A DISPOSABLE, DISPENSING VALVE FOR NON-CONTACT MICROLITER APPLICATIONS IN 96-WELL PLATE FORMAT

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ABSTRACT

We present a miniaturized, disposable dispensing valve for the microliter range, applicable as consumable to process 96-well plates. The new valve design is adapted to fit into a 9 mm grid and derives from the miniaturization study of a previous functional model [1]. The outer diameter of the valve, including actuating coil, was reduced from 16 mm to 8.5 mm without performance restrictions, thus made compatible for 96-well plate processing. Also the actuation current was reduced from 10 A to 5 A. The valve enables the dosage of target volumes in the range between 230 nL and 5 µL with coefficients of variation (CVs) below 2%. The current performance coincides with similar commercially available systems with the decisive advantage of material costs below 1 €.

KEYWORDS

non-contact dispensing, electromagnetic valve, normally closed, disposable, 96-well plate format

INTRODUCTION

The requirements concerning dispensing performance of liquid handling systems in terms of precision and trueness are increasingly growing. Also the risk of cross-contamination and the need of expensive cleaning steps are omnipresent issues. Therefore, disposable components and non-contact dispensing technologies are preferred, which are hardly available on market.

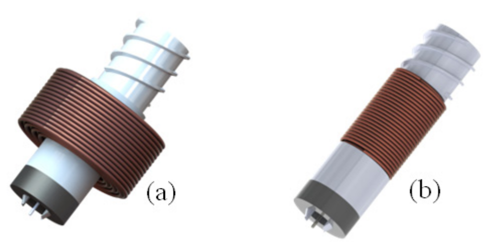

Figure 1: Schematic drawing of the functional model (a) [1] and the novel miniaturized (b) design of the disposable, non-contact dispensing valve.

In a previous work [1], we developed a disposable, normally-closed, non-contact dispensing valve focused on requirements given from industry and research [2]. The major drawbacks of that functional model were the large size with an overall outer diameter of 16 mm (including actuation coil, see fig. 1(a)), and the heat coupling, induced by the required high actuation currents. For pressure-time controlled valves, the flow rate and therefore the dispensed volume is depending on the nozzle dimension and the fluid properties. In this case, the coil is in direct contact with the valve body, so a high actuation current will heat up the valve and the containing fluid. The temperature will influence the viscosity of the fluid which will lead to a higher flow rate, thus an increased dispensed volume for pressure-time controlled systems. Therefore, the actuation current has to be reduced in order to minimize this influence on the dosing performance.

MINATURISATION STUDY

To enable a parallel application of multiple valves, in order to process 96-well plates by individual channels, the geometry of the valve requires an outer diameter of below 9 mm which was a crucial issue for the realization of the presented work. Also the actuation currents had to be reduced to lower the heat coupling into the liquid.

Working principle and acting forces

The miniaturization study is based on the theoretical consideration of three general forces acting on the valve plunger during actuation [3]. The individual forces are: a) the force between the coil and the plunger $F_{plunger}$, b) the force between the normally-closed (NC) ring magnet and the plunger $F_{RingMagnet}$ and c) the pressure force $F_{pressure(open)}$ as illustrated in fig. 2.

The movement of the plunger is controlled by the coil current and the induced opening force $F_{plunger}$ which is dependent on the distance between the coil and the plunger and their dimensions. In the normally closed state, the plunger is contact with the valve seat because of the attractive force $F_{RingMagnet}$ exerted by the NC magnet and the pressure force $F_{pressure(open)}$ as illustrated in figure 2. In order to open the valve, the two closing forces have to be overcome by applying a positive current pulse, whereby a magnetic field is generated, which exerts a force on the plunger higher than the closing forces and opens the valve. After the current is turned off, the plunger moves downwards again (see figure 2). The dispensed volume can be controlled by either varying the applied external actuating pressure, the nozzle dimensions or the current pulse length.

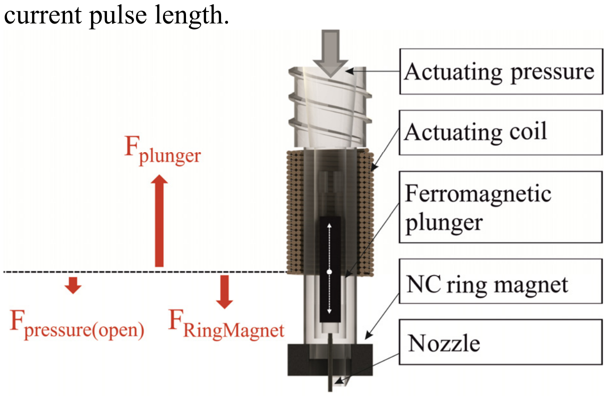

Figure 2: Cross section of the disposable, electromagnetic dispensing valve and the three main forces acting on the ferromagnetic plunger.

$F_{Plunger}$ acts as opening force which needs to overcome the closing force ($F_{RingMagnet} + F_{pressure(open)}$) to enable the movement of the plunger and the actuation of the valve. These three forces can be calculated analytically with focus on the geometrical miniaturization of the valve.

Force between two permanent magnets

First, the force $F_{RingMagnet}$ between a permanent ring magnet and a permanent cylindrical magnet, both with axial magnetization is calculated. In Ravaud et. al. [3] the force between two permanent ring magnets is calculated by using the charge model. This model can be used due to the constant magnetization of the permanent magnets. Each magnet can be described by two charged planes located on the upper and lower surface of the magnet. Analogically, the force between a ring magnet and a cylindrical magnet can be calculated. $F_{RingMagnet}$ is depending on the dimensions of the magnet and the magnitude of the magnetization.

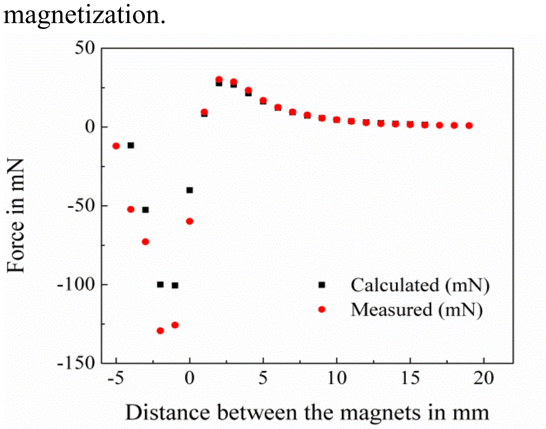

Figure 3: Measured (red) and calculated (black) force $F_{RingMagnet}$ between a plunger and a NC magnet in correlation with the distance between the magnets.

Using a hard ferrite as NC ring magnet with an inner diameter of 4 mm, an outer diameter of 8 mm and a height of 3 mm and a NdFeB magnet with an outer diameter of 2 mm and a height of 10 mm as plunger (cf. figure 2) leads to a maximum calculated force $F_{RingMagnet}$ of 30.11 mN at a distance of 2 mm between attractive planes of the two magnets (cf. fig. 3).

Pressure force

The second closing force is the pressure force which appears from the external actuating pressure required to drive the valve. Therefore, the pressure force $F_{pressure(open)}$ can be calculated with the following formula:

$$d\vec{F}_{pressure(open)} = \int_A p \, d\vec{A} \qquad (1)$$

where $F_{pressure(open)}$ is the pressure force in N, p is the pressure in bar and A is the surface in m².

In the normally-closed state the plunger is in contact with the valve seat. The upper side of the plunger is exposed to a pressure force $F_{pressure(open)}$ acting on the whole surface $\pi r^2_{plunger}$. This force is determined as positive. On the other side of the plunger which is in contact with valve seat, the pressure force acts in the opposite direction (negative). On this side, the force acts on the cross section which is not in contact with the valve seat $\pi(r^2_{plunger} - r^2_{nozzle})$. After adding these forces one gets the pressure force acting on the cross section of the outer diameter of the nozzle in direction of the external applied pressure:

$$F_{pressure(open)} = p_{ext} \pi r^2_{nozzle} \qquad (2)$$

Force between coil and plunger

In [4] the force between a coil and a permanent magnet is calculated by using the charge model described in [3]. The force $F_{Plunger}$ is dependent on the coil dimensions (windings, height, length, inner and outer diameter and wire diameter), the distance between the coil and the plunger, the current and the plunger properties and dimensions. For this study, a NdFeB magnet with an outer diameter of 2 mm and a height of 10 mm was used as plunger, and the minimized target current was set to 5 A. A pressure of 2 bar is specified to be the maximum applicable actuation pressure.

The required opening force $F_{Plunger}$ can then be calculated by:

$$F_{Plunger} > F_{RingMagnet} + F_{pressure(open)}$$
$$> 30.11 \text{ mN} + 101.1 \text{ mN} = 131.81 \text{mN} \qquad (3)$$

$F_{plunger}$ needs to overcome the maximum calculated closing force of 131.81mN, to guarantee a reliable functionality of the valve for the entire actuation pressure range. The outer diameter of the coil was set to 8.5 mm. By reducing the inner diameter of the coil, the opening force could be increased. But this dimension could not be reduced to an arbitrarily low value, because of the minimal required wall thickness of the valve which was set to 1.2 mm to guarantee no deformations for actuating pressures of 2 bar. Based on theoretical considerations in [4], the design rules for the valve miniaturization could be identified, which are listed in table 1. This configuration entails a maximum opening force of $F_{plunger}$ of 150.15 mN.

Table 1: Comparison of the dimensions of the old [1] and the new design of the disposable, electromagnetic dispensing valve.

	Old design [1]	New design
Outer diameter coil	16 mm	8.5 mm
Inner diameter coil	9 mm	5.5 mm
Length coil	8.5. mm	12 mm
Number of windings	105	72
Peak current	10 A	5 A
Overall length valve	27.1 mm	29.35 mm

FABRICATION

Based on the investigated design rules, a first prototype was fabricated. The two parts of the valve body are fabricated with a 3D-printer working with the MultiJet Moldeling (MJM) technology, where high viscose urethane acrylate printed structures become solid three-dimensional bodies after a UV curing process. The used transparent material is "Visijet EX 200".

In figure 5, an exploded drawing of the valve body is shown. The body consists of two individual parts, whereas part one consists of a Luer Lock connection to the reservoir, the magnet stop and the duct structures for the plunger, necessary to minimize the tilting, lower the friction and to guarantee a parallel movement of the plunger. Part two consists of the clamps for the NC magnet and a hole to mount the nozzle. The nozzle is made of a either a PI or steel capillary tube which is glued inside the hole with a defined height of 0.5 mm of the valve seat.

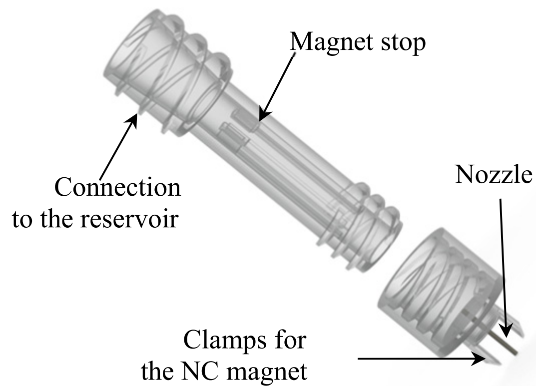

Figure 5. Exploded drawing of the two-part valve body with mounted nozzle.

The used magnet stop defines the maximum stroke length of the plunger to 2.5 mm. The plunger is coated with a Parylene C layer and a 1mm thick silicone sealing layer, with a shore hardness of A60, is glued on top of the plunger. Afterwards, the plunger is inserted into part one which was previously inserted into the actuation coil. Finally, the assembly is closed by part two by a Luer-Lock thread.

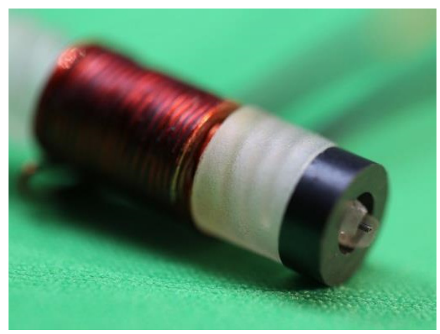

Figure 6: Prototype of the disposable, non-contact dispensing valve fabricated applying a 3D printing process.

In order to cover a wide area of applications, different nozzles are used to obtain different minimum volumes and flow rates, cf. table 2.

Table 2: Influence of the dimensions of the nozzle at a constant actuating pressure of 200 mbar on the flow rate and the volume range of the dispensing valve.

ID nozzle	Length nozzle	Flow rate	Min. volume
200 µm	16.5 mm	43 µL/s	200 nL
200 µm	5.5. mm	80 µL/s	400 nL
230 µm	5.5 mm	130 µL/s	1 µL

RESULTS

In order to characterize the droplet ejection process, the droplet volume has to be determined gravimetrically. The dispensing performance was characterized applying the GRM method [5].

The first characterization study focuses on the reproducibility of the valve, expressed by the coefficient of variation (CV) given in percent. It describes the ration between the standard deviation *s* and the mean volume $\bar{V}$ of 24 individual measurements.

$$\mathrm{CV}_{\text{intra-run}} = \frac{s}{\bar{V}} = \sqrt{\frac{\frac{1}{n-1}\sum_{i=1}^{n}(d_i - \bar{V})}{\bar{V}}} = \quad (4)$$

Where d_i is the volume of a single dispense in nL and n the number of dispense.

As nozzle we used a metal capillary with an inner diameter of 200 µm and a length of 5.5 mm. The actuation pressure wars set to 160 mbar to guarantee a suitable droplet tear-off. The number of dispenses per run were set to 24 dispenses to get a reliable statistic. The actuation time of the valve was varied between 1 and 60 ms.

In figure 7, each measured volume point in the diagram states the mean volume $\bar{V}$ of one run with 24 dispenses. The valve reveals an excellent performance for water as dispensing medium, cf. figure 7. The CV varies between 0.3% and 2.0% for a volume range between 400 nL and 4.2 µL.

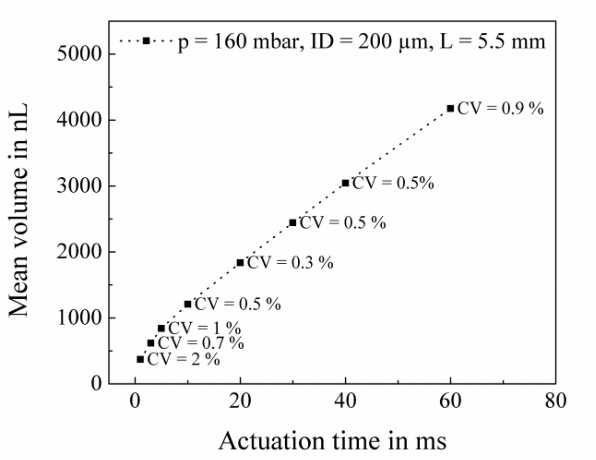

Figure 7: The dispensing performance shows a linear dependency between the actuation time and the dispensed mean volume. Each data point represents the mean volume of one run of 24 individual measurements. Percentages state the respective CV.

As shown in figure 7, the mean volume $\bar{V}$ and the actuation time t show a linear correlation for an actuation time above 10 ms. In order to evaluate the non-linear behavior for $t < 10$ ms, the flow profile was recorded by a flow sensor from the Sensirion AG mounted between the reservoir and the dispensing valve. We examined that for actuation times less than 10 ms, the flow profile is not fully established. This behavior explains the non-linear range in figure 7 for an actuation time between 1 ms and 10 ms.

SUMMARY

In summary, we successfully miniaturized the functional model of the existing valve to an allover outer diameter of 8.5 mm without any performance restrictions, implying the arrayability of the valve in a 9 mm pitch for 96-well plate applications. The decrease of the actuation current by 50% entails less heat transfer to the sample liquid, thus improves the valve accuracy and reproducibility. Furthermore, we were able to adjust the desired volume range and flow rate by using nozzles with different dimensions. The performance of the developed prototype can already compete with commercially available dispensing valves, implying a cost effective and clean application and the possibility of fabrication by injection molding processes.

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