m-Trap™

Dedicated High-resolution Optical Tweezers

m-Trap I Product Brochure

The m-Trap™ is the first dedicated optical tweezers instrument specifically developed for high-resolution single-molecule force spectroscopy research. Ultra-high force resolution and stability, with incredible throughput and ease-of-use, all at an unprecedented price level.

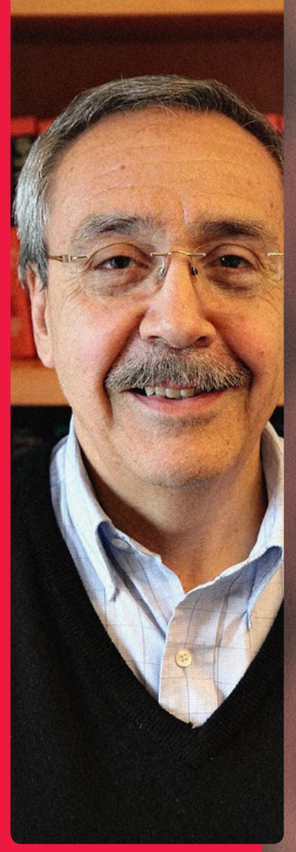
LUMICKS
Capture Molecular Interactions

C-Trap | **m-Trap** | AFS | z-Movi

The key to unlocking dynamic single-molecule analysis

Our dream is to unlock single-molecule analysis. Understanding the root causes of diseases at the molecular level is one of the greatest scientific challenges of today. Expanding the knowledge of biological processes that are at the basis of disease is key for prevention and the development of future cures. We aim to create the best possible tools for researchers to perform high-quality, high-throughput single-molecule experiments in the most accessible manner.

With this in mind, we developed the m-Trap™: a dedicated high-resolution optical tweezers instrument which lowers the price barrier for access to state-of-the-art single-molecule force spectroscopy without any compromise on key performance specifications.



Prof. Carlos Bustamante

HHMI investigator and professor at the University of California, Berkeley

On the importance of single-molecule research.

Adapted from Bustamante, Carlos. "Optical Tweezers: Single Molecule Manipulation in Biochemistry" Lecture, iBiology, September 2010.

*"Single-molecule experiments allow you to follow the dynamics of the reactions; not just the average behavior of molecules, but how individual molecules behave over time, providing **incredible insights** into the function of individual biomolecules."*

A new milestone for single-molecule research

The m-Trap™ optical tweezers was developed to lower the price barrier of advanced single-molecule force spectroscopy instrumentation without compromising on performance characteristics.

We went back to the essence of force spectroscopy. Every single component, every process, has been considered and measured to be truly useful and enhances the user's experience.

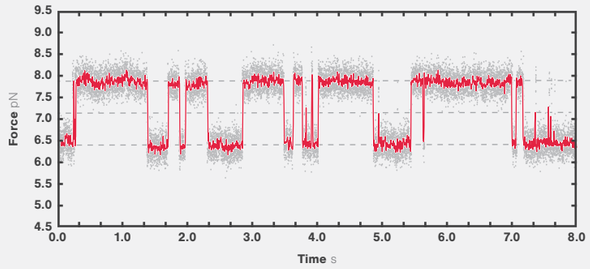
The m-Trap is capable of manipulating and characterizing structural transitions and interactions of biomolecules at the Angstrom scale with ultra-high force resolution, stability and throughput.

Want to learn more about LUMICKS?
Visit www.lumicks.com for more information!

Activity, states, and conformational changes

The m-Trap enables you to detect discrete conformational changes within a protein or DNA molecule. By keeping the traps at fixed position while measuring tension fluctuations caused by intramolecular conformational transitions with ultra-high sensitivity you can detect the most transient and rarest states. Moreover, measuring the activity and states of molecular motors over DNA or filaments is achieved with sub-nm stepping resolution, thereby resolving biomolecular processes with extremely high detail.

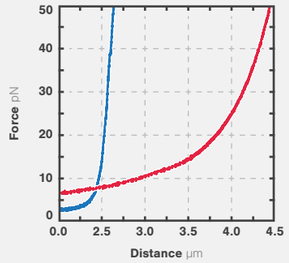
By tethering the molecule between two optically trapped beads and measuring force fluctuations, while holding the traps at a fixed distance, equilibrium dynamics are revealed. Observation of transitions between extremely short-lived states within molecules and characterization of conformational transitions during long periods of time is easily achieved.

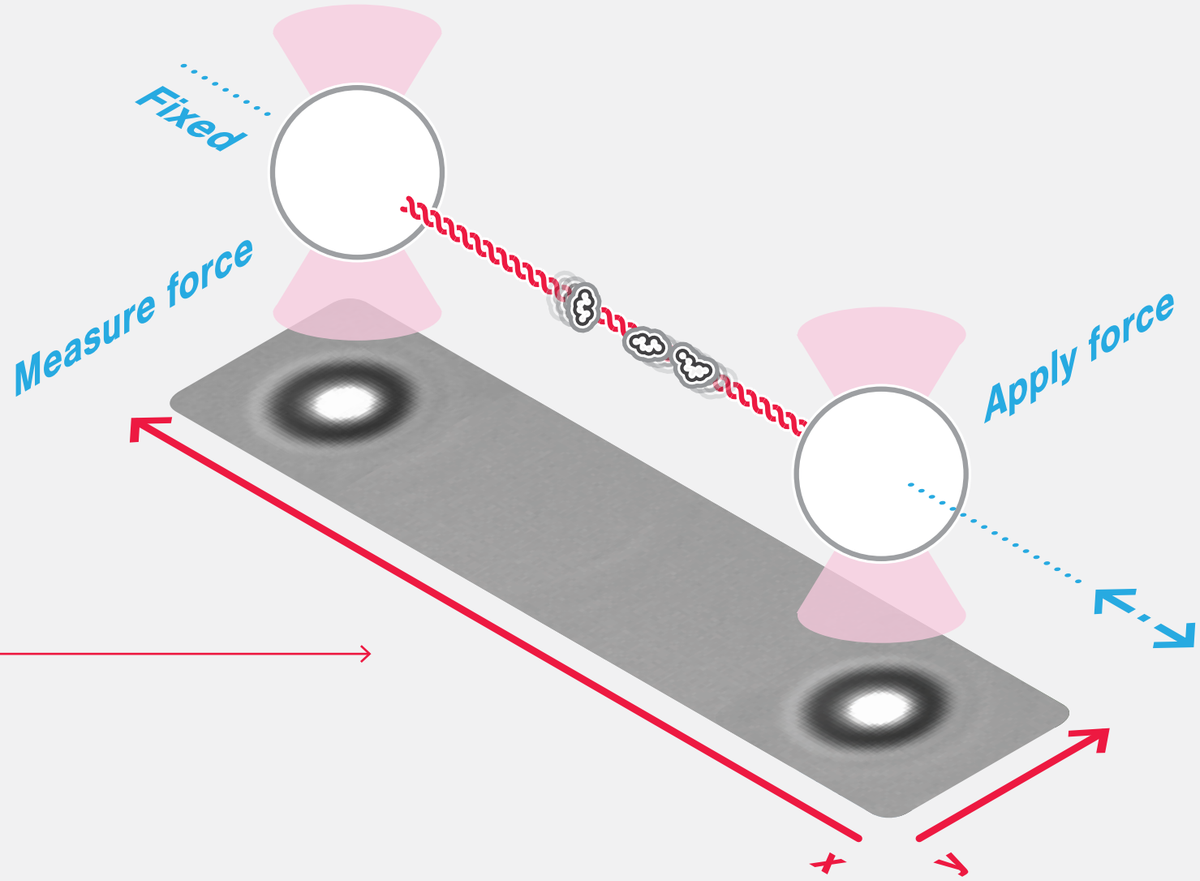


Force extension, and manipulation of single molecules

With the m-Trap high-resolution optical tweezers, we can both manipulate individual molecules, thereby inducing transitions in a controlled manner, but also to enable readings of force and distance values over time with sub-pN and sub-nm resolution.

Optical tweezers can be used to trap beads and tether in-between a single molecule, such as a double-stranded DNA (dsDNA). By stretching the dsDNA it becomes possible to obtain the characteristic force-distance curve and determine the mechanical properties of the tethered biomolecule.





Manipulation and force spectroscopy measurements at the single-molecule level

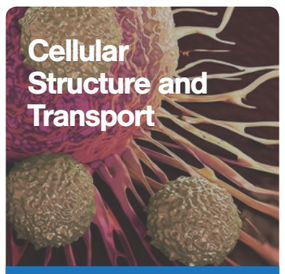
The structural dynamics of biomolecules can be measured in a matter of minutes, while long- and short-lived conformational states within a biomolecular structure can be recorded over long periods of time.
With the m-Trap, scientists are now able to reveal novel detailed information on a wide range of biomolecular mechanisms, which ultimately lead to groundbreaking discoveries.

Applications

Dedicated high-resolution optical tweezers

Using LUMICKS' pioneering m-Trap optical tweezers, scientists of all biological disciplines and backgrounds are able to study and discern the high complexities of molecular processes with base-pair resolution.

Browse the applications →

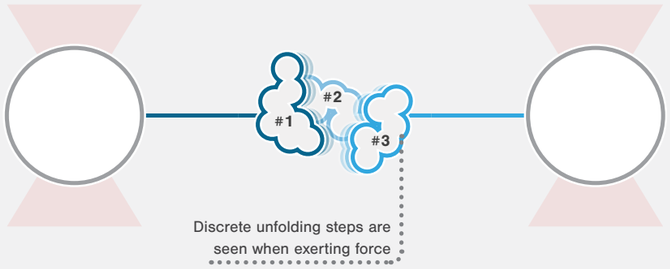


Multi-domain Protein Unfolding

Study protein unfolding steps and equilibrium dynamics.

Studying how proteins fold correctly and undergo conformational changes to accomplish their biological function is a valuable method that produces groundbreaking discoveries in the field of biology and biophysics; however, few techniques allow this study in a **non-static fashion**.

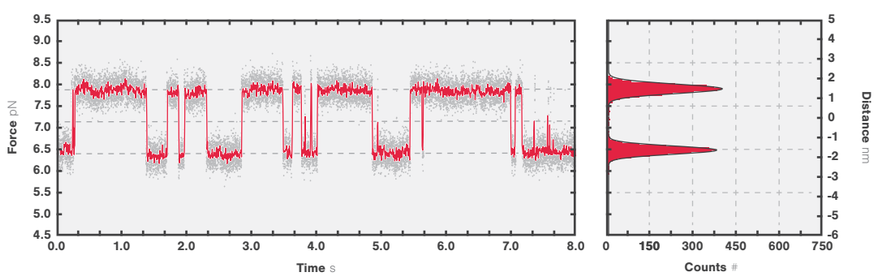
Using the m-Trap optical tweezers, both unfolding and refolding can be observed, as well as **highly detailed equilibrium dynamics**. This, in turn, allows scientists to study intermediate states in the unfolding process, identify the protein **(un)folding pathway**, and map its **energy landscape**—providing valuable information of the structure-function of the protein.



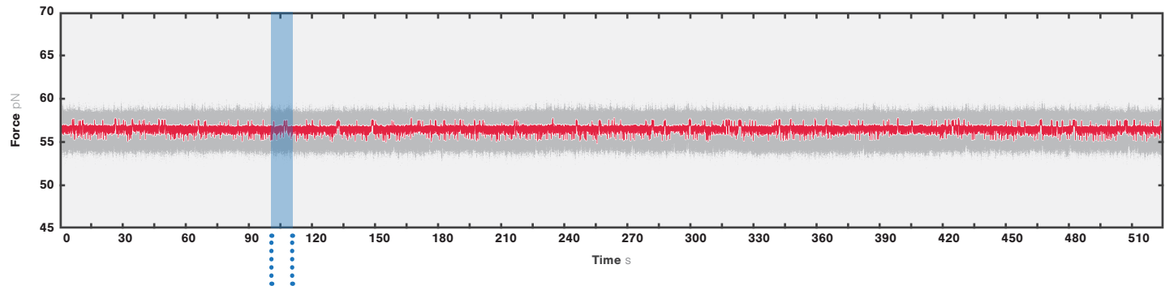
Multi-domain protein unfolding

Optical tweezers are used to trap beads while a protein is tethered using DNA-handles. The (un)folding of the protein is controlled by moving the beads while the force and distance are measured simultaneously. **Equilibrium dynamics** showing the transition between short-lived intermediate states can be studied because of the intrinsic distance clamp which keeps the traps at a fixed distance, while force fluctuations are measured. When this is applied to calmodulin, the equilibrium fluctuations and relative probabilities between the states can be observed with a force resolution of <0.1 pN at 100 Hz.

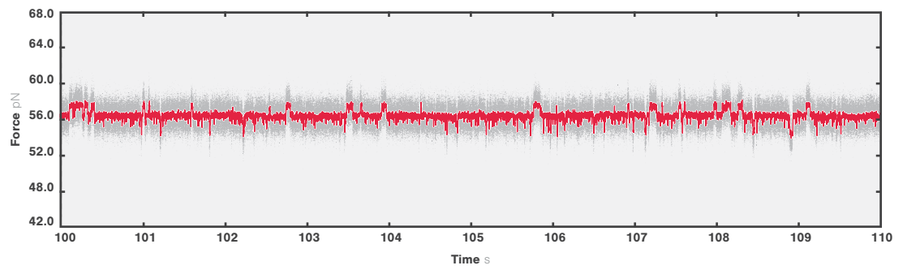
Figure 1 shows that calmodulin switches between two major states, without a clear preference, and that intermediate steps can be resolved as calmodulin occasionally jumps to a third state for short periods of time, as shown by the dashed grey lines.



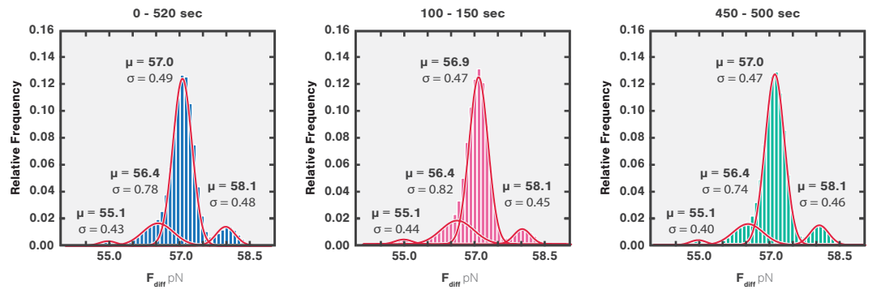
1 Force trace of equilibrium measurements over 10 seconds displaying the structural fluctuations of a single calmodulin molecule. Grey data is shown at a 2.5 kHz sampling rate while the red line shows raw data decimated to 200 Hz. The histogram on the right shows the two major states, while the third intermediate state becomes negligible due to its transitory existence. Sample obtained with courtesy of UC Berkeley, Bustamante Lab.



2 Force trace recorded over 520 seconds corresponding to a single dsDNA molecule (8.4 kbp) held at a constant distance using optically-trapped polystyrene beads (Ø= 0.8 µm). The trap stiffness was set at 0.5 pN/nm. Data were recorded at 50 kHz (gray) and decimated to 100 Hz (red).



3 Fragment with a duration of 10s of the trace shown within the blue inset in **Figure 4**.



4 Histograms of the force values collected for the full trace and for values collected during two different fragments of 50 seconds. The mean and sigma values are reported for each peak obtained from a Gaussian fit.

The m-Trap's ultra-high stability makes it possible to characterize the properties of conformational transitions occurring during protein (un)folding over extremely long periods of time. To demonstrate this, **Figure 2** shows **spontaneous conformational transitions** occurring within a dsDNA molecule at ~56 pN for almost 10 minutes. When looking at a 10 s set of the complete trace, fast transitions between multiple states are clearly visible (**Figure 3**).

The histogram analysis for both the entire 520 s trace and two 50 s sections of the main trace (**Figure 4**) show identical features, indicating that the experiment was performed without altering the transition kinetics due to unwanted force drift. When this is applied to protein (un)folding studies, the equilibrium fluctuations and relative probabilities between the states can be observed with a force resolution of <0.1 pN at 100 Hz and a force drift of <0.3 pN over minutes.

Read more:

Mashaghi et al.
Nature (2016)
Neupane et al.
Science (2016)
Pelz et al.
Nature Communications (2016)

DNA/RNA–Protein Interactions

Study molecular mechanisms involved in DNA repair, replication, transcription, translation, and organization.

Optical tweezers can be used to measure in real-time the **activity** and **states** of motor proteins, such as DNA and RNA polymerase. Single-molecule studies of stepping behavior of biomolecular motors will supply crucial new information about their enzymatic mechanisms.

Using optical tweezers, a tethered DNA or RNA template can be probed or manipulated to trigger different structural conformations. The m-Trap allows performing these manipulation steps while simultaneously monitoring the mechanical the effect generated by proteins involved in DNA processes. This is achieved with the m-Trap's unparalleled **basepair** and force resolution of <0.1 pN enabling the in-depth investigation of biological processes in unprecedented detail.

Cellular Structure and Transport

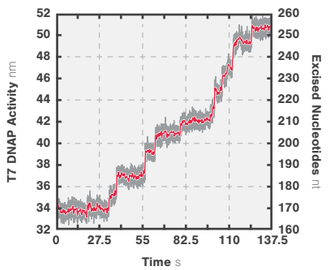
Force extension and manipulation of polymers and protein filaments.

Polymers and filaments can be manipulated with the high-resolution optical tweezers while simultaneously measuring force and extension data. Because of the extremely high escape force of the m-Trap, biomolecules can be probed up to the **nanoNewton regime.**

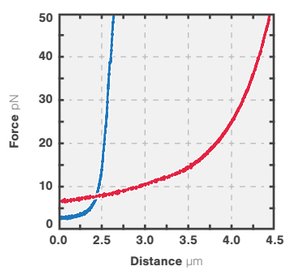
Activity and conformational changes

A DNA molecule can be caught and stretched by a constant force using the optical tweezers, while a single DNA polymerase protein replicates the DNA. As the DNA polymerase incorporates nucleotides, single-stranded DNA becomes double-stranded; thus, the end-to-end length of the DNA molecule and the distance between the two traps becomes smaller, which can be measured in high resolution. This way the **activity events** of the polymerase can be measured.

Figure 1 shows measured data of the activity of T7 DNA polymerase, which participates in DNA replication. Optical tweezers hold a DNA construct (8.3 kbp), tethered between two beads (Ø =1.86 µm) at a force of 45 pN to observe force-induced exonucleolysis at the single-molecule level. The stiffness of the DNA changes as more double-stranded DNA becomes single-stranded (**Figure 2**), allowing the activity of the polymerase to be measured. Short activity bursts of 3 to 10 nucleotides are observed interspersed by frequent pauses of varying duration.



1 Activity bursts of DNA polymerase.



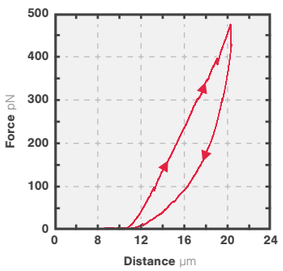
2 Force-distance curves of double-stranded DNA (blue) and single-stranded DNA (red).

Polymers and protein filaments

The mechanical properties of for example microtubules, as illustrated above, can be measured at the single-molecule level by tethering the biomolecule between two optically trapped beads. By simultaneously stretching the individual filaments and measuring the force and extension, it becomes possible to obtain the characteristic **force-distance curve** and determine the **mechanical properties** of the protein filament.

The measured data in **Figure 1** shows the extension of a vimentin intermediate filament, a fundamental constituent of the cytoskeleton. In this experiment, an individual vimentin filament is held between two optically trapped beads.

The force-distance curve is measured while stretching and relaxing the intermediate filament at a slow speed, allowing for structural equilibrium. The retraction curve shows evident hysteresis due to the remodeling of the vimentin filament under high tension.



1 Force-extension curve of a vimentin filament

Read more

Block et al.
Physical Review Letters (2017)

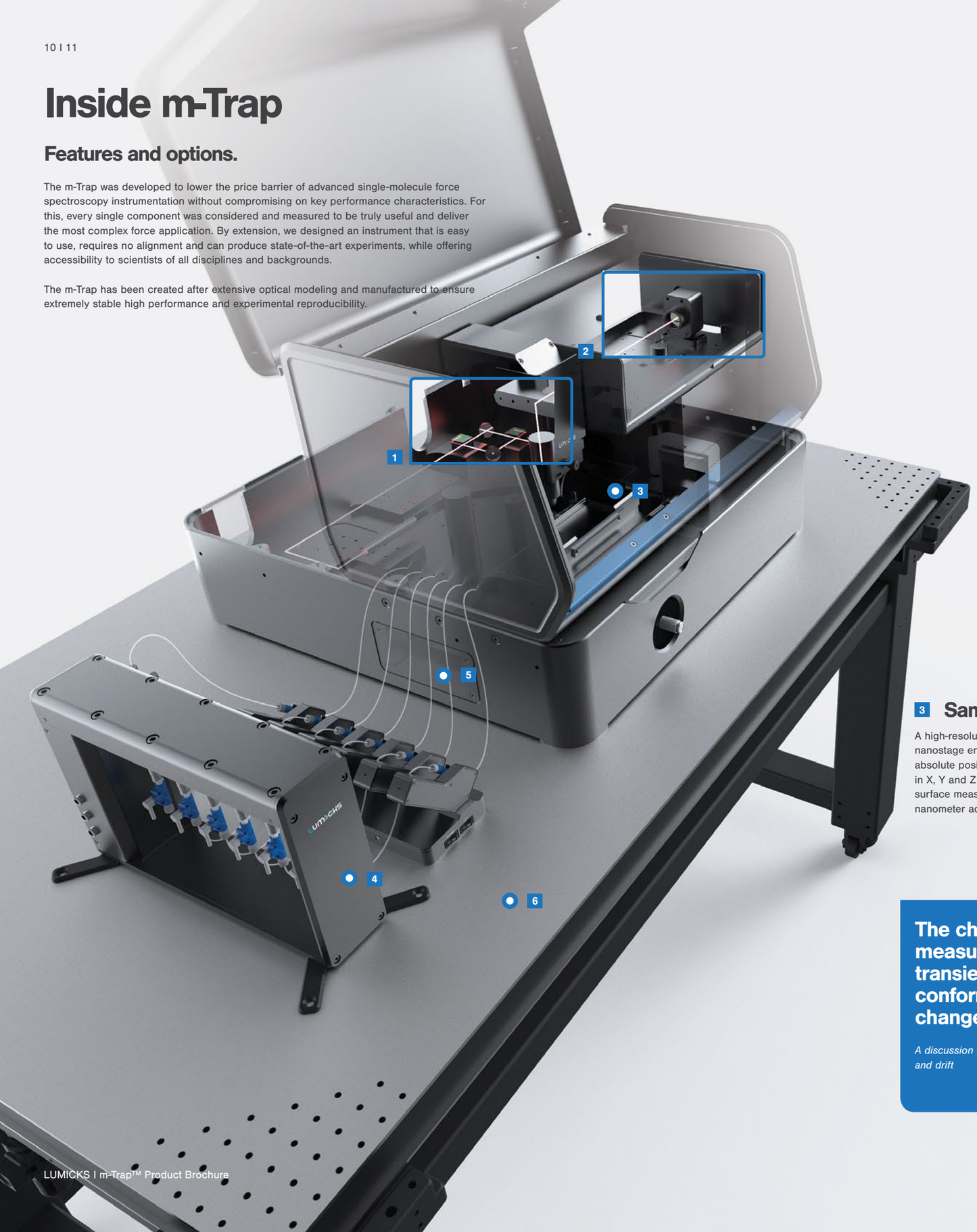
Data courtesy of Prof. Sarah Köster at the University of Göttingen.

Inside m-Trap

Features and options.

The m-Trap was developed to lower the price barrier of advanced single-molecule force spectroscopy instrumentation without compromising on key performance characteristics. For this, every single component was considered and measured to be truly useful and deliver the most complex force application. By extension, we designed an instrument that is easy to use, requires no alignment and can produce state-of-the-art experiments, while offering accessibility to scientists of all disciplines and backgrounds.

The m-Trap has been created after extensive optical modeling and manufactured to ensure extremely stable high performance and experimental reproducibility.



1 Manipulation

The m-Trap is equipped with two ultra-stable optical traps for manipulating a single biomolecule. The optical tweezers configuration consists of one trap that can be operated individually in x-direction and one trap with a fixed position. The extreme stability of less than 0.3 pN over minutes enables long acquisitions at a constant distance revealing even the rarest states, otherwise hidden by Brownian motion or instrumental drift.

2 Force detection

The force on the sample is measured with sub-picoNewton resolution on one of the traps through an ultra-sensitive position sensing detector. Tension values ranging from a few tenths of pNs to the nN level and beyond can be applied and measured. This allows for monitoring extremely small steps on a broad regime, relevant for example in protein unfolding experiments.

3 Sample control

A high-resolution piezo-controlled nanostage enables the repeatable and absolute positioning of the sample in X, Y and Z and can be used for surface measurements with sub-nanometer accuracy.

4 Microfluidics

Flip over to the next page to learn more about the power of our full microfluidic workflow!

5 m-Trap Flex

The m-Trap Flex option provides access to the optical path, allowing for the integration of custom hardware. Imaging and spectroscopy techniques can be added to the m-Trap offering full flexibility to combine locally developed optical hardware with the m-Trap's ultra-high force resolution and stability.

6 Stabilization

The m-Trap can be delivered with a pressure-stabilized optical table. Depending on your requirements, LUMICKS can find the optimal solution for ultra-stable experiments with minimal noise.

The challenge in measuring small, transient, and rare conformational changes

A discussion on resolution, stiffness and drift

Due to the motion of the of the water molecules that continuously bombard the object that is measured with the optical trap, there is an intrinsic floor on force noise on the measurement. In order to still be able to measure the smallest conformational changes, you need extremely stiff optical traps to quench the motion of the trapped bead, so that the smallest displacements are revealed by the high-resolution optical trap measurement.

Very low drift is required to enable long measurements to average out the noise, to reveal small steps and/or rare states. Additionally, in a typical case of a multi-state biological system, extremely low drift is also required to avoid change in tension on the molecule, which would skew the populations of the different states.

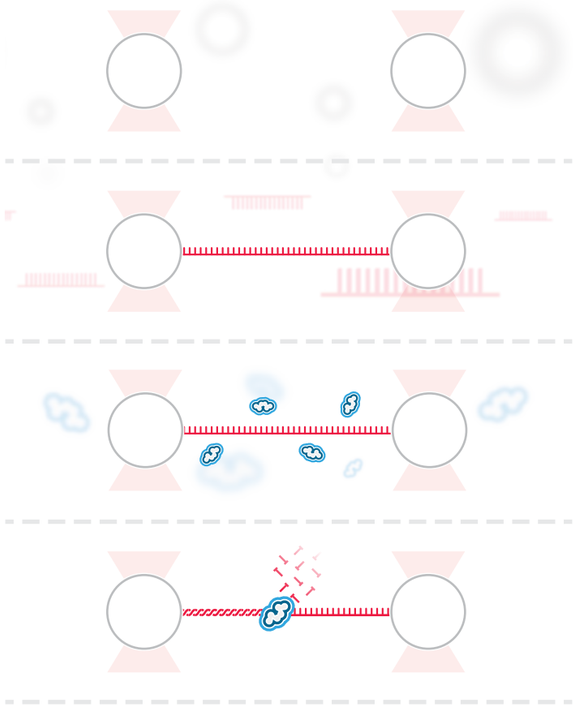
The LUMICKS solution

Unlike microscopy bolt-on tweezers, the m-Trap's purpose-built body has been fully optimized to provide extreme force stability and resolution. With drift below 0.3 pN over minutes and a trap distance resolution of less than 3A (at 100 Hz), we achieve the highest combination of force/time resolution.

u-Flux Microfluidics

A highly stable microfluidic system for single-molecule experiments.

u-Flux has been developed as an easy-to-use high throughput solution dedicated for single-molecule applications. The microfluidic flow cell provides multiple adjacent laminar flow channels that do not mix (no physical barriers are involved). Flow channels can be independently switched on and off through automated fluidic valves.



1 Bead Trapping
The first flow channel is filled with small beads which are trapped in the focal point of the optical tweezers, allowing you to manipulate and exert high forces on your sample.

2 Tether Formation
The traps are moved to the second channel, filled with a biomolecule of interest—in this example DNA. In this channel, the biomolecule is tethered between the beads.

3 Protein Incubation
DNA is incubated in the third channel with a protein or multiple proteins of interest, in this case a DNA polymerase.

4 Force Measurement
The fourth channel contains a buffer solution and is used to perform measurements. The activity of the proteins on the DNA events are quantified by the force measurement.

User insights

Dr.
Zdeněk Lánský
BIOCEV

"We are now able to construct and investigate complex macro-molecular assemblies because of the microfluidics system integrated into our setup."

Twist-lock syringes

Sample loading is easily performed by directly pipetting your sample(s) into the syringes. The twist-lock syringe adaptor with bayonet fitting allows for quick and easy refilling of individual syringes.

Remote control

Automated flow control and valve switching allow for an optimal remote operation to perform robust measurements with high throughput. Using the software, you are able to regulate the pressure and control each of the channels with simple clicks or with a scripting plugin for automation.

Reliable and precise

The pressure driven flow in combination with the monolithic glass flow cell provides an extremely stable and repeatable experimental environment. The laminar flow permits the sequential assembly of single-molecule assays and the controlled triggering of biochemical reactions by exposing the molecule of interest to different buffer environments at specific time-points.

Repeated use

The monolithic glass design allows for re-use. Even highly-concentrated chemical solutions can be cleaned quickly and effectively.

Introducing:

Bluelake

An intuitive single-molecule software suite for high throughput correlated experiments.

Designed from the ground up, our brand new software suite **Bluelake** provides intuitive controls that bring you closer to your experiment and enable the highest experimental throughput. Manipulate your sample directly with simple mouse and joystick movements, and fully automate your measurement with our powerful Python scripting engine.

With a click of a button, you perform complex single-molecule experiments and gather simultaneous force, bright-field, and instrument status data streams. The new timeline feature ensures you can focus on the data that matters, and never lose anything of value.

True correlation

Bluelake was designed to control all aspects of the m-Trap from a single interface. The trap positions, force data and bright-field images are acquired using the same software package, making the experiments truly correlative. All data streams are saved in the same single data file and synchronized using the same hardware clock.

High performance

By focusing on the ultimate performance of the software, we ensure that the user interface remains smooth and responsive, even when performing the most demanding experiments. Because of the unique GPU rendering technique of **Bluelake**, it provides fast, quick and smooth data navigation through extremely large datasets. Visualize your data in real-time, even at acquisition frequencies up to **2.5 MHz**.

Auto-save functionality

Our intuitive timeline interface for data storage automatically generates a structured overview of the state of your experiments, allowing for **fast and smooth navigation** through **multiple days of typical measurements**. The fully correlated data streams can be viewed, compared and exported during—or after your experiment. In addition, the extensive list of metadata is always streamed to disk, ensuring that you will never miss anything of value and will always be able to reproduce your experiments.

An open data standard and open source initiative

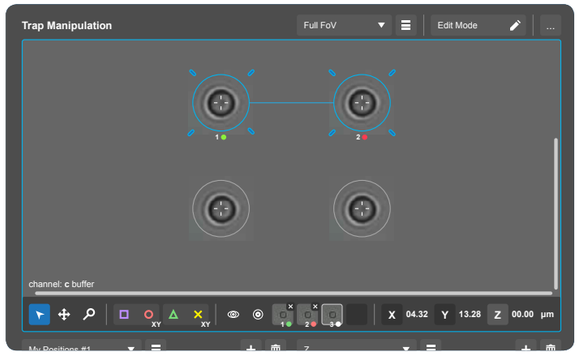
Data integrity is a key aspect of scientific instrumentation. All data of the m-Trap is stored in the standardized HDF5 open data format, which ensures that data can be accessed by anybody independent of LUMICKS software. Besides that, it is our philosophy that the user has direct access to the raw data and all data processing algorithms within the software (e.g. power spectrum fitting). This gives you **full flexibility** to understand, inspect, adapt, share and publish the data algorithms used within the instrument for online and offline data analysis. By storing extensive metadata about your experiments and saving the data in an open file format, ensures better reproducibility of your experiments and raw data that are easily accessible.

User insights

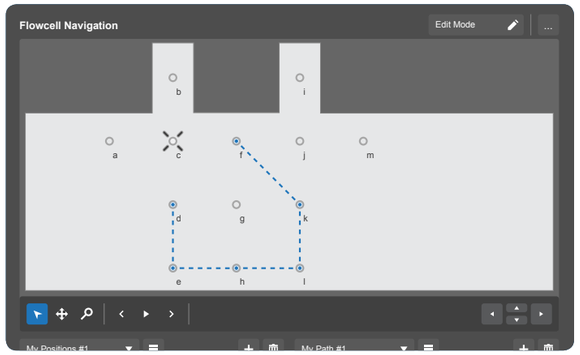
Prof. Ben Schuler
University of Zurich

"The user-friendly software combined with the high-throughput experimental workflow and the dedicated training we received from LUMICKS, has fully equipped us to perform state-of-the-art single molecule force spectroscopy experiments in no time."

Bead trapping



Flow cell navigation



Ease of use

Bluelake provides intuitive controls that bring you closer to your experiment. The software is developed in such a way that it gives you all the controls you need in an easy and intuitive manner. Whether you are visually navigating through the laminar flow cell on screen, or selecting the area you wish to scan in the bright-field camera tab, our user-centered approach provides you with an intuitive experience that is accessible for anyone.

Automation and scripting with Python

Repeatable experiments are key for gathering statistically relevant quantities of data and publishable results. The m-Trap software allows for automation through the implementation of:

Programmable controls that automate basic procedures, such as predefined trap calibration, force-extension measurements, force-clamp experiments and predefined sample-stage trajectories, making measurements faster and less prone to human or random errors.

Scripting with full access to all relevant system parameters and data streams to allow the user to fully automate any kind of repeated experimental procedure, enabling to perform experiments autonomously.

```
trap.clear()  # to get rid of any existing bead
stage.move_to("beads")
fluidics.open(1, 2, 3, 6)  # depends on experiment

while trap.match_score < 30:
    if 0 < trap.match_score < 30:
        trap.clear()  # bad bead, BAAAD bead! >:(
        pause(1)  # second

stage.move_to("buffer")
fluidics.close(1, 2, 3, 6)
```

Catching beads with 11 lines of code

Here we show the power of **Bluelake**'s scripting features; **automated bead catching**. The software moves the traps into the bead channel, and selectively catches beads that fit the user's set criteria. The moment the perfect beads are trapped, the flow is stopped and the sample is automatically moved to the buffer channel, ready for you to start the next step of your experiment.

Spec sheet

Unique and enabling features of m-Trap.

Optical Tweezers

Force resolution	< 0.1 pN at 100 Hz (1 µm beads at 0.3 pN/nm trap stiffness)
Maximum escape force	> 1000 pN using 4.5 µm polystyrene beads
Force stability	< 0.3 pN over 2 minutes
Trap distance resolution	< 3 Å at 100 Hz
Minimal incremental step size	2 nm
Live bead tracking accuracy	< 3 nm at 100 Hz using video analysis , simultaneous with force and fluorescence detection
Field of movement (FoM)	38 µm (x)
Trap type	Continuous wave for unparalleled stiffness, stability and precision
Number of independent traps	2
Trap positioning capability	One fixed, one moveable in x

Dual optical tweezers; for manipulating single biomolecules with high stability and precision.

Force detection; measured on one trap with an extremely high escape force (>1000 pN), force stability (<0.3 pN over 2 minutes) and force resolution (<0.1 pN at 100 Hz); for probing different biological systems with a large dynamic range, while measuring very small force steps.

Trap steering; providing 2nm positioning accuracy applicable over a range of 38µm; for providing accurate trap movement over a large field-of-view.

Video-based bead-tracking; with an accuracy <3nm at 100 Hz for independent distance tracking.

Integrated software suite; with optimized workflow; for high throughput single-molecule experimentation by trapping microspheres, tethering and subsequently manipulating biomolecules within minutes.

Standard sample holder; to clamp microscope slides and/or coverslips containing the sample.

LUMICKS is committed to standing by you to ensure your instrument performs to specification throughout its lifetime, provide you with access to our experts for application support and service to facilitate the fastest time to result for your experiments.

Microfluidics

Multi-channel laminar flow microfluidics system; without physical barriers between the channels; for introducing reagents in a controlled manner and *in-situ* assembly of a wide range of complex, multi-step single-molecule assays.

Remote fluidics valve control; for programming the software user interface for high data throughput applications.

Software

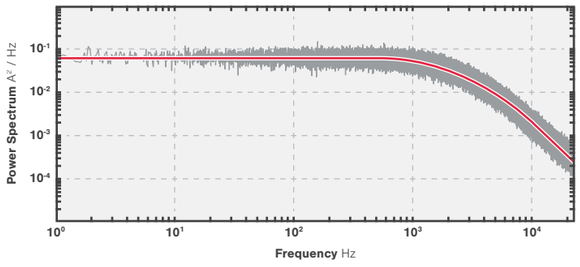
New Bluelake software suite with optimized workflow; for high throughput single-molecule experimentation by trapping microspheres, tethering and subsequent manipulation and imaging of biomolecules within minutes.

Software support; at LUMICKS, we have a software team working relentlessly to continuously optimize and adapt the m-Trap software for novel applications. We work with our users to implement features that help them improve their research capabilities, enhancing the possibilities of the system with every release

General

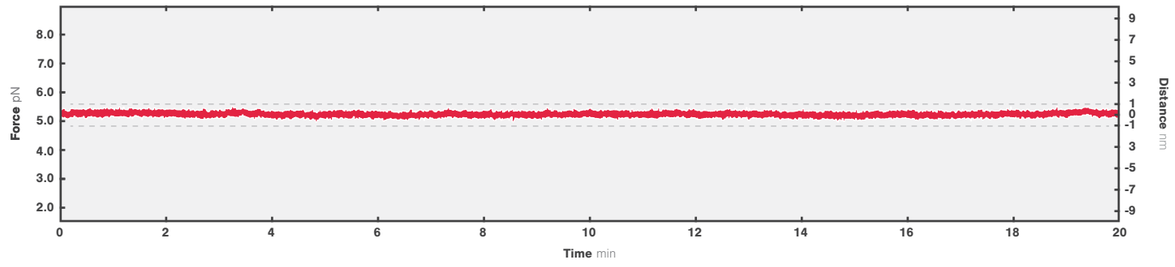
High-resolution piezo-controlled nanostage; for surface assays and repeatable and absolute positioning of the sample.

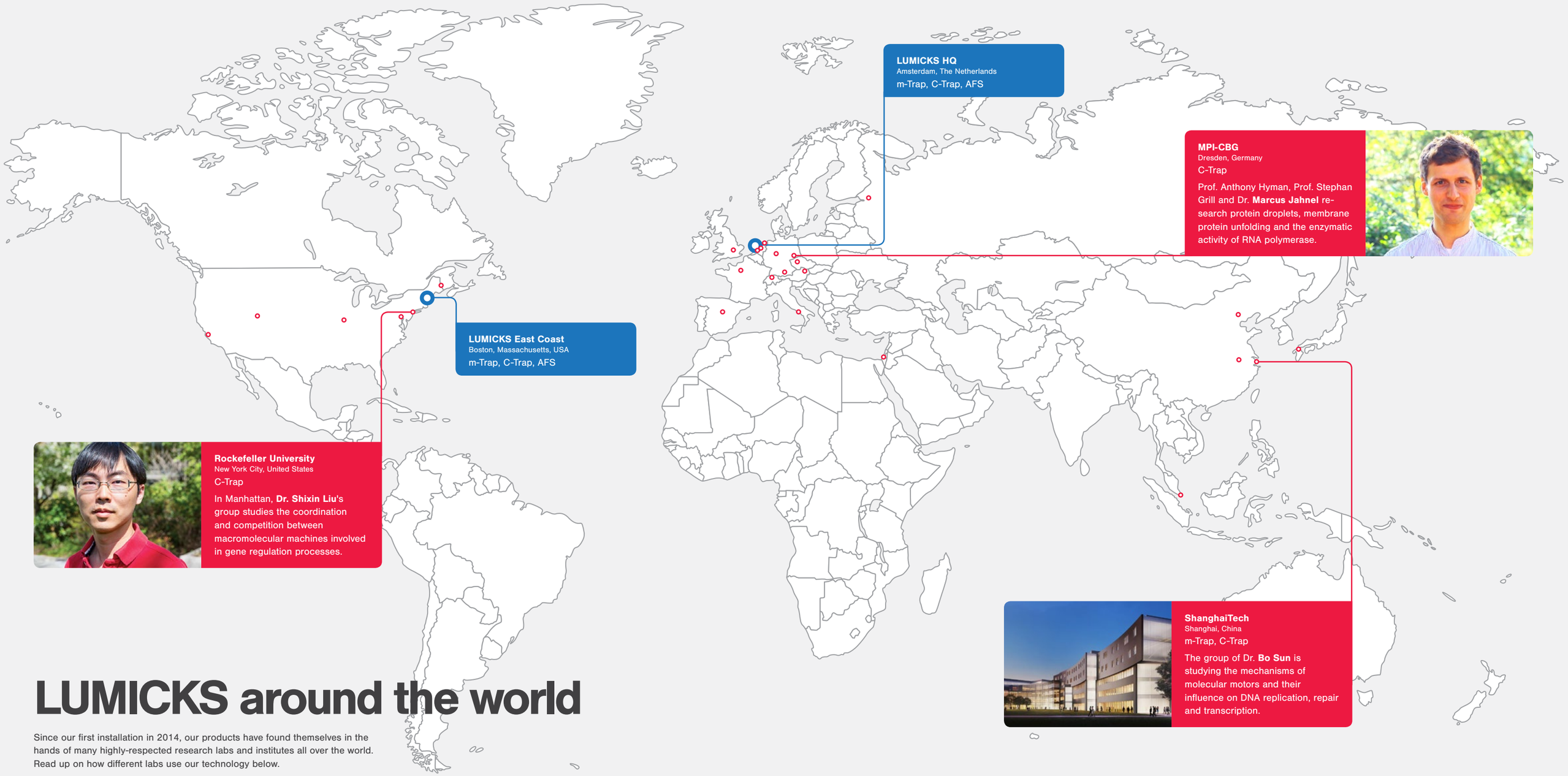
On-site application and scripting training; for expert support from our specialists dedicated to the customer's scientific application.



Power spectrum (acquisition time of 5 minutes)of the Brownian motion in the X-direction of an optically-trapped 1.00 µm polystyrene bead. Raw data were binned in 20 points bins (grey), which were then used for performing a 2-step fit (red).

Force trace recorded over 20 minutes to a single dsDNA molecule (8.4 kbp) held at a constant distance using optically-trapped polystyrene beads (Ø= 1.0 µm). Data are shown at 100 Hz





LUMICKS around the world

Since our first installation in 2014, our products have found themselves in the hands of many highly-respected research labs and institutes all over the world. Read up on how different labs use our technology below.

UC Berkeley
Berkeley, California, USA
C-Trap *SR*, u-Flux

Göttingen University
Göttingen, Germany
C-Trap

BIOCEV
Prague, Czech Republic
C-Trap

Ludwig Maximilian University
Munich, Germany
AFS

Imperial College London
London, United Kingdom
C-Trap, AFS

FOM Institute AMOLF
Amsterdam, The Netherlands
C-Trap

Pasteur Institute
Paris, France
AFS

Max F. Perutz Laboratories
Vienna, Austria
AFS

Johns Hopkins University
Baltimore, Maryland, USA
C-Trap, AFS

VU University
Amsterdam, The Netherlands
C-Trap, AFS, u-Flux

Kyushu University
Kyushu, Japan
AFS

Colorado State University
Fort Collins Colorado, US
AFS

University of Zürich
Zürich, Switzerland
C-Trap

University of Groningen
Groningen, The Netherlands
C-Trap

Hefei University of Technology
Heifei, China
AFS

CSIC Madrid
Madrid, Spain
AFS

LUMICKS Suppport

Our application scientists constantly travel around the globe to conferences and institutes to perform demonstrations, jobs, training and hands-on workshops. The whole LUMICKS team focuses on offering the best possible support for your research needs. Interested in how the m-Trap works and what it can do for your research? Reach out to us to experience the possibilities yourself!

LUMICKS - Capture Molecular Interactions

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Capture Molecular Interactions