384 Channel Parallel Nanoliter/Microliter Non-Contact Induction Based Fluidics with Millisecond Dispensing onto MALDI Plates and into Array Tape™

Terry Rusch – Douglas Scientific, Alexandria, MN

Andrew D. Sauter Jr., Andrew D. Sauter III – Nanoliter LLC, Henderson, NV

Introduction

The ability to perform non-contact, multichannel dispense operations in the low microliter and nanoliter volume range is highly desired in high throughput laboratory operations. The lower volume parallel dispense translates directly into cost savings per data point. This study was conducted to demonstrate the feasibility of low volume non-contact dispense using the Nanoliter Wave induction based fluidics (IBF) technology in conjunction with the Douglas Scientific high throughput Nexar™ fluid handling instrument and Array Tape™ platform.

The initial study results presented here demonstrate for the first time the viability of these technologies to provide an economical, non-contact, low volume, 384 channel parallel fluid dispense. Based upon our research, we believe this to the be the first time that 384 channel parallel non-contact, millisecond nL, µL dispensing has been reported.

Background

Induction based fluidics (IBF) was developed to dispense, treat, and otherwise manipulate small volume liquids in a non-contact format. This technology has proven to be adaptable to countless fluid handling applications and volumes from microliter to picoliter have been successfully managed and delivered. IBF uses electric fields to launch, direct and optionally measure liquids fired at targets of all types. IBF can transform syringes, pipettes, pumps and LC's into non-touch parallel nL dispensers or instrument introduction devices. IBF has been shown to dispense liquids to/from humans, in a non dispersive manner and to fly even viscous liquids up! Nanoliter LLC is the leader in IBF with many patents surrounding the technology. They have developed and successfully used their CoolWave™ IBF technology to demonstrate major (100x) increases in MALDI analysis and precision for proteins, peptides, and synthetic polymers.

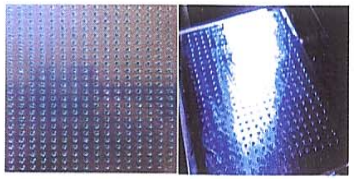
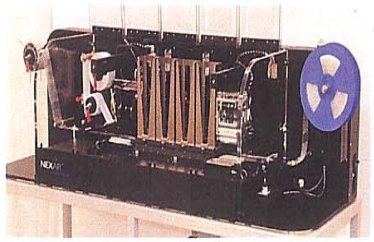


Figure 1. 300nL and 250nL - 384 Channel Dispenses into Array Tape™ and onto MALDI plate shot in 1 ms

Methods

The equipment used to conduct this study was specifically selected to meet the desired goals of high throughput, non-contact, low volume, multichannel dispensing. To meet the desired requirement for both high throughput and multichannel dispensing we selected the Douglas Scientific Array Tape™ platform including their Nexar™ fluid handling.system (Figure 2).

Figure 2. Nexar Dispensing Instrument



The Nexar system was equipped with a Roche 384 tip positive displacement dispensing head in a positioning rail module. This system has recently demonstrated significant gains in screening volumes and is being positioned as a next generation high throughput screening solution. The Array Tape platform allows for continuous in-line processing in a very flexible and cost effective medium. The benefits that the tape provides as compared to a standard 384 well microtiter plate include: cost, well volume, reduced thermal mass, and reduced waste. (Figures 3 and 4)

Figure 3. Microtiter Array Tape™

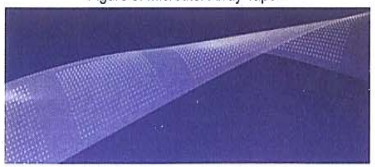
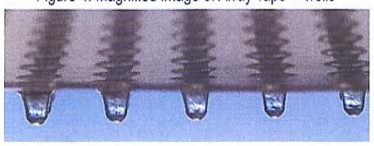


Figure 4. Magnified image of Array Tape™ wells



The Nanoliter Wave technology using induction based fluidics (IBF) was selected as the enabling technology to allow for rapid multichannel non-contact dispensing. The standard electronics for the IBF dispensing was upgraded to handle the configuration. Nanoliter's IBF technology was appended to the Nexar™ instrument at the Nanoliter facility. Standard 10µL CyBio tips trays where used with the Roche head for dispensing. The 25µL CyBio tips were also tested. Dispensing was tested at a range of volumes in the microliter to nanoliter range. Samples were dispensed onto both MALDI plates (Figure 5) and Array Tape™ (Figure 6). These new data and lower volume (50nL and less) dispenses are currently being assessed for accuracy and precision in collaboration with National Instrument. This is believed to be the first time that 384 channel parallel nL and µL dispensing has been presented.

Figure 5. 384 channel non-contact 2µL dispense on to MALDI Plate

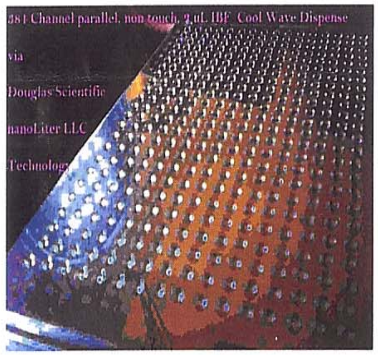
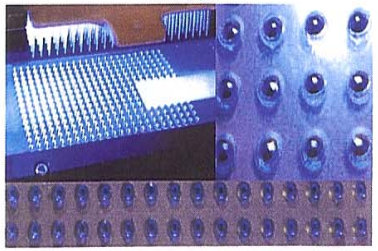


Figure 6. 384 channel non-contact parallel dispensing into Array Tape™



Results and Discussion

The speed of parallel dispense operations for analytical assays has clear benefits. This initial development and demonstration of 384 channel non-contact dispensing in the microliter and nanoliter range shows the potential of the combined system to provide the desired result. The new electronics from Nanoliter provided the increased capability needed to perform the parallel 384 channel non-contact dispensing using IBF with a single energy source. The IBF modifications to the Nexar system allowed for non-contact dispensing in the µL and nL range with good to excellent results down to 100nL. IBF is capable of smaller volume dispensing through the modification of other dispense system variables, most notably dispense tip design. The 10µL tips used dispensed well at the higher volumes but are not designed for the smaller nanoliter volumes. There are many configuration variables that could be improved upon to lower the volume dispense. Future development is required to integrate the full Nexar liquid handling functionality with the added IBF electronics.

Conclusion

This study was successful in demonstrating for the first time rapid, low volume, non-contact, 384 channel parallel dispensing.

Non-Contact, parallel dispenses in volumes ranging from 25µL to 100nL were successfully performed in the millisecond time frame.

These initial feasibility tests using IBF and the Nexar fluid handler provide the necessary information to further develop a highly economical 384 channel non-contact parallel dispensing system for high throughput laboratory automation.

References

1. T. Tu, A. D. Sauter, Jr., A. D. Sauter III and M.L. Gross, Improving Intensity and Sensitivity of MALDI Signals by Nanoliter Volume Spotting, poster session presented at ASMS 2007, Indianapolis, IN, June 2007. Also, *Journal of the American Society of Mass Spectroscopy* 2008, 19, 1086-1090
2. Hilker, B.; Clifford, K. J., A. D. Sauter Jr., A.D. Sauter III; A.D.; Gauthier, T.; Harmon, J.P. Electric Field Enhanced Sample Preparation for Synthetic Polymer MALDI-TOF Mass Spectrometry via Induction Based Fluidics (IBF). Accepted for publication in Polymer 12/09. Also see J. Harmon ASMS 2009.
3. Brent Hilker, Kevin J. Clifford, Andrew D. Sauter Jr, Andrew D. Sauter III, and Julie P. Harmon,. Measuring Charge For The Real Time Induction Based Fluidic MALDI Dispense Event Verification and Nanoliter Volume Determination. Accepted JASMS, 2/09.
4. "Capillary flow as the cause of ring stains from dried liquid drops" Robert D. Deegan, Olgica Bakajin,Todd F. Dupont, Greg Huber, Sidney R. Nagel, and Thomas A. Witten, in Nature 389, 827 (1997).
5. US Patent 6,149,852 and four pending patents.