ELASTO-TWEEZERS: A NOVEL PLATFORM FOR HIGH-PRECISION CELL ELASTICITY MEASUREMENTS

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ABSTRACT

Here we report the development of an optical-tweezer based setup for the automatic characterization of cell mechanical properties, using dual-beam optical trap, microfluidic-assisted pre-patterning of bead-cell-bead complexes and video-based force detection.

INTRODUCTION

The mechano-elastic properties of human cells are essential for their function. In certain diseases like some types of cancer and cardiomyopathies those properties are altered, which correlates with abnormal behavior of cells [1, 2]. Therefore, high-throughput and high-resolution measurements of cell elasticities is of great interest not only to provide insights into the pathomechanisms of these diseases, but also for diagnosis purposes.

EXPERIMENTS AND RESULTS

To this end we developed a dual-beam optical tweezers setup with video-based force detection to directly measure both the forces applied to a cell with piconewton resolution and the cell deformation with sub-micrometer resolution. We couple functionalized beads to the cell surface that act as handles for stretching experiments (Fig. 1&3), which allows us to perform all elasticity measurements on living cells in suspension and with superior sensitivity compared to other techniques like optical stretchers and atomic force microscopy (AFM). Furthermore, with our time resolution of 2 ms we are able to determine both the elastic and the viscous properties of the cells. This novel setup is combined with custom-designed microfluidic cartridges (Fig. 2) to automatically and reliably pattern cells and beads at specific positions. The beads and cells are automatically trapped and coupled with each other using the optical tweezers to yield the desired bead-cell-bead complexes. This way, we are aiming at a throughput of 30 – 60 elasticity measurements per hour. We have characterized the elasticity of HEK293 (human embryonic kidney) cells (Fig. 4), as well as skin fibroblasts. In particular, we analyzed the TMEM43-p.S358L mutation, which is linked to arrhythmogenic right ventricular cardiomyopathy (ARVC) and which has previously been examined with AFM.

CONCLUSIONS

The system was designed with flexibility and adaptability in mind. Completely encapsulated in a single microscope deck, it can easily be combined with other analysis techniques, such as fluorescence microscopy to study intracellular processes during stretching or to correlate mechanical properties with other phenotypic results.

FOUNDING

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REFERENCES

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[2]. Y. Ding et al., Sci. Rep. 7, 45575 (2017)

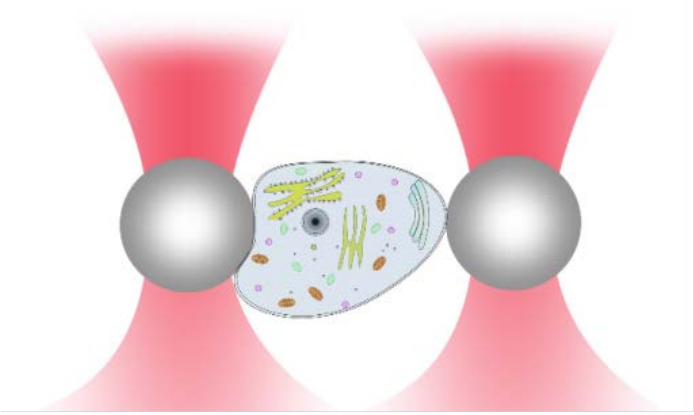

Fig. 1: Schematic of the general measuring principle. NH_2 functionalised polystyrene beads are trapped in two optical beams. The cell attaches non-specifically to the negatively charged particle surface.

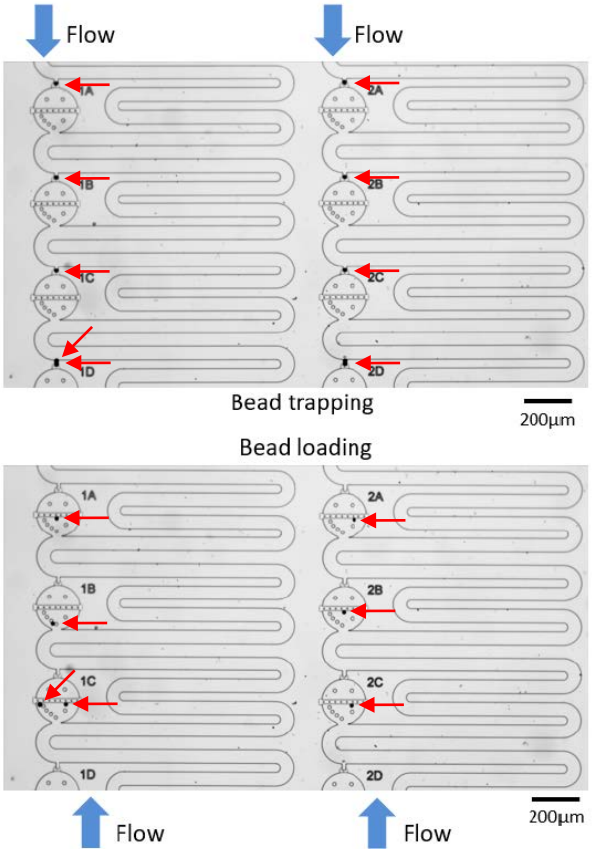

Fig. 2: Pictures of our microfluidic system after loading of beads (red arrows) (top) and after redirection into the chambers (bottom).

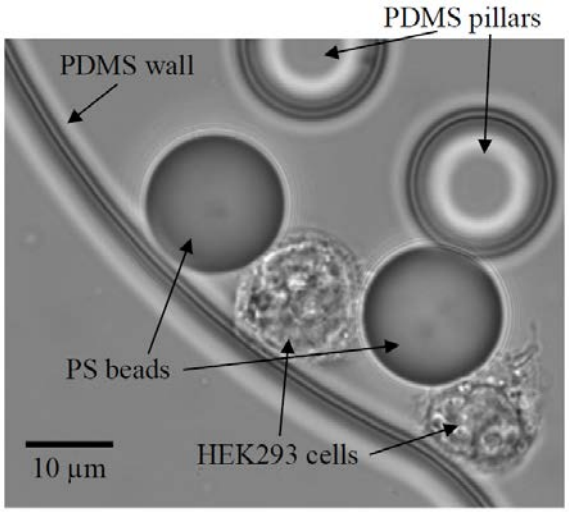

Fig. 3: Video frame of a HEK293 cell trapped between two 15µm NH_2 functionalized polystyrene (PS) beads in the microfluidic device..

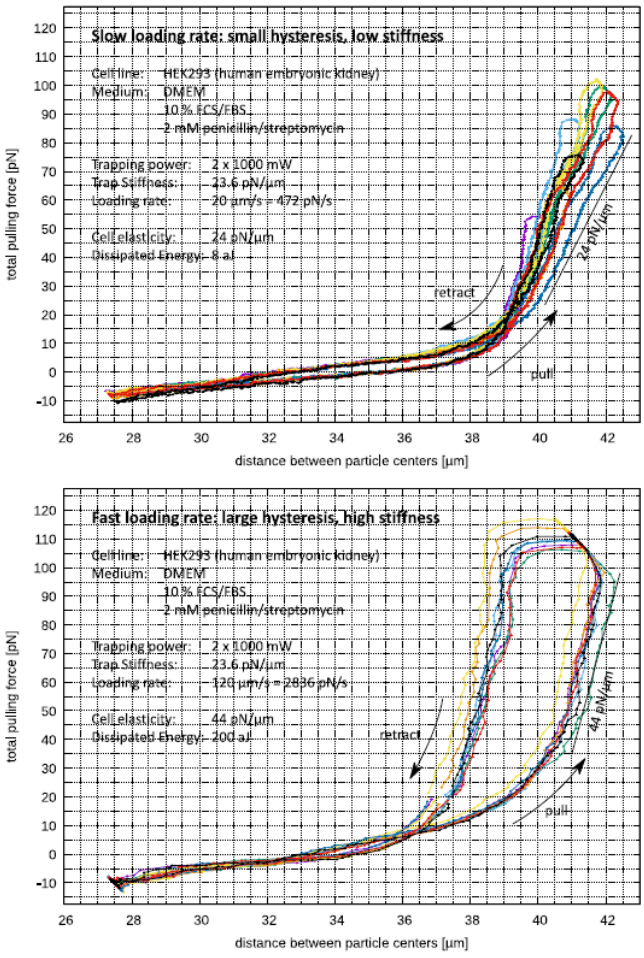

Fig. 4: Elasticity measurements of HEK293 cells with slow (top) and fast (bottom) loading rate. For fast loading rate, hysteresis between pulling and relaxation is visible. Integration over the area between the curves yields a dissipated energy of ~200 aJ per stretching cycle.