High throughput nanoliter pipetting with the MCA 384

Scientists working in the Screening Unit at the Institute for Molecular Pharmacology in Germany are finding the low volume pipetting capability of the MultiChannel Arm™ 384 beneficial for the investigation of siRNAs and small molecule compound screening.

LEIBNIZ-INSTITUT FÜR MOLEKULARE PHARMAKOLOGIE

The Leibniz-Institute for Molecular Pharmacology (FMP), based in Berlin, Germany, is an academic center offering open access RNAi and small molecule compound screening. FMP's Screening Unit has automated these processes on a Freedom EVO® platform, taking advantage of the low volume pipetting capability of the MultiChannel Arm (MCA) 384. Martin Neuenschwander, automation scientist at FMP, explained: "We have been using laboratory automation for small molecule screens for several years, and have four Freedom EVO 200 platforms equipped with a variety of liquid handling arms, including MCA 96, MCA 384 and eight-channel Liquid Handling (LiHa) Arms, as well as Robotic Manipulator (RoMa) Arms. For compound screening, material is often limited, and it is also important to keep the DMSO concentration below 1 %. We needed to pipette volumes down to 300 nl, and invested in a new Freedom EVO platform optimized for this work."

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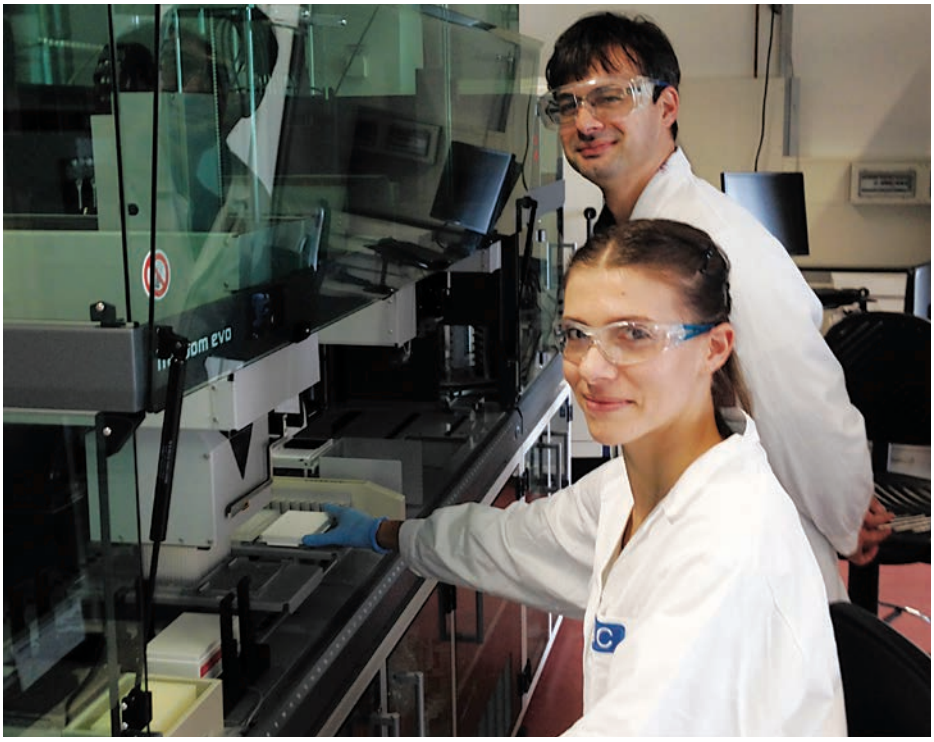
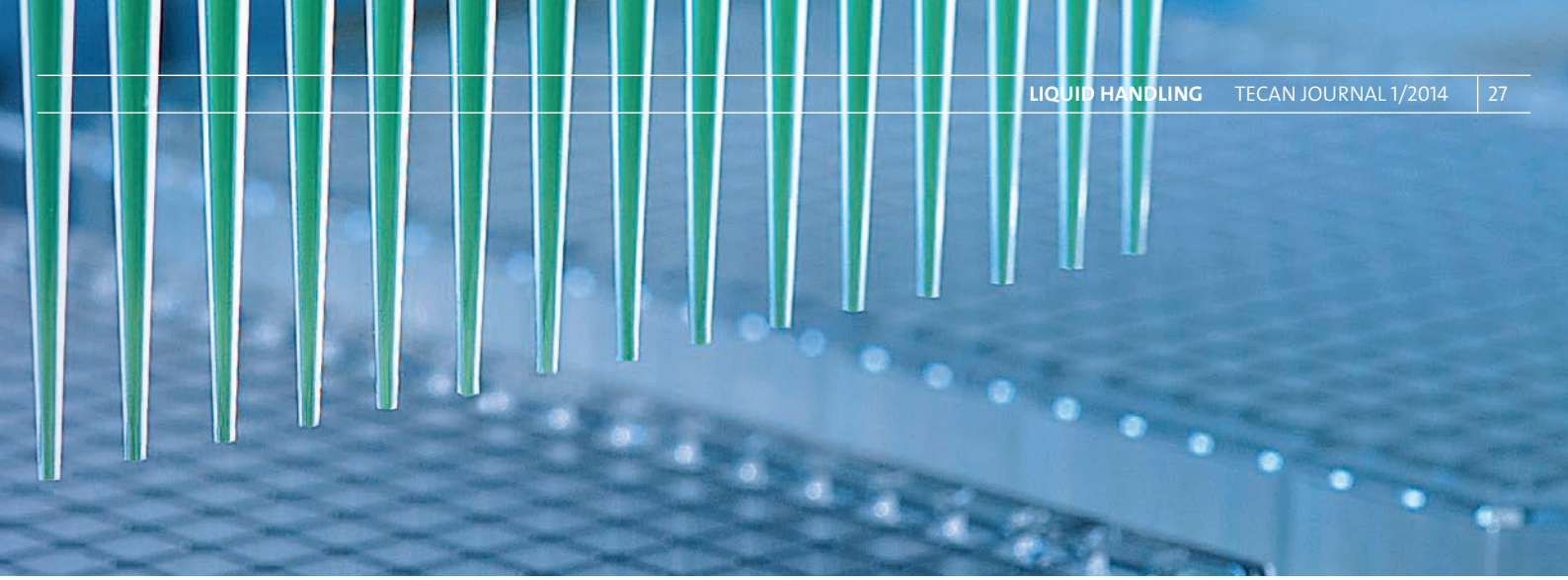


Katina Lazarow and Martin Neuenschwander with FMP's Freedom EVO workstation

"The new workstation is equipped with an MCA 384, a Carousel LPT 220 EVO™, a wash station, a HydroSpeed™ plate washer and a Safire²™ microplate reader, as well as two small LiCONiC incubators. Using the 15 µl tips, we performed some experiments pipetting two different colored dyes in DMSO, adjusting the liquid classes as necessary to achieve linearity down to 300 nl. In a second study, these adjusted liquid classes were used to demonstrate pipetting reproducibility, taking a fresh tip box for each experiment. These studies showed the MCA 384 can accurately and reproducibly pipette down to 300 nl without the need to use any special techniques, allowing us to reduce our assay volumes to just 30 µl while still maintaining a DMSO concentration of less than 1 %."

Martin continued: "Another big advantage of the system is that we can perform serial dilutions within individual plates, which is ideal for IC_{50} determinations. With our previous system, we had to copy the entire plate, performing dilutions across several different plates. With the MCA 384, we have the capability to select just one column, allowing us to perform dilutions in the same plate. We can do everything with just two plates now, whereas before we always had at least 20 to measure. In addition, the layout of the Freedom EVO workdeck is easily reconfigured in house, enabling us to add additional carriers to meet future needs – for example to accommodate 1,536-well plates – or to integrate other modules such as readers or incubators into the workstation. It gives us so much more flexibility."

Martin added: "We control almost everything from Freedom EVOware®, which is perfect for rapid, high throughput screening using fairly simple worklists, while still allowing the more complex programming for assays where the timing is crucial. In addition, we can carry



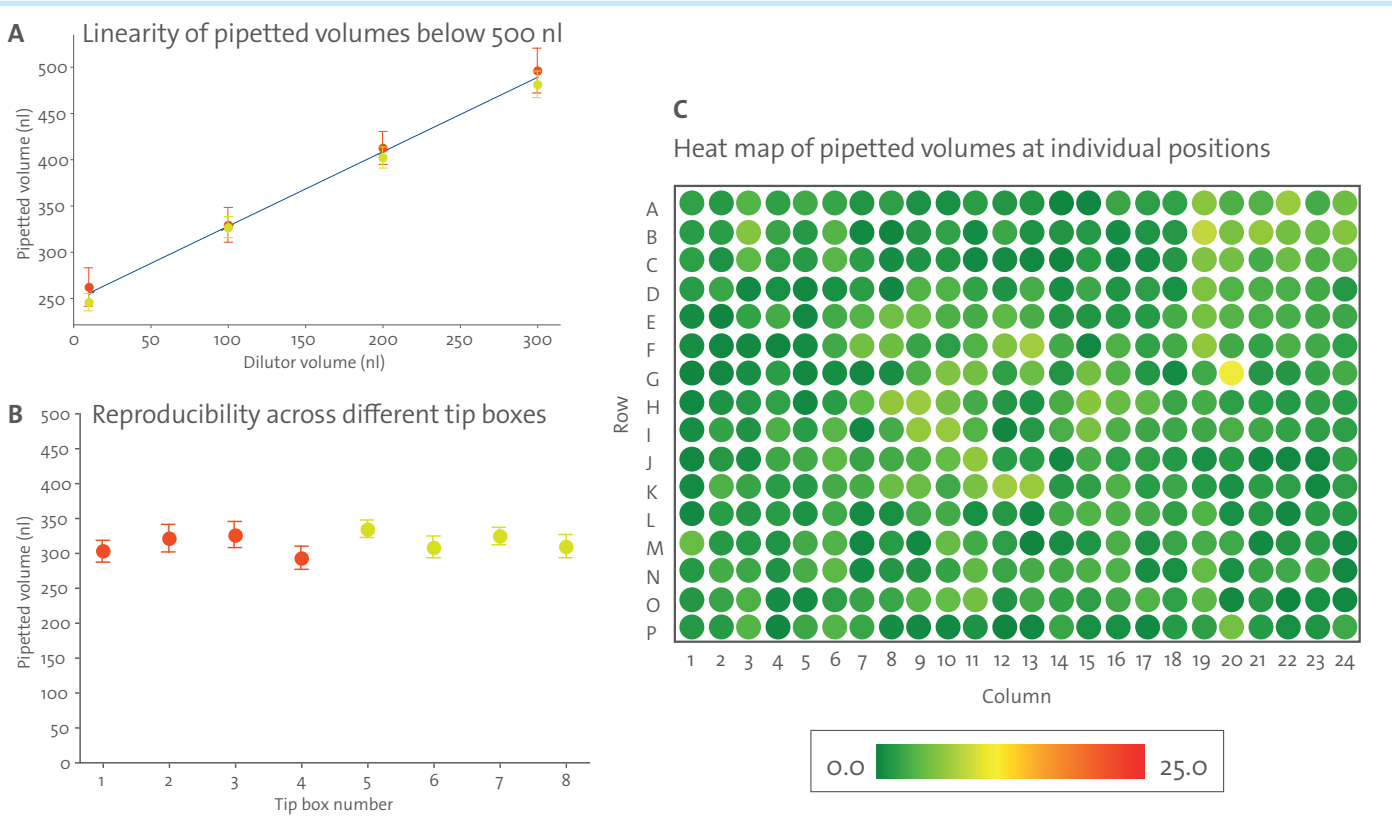
out longer experiments needing overnight measurements, for example cell-based assays monitoring fluorescence intensity, ensuring that there are no gaps in the data."

Katina Lazarow, a scientist from the RNAi screening core facility, added: "The Screening Unit is also responsible for RNAi screening, and has two libraries of siRNAs stored in 384-well microplates. The new Freedom EVO is also used to perform transfections for these screens, which involves transferring the siRNAs into assay plates, adding the cells and, at a later date, changing the medium. The system also prepares the plates for reading, removing the medium and adding other solutions as necessary. Previously, we used fixed tips for all our liquid handling protocols, but disposable tips are more suitable for siRNA and semi-sterile processes. We are able to use the MCA 384 with 125 µl disposable filter tips to pipette 4 µl volumes, and have demonstrated a CV of below 1 % with good reproducibility across the plate. The MCA is also particularly suitable for assays where cells do not adhere well. By pipetting very slowly, we can ensure that the cells are not disturbed, which is critical for microscopy applications."

"I only began using the Freedom EVO about a year ago, but very quickly learnt how to write the scripts and use the workstation; it is really good to work with. The big advantage of the Freedom EVO workstation is that it makes it possible to perform high throughput whole genome screening in 384-well plates. The system is very reproducible and accurate, and using the MCA with disposable tips allows very clean working, eliminating any risk of cross-contamination," Katina concluded.

To find out more about Tecan's MultiChannel Arm 384, visit **www.tecan.com/mca384**

To find out more about the Screening Unit at FMP, visit **www.fmp-berlin.info/core-facilities/screening-unit/screening-unit/intro.html**



A: Pipetting performance showed good linearity at volumes of less than 500 nl. **B**: Excellent pipetting reproducibility was achieved at 300 nl.
C: The high reproducibility of pipetting across a microplate is clearly shown by a heat map of % CVs