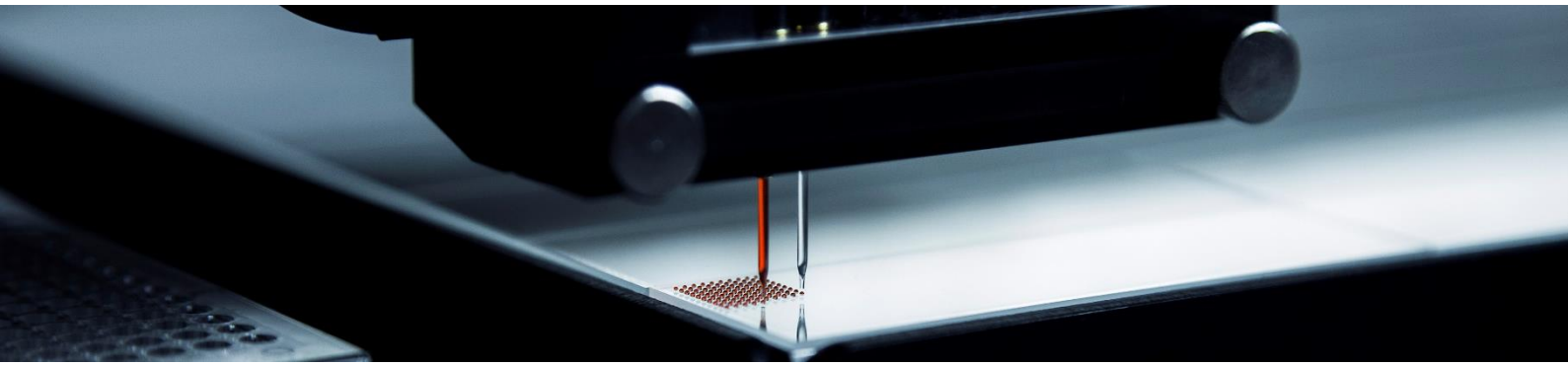

sciPULSE ULTRA LOW VOLUME - Dispensing of small droplets in the range of 18 -180 pL

Abstract

SCIENION's sciFLEXARRAYER platforms are equipped with Piezoelectric Dispense Capillaries (PDCs) that enable dispensing of low volumes for miniaturized applications such as microarrays or biosensors. Here we show that sciPULSE ULTRA LOW VOLUME, a hardware device combined with a specific software package and compatible with all sciFLEXARRAYERs, enables the reduction of drop volume to below 20 pL and the decrease in spot diameters. This is of special interest for miniaturization and multiplexing of diagnostic applications to optimize costs, sensitivity and speed.

Introduction

SCIENION's core technology sciDROP PICO, implemented in the sciFLEXARRAYER precision dispensing platforms, is based on piezo-driven pulses on an inert glass capillary for accurate and precise droplet deposition under various conditions. When an electrical voltage is applied to the integrated piezoelectric materials, the electrical energy is converted into mechanical energy. In the sciFLEXARRAYER platforms, Piezoelectric Dispense Capillaries (PDCs) transmit the transfer of the mechanical energy to the fluid inside the PDC as a defined wave function. This results in a pressure wave that oscillates in the fluid followed by interference and a drop will be displayed out of the PDC orifice.
The size and shape of the generated droplets depend on many different factors such as the size and the individual parameters of each PDC, including voltage, pulse and frequency. Besides the PDC parameters, the stability of the droplet is influenced by the viscosity, surface tension or density of the fluid. The correct adjustment of the spotting parameters of different sample types is often time-consuming and requires experimental experience. To overcome high development costs due to time consuming implementation of protocols, SCIENION offers the sciPULSE solution.

With the standard settings of the sciFLEX software, dispensing of droplets with volumes from 200 pL to 800 pL (Figure 1) is achieved. For dispensing of challenging samples as well as the reduction of drop volumes below 200 pL, the sciFLEXARRAYER solution sciPULSE is applied. sciPULSE is a specific hardware device including software that enables changing the setup of the standard sciFLEX software. Two sciPULSE software packages exist: sciPULSE LOW VOLUME (see also application note sciPULSE LOW VOLUME) for the generation of droplets between ~ 150 - 220 pL and sciPULSE ULTRA LOW VOLUME for the dispensing of droplets below ~ 180 pL to as little as 18 pL (Figure 1).

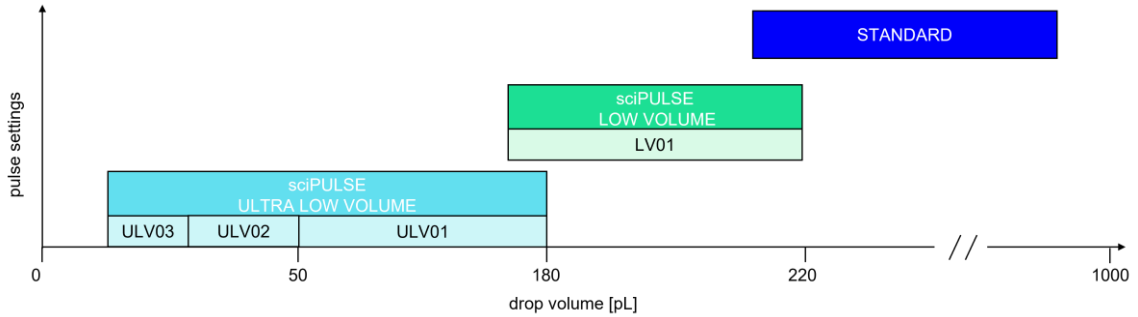

Figure 1 Overview of achievable drop volumes with standard pulse, sciPULSE LOW VOLUME and sciPULSE ULTRA LOW VOLUME pulse. The sciFLEX software can be operated with standard settings (dark blue) and lead to the generation of droplets between 200 – 800* pL. The sciPULSE LOW VOLUME (green) including the LOW VOLUME (LV01) pulse facilitates dispensing below 220 pL. The sciPULSE ULTRA LOW VOLUME application package (light blue) enables the generation of droplets in the volume range of 18 - 180 pL depending on the used pulse shape ULTRA LOW VOLUME (ULV01-03). ***Please note** that exact achievable drop volumes depend on many parameters, such as PDC size, sample type and configuration.

Here we show that the sciFLEXARRAYER solution sciPULSE ULTRA LOW VOLUME facilitates the adjustment of the optimal PDC parameters for the generation of droplets between 18 – 180 pL.

Importantly, sciPULSE ULTRA LOW VOLUME can be used for miniaturized applications to reduce droplet volumes and spot sizes, as it generates droplets as little as 18 pL and spot diameters below 30 µm with the PDC 60 that normally interacts in the volume range of 220 – 300 pL (Table 2).

Materials and methods

Drop formation with standard pulse

SCIENION offers different PDC sizes to achieve specific drop volumes with standard settings that are shown in Table 1. Typical drop volumes range from 300 pL to 500 pL, which lead to spot diameters of 130 µm to 250 µm depending on the surface wettability of the substrates and the spotting samples. For smaller sample volumes, reduced spot diameters and challenging samples the sciPULSE application packages can be integrated into the sciFLEXARRAYER platforms.

Table 1 PDC sizes and correlating drop volume range with standard software settings

Size	Volume range [pL]
PDC 60	220 - 300
PDC 70	300 - 360
PDC 80	360 - 440
PDC 90	440 - 520

Applying sciPULSE ULTRA LOW VOLUME

The sciPULSE ULTRA LOW VOLUME application package in the sciFLEX software allows the generation of droplets between 18 – 180 pL with SCIENION's PDCs.

The setup of PDC consists of a few easy steps:

1) In the Nozzle Setup Tab of the sciFLEX software, the sciPULSE button is found
2) The pulse list opens by clicking the sciPULSE button
3) Select the desired pulse shape "ULV01", "ULV02" or "ULV03" and press send
4) Depending on the selected sciPULSE pulse shape decrease the initial Voltage [V] by:
    - 35% ± 10% for sciPULSE "ULV01" to dispense drop volumes of 50 – 180 pL
    - 50% ± 10% for sciPULSE "ULV02" to dispense drop volumes of 30 – 50 pL
    - 50% ± 10% for sciPULSE "ULV03" to dispense drop volumes of 18 – 30 pL

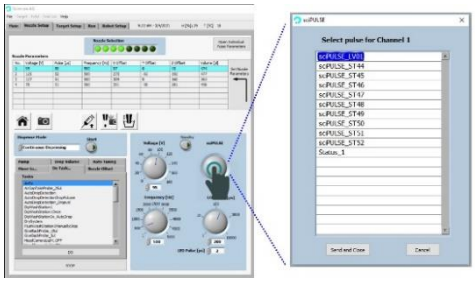

Figure 2. Nozzle Setup tab of the sciFLEX software and pulse list

Results and discussion

Drop Volume can be significantly reduced using sciPULSE ULTRA LOW VOLUME (ULV)

To compare how much volume reduction per PDC size can be achieved using standard, ULV01, ULV02 and ULV03 pulse shapes were loaded in the sciFLEX software with either a PDC 60,70,80 or 90. In Figure 3 exemplified results are shown: Due to the different opening diameter of every PDC size, ULV2 and ULV3 pulse shapes can only be applied with a PDC 60 and/or 70 (Figure 3). In general, the utilization of ULV01, ULV02 and ULV03 resulted in a drastic drop volume reduction compared to applying standard software settings of the individual PDCs. For ULV01 pulse shape, a volume reduction of more than 60% for every applied PDC could be achieved. Applying ULV2 resulted in drop volumes below 50 pL and a volume reduction of more than 80 % with the PDC 60 and 70. The ULV03 pulse shape led to the most drastic effects with > 90% volume reduction and drop volumes below 30 pL when used with the PDC 60.

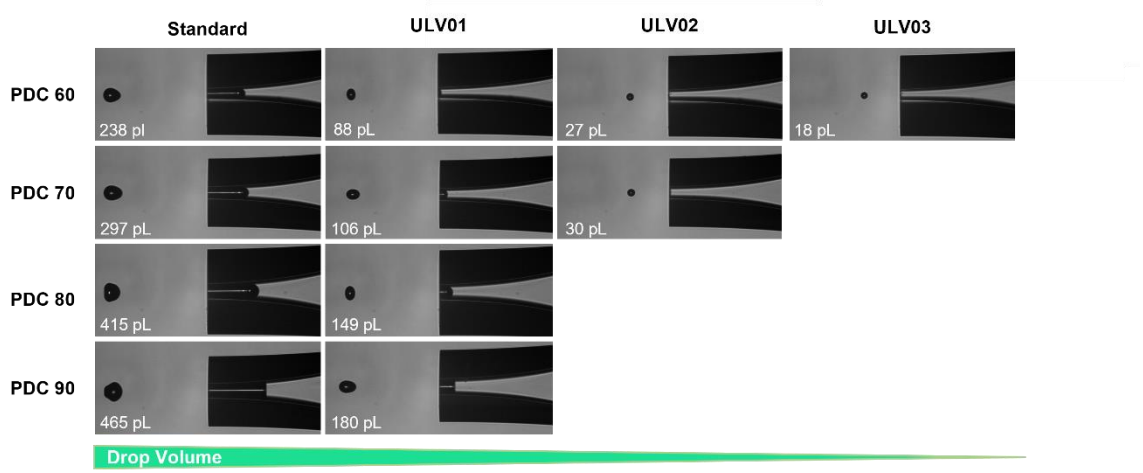

Figure 3 Examples of achievable drop volumes applying sciPULSE ULTRA LOW VOLUME pulse shapes ULV01, ULV02 and ULV03 with different PDC sizes. For every PDC size, the dispended drop volume can be reduced by applying at least one of pulse shapes of the sciPULSE ULTRA LOW VOLUME packages. Exemplified results are shown. To validate the results in total 17 PDC 60, 9 PDC 70, 13 PDC 80, and 7 PDC 90 were tested. Different voltages were applied to determine the achievable volume range of each individual PDC.

Spot diameters can be significantly decreased using sciPULSE ULTRA LOW VOLUME

Aside from the reduction of total printed material, miniaturization may also require the deposition of reagents onto very small areas such as for printing onto defined sensor structures, covering sensing electrodes or filling microwells. Here, a small drop volume and respectively a small spot diameter is of advantage. Applying sciPULSE ULTRA LOW VOLUME allows arrays to be much narrower. Due to the reduced drop volumes also the spot diameter can be reduced significantly. Therefore, the achievable spot diameters for different drop volumes where compared. Using a PDC 60 with standard pulse or ULV01, ULV02 or ULV03 pulse shapes, 20x20 arrays with a defined dot pitch of 100 µm were printed. With standard settings, the array could not be printed because the spots merged due to the high drop volumes applied in a limited space. Using ULV01, ULV02 or ULV03 the drop volumes as well as the spot diameters could be reduced to as low as 24 µm, so

that 20x20 arrays could be printed.
In summary, sciPULSE ULTRA LOW VOLUME enables the possibility to increase the number of reaction sites or replicates in a microarray to extend multiplexing capacities.

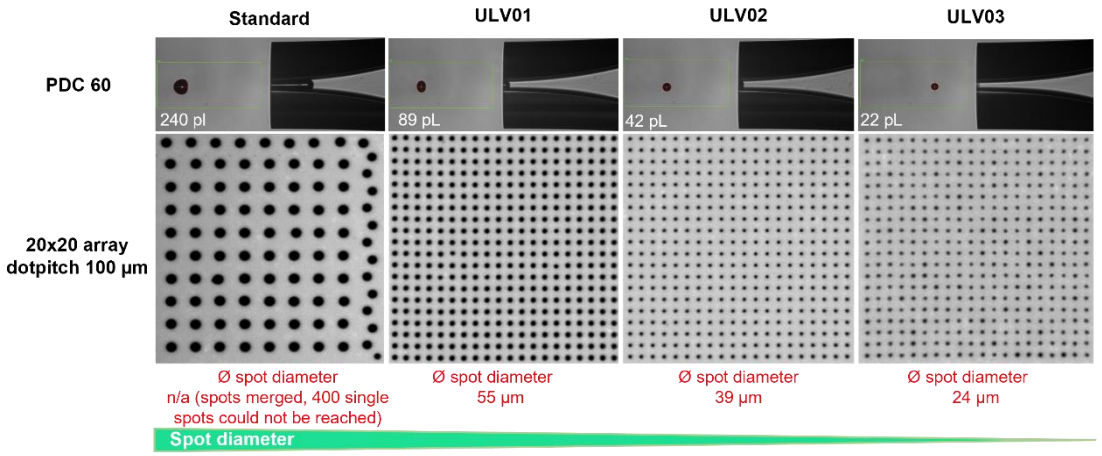

Figure 4 Comparison of printing with standard pulse and sciPULSE ULTRA LOW VOLUME. A 20x20 array with a dot pitch of 100 µm was printed on a hydrophobic glass slide. Due to the narrow dot pitch the spots merge with standard setup whereas applying sciPULSE ULTRA LOW VOLUME leads to a uniform array.

sciPULSE ULTRA LOW VOLUME is universally applicable in all SCIENION'S dispensing platforms

The sciPULSE ULTRA LOW VOLUME is applicable in all dispensing platforms offered by SCIENION including the sciFLEXARRAYER S3, S12, SX, S100 as well as Cellenion's single cell dispensing platform cellenONE® (data not shown).

Conclusion and future direction

- sciPULSE is an easy solution to go beyond the standard parameters such as droplet volumes, spot diameter or viscosity of the currently available PDCs.
- Using sciPULSE ULTRA LOW VOLUME enables the reduction of droplet volumes to 18 -180 pL with SCIENION's PDC 60,70, 80 or 90
- Using the sciPULSE ULTRA LOW VOLUME enables the reduction of spot diameters down to 24 µm on an optimized target surface
- Smaller drop volumes and spot diameter allow for the increased number of spots on a certain area with regards to multiplex applications

The sciPULSE ULTRA LOW VOLUME is one of the currently available application packages for the generation of reduced drop volumes. In the future more sciPULSE application packages will be released that enable the dispensing of challenging samples that can't be facilitated by the standard settings of the sciFLEX software such as high viscosity or organic solvents.

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