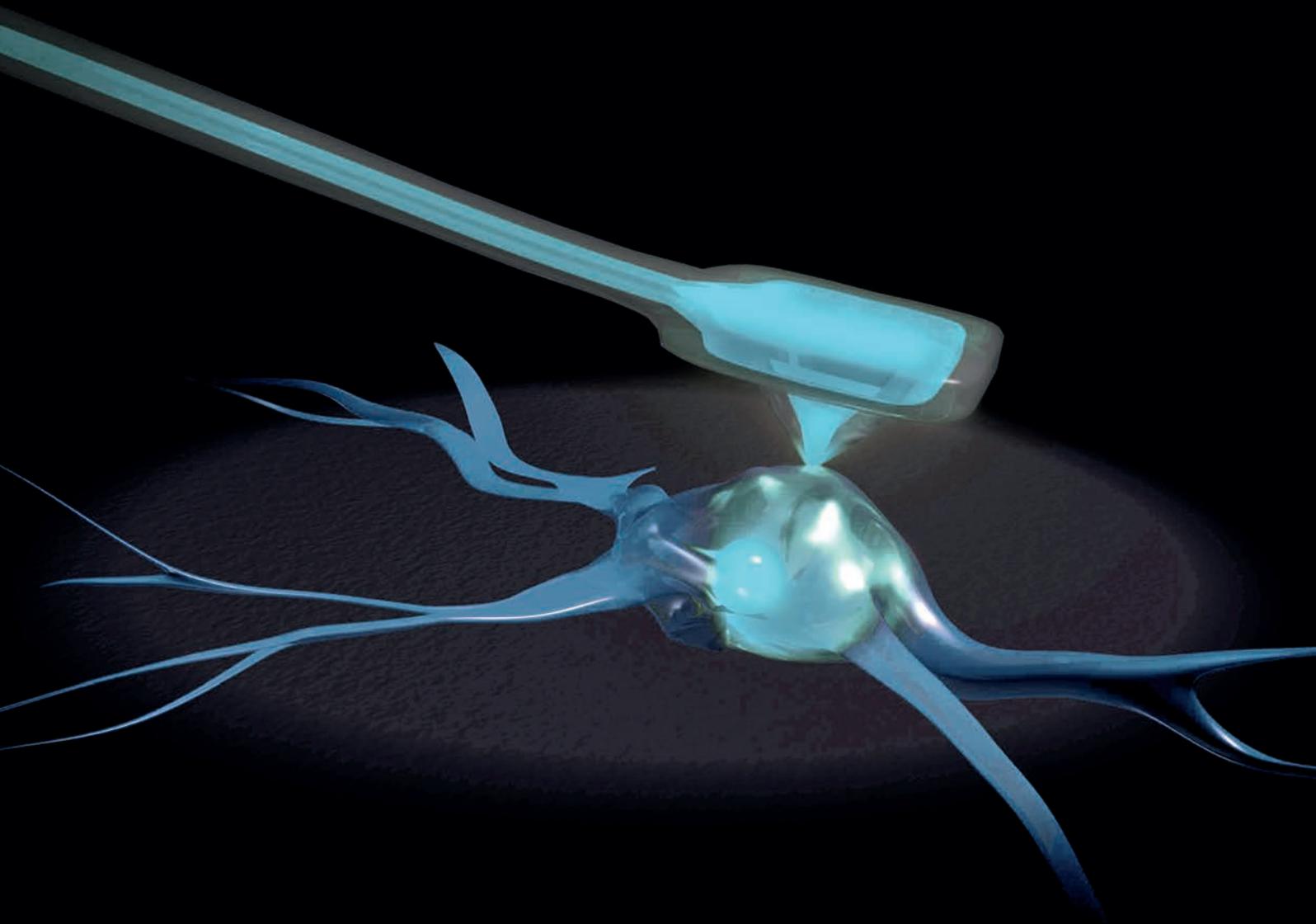


FluidFM® BOT

FOR NANO-INJECTION
INTO ADHERENT CELLS.

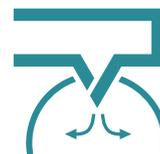


FluidFM[®]
SINGLE CELL EXPERIMENTS
REINVENTED.

A POWERFUL TOOL FOR SINGLE CELL BIOLOGY.

FluidFM® BOT SYSTEM

With the FluidFM BOT system for nano-injection into adherent cells and the patented FluidFM nanosyringe, you can perform nano-injection with a vast variety of materials of your choice selectively into either cytoplasm or nuclei of adherent cells. This is achieved in a cell-context preserving, non-destructive and measurable manner.



FluidFM nano-injection combined with other FluidFM applications, such as nano-extraction and cell isolation, makes the FluidFM BOT an incredible tool for biologists. The FluidFM BOT system has been designed specifically to achieve a throughput that can address bottlenecks in the pipelines of pharmaceutical drug development and genetic editing at the single cell level.



FluidFM® BOT SYSTEM. A complete stand-alone system for FluidFM cell applications (the tailor-made incubator is not shown).

THE SOLUTION FOR YOUR RESEARCH QUESTIONS.

FluidFM nano-injection is the tool to overcome many of your current experimental limitations:

- How can I reliably inject into cells that are smaller than oocytes?
- How can I perform gene engineering on cells that are hard to transfect?
- How can I selectively deliver a compound into the nucleus or the cytoplasm?

SELECTED RESEARCH AREAS.

The following research areas can greatly benefit from the unique features of the FluidFM BOT system, amongst others:

- Gene engineering
- Epigenetics
- Pharmaceutical drug development
- Toxicology
- Stem cell research
- Cancer cell research
- Cell line development

PRECISE

IN CYTOPLASM OR NUCLEUS

FAST

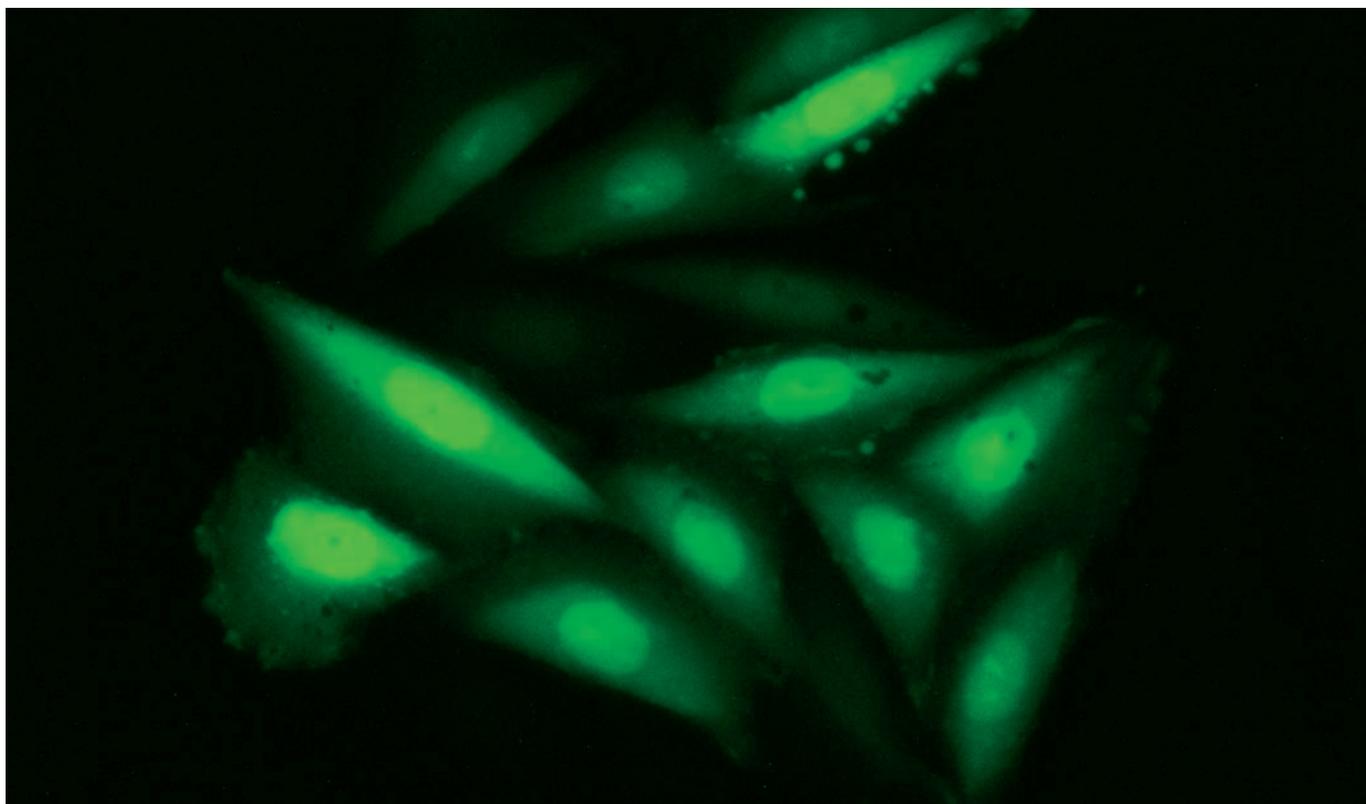
100+ CELLS / HOUR

GENTLE

~ 95% CELL VIABILITY

MEASURABLE

FEMTOLITER INJECTED VOLUMES



INJECTED ADHERENT CELLS. Gentle and fast delivery of Lucifer Yellow dye into CHO cells.

ANY SOLUBLE COMPOUNDS.

FluidFM[®] – RELIABLE NANO-INJECTION

The FluidFM BOT is an unmatched tool to introduce a vast variety of materials of your choice into an adherent cell.

From small molecules to proteins, RNAs, and plasmids, the FluidFM nanosyringe can be loaded with – and thus deliver – virtually any kind of liquid-based solution.

The high level of efficiency of injection using the FluidFM BOT system has already been demonstrated in various kind of cell types, including:

- Human cervical cancer cells (HeLa)
- Human Embryonic Kidney cells (HEK)
- Chinese Hamster Ovary cells (CHO)
- Human induced Pluripotent Stem cells (iPS)
- Mouse primary hepatocytes
- ...

SELECTED PUBLICATIONS.

O. Guillaume-Gentil, E. Potthoff, D. Ossola, et al. Force-controlled fluidic injection into single cell nuclei. (2013) *Small*, 9(11), 1904–1907. doi:10.1002/smll.201202276

A. Meister, M. Gabi, P. Behr, et al. FluidFM: Combining atomic force microscopy and nanofluidics in a universal liquid delivery system for single cell applications and beyond. (2009) *Nano Letters*, 9(6), 2501–2507. doi:10.1021/nl901384x



FLUORESCENT MARKERS

LUCIFER YELLOW, ALEXA FLUOR[®], ...

PROTEINS

ANTIBODIES, CHROMATIN REMODELERS, ...

NUCLEIC ACIDS

RNA, DNA INCLUDING PLASMIDS, ...

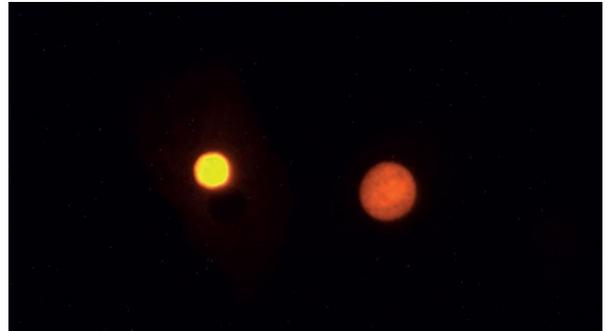
DIRECTLY INTO THE NUCLEUS.

FluidFM® OPTIMIZES CRISPR-Cas DELIVERY

Perform fast FluidFM nano-injection of CRISPR-Cas complexes, especially into cells that are difficult to target with conventional CRISPR delivery methods.

Using the FluidFM BOT to deliver your CRISPR-Cas complex, you can selectively choose the cells you want to inject within a cell culture. In addition, with FluidFM nano-injection, deliver your CRISPR-Cas complex directly where it is required: the nucleus. This is performed without affecting the neighboring cells.

For experiments with mouse primary hepatocytes (image on the right), the injection time is only 2 seconds per nucleus with a gentle 75 mbar pressure corresponding to approximately 130 femtoliters of injected volume.

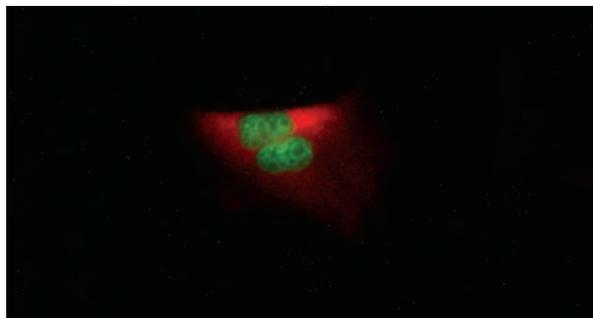


FluidFM® NANO-INJECTION OF CRISPR-Cas9. Fluorescently labeled CRISPR-Cas9 ribonucleoprotein complexes delivered into mouse primary hepatocyte nuclei.

IDEAL FOR DIFFICULT TO TRANSFECT CELLS.

FluidFM® NANO-INJECTION ENHANCES PLASMID TRANSFECTION

Transfection of plasmids with FluidFM nano-injection enables the delivery of genetic material even into difficult to transfect cells and in a faster and, for the cells, less stressful manner than with conventional methods.



FluidFM® NANO-INJECTION OF PLASMIDS. pmCherry-TRIM21 and pEGFP-UHRF1 expression in CHO cells 3 hours after nano-injection.

The FluidFM BOT system is able to transfect more than 100 cells per hour, with a transfection efficiency of over 80%. This can be achieved with one single FluidFM nanosyringe.

In contrast to conventional transfection methods, no toxic compounds are necessary to allow the DNA vector to enter the cell.

Observe the expression of your plasmid sooner than with conventional transfection methods. Because we bring the plasmid directly into the nucleus, protein expression can be detected as early as 3 hours after the FluidFM nano-injection (image on the left).

CUTTING-EDGE

INJECT INTO DIFFICULT TO TRANSFECT CELLS

PRECISE TARGETING

SELECT THE NUCLEI TO BE INJECTED

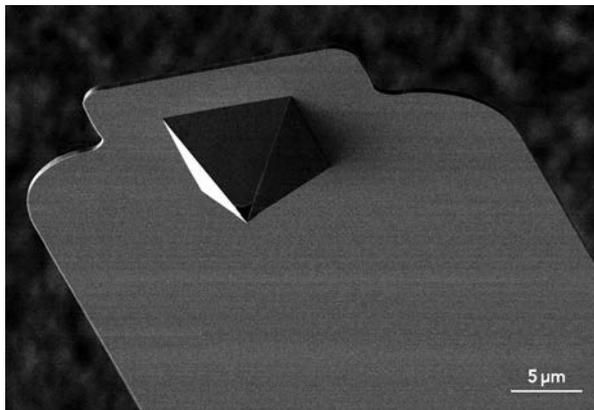
CELL-FRIENDLY

NO TOXIC COMPOUNDS

GO BEYOND.

STATE-OF-THE-ART TECHNOLOGY

Conventional injection using glass micropipettes has its limits: These include difficulties in injecting into adherent cells, time-consuming experiments and limited cell viability. FluidFM overcomes these limits and gives access to complementary single cell applications.



FluidFM® nanosyringe. Patented FluidFM nanosyringe with pyramidal tip and an 800 nm side-aperture.

EASILY INJECT INTO ADHERENT CELLS.

Ease of use has been engineered into the FluidFM BOT system from the very beginning so that any researcher can successfully inject into adherent cells and even can determine whether the nucleus or the cytoplasm should be injected. This is made possible by the small size of the FluidFM nanosyringe, which is probably the smallest mass-made syringe in the world, with its 800 nanometer aperture at the tip of the pyramidal probe. Besides, our in-house designed FluidFM microfluidics control system enables precise pressure and spatial control and our integrated FluidFM ARYA operator software intuitively guides through the FluidFM nano-injection workflow.

TIME-SAVING EXPERIMENTS.

FluidFM nano-injection saves time and reagents: The preparation of a FluidFM nano-injection experiment requires less than 15 minutes, from the loading of the nanosyringe to the calibration of the system before injecting the first series of cells. The same FluidFM nanosyringe, loaded with only 1 μ l of the compound to inject, can, in theory, be used to inject millions of cells. However, in practice, FluidFM nano-injection into more than 3000 cells can be achieved within a working day.

GROUNDBREAKING

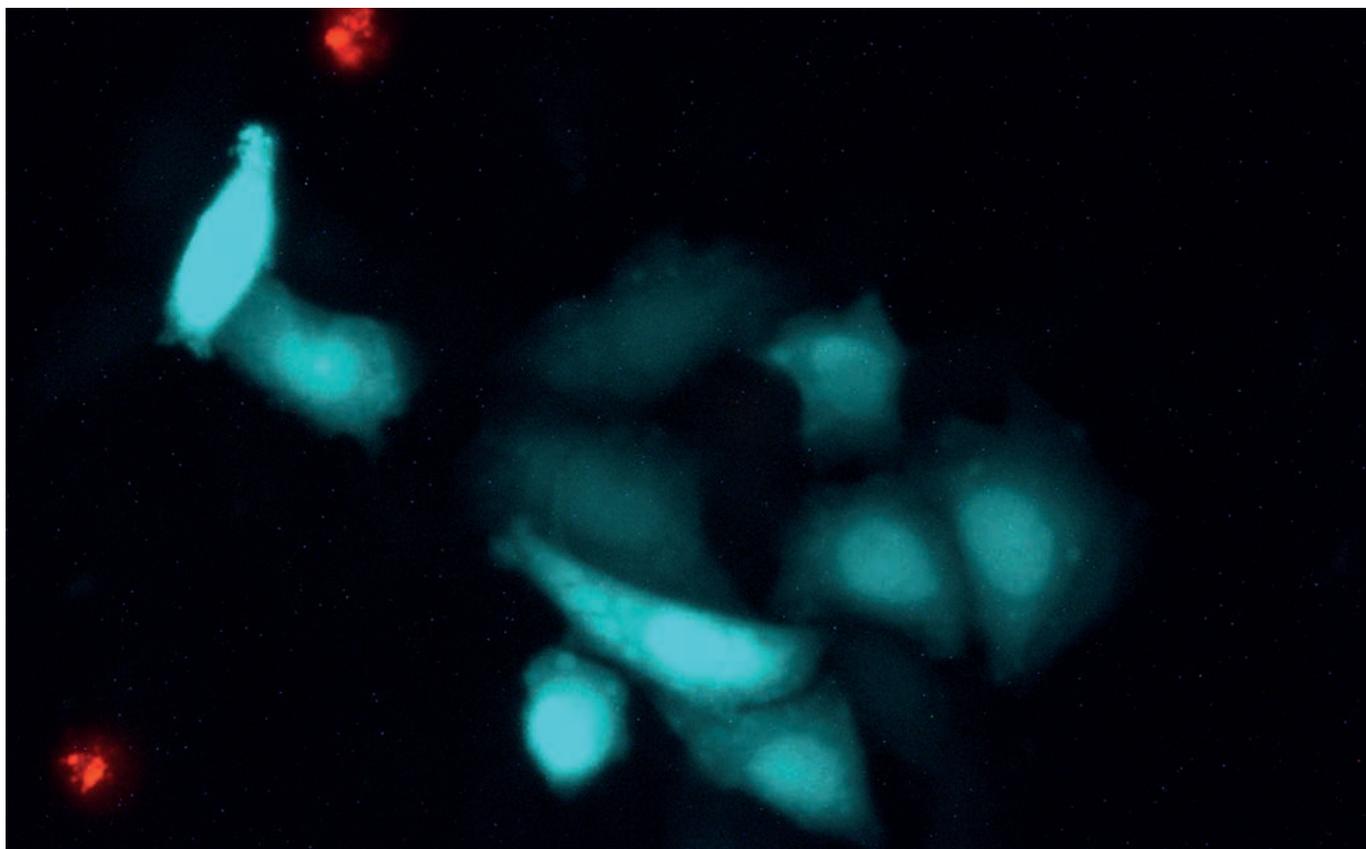
OVERCOME TRADITIONAL INJECTION-LIMITS

NANOSYRINGE

INJECT INTO ADHERENT CELLS

TIME-SAVING

15 MINUTES PREPARATION TIME



CELL VIABILITY ASSAY. After FluidFM nano-injection, propidium iodide has been added to the culture medium to stain dead cells (red). The injected cells (blue) showed viability over 95% (experiment conducted on more than 50 cells).

HIGH CELL VIABILITY.

The design of the FluidFM nanosyringe has been optimized to significantly minimize the cross-sectional area of its apex that is in contact with the cell membrane at the moment of penetration. This very sharp apex of the tip of the pyramidal shaped FluidFM nanosyringe combined with smooth and controlled movement, results in cell viability ~ 95%. Thus, with FluidFM nano-injection, different compounds can be injected at different time points into the same cell in a cell-context preserving and non-destructive manner. Due to the tailor-made incubator, the injected cells can also be cultivated and analyzed, and their evolution captured over time with integrated tracking and time-lapse photo and video features.

MORE THAN NANO-INJECTION

The hollow probe technology of FluidFM allows researchers to also perform other cutting-edge bioscience experiments on the same semi-automated FluidFM BOT system:



Cell isolation

Isolate single adherent or suspended cells in a cell-context-preserving and non-destructive manner.



Single cell nano-extraction

Extract the content of individual cells directly in their native environment while preserving the cellular context and without affecting cell viability.



Spotting

Print spots and high-density arrays with nanometer precision, useful for example in biosensing to create protein or DNA arrays.



Nanolithography

Print complex patterns with many types of biological particles at the nanometer scale.

GENTLE

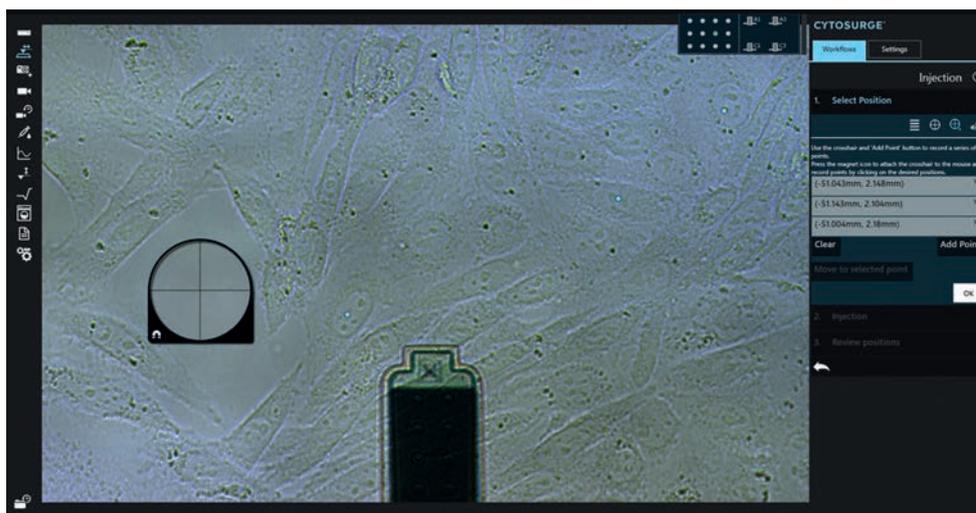
~ 95% CELL VIABILITY

INTEGRATED TRACKING

TIME-LAPSE PHOTO & VIDEO FUNCTIONALITY

GO BEYOND

NANO-INJECTION + OTHER APPLICATIONS



FluidFM® ARYA OPERATOR SOFTWARE. Simple point and click cell selection boosts your productivity.

AMAZINGLY EASY TO USE.

TOWARDS FULL AUTOMATION

Selecting the targeted cells has never been easier: With our in-house developed FluidFM ARYA operator software, you see a high definition image of the cells on the screen. Point and click on the cytoplasm or nucleus of the cells you want to target and click on "OK". It is as straightforward as that.

Simple preparation and extensive automation and data management combined with our user-friendly and intuitive ARYA software allows any user to inject over a hundred cells per hour. For the FluidFM nano-injection of Lucifer Yellow dye into HeLa cells for example, average injection rates of 200-300 cells per hour can easily and regularly be reached.

The FluidFM nano-injection-specific workflow within ARYA allows all users to be in full control of their experimental parameters and to optimize them depending of the type of cells that are to be injected.

Due to the fully programmable FluidFM nanosyringe exchange and washing features, as well as automatic sample swapping, all experiments are executed in a clean and precise fashion, reducing contamination risks and human error to a minimum, whilst boosting productivity.

SIMPLE

INTUITIVE SOFTWARE & WORKFLOWS

STRAIGHTFORWARD

POINT & CLICK TO INJECT

HIGH PRODUCTIVITY

HIGH LEVEL OF AUTOMATION

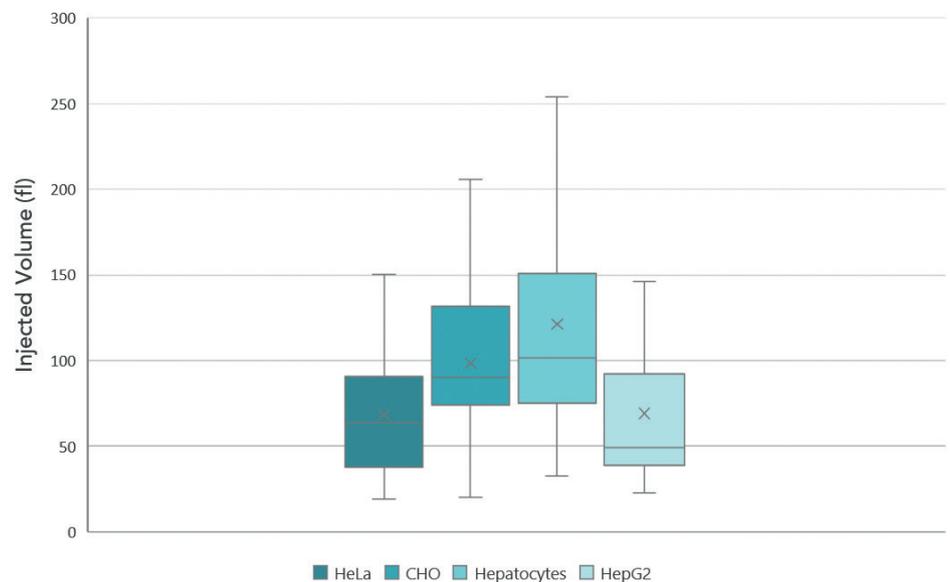
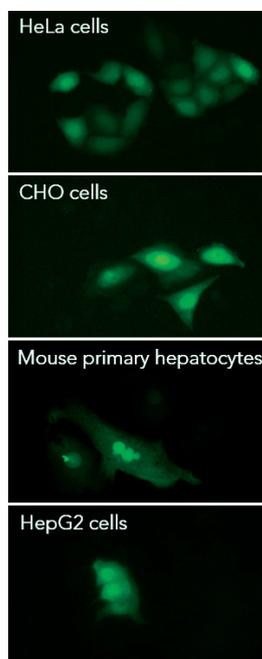
DOWN TO FEMTOLITERS.

INJECTED VOLUME CALCULATION

Knowing the injected volume is key for many experiments, for example when determining a dose-response relationship. With FluidFM nano-injection, you can now precisely calculate the volume of the compound that you have injected in each and every single cell.

Even within the same cell type, every single cell presents different physical properties. Therefore, the injected volume will differ from one cell to another even when keeping the same parameters for the injection. Working with fluorescent compounds, the microfabricated FluidFM nanosyringe serves as a precise reference for calculating the injected volume.

The inherent manufacturing precision and the constant dimensions of the FluidFM nanosyringe and its inner channel make it possible for the FluidFM nanosyringe to provide a reference intensity per femtoliter. After injection, the fluorescence intensity of each cell is compared to this reference intensity, allowing you to precisely calculate the injected volume. A provided ImageJ macro will guide you all along this process.



CALCULATION OF INJECTED VOLUMES. Four different cell types have been injected with luciferase yellow, using similar parameters. Three independent experiments have been performed for each cell type, with a minimum of 50 cells injected per experiment.

PRECISE

FEMTOLITER SCALE

SIMPLE

IMAGEJ MACRO PROVIDED

RELIABLE

HIGH MANUFACTURING PRECISION

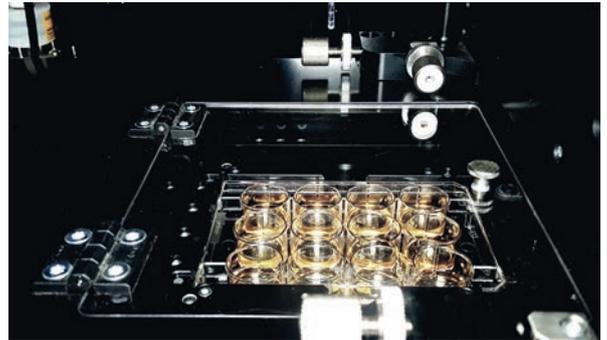
FULLY INTEGRATED SYSTEM.

FluidFM® BOT

A high level of automation coupled with intuitive instrument operation have proven to be particularly important for single cell research.

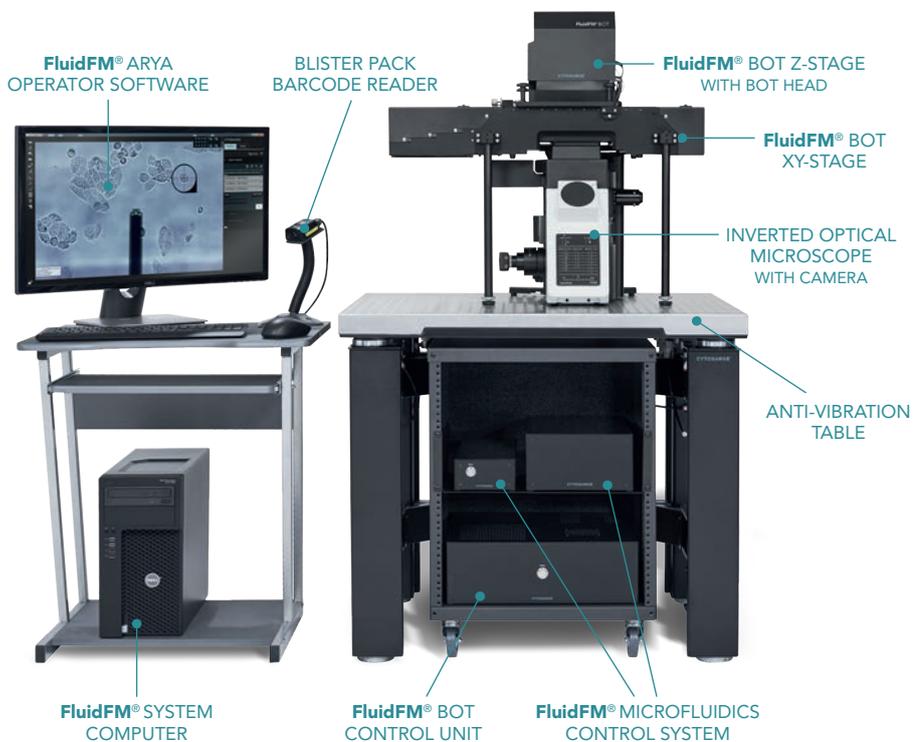
The FluidFM BOT system takes single cell injection to the next level, thanks to the high-precision XY- and Z-stages, an in-house designed FluidFM microfluidics control system, the user-friendly proprietary FluidFM ARYA operator software and extensive automation.

The FluidFM BOT is a complete stand-alone system which includes all essential elements such as a fully integrated motorized inverted microscope and an anti-vibration table with its own pressure pump assuring stable FluidFM



High compatibility. The FluidFM BOT meshes well with cell culture dishes and well plates.

experiments. The system also includes a tailor-made incubator with a HEPA filter and UV light to minimize contamination. A dedicated barcode reader gives access to the relevant probe characteristics and quality control data. Finally, an optimized computer and a high definition monitor enable smooth operation of the ARYA software and all FluidFM BOT system components. The systems is delivered with a set of 20 FluidFM probes, including FluidFM nanosyringes for nano-injection and nano-extraction and FluidFM micropipettes for cell isolation.



FluidFM® BOT SYSTEM. A complete stand-alone system for FluidFM cell applications (the tailor-made incubator is not shown).

COMPLETE
STAND-ALONE SYSTEM

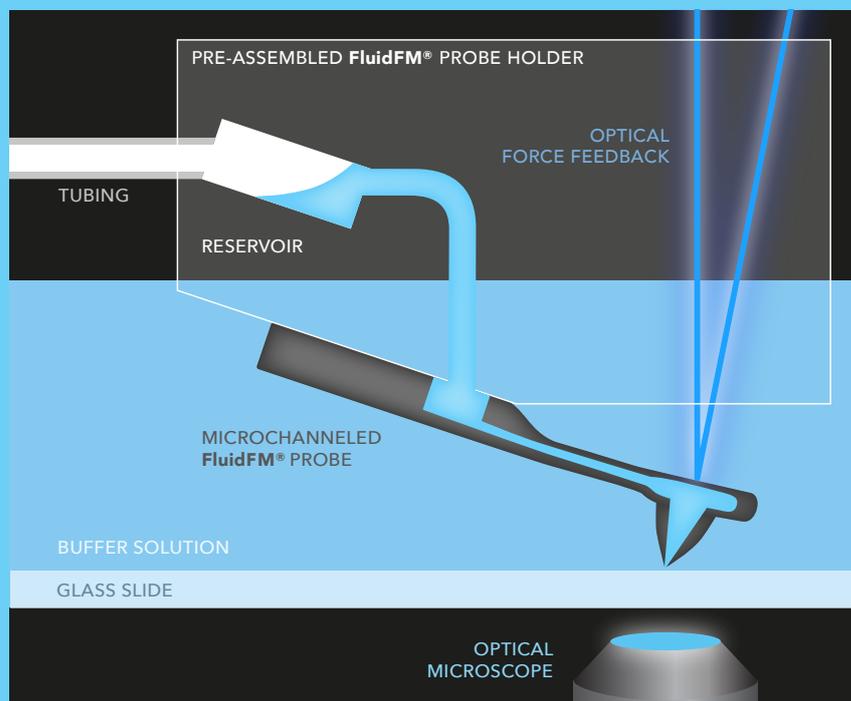
ARYA SOFTWARE
FULL EXPERIMENTAL CONTROL

HIGHLY AUTOMATED
TAKE SINGLE CELL RESEARCH TO THE NEXT LEVEL

CUTTING EDGE & UNIQUE.

FluidFM® TECHNOLOGY

FluidFM technology unites the best features of microfluidics and force microscopy by introducing a microscopic channel into force sensitive probes. The result is the FluidFM probe, such as the FluidFM nanosyringe, the heart of our patented FluidFM technology.



THE UNIQUE FluidFM® TECHNOLOGY. Synergy of microfluidics and force microscopy.

Through the microfluidic channel inside the FluidFM probes, soluble molecules and nanoparticles can be dispensed or aspirated through a sub-micrometer aperture at the tip. These apertures can be as small as 300 nm (for FluidFM nanopipettes) enabling the handling of femtoliter volumes by precisely controlling positive and negative pressures with sub-mbar precision.

The force-sensing capability of FluidFM probes provides a reliable feedback about physical interactions enabling the precise and gentle manipulation of cells, microscopic objects and micro-structured surfaces.

The seamless control of the hollow FluidFM probes through our in-house designed FluidFM microfluidics control system and the nanometer-precision XY- and Z-stages via our intuitive FluidFM ARYA operator software makes the FluidFM BOT system so unique.

HIGH QUALITY
MICROFABRICATION

PRECISE
FEMTOLITER LIQUID VOLUMES

DIVERSE
12+ APPLICATIONS

CONTACT US.



ALEXANDER SERRE
SALES & MARKETING DIRECTOR

alexander.serre@cytosurge.com
+41 43 544 87 10



DR. PAUL MONNIER
LIFE SCIENCE APPLICATION SCIENTIST

paul.monnier@cytosurge.com
+41 43 544 87 08

VISIT US.

BIO-LAB (BSL-2)

WWW.CYTOSURGE.COM



FluidFM®
GO BEYOND.

CYTOSURGE®

CYTOSURGE AG, SÄGEREISTRASSE 25, 8152 GLATTBRUGG, SWITZERLAND
PHONE +41 43 544 87 00, FAX +41 43 544 87 09, WWW.CYTOSURGE.COM

CYTOSURGE SWISS
INNOVATION 