FluidFM® BOT
FOR NANO-INJECTION INTO ADHERENT CELLS.
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 cytoplasms 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.

**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

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

**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.**


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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.

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).

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

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 µl 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.

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

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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.

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).
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 on 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.
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.
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 experiments. The system also includes a tailor-made incubator with a HEPA filter and UV light to minimize contamination. A dedicated bar code 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.

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

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.
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