About Micronit

Micronit Microtechnologies B.V., founded in 1999, with development and manufacturing facilities in The Netherlands and Germany, provides innovative lab-on-a-chip and MEMS solutions using micro- and nanotechnologies. Solutions that help customers improve their products and research, contributing to the quality of life. Research & prototyping services, creative product development and quality manufacturing are its core businesses. Micronit is ISO 9001 and ISO 13485 certified. See www.micronit.com for more information.

References

[1] National Cancer Institute - https://www.cancer.gov/about-cancer/understanding/statistics

[2] Microfluidic Isolation of Circulating Tumor Cell Clusters by Size and Asymmetry. Sam H. Au et al. Sci Rep. 2017; 7: 2433

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[4] Food for Thought Look Back in Anger – What Clinical Studies Tell Us About Preclinical Work. Thomas Hartung ALTEX, 2013; 30(3): 275–291.

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Microfluidics, the engine behind life-changing healthcare

Microtechnologies refer to all the technologies involving designs and features on a micrometre scale. Among these microtechnologies, microfluidics is considered one of the main breakthroughs of this decade. Microfluidics is the science of manipulating small volumes of liquids, usually on microchips made with semiconductor manufacturing techniques and containing small channels, which enable accurate control of liquids and chemical reactions. Because of the use of small volumes, quicker temperature shifts and faster liquid displacement is made possible. Moreover, microfluidics enables the automation and integration of complex operations on-chip, with reduced sample and expensive reagent volumes. With such properties, microfluidics obviously fits applications in healthcare along with other MEMS technologies.

Microfluidic technologies have been around for a while, but only in the last few years have certain applications started benefiting from microfluidic breakthroughs. First, next-generation sequencing (NGS) found new possibilities enabled by microfluidics: Illumina's technology, based on glass microfluidic flow cells, is dominating the market and enables sub-$1,000 genome sequencing. In the meantime, other technologies have become serious competitors: nanopore sequencing is currently the new centre of attention in the NGS field, with companies such as Oxford Nanopore now scaling up their production of microfluidic flow cells equipped with solid-state nanopores.

Since 2014, point-of-care testing (POCT) has been reaping microfluidic technologies' full benefits, with many products finally reaching the market. Molecular diagnostics for decentralised use is particularly impacted, with the first molecular diagnostics platforms available for use by untrained users. Examples are the Alere i and Roche cobas LIAT platforms, which run flu/RSV tests that include DNA amplification but remain extremely simple for the user. A large number of applications has recently taken off thanks to microfluidic technologies, including digital PCR and emergency testing for cardiac markers. These applications continue to drive growth in the microfluidics industry, with cutting-edge technologies enhancing daily healthcare at a number of levels, from practitioners to patients themselves.

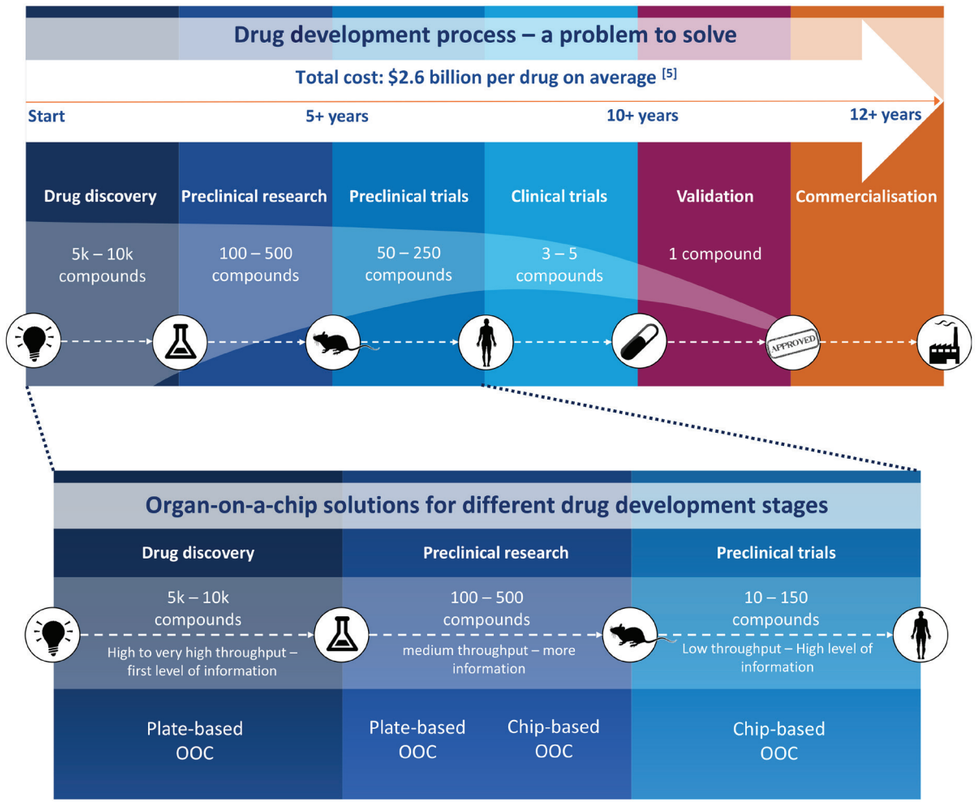
New applications that can have a significant impact on healthcare

New applications made possible by the use of microfluidics techniques are entering the market both in the field of diagnostics and in pharmaceutical research.

In the field of diagnostics, probably the most promising applications of microfluidics are in the field of oncology. As of today, most tests using microfluidics devices are targeting infectious diseases and chronic diseases (diabetes, cardiac conditions, kidney failure, psychiatric disorders), but few tests have been targeting cancer biomarkers as there are still few circulating blood or

urinary biomarkers for cancer. This is where liquid biopsy combined with single cell analysis methods will play a major role in the next decade, bringing new tools to extract and analyse circulating cancer cells for diagnosis, prognosis and treatment monitoring. Approximately 40% of men and women will be diagnosed with cancer at some point in their lives [1], hence cancer is a rising concern in every country in the world - liquid biopsy and single cell analysis aim to add a new weapon to the arsenal of oncologists. However, liquid biopsy devices are very challenging to build because of the very precise microstructures required to sort circulating tumour cells (CTC). Indeed, new CTC selection methods are based on cell size and deformability. The challenge is huge, as microfluidic chips must enable rapid detection of one CTC among billions of blood cells. Several innovative designs are used to this end, from high and very thin micropillars (high aspect ratio structures) poised to slightly change larger cells' trajectory within a microfluidic chamber [2], to inertial microfluidic chambers which trap CTC and allow other cells to flow out of the chamber (requiring very precise geometry, such as Vortex Biosciences' technology).

In the field of pharmaceutical research, organs-on-chips may change the current inefficient paradigm of the drug development process. An organ-on-a-chip is a combination of microtechnology and biology aimed at reconstituting the physiological and mechanical functions of human organs in the form of microengineered devices lined with living cells. Precisely controlled fluid flows combined with mechanical cues and tissue-tissue interfaces enable dynamic models that are expected to be much more relevant than conventional static cultures or animal models. These current methods are not predictive enough however, with about 90% of drugs validated on these models failing during clinical trials because of toxicity or lack of efficacy [3][4]. Indeed, bringing a new drug to the market takes about 12 years and costs several billion dollars. Organs-on-chips have the potential to address the colossal issues of delay and drug development cost, developing a new tool closer to human physiology.



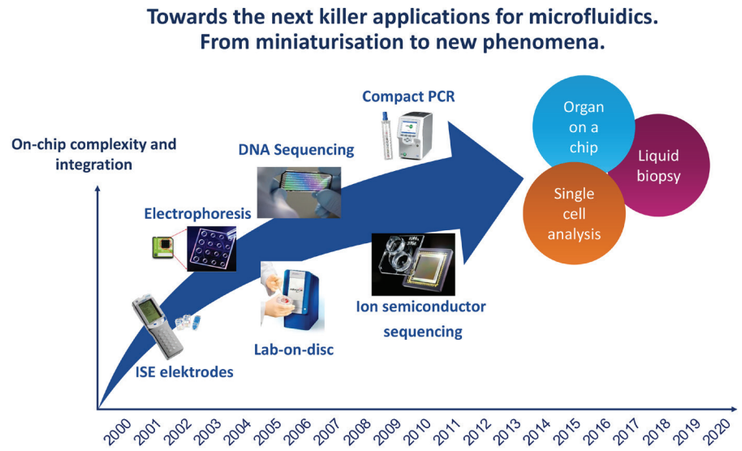
[5] Tufts Center for the Study of Drug Development
Data from the Organs-on-Chips report (Yole Développement, 2017).

Focus on technical and manufacturing capabilities

Such rapid and impressive progress in the field of diagnostics and medical device development can be explained by the direction taken by technology developers. Until recently, the focus was mainly on the miniaturisation of existing systems and processes found in laboratories, such as capillary electrophoresis and PCR, to enable parallelisation. Now the focus has switched to new developments thanks to process and materials innovation, with the emergence of totally new applications leveraging microfluidic technologies' possibilities.

Such improvements significantly enhance medical device development. With innovative diagnostic tests, early detection of disease has now become a reality, paving the way for preventive actions and personalised medicine and leading to better health and higher life expectancy. Technology is helping clinicians in their daily activities, automating data handling and analysis and giving them more time to focus on their interaction with patients. Globally, systems are flexible, scalable and more efficient. Complex sample preparation can now be automated at a high throughput, allowing lab technicians to focus on other parts of the workflow such as data analysis.

These breakthroughs are only possible because of the progress that has been made by both top designers and top manufacturers. With the right capabilities and growing experience in the field, myriad possibilities are offered by microtechnology companies that may lead to improvements in healthcare. For such critical applications, where the challenge can be as critical as saving a patient's life, selecting average quality is not an option. Only the best manufacturers and those who can adapt quickly are able to unleash the potential of microtechnologies.



Data from Status of the Microfluidics Industry report (Yole Développement, 2017).