



# SENSORS AND WEARABLES FOR PRECISION MEDICINE

**Lars M. Steinmetz**

Stanford University, School of Medicine (USA)

Stanford Genome Technology Center (USA)

European Molecular Biology Laboratory (Heidelberg)

# DECLARATION OF INTERESTS



Co-founder  
Sophia Genetics SA, Switzerland

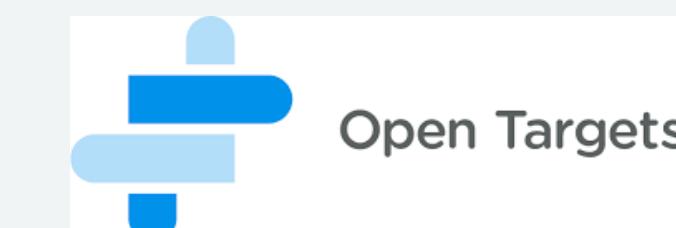


Co-founder & Board of Directors  
Levitas Bio Inc, USA

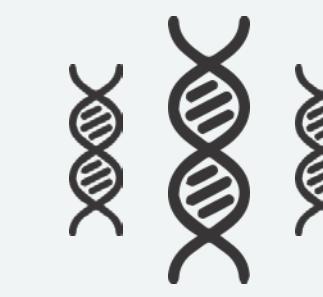


Co-founder & Board of Directors  
Recombia Biosciences, US

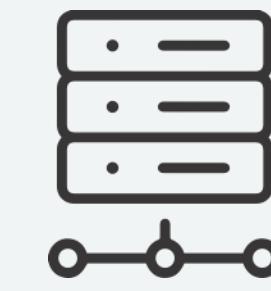
## FUNDING ACKNOWLEDGEMENTS



# TECHNOLOGY IS RESHAPING HEALTHCARE



Secure  
sequencing  
for every person



A.I.-driven  
diagnoses and  
monitoring



Real-time  
monitoring with  
sensors



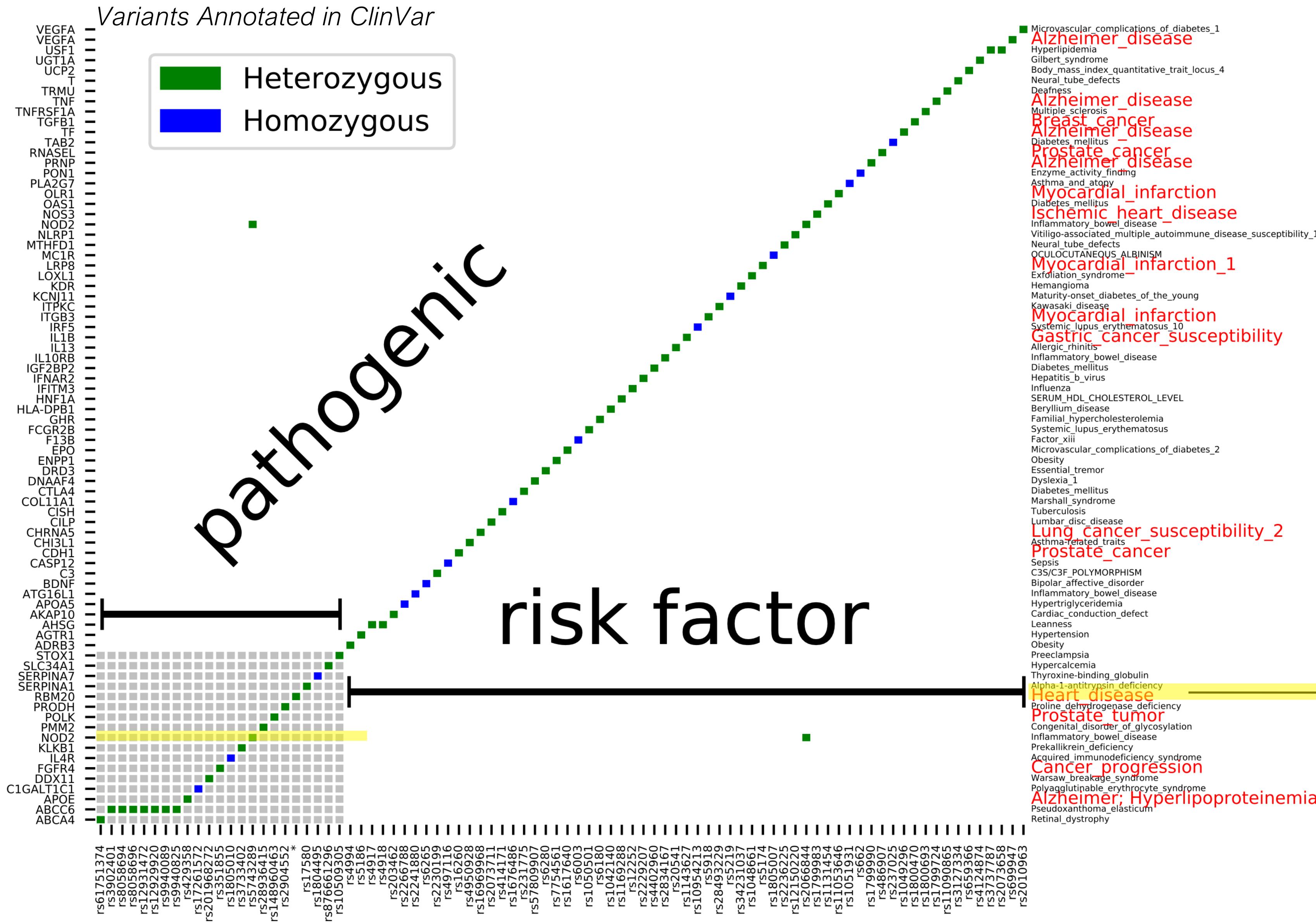
Personalized  
treatment  
and diet



DISEASE  
PREVENTION

DISEASE  
TREATMENT

# PREDISPOSING RISK VARIANTS IN A “HEALTHY” GENOME



Multiple cancer predisposing variants in particular gastric, prostate, lung.

RBM20 mutations very rare; 3% of DCM.

Penetrance and mortality high. Avg. life expectancy 45 years in several families.

APOE4 (24% carriers); Risk for atherosclerosis and Alzheimer's disease (AD odds het: 3x, hom 15x).

# ACTIONABLE INSIGHTS



CTGATG  
AGGTAC  
AGGGCT  
CATGGT  
CAGGTT  
GCACTG



ACMG currently classifies 73 genes as actionable.

Our knowledge of disease variant actionability needs to expand



Sequencing gives us useful info, however...

**Your genome is not your destiny!**

We need improved technologies to read and heal genomes

# SOPHiA GENETICS, a global health tech company democratizing data-driven medicine

## to drive better health outcomes and economics worldwide



790 +  
Health care institutions



70 +  
Countries



>1,000,000  
Patient genomic profiles



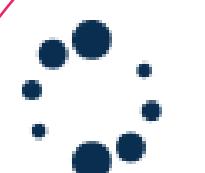
500 +  
Employees



# Connecting Healthcare Institutions Worldwide

## Artificial intelligence + cloud-based software-as-a-service platform to democratize data driven medicine



 **SOPHiA GENETICS™**

promotes global knowledge sharing

standardization and analysis of digital health data

from oncology to inherited disorders

# THE RECORD BREAKERS: RAPID GENOME SEQUENCING AT STANFORD



Euan Ashley  
(Stanford)



John Gorzynski  
(Stanford)

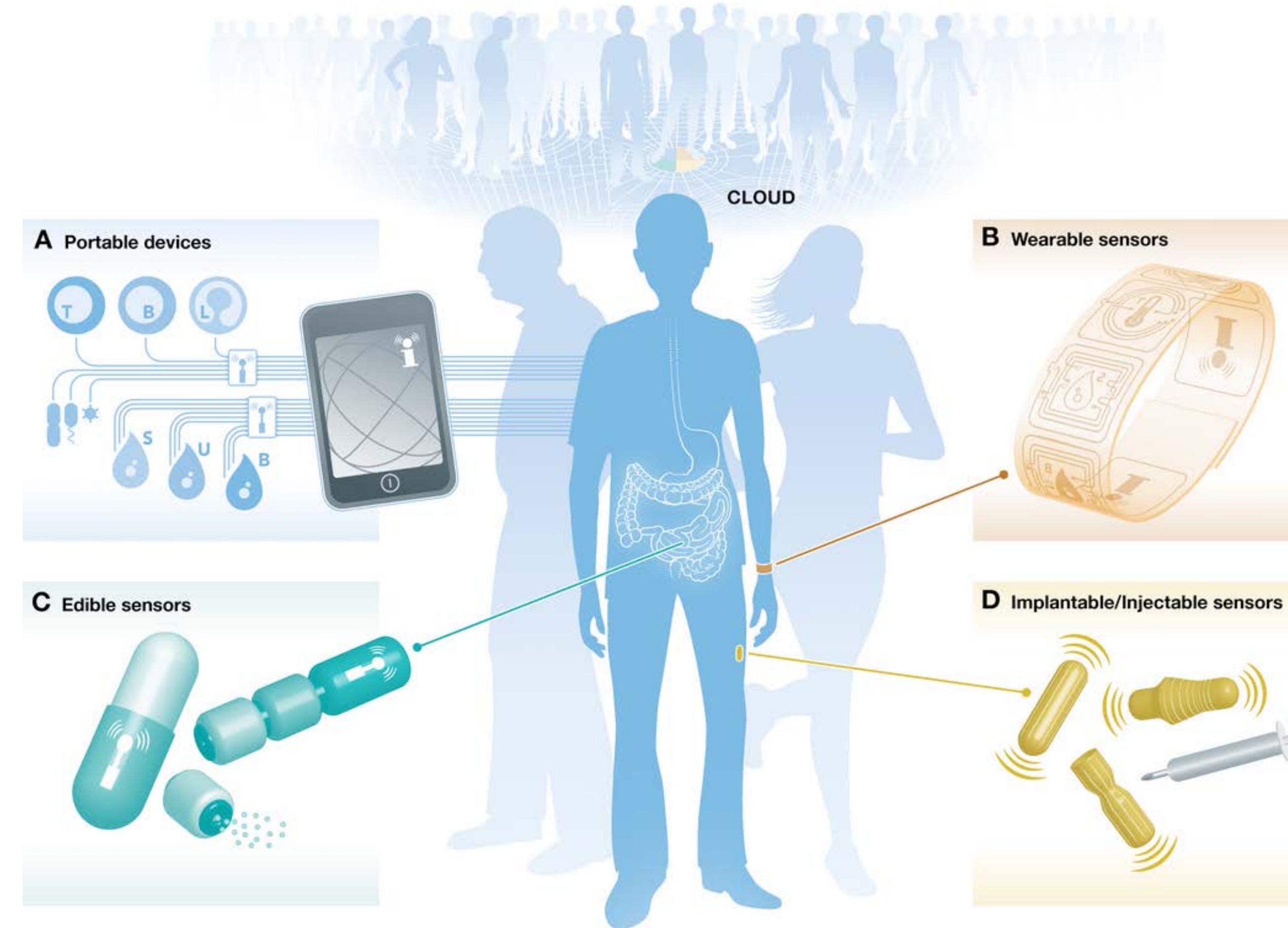
Gorzynski J et al. **N Engl J Med** (2022)

Gorzynski J et al. **Circ Gen** (2022)

Goenka S et al. **Nat Biotech** (2022)

- Guinness world record set on Feb 16, 2022: Sequencing a whole human genome in **5 hours!**
- Employing rapid Nanopore whole genome sequencing & AI to diagnose critically ill patients
- Sequenced the genomes of 12 patients with ~50x coverage, identified **5 cases** with genetic variants -> definitive diagnosis
- 1 diagnosis of known DCM mutation in an adolescent with cardiogenic shock -> immediate referral for heart transplant

# PORTRABLE, WEARABLE, EDIBLE AND IMPLANTABLE SENSORS



## Wearable Technology

### **Biomarker monitors**

(Glucose, temperature, caloric intake, stress, urine, blood, sweat...)

### **Activity trackers**

(Exercise, heart rate, sleep...)

### **Replacements**

(3D printed limbs, organs,...)

Emphasis on *health* as well as treatment

Steinmetz & Jones, Mol Syst Biol (2016)

# PERSONALISED, CONTINUOUS MONITORING



MY HABITS

INSIGHTS

DATA

5,300

Lars Steinmetz  
Level 4

TUE - SEP 22

Yesterday 23 Sep 2013

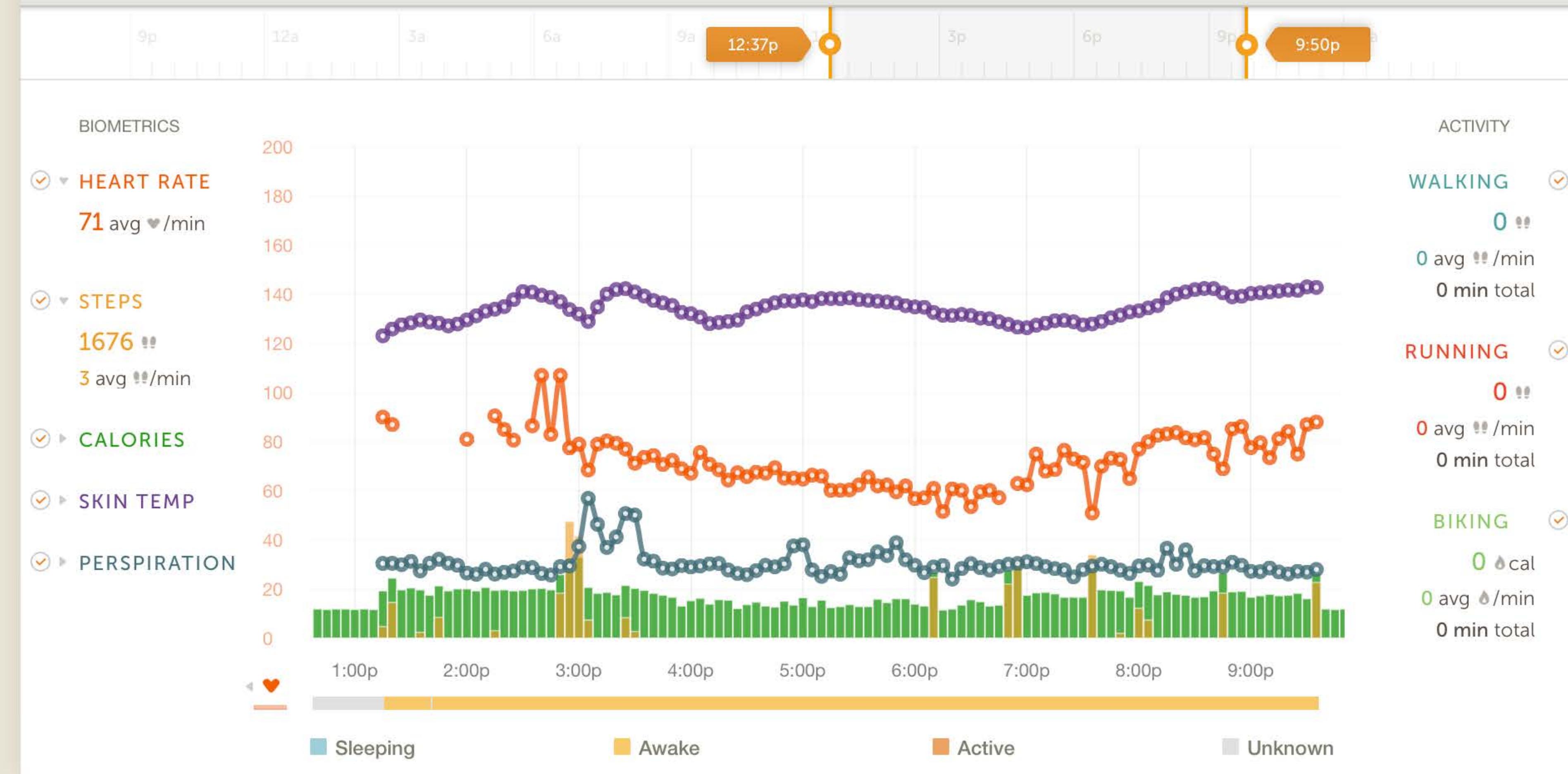
Last updated: an hour ago

Today

TODAY - SEP 24

## Activity Details

Wednesday 23 Sep

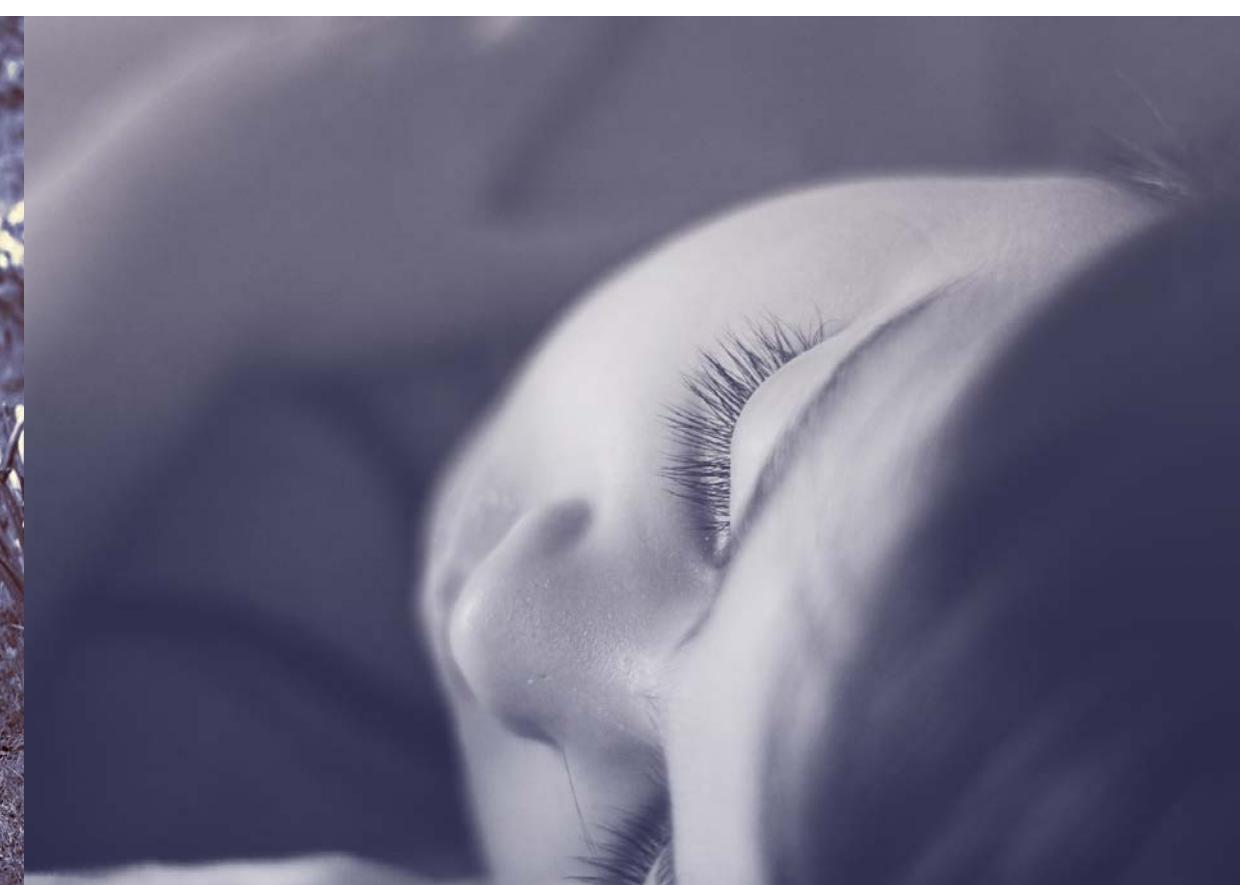


# mitoWEAR: MONITORING MITOCHONDRIAL DISORDERS

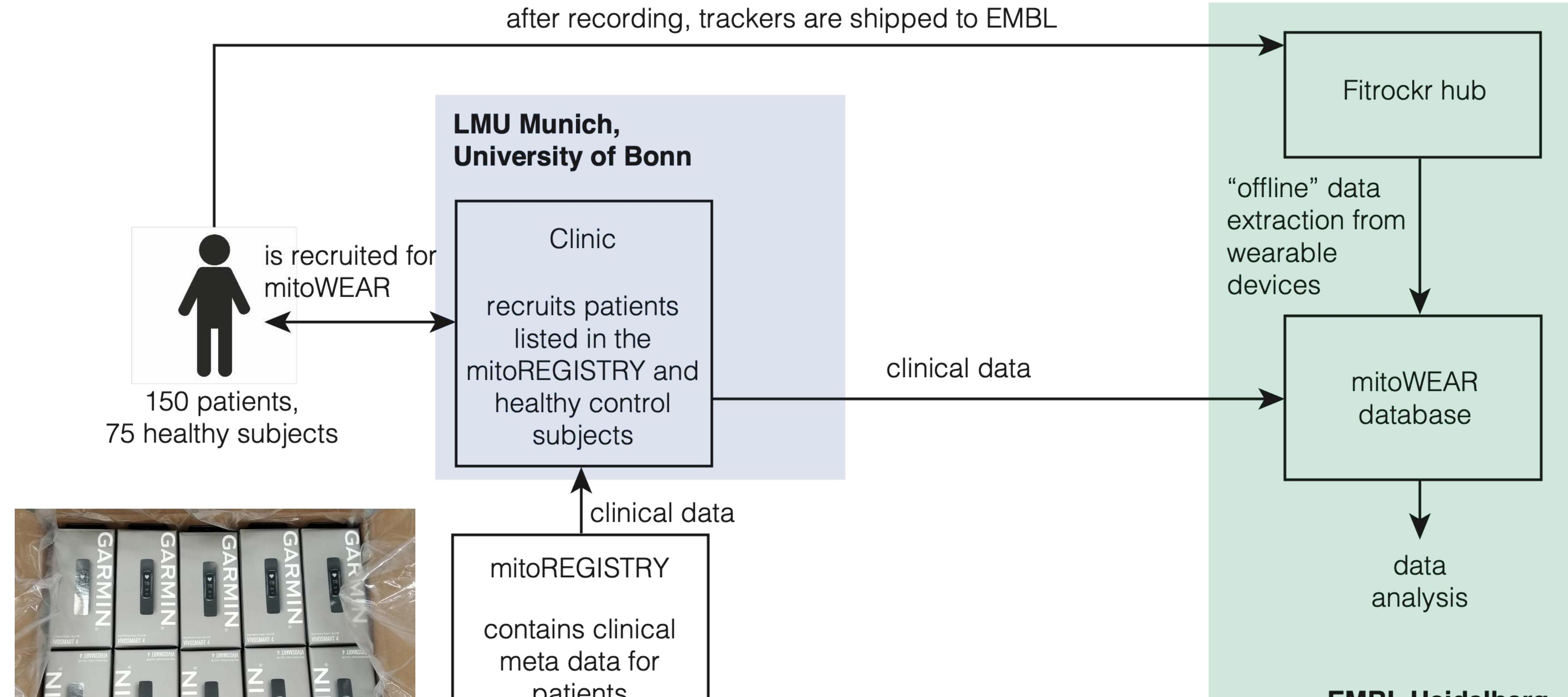
**mitoWEAR**  
Using wearable sensors to aid  
diagnosis and reporting of  
mitochondrial diseases without  
frequent trips to the clinic



Continuous monitoring in a patient's home environment can provide more accurate, representative data



# mitoWEAR: USING WEARABLES TO DIAGNOSE MITOCHONDRIAL DISEASE



Benedikt  
Rausher



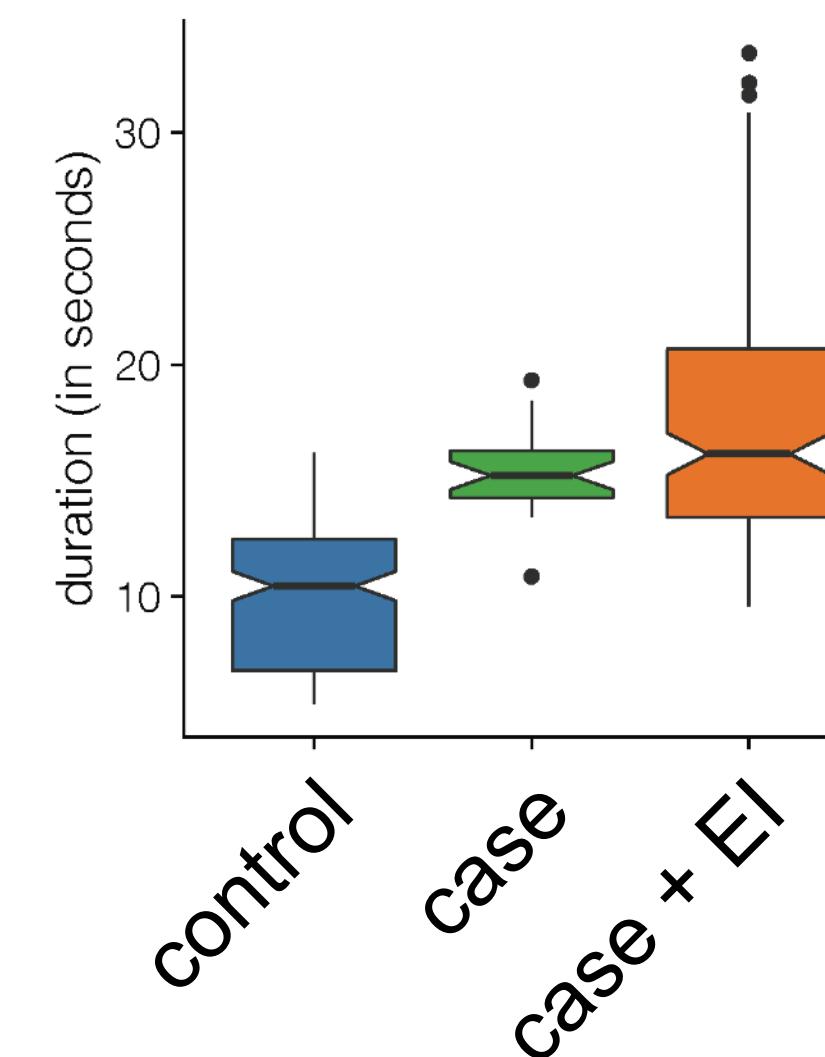
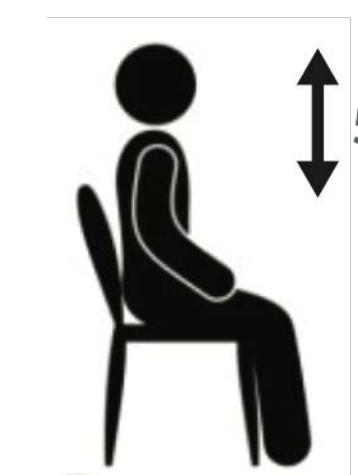
Bundesministerium  
für Bildung  
und Forschung

**mitoNET**  
DEUTSCHES NETZWERK  
FÜR MITOCHONDRIALE  
ERKRANKUNGEN

# EFFECTS OF EXERCISE INTOLERANCE ON PERFORMANCE IN EXERCISE TESTS

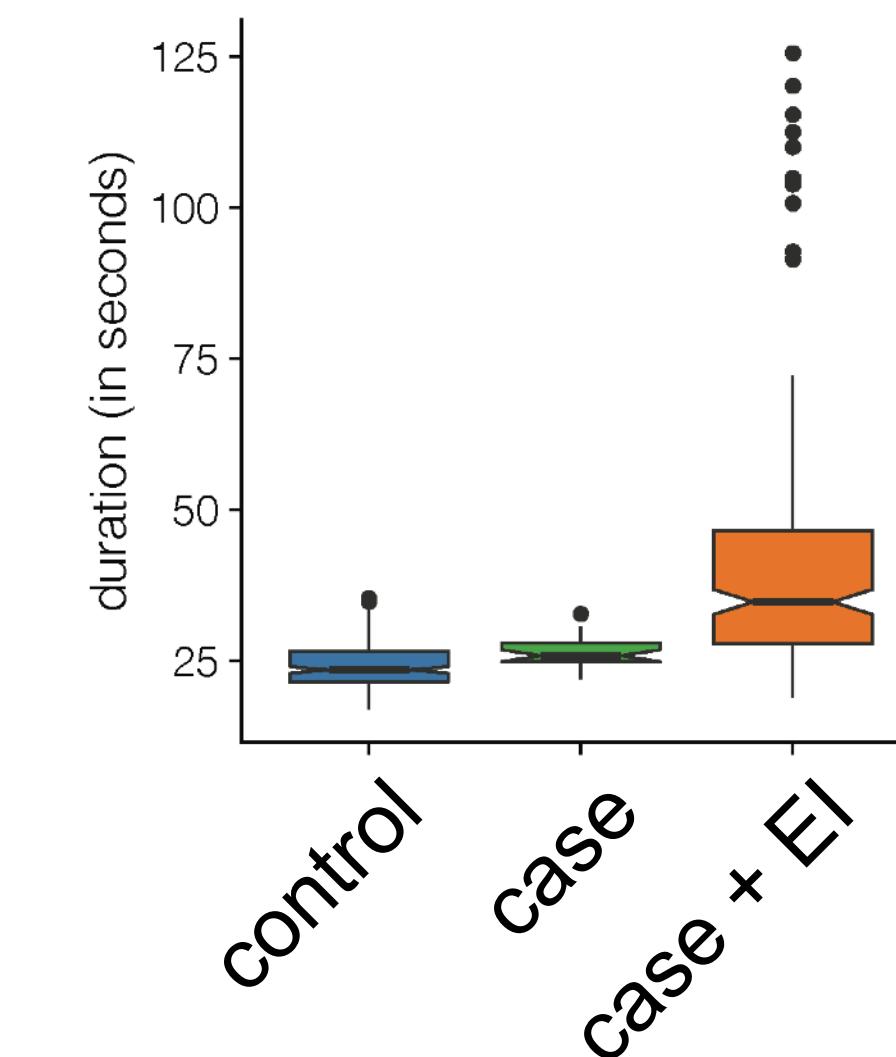
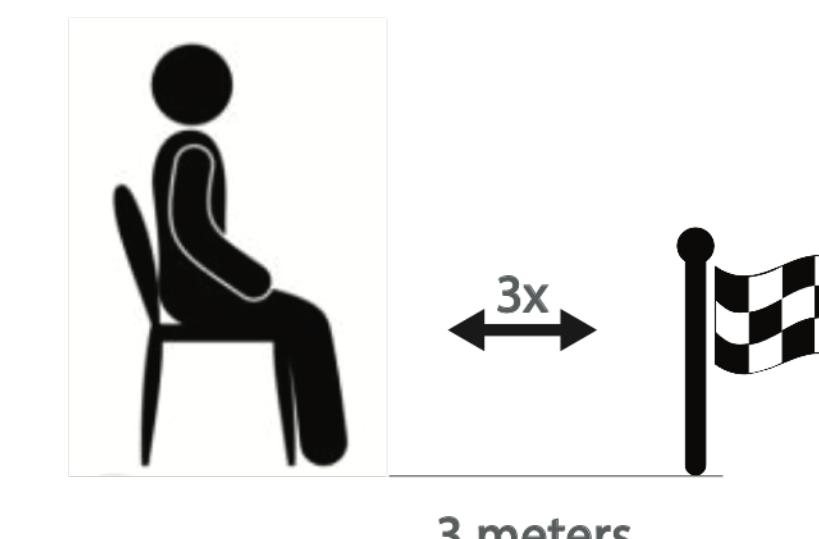


**5 Times Sit-to-Stand Test**  
determine speed

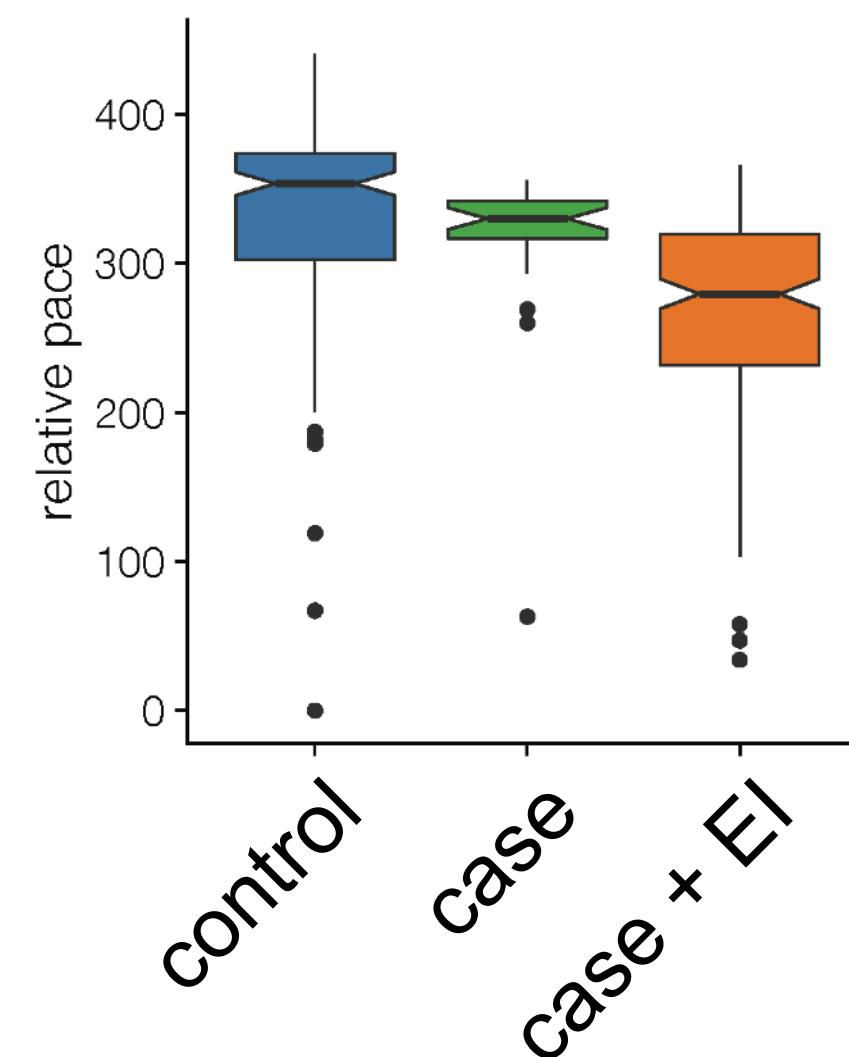


case = diagnosed mitochondrial disease  
EI = exercise intolerance

**Timed Up and Go Test**  
determine speed  
determine response to protracted effort



**6 Minute Walk Test**  
determine pace  
determine response to protracted effort



# USING YOUR SMARTWATCH FOR DIAGNOSIS: MyPhD EXAMPLE



Mike Snyder  
(Stanford)

<https://innovations.stanford.edu/wearables>

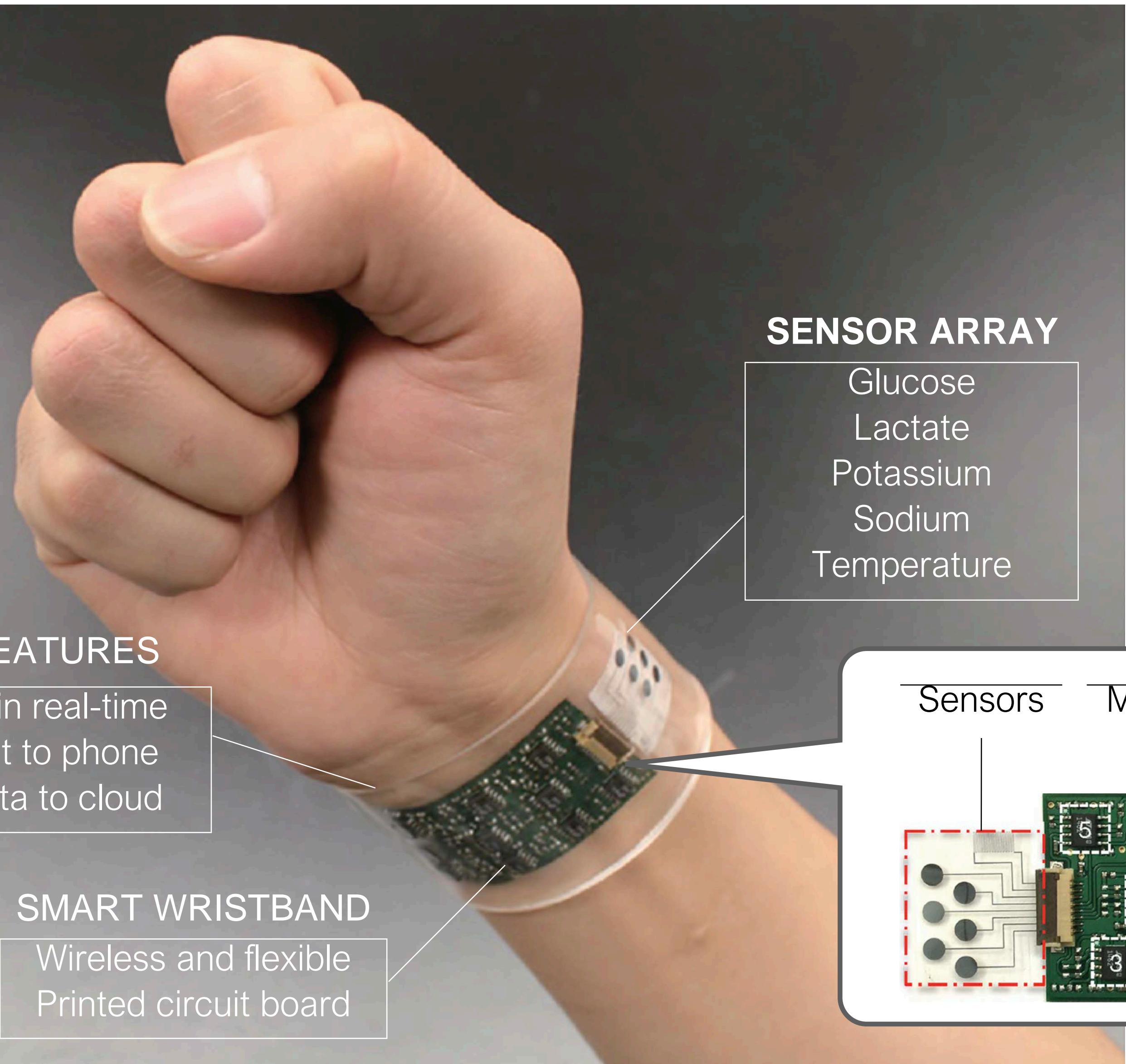
## Pre-symptomatic detection of COVID-19 from smartwatch data

Tejaswini Mishra, Meng Wang, Ahmed A. Metwally, Gireesh K. Bogu, Andrew W. Brooks, Amir Bahmani, Arash Alavi, Alessandra Celli, Emily Higgs, Orit Dagan-Rosenfeld, Bethany Fay, Susan Kirkpatrick, Ryan Kellogg, Michelle Gibson, Tao Wang, Erika M. Hunting, Petra Mamic, Ariel B. Ganz, Benjamin Rolnik, Xiao Li & Michael P. Snyder

*Nature Biomedical Engineering* 4, 1208–1220 (2020) | [Cite this article](#)

- Correctly flagged signs of COVID-19 before (or as) symptoms arose, 63% of the time.
- Continuous spike in resting heart rate, fewer steps & extra sleep trigger a health alert
- Algorithm doesn't replace diagnostics but provides early warning sign for illness

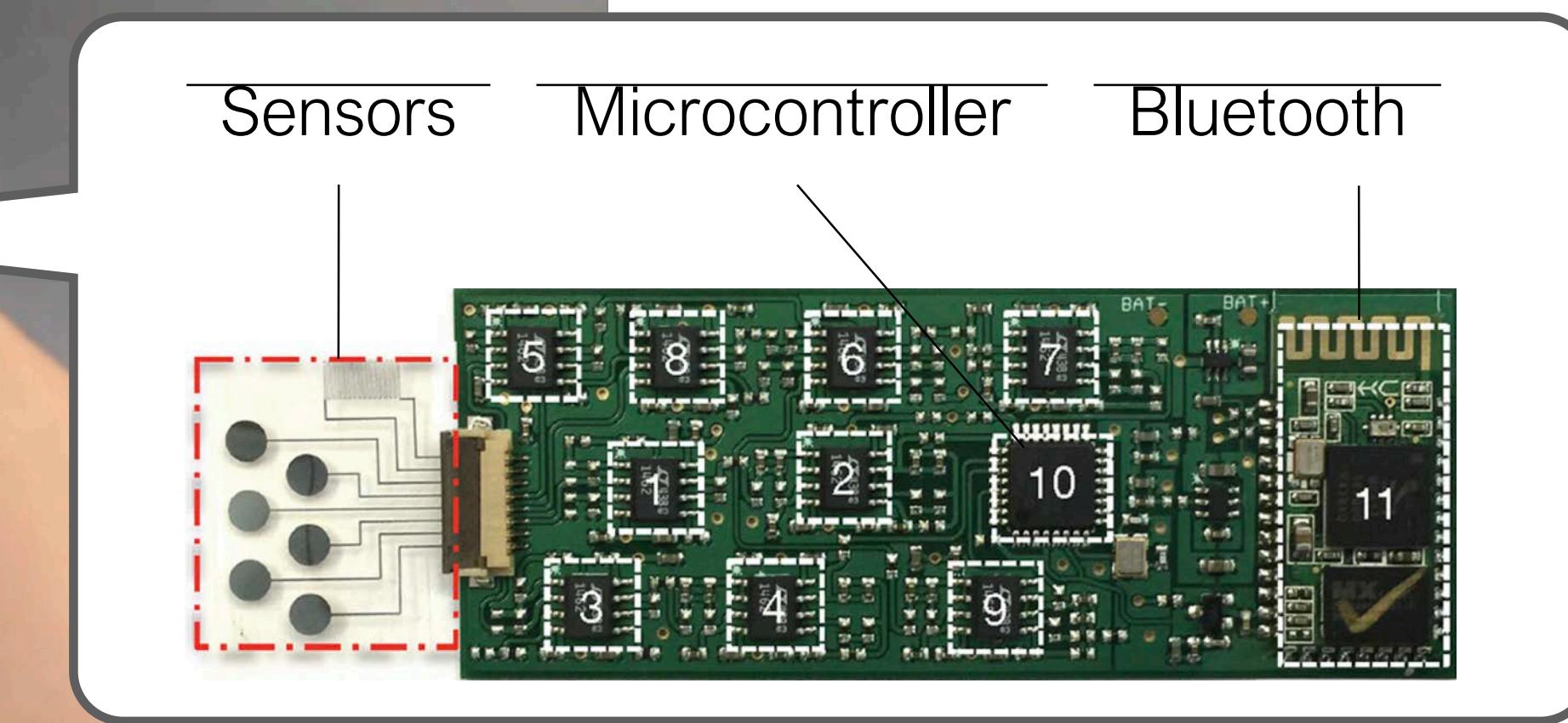
# FULLY-INTEGRATED WEARABLE SENSOR ARRAYS ( FISA )



## MULTIPLEXED IN-SITU PERSPIRATION ANALYSIS

*Sweat is a non-invasive way to detect wellness*

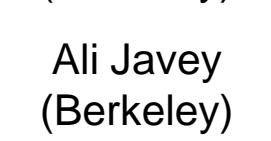
Gao\*, Emaminejad\* et al. **Nature** (2016)



Sam Emaminejad  
(Stanford, Now UCLA)

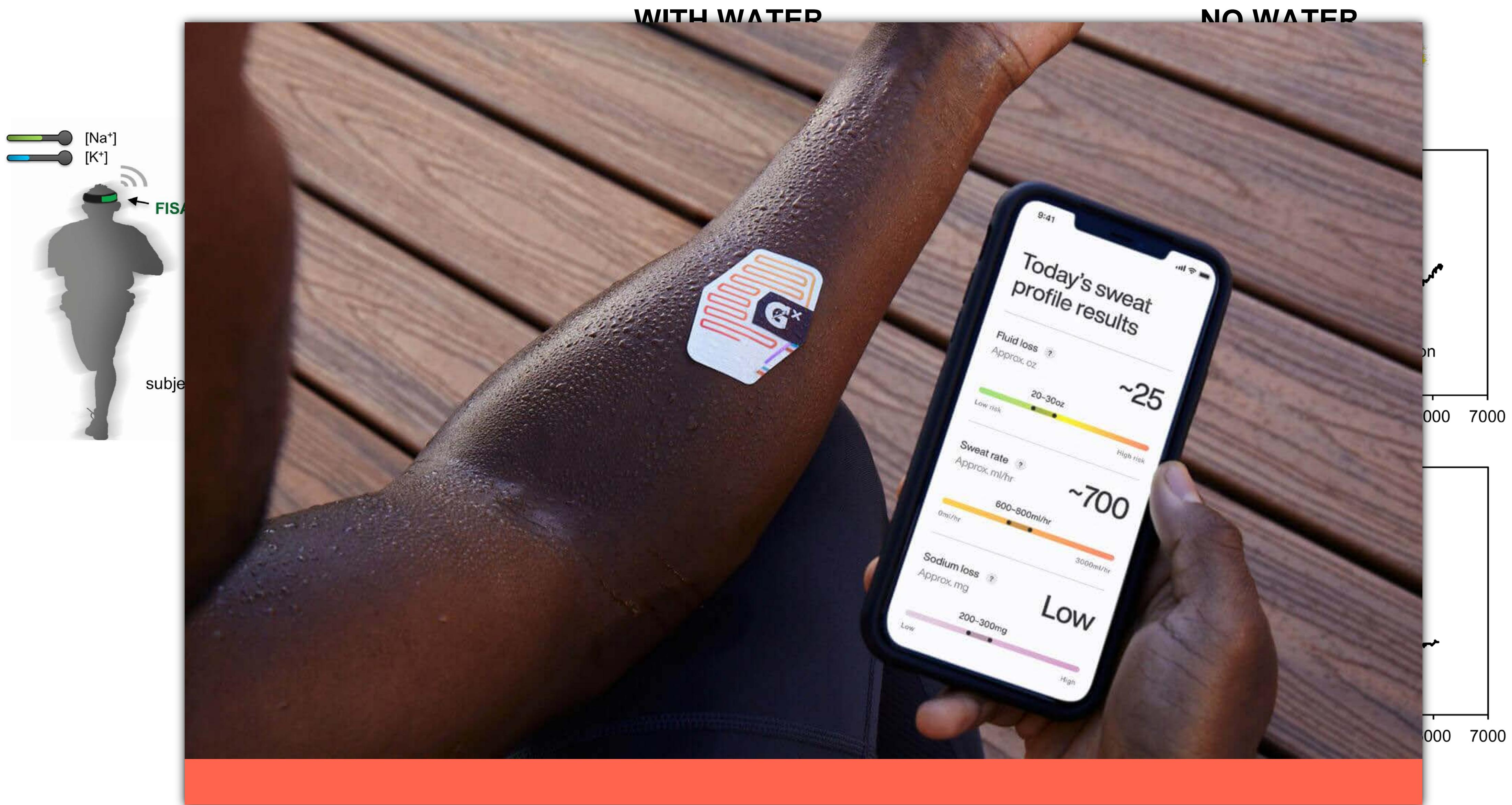


Wei Gao  
(Berkeley)



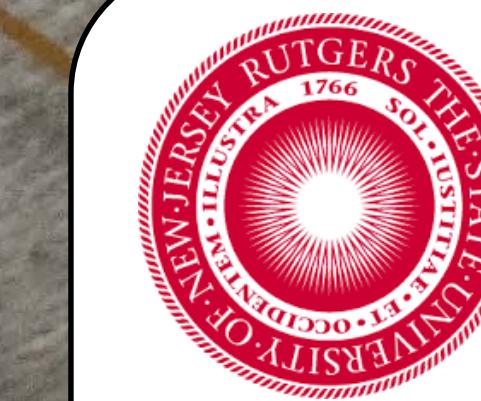
Ali Javey  
(Berkeley)

# USING SWEAT SENSORS TO DETECT DEHYDRATION



## POC home testing device for infectious pathogens:

- ✓ simple (no specialized equipment)
- ✓ fast (within minutes)
- ✓ flexible (multiple pathogens, multiplexing)



Rutgers  
Mehdi Javanmard  
Muhammad Tayyab



Yale  
Curt Scharfe

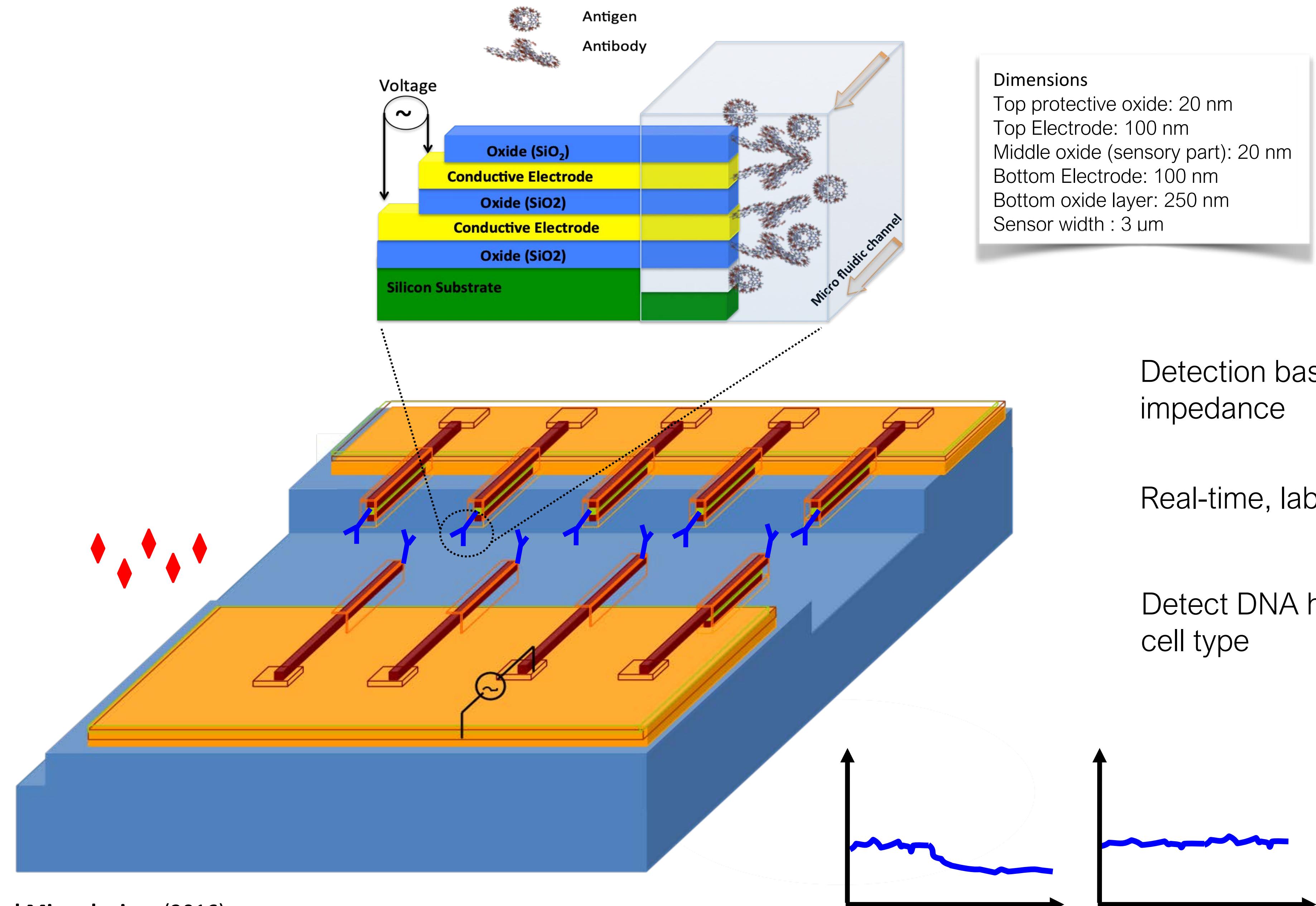


Stanford  
Lars Steinmetz  
Peter Griffin



Karolinska  
Vicent Pelechano

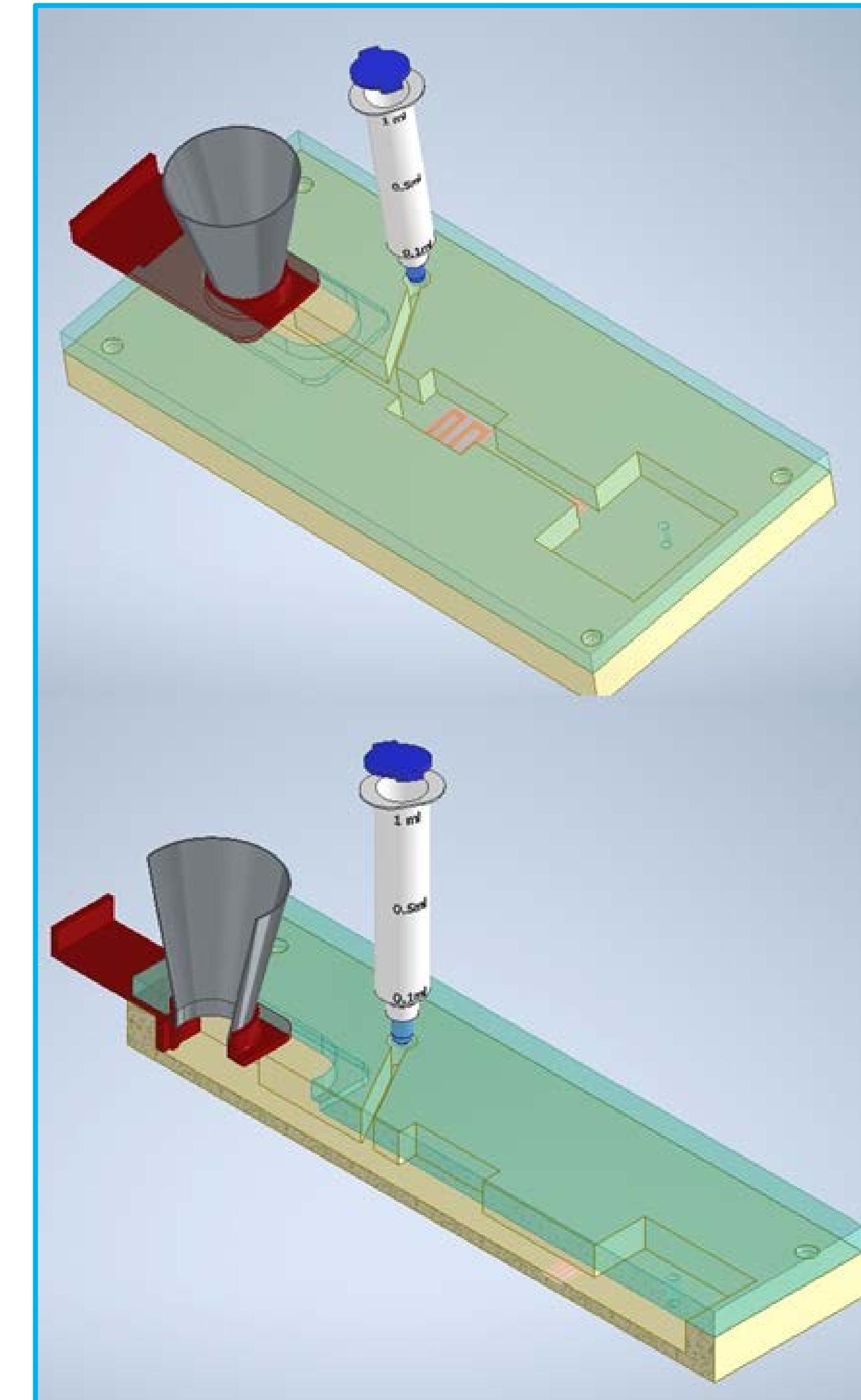
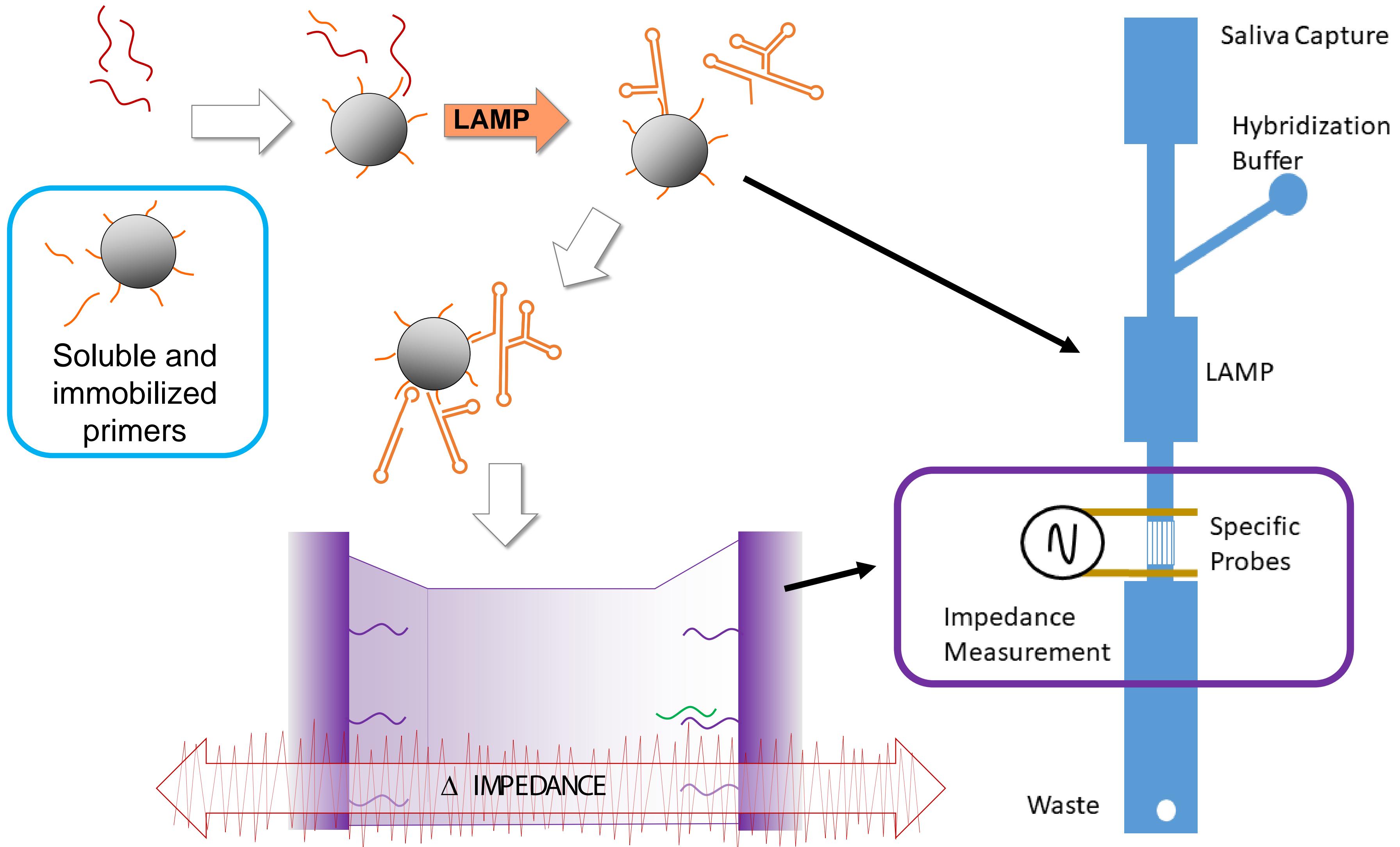
# NANONEEDLE BIOSENSORS FOR AT-HOME BIOMARKER MONITORING



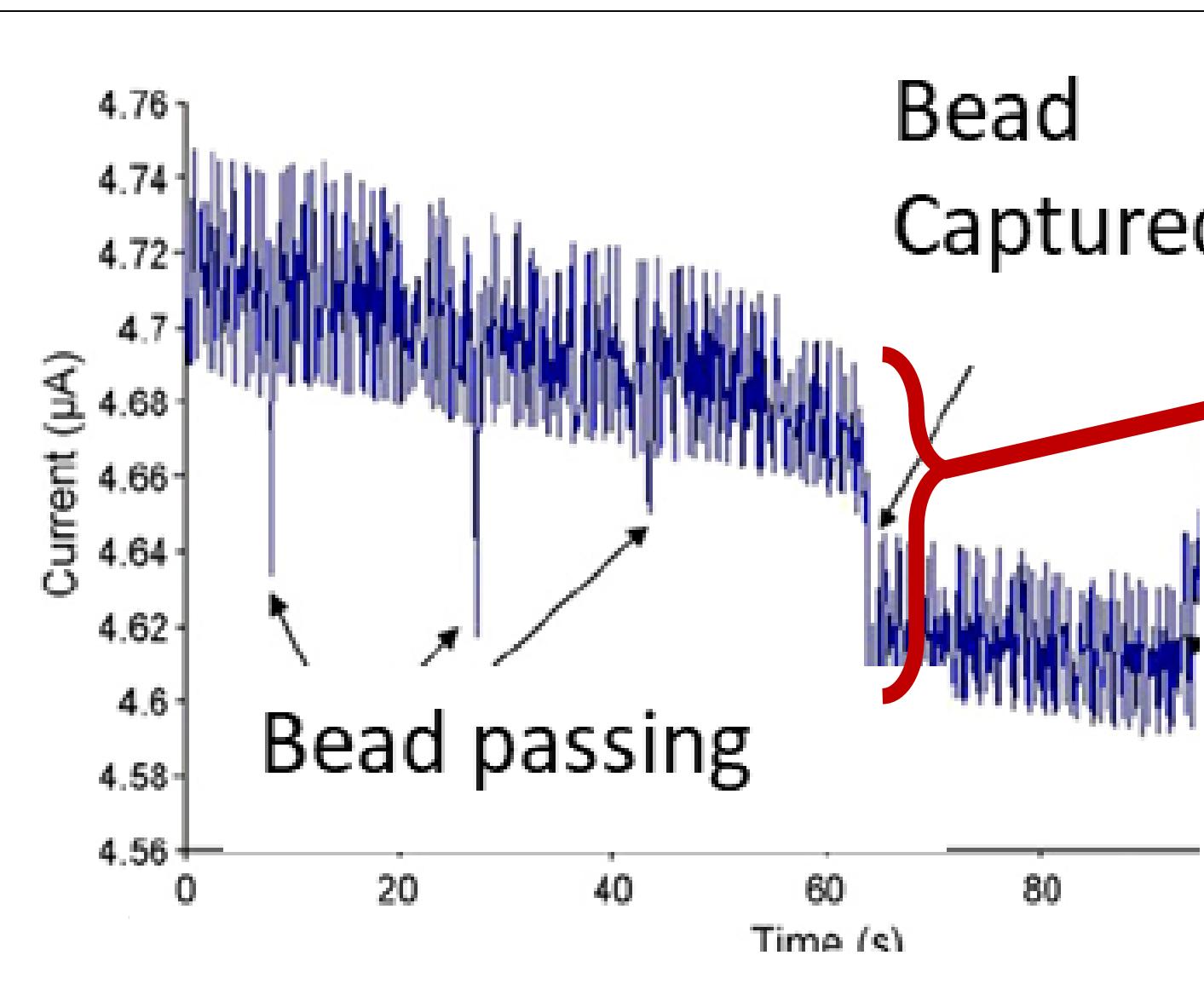
# HYBRIDIZATION-BASED IMPEDANCE DETECTION OF NUCLEIC ACIDS

LAMP = Loop-mediated isothermal amplification (*no thermocycler required*)

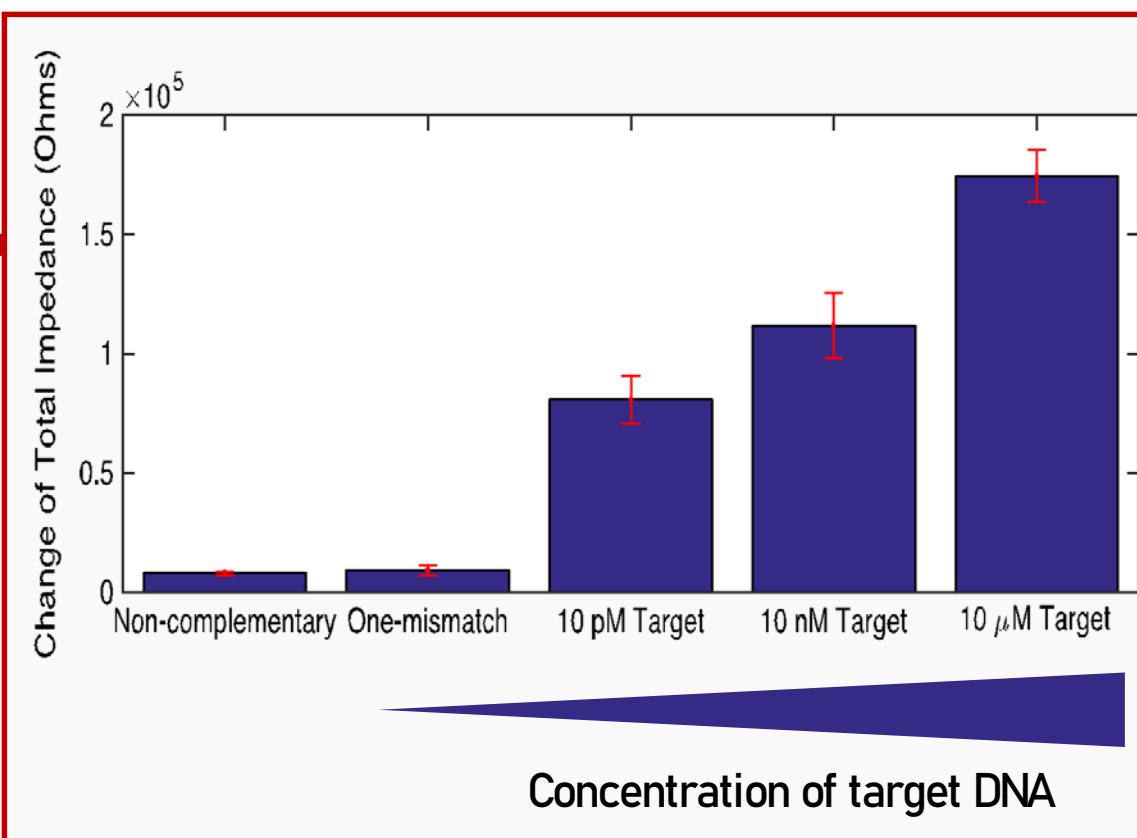
Viral RNA



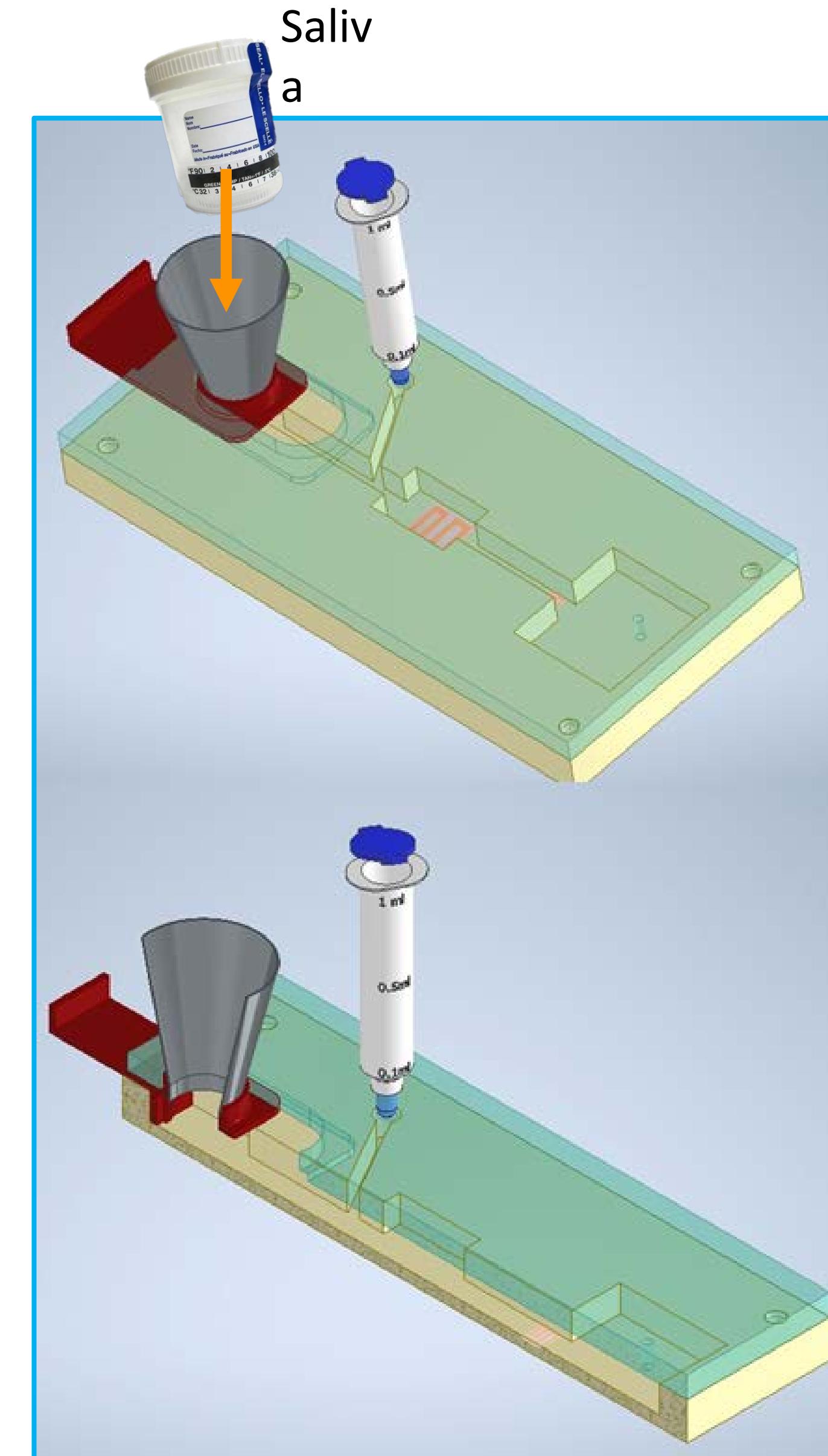
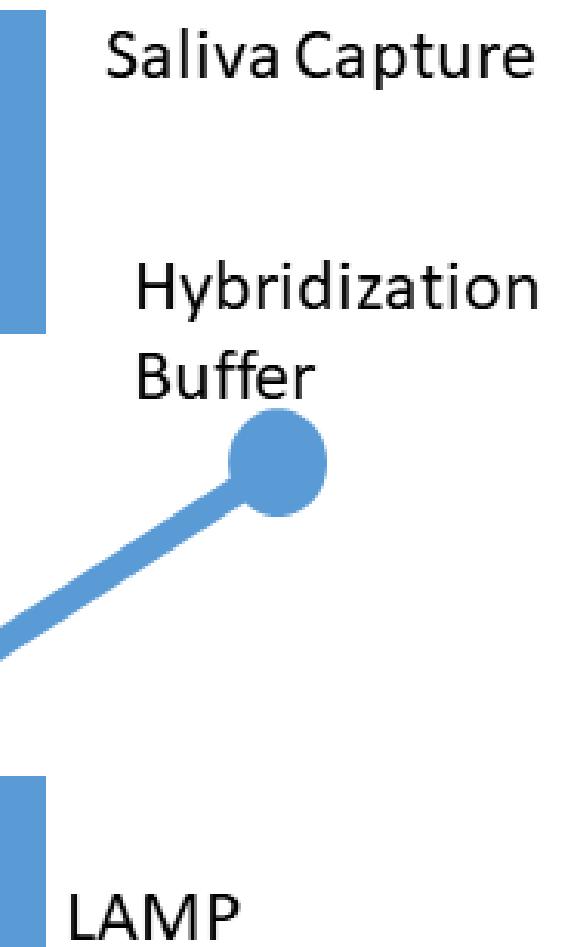
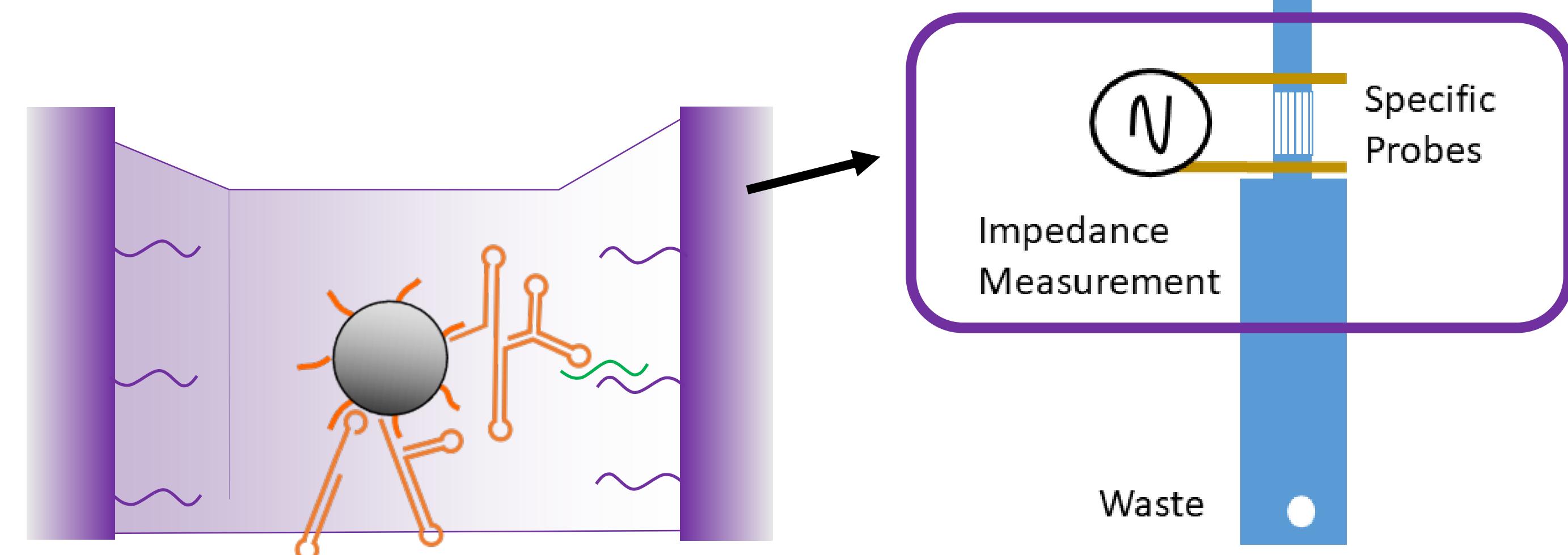
# HYBRIDIZATION-BASED IMPEDANCE DETECTION OF NUCLEIC ACIDS



Impedance change scales  
with amount of amplicon



Esfandyarpour et al. *Biomed Microdevices* (2016)



# MAGNETIC LEVITATION TECHNOLOGY



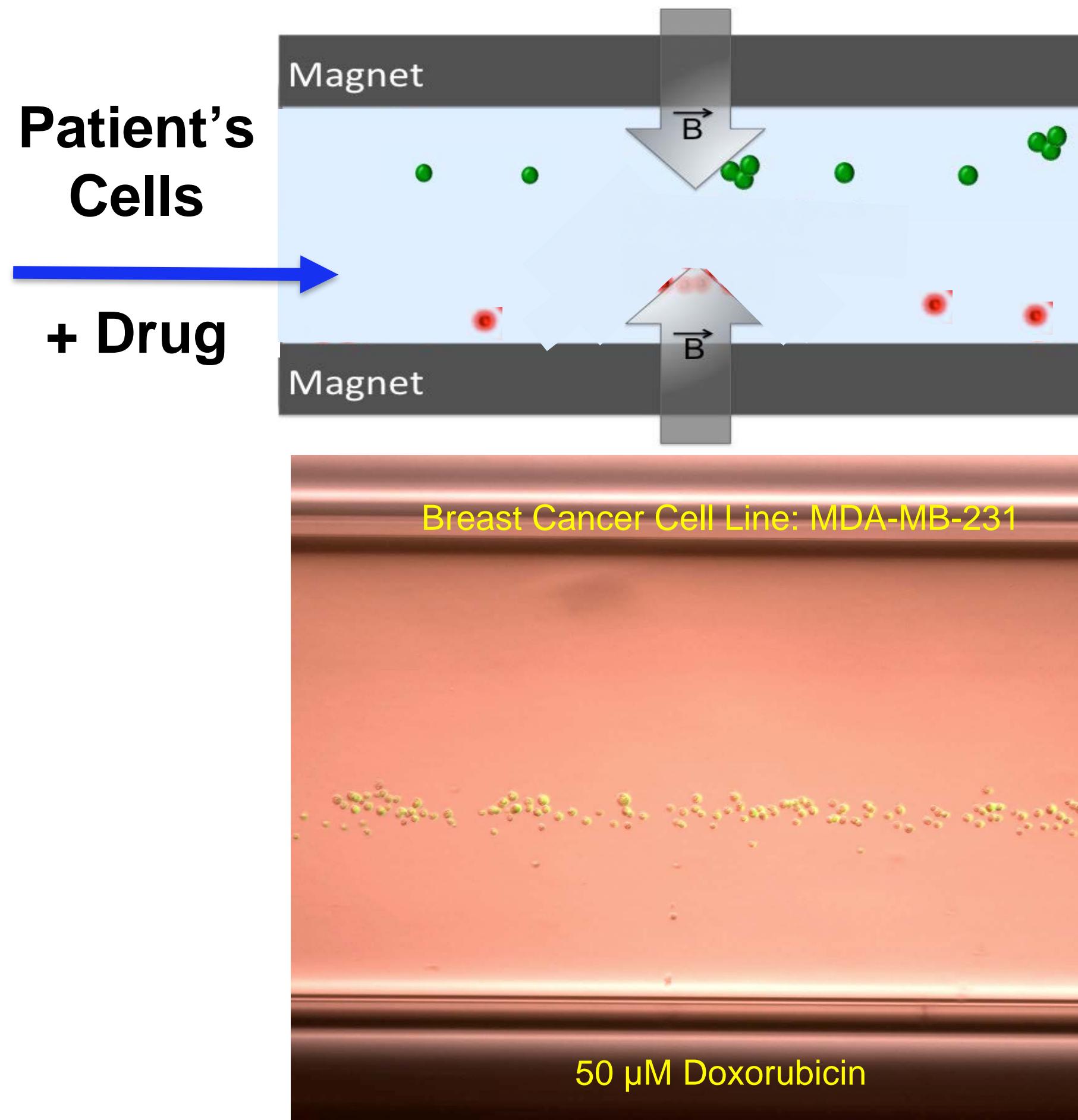
Gozde  
Durmus



Huseyin  
Tekin



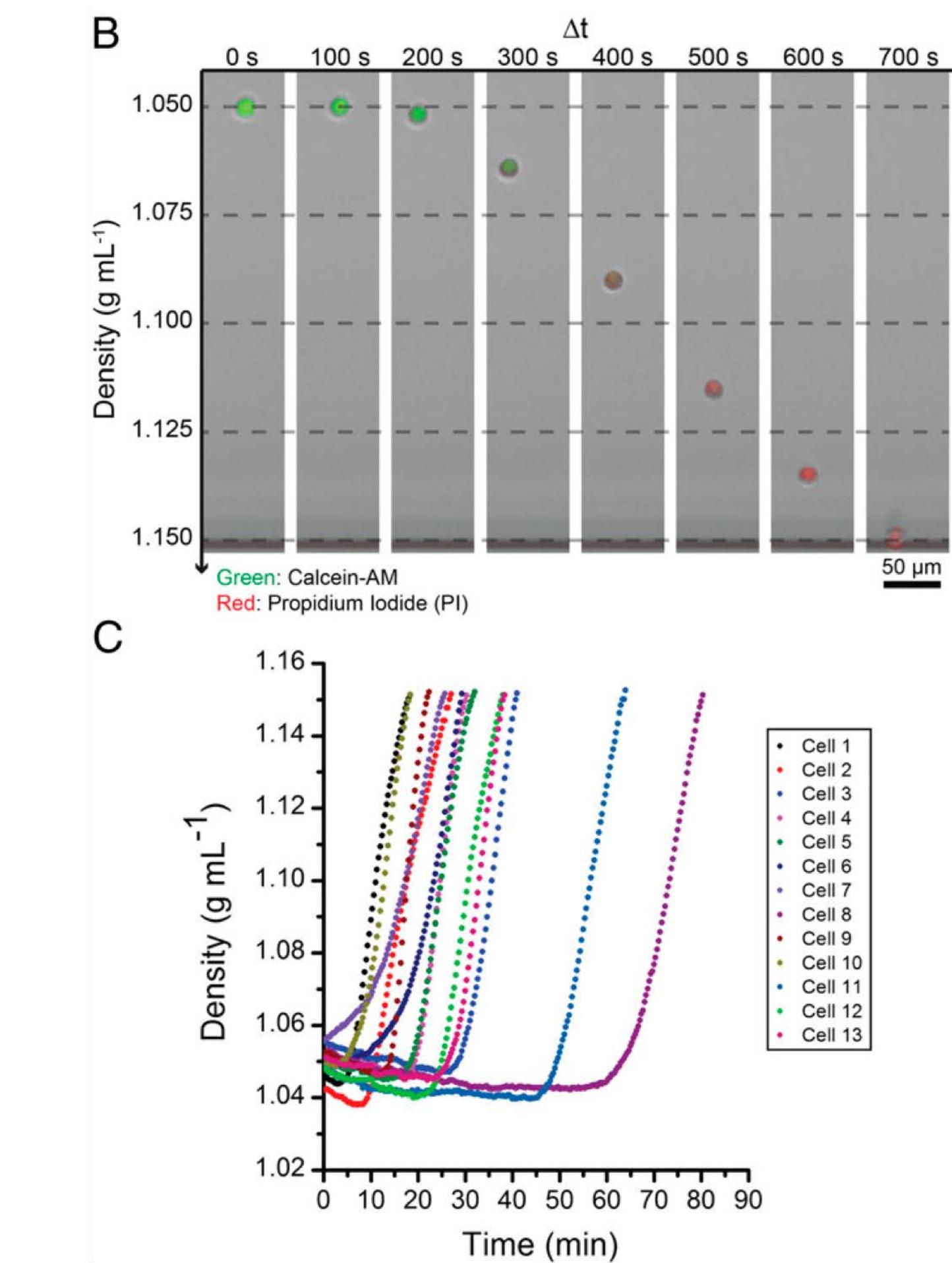
# REAL-TIME MONITORING, PREDICTIVE DECODING, AND MODELING OF CELLULAR EVENTS



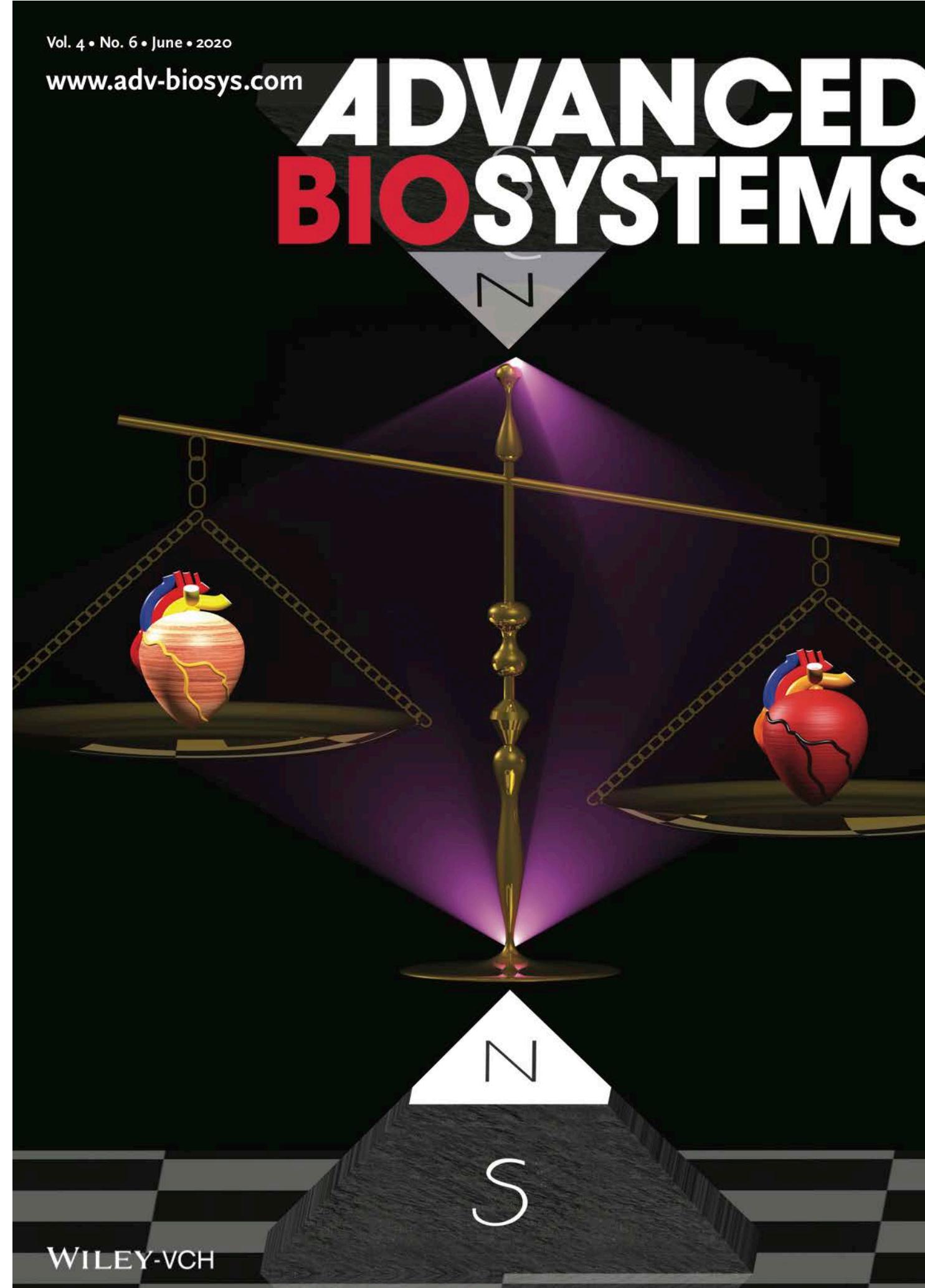
Live Cells  
Dead Cells

Breast Cancer Cell Line: MDA-MB-231

50  $\mu\text{M}$  Doxorubicin



# MAGNETIC LEVITATION TECHNOLOGY FOR CARDIOMYOCYTES



Vol. 4 • No. 6 • June • 2020  
[www.adv-biosys.com](http://www.adv-biosys.com)

## ADVANCED BIOSYSTEMS

Inside Front Cover | Free Access |

**Cell Sorting: Levitating Cells to Sort the Fit and the Fat (Adv. Biosys. 6/2020)**

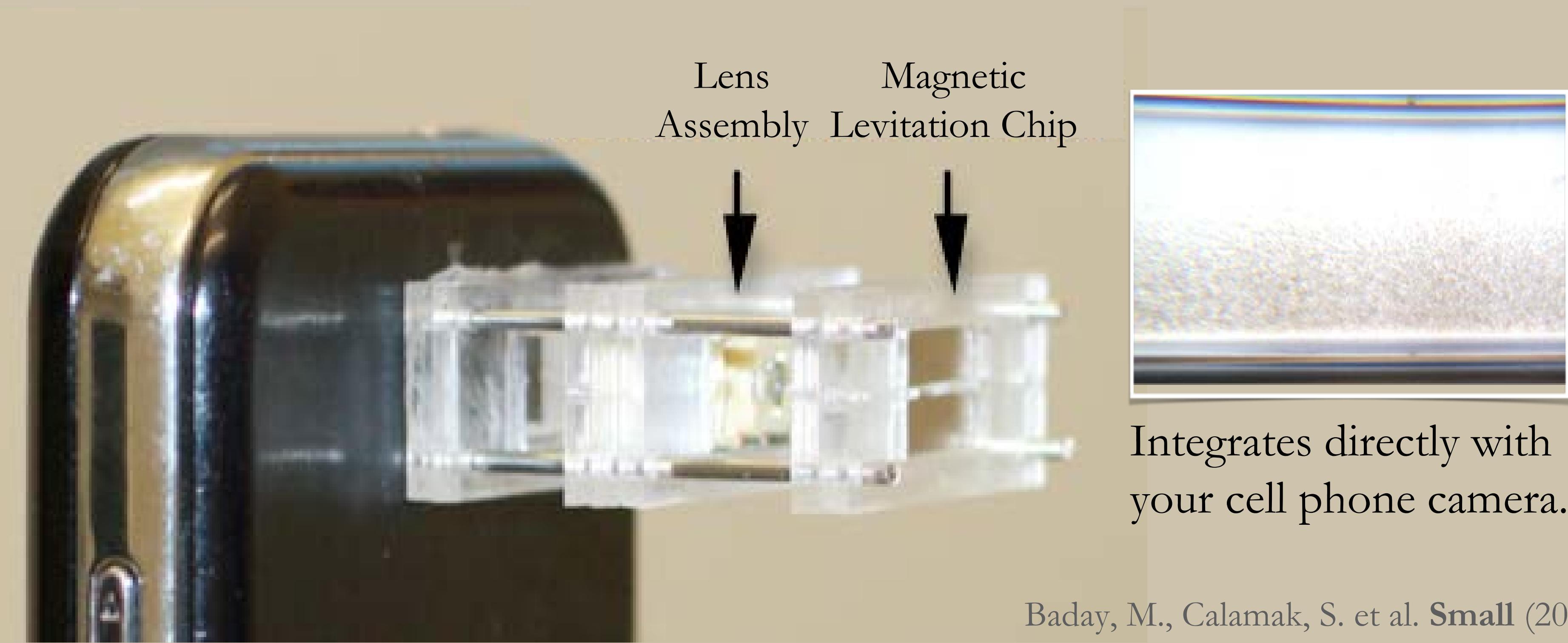
Nazan Puluca, Naside Gözde Durmus, Soah Lee, Nadjet Belbachir, Francisco X. Galdos, Mehmet Giray Ogut, Rakhi Gupta, Ken-ichi Hirano, Markus Krane, Rüdiger Lange, Joseph C. Wu ... [See all authors](#) ▾

First published: 12 June 2020 | <https://doi.org/10.1002/adbi.202070062>

- Magnetic levitation of iPSC-CMs from patient with neutral lipid storage disease
- Density sorting based on lipid content in real-time
- Possible applications for DCM phenotypes?

# i-Lev

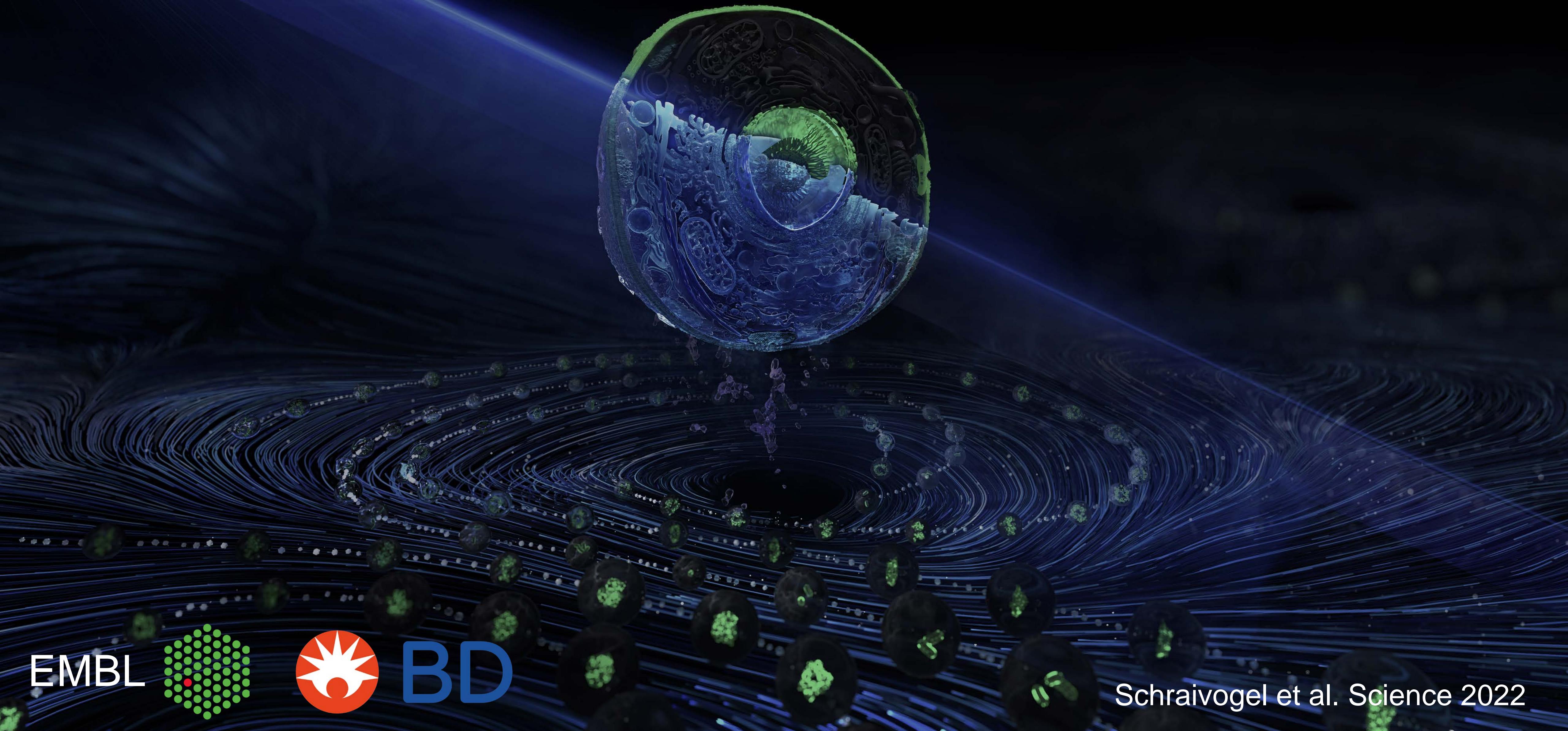
Magnetic levitation.  
Now on your phone.



Integrates directly with  
your cell phone camera.



# HIGH-SPEED IMAGE-ENABLED CELL SORTING



# ICS ALLOWS SINGLE-CELL PHENOTYPING AT 15,000 CELLS/SEC



Schraivogel *et al.* Science (2022)



et al.

Daniel  
Schraivogel

Sara  
Cuylen

Eric  
Diebold



► ICS developed by BD Biosciences

# COMBINING MICROSCOPY AND CELL SORTING IS A DIFFICULT TASK



**Problem: Blur free images of fast flowing cells**

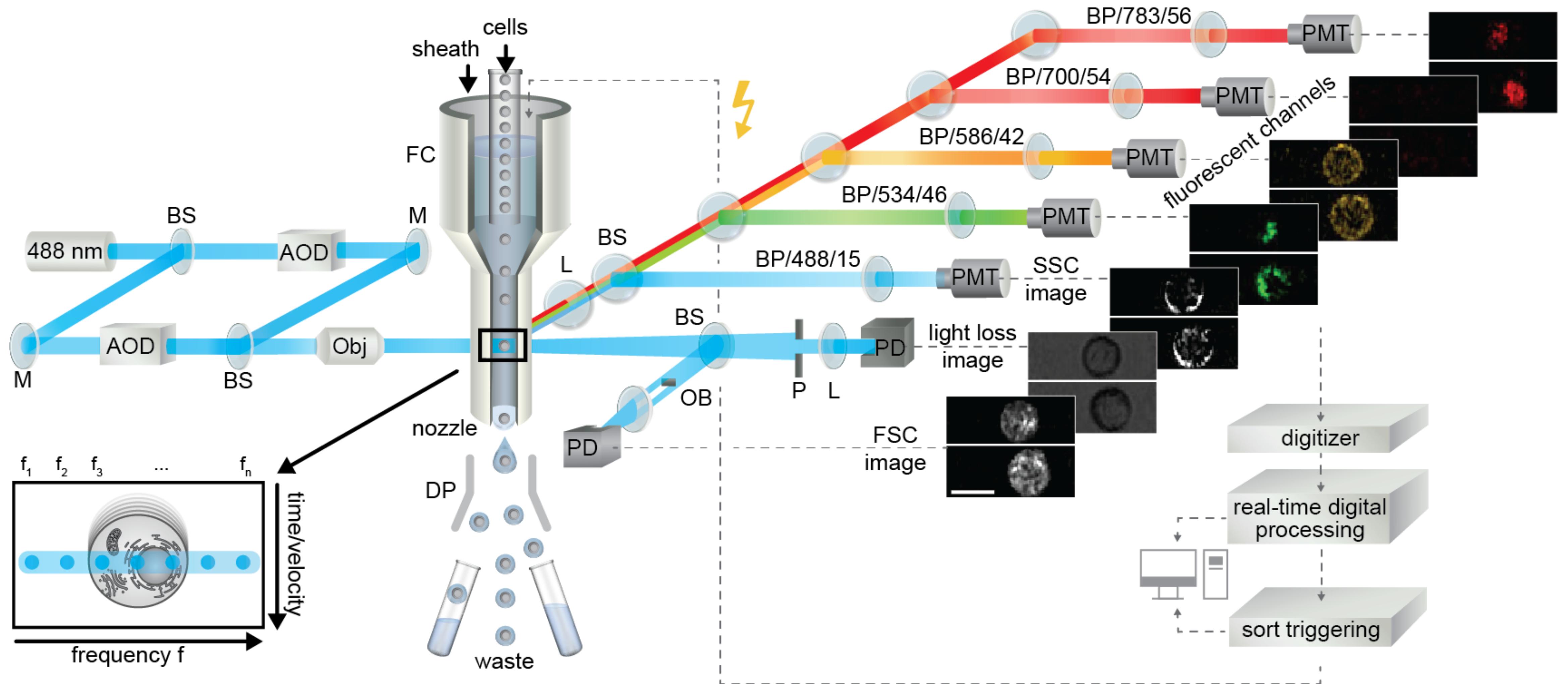
Solution: Ultra-fast imaging methods with or without fluorescence



**Problem: Real-time image reconstruction + analysis**

Solution: Low latency electronics to reconstruct + analyze images on-the-fly

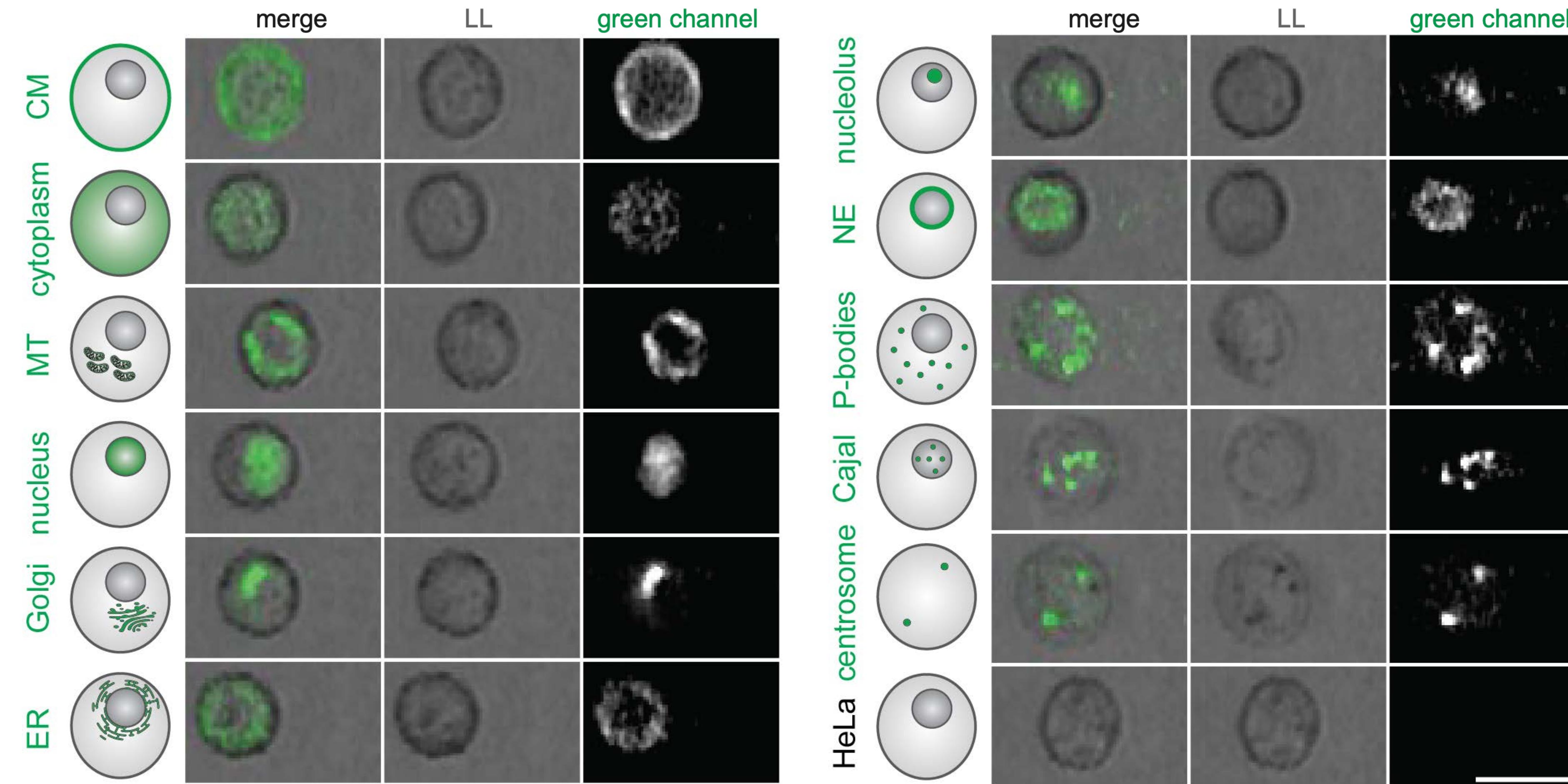
# FUNCTIONALITY OF ICS



FIRE = Fluorescence Imaging using  
Radiofrequency-tagged Emission  
Diebold et al. Nat Photonics 2013

Schraivogel et al. Science 2022

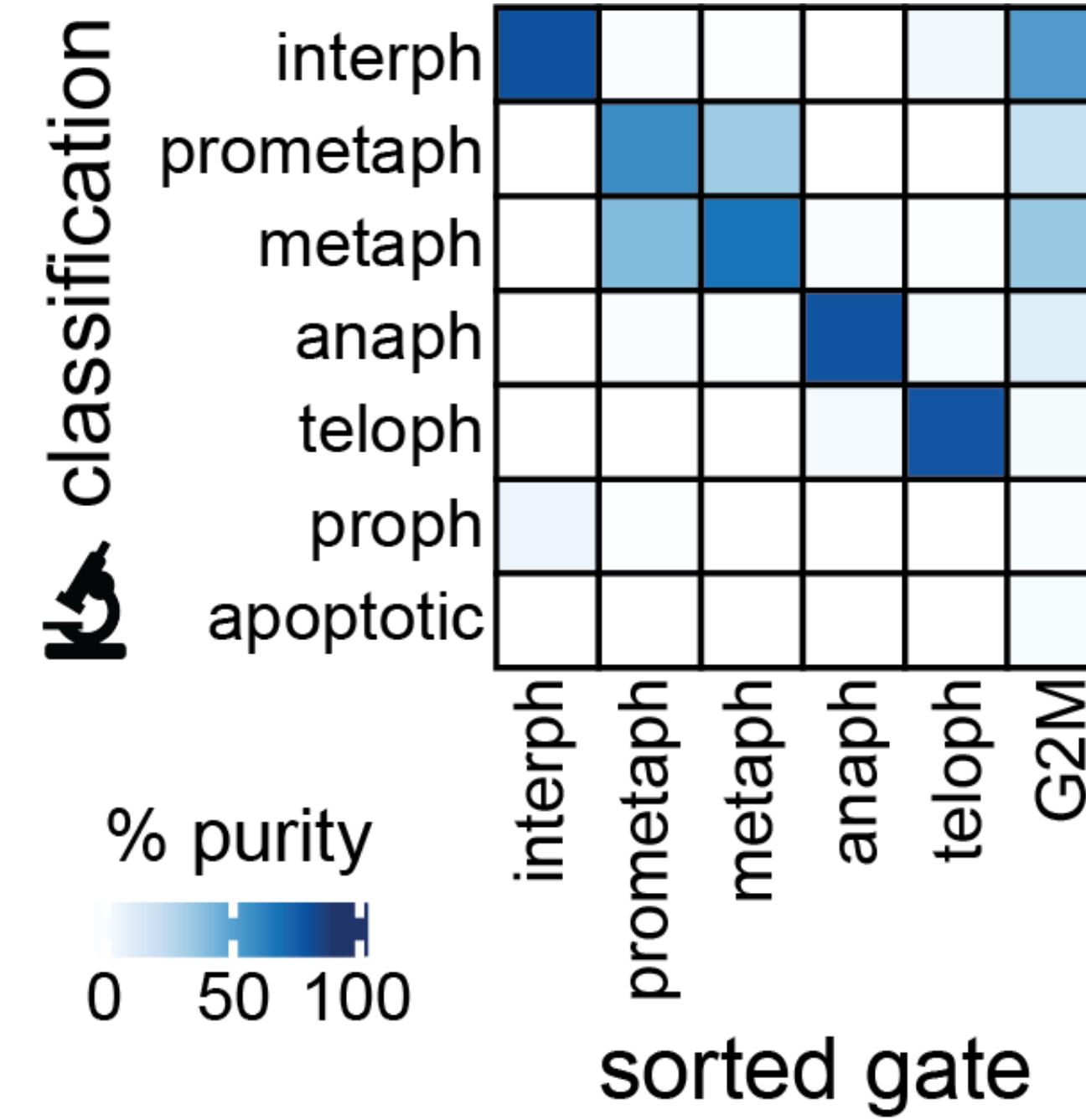
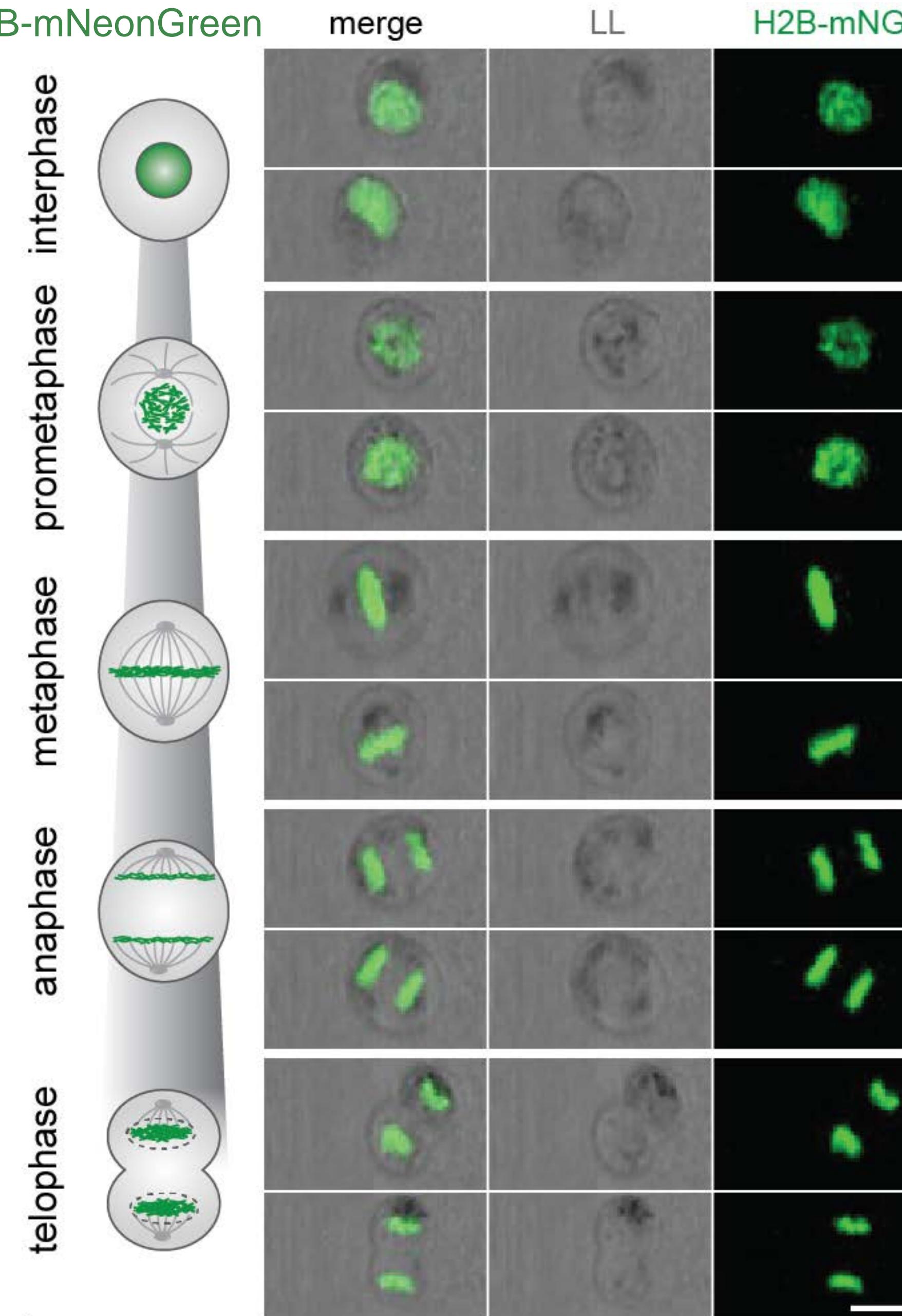
# MULTICOLOR IMAGING IN MICROSECOND TIMESCALE



→ Isolation of a broad range of microscopic phenotypes at speeds up to 15,000 cells/s!

# SORTING OF MITOTIC CELL CYCLE PHASES

HeLa H2B-mNeonGreen



# INFECTIOUS DISEASES

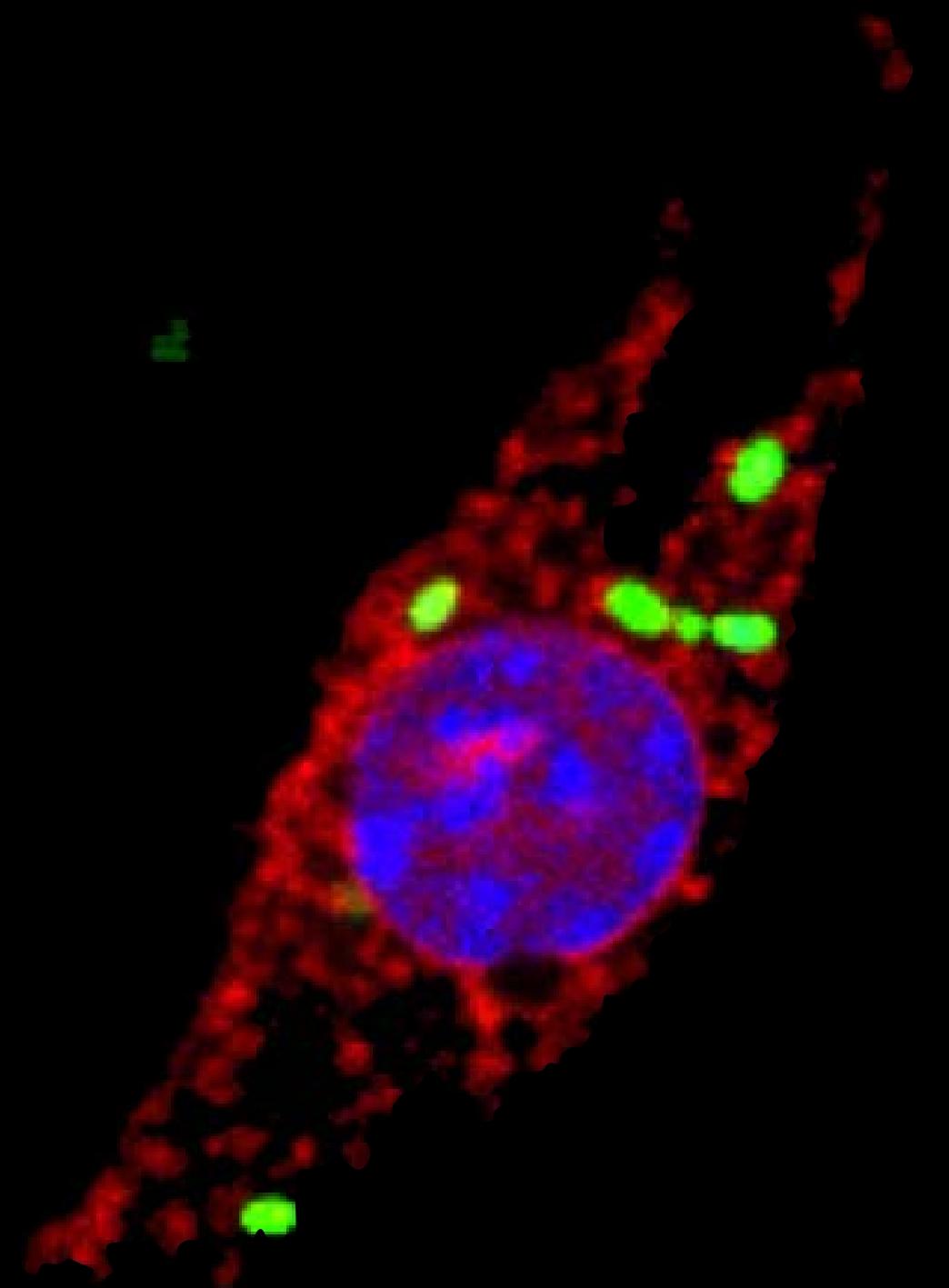
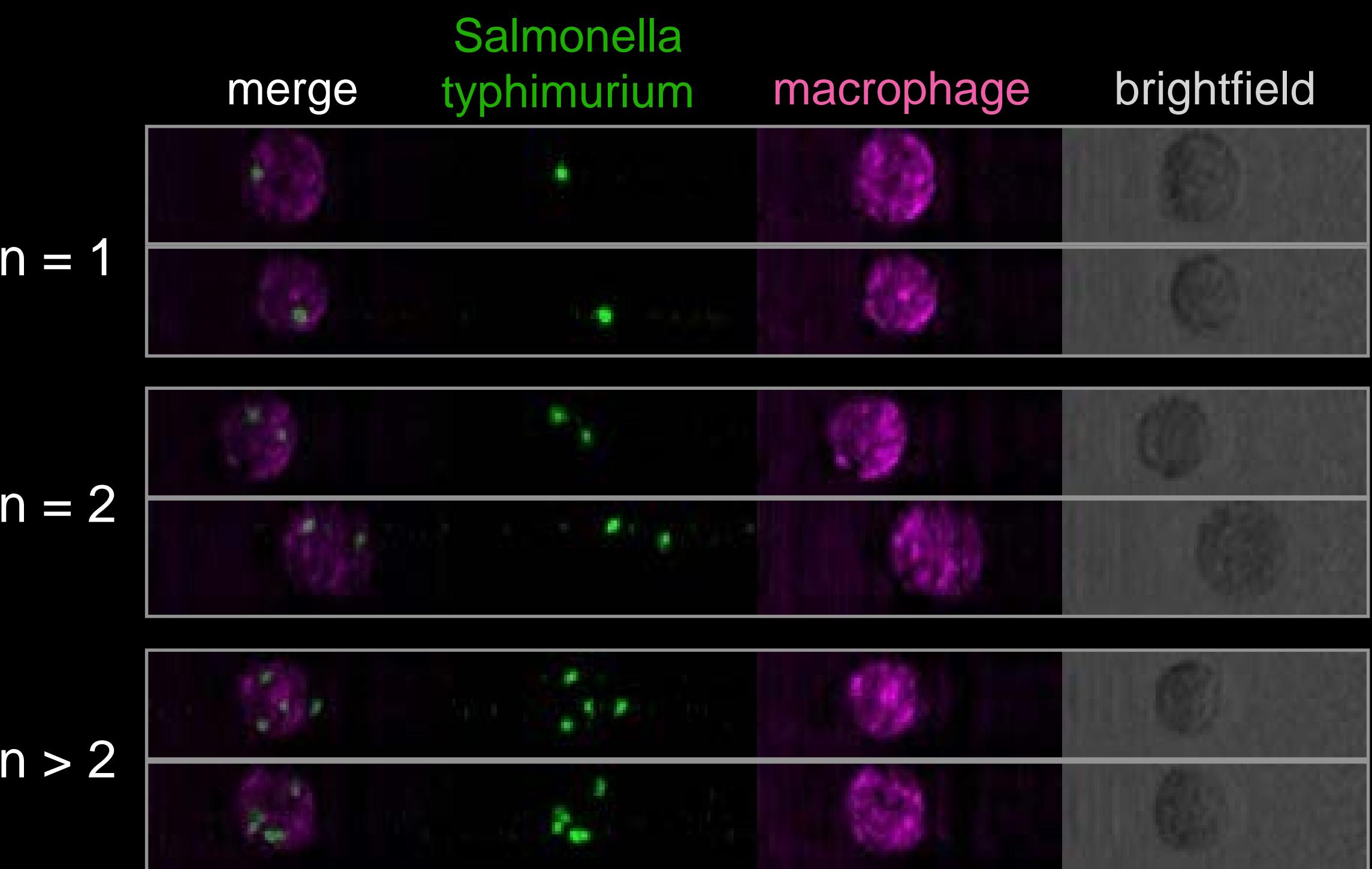
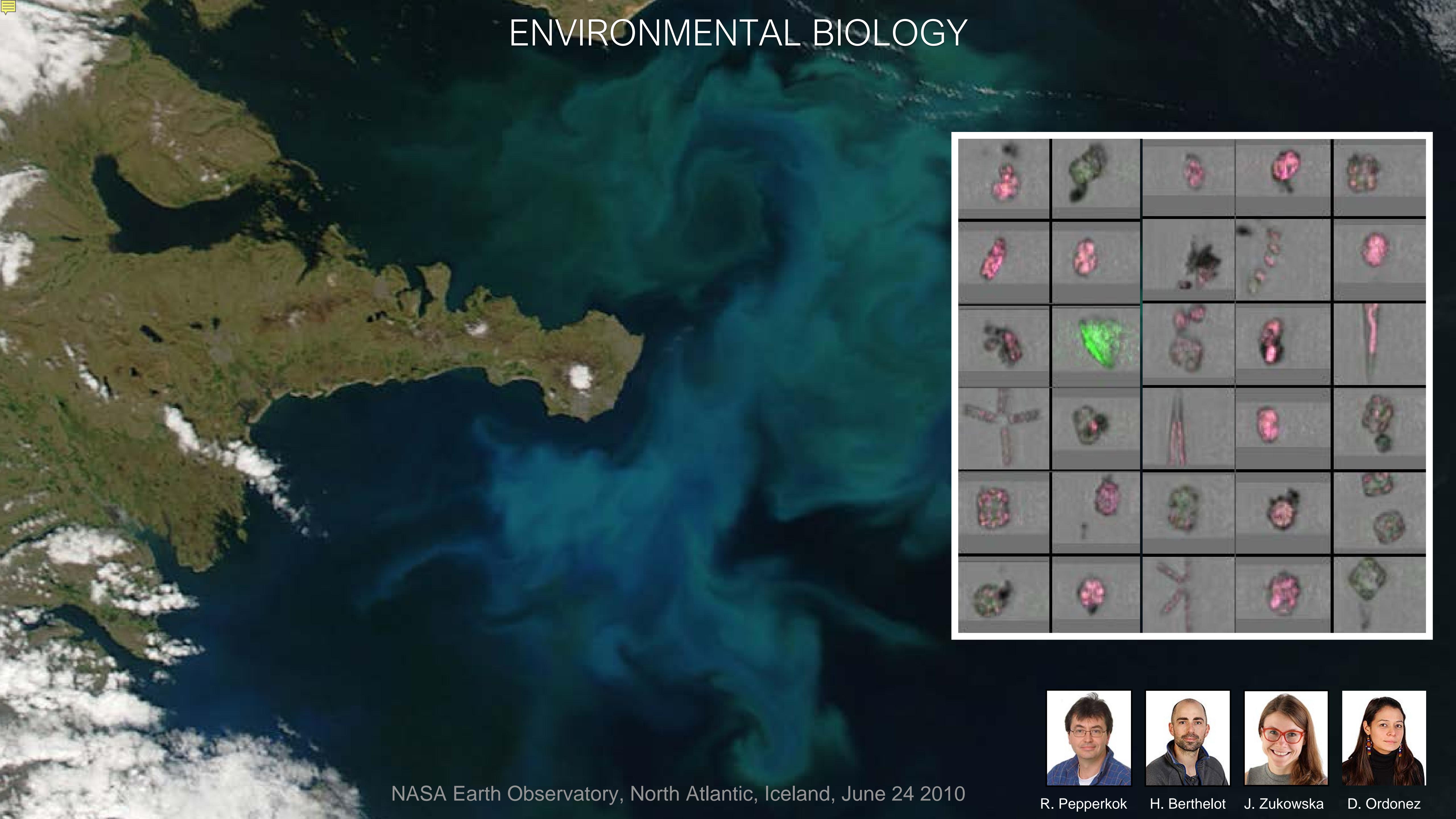


Image credit: Joel Selkirk/EMBL



C. Ciolfi-Mattioli   R. Avraham   D. Schraivogel



# ENVIRONMENTAL BIOLOGY

NASA Earth Observatory, North Atlantic, Iceland, June 24 2010

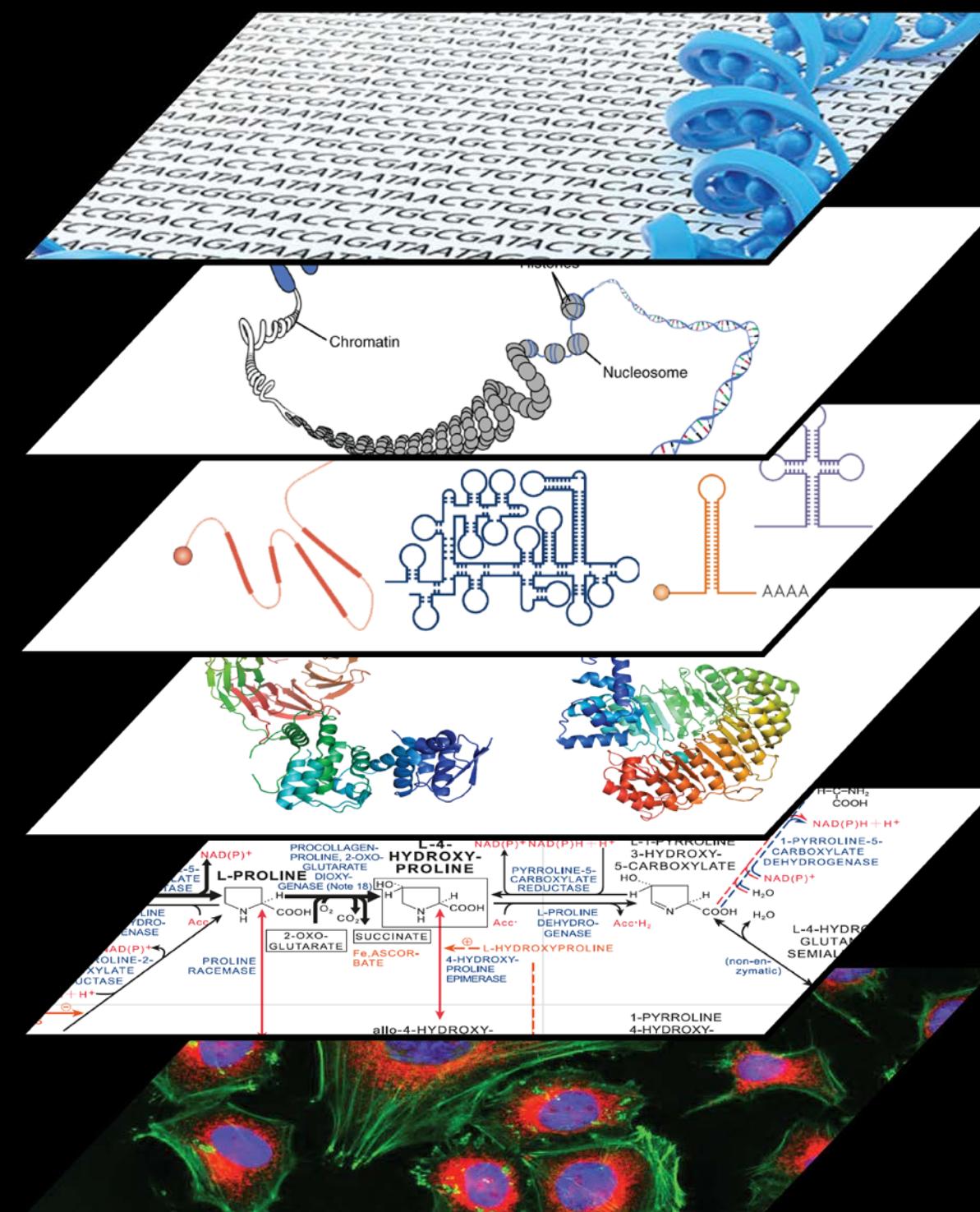
R. Pepperkok

H. Berthelot

J. Zukowska

D. Ordonez

# SINGLE-CELL MULTOMICs



*Perturbation*

Perturb-seq

*Genome*



*Epigenome*



*Transcriptome*



TAP-seq

*Proteome*

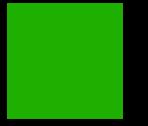


CITE-seq

*Metabolome*



*Phenotype*



ICS

*Spatial*





# THE FUTURE OF MEDICINE IS GLOBAL & PERSONALIZED

DIGITAL INNOVATIONS, BIG DATA & PRECISION EDITING  
ARE CHANGING THE WAY WE APPROACH HEALTHCARE

# ACKNOWLEDGEMENTS



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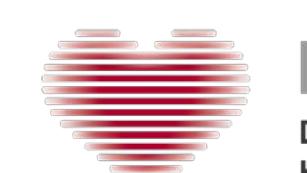
Wu Wei

Christoph Dieterich

EMBL Cores (*Animal,  
Protein, Cytometry, Genomics*)  
... and many more!



Bundesministerium  
für Bildung  
und Forschung



DZHK  
DEUTSCHES ZENTRUM FÜR  
HERZ-KREISLAUF-FORSCHUNG E.V.



# OPEN POSITIONS

