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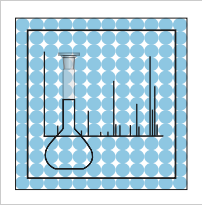

Highlights of Analytical Sciences in Switzerland

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Microdroplet Arrays for High-Throughput Analysis and Biochemical Assays

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Students and technicians working in a biochemical, pharmaceutical, or biology-oriented lab know very well the tedious procedure of filling multi-well plates (*e.g.* with 96 or 384 wells) for biochemical analyses or for cell assays. Repeating the same pipetting steps again and again is laborious, boring and produces often experimental mistakes. For large numbers of experiments, robotic systems are replacing humans to fill the wells faster, more precise and in a systematic way. For very high throughput, it is still time-demanding as well as compound- and resource-consuming.

We developed microdroplet arrays as an efficient alternative, enabling automated sample handling and miniaturisation of sample volumes in the sub-nanolitre range.[1] Moreover, the number of experiments that can be done on a single platform can be massively increased. Fig. 1 shows such a glass platform which can hold up to 7'200 droplets. Upscaling is straightforward – we already fabricated plates for up to 100'000 droplets. The key is the surface of the glass which is hydrophilic where the aqueous sample droplets will be placed, and hydrophobic everywhere else. The hydrophilic areas are comparable to the wells on a multi-well plate; however, no walls surround the droplets. Instead, they are covered by an oil to prevent evaporation. We use these microdroplet arrays for a variety of biochemical assays and long-term studies with cells, where we monitor the droplets by brightfield or fluorescence microscopy. We also use mass spectrometry to assess the content (usually, matrix-assisted laser desorption/ionization (MALDI) mass spectrometry).

The ultra-high throughput is essential in many applications such as single-cell analysis or testing a large library of compounds. For example, aiming at antibiotic drug testing, bacteria growth is monitored while the cells are exposed to several compounds in varying concentrations. We can perform experimental series with a single compound but also combinations of two or more compounds in a systematic way within a single experiment. The effect of the compounds (*e.g.* bacteriostatic or bactericidal) can be derived within hours as well as the minimal inhibitory concentration (MIC). **Further automation and integration of data analysis is currently on the way to increase the number of compounds that can be tested and make use of the full potential of a 100'000-well plate, which drastically reduces time and consumables for high throughput analysis.**

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Reference

[1] R. Strutt, B. Xiong, V. F. Abegg, P. S. Dittrich, *Lab Chip* **2024**, *24*, 1064, https://doi.org/10.1039/D3LC01024D.

Fig. 1. Photograph of a microdroplet array next to a 96-well plate. The glass plate carries picoliter droplets in high density (inset). When used in an experiment, these droplets are covered by oil to prevent evaporation. The platform is used to test the effect of antibiotic compounds on bacteria (data left side), achieved by assessing viability and morphology of the cells.

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