Non-contact micro dispensing technologies for science and industry

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Abstract:
Non-contact micro dispensing technologies have turned out to be ubiquitous tools in various industries and applications over the past decades. The well-known ink-jet printing technology – to give a prominent example – has paved the way to digital printing and still plays an important role in industrial fabrication together with micro-dispensing valves used in a large variety of applications. Though, both of these technologies are wide-spread and mature, it is often disregarded that they cannot enable all applications currently sought after in science and industry. Certain applications in the life sciences, and increasingly also in industry, require dedicated non-contact dispensing technologies with specifications significantly different from ink-jet and valve technology. This article discusses the most important requirements that guide the development and application of novel non-contact dispensing technologies such as massive parallel dispensing, disposable dispensing components and high temperature dispensing devices. Selected technologies developed in the past to address such needs are reviewed.

Keywords: Non-contact printing, dispensing, droplet generation, liquid handling

Introduction

Non-contact micro dispensing and droplet based digital printing technologies such as ink-jet technology are becoming increasingly important in the context of industrial fabrication as well as for life-science applications. Common to all of these technologies is the fact that they can deliver a liquid aliquot as free flying droplet to the target without mechanical contact – hence the name non-contact technology. The specific strengths of the well-known ink-jet technology are attributed to small droplet volumes of only a few picoliters, the high printing frequency as well as the random access to any nozzle of the printhead. For a long time this made ink-jet the technology of choice for office and digital printing applications. Nowadays, ink-jet technology moves increasingly into industrial and life-science applications like fabrication of displays, organic light emitting diodes, micro arrays or even printing of living biological cells [1 – 3].

In view of the fact that ink-jet technology has been so successful in a variety of applications the question arises why are there other non-contact micro dispensing technologies needed? One could assume that making small droplets in the picoliter range – like with ink-jet – is the most difficult task and any other application requiring larger droplet volumes could be achieved by using many of the smaller droplets. However, a closer look reveals that droplet size and printing frequency constitute only a small fraction of the properties that have to be considered for the selection of the most suitable non-contact dispensing technology for a given task. For example, the capability to operate with a large variety of different liquids is a very important requirement in life-science applications, which is not met very well by ink-jet technology. In order to make an ink-jet printing process run reliably it takes a considerable amount of optimization with respect to the ink (i.e. the liquids to be printed) and the operation parameters of the printhead. In many life science applications therefore dispensing valves are used for non-contact dispensing of liquid volumes in the nanoliter to microliter range. Such valves work by discharging a liquid from a pressurized reservoir through a nozzle by opening the valve with high dynamics for very short times (~ miliseconds). Once calibrated for each liquid, such valves can typically operate with a large variety of liquids, Furthermore, many valves support also aspiration which makes it possible to take up the liquids through the nozzle to realize automatic liquid exchange – a functionality that is not supported by conventional ink-jet devices. This brief comparison between ink-jet and valve technology illustrates how important it is to consider the whole workflow that a non-contact dispensing device has to perform. It is obvious that a digital printing application has other challenges than the fully automatic assembly of biochemical assays out of a millions of different compounds. Therefore, it is of highest importance to consider the specific requirements of a given application carefully to find the most appropriate solution.

In the following sections first an overview of the most significant requirements for non-contact dispensing applications is given. Afterwards, examples of non-contact dosage methods are reviewed that have been published by the author and co-workers previously. Reference is made to the requirements and specifications that make these approaches particularly suited for the given application as well as significantly different from ink-jet or dispensing valve technology.

Non-contact dispensing requirements

Each printing, dispensing or coating application has its unique requirements in terms of the liquids and their properties, the dispensing performance that has to be achieved as well as other requirements like operating conditions or commercial considerations. For the purpose of the following discussion the most important requirements are grouped into four main categories. The examples given within each category below are by far not complete and for each application careful considerations are necessary to determine all relevant requirements.

Liquids

The material properties of the liquids to be dispensed are of course one of the main factors to be considered. The physical properties i.e. the rheology of the liquid is often described by parameters like viscosity, density, surface tension and vapour pressure for simple liquids. More complex liquids might exhibit in addition non-Newtonian behaviour or can contain particles in suspension. Such physical properties are very important to determine whether a certain liquid formulation is printable at all with a certain dispensing technology. The chemical properties of the liquids – as important as the physical ones – are determining the choice of the right materials to be used for the fabrication of a dispensing device. In many applications a dispensing technology that could work with a specific liquid in terms of its physical properties cannot be applied, if the ink chemically reacts with the involved materials, deteriorating the device and/or the printing results.

Performance

The performance of a dispensing technology is often considered in terms of the liquid volume of the produced droplets (i.e. microliter, nanoliter, picoliter or femtoliter) and by the precision and accuracy the droplets can be created with. In some applications – like digital printing for example – the volume accuracy might be less important but the droplet frequency can be crucial to achieve a certain flow rate of liquid. Further requirements are often related to the fact, whether a dispensing system operates with different liquids and how far the performance is independent of the liquid. And finally also the adjustability of the liquid volume per droplet plays an important role, if a specific volume is to be delivered accurately.

Workflow

The total workflow of the dispensing or printing process is also of high significance for the choice of a suitable technology. Whether one single liquid, a couple of well-known liquids or thousands of unknown liquids are to be handled makes a significant difference. The total number of different liquids and how often these liquids have to be exchanged, for example in a biochemical screening process, limits the amenable technologies. If liquids are to be exchanged frequently means for automated loading, cleaning or exchanging of disposable parts are required. This is even more challenging if all the liquids exhibit unknown or different properties and the performance requirements are high.

Whether a certain workflow is manageable with a specific technology at all also depends on considerations related to throughput and economy. A serial process using one or a few dispensing nozzles cannot level up with a technology working with hundreds of nozzles in parallel in terms of throughput. When applying many nozzles in parallel it is important whether these nozzles are controlled independently, or whether they dispense all at the same time to reproduce a fixed pattern given by the layout of the printhead.

As far as economy is concerned very often the dead volume i.e. the amount of liquid that inevitably remains in the dispensing device is of high importance, since it determines how much liquid is left unused. For expensive liquids – for example in pharmaceutical applications – a low dead volume can be a major requirement. On the other hand the costs of the dispensing device itself can be the crucial point, if large numbers of such device are required for a consumer application for example.

Other

Apart from the main workflow often secondary requirements have to be considered, too. In biological or medical applications often concerns about cross-contamination are raised. In some applications therefore cleaning is not admissible and all liquid contaminated parts have to be disposable and easily exchangeable. In the medical context also the materials from which a dispensing device is made of can be of high relevance; not only with respect to the interaction with the dispensing liquid, but also with respect to interaction with the human body (e.g. for implantable devices) or with respect to interference with biochemical ingredients (e.g. within biochemical assays).

Dispensing Well Plate (DWP) Technology

Modern drug discovery strives to develop new drugs through identification of potential drug candidates from a large number of different chemical compounds contained in the proprietary libraries of pharmaceutical companies. The fully automated process of experimental identification of drug-like substance is termed high throughput screening (HTS). It enables the testing of millions of chemicals per day. In HTS, the drug candidates are studied by biochemical assays modelling the targeted physiological interaction in-vitro [4]. Such tests are performed in standardized containments termed micro well plates. Today, well plates with 384 or 1536 wells on an area of about 80 x 120 mm size are handled routinely. To push the limit of HTS, assay volumes ranging from 2 µl to 5 µl are about to be miniaturized even further and the throughput of plates is continuously accelerated. Since the liquid handling i.e. filling of the well plates with reagents and compounds is usually the bottleneck, pipetting and dispensing systems are required that can handle volumes in the nanoliter range and operate in a multi-parallel fashion compatible with the standardized well plate format [5]. The dispensing well plate (DWP) presented here as an example for massive parallel liquid delivery is designed to address this issue.

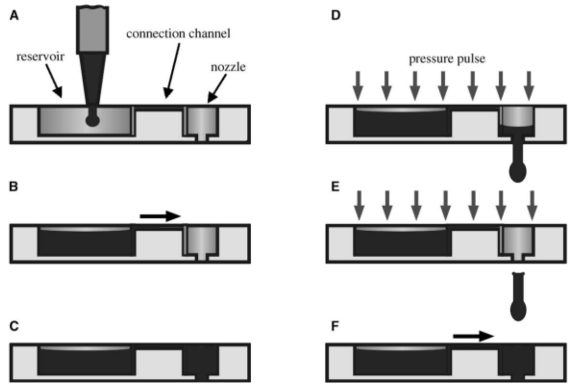

Fig. 1: *Sketch of the working principle of the DWP*

Working principle

The complete dispensing system consists of a pneumatic actuation unit driving a printhead termed DWP. The DWP consists of a number of individual dispensing units arranged very closely at conventional well plate spacing. Prototypes with 24, 96 and 384 individual units at a pitch of 4.5 mm and 2.25 mm have been realized so far using different micro-machining approaches [6]. Each dispensing unit of a DWP consists of three basic elements, which are shown in Fig. 1 and Fig. 2 in detail: a reservoir, a connection channel and a nozzle chamber.

Before operating the system, the reservoirs are filled with liquid by conventional pipetting systems. The whole DWP is then inserted into the actuation unit. The dispensing process then proceeds as illustrated in Fig. 1. Due to capillary forces, the nozzle chambers are always filled completely via the connection channels. By applying a pressure pulse to the whole upper surface of the DWP, the liquid contained in the nozzle chambers is driven out completely.

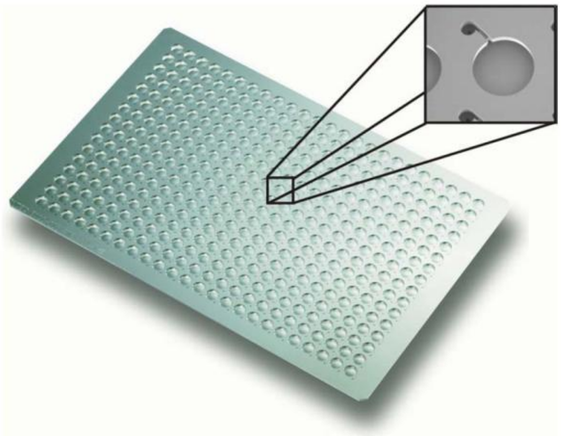

Fig. 2: *384-channel DWP made from silicon*

Because the reservoir and nozzle chamber are exposed to the same pressure head, no pressure-driven flow occurs within the connection channel during jet ejection. Thus, essentially the volume confined in the nozzle chamber is dispensed, which accounts for the high accuracy and robust performance of the technology. After switching off the driving pressure, the nozzle chambers refill again from the reservoirs by capillary forces. Multiple dispensing cycles are possible.

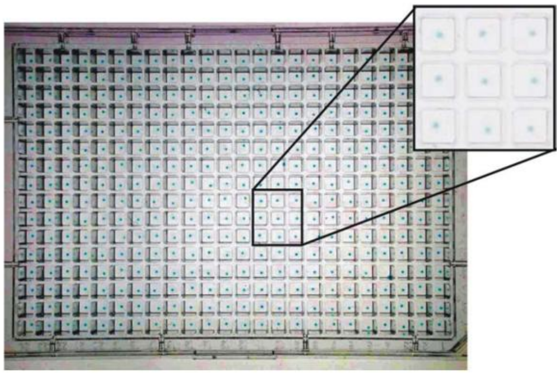

Fig. 3: *384 droplets of DMSO printed simultaneously into a micro well plate by the DWP technology.*

Experimental results & discussion

Due to the described working principle the DWP performs as a fixed-volume dispenser. In contrast to most other dispensing technologies, the dosage volume is mainly determined by the geometrical volume of the nozzle chamber. It is hardly affected by liquid properties and external parameters like pressure head and pulse duration (cf. Fig. 4). Thus, basically the machining precision of the fluidic structures — especially the nozzle chamber — determines the dispensing accuracy.

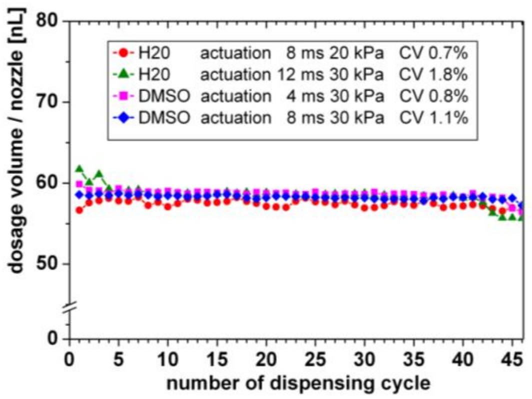

Fig. 4: *Dispensed volume per single nozzle for different liquids (water, DMSO) and actuation parameters (pressure head and pulse duration).*

TopSpot Technology

In the last decade, microarrays became a widely applied tool for genomic and proteomic analysis [7]. Today, microarrays are increasingly applied in a medical diagnostic context for molecular diagnostics or personalized medicine applications. While the DNA microarrays for genomic research (i.e. high density microarrays) usually feature ten thousands of gene sequences, diagnostic microarrays consist of only ten to hundreds of different protein or oligonucleotide bio-markers for a specific physiological condition or disease (i.e. low density micro arrays). As different as the spot numbers are the required numbers of microarrays being fabricated: For a research project ten to hundred high density microarrays might be sufficient. A diagnostic application, when applied routinely, requires thousands to millions of identical low density microarrays per year. Therefore, the production requirements for low- vs. high-density microarrays in terms of total number of spots as well as total number of printed arrays are very different.
There are many ways to fabricate microarrays [8]. A very prominent way is non-contact spotting of the oligonucleotides or proteins dissolved in liquids. The spots printed onto the substrate should be small and in close proximity, to enable fast and sensitive analysis. For high-throughput microarray production it is therefore desirable to spot many different liquids simultaneously. Similar like with the DWP presented in the previous section, but at much lower volumes and in form of an array with a small pitch (typically between 50 to 500 µm). A technology fitting to these requirements is the TopSpot technology.

Working principle

The basic elements of the TopSpot technology as presented previously [9] are a micromachined printhead made from silicon and Pyrex glass, an elastomer sheet and a piston. The elastomer sheet is placed between the piston and the printhead on top of the nozzle array. The piston is actuated by a piezo stack actuator enabling displacement of the elastomer up to 15 µm. The movement of the piston thus creates, by the elastomer sheet, a direct displacement of the liquid contained in the nozzles which causes droplets of 300 to 1500 pl to be ejected from all nozzles simultaneously. The filling of the printhead takes place through capillary forces: Surface tension transports the liquid filled into each reservoir to the corresponding nozzle. Also the refill after droplet ejection is accomplished by capillary forces similar to the DWP and ink-jet devices.

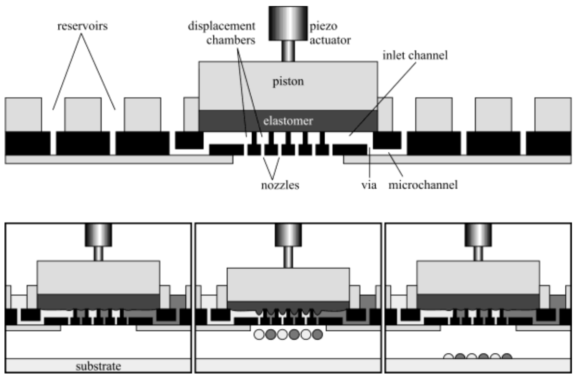

Fig. 5: *Sketch of the TopSpot printhead and working principle.*

Experimental results & discussion

In comparison to the DWP the droplet volume produced by the TopSpot method is not just significantly smaller but can be controlled by the actuation parameters (cf. Fig. 6). This enables an adjustable droplet volume in contrast to the fixed volume of the DWP. Another difference provided by the TopSpot technology is the format change of the print pattern from a large pitch of the reservoirs (4.5 mm) to a small pitch (500 µm) of the printed droplet array. This feature enables less automation since one low density micro array can be printed in "one shot". Medium density micro arrays can be created by repeated dispenses from printheads loaded with different liquids. Smaller pitches are feasible by interlaced printing (e.g. 250 µm) as well.

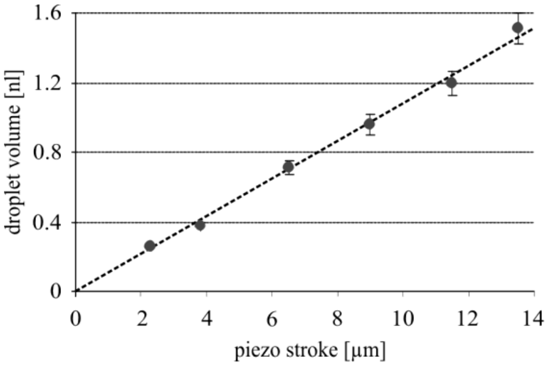

Fig. 6: Droplet volume as a function of piezo stroke for the TopSpot technology.

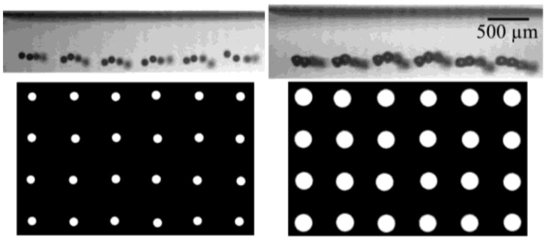

Fig. 7: Droplets in flight (top) and corresponding printed array (bottom) for small resp. large droplets.

LotSpot Technology

A variation of the presented TopSpot technology – referred to as LotSpot technology – can be applied for printing of hot liquid metal for industrial applications [10]. In microelectronics, for example, the creation of small solder balls on microelectronic chips (bumping) is one production step that occurs in various contexts and that requires high throughput [11].

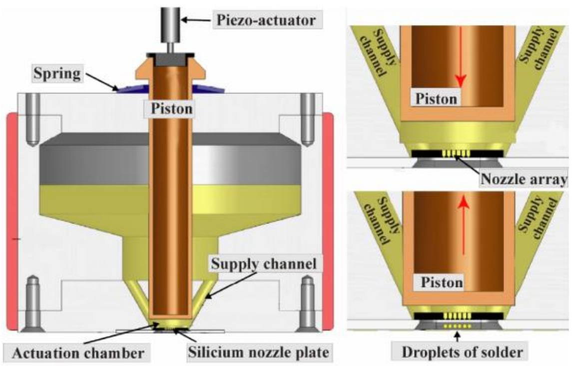

Fig. 8: Sketch of the LotSpot printhead illustrating thermal decoupling of the piezo actuator from the nozzle plate and the supply form a single reservoir.

Working principle

The LotSpot technology was made amenable for high temperature applications by a heated printhead and a thermally isolated piezostack actuator (cf. Fig. 8). Otherwise, the configuration is quite similar to the TopSpot technology. However, in detail there are some considerable differences: First of all there is only one type of liquid used in the LotSpot printhead. Therefore, no micro channels connecting the nozzles with individual reservoirs are required, but the molten metal is directly available from one large reservoir above the nozzle array. Through this reservoir the actuating piston is directly immersed into the liquid as shown in Fig. 8. Thus, no elastomer is required between piston and nozzle for conversion of the mechanical displacement into liquid flow.

Experimental results & discussion

It has been shown in experiments that the droplets produced by the LotSpot technology can be adjusted in the range between 0.4 and 1 nl volume. By variation of the temperature of the solder between 290 and 340°C the volume as well as the shape of the solidified structures on the substrate could be influenced. Thus, parameter optimization for specific applications can be performed if necessary.

In the presented example nozzle plates with 4 x 4 nozzles at a pitch of 500 µm where used (cf. Fig. 9). But of course nozzles arrays corresponding to a specific chip layout can also be realized for direct bumping of a complete die. In contrast to the other technologies presented before, the main challenge here was not the large number of different liquids, but the high operating temperatures to be achieved. Temperatures up to 340°C have been demonstrated that cannot be achieved by conventional ink-jet devices due to the fact that the Curie-Temperature of the piezos would be exceeded.

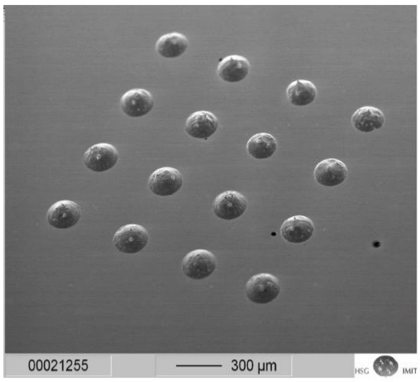

Fig. 9: Micrograph of a printed solder array on a gold surface.

Discussion

The technologies presented as examples provide massive parallel dispensing with high accuracy and precision, which makes them particularly well suited for high-throughput applications. In contrast to ink-jet technology on the one hand no digital printing is support i.e. the nozzles cannot be triggered individually, but all nozzles are dispensed simultaneously. Thus, the printed pattern is fixed by the printhead design. On the other hand a much larger number of different liquids can be handled within in one printhead compared to ink-jet devices. For the DWP and TopSpot technology printheads with 384, 96 and 24 different liquids have been realized so far. As far as the LotSpot technology is concerned the main difference to conventional ink-jet-devices is that through the thermal isolation of the piezo stack actuator the LotSpot technology can operate at much higher temperatures, enabling the printing of liquid metals. So far, maximum temperatures of 340°C have been realized in experiments. Such elevated temperatures cannot be achieved with conventional ink-jet devices where the piezo actuators are not thermally isolated and must not be heated above their Curie-Temperature.

Apart from the massive parallel dispensing capability there are several other features provided by the individual technologies presented as examples that can be of significance in selected applications. If for example a consistent dispensing performance with different liquids is needed, the DWP technology is particularly well suited. Due to the definition of the dispense volume by the micromachined nozzle, different liquids can be dispensed with the same parameters consistently. However, if precisely adjustable droplet volumes are required other technologies like for example the TopSpot or LotSpot technology are better suited. Both of these technologies exhibit an adjustable droplet volume that can be controlled by the piezo actuator. Because the piezo stack actuator creates much larger displacements than the single layer piezo actuators usually applied in ink-jet devices, the range of liquid viscosities as well as the range of attainable droplet volumes is much larger for these technologies compared to conventional ink-jet devices.

Another specific feature provided by the TopSpot and LotSpot technology is the fixed print pattern (i.e. the array layout) pre-defined in the printhead. This enables to replicate this pattern much faster compared to the situation where several dispensing devices are moved by automation equipment to assemble the printed pattern each time again from a number of individual dispenses. A feature that is particularly important for high throughput applications.

Finally, one feature is common to all of the presented technologies: In contrast to most other non-contact dispensing technologies the actuation mechanism is not part of the printhead itself. All liquid contaminated parts can be removed from the actuator and – if required for safety reasons – be disposed, while the actuator is re-used again. Considering the printheads as disposable parts is of course only possible, if the fabrication costs for the printheads are sufficiently small like for example enabled by injection moulding or for small size silicon parts.

Obviously, the presented examples mainly stress the requirement of massive parallel dispensing which is essential for high throughput applications. But of course there are other applications where the focus might be more on the cross contamination free dispensing with disposable components, printing of liquids with challenging rheology or generating droplets under harsh ambient conditions, etc. To satisfy such requirements the research and development of novel non-contact dispensing technologies as well as fabrication technologies to manufacture dispensing devices from various materials will certainly also continue in the future.

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