impetux
The Force of Light

SENSOCELL

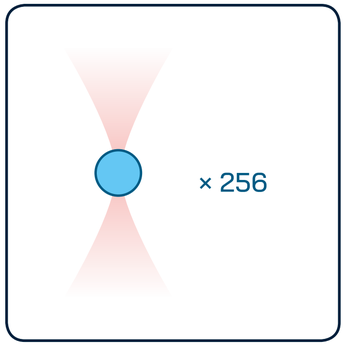
Optical Tweezers for Cell and Tissue Mechanobiology

SENSOCELL is the only optical tweezers platform that allows measuring biological forces within living cells and tissues without needing any previous calibration by the user

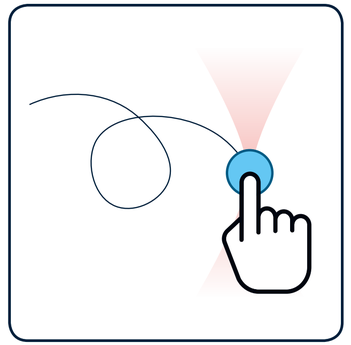
Version 2021-01

Optical manipulation

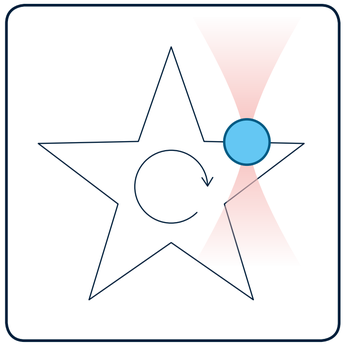
Accurate, extensive and flexible control over multiple traps



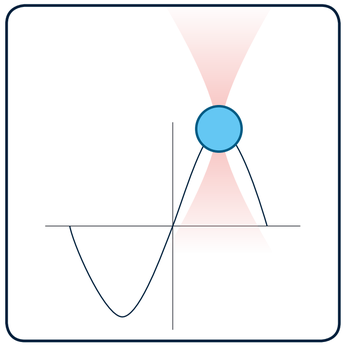
Up to 256 traps



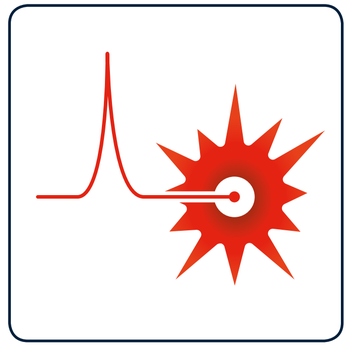
Click & drag mode



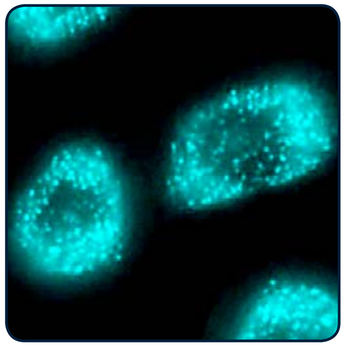
Custom trajectories



Custom oscillations



5W, 1064nm laser source



BF, epi-FL, confocal, TIRF

SENSOCELL's optical manipulation module allows generating **up to 256 simultaneous traps** over a working field of 80×80 µm *(for a 60× objective)* reaching trapping forces up to 500 pN. Based on acousto-optic deflection technology, the system allows trap steering at high frequency *(25 kHz)*.

Owing to its **customizable & automatized routines**, our control software suite LightAce enables precise, extensive and flexible control over multiple traps. Apply predefined **oscillations and/or trajectories over multiple traps** or control them using the ***click & drag*** mode. Apply static *(256 traps)* or dynamic *(32 traps)* **trap patterns**.

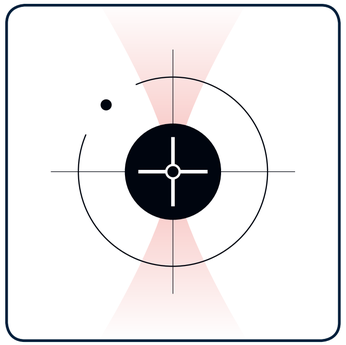
SENSOCELL is **compatible with a wide variety of imaging techniques** simultaneously working during trap manipulation and force measurement experiments.

The system includes a racked case with all electronics and an ultra-low noise single frequency laser source *(5W, 1064 nm)*.

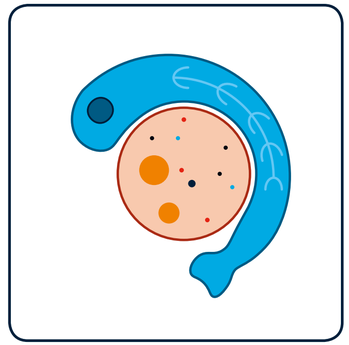
Trapping of multiple *E. coli* bacteria. Using two traps per specimen allows controlling their orientation

Direct force measurements

A unique force sensor based on light momentum analysis

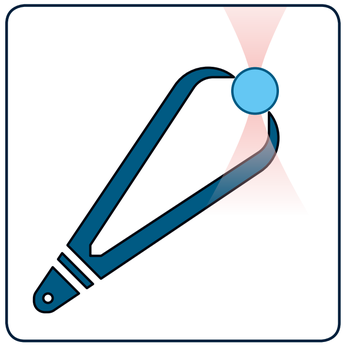


No calibrations



In vitro & in vivo

Force resolution	< 50 fN
Accuracy (typ.)	< 10 %
Position resolution	< 1 nm



Force clamp mode

Prevent cell damage

Our unique force sensor technology based on **light momentum analysis** directly yields the force applied by the optical tweezers via a constant that is unique, permanent and calibrated at factory. **No calibrations** by the user are required to start measuring. The sensor can be installed and set in operation through a simple procedure even by non-expert users.

Forces can be measured on trapped exogenous spherical particles or directly on endogenous trappable cellular structures such as lipid vesicles, membranes, nuclei or whole cells, **even inside living tissues**.

Perform simultaneous **direct force measurements** over multiple independent traps and obtain accurate determination of the trapped particles positions.

Use our implemented **Force Clamp** mode to have absolute control of pulling and pushing force rates.

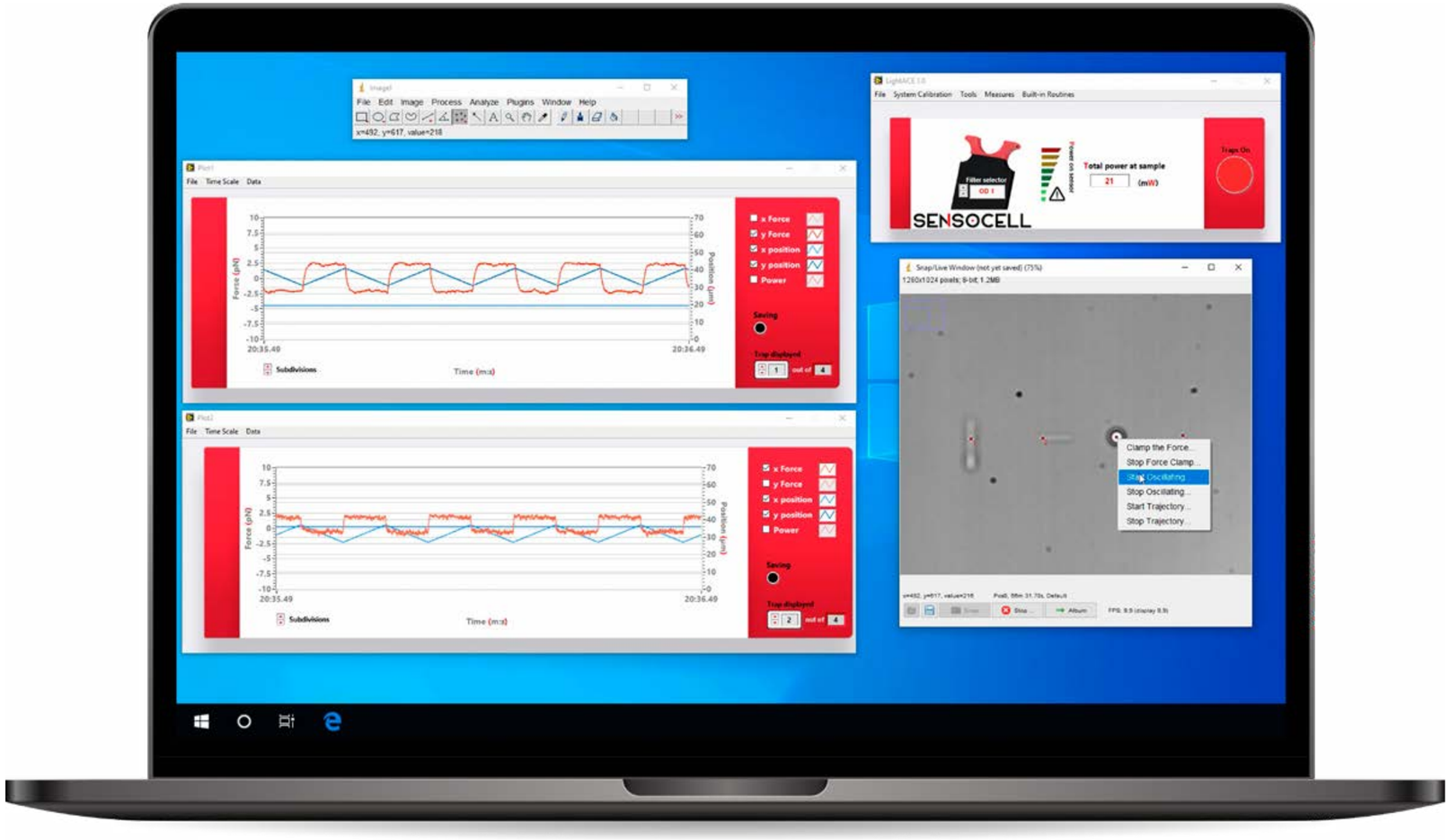
The sensor continuously monitors laser power at the sample plane giving **maximum control** over the irradiation levels imposed on your samples.

LightAce control software suite

Powerful, flexible, intuitive and user-friendly

LightAce is our control software suite for **SENSOCELL** based on the integration of LABVIEW *(National Instruments)*, ImageJ and µ-Manager. **Easy and intuitive** to work with, our LightAce software will allow you to:

- **Take control over multiple optical traps** and read real time force & position data for each trapped target; apply force clamping or launch built-in routines. Simply selecting the different options on the interface menu, LightAce offers you an **incredible set of trapping, manipulation & measurement capabilities!**

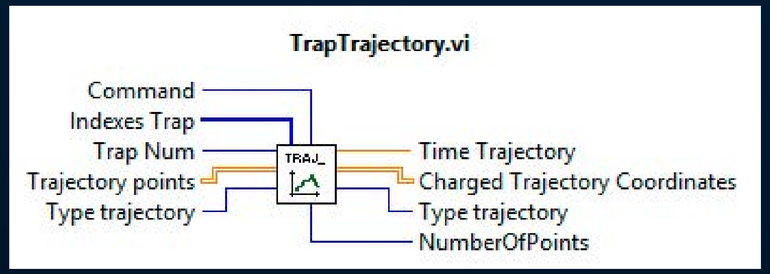


- Use our predefined and customizable automated routines or **create your own routines** using our simple and flexible LightAce Software Development Kit *(SDK)* completed by a variety of examples.

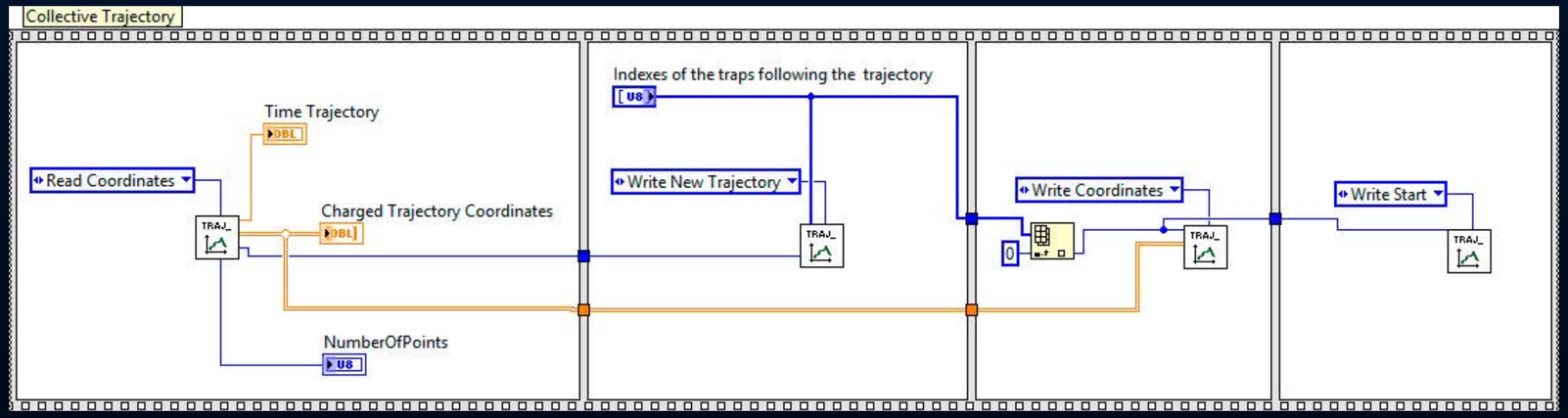
Our best efforts have been dedicated to create a **user-friendly** GUI. After a short training course given by our engineers, non-experts users can start working immediately and plan experiments from the very beginning.

How to Create your own routines using LightAce SDK

1. Choose .vi functions among the LightAce SDK library

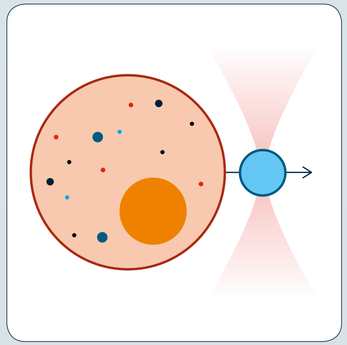


2. Customize your selected .vi functions by setting their input parameters values



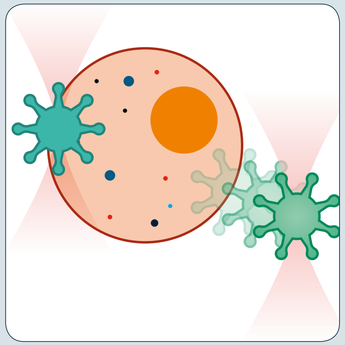
3. Combine them to create complex routines controlling all features of SENSOCELL

Applications for cell & tissue mechanobiology



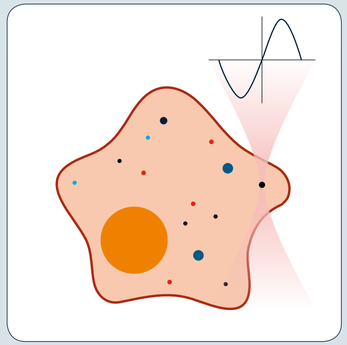
Tether pulling

Study cell membrane mechanics in cells and explants performing tether pulling experiments. Use our customizable routines or create your own tether pulling routines.



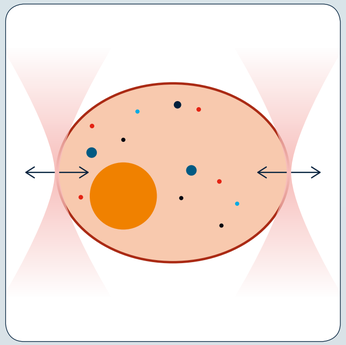
Immune Cells Interactions

Manipulate whole cells to engage cell-cell interactions and measure their interaction forces while having absolute control on cells orientation and contact time.



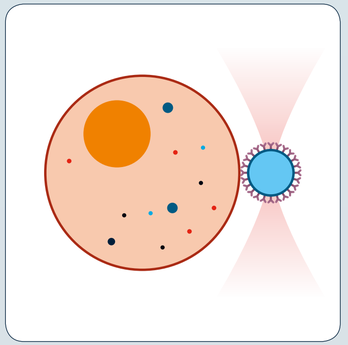
Active Micro-Rheology

Perform active & passive micro-rheology experiments in viscoelastic media like cell's cytoplasm, hydrogels or biofilms.



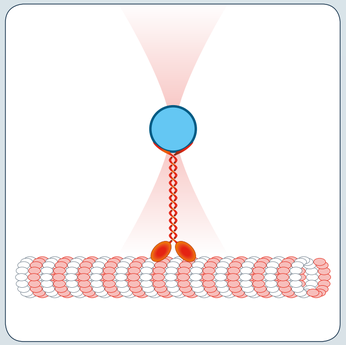
Cell & Nucleus Deformation

Study cell membrane and cell nucleus mechanotransduction pathways by stretching the cell as a whole or manipulating the cell nucleus.



Cell-ECM Mechanics

Study the dynamics and forces of transmembrane mechanoreceptors in cell-ECM interactions at the single-molecule level.



In vivo Protein Motors Activity

Study the activity and kinetics of protein motors in vitro and in vivo. Measure stall forces of protein motors and observe tug-of-war and cooperating phenomena.

Application example I

Tether pulling

Using IMPETUX's **SENSOCELL** optical tweezers platform, a membrane tether pulling experiment *(Michael Krieg's lab, ICFO)* was performed by adhering a 1 µm optically trapped fluorescent bead to a **neuron**. When the adhered bead is pulled away, a lipid filament *(tether)* is extruded from the cell surface *(Fig.1)*.

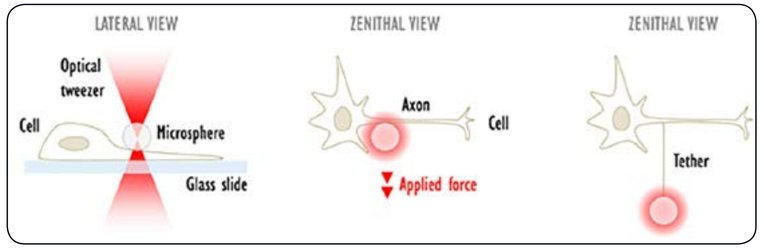


Fig.1 Top: scheme of a tether pulling experiment performed on a neuron.

Using a **customized routine**, the tether is elongated during consecutive pulling steps producing force peaks. After each pulling step, the bead is kept fixed for a certain period of time. During this time, the cell adds material to the membrane tether and the force signal decays. Different pulling rates can be applied at subsequent steps using **SENSOCELL**'s customizable routines. The **system monitors the applied force and bead position** at real time.

Below, *Fig. 2* shows the force and trap position data for each subsequent pulling and relaxation steps. In this case, the tether is pulled at increasing speeds to produce force peaks of increasing height. A model is used to fit the force decay response during relaxation.

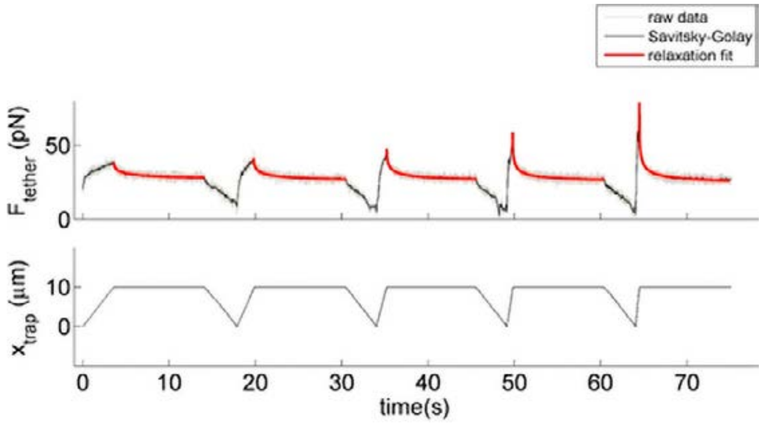


Fig.2 Force and trap position signal during a tether pulling experiment performed on a neuron axon. The pulling rate is increased for each subsequent step. Fitting of force data during the relaxation process after each pulling step is shown in red.

The same type of experiment was performed on HELA cancer cells. *Fig. 3* shows the formed membrane tether generated from a HELA cancer cell and attached to the pulling bead:

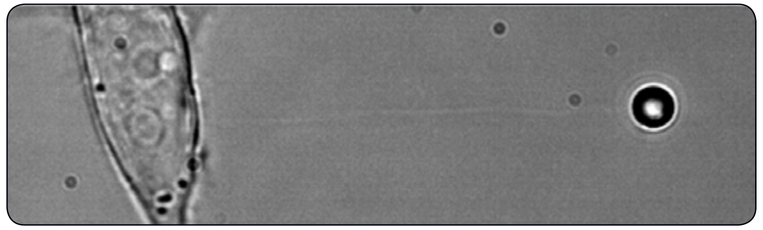


Fig.3 Membrane tether formed from a HELA cancer cell during an experiment.

Similarly, *Fig. 4* shows the force and trap position data obtained two different experiments performed on **HELA cancer cells** *(blue and red data are for high and low pulling rates respectively)*. Note that the force signal has negative sign due to the chosen pulling direction.

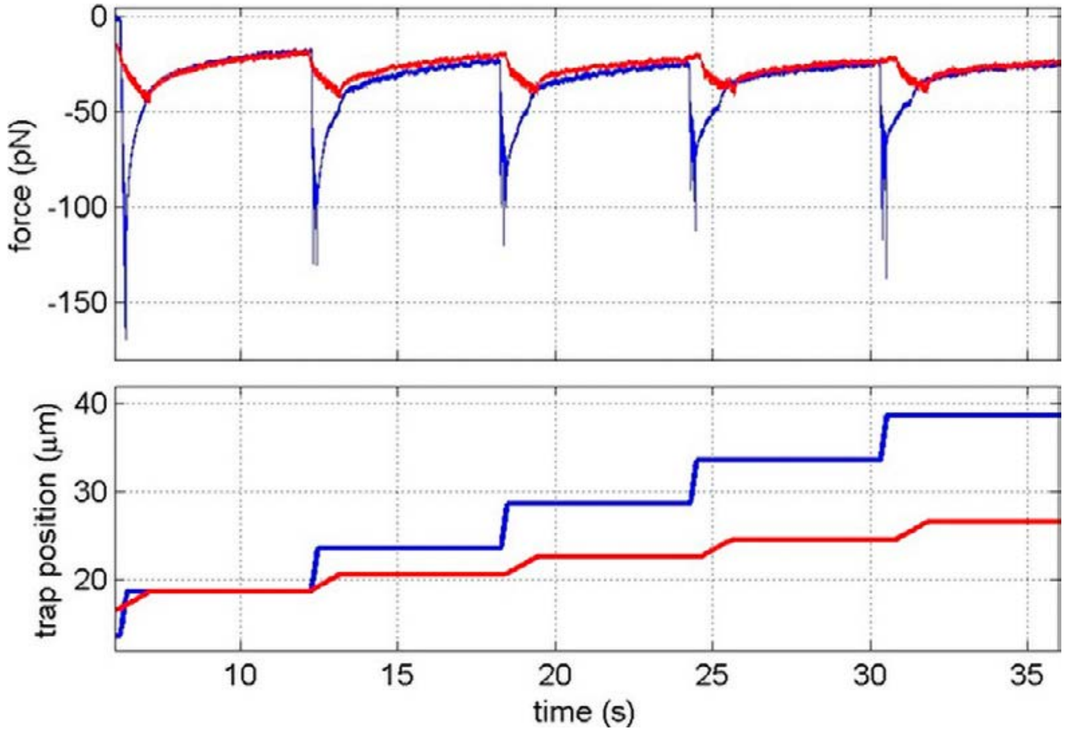


Fig.4 Force and trap position data obtained during two different *(blue and red data)* experiments performed on a HELA cancer cells. The applied pulling rate is higher for the blue data than for the red data.

Application example II

Cell nucleus deformation

SENSOCELL was used* to probe intracellular nucleus mechanics *(Verena Ruprecht's lab, CRG and Stefan Wieser and Michael Krieg's labs, ICFO)* in **cell extracts from zebrafish embryos**:

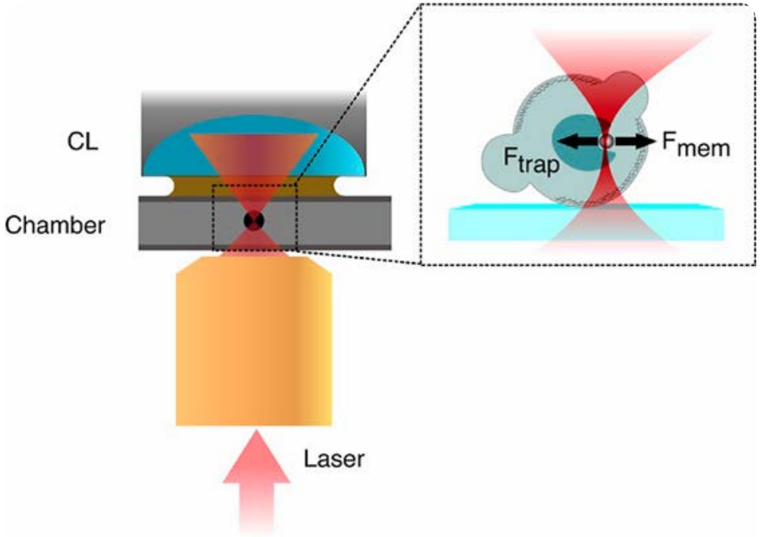


Fig.1 Injected microspheres are used to indent the cell nucleus in both suspended and confined cells from Zebrafish embryos. Source: extracted from*.

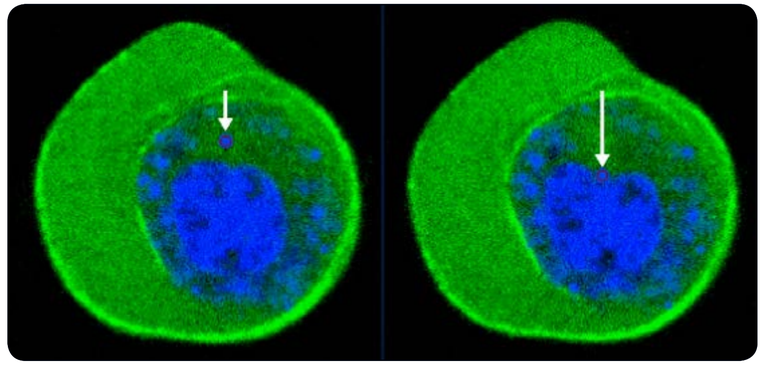


Fig.2 Cconfocal imaging of a cell nucleus indentation experiment performed with SENSOCELL optical tweezers system in a zebrafish stem cell *(green)*. The trapped microsphere *(white arrow)* is pushed against the nucleus *(in blue)* to squeeze it.

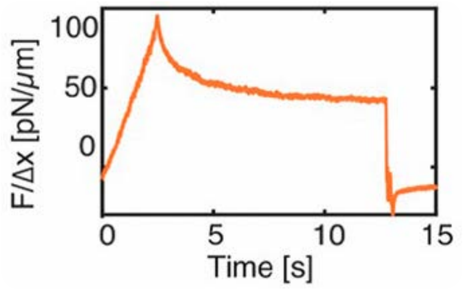
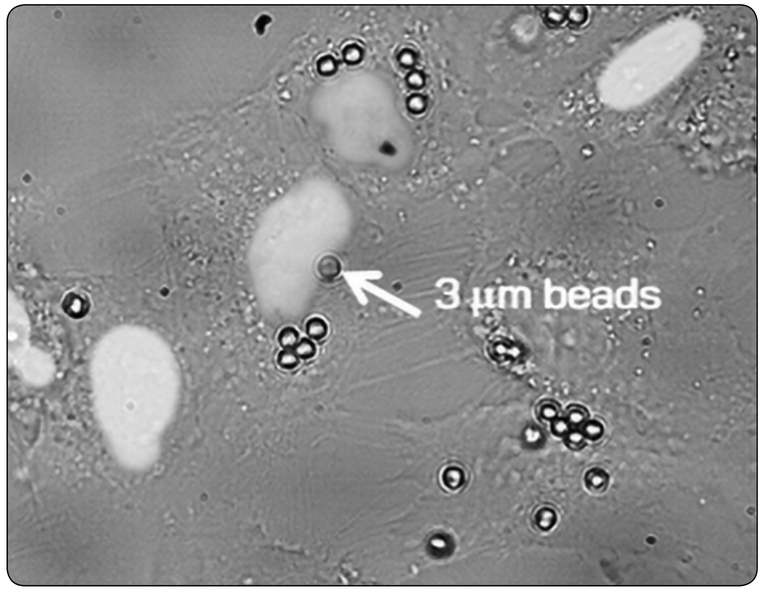


Fig.3 Example of a **nuclear force profile** normalized to nuclear indentation. After the microsphere gets in contact with the nucleus, the force exhibits a characteristic time relaxation. At t=13s, the particle is moved away.

* V.Venturi, F.Pezzano, F.Català-Castro, H.-M.Häkkinen, S.Jiménez-Delgado, M.Colomer-Rosell, M.Marro-Sánchez, Q.Tolosa-Ramon, S.Paz-López, M.A.Valverde, P.Loza-Alvarez, M.Krieg, S.Wieser and V.Ruprecht, "The nucleus measures shape deformation for cellular proprioception and regulates adaptive morphodynamics" Science 16 Oct 2020, Vol.370, Issue 6514, eaba2644. DOI: 10.1126/science.aba2644

Similar data has been obtained with **SENSOCELL** in preliminary tests using **HELA cancer cells and RPE-1 human retina cells** *(samples were kindly provided by Dr. Aastha Mathur from M. Piel's lab at Institut Curie)*. In this case, 3µm beads were internalized in the cells by phagocytosis:



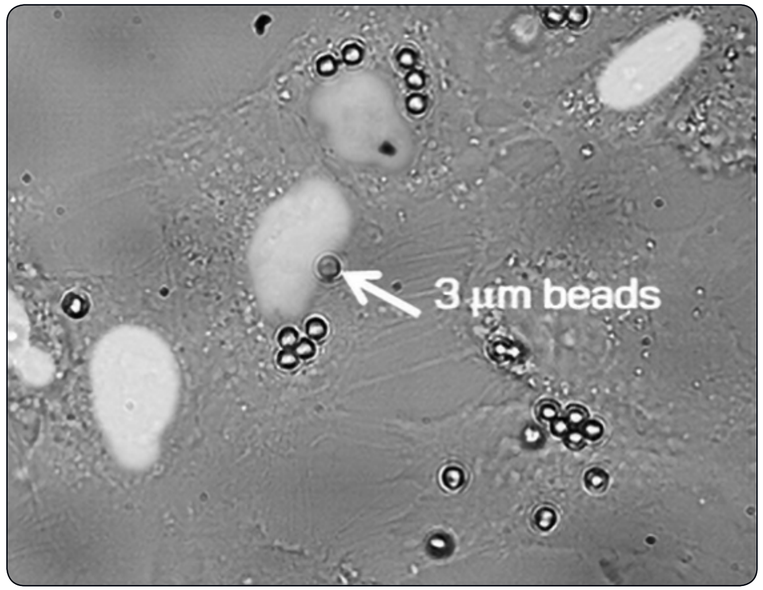


Fig.4 HELA cancer cells *(left)* and RPE-1 cells *(right)* with internalized microspheres that were optically trapped and manipulated to indent the fluorescently labelled cell nuclei.

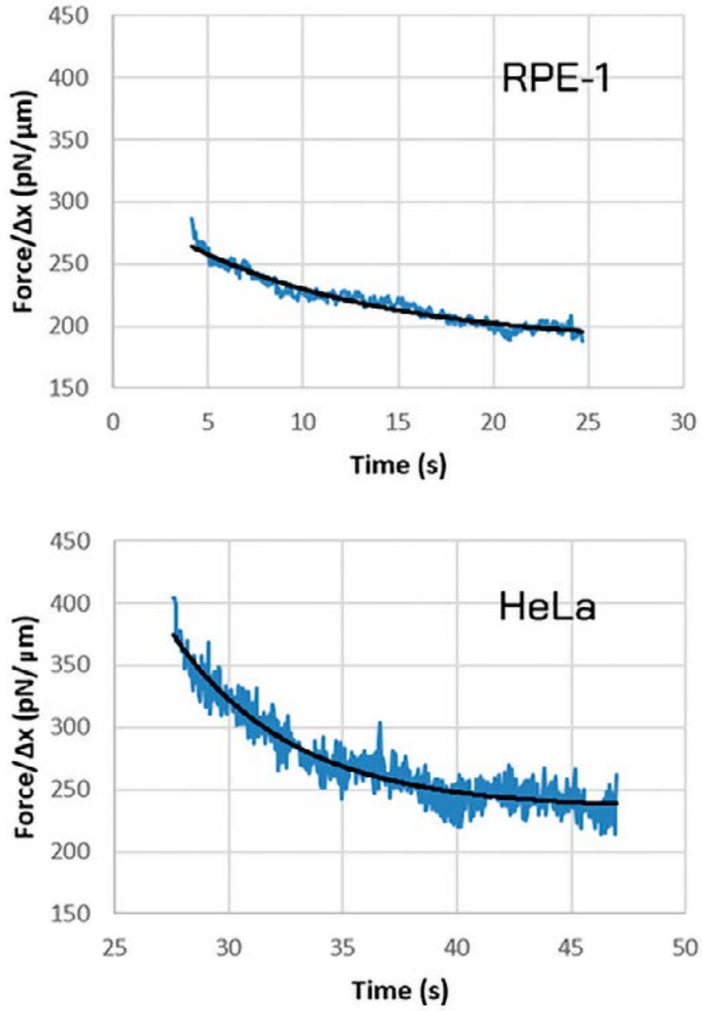


Fig.5 Relaxation of the applied force normalized to nuclear indentation for tests using HELA and RPE-1 cells.

Application example III

Active micro-rheology of soft gels and living cells

Here we show how the micro-rheology module of the **SENSOCELL** optical tweezers system can be used to measure the **viscoelastic properties of extracellular matrices or living cells**, with stiffnesses ranging from tens of Pa to **several kPa** and at probing frequencies up to the **kHz regime**.

The active micro-rheology routine in our **SENSOCELL** optical tweezers system was used to get the complex shear moduli of polyacrylamide gels with embedded micrometer beads

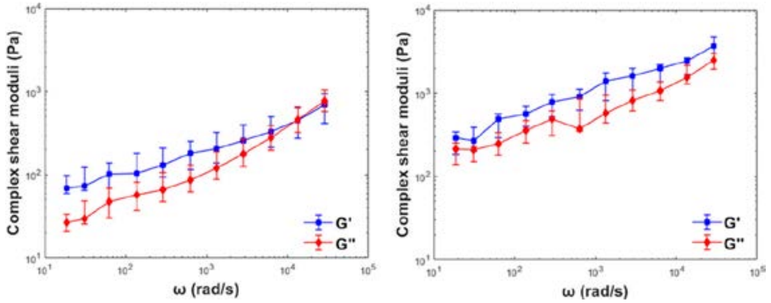


Fig.1 Example of the frequency-dependent behavior of the complex shear moduli of soft polyacrylamide gels. Blue symbols indicate storage modulus *(G')* and red symbols indicate loss modulus *(G")*. Symbols are median values and error bars indicate Q1 and Q3 ranges. N = 13 beads probed for this experiment.

Next, we present some preliminary data of micro-rheology tests carried out inside **mouse oocytes and mouse early embryos** *(samples were kindly provided by Dr.Maria Almonacid from College de France and Dr.Jean Leon Maitre from Institute Curie)*. For these tests, **no beads were internalized**. Instead, **endogenous vesicles** located inside the cells' cytoplasm were optically trapped and **used as probes**. The vesicles were forced to oscillate sinusoidally with 200 nm amplitude at increasing frequencies *(10 Hz to 100 Hz)*. Below we show the frequency-dependent behaviour of the complex shear moduli obtained for some of these tests.

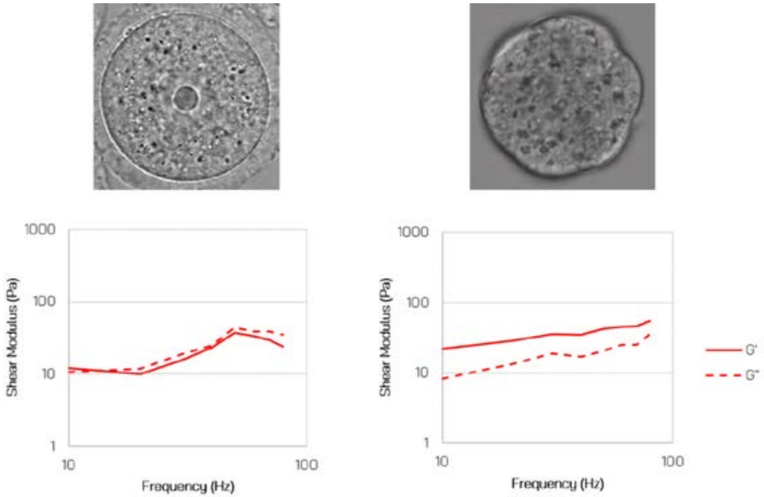


Fig.2 Example of the frequency-dependent behaviour of the complex shear moduli data obtained for tests carried out inside the cytoplasm of mouse oocytes *(left)* and early mouse embryo cells *(right)*.

Application example IV

Cancer cells & T-cells interactions

The study of cell-cell interactions is of great importance in research fields like immunophysics. Our optical tweezers platform **SENSOCELL** allows trapping and manipulating multiple cells simultaneously in such a a way that cell-cell contacts can be easily established in a precise manner. Users can control the cells' orientation and contact time. In this example *(Fig.1)* we show how contact is engaged between a neuroblastoma cancer cell and a T-cell using two optical traps. The first trap *(trapping the cancer cell)* is fixed while the second trap *(over the T-cell)* is moved using the "click & drag" mode. The T-cell is moved towards the cancer cell and contact is established. After 10 s, the T-cell is pulled away and an **adhesion force** is measured.

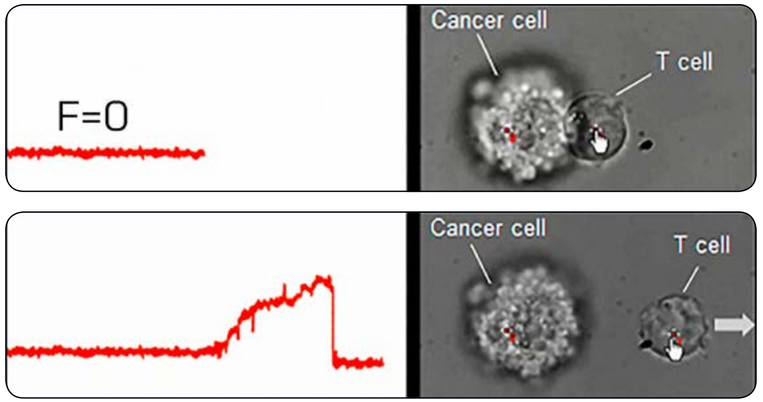


Fig.1 Cell-cell interaction established between a neuroblastoma cancer cell and a T-cell.

Initially, the measured trapping force is zero *(red curve)*. After 10 s, the T-cell is pulled away and an increasing force is measured. When the applied force is high enough to break the bond between the two cells, the measured force drops to zero. In this case **the adhesion force** was measured to be 21 pN. In collaboration with **Dr. Carlos Barcia** from Autonomous University of Barcelona. The same type of experiment was carried out for **lymphoma cancer cells** and **3 immune cell** lines expressing different receptors in collaboration with **Dr. Manel Juan Otero** from the Hospital Clínic of Barcelona.

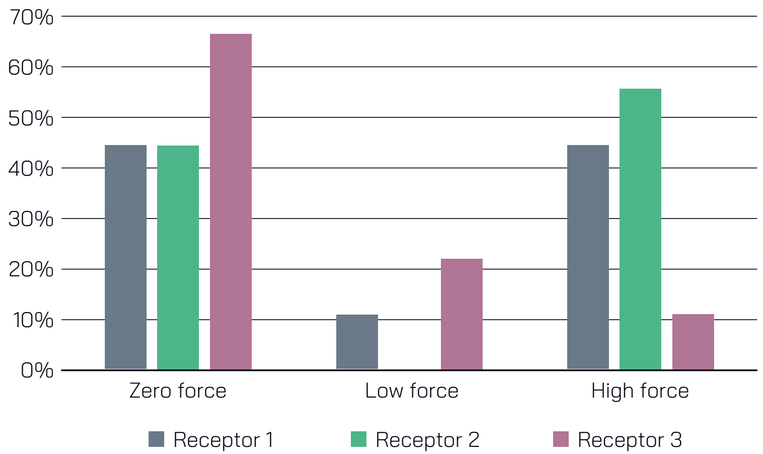
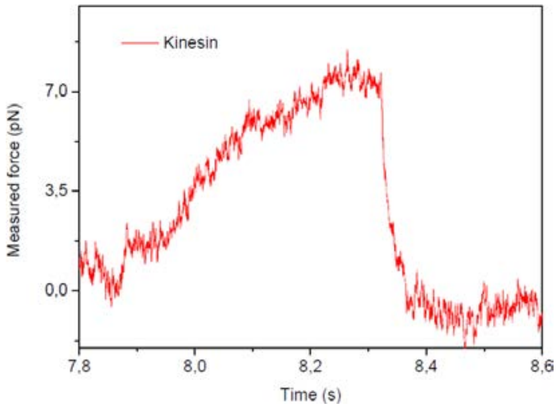


Fig.2 Statistics of cell-cell adhesion forces measured for lymphoma cancer cells in contact with immune cells expressing different receptors after a contact time of 15 s. Each bar represents the data for a set of 9 different samples of each cell type.

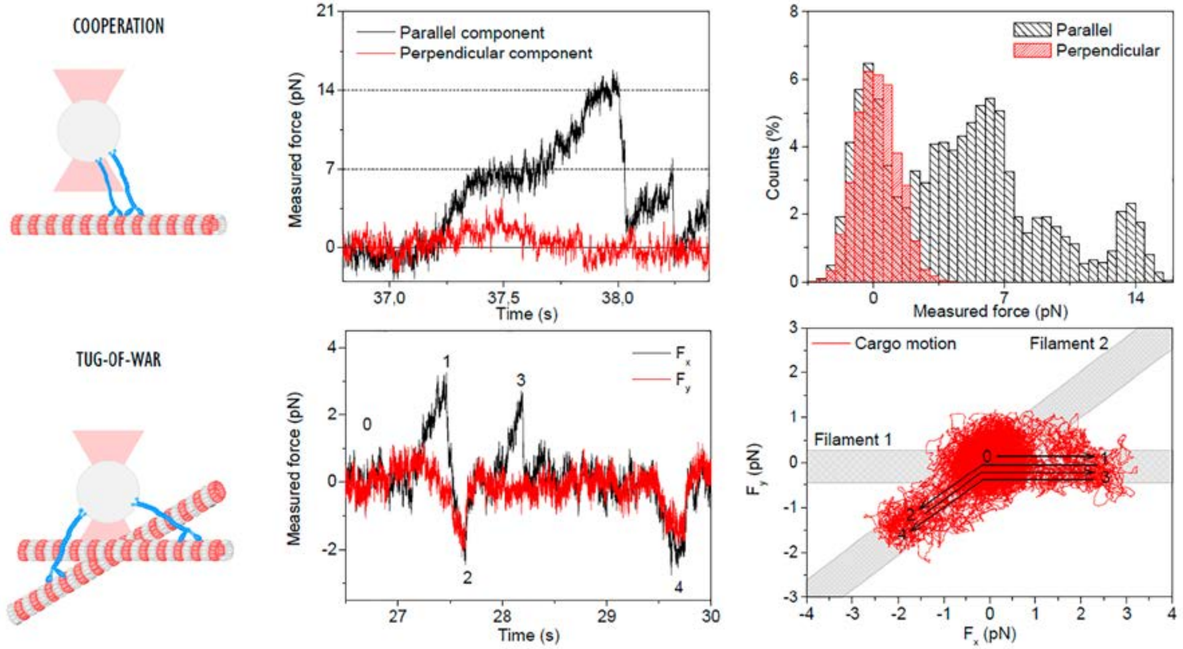
Application example V

Measurement of the stall force of kinesins in living cells

Motor proteins are responsible for different fundamental biological processes inside cells. One of these functions, of vital importance for the cell survival, is the intracellular transport of vesicles and organelles. Kinesin is the microtubule-based protein that performs the plus-end-directed motion. The protein generates the mechanical work required to move cargos, by means of the hydrolysis of ATP molecules. In cells, lipid droplets can be used as targets for trapping and analysis of the force of the motor proteins propelling them. Here we show the measurement of the stall force of one of these lipid droplets in an A549 cell:



Measurement of **forces inside cells** allows exploring the rich interplay between multiple motor proteins simultaneously pulling on the same vesicle/organelle. Below is an example illustrating two opposed scenarios: cooperation and competition;



Graphics; Force curves for a lipid droplet in an A549 cell pulled by multiple molecular motors in different scenarios: in cooperation and in competition. The two components of the force *(parallel and perpendicular to the filament)* are shown.

impetux
The Force of Light

Optical tweezers for mechanobiology

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