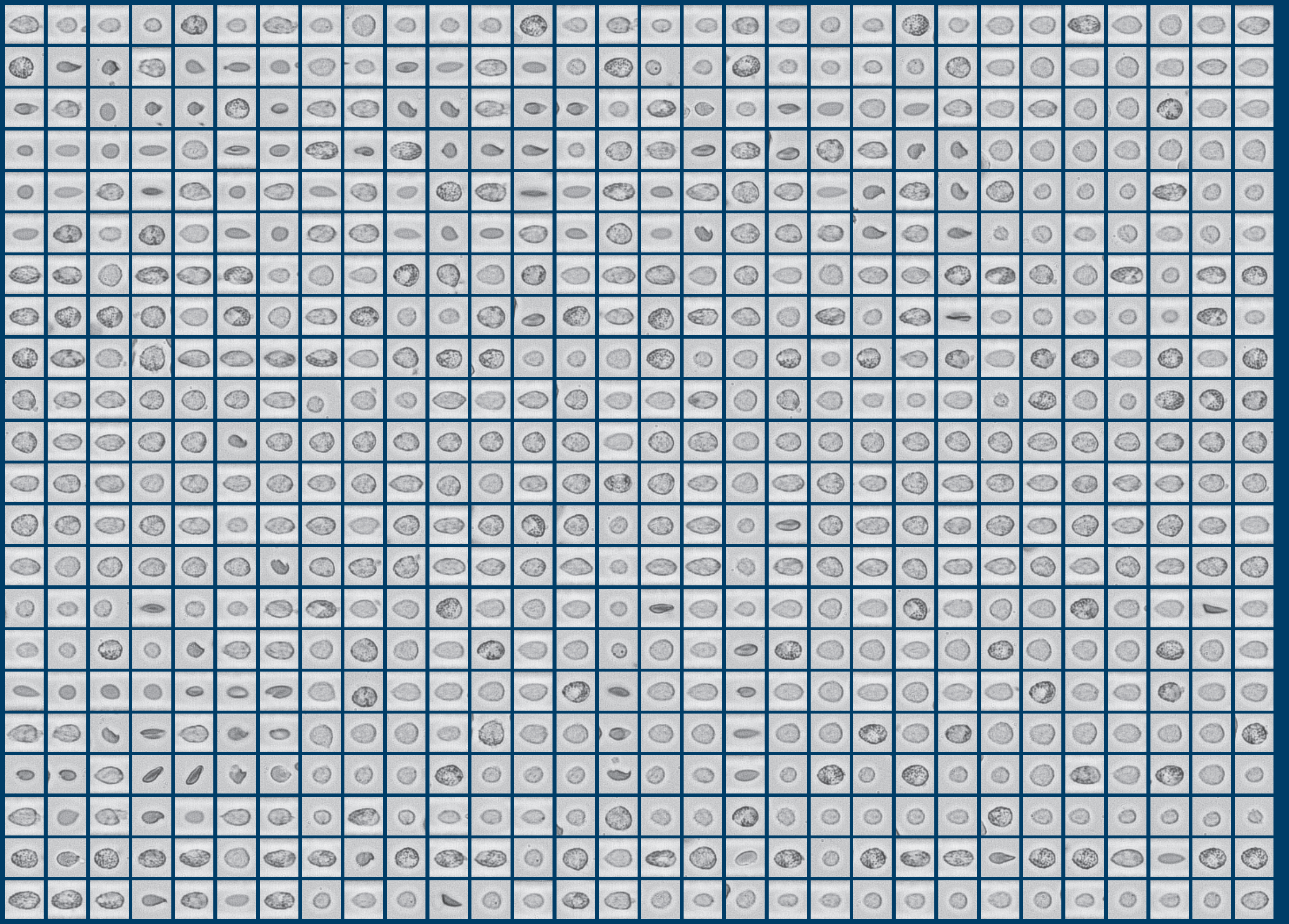
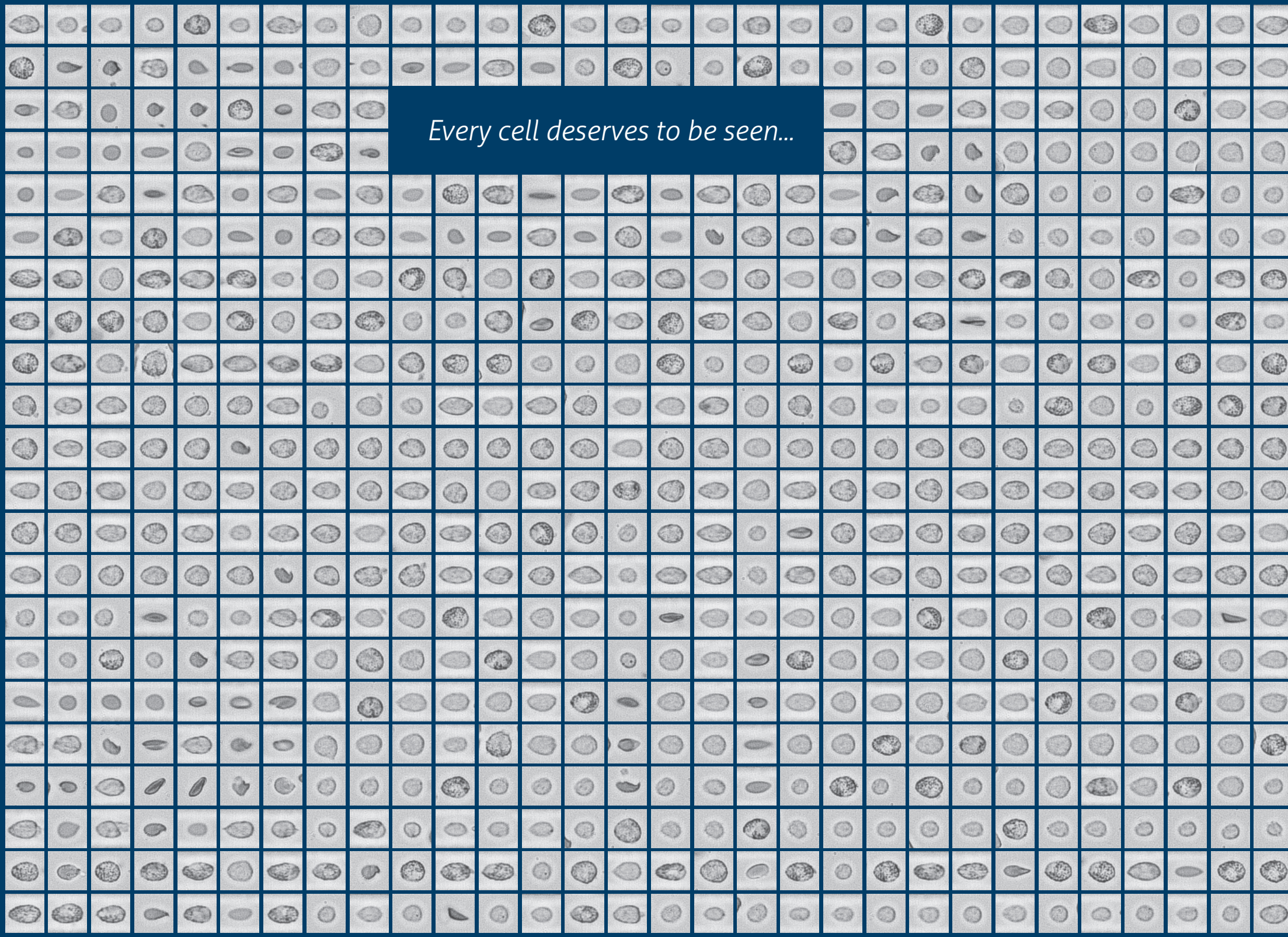
ZELLMECHANIK DRESDEN

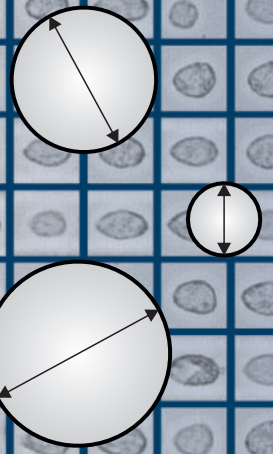
more senses for science



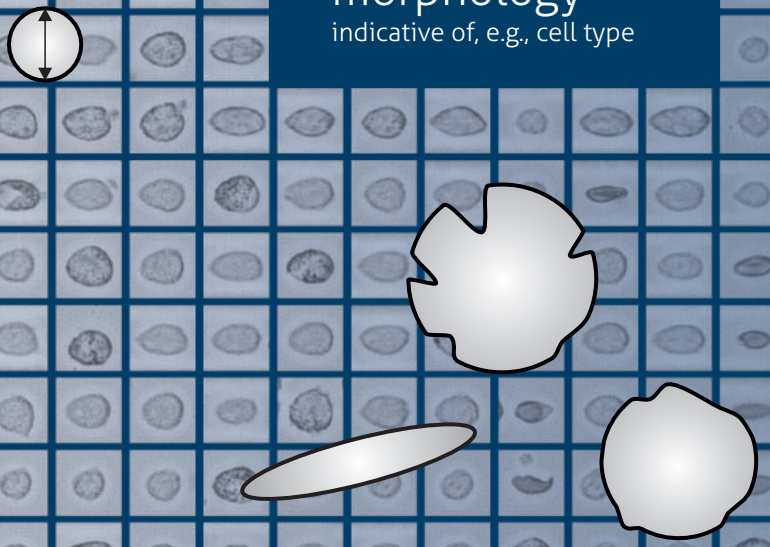

Every cell deserves to be seen...

...for its visible features...

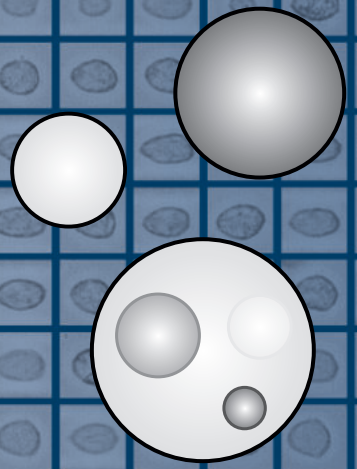
size
indicative of, e.g., cell growth



morphology
indicative of, e.g., cell type



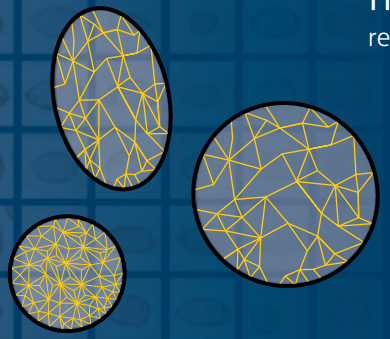
brightness
indicative of, e.g., cell content



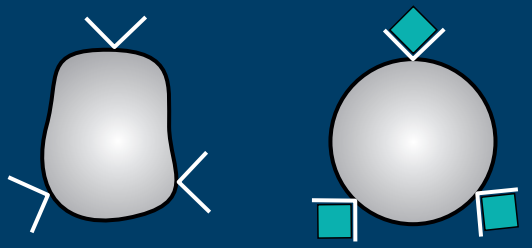
...and for its hidden properties.

mechanical characteristics

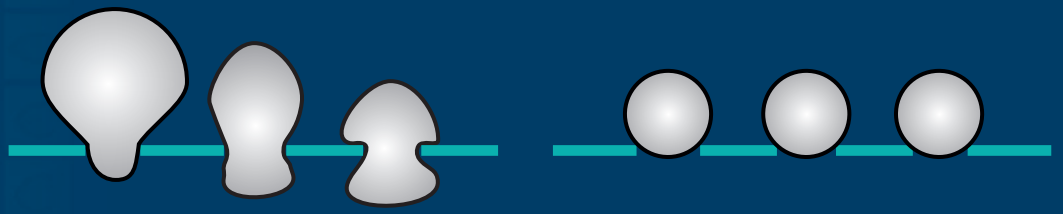
reveal, e.g., ...



... cell activity and activation states



... migratory abilities

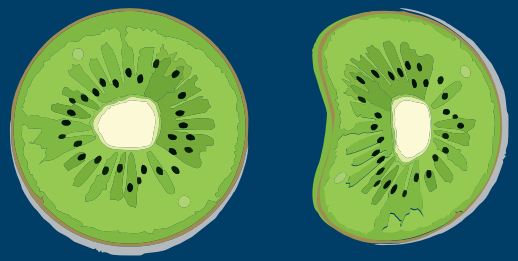


... memory of former cellular environment

WHY WE CARE ABOUT CELL MECHANICS:

Creating, sustaining and sensing mechanical forces are fundamental elements in cell-cell and cell-substrate interactions as well as cellular function. Therefore, cell mechanics constitutes a key scientific target for investigating topics ranging from development to disease. We offer the tools that give you the tactile sense necessary to uncover the inner mechanical features of cells.

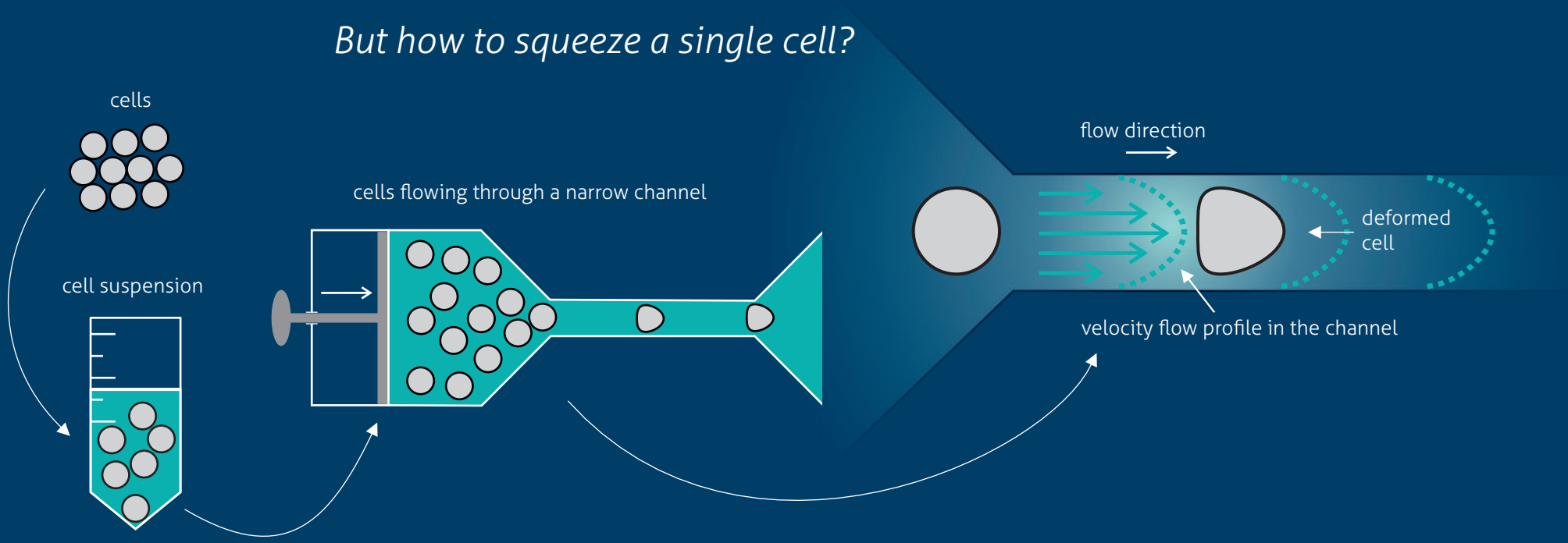
IMAGING FLOW CYTOMETRY FOR CELL MECHANICS



On the macro-scale, testing the mechanical response is intuitive. To determine if a fruit is ripe, you may gently squeeze it and the degree of deformation will depend on the force of your fingers and the properties of the fruit. Similarly, testing a single cell yields a response that depends on the cytoskeleton, nucleus, membrane and sub-cellular structures.

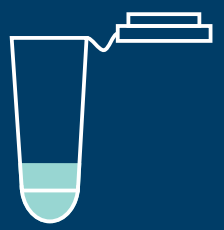
METHOD & TECHNOLOGY

But how to squeeze a single cell?

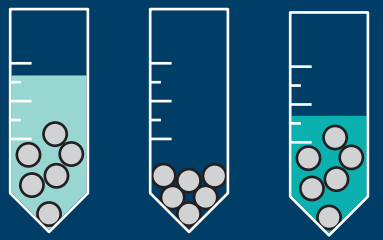


Deforming cells with hydrodynamic forces: The surrounding fluid generates forces that deform individual cells when they travel through a narrow channel. These forces originate from friction within the fluid, which increasingly reduces the flow velocity closer to the channel wall. A cell in the channel is exposed to the resulting velocity gradient in the liquid and experiences a force field that applies a gentle squeeze. High-speed imaging reveals the resulting cell deformation. The degree of deformation is indicative of the stiffness of the cell.

REAL-TIME DEFORMABILITY CYTOMETRY (RT-DC)



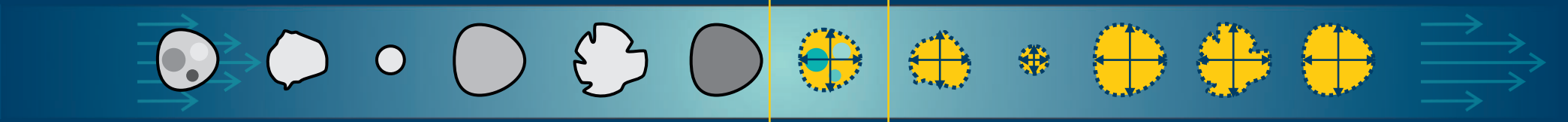
+ **low sample volume**: starting from 30 µl and 10 000 cells



+ **easy sample preparation**: take up in measurement buffer, load sample and start experiment

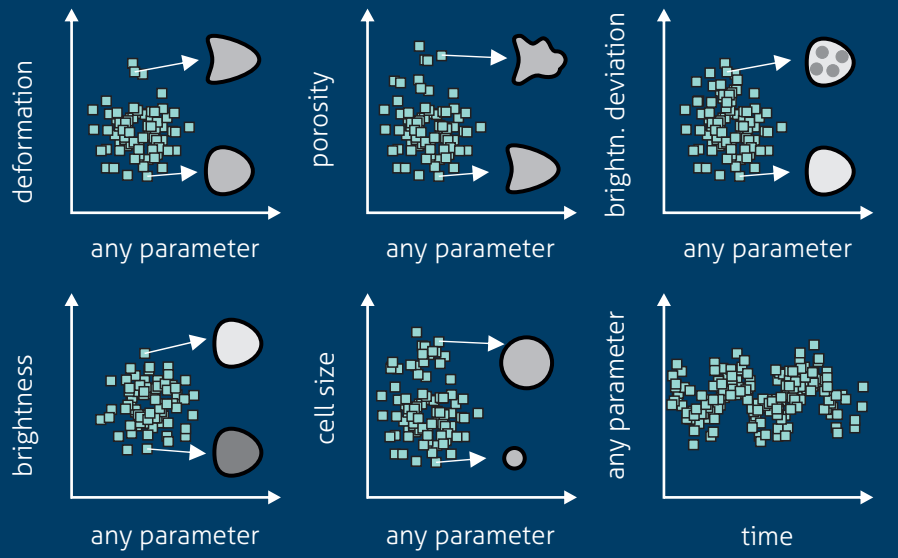
+ **image of every cell**: inspect interesting events with your own eyes
+ **label-free**: as long as cells are discernible by their intrinsic properties, no artificial labels and no hypotheses of molecular targets are necessary during mechanical probing
+ **high speed and high throughput**: measure and analyze up to 1000 cells per second, typical time from sample preparation to results: 15 minutes
+ **non-destructive**: sample reusable, >90% viability (Otto et al., Nature Methods, 2015)

real-time analysis



area
height
width
aspect ratio
circularity
deformation
inertia ratio
porosity
brightness
brightness deviation

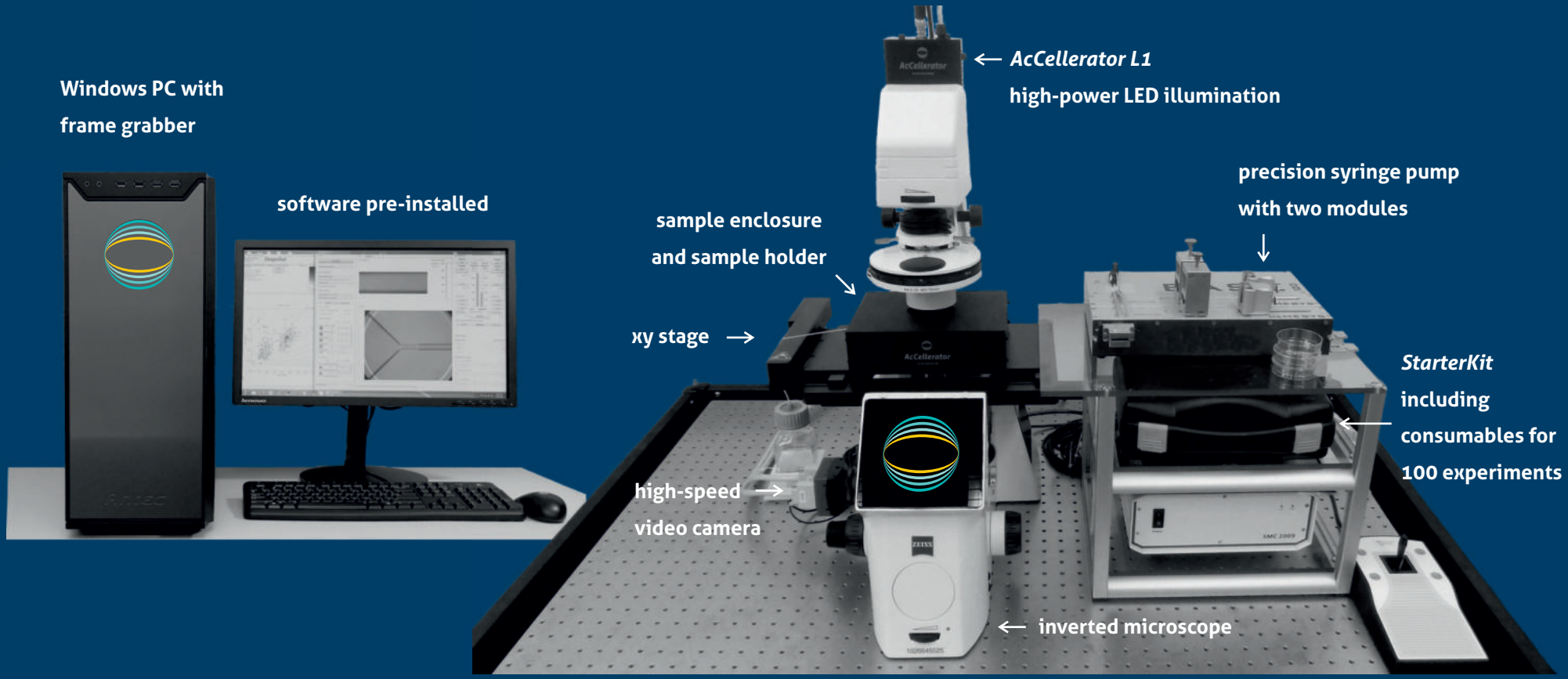
+ **analysis in real-time**: no need for cell purification/isolation; possibility to focus your measurement on a sparse subpopulation
+ **cell brightness**: distribution and average of pixel intensity allow identification of certain cell types and their content
+ **cell size**: true cell dimension form image
+ **cell shape**: immediate calculation of deformation and additional morphology parameters like porosity



METHOD & TECHNOLOGY

AcCellerator

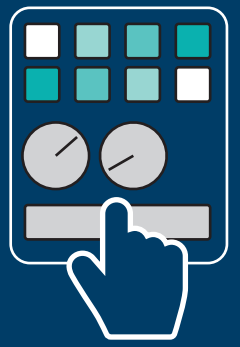
The *AcCellerator* is your door to the world of cellular mechanics. Extend your research methods with a quantitative cell characterization device that detects properties, responses and function that would otherwise remain hidden.



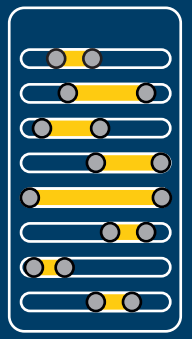
The *AcCellerator* is a high speed imaging cytometer for mechanical cell characterization through real-time deformability cytometry measurements. Designed as an extension to an inverted microscope, the combination of hardware and software solutions ensures unprecedented comfort and flexibility for cell mechanical measurements. Our *InitialService* includes delivery, installation and user training as well as all the consumables necessary for your first experiments.

Shape-In and *Shape-Out* - SOFTWARE FOR ACQUISITION AND ANALYSIS

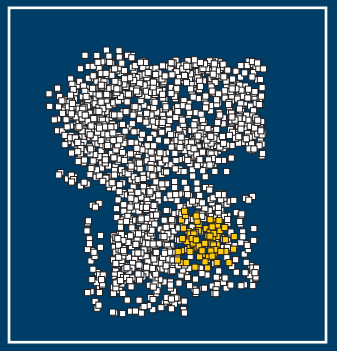
***Shape-In* is the data acquisition software and control center of the *AcCellerator*:**



control



gate



live-plot

storage

Shape-In allows you to define your measurement parameters and to control measurement conditions. The created data file contains information on all detected events including image data, deformation data and morphology data. Real-time gating allows you to focus on a subpopulation of cells within a heterogeneous sample.

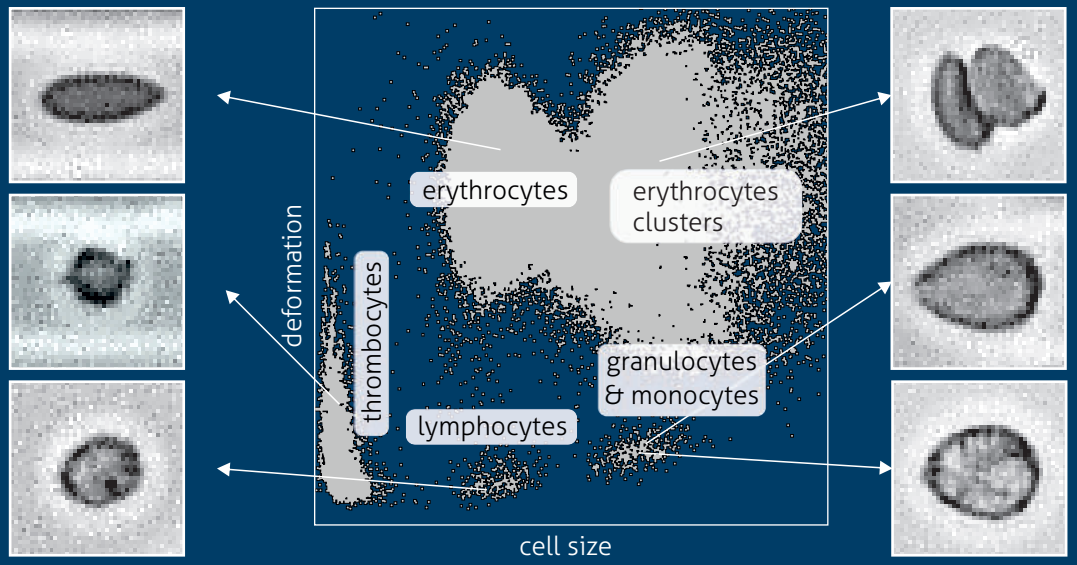
***Shape-Out* is the data analysis and visualization software:**

Shape-Out is designed as an open source software to grant our customers full access to the analysis process. It allows you to inspect and analyze your data by:

- filtering/gating
- visualizing
- calculating elastic moduli
- determinig statistics (e.g. comparison by linear mixed models)

You may export your data to another file format like .fcs, .tsv, .avi, .png.

click-to-inspect feature

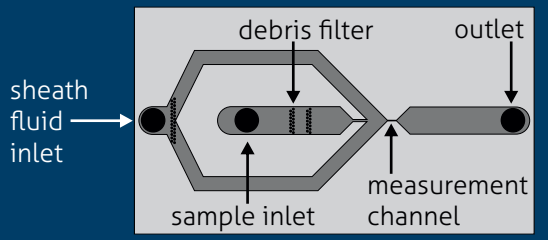


PRODUCT

FlicXX and *CellCarrier* - THE CONSUMABLES

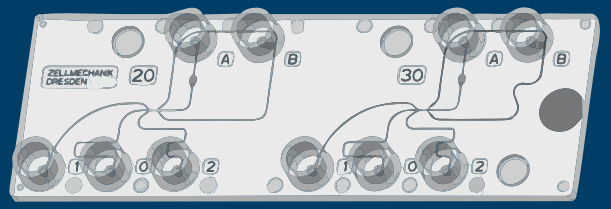
The microfluidic channel device *FlicXX* and the measurement buffer *CellCarrier* are at the heart of each experiment. The modular single use design of *FlicXX* prevents sample cross-contamination and ensures optimized conditions for every experiment. *FlicSo* is a high quality plastic chip for active cell sorting with the *SortingModule*.

Flic15, Flic20, Flic30, Flic40



- glass (borosilicate): 0.19-0.23 mm
- PDMS (Polydimethylsiloxane)
- we offer 15, 20, 30 and 40 µm channel cross-sections (± 7%)

FlicSo



- one chip provides two channels: 20 µm and 30 µm
- designed for 2-way sorting experiments using the *SortingModule*
- easy connection between tube and *FlicSo* through Luer connectors
- comes with two triple-container for connecting sorting pressure and collecting target and default samples

CellCarrier, CellCarrierB

- sterile filtered PBS
- < 1% methyl cellulose to adjust the viscosity
- pH: 7.4
- Osmolarity: 310-330 mOsm/kg
- Viscous, transparent fluid

FlicXX are microfluidic chips with a narrow measurement channel of a cell-type specific cross-section. The channel layout includes a cell focusing sheath geometry. We offer 15, 20, 30 and 40 µm channel cross-sections (*Flic15*, *Flic20*, *Flic30*, *Flic40*). *CellCarrier* is a measurement buffer with fine-tuned viscosity to ensure high reproducibility of experiments. The composition of *CellCarrier* is optimized for mammalian cells and based on phosphate buffered saline with <1 % methyl cellulose. We offer two different viscosities to cover a broad range of cell stiffnesses and custom compositions of *CellCarrier* on demand.

SERVICES

InitialService

delivery to the lab

installation, configuration, test run

user training

CustomService

sample buffer customization
(*CellCarrier* with custom viscosity
and/or composition)

channel-size customization
(design and production of
non-standard channel-sizes)

ServiceContract

assistance with experiment design

assistance with data interpretation

software upgrades

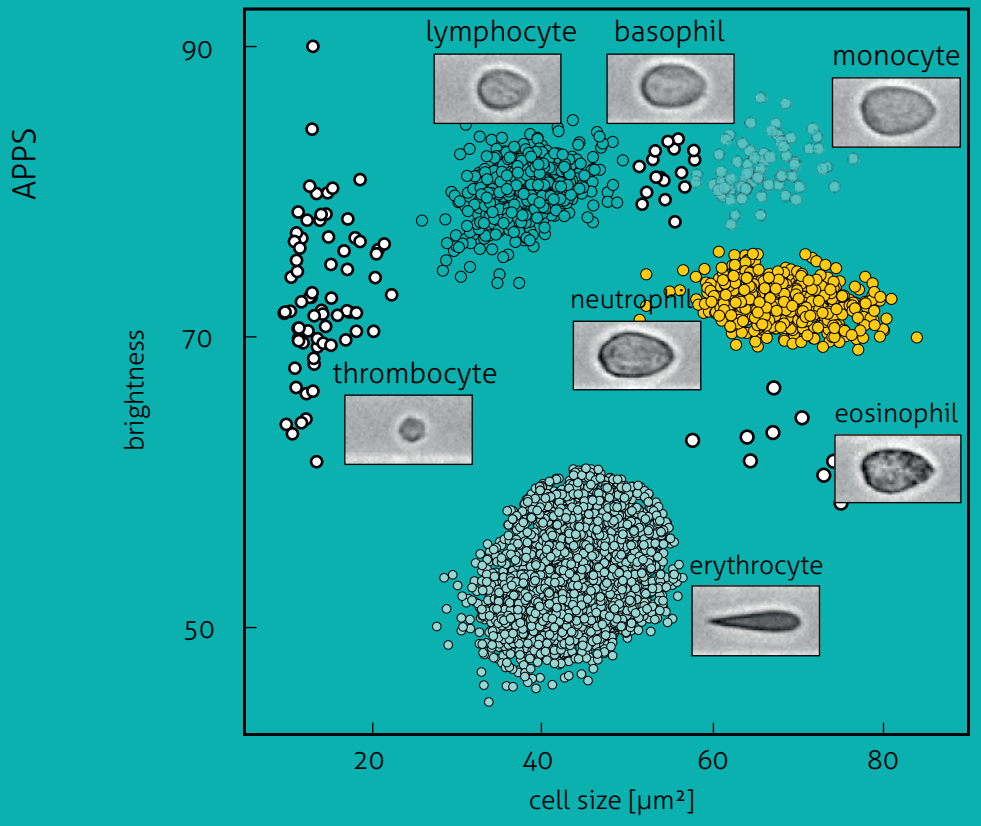
Pre-trial: if you want to test the feasibility of *AcCellerator* measurements with your sample, please contact us.

If you need any assistance feel free to call, write or visit us anytime. We are personally available for our customers.

PUBLISHED APPLICATIONS: WHOLE BLOOD

Discern blood cell types:

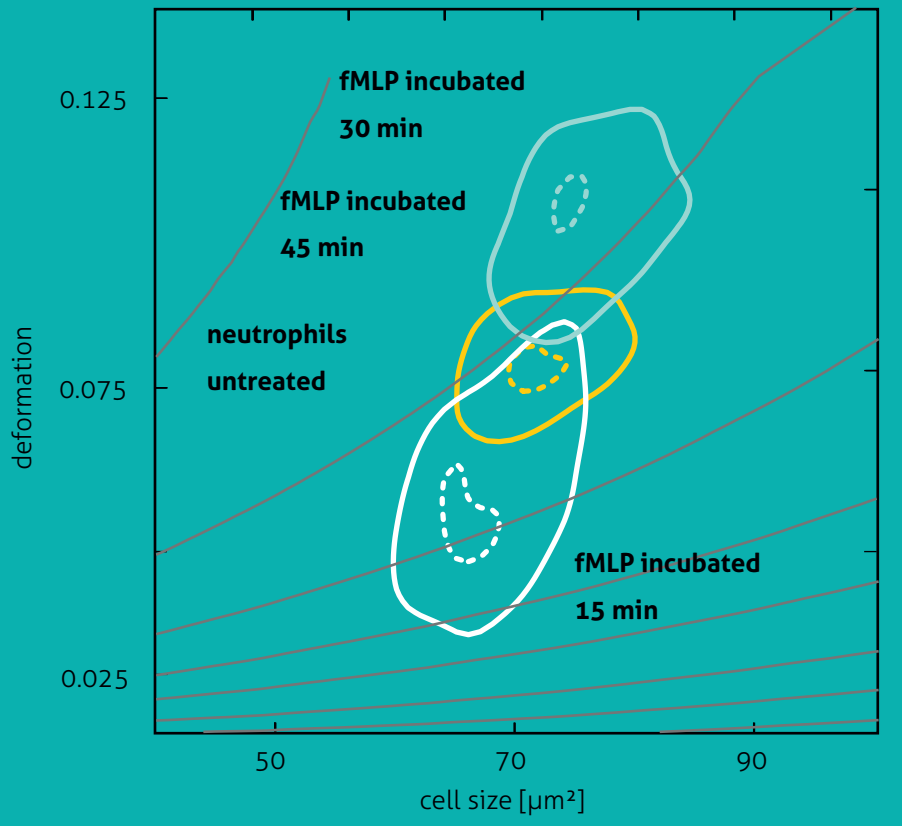
Many cell types are distinguishable by properties of their images like brightness and size. In whole blood samples, this enables the identification and further analysis of erythrocytes (red blood cells), thrombocytes (platelets) and even subpopulations of leukocytes (white blood cells) without the need of labeling or cell purification.



Töpfner et al., elife, 2018

Resolve kinetics in neutrophil activation:

High measurement rates and fast sample preparation allow for observation of kinetic processes. The plot below shows the change of mechanical properties when neutrophil granulocytes from freshly drawn blood are exposed to formyl-methionyl-leucyl-phenylalanin (fMLP). The tripeptide fMLP is released by many bacteria and signals an infection to cells of the immune system.

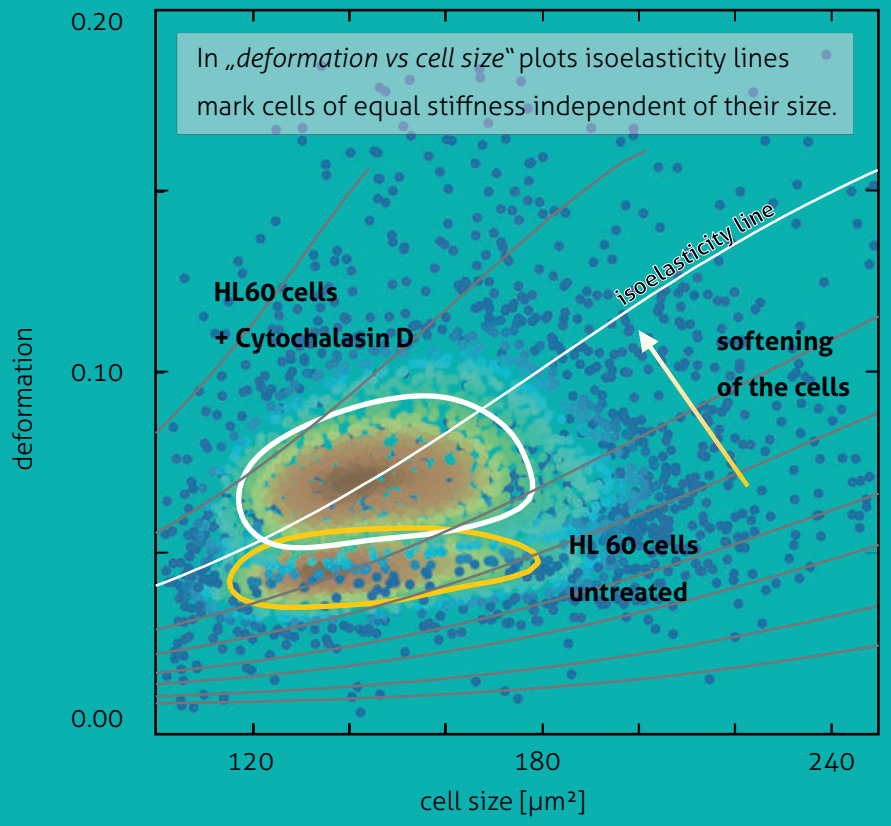


Töpfner et al., elife, 2018

PUBLISHED APPLICATIONS: CULTURED & STEM CELLS

Detect changes of the cytoskeleton:

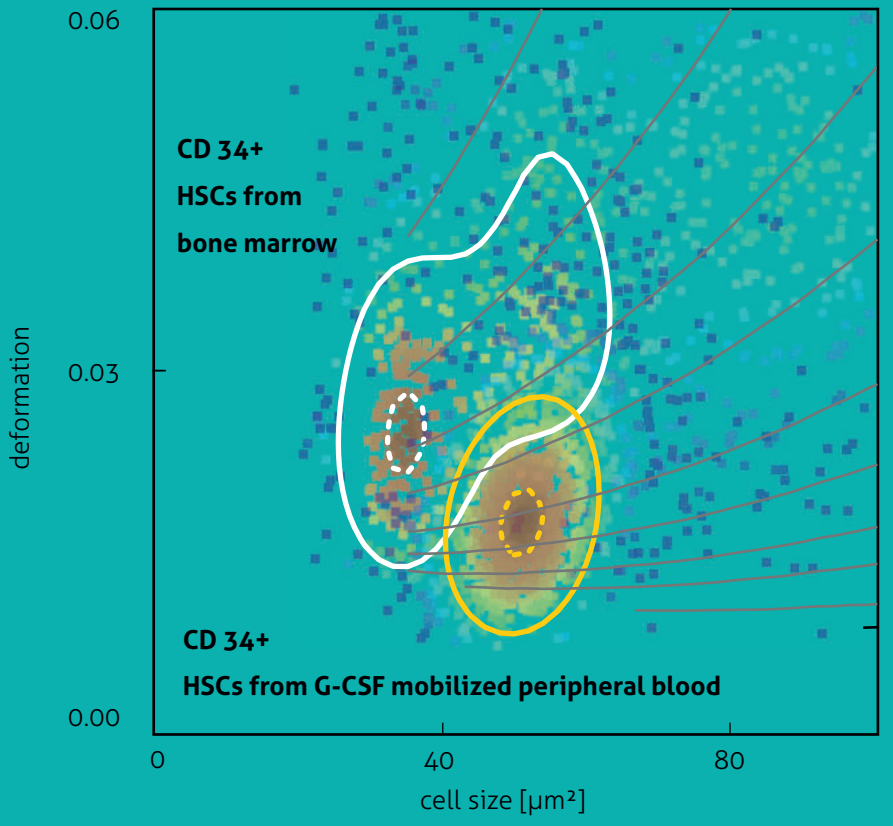
Alterations of the cytoskeleton can be quantified through mechanical analysis. The depletion of actin microfilaments by Cytochalasin D results in a higher deformation and therefore, reduced stiffness of HL60 cells. The plot below shows the superposition of treated and untreated cells.



Golfier et al., Cytoskeleton, 2017

Investigate effects of past conditions:

Primary human hematopoietic stem cells (HSCs), are commonly identified by the presence of the transmembrane protein CD34. The plot below compares CD34+ cells obtained from bone marrow and CD34+ cells that were mobilized into peripheral blood by the granulocyte colony–stimulating factor (G-CSF). While identical according to their CD34+ classification, HSCs derived from peripheral blood are stiffer than HSCs derived from bone marrow.

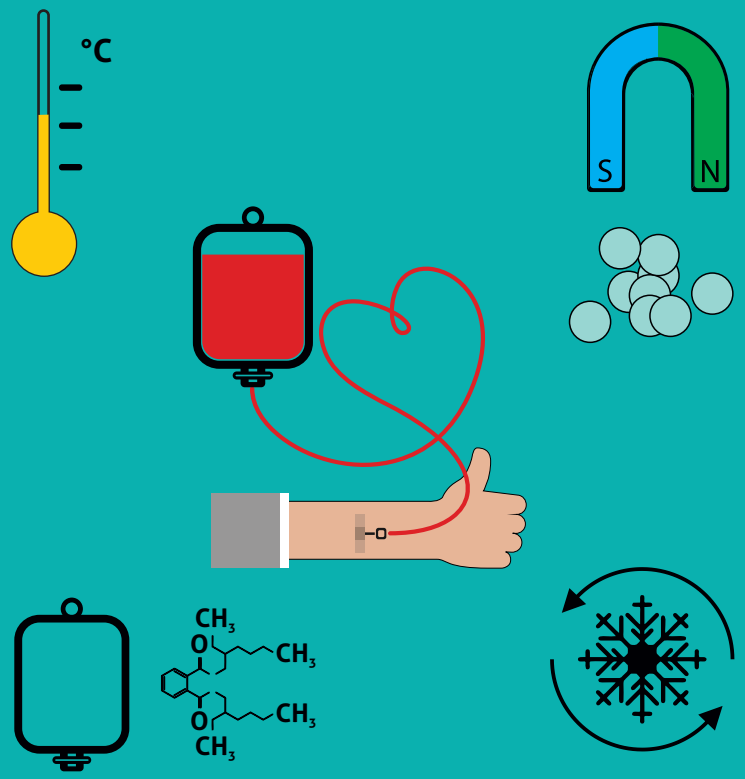


Otto et al., Nature Methods, 2015

PUBLISHED APPLICATIONS: TRANSLATIONAL MEDICINE

Quality control of blood products:

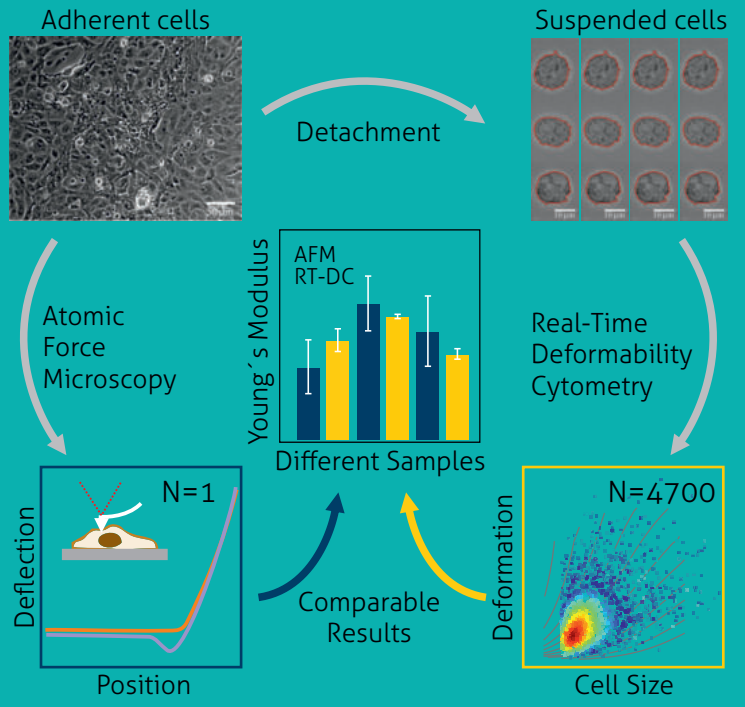
RT-DC can be used to monitor the status of e.g. platelet concentrates, red blood cells or hematopoietic stem cells. A study shows the impact of storage temperature, intracellular changes by nanoparticle exposition, impact of plasticizers in PVC blood bags and the influence of cryoprotectants on the rheology and other biophysical properties of the stored cells.



Aurich et al., Lab on a Chip, 2020

Label-free characterization of suspended cardiomyocytes:

Researchers explored the potential of RT-DC to characterize human-induced pluripotent stem cells - derived cardiomyocytes, which are an important cell type of the heart. They showed that high-throughput mechanical characterization is capable to monitor subtle changes in the structure of these cells. Utilizing these results might allow to label-free assess these cells before transplantation and without the need of fluorescent markers.

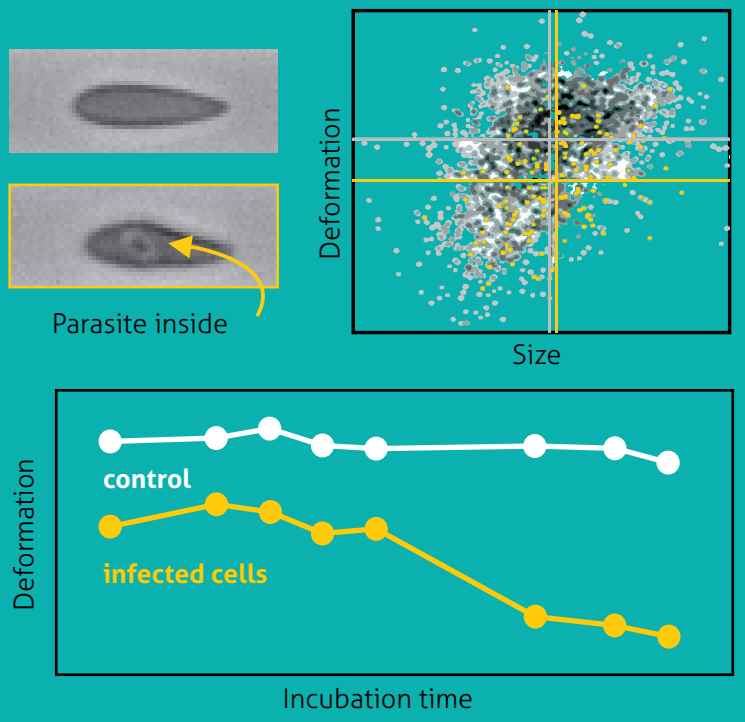


Pires et al., Phil. Trans. R. Soc. B , 2019

PUBLISHED APPLICATIONS: IMAGING CYTOMETRY

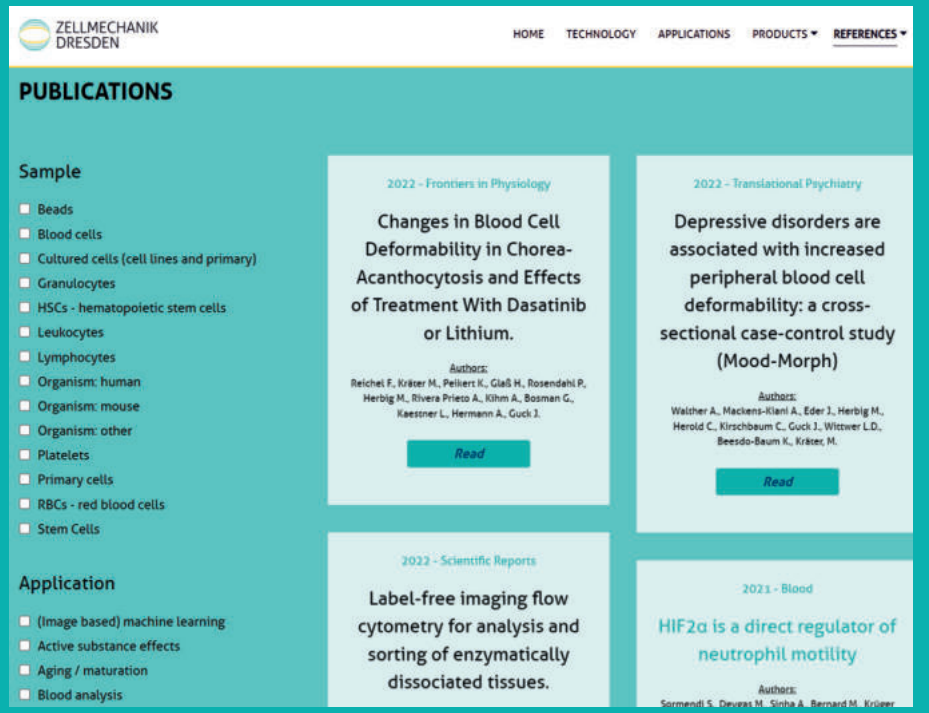
Parasite detection:

Using the *AcCellerator* to detect infiltration of the malaria parasite inside red blood cells based on mechanical cell changes. In addition, the RT-DC software feature to acquire bright-field images of each single cell was capable to identify the parasite directly inside the cell. This suggests the possibility of parasite detection directly from an image analysis. A process, which can be carried out in seconds.



Toepfner et al., eLife , 2018

Many more scientific publications can be found on our website under references. We maintain a huge online database of publications that can be searched by samples, application, devices and type of publication.

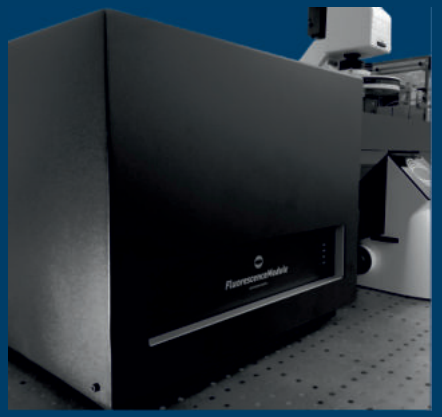


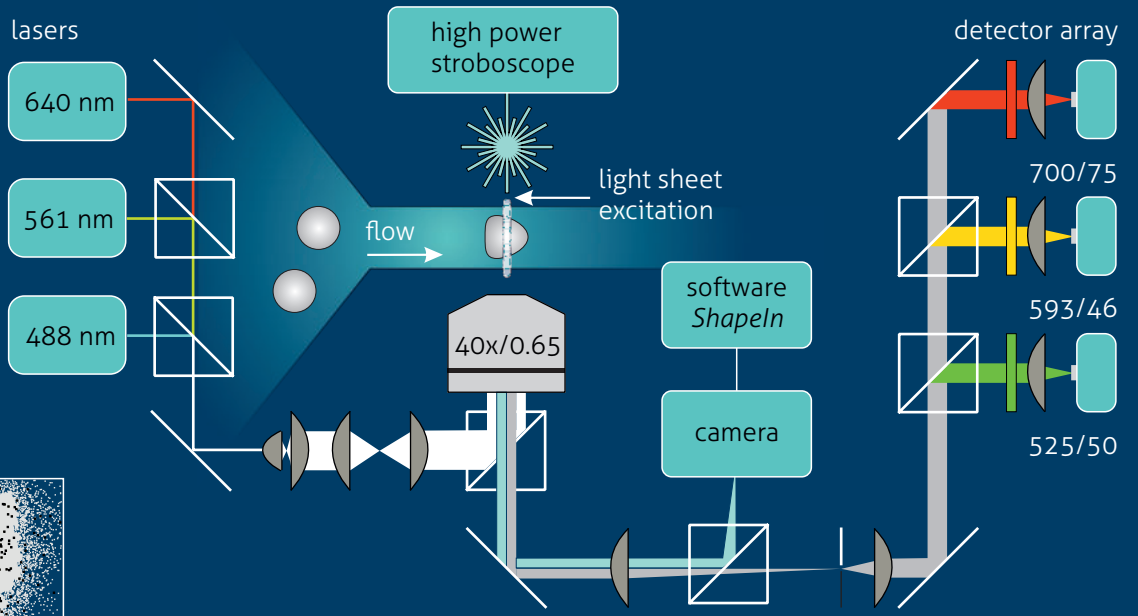
Visit www.zellmechanik.com!

PRODUCT

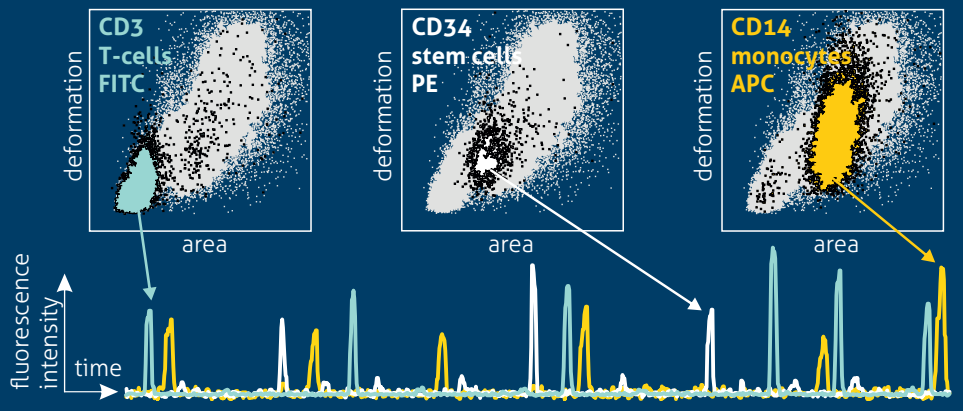
FluorescenceModule - ADD-ON FOR FLUORESCENCE DETECTION

The *FluorescenceModule* turns your *AcCellerator* into more than a classical flow cytometer with an additional channel for cell mechanics. It adds a powerful tool to your life science lab - ready to solve your questions by providing an unexpected perspective.



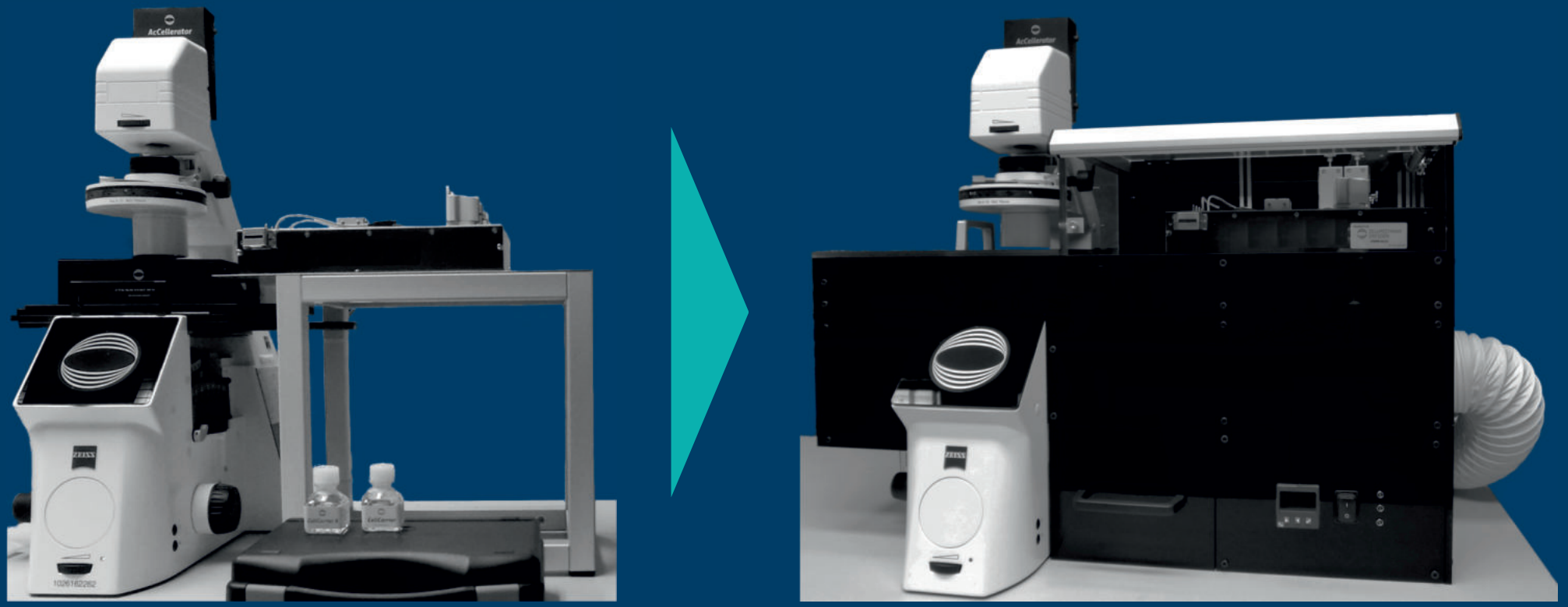


adapted from Rosendahl et al. Nature Methods, 2018



In biological research, identification and quantification of cells and cellular processes are commonly assessed by fluorescence flow cytometry. The *FluorescenceModule* and the *AcCellerator* combine the advantages of fluorescence flow cytometry and RT-DC in a novel method termed real-time fluorescence deformability cytometry (RT-FDC). The unique design of confined light sheet excitation allows for 1D fluorescence imaging in up to three detection channels. In addition to all RT-DC parameters, fluorescence signals are analyzed for peak shape in real-time at a rate of up to 1 000 cells per second. The fluorescence raw data are also available for post-measurement evaluation providing the opportunity to tailor your own analysis to your specific questions and needs.

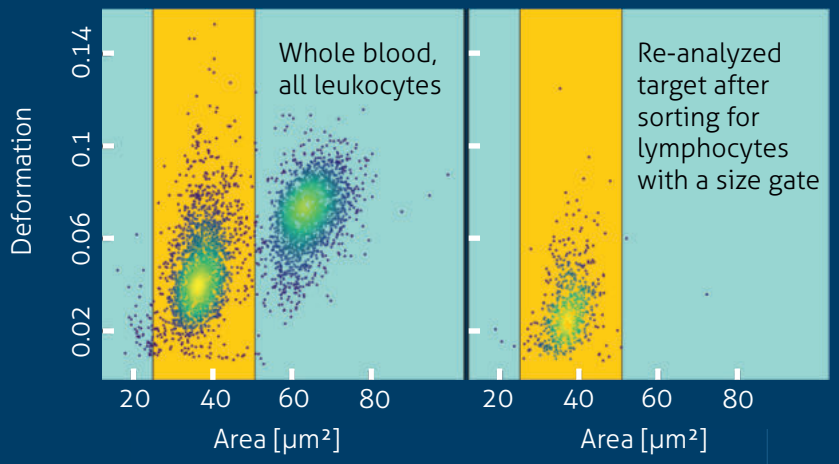
HeatModule - ADD-ON FOR TEMPERATURE CONTROL

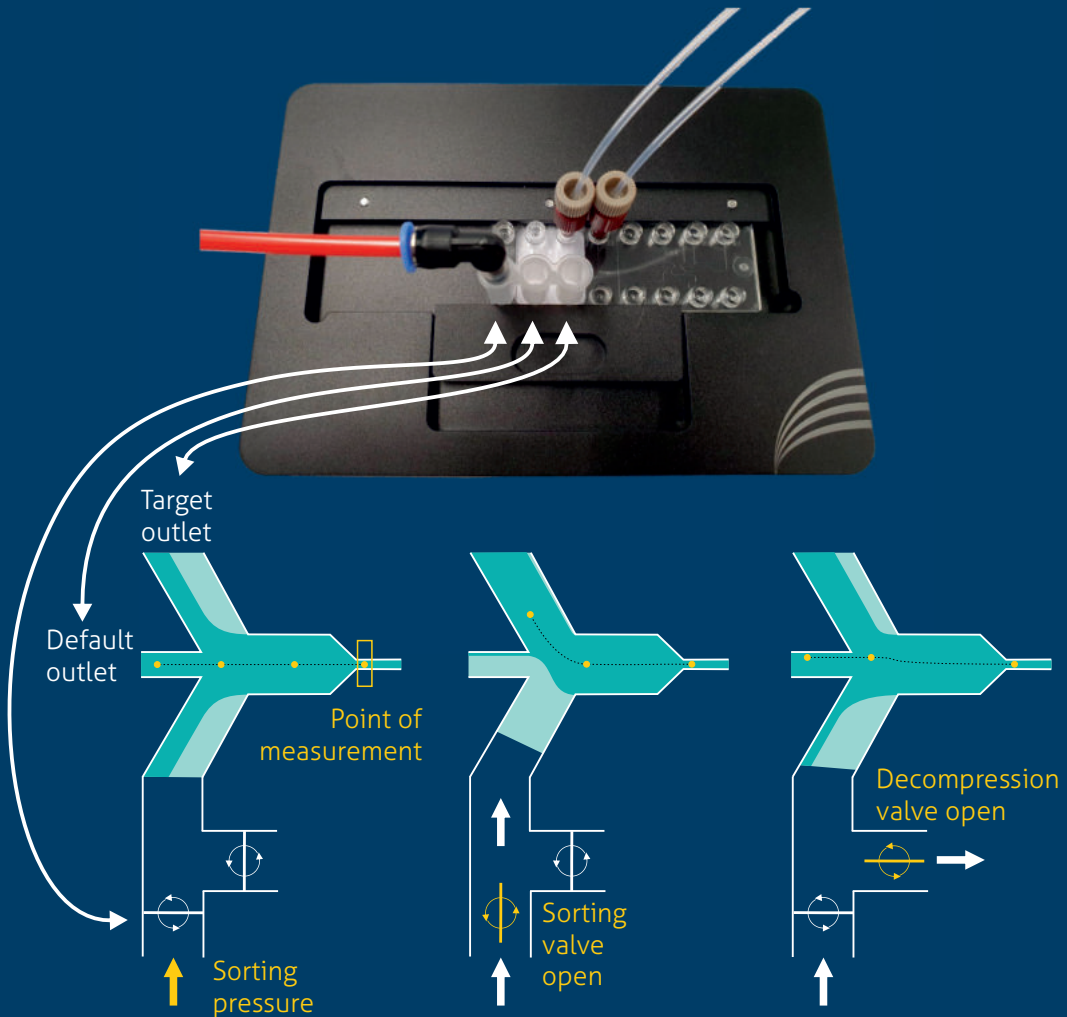


The *HeatModule* enables measurements at physiological temperatures. To realize a controlled environment at stable temperatures, a box encapsulates large parts of the *AcCellerator*. The *HeatModule* contains a 300 W heater and several, silent ventilators to efficiently distribute the heated air. A sensor in close proximity to the sample and a control unit stabilize a desired temperature with high precision between room temperature and 37°C. Fast temperature recovery after enclosure opening, e.g. for sample replacement, is ensured by an air recycling and circulation system.

PRODUCT

SortingModule - ADD-ON FOR LABEL-FREE CELL SORTING

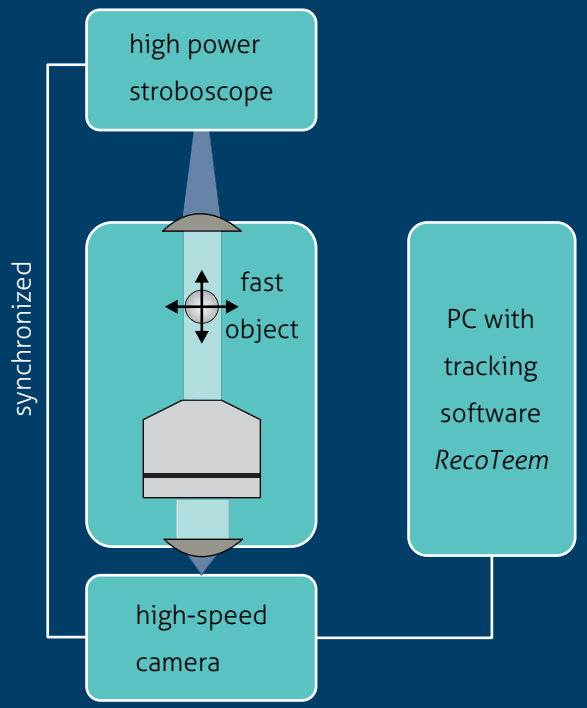




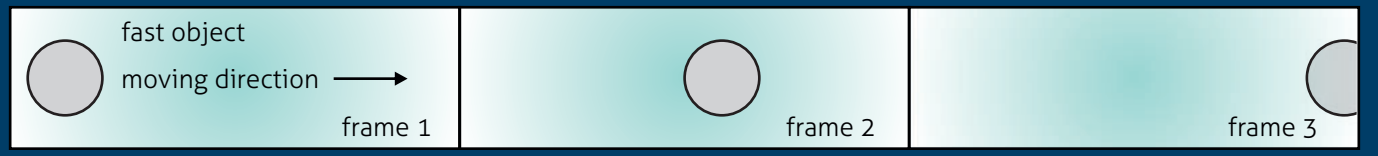
Unlock the power of real-time data with the *SortingModule*. Seamlessly sort based on any cell property detected by the *AcCellerator* or the *FluorescenceModule*. Experience stress-free sorting with our gentle pressure-driven flow-shift design. Opt for label-free sorting based on morphology/rheology, fluorescence signals, or a mix of both. Our *FlicSo* microfluidic chips come in 20 and 30 µm channels. Achieve sorting rates of 50 cells/s and measurements of 100 cells/s, leading to an several 10k cells in a typical experiment, depending on initial target concentration.

DeCellerator - HIGH SPEED VIDEO RECORDING

scheme of the video microscope



standard video microscopy



fast video microscopy with fast particles and motion blurring

***DeCellerator* : fast video microscopy and synchronized microsecond illumination**

The *DeCellerator* is a high-speed, brightfield video microscope, that uses synchronized, microsecond, high intensity LED light flshes to suppress motion blurring. This enables extreme slow motion video recordings. Full frame images can be recorded at up to 500 frames per second and recording of up to 10 000 frames per second is possible in reduced regions of interest using our designated acquisition software: *RecoTeem.*

ABOUT US

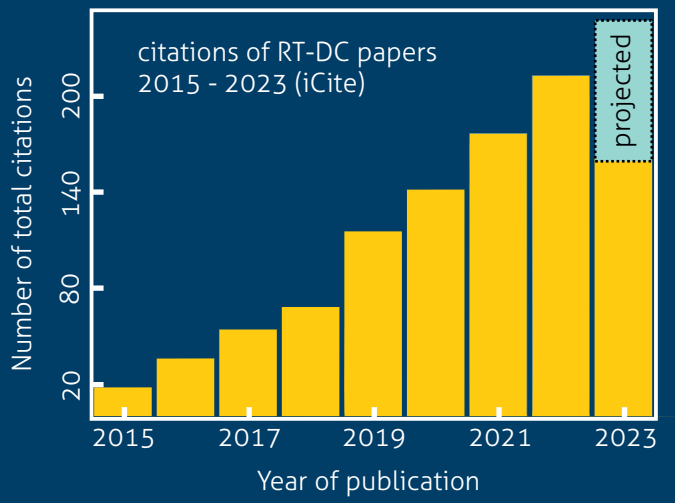
EMPOWERING RESEARCH THROUGH INNOVATION

We believe in the power of research.

With strong commitment, we stand alongside life scientists, supporting their scientific aspirations on a global scale. By introducing subtle shifts in perspective, we quietly encourage the birth of disruptive applications that will reshape the norm.

From conception to creation, we engineer, craft, and bring to life cutting-edge devices and applications for label-free cell analysis.

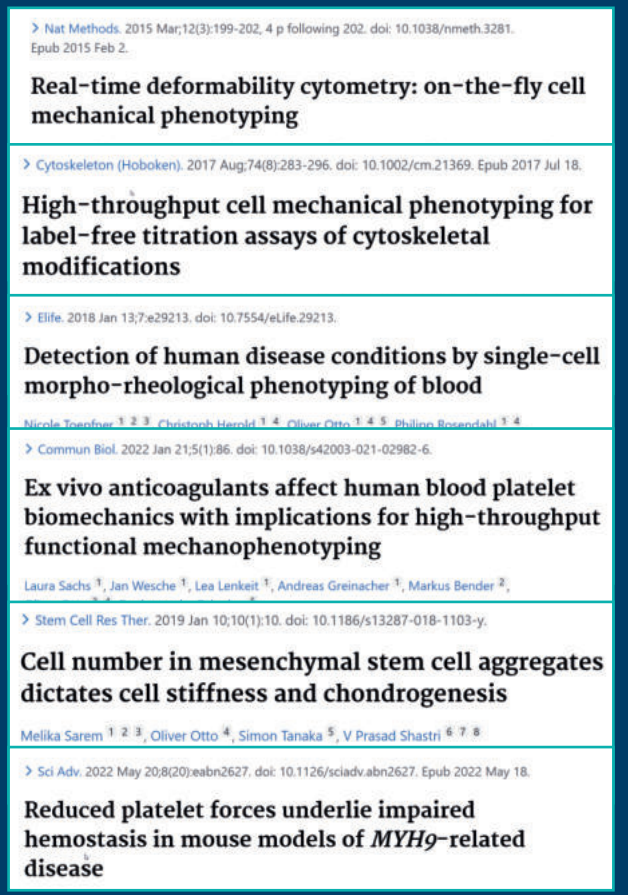
Our products serve as catalysts, unraveling the intricate mechanisms of cell reactions and providing unprecedented insights into their world. They illuminate pathways to address profound systemic and holistic research endeavors. Embark on a journey where research boundaries are pushed, guided by unobtrusive breakthroughs that inspire the scientific community.



> 20 Machines at different research facilities

> 40 independent peer reviewed publications

> 1000 Citations of RT-DC related papers



> Nat Methods. 2015 Mar;12(3):199-202, 4 p following 202. doi: 10.1038/nmeth.3281. Epub 2015 Feb 2.

Real-time deformability cytometry: on-the-fly cell mechanical phenotyping

> Cytoskeleton (Hoboken). 2017 Aug;74(8):283-296. doi: 10.1002/cm.21369. Epub 2017 Jul 18.

High-throughput cell mechanical phenotyping for label-free titration assays of cytoskeletal modifications

> Elife. 2018 Jan 13;7:e29213. doi: 10.7554/eLife.29213.

Detection of human disease conditions by single-cell morpho-rheological phenotyping of blood

> Commun Biol. 2022 Jan 21;5(1):86. doi: 10.1038/s42003-021-02982-6.

Ex vivo anticoagulants affect human blood platelet biomechanics with implications for high-throughput functional mechanophenotyping

Laura Sachs [1], Jan Wesche [1], Lea Lenkeit [1], Andreas Greinacher [1], Markus Bender [2],

> Stem Cell Res Ther. 2019 Jan 10;10(1):10. doi: 10.1186/s13287-018-1103-y.

Cell number in mesenchymal stem cell aggregates dictates cell stiffness and chondrogenesis

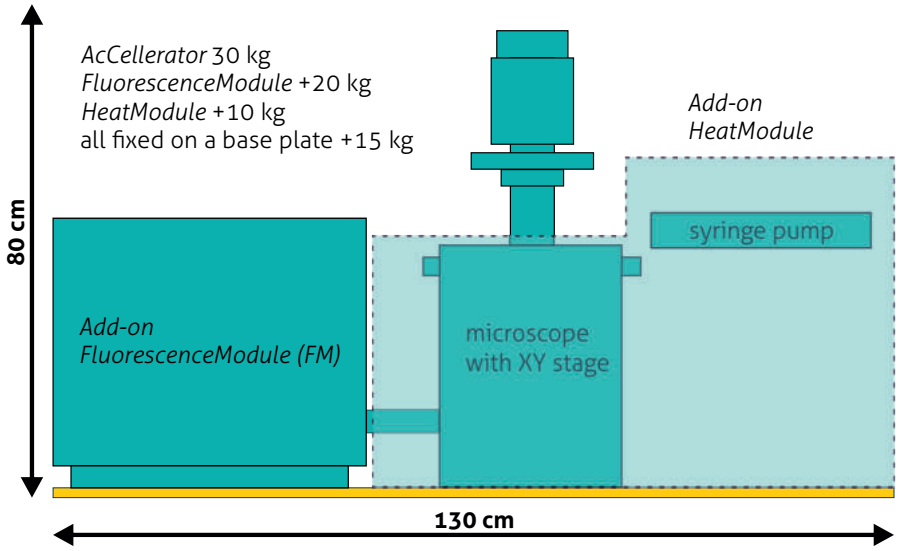
Melika Sarem [1 2 3], Oliver Otto [4], Simon Tanaka [5], V Prasad Shastri [6 7 8]

> Sci Adv. 2022 May 20;8(20):eabn2627. doi: 10.1126/sciadv.abn2627. Epub 2022 May 18.

Reduced platelet forces underlie impaired hemostasis in mouse models of *MYH9*-related disease

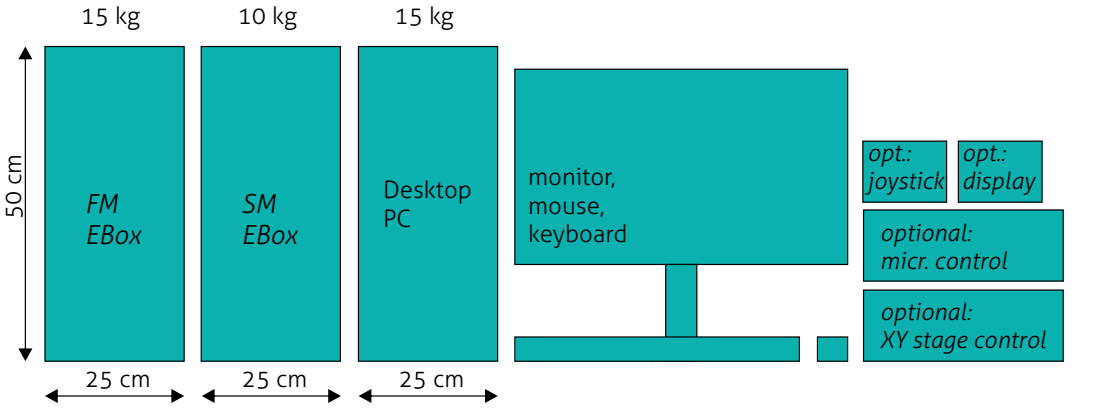
CUSTOMERS, FRIENDS, FANS - WORLDWIDE

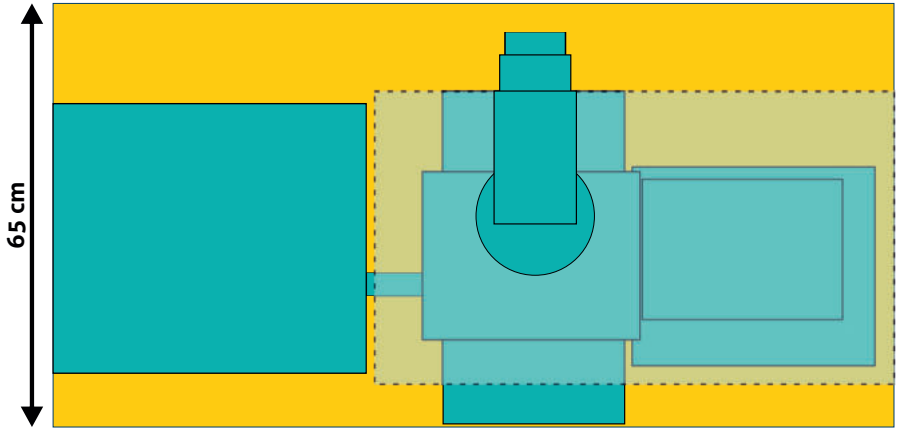
DIMENSIONS



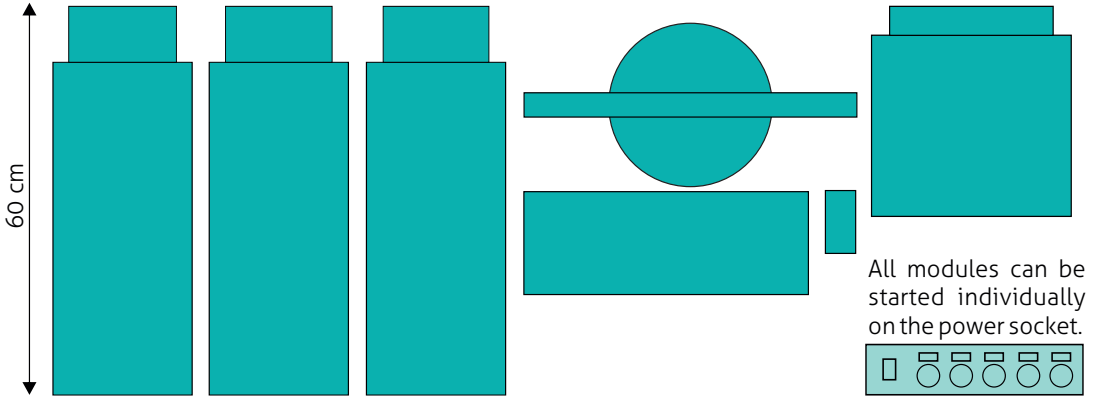
FRONT-VIEW

The *EBox*es contain various electrical and mechanical components and can be freely placed within 2m from the module.





TOP-VIEW



EN 61326-1 Electrical equipment for measurement, control and laboratory use
EN 61010-1 Safety requirements for electrical equipment for measurement, control and laboratory use
EN 60825-1 Safety of laser products

max. 300 W, 100-240 VAC, 50/60 Hz

Please, check our website for latest updates!

SPECIFICATIONS

ENVIRONMENT

- operation temperature: 15 - 40°C
- air humidity: 20 - 75 %, non-condensing
- table recommended: passive damping
- room temperature stability: ± 1K

OPTICS

- brightfield, objective: 40x NA 0.65
- CMOS camera: full frame 1024 x 1280 pixel, 8-bit
- typical ROI: 250 x 80 pixel
- resolution: 340 nm/pixel
- LED: blue (460 nm) or red (623 nm) , 2 µs pulses

LASERS

- up to 3, typically 488 nm, 561 nm, 640 nm (40-100 W) customer choice

DETECTION CHANNELS

- up to 3, typically 500-550 nm, 570-616 nm, 663-737 nm customer choice

SPEED

- cell analysis depending on cell concentration, up to 1 000 cells/second using our software *Shape-In 2*
- videos: up to 10 000 frames/second using our software *RecoTeem*
- sorting up to 50 cells/second while analyzing 100 cells/second

SAFETY

- laser interlock switches on the *FluorescenceModule*, safety covers, completely enclosed lasers: class 1 laser product
- data protection with backup hard drive
- overheat protection in the *HeatModule*

MAINTENANCE, SERVICE

- occasional test of optical stability with fluorescent beads

PATENTS

- EP3036520, US10571387B2, EP3721231A1

Please, check our website for prices!

ZELLMECHANIK
DRESDEN

Version:2.0

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