Available online at www.sciencedirect.com
SCIENCE DIRECT®
Sensors and Actuators A 116 (2004) 483–491
SENSORS AND ACTUATORS A PHYSICAL
www.elsevier.com/locate/sna

The dispensing well plate: a novel nanodispenser for the multiparallel delivery of liquids (DWP Part I)

Peter Koltay*, Reinhard Steger, Benjamin Bohl, Roland Zengerle

IMTEK, University of Freiburg, Laboratory for MEMS applications, Georges-Koehler-Allee 103, D-79110 Freiburg, Germany

Received 13 November 2003; received in revised form 18 May 2004; accepted 21 May 2004
Available online 23 July 2004

Abstract

This paper reports on a novel dispensing system for the massive parallel delivery of liquid volumes in the range of 50 nL. Due to the similarity of the device to conventional microwell plates used for storage of liquids, the device has been termed “dispensing well plate” (DWP). In contrast to other known microdispensers the DWP can consist of up to 1536 dispensing units in parallel all holding different reagents. The dispensing units can be arranged very closely at the pitch of conventional microwell plates (2.25 or 4.5 mm). Driven by pneumatic actuation a fixed volume of different liquids can be dispensed simultaneously and contact free into microwell plates or onto flat substrates. By this the liquid-handling in many chemical, biochemical and pharmaceutical applications—especially within high throughput screening (HTS)—can be speed up by a factor 10–100. In this paper the basic operation principle of the device is presented and experimental evidence is given of its extraordinary performance: a reproducibility of 2–5% and a homogeneity within individual droplet arrays of 1–2% has been measured as well as viscosity independent performance for liquids in the range from 1 to 5 mPas. The fabrication of DWP prototypes by different micromachining technologies based on silicon dry etching and SU-8 technology is described and various DWP prototypes with different dosage volumes are presented.

Keywords: Non-contact dispenser; Jets; High throughput screening; SU-8

1. Introduction

In modern drug discovery, potential drug candidates have to be identified from a huge number of different chemical compounds. The process applied for this purpose is called high throughput screening (HTS). It allows for the testing of several 100 000 chemicals per day. In HTS biochemical assays are performed in standardized containments termed microwell plates. Today well plates like displayed in Fig. 1(a) with 384 or 1536 wells at a pitch of 4.5 or 2.25 mm are handled within automated equipment. Around 1000 dispensing cycles per minute are accomplished currently by conventional pipetting systems. To push the limit of HTS, assay volumes ranging from 2 to 5 μL have to be miniaturized even further and the liquid handling has to be accelerated [1–4]. Therefore pipetting and dispensing systems are required which can handle volumes in the nanoliter range and operate in a multiparallel fashion compatible to well plate formats. The DWP system presented in this paper is able to speed up the liquid handling process in HTS by a factor of 10–100 while at the same time reducing reagent consumption from the microliter to the nanoliter range.

2. System description

The complete DWP system consists of a pneumatic actuation unit driving a microfluidic chip termed “dispensing well plate” (DWP) displayed in Fig. 1(b). The DWP-chip itself consists of a number of dispensing units arranged very closely at conventional well plate spacing. Prototypes with 24 and 96 independent units at a pitch of 4.5 and 2.25 mm have been realized so far using different micromachining approaches (see below). Typically the dispenser array is surrounded by an unstructured border enabling better handling and sealing of the upper surface. Each dispensing unit of a DWP consist of three basic elements which are shown in Fig. 2 in detail: a reservoir, a connection channel and a nozzle chamber.

Before operating the system the reservoirs can be filled with liquid by conventional pipetting systems. The whole DWP is then inserted into an actuation unit described below. The subsequent dispensing process proceeds like illustrated

* Corresponding author. Tel.: +49 7612037413; fax: +49 7612037539.
E-mail address: koltay@imtek.de (P. Koltay).

0924-4247/$ – see front matter
doi:10.1016/j.sna.2004.05.038

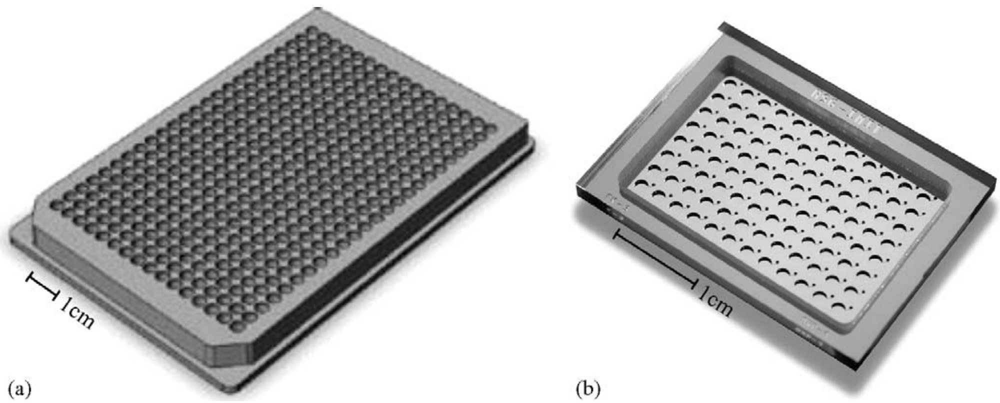

Fig. 1. (a) Conventional microwell plate with 384 wells at pitch of 4.5 mm, (b) photograph of a DWP-prototype with 96 dispensing units at a pitch of 2.25 mm micromachined in silicon and Pyrex glass.

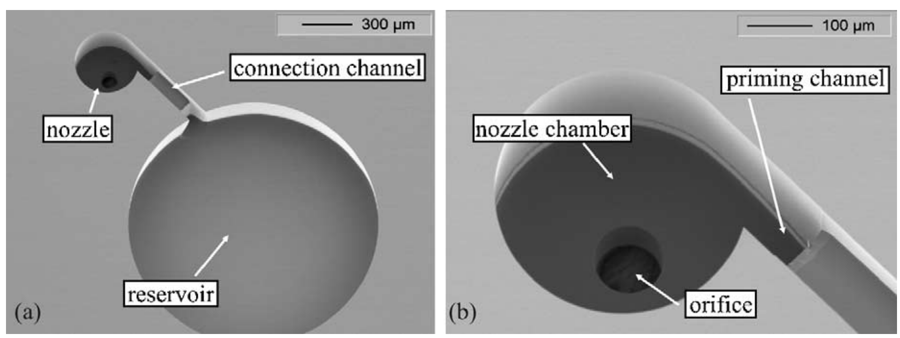

Fig. 2. SEM micrograph of: (a) a single dispensing unit of the DWP micromachined in silicon, (b) a close up of the nozzle chamber.

in Fig. 3: due to capillary forces the nozzle chambers are always filled completely via the connection channels from the reservoirs (Fig. 3(b) and (c)). By applying a pressure pulse to the whole upper surface of the DWP the liquid contained in the nozzle chambers is driven out completely (Fig. 3(d) and (e)). Since reservoir and nozzle chamber are exposed to the same pressure head no pressure driven flow occurs within the connection channel. Thus essentially the volume confined in the nozzle chamber is dispensed. No flow through the connection channel occurs during jet ejection which accounts for the high accuracy and robust performance of the device. After switching off the driving pressure, the nozzle chambers refill again from the reservoirs by capillary forces (Fig. 3(f)). Therefore multiple dispensing cycles are possible.

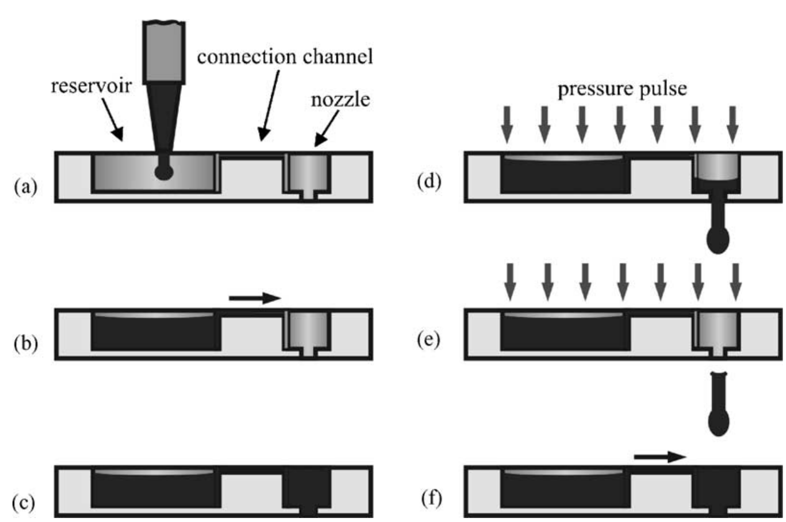

Fig. 3. Schematic illustration of the DWP working principle: (a) filling of the DWP, (b) capillary priming of the nozzle, (c) DWP ready for dispensing, (d) actuation of the DWP by pneumatic pressure, (e) complete depletion of the nozzle chamber during jet ejection, and (f) refilling by capillary forces.

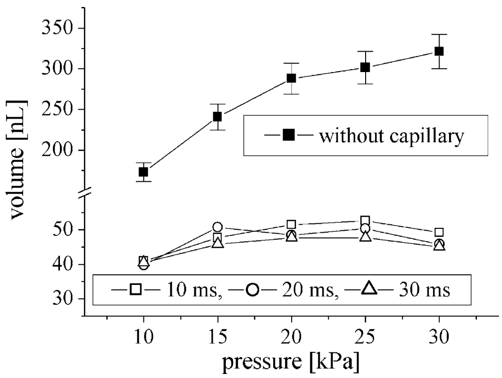

Fig. 4. Dosage volume of dimethylsulfoxide (DMSO) as a function of pressure head and pulse duration. Compared are the values for the DWP prototype displayed in Fig. 5(a) (hollow symbols) and a pressure controlled dispenser concept consisting of a well with a orifice in the bottom without capillary channel (full squares).

Due to this unique working principle the DWP performs as a fixed volume dispenser. The dosage volume is mainly determined by the geometrical volume of the nozzle chamber, and it is hardly affected by liquid properties and external parameters like pressure head and duration. Thus basically the machining precision of the fluidic structures—especially the nozzle chamber—determines the dispensing accuracy. Therefore the DWP method is much more robust and accurate, than for example, a purely pressure controlled dispenser: imagine for example, a dispenser consisting of a reservoir with a small hole drilled into its bottom. If this device is driven by a pneumatic pressure similar to the DWP, the dispensed volume is extremely sensitive to the driving pressure and liquid properties. Experiments with such a type of dispenser have been conducted, and the results displayed in Fig. 4 (black squares) clearly state a strong dependence of the dosage volume on the pressure head. In contrast to this the dosage volume of the DWP is independent on pressure head and pulse duration. The same experiment conducted with a DWP prototype as displayed in Fig. 4 exhibits no dependence of the dosage volume on the pressure pulse. The same dosage volume has been obtained for pressure heads between 10 and 30 kPa and pulse durations between 10 and 30 ms. The dosage volume also corresponds very well to the geometrical volume of the nozzle chamber of about 50 nL in that case. Thus essentially the liquid contained in the nozzle chamber has been dispensed. This proves the described working principle and also the robustness of the method. The small scattering of the data in Fig. 4 is explained by the error of the measurement of about 7%.

3. Fabrication technology

3.1. Fabrication requirements

Though the working principle of a DWP is quite simple, which generates its robust performance, the fabrication of DWP-type dispensers is not trivial. The main challenges with respect to fabrication are:

1. The nozzle chambers have to be machined very precisely within a few micrometer tolerance, because their dimensions essentially determine the dosage volume.
2. A high yield is indispensable because if one dispensing unit out of an array (typically 384 or 1536 individual units) fails the whole chip must be rejected.
3. Usually the DWP and the target well plate have the same format of arraying dispensing units and wells. This means up to 1536 dispensing units with feature sizes down to 50–100 μm have to be manufactured on a large area of approximately 8 cm × 12 cm.
4. The applied materials must be stable against aqueous solutions and DMSO, which are the most prominent solvents used in HTS-applications. This restricts the use of plastic materials severely.
5. A DWP should be ideally about 1–5 mm thick to accommodate an appropriate liquid reservoir of 5–20 μL or if requested even bigger.
6. The whole device preferably for many medical and pharmaceutical applications needs to be disposable which requires the use of cheap materials (e.g., plastics).

These fabrication requirements cannot be met by conventional silicon micromachining, because of the thickness requirement and the material's price. Therefore low cost production processes have to be developed for mass fabrication. In principle injection molding or hot-embossing would be ideal fabrication methods for large volume production. But creating the through holes in a massive parallel way as required is still an unresolved issue with these technologies.

Despite of the mentioned constraints silicon micromachining has been applied for the fabrication of the first prototypes for proof of principle due to its simplicity. Later on an alternative fabrication method based on SU-8 has been investigated which might be optimized to yield a low cost production process for full size DWPs.

3.2. Fabrication of silicon prototypes

For experimental validation of the DWP method first prototypes were fabricated by silicon micromachining. The functional elements, i.e., the reservoirs, the channels and the nozzles, were realized by deep reactive ion etching (DRIE). The DWP chips were enforced by a Pyrex frame for mechanical stability. The silicon chip and the Pyrex frame were connected by anodic bonding [5]. Prototypes with 96, respectively, 24 dispensing units at a pitch of 2.25 mm with reservoir volumes around 800 nL and dosage volumes around 50 nL have been fabricated (see Figs. 1(b) and 5(a)). Typical dimensions of the chips are summarized in Table 1.

The applied fabrication process is illustrated in detail in Fig. 6. A 4 in. silicon wafer with a thickness of 525 μm is oxidized double sided by a wet oxidation process. First the

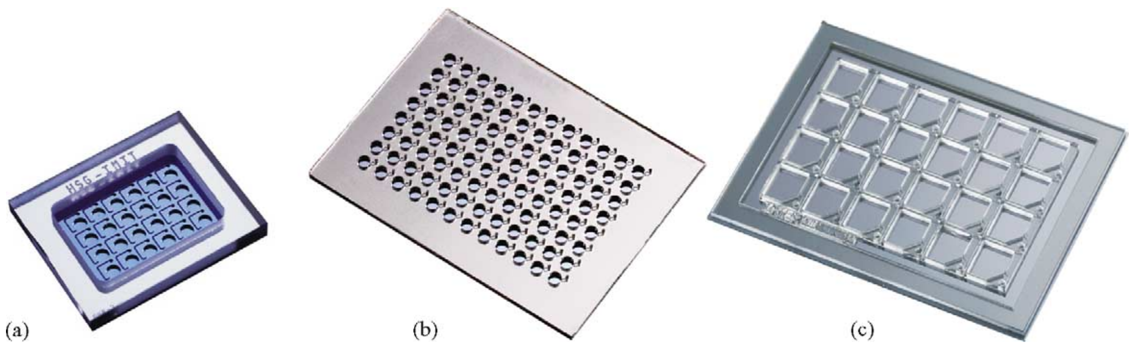

Fig. 5. Fabricated DWP prototypes: (a) silicon prototype with 24 dispensing units at a pitch of 2.25 mm, (b) silicon/SU-8 prototype with 96 dispensing units at a pitch of 2.25 mm, and (c) silicon/SU-8 prototype with 24 dispensing units at a pitch of 4.5 mm.

Table 1
Typical dimensions of the silicon prototypes

Reservoir	
Volume (nL)	800
Connection channel	
Length (μm)	150–3800
Height (μm)	40–425
Width (μm)	50–200
Nozzle chamber	
Depth (μm)	425
Diameter (μm)	385
Nozzle orifice	
Depth (μm)	100
Diameter (μm)	50–200

oxide layer on the reservoir side is structured by a standard lithographic process and a wet etching process using buffered hydrofluoric acid (HF) (a). This layer is used as an etch mask for the connection channels later on. Then a structured photoresist is prepared on top of the oxide defining the reservoirs and the nozzle chambers. These are subsequently etched 325 μm deep by deep reactive ion etching (DRIE) (b) and (c). After removal of the photoresist a second dry etching process is performed 100 μm deep to realize the connection channels between the reservoirs and the nozzle chambers (d). The oxide layer structured in (a) acts as etch mask. After the removal of silicon oxide the reservoir side of the DWP chip is finished (e). To create the nozzle orifice the whole wafer is oxidized again (f). The oxide layer is opened at the back side of the wafer by standard lithography and a dry etching process. The nozzle orifices are afterwards etched by DRIE. Both resist and oxide layer act as etch mask on the nozzle plate. The oxide layer on the upper side of the wafer forms the etch stop layer (f). After the removal of the oxide layers by wet etching in buffered-HF (g) the DWP chips are enforced by a Pyrex frame through anodic bonding and diced subsequently.

3.3. Prototypes manufactured in SU-8 hybrid technology

To embark upon the long-term objective of a disposable DWP device a hybrid process based on SU-8 has been investigated. The fabrication technology applied to produce DWP prototypes like the ones displayed in Fig. 5(b) and (c) makes use of a multilayer structure of the photodefinable epoxy SU-8 on a silicon wafer. The nozzle orifices are fabricated in the silicon wafer, while the other structures like

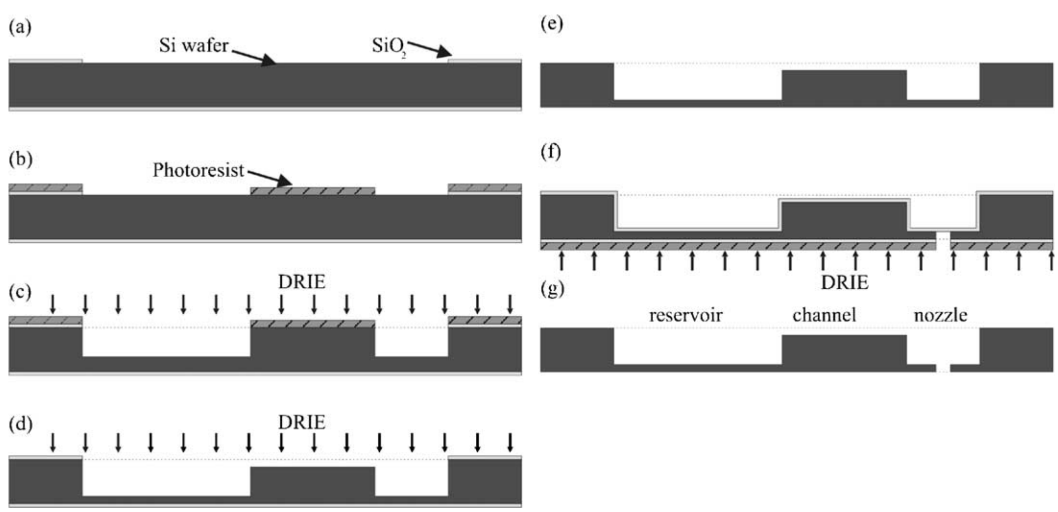

Fig. 6. Fabrication process used for the silicon prototypes.

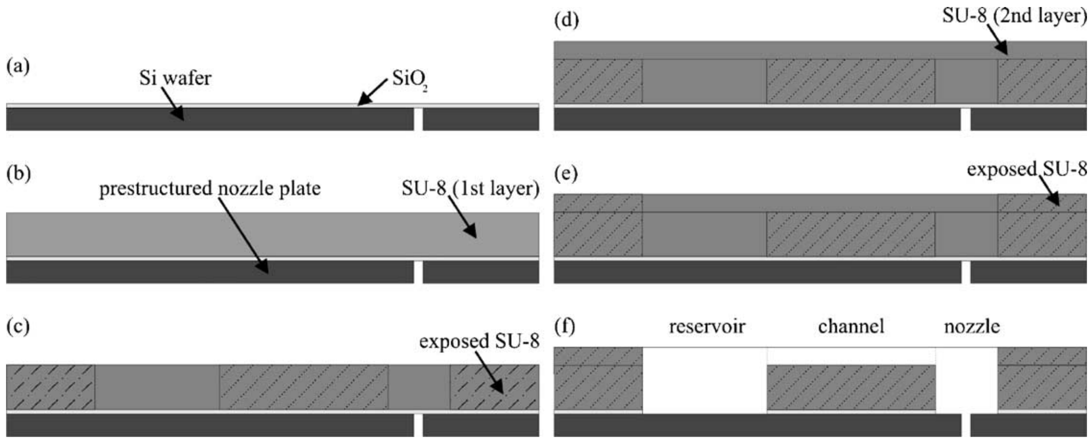

Fig. 7. Description of the SU-8 fabrication process.

reservoir, connection channel and the upper part of the nozzle chambers consist of SU-8 as functional material. SU-8 technology is compatible with standard silicon processing conditions and multilayer structures can be patterned with standard mask aligners. The applicability of SU-8 as a functional material for microfluidic structures and its stability against aqueous solutions and DMSO have been demonstrated before [6–9].

For the shown prototypes silicon has been used as nozzle plate due to its availability in our lab. But in principle also (cheaper) polymer materials can be applied, if sufficiently precise nozzles can be manufactured. In the presented case the silicon nozzle plate has been realized by reactive ion etching like for the silicon prototypes. The orifices were etched through a whole 380 μm Si wafer arranged in an array of 2.25 mm, respectively, 4.5 mm pitch. A silicon oxide layer acts as the etch stop (a). Onto this oxide layer the reservoirs, the channels and the nozzle chambers can be fabricated using SU-8 technology. The complete SU-8 process is sketched in Fig. 7: we have used Nano™ SU-8 100 from MicroChem Inc. [10]. First a 200–600 μm thick layer of the SU-8 is spin coated onto the structured silicon wafer (b). An extended pre-bake is performed at 115 °C to increase the viscosity of the SU-8, because solvent contained in the SU-8 is vapourized. Thus gravity leads to annihilation of the edge bead and other possible variations of the layer thickness. Cooling down with a slow temperature ramp between 60 and 50 °C allows the polymer molecules to re-crystallize and reduces the mechanical stress in the layer. After pre-bake the reservoirs and nozzle chambers are exposed into the SU-8 (c). By spin coating a second layer of SU-8 (50–100 μm) – the layer for the connection channels – is created (d). After an other pre-bake both SU-8 layers are exposed and a post-bake is performed (e). Subsequently both SU-8 layers are developed simultaneously. Finally the silicon oxide layer, which covered the nozzle orifices is removed inside the nozzle by a wet etching process (f).

4. Experimental characterization

To drive the micromachined DWP-chips a prototype actuation unit has been constructed, which consists mainly of a pressure chamber that can be pressurized by two pneumatic valves. A sketch as well as a picture of this unit and a herewith dispensed array of DMSO are displayed in Fig. 8. Using this actuation unit experiments have been carried out to characterize the dispensing performance of the various DWP-prototypes.

4.1. Gravimetric measurements

The presented DWP prototypes have been intensively characterized by gravimetric measurements. The overall dispensed mass has been measured with a microbalance accounting for systematic errors due to evaporation or adsorption. From this data the mean dosage volume per channel has been calculated. In order to prove the working principle the influence of pressure head and pulse duration on dosage volume was studied. The results of these experiments (cf. Fig. 4) support the assumption, that essentially the volume contained in the nozzle channel is dispensed and no significant flow from the reservoir occurs during dispensing. No pressure dependence of the dosage volume has been detected which proves the fixed volume dispensing concept.

Using a solution of water with 0.005% surfactant (Nonidet, P40 Substitute from Fluka) and DMSO as dosage media the reproducibility for the DWP prototypes displayed in Fig. 5(b) and (c) has been determined. The surfactant has to be added to the water because the contact angle of water on SU-8 is close to 90°, which hampers reliable self priming. By adding Nonidet the wetability could be enhanced and a reliable priming of the nozzles could be achieved. The average dosage volumes per dispensing unit displayed in Fig. 9, as a series of consecutive shots shows, that identical volumes are obtained for the differ-

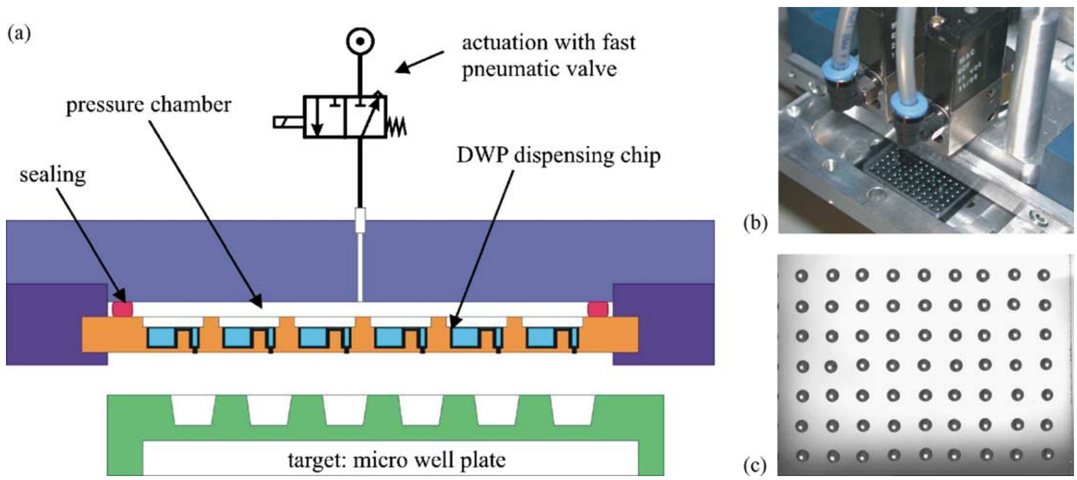

Fig. 8. (a) Schematic of the actuation unit, (b) close up of DWP inserted into the pressure chamber, and (c) array of approximately 50 nL dispensed DMSO droplets.

ent liquids. This observation supports the fixed volume dispensing concept outlined before. Therefore, it can be expected that also other solvents can be dispensed with similar accuracy.

Furthermore the experiments especially exhibit a good reproducibility of around 3% in all cases. In combination with the robustness of the method discussed before, this constitutes the basis for the excellent performance of the DWP. The main difference between the DWP-prototypes with 24 dispensing units (384 format), respectively, 96 dispensing units (1536 format) is given by the fact, that for the 1536 format the reservoir depletion sets in much earlier. The reservoir volume of the 96 channel prototypes of about 800 nL is depleted within 16 shots, while the larger reservoirs of the 24 channel devices of more than 6 μL enable continuous dispensing. Therefore one important goal for the further optimization of the 1536 format is to enhance the SU-8-thickness from 500 μm to more than 1000 μm to be able to accommodate more liquid.

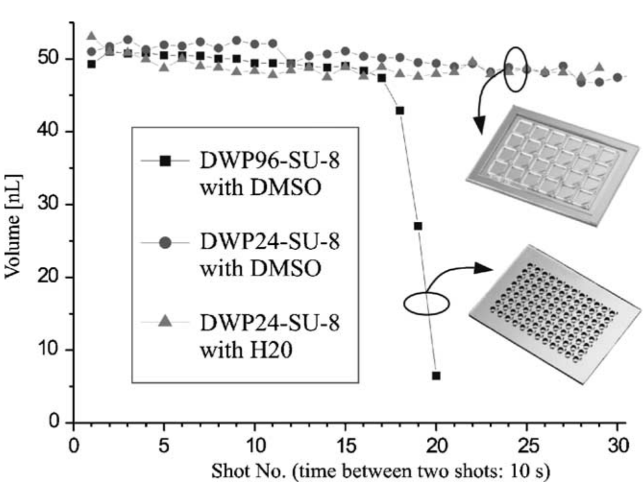

Fig. 9. Reproducibility of the dispensing process for DMSO and water.

4.2. Jet quality

Based on the gravimetric experiments discussed so far only statements regarding the average dosage volume per dispensing unit are possible. In order to find out if the jet generation occurs homogenously over all nozzles stroboscopic imaging has been applied. Pictures of the orifice array have been taken at different times after starting a repeated dispensing process with a frequency of 1 Hz which are displayed in Fig. 10. In the photographs three neighboring orifices are visible in the focal plane. It can be seen clearly, that the jet generation proceeds reproducibly and homogenously. At a nominal pressure head of 20 kPa the jets escape from the 100 μm wide nozzles at a speed of approximately 1.6 m/s and terminate in a spray of liquid after jet tear off. This is due to the fact, that the density of air is much smaller than the density of the used liquids, which causes a high-speed air flow after jet tear off. Due to the Venturi effect this air flow generates a spray which transports liquid out of the nozzle. How much liquid is transported with the spray is essentially determined by the nozzle shape as discussed in more detail in [11].

Though the spray effect degrades the jet quality, the dosage accuracy is hardly affected. Even the droplets generated on a flat substrate like displayed in Fig. 8(c) typically do not exhibit any satellites if the distance to the DWP during dispensing is small enough (approximately <1 mm). In this case the narrow opening angle of the spray causes all sprayed droplets to rejoin the leading part of the liquid on the substrate. Another unintended side effect of the spraying is the formation of a corona of droplets around the orifices on the nozzle plate (see Fig. 10). This is presumably due to the electrostatic charging of the droplets during the ejection process and might cause degradation of the surface properties or cross contamination during extended use of the DWP. Therefore the reduction of the spray effect is a major target for further optimization.

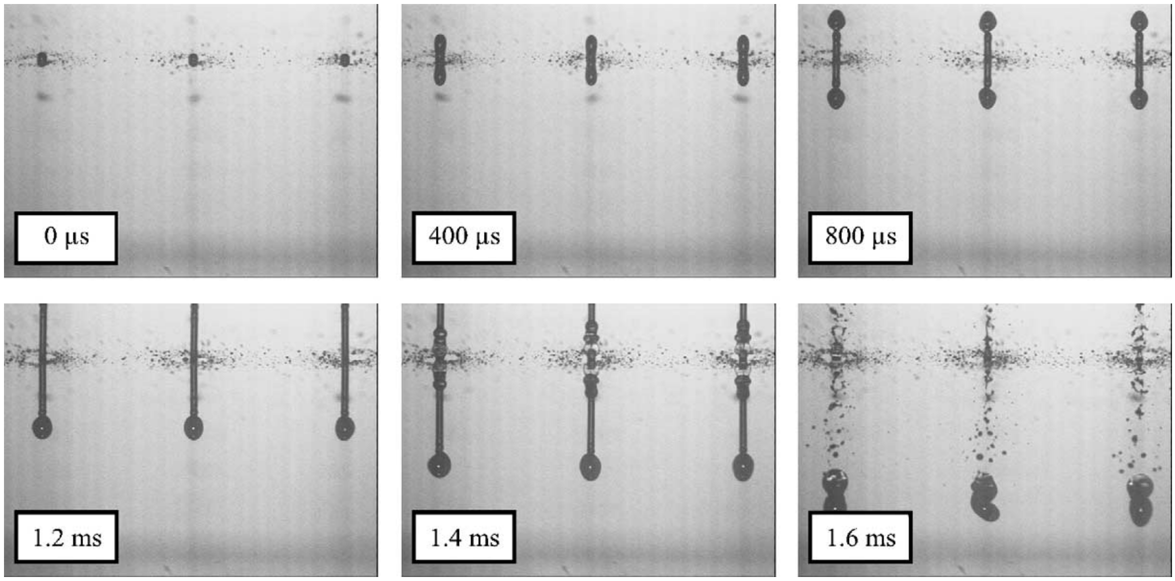

Fig. 10. Stroboscopic images of the jet ejection from three nozzles of a DWP at successive points in time (dispensed medium: DMSO). The jets visible right above the orifices are just mirror images of the real jets moving downwards.

4.3. Bio-chip reader measurements

In order to derive a statistics of the droplet distribution within a simultaneously dispensed droplet array, measurements with a bio-chip reader (type: LaVision BioTec BioAnalyzer 4F) have been conducted. DMSO has been labelled with Dye630 (0.2 mol/L, emitting at 630 nm) and has been dispensed onto a glass slide using the DWP prototype displayed in Fig. 5(a). Due to the fact, that DMSO is hygroscopic, the droplets on the slide do not dry and the fluorescence signal is correlated very well with the droplet volume. This has been proven by a prior calibration. The calibration has been carried out by dispensing a series of volumes from 5 to 60 nL with a single channel NanoJet-type nanodispenser [12]. The dispenser itself has been calibrated before by gravimetric measurements. Thus the volume of the dispensed droplets was accurately known. Then the same volumes have been dispensed onto a glass slide and the fluorescence picture displayed in Fig. 11(a) has been taken. By integrating the total signal over each spot and applying a linear fit, the slope of the calibration curve has been determined to be 77 873 ± 687 counts/nL.

Based on the calibration the absolute volume of the individual droplets dispensed by a 24 channel DWP has been determined. The fluorescent image of the array spotted onto a glass slide is displayed in Fig. 11(b). The picture shows, that the homogeneity of the dispensing process and also the quality of the droplets is very good. An equal signal distribution without satellite droplets can be observed. The quantitative analysis reveals that an excellent CV of 1% could be obtained. The determined mean volume of 42.9 ± 0.6 nL is slightly smaller than the values obtained by gravimetric measurements (48 ± 3.5 nL, cf. Fig. 4). The small systematic deviation of the measurements might be attributed to a slight drift of the camera signal over time. To avoid this source of systematic error the calibration should be better performed on the same slide as the measurement (i.e., taking the pictures in Fig. 11(a) and (b) si-

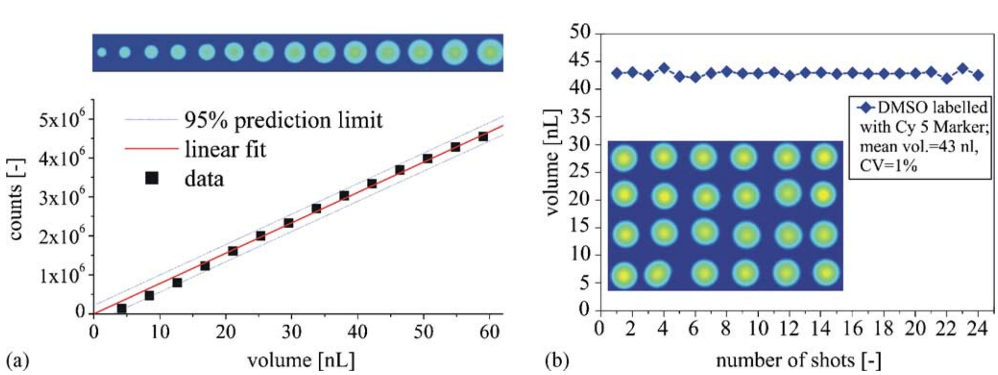

Fig. 11. (a) Fluorometric image of a 5–60 nL droplet series and corresponding calibration line dispensed with NanoJet, (b) fluorometric image of a droplet array dispensed by a DWP-prototype and corresponding volumes per droplet.

multaneously). Compared to the gravimetric measurements the fluorometric method provides more information and is much more accurate (relative error of 1.3%) but also more complicated. It is furthermore restricted to hygroscopic liquids, otherwise a precise evaporation control would be required.

4.4. Plate reader measurement

The ultimate application the DWP has been designed for is the filling of well plates with nanoliter quantities. Therefore the performance when dispensing into well plates has been studied using fluorometry, which is a common technique in HTS to read out the results of assays performed in well plates. In the present case this is however a very difficult task because on the one hand commercial plate readers require at least volumes of 2–5 μL to be able to read the fluorescent signal in a well plate. Thus the volume of interest (e.g., 50 nL) forms only about 1–2% of the total assay volume. On the other hand the filling of the well plates with 2–5 μL by standard liquid handling equipment already causes an error of about 2–5% (CV over a well plate) corresponding to an absolute value of 40–250 nL. This results in a signal to noise ratio of <1. Therefore extra care has to be taken to filter the signal of interest out of the measured noise. A method for this specific purpose has been developed. It relies on the use of two different dyes and an extra calibration of the assay volume before dispensing the nanoliter volumes, which is very tedious. Despite the large effort the method is not very reproducible and accurate. Therefore the following results of experiments performed in well plates should be interpreted only qualitatively.

Measurements have been carried out using the silicon DWP prototype with 96 wells (cf. Fig. 1(b)), a Wallac Victor^{2TM} plate reader [13] and a Cartesian synQuad system [14]. The experimental procedure has been like follows: first a 1536 well plate has been prepared by filling a segment of 96 wells each with 5 μL of DMSO labelled with the dye Umbelliferone (50 μmol/L, emitting at a wavelength of 460 nm) using the Cartesian synQuad dispensing system. Then the fluorescence signal of the Umbelliferone has been determined using a Wallac Victor^{2TM} plate reader. From a volume calibration curve performed beforehand the volume contained in each well of the plate could be determined depending on the count signal of the fluorometry. Since the calibration process exhibited a pour reproducibility large systematic errors of the absolute measured volume dispensed with the synQuad system have to be suspected. Then a solution of another dye, Europium (0.36 μmol/L emitting at 616 nm) in DMSO has been loaded into the DWP and was dispensed into the pre-filled 96 wells of the target well plate. The Europium counts correspond to the concentration of Europium in the final solution, which depends on the quality of dispensing the 5 μL of DMSO with the synQuad system. By applying a correction procedure based on the signal obtained from the Umbelliferone reading the volume

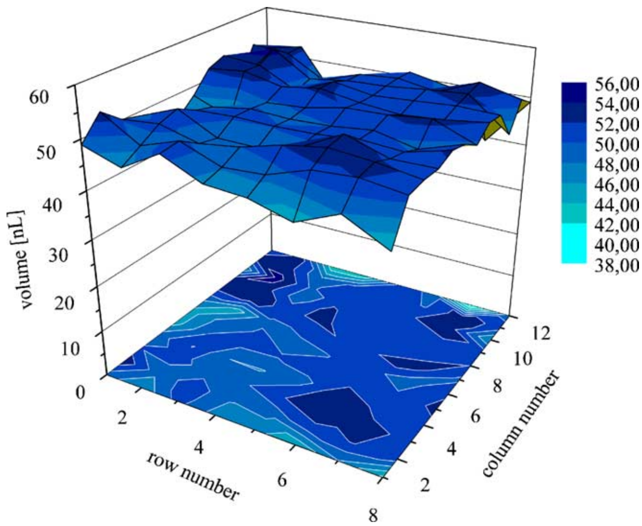

Fig. 12. Volume distribution inside the well plate.

dispensed by the DWP could be determined in each well separately.

The results of these measurements are shown in Fig. 12. A good CV of the volume distribution over the 96 wells of the DWP of slightly <6% could be achieved. Taking into account the much better results obtained with the chip reader equipment the reason for the higher CV might as well be found in the delicate and error prone experimental setup of the plate reader measurements. Nevertheless even a CV of 6% at a dosage volume of 50 nL is still excellent and sufficient for most applications. The experimentally determined volume of about 50 ± 5 nL is in fair agreement with the gravimetric measurements but might suffer at the same time from systematic errors due to the described calibration problems.

5. Summary and outlook

A novel method for massive parallel dispensing of liquids in the nanoliter range has been presented. The proposed DWP method has been studied experimentally using prototypes fabricated by different micromachining techniques. Their dispensing performance was successfully characterized by gravimetric and fluorometric experiments. The DWP prototypes were able to deliver fixed volumes of between 43 and 50 nL with a CV as low as 1% when dispensing an array of 24 droplets simultaneously onto a slide and measuring fluorescence with a bio-chip reader. Dispensing into well plates with a 96 channel prototype did yield a CV better than 6% measured with a Victor^{2TM} well plate reader.

The proposed DWP method has been proven to be very accurate, scalable, simple and robust. A reproducibility of the mean dosage volume of better 3% has been obtained by gravimetric measurements for all prototypes dispensing aqueous solutions or pure DMSO. The DWP-technology therefore has the potential to speed up the liquid handling in HTS by a factor of 10–100 and to reduce reagent consumption by a factor of 10 in the future. To achieve this goal full size prototypes with 384 dispensing units on the size of a well plate have to be fabricated and characterized in the future. The applicability of the DWP method in a HTS laboratory environment has to be demonstrated and minor problems related to the discussed spray effect have to be overcome.

Acknowledgements

The financial support of Wallac, Oy is gratefully acknowledged. The authors are indebted to Gerhard Birkle and Bastian Birkenmeier for performing part of the experiments.

References

[1] J. Burbaum, Miniaturization technologies in HTS: how fast, how small, how soon? Drug Discov. Today 3 (1998) 313–322.
[2] J. Major, Challenges and opportunities in high throughput screening: implications for new technologies, J. Biomol. Screen. 3 (1998) 13–17.
[3] M. Divers, What is the future of high throughput screening? J. Biomol. Screen. 4 (1999) 177–178.
[4] J. Comley, Nanolitre Dispensing—On the Point of Delivery, Drug Discovery World, Summer 2002, pp. 33–44.
[5] W. Menz, et al., Microsystem Technolgy, Wiley–VCH-Verlag, Weinheim, Chapter 9.5, pp. 425–427.
[6] H. Lorenz, et al., SU-8: a low-cost negative resist for MEMS, J. Micromech. Microeng. 7 (1997) 121–124.
[7] R.J. Jackman, et al., Microfluidic systems with on-line UV detection fabricated in photodefinable epoxy, J. Micromech. Microeng. 11 (2001) 263–269.
[8] D.S. Kim, et al., Microchannel filling flow considering surface tension effect, J. Micromech. Microeng. 12 (2002) 236–246.
[9] J. Krüger, et al., Development of a microfluidic device for fluorescence activated cell sorting, J. Micromech. Microeng. 12 (2002) 486–494.
[10] http://www.microchem.com/products/.
[11] P. Koltay, et al., Theoretical evaluation of the dispensing well plate method (DWP Part II), Sens. Actuat. A, in press.
[12] P. Koltay, et al., Microdispenser array for highly parallel and accurate liquid handling, SPIE's MICRO/MEMS 2001, Adelaide, Australia, December 2001.
[13] http://las.perkinelmer.com/.
[14] http://www.cartesiantech.com/.

Biographies

Peter Koltay studied physics at the Universities of Freiburg (Germany) and Budapest (Hungary) and obtained his PhD from the University of Freiburg 1999 for his work on solar cells and photo-voltaic modules. End of 1999 he joined the laboratory of Prof. Zengerle at the Institute for Microsystem Technology (IMTEK) of the University of Freiburg. There he is heading the pL and nL dispensers group and the group fluidic simulation. His research interests are especially related to the development of microfluidic liquid-handling devices for various life-science applications as, for example, microdispensers, modeling of free surface flows and simulation of microfluidic devices by system simulation and computational fluid dynamic simulation.

Reinhard Steger studied mechanical engineering at the Fachhochschule Karlsruhe. From 1991 to 1999 he worked at Ferromatik Milacron Maschinenbau GmbH in Malterdingen, Germany, in the field special processes in injection molding of plastic parts. From 1997 to 1999 he headed the department of application engineering of Ferromatik Milacron. In 2000 he joined the laboratory of Prof. Zengerle at the Institute of Microsystem Technology (IMTEK) for conferral of a doctorate. In the group of Prof. Zengerle he is responsible for the plastic manufacturing of microfluidic systems and works especially on the development of the dispensing well plate.

Benjamin Bohl obtained his graduate degree in civil engineering in microsystem technology in 2003 at the University of Freiburg, Germany. The topic of his diploma thesis was the evaluation of a novel fabrication technology and design optimization for a highly parallel dispensing system according to the DWP principle. Since 2003 he is working as a R&D engineer in Prof. Zengerle's laboratory for MEMS Applications at the Institute of Microsystem Technology (IMTEK). His main task is the development of technologies for rapid prototyping and production of microfluidic systems.

Roland Zengerle is the head of the Laboratory for MEMS Applications at the Institute of Microsystem Technology (IMTEK) at the University of Freiburg, Germany. Prior to that he was from 1995 to 1999 the head of the microfluidics department at the Institute for Micro and Information Technology of the Hahn-Schickard-Society (HSG-IMIT) and still all his work is done in close cooperation with the HSG-IMIT. His research is focused on microfluidics and covers topics like miniaturized and autonomous dosage systems, nanoliter and picoliter dispensing techniques, lab-on-a-chip systems, microreaction technology as well as micro and nanofluidics simulation. He co-authored more than 120 technical publications and 20 patents. He serves on the international steering committee of the IEEE-MEMS conference as well as on the technical program committee of the bi-annual Actuator conference. He is the European editor of the newly launched Springer Journal of Microfluidics and Nanofluidics.