Blood Under Stress

Physical Testing of Cells

Martin Kräter

rivercyte

The future of blood analysis.

PHYSICAL PHENOTYPING AND WHY?

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Mechanical probing reveals information about patho-physiological processes

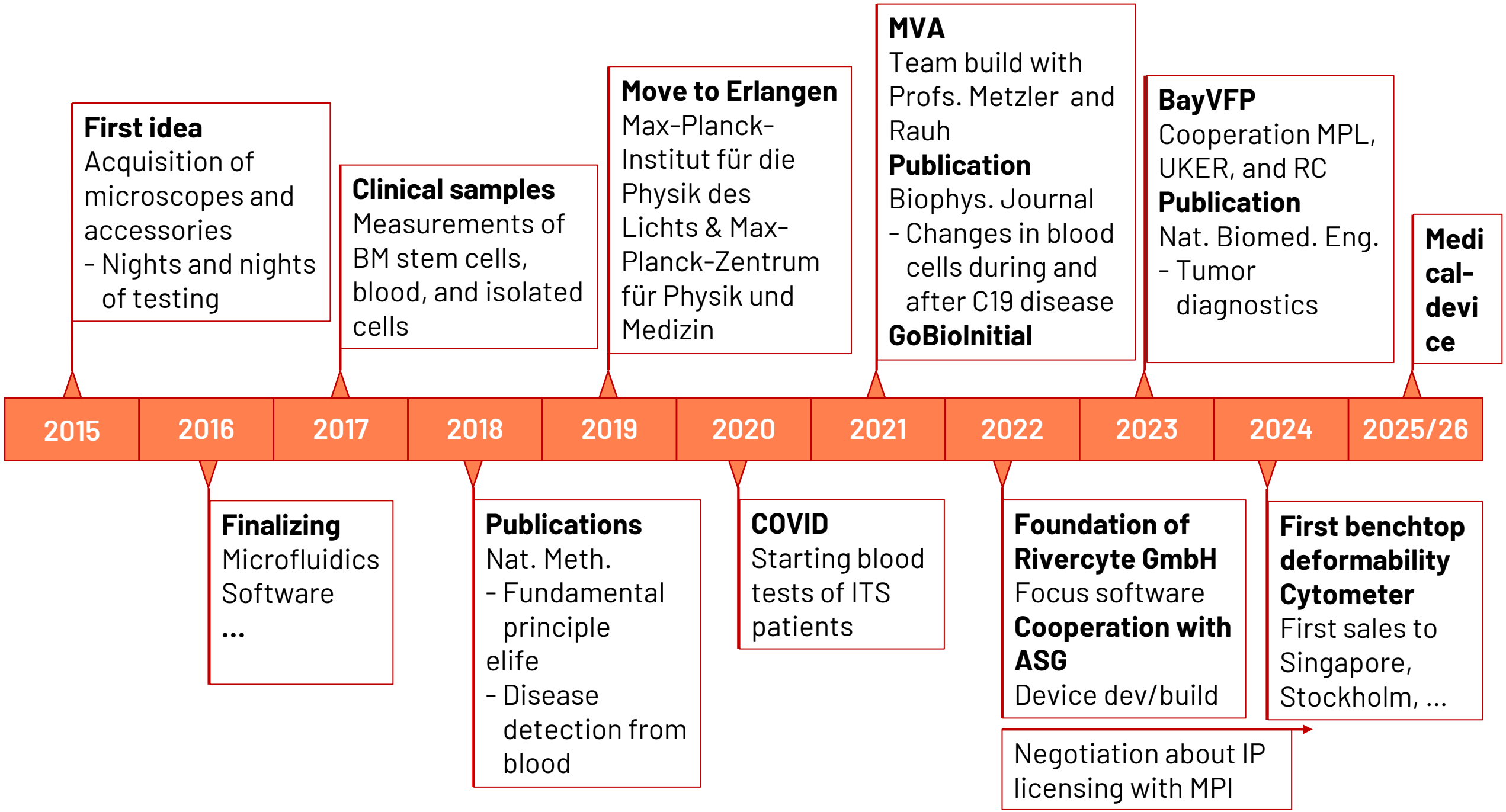
https://www.wikihow.com/images/thumb/7/7c/Tell-if-an-Avocado-is-Bad-Step-3-Version-3.jpg/v4-728px-Tell-if-an-Avocado-is-Bad-Step-3-Version-3.jpg.webp

https://www.smarticular.net/wp-content/uploads/2019/12/braune-avocados-essbar-verwerten-1-fb.jpg

Technology to „feel“ for changes is

1. More than 1000 years old

2. Missing in cell-based diagnostics



Lautenschläger et al., *PNAS* (2009)
Guck et al., *Integr. Biol.* (2010)
da Silva et al., Biometerials (2010)

da Silva et al., *Integr. Biol.* (2011)
Ekpenyong et al., *PLoS One* (2012)
Min et al., *PNAS* (2014)

2015

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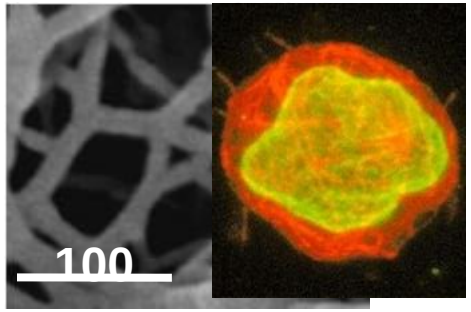
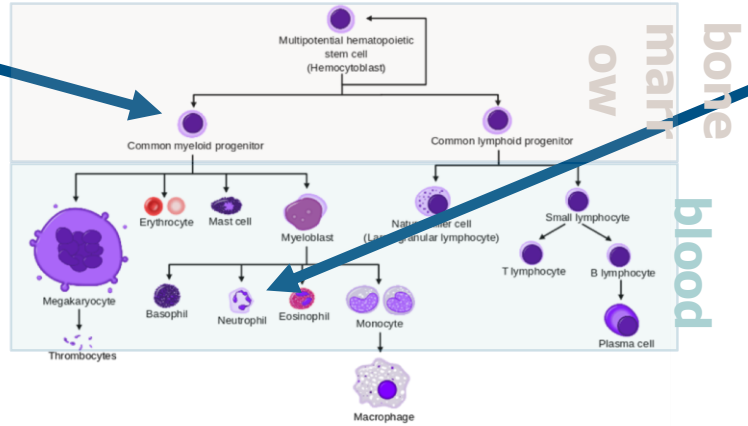
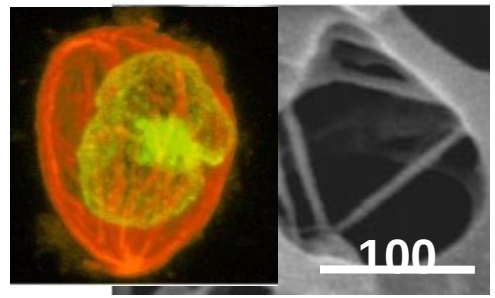
Precursor cell (in bone marrow)

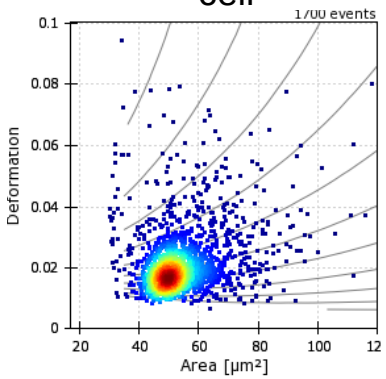




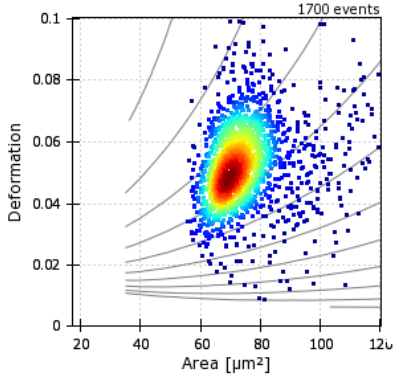
Neutrophil (in blood)



Precursor cell



Neutrophil



Functional readout by mechanical probing

2015

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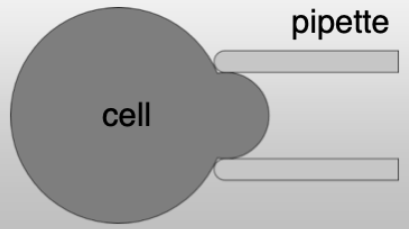
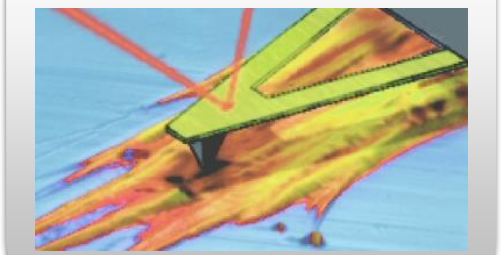
Throughput

10 cells/h — 100 cells/h

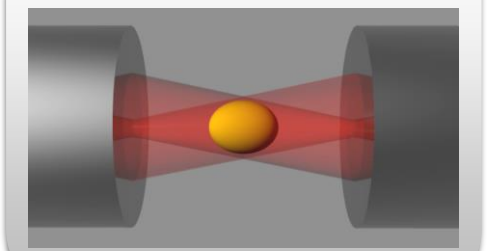
Micropipette aspiration



Atomic force microscopy



Optical stretcher



Maloney et al., *Biophys J* (2010)
Boyde et al., *Phys Rev E* (2010)
Ekpenyong et al., *PLoS One* (2012)
Chalut et al., *Biophys J* (2012)
Boyde et al., *Acta Mechanica* (2012)
Boyde et al., *Appl. Opt.* (2012)
Bellini et al., *Biomed. Opt.* Express (2012)
Min et al., *PNAS* (2014)
Faigle et al., *Lab Chip* (2015)

Guck et al., *Phys Rev Lett* (2000)
Guck et al., *Biophys J* (2001)
Guck et al., *Biophys J* (2005)
Wottawah et al., *Phys Rev Lett* (2005)
Lu et al., *PNAS* (2006)
Lincoln et al., *Biomed. Microdev.* (2007)
Remmerbach et al., *Cancer Res* (2009)
Lautenschläger et al., *PNAS* (2009)
Boyde et al., *JOSA A* (2009)

Deformability Cytometry

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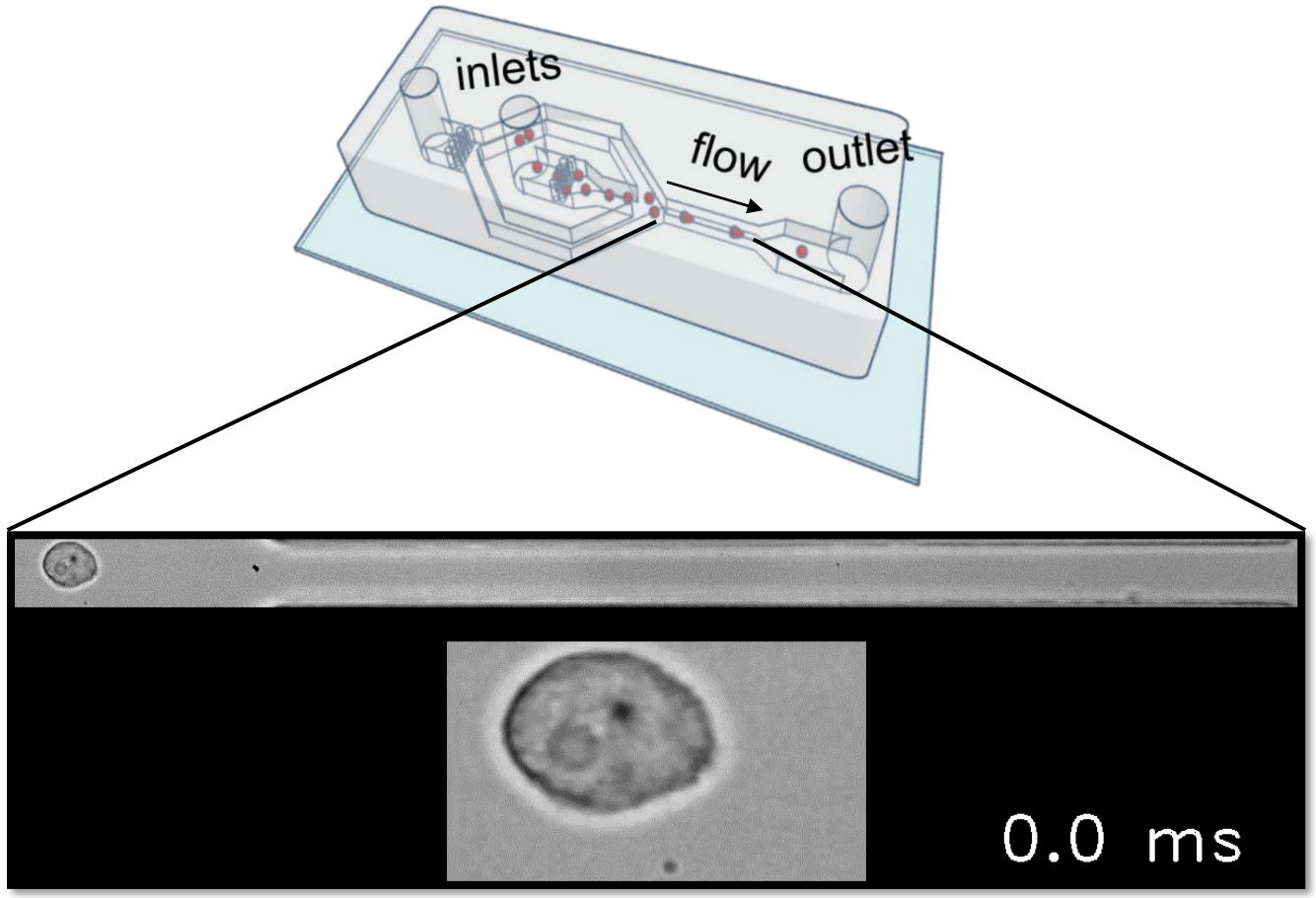
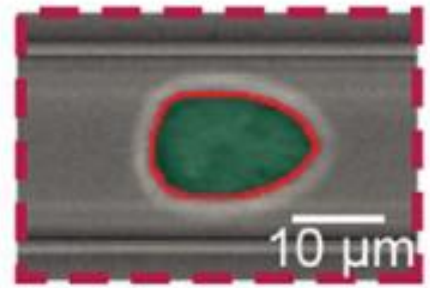
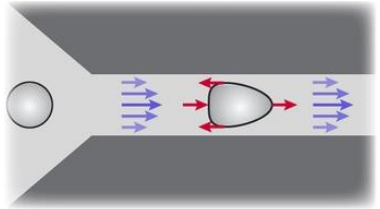


Its mechanical and other physical properties are quantified





$$\text{Deformation} = 1 - \underbrace{\frac{2\sqrt{\pi\,\text{Area}}}{\text{Perimeter}}}_{\text{Circularity}}$$

Video by MPL,CCO license

36,000 times faster than older technology

2018

Advanced Blood Measurement

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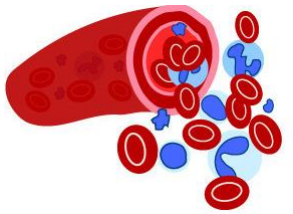
Measurement

10 mins
< 3 µl



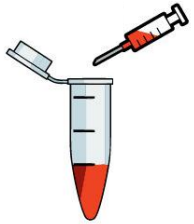
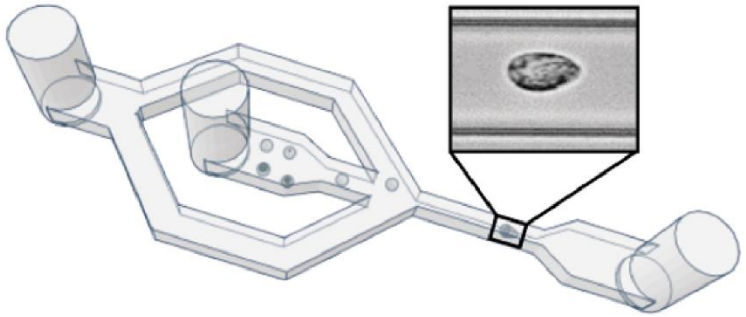


Image acquisition

Fast imaging
Accurate flow

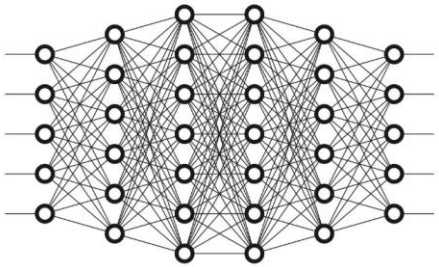


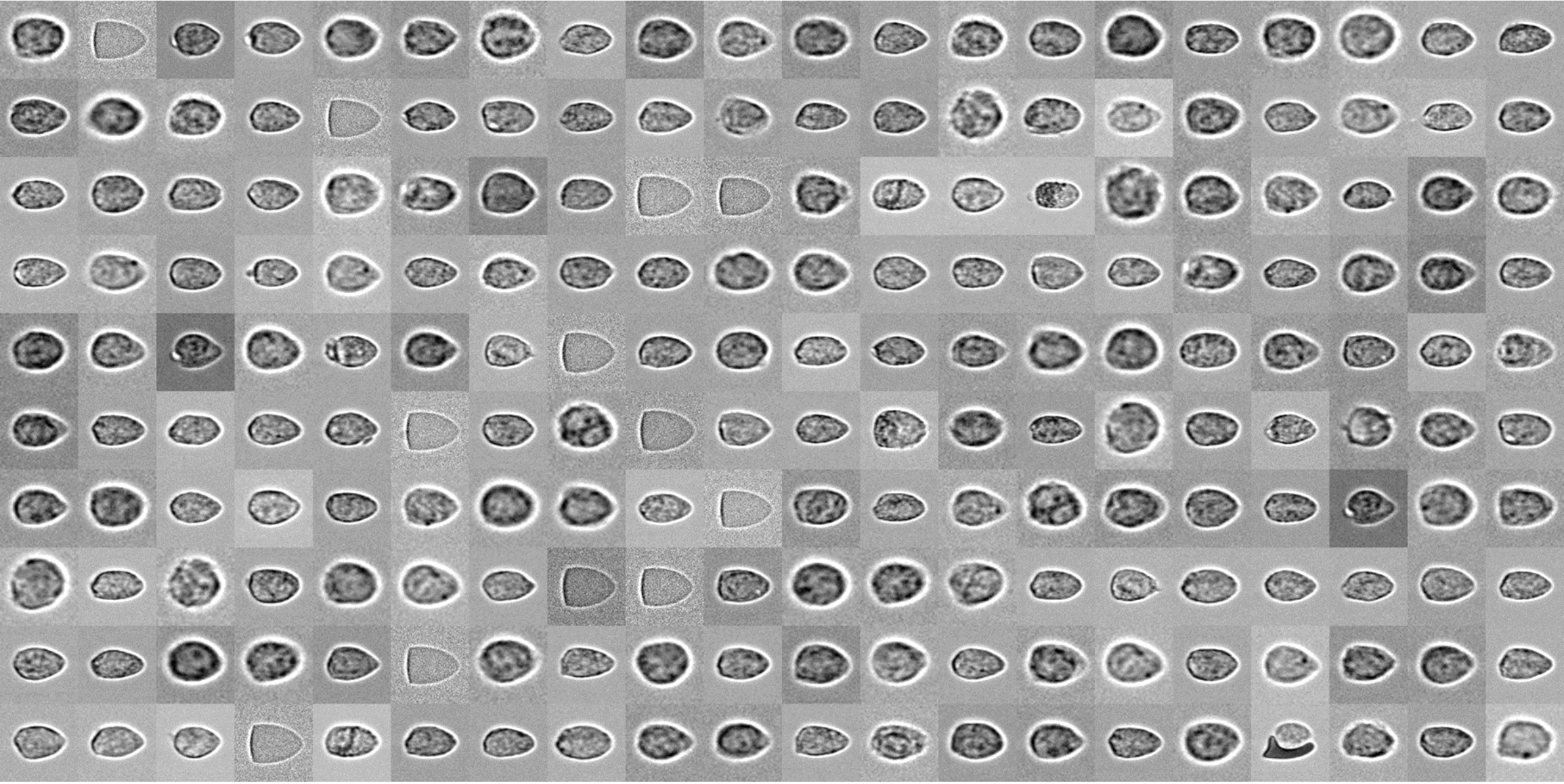
Analysis

Detection

Classification

Diagnosis

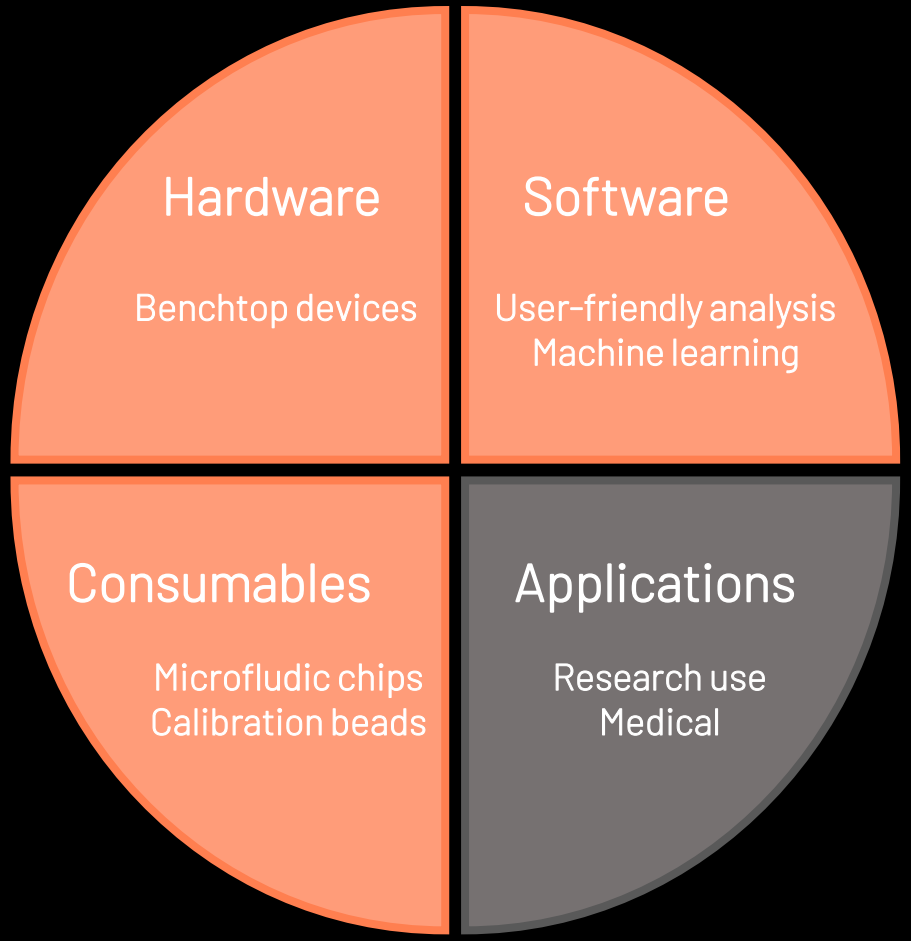




= number of cells measured each 0.1 second

Naiad and Friends

2022



Diagnostic Features

2023

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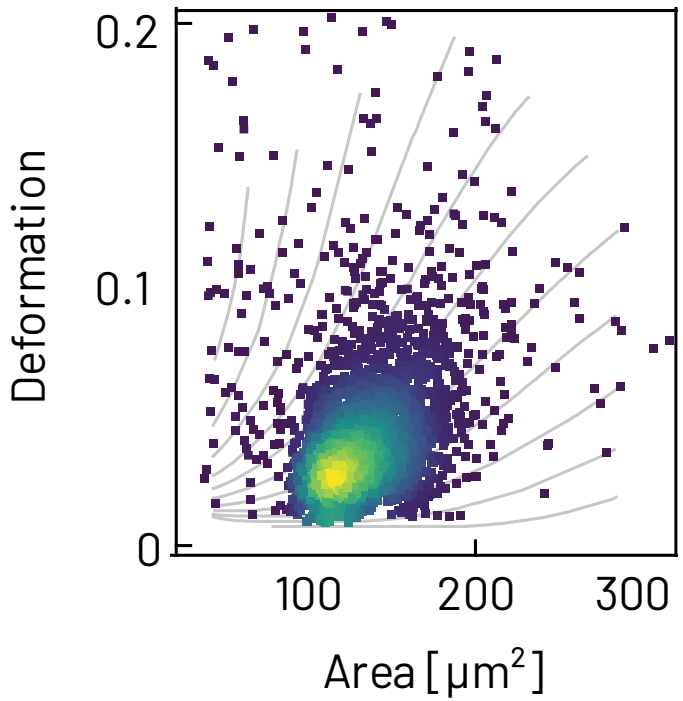
- Brightfield image
- Deformation
- Cross-sectional area
- Young's modulus
- Aspect ratio
- Brightness
- Texture
- Surface roughness

....

> 27 features



Statistical and ML-based approaches for diagnosis

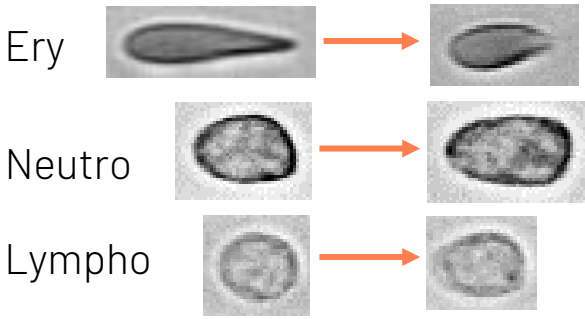
Applications

Soteriou et al., Nat Biomed Eng 2021

Tietze et al., Adv Sci 2019

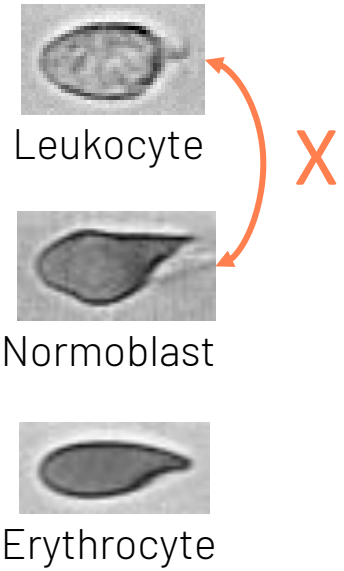
Reichel et al., Lab Chip 2024

COVID blood



Kubankova et al., Biophys J 2021

Neonatal diagnostics



Disease Fingerprint

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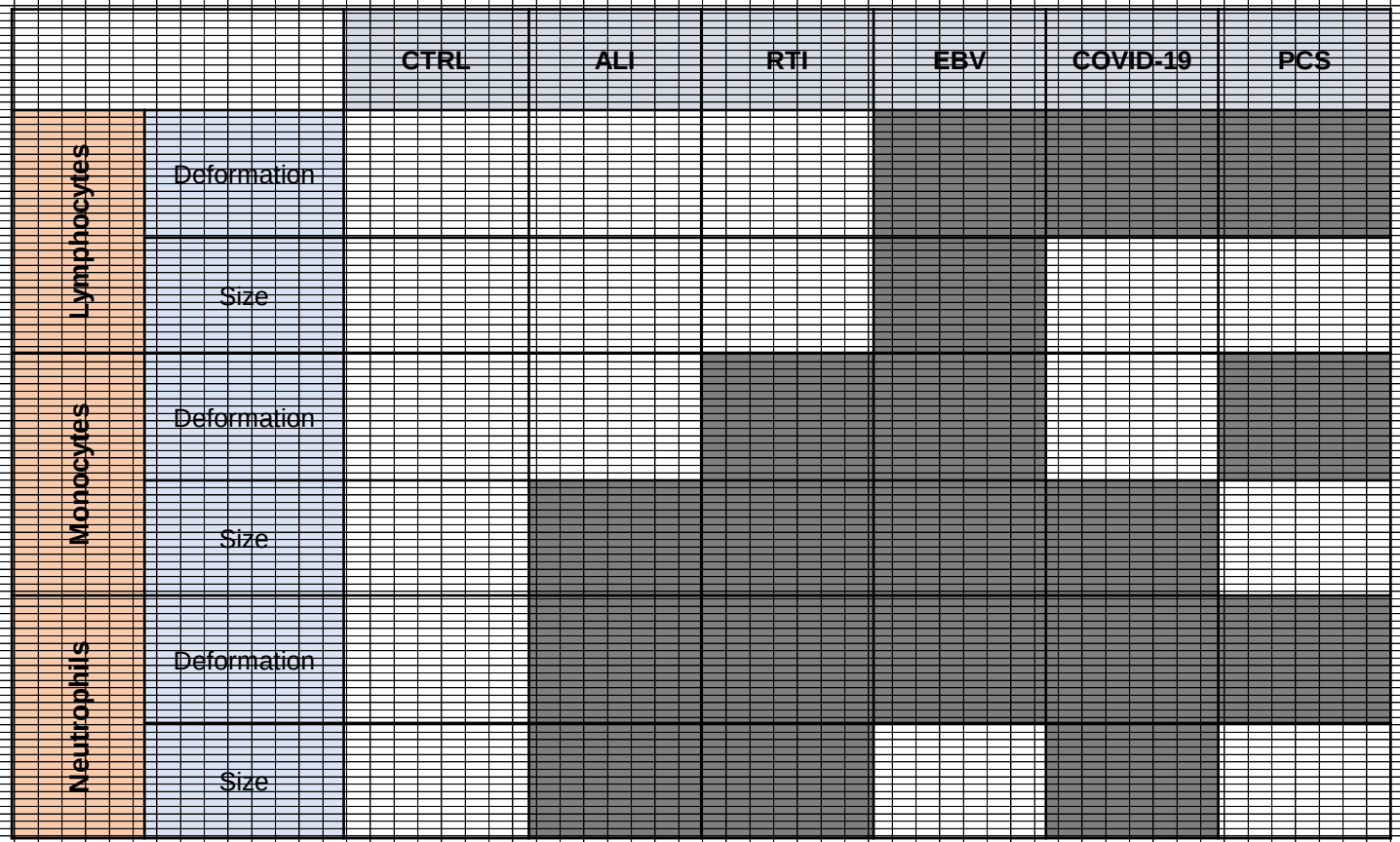
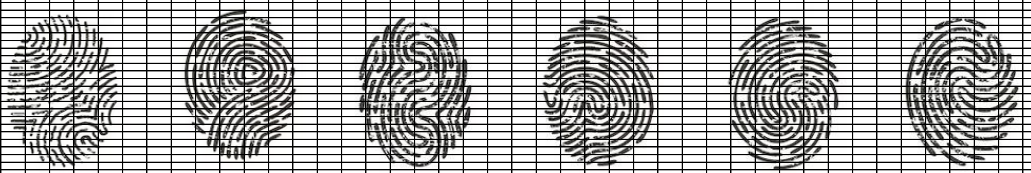


No difference

Difference to CTRL

ALI - Acute Lung Injury
RTI - Respiratory Tract Infection
EBV - Epstein Barr Virus
PCS – Post-COVID Syndrome



MAX PLANCK INSTITUTE FOR THE SCIENCE OF LIGHT

Toepfner et al., Elife 2018
Kubankova et al., Biophys J 2021

Rivercyte GmbH founder team

Founded in April 2022

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Felix Dirla

CEO

- 25 years of professional experience (product development, production management, marketing & sales, quality management, regulatory affairs, HR, finance)
- 18 years of entrepreneurship and executive management in IVD

Dr. Shada Abuhattum

- 10 years experience in cell mechanics, data analysis and mathematical modelling
- 6 years experience in product development
- 3 years experince in IP analysis, patent editing and drafting
- PhD Physics, FAU Erlangen-Nürnberg

Dr. Markéta Kubánková

- Leader of Medical Valley Award project at the Max Planck Institute for the Science of Light
- 10 years of experience in cell biophysics, data analysis and AI
- PhD Chemical Physics, Imperial College London

Dr. Martin Kräter

- Coordinator of clinical projects at the Max Planck Institute for the Science of Light
- 10 years of research experience in biological and biochemical cell analysis
- PhD Hematology, University Hospital Dresden

Dr. Paul Müller

- Senior data analyst at the Max Planck Institute for the Science of Light
- 10 years hands-on experience in software development
- Development and maintenance of core libraries, end-user programs and data repositories
- PhD Physics, TU Dresden

Dr. Salvatore Girardo

- Head of Lab-on-a-Chip technology platform at Max Planck Institute for the Science of Light
- 15 years of experience in microfluidics
- PhD Nanoscience, University of Salento, Italy

Prof. Jochen Guck

- Director of the Max Planck Institute for the Science of Light
- 25 years of research experience in biophysical cell analysis
- PhD Physics, University of Texas, Austin

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1,500,000 Images Say a Lot About 1 Patient

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Open positions

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Articles

Demos & other events

ACKNOWLEDGEMENT

Bundesministerium für Bildung und Forschung

Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit

Bayerisches Staatsministerium für Wissenschaft und Kunst

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Benedikt Hartmann
Maximilian Schlögel
Eoghan O´Connell
Raghava Alijanga
Felix Reichel
Nadine Ströhlein
Jeff Harmon
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GUCKLAB

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ML-Based Pipeline

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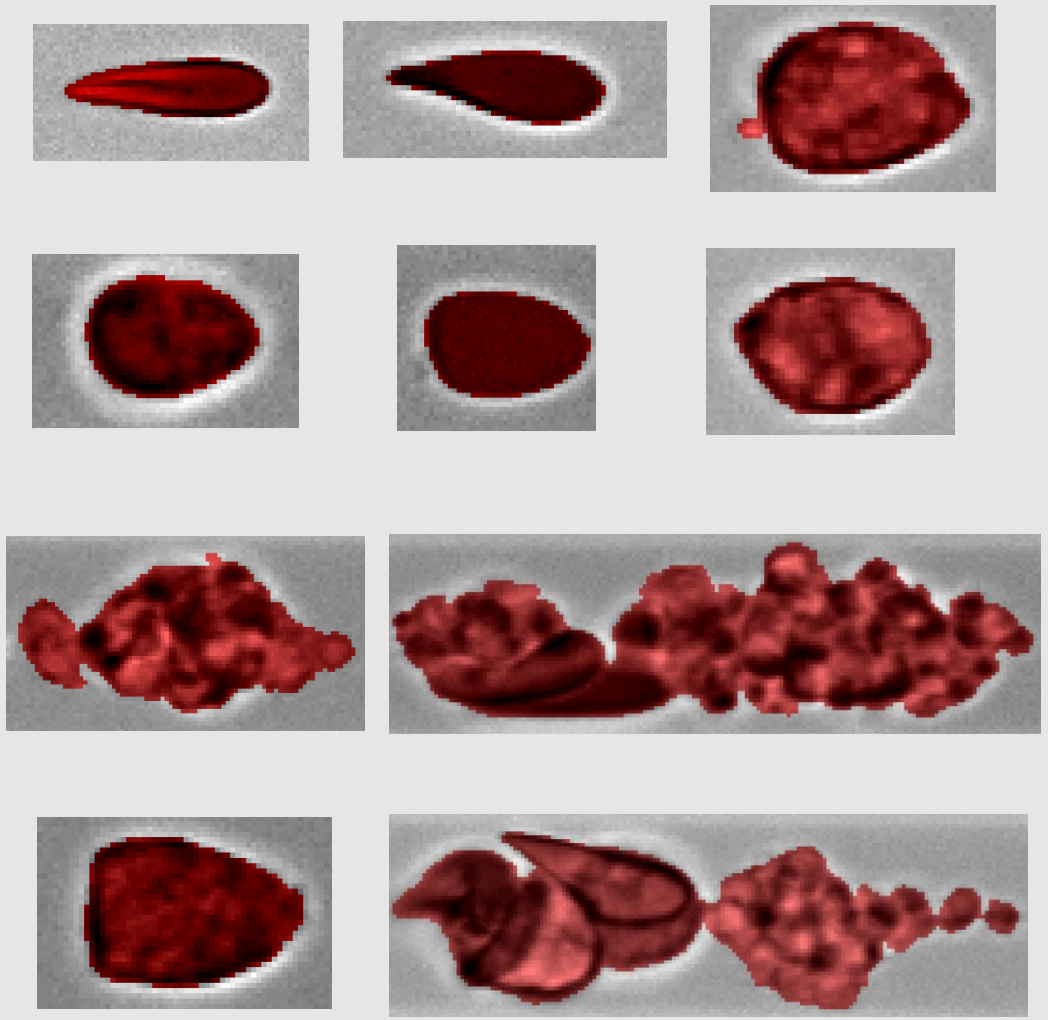
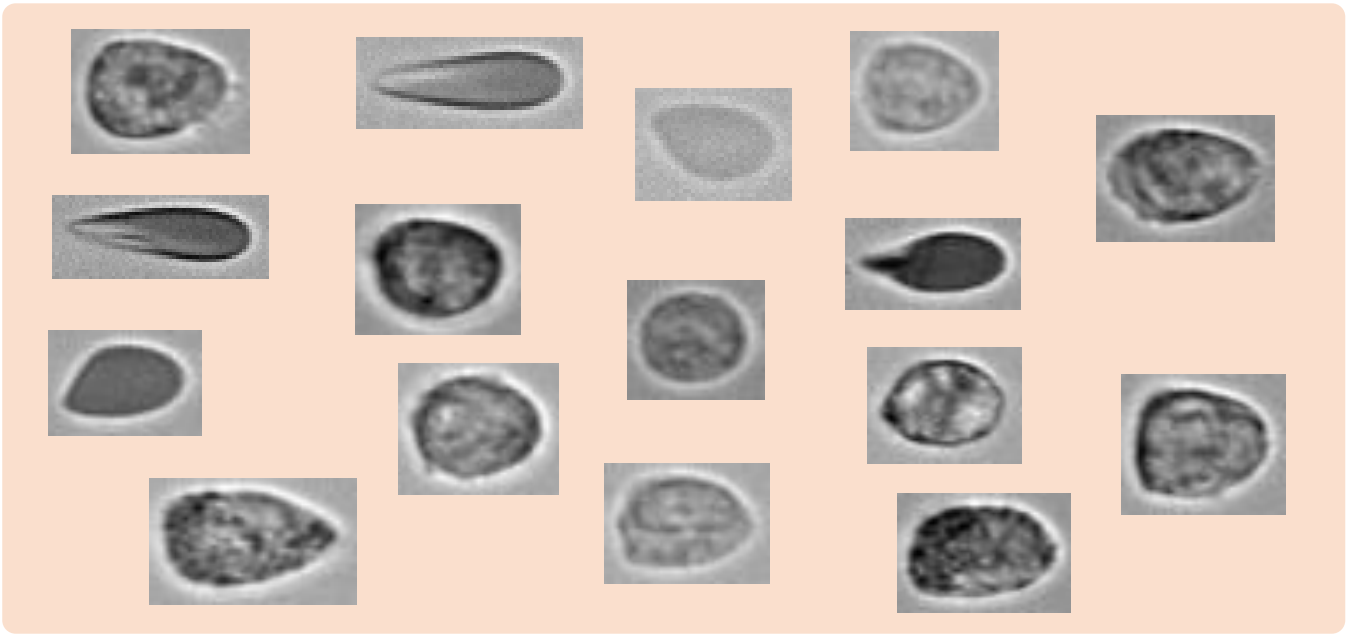
Segmentation



Classification



ML-Based Pipeline

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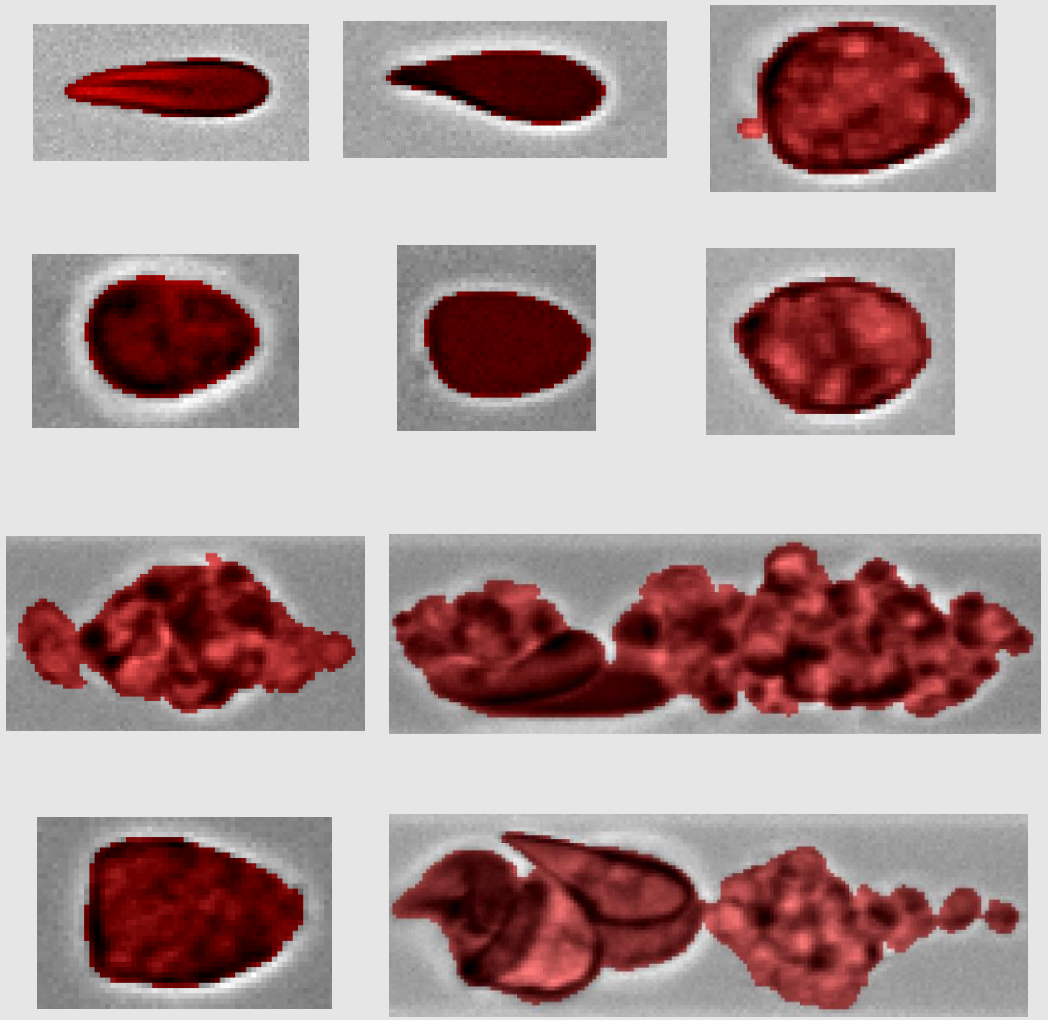
Segmentation



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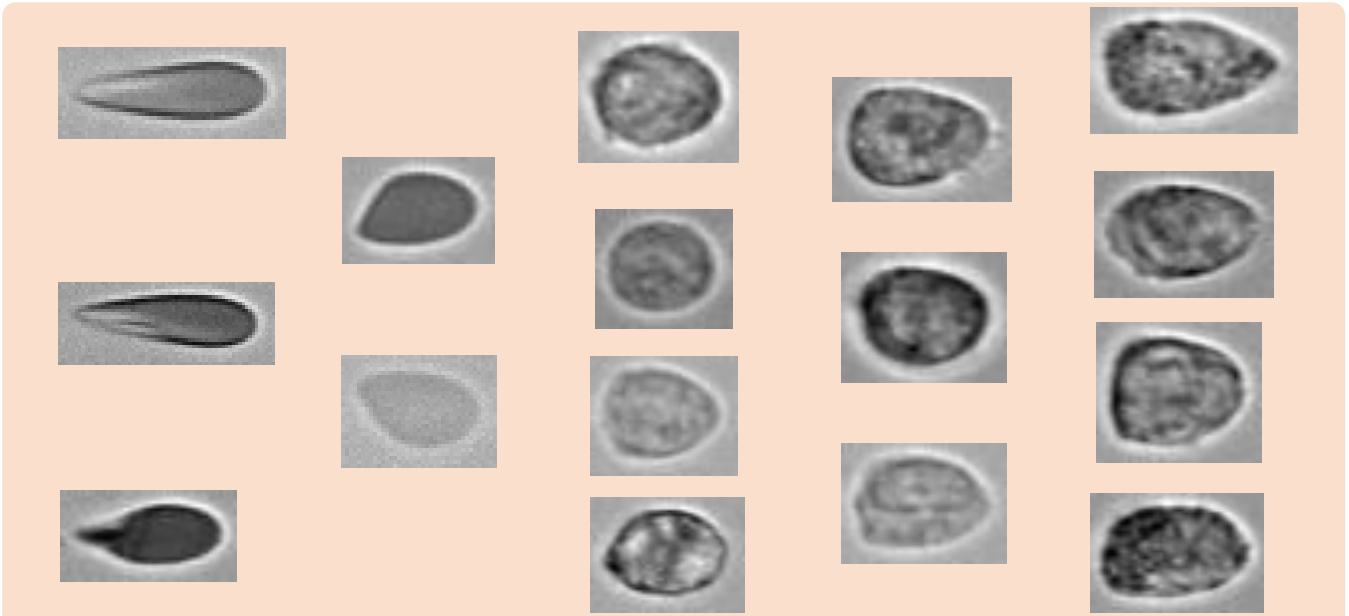

ML-Based Pipeline

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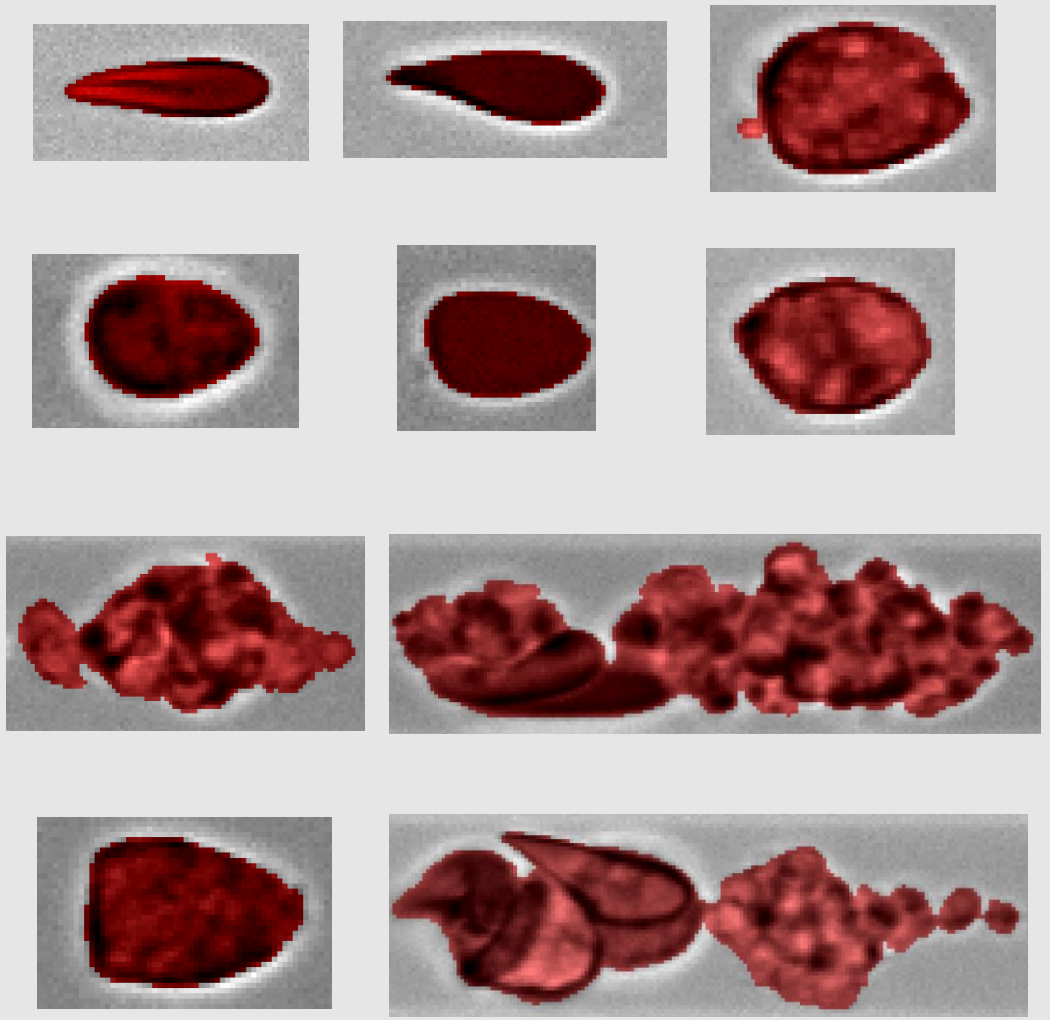

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