Studies into mechanics of single cells have rapidly evolved during past decades with significant implications towards mammalian health. Cells experience mechanical deformation due to external forces and geometric restrictions as any other engineering material. Moreover, mechanical forces are indispensable to living cells and mechanical properties of the cells are playing important role in many processes in living organisms. Characterizing mechanical properties of biological cells is crucial in understanding cellular structures and physiological functions, predicting cellular responses to mechanical cues and stimuli, and correlating cell mechanical properties with pathophysiological conditions.

It can be found that most of the reported in the literature tools and methodologies relate to investigations on small cells (i.e. red blood cells, cancer cells, leucocytes etc) with diameter significantly below 50 μm and with very low-throughput (one cell per tens of minutes for example by atomic force microscopy AFM) or high-throughput (hundreds of cells per second by the use of microfluidic solutions). But there is a gap in microfabricated scientific instrumentation and methodology of cell mechanical characterisation dedicated for mid- to large-size cells (50-150 μm in diameter) with medium throughput (up to few cells per minute or measurement session). Another key limitation to each of these techniques is equipment complexity. Each of the experimental setups is challenging to operate, and requires skilled and trained operators. Peripheral equipment can be expensive and is rarely portable (for example AFM or fast and high resolution cameras in microfluidic solutions), making measurements outside a lab environment or even in non-specialized lab quite challenging. Though an ideal solution to probe single cell mechanics does not yet exist but microfabricated approaches have been designed to alleviate some of these issues.

In this project as scientific problem that we recognized and aim to solve is to fill mentioned above gap by development of a novel MEMS-based research tool (called in this project as MEMS deformability microcytometer) and methodology. The research hypothesis of the projects is that it is possible to automatically and fast determine mechanical properties of important from biological point of view cell - medium and large in diameter (for example mammalian oocytes) by novel MEMS-based tool co-working with innovative research methodology utilizing multiparametric image-based detection collected by reflective and/or fluorescence microscopy.

The deformability microcytometer consists of MEMS chip with microfluidic circuits for controlled single cell deformation and transport, pressure and fluid management units for precise control of actuation pressure and flow of the cell, biological inverted microscope with digital camera for cell images capture and computer with specialised software for experiment control and image analyse. Investigated cell is deformed by deflected thin silicon membrane and glass substrate. Deflection of the membrane is controlled by precis pressure actuation. Thus the cell is squeezed like a balloon between two plates. Images of the deformed cell are next analysed and a set of parameters, related to cell mechanical properties, are visualised and presented. Except cell delivery to the inlet reservoir and cell pick up from the outlet reservoir all listed above steps are done automatically by the use of pressure/flow controllers and specialised software.

The project proposal presents innovative solution and opens a new exciting perspective for wider scientific applicability of mechanical characterisation of cells with special attention paid to biologically important ones like oocytes (mouse and porcine). One of the expected outcome of the project will be breaking methodological and instrumentational barriers in research teams that were not involved in mechanical aspects of the cell due to lack of specialized (and expensive) scientific instrumentation and research experience in the field. Natural consequence of this project will be application of the developed methodology and instrumentation for more complex and life-science oriented investigations on oocytes (or even embryos) mechanical properties and their correlation with biological potential. Due to limited time, founds and competences of the team realizing this project, these issues will not be discussed in the project. From the point of view of technical sciences, next step may be integration of developed in the project MEMS and microfluidic structures with image sensors. Thanks to lens-free holography it will be possible to develop all-on-chip microscope for mechanical characterisation of the cells, which would be a next major breakthrough in the field.