Dispensing Well Plate: A Highly Parallel Nanoliter Liquid Handling Device for HTS

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Abstract
Pharmaceutical research experiences an increasing need for highly parallel dispensing technologies to speed up drug development. For testing new compounds in well plates about 1,000 dispensing cycles per minute can be handled today. In order to improve this throughput by a factor 10 to 100 we developed the "Dispensing Well Plate" (DWP^{TM}) [1, 2]. The DWP system is able to deliver a fixed volume of up to 1,536 different liquids simultaneously and contact free into micro well plates or onto flat substrates. The DWP device consists of individual microstructured dispensing units arrayed in the format of a standard micro well plate (approx. 81 x 123 mm). Each dispensing unit comprises of three basic elements: a reservoir, a connection channel and a nozzle (figure 1,2). The device is operated by a simple pneumatic actuation unit, which applies a pressure pulse on the whole upper surface of the plate to eject all nozzles simultaneously. Hereby the dispensed volume is determined by the geometric volume of the nozzle. The dosage volume can be adapted in the range of 10 nL to 1,000 nL by appropriate design of the DWP.

In this paper we present for the first time a full size DWP-prototype with 384 individual dispensing units compatible to the 384 well plate standard. DWP dispensers have been fabricated by high-speed micro milling in plastic materials like for example COC (figure 1) and also by lithographic techniques in epoxy material (SU-8). The achieved fabrication tolerances of less than 5 µm result in an excellent dispensing performance of the system. A reproducibility of 2-5% and a homogeneity within individual droplet arrays of about 5% (figure 3) has been measured. We found a viscosity independent performance for liquids in the range from 1 to 5 mPas.

In the final paper the DWP working principle will be briefly presented along with latest results obtained in 384-well plates. The dispensing accuracy of the various prototypes in this format is addressed by fluorometric measurements. Furthermore the applicability of the DWP dispensing technology within HTS and the related miniaturization potential is demonstrated by performing miniaturized kinase assays. In this context different configurations of the DWP have been applied for compound reformatting (dosage volume 50 nL) as well as for bulk reagent dispensing (dosage volume 1000 nL). Finally also the possible use of DWPs as storage plates will be briefly discussed.

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References

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[2] P. Koltay et al; "Dispensing Well Plate (DWP): A highly integrated nanoliter dispenser dispensing system"; Proc. Transducers 2003, Boston, pp. 16 -19

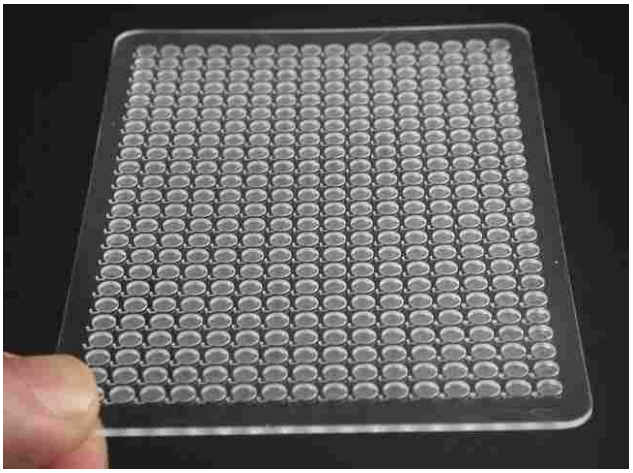

Figure 1: Photograph of a 384-unit DWP made of COC (size 120x80 mm²; pitch: 4.5 mm).

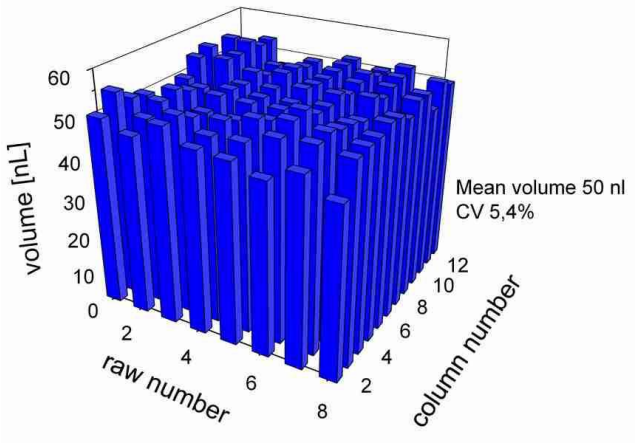

Figure 3: Volume distribution inside the well plate. (Measurements have been carried out using a DWP prototype with 96 wells, a Wallac Victor^2 plate reader and an Europium label (0.36 µMol/L emitting at 616 nm) in DMSO

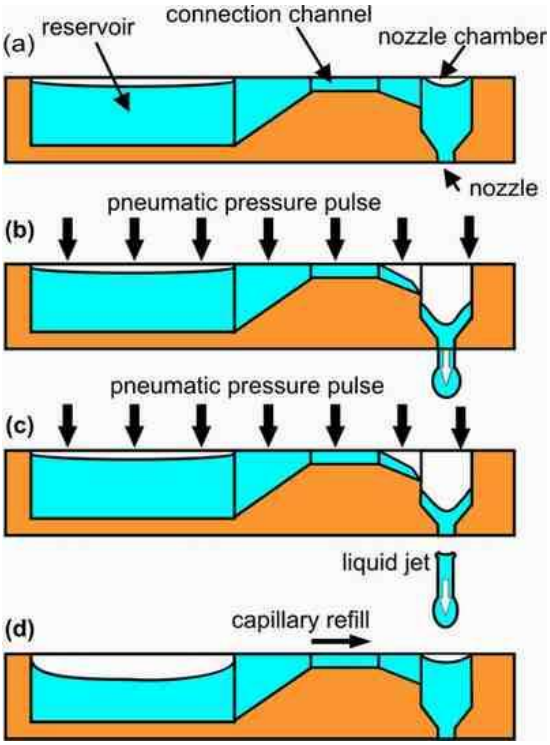

Figure 2: DWP Dispensing process: a) basic elements b) Jet ejection by pneumatic actuation c) dispensed volume defined by volume of nozzle chamber d) refilling by capillary forces when pneumatic pressure turned off