FluidFM: combining AFM and microfluidics for single-cell perturbation *in vitro*

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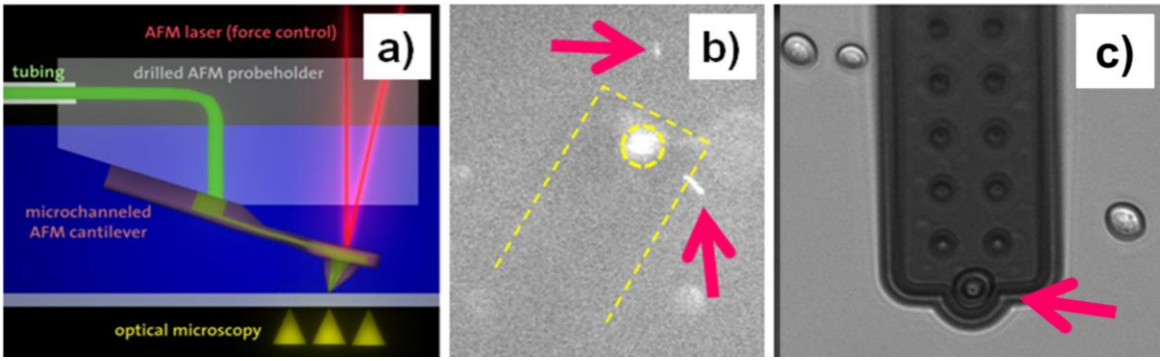
Glass micropipettes are the typical instrument for intracellular injection, patch clamping or extracellular deposition of liquids into viable cells. The micro pipette is thereby slowly approached to the cell by using micro manipulators and visual control through an optical microscope. During this process, however, the cell is often mechanically injured which leads to cell death and failure of the experiment. To overcome these challenges and limitations of this conventional method we developed the FluidFM technology, an evolution of standard AFM microscopy combining nanofluidics via cantilevers with integrated microfluidic channel [1]. The channel ends at a well-defined aperture at the apex of the AFM tip while the other extremity is connected to a reservoir. The instrument can therefore be regarded as a multifunctional micropipette with force feedback working in liquid environment.



a) *Scheme of the FluidFM.* ***b)*** *Two fluorescent viruses ejected from a microchanneled cantilever.* ***c)*** *A yeast attached by underpressure at the aperture of a microchanneled cantilever.*

We are focussing on three applications for single-cell biology [2]: i) cytosolic and intranuclear injection, ii) cell adhesion, and iii) single virus deposition on cell surfaces.
At the same time we are using the FluidFM as lithography tool in liquid [3].

[1] A. Meister et al, Nano Lett (2009) 9:2501
[2] O. Guillaume-Gentil et al, Trends Biotech (2014) 32:381
[3] R.R. Grüter et al, Nanoscale (2013) 5:1097