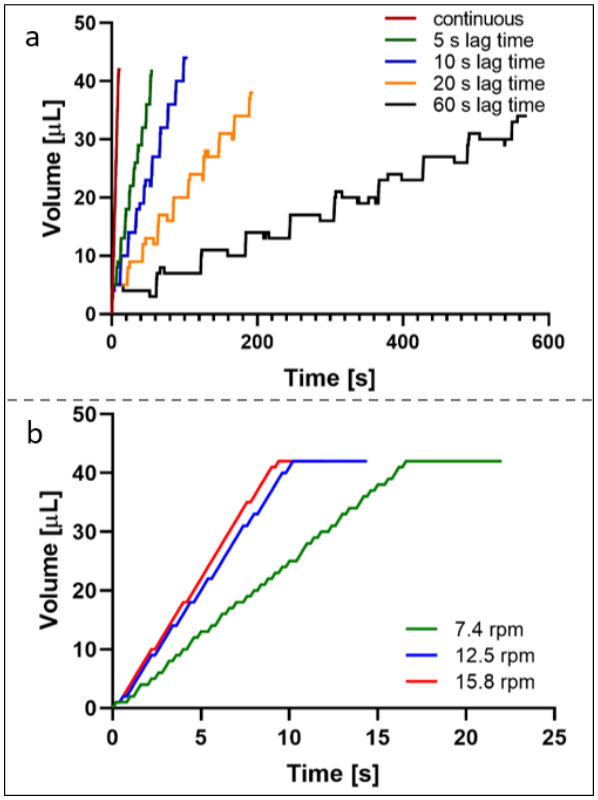

Figure 5. Four rollers pump performances:cumulative release over ten pump operation steps in one representative experiment when varying lag time (at 15.8 rpm) (a) and rotation speed (when in continuous rotation) (b).

Data post processing enabled to calculate pumps resolution to be compared with theoretical doses. Single step output results were grouped based on lag time and plotted as boxplot for both pump designs, as in “Fig. 7”. Multiple coupled t-tests highlighted the absence of statistically significant differences (p-value > 0.01) when varying operating speed and lag time.

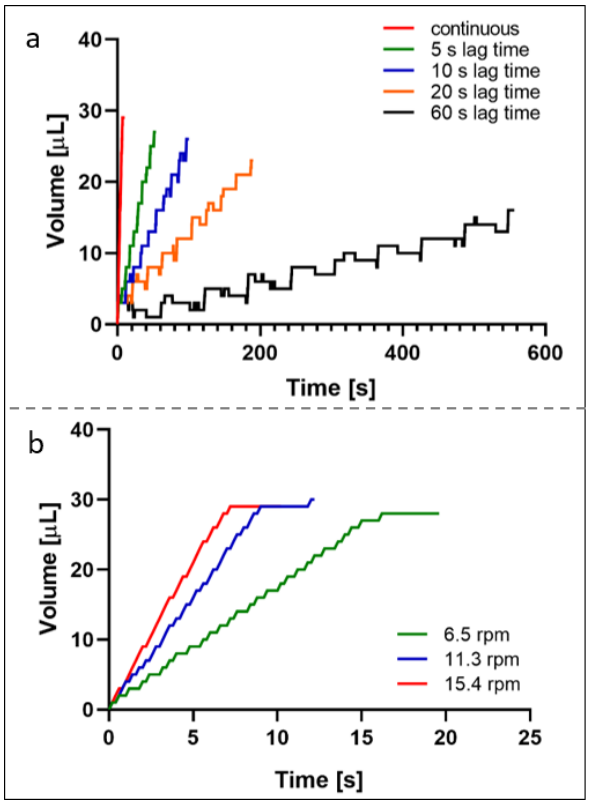

Figure 6. Five rollers pumpperformances: cumulative release over ten pump operation steps in one representative experiment when varying lag time (at 15.4 rpm) (a) and rotation speed (when in continuous rotation) (b).

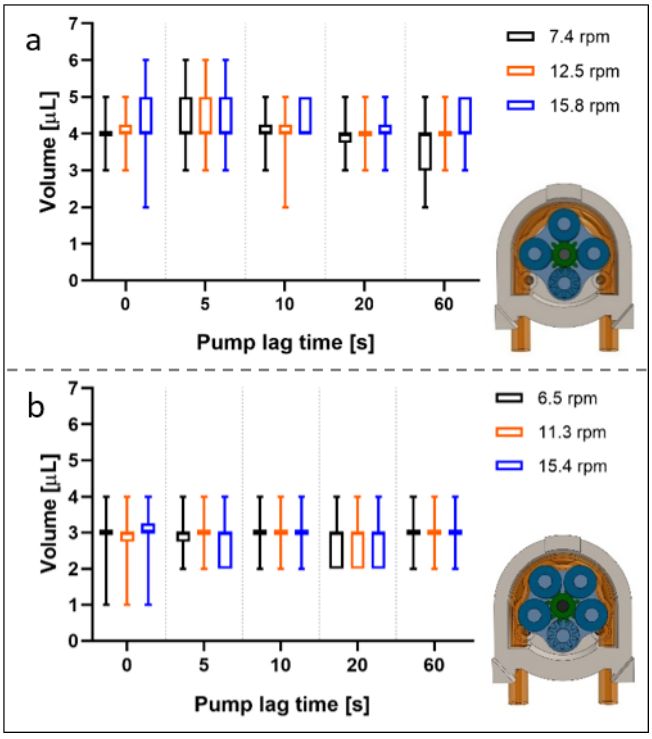

Figure 7. Peristaltic rotary pump in single step release (three sets of ten) for the four (a) and five (b) rollers pump. No statistically significant differences emerged (p-value > 0.01).

Based on the cumulative results in continuous mode reported in "Fig. 5a" and "Fig. 6a", it can be observed that with long lag times the cumulative volume decreased due to evaporation from the Petri dish. On the other hand, speed variation ("Fig. 5b" and "Fig. 6b") did not significantly affect the release. Output fluctuations in "Fig. 5a" and "Fig. 6a" are mostly related to balance resolution and environmental factors. However, by looking at the single step release reported in "Fig. 7", the output variance increased for both pumps when operating in continuous mode (*i.e.* lag time = 0). Interestingly, the presence of a lag time between consecutive steps led to a greater output precision, especially for the five rollers pump.

For the four rollers pump, the experimental average dosing volume for a single step release resulted 4.11 µL (median value: 4 µL). For the five rollers pump, the experimental average dosing volume for a single step release was 2.88 µL (median value: 3 µL). These experimental outputs can be considered acceptable when comparing with theoretical predictions, shown in Table I. The difference between the theoretical and the experimental output was +8% for the four rollers pump and +27% for the five rollers pump. This discrepancy can be ascribed to mechanical tolerances associated with the prototyping steps, leading to suboptimal tube compression, and to a limited resolution of the measurement system.

IV. Conclusion

This paper proposes the design and characterization of a dosing system based on a peristaltic rotary pump. The performance of the proposed dosing systems was poorly affected by speed and lag time variations. In addition, the median and average values of the dosing resolution resulted in good accordance with theoretical calculations. This confirms the reliability and precision of the proposed pumps and their suitability to intermittent operation and various rotational speed conditions. In this framework, the paper successfully reports about the employment for the first time of small size rotary peristaltic pumps operated in non-continuous mode, in contrast with traditional peristaltic pumps with continuous operation. The peristaltic pump is easily scalable to 6 or more rollers based on available space and required output volume.

These pumps can solve the issue of the contact between fluids and pump mechanisms, thus avoiding leakages and fluid contaminations. Furthermore, the use of rotary actuator enables to reduce powering and driving issues, which are always crucial in wearable and implantable medical devices.

The results shown in this paper can lead to an effective intermittent use of peristaltic pumps in a wide variety of medical applications, including the integration in implantable devices for a precise and temporized release of drugs and hormones.

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