

BioQantSense

WORKSHOP

NIMOCHIP – a Lab-on-a-chip device for advanced diagnostics

Pavle R. Andjus

*Center for laser microscopy,
Faculty of Biology University of Belgrade
SERBIA*



PHOTONICA 2023, Belgrade, 31.08.2023.

Disclosures

- Signed co-authorship agreement for NIMOCHIP
- Signed NDA, PoC project ID 5360 (Innovation Fund RS)
- Board member of *dAlignostics Ltd*

General features of ALS

Primary characteristic:

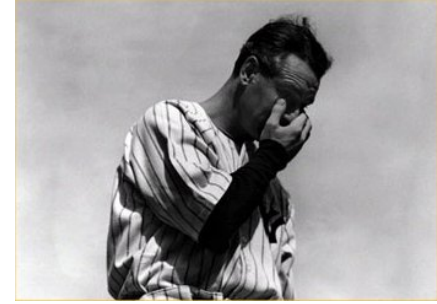
Selective dysfunction and death of neurons in the motor pathways of the *spinal cord*, *brain stem* and *motor cortex*

Symptoms: Generalized weakness, muscle atrophy and paralysis

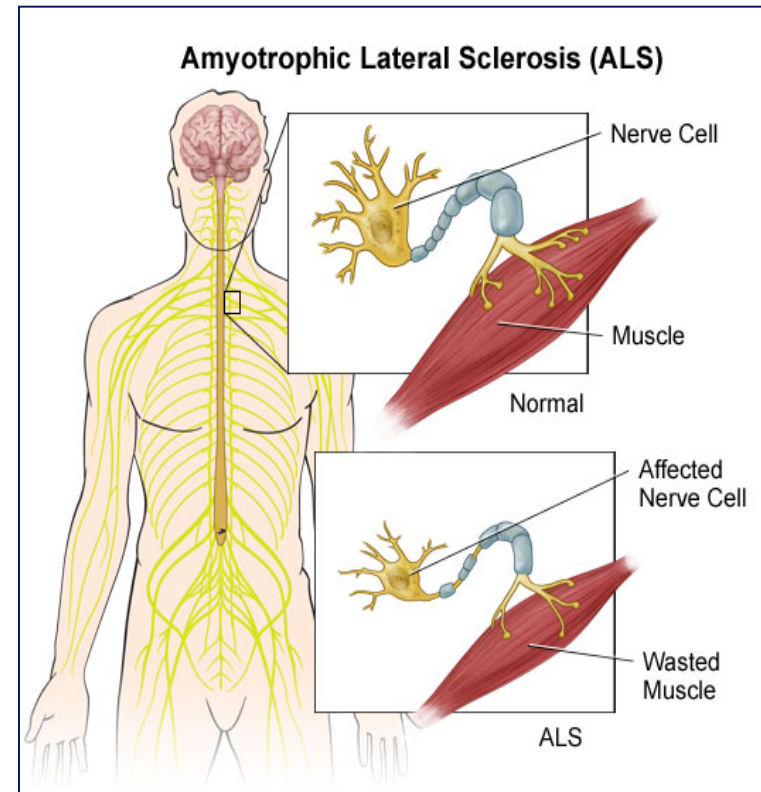
Cause of death – paralysis of respiratory muscles (1-5 years after 1st symptoms)

Majority of cases (90%) are without known genetic background (sporadic ALS), while only 10% has a known genetic background (familial ALS).

Uncurable.



**Lou Gehrig
(1903-1941)**



Sporadic ALS model – immune mechanism

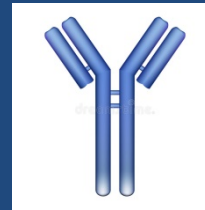
neurons in culture

Journal of Physiology (1997), 504.1, pp.103–112

Immunoglobulins from motoneurone disease patients enhance glutamate release from rat hippocampal neurones in culture

Pavle R. Andjus, Zorica Stevic-Marinkovic and Enrico Cherubini*

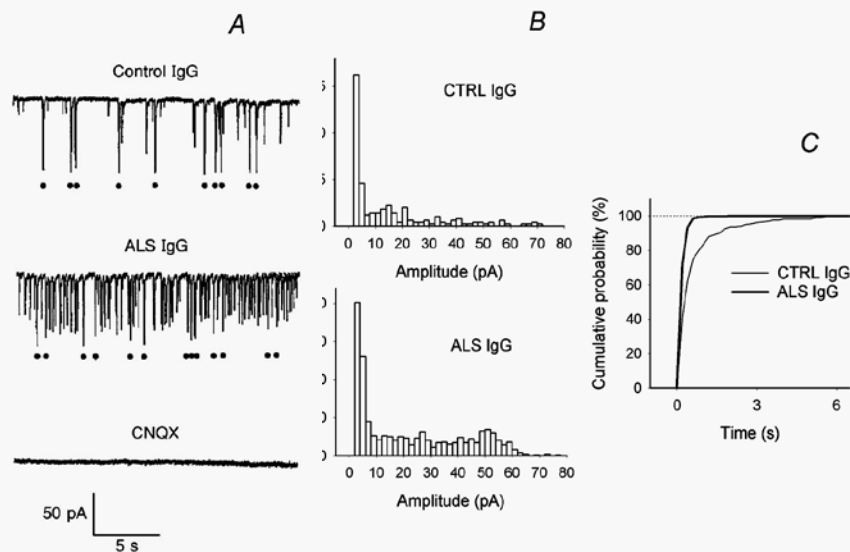
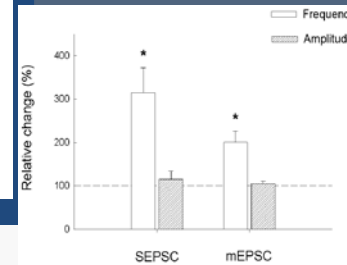
*Biophysics Sector and INFM Unit, International School for Advanced Studies (SISSA),
Via Beirut 2-4, 34014 Trieste, Italy*



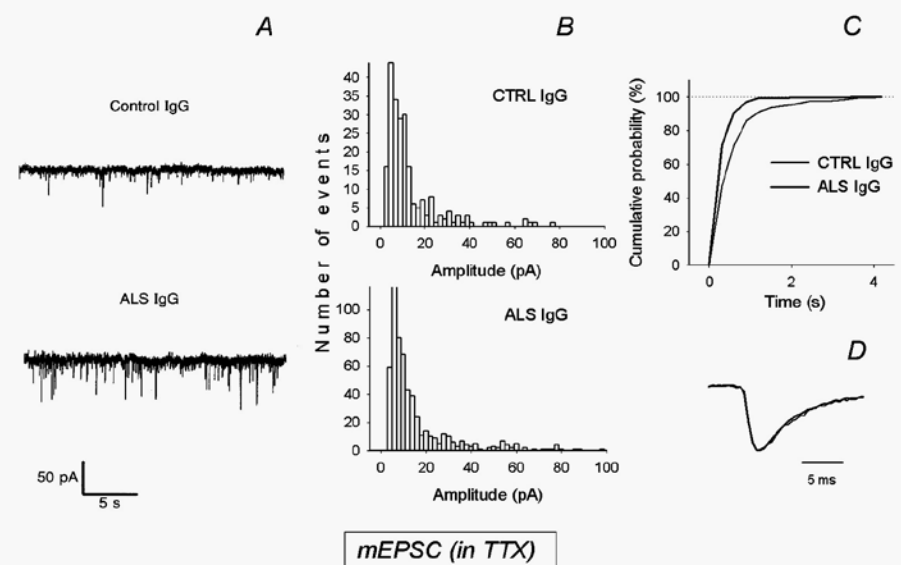
Enrico Cherubini



Zorica Stević

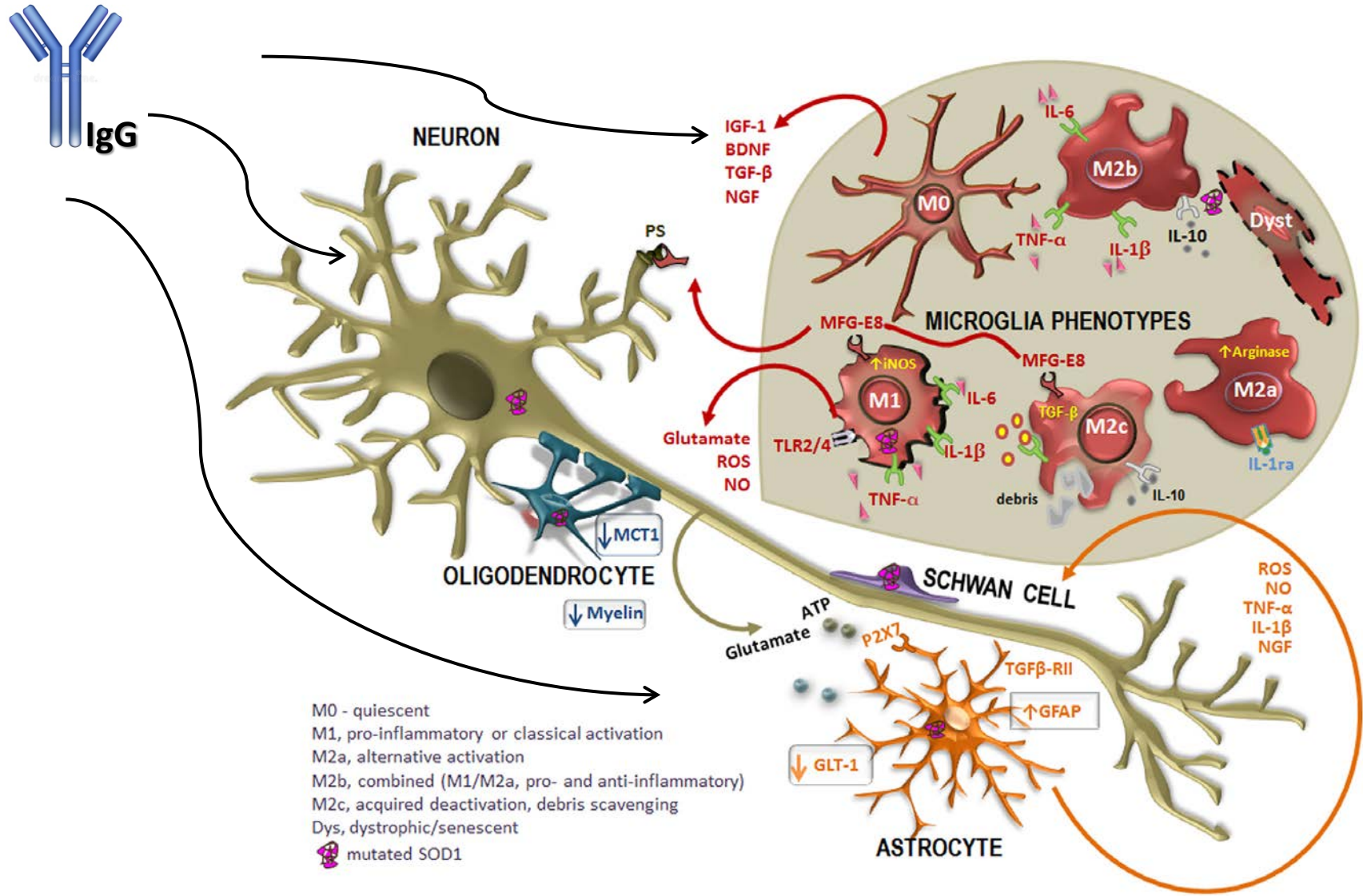


sEPSC



mEPSC (in TTX)

NON-CELL AUTONOMOUS PATHO-MECHANISM OF ALS



The effect of ALS IgGs on intracellular calcium concentration



Contents lists available at SciVerse ScienceDirect

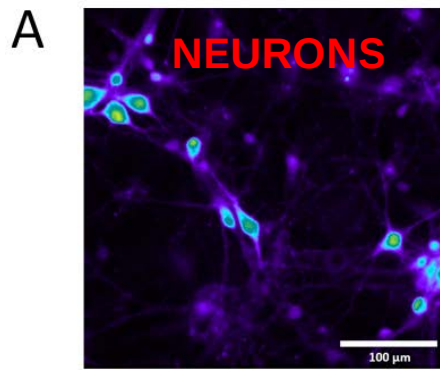
Cell Calcium

journal homepage: www.elsevier.com/locate/ceca

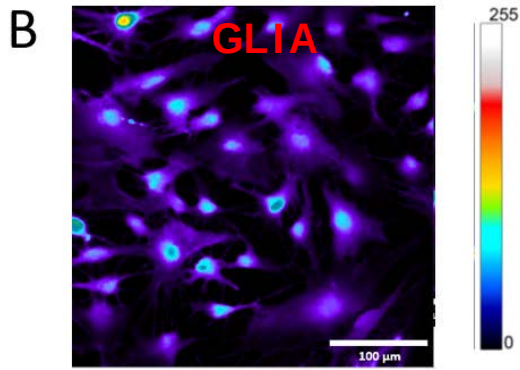


Immunoglobulins G from patients with sporadic amyotrophic lateral sclerosis affects cytosolic Ca^{2+} homeostasis in cultured rat astrocytes

Milena Milošević^{a,c,1}, Matjaž Stenovec^{a,b,1}, Marko Kreft^{a,b,d}, Vladimir Petrušić^e, Zorica Stević^f, Saša Trkov^{a,b}, Pavle R. Andjus^{c,**}, Robert Zorec^{a,b,*}

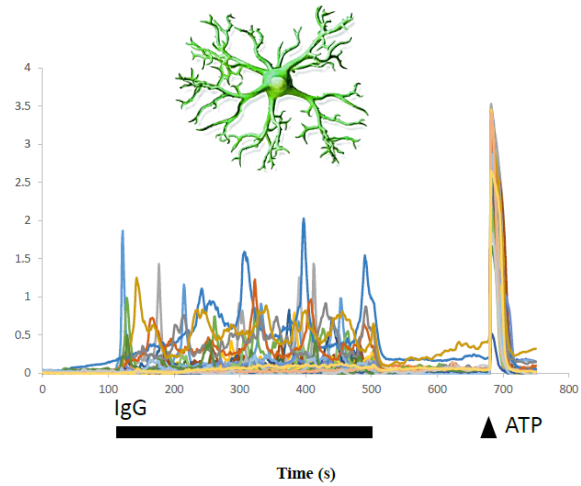
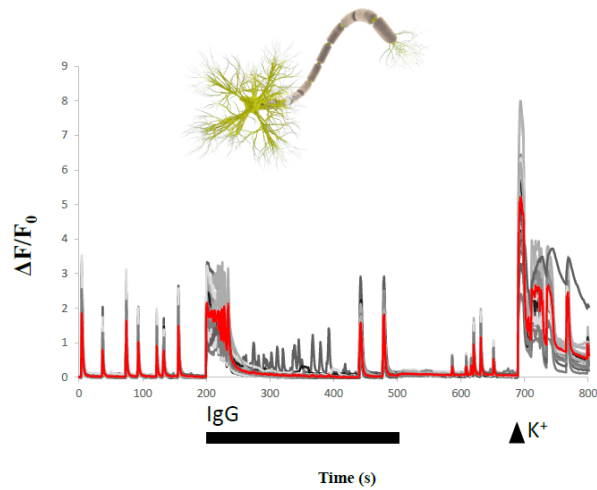


Hippocampal neurons

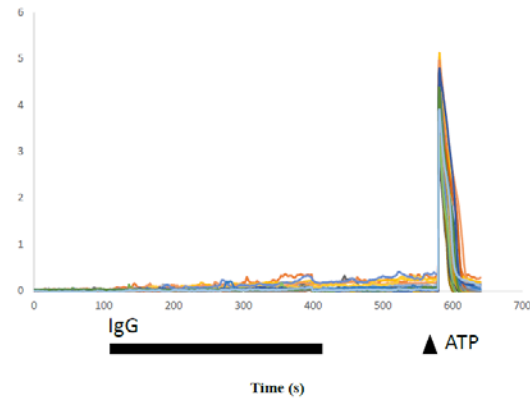
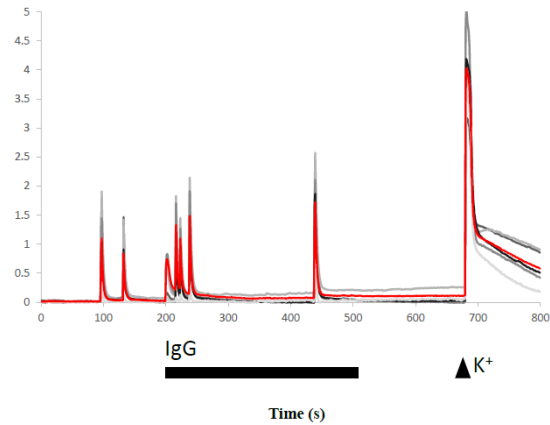


Cortical astrocytes

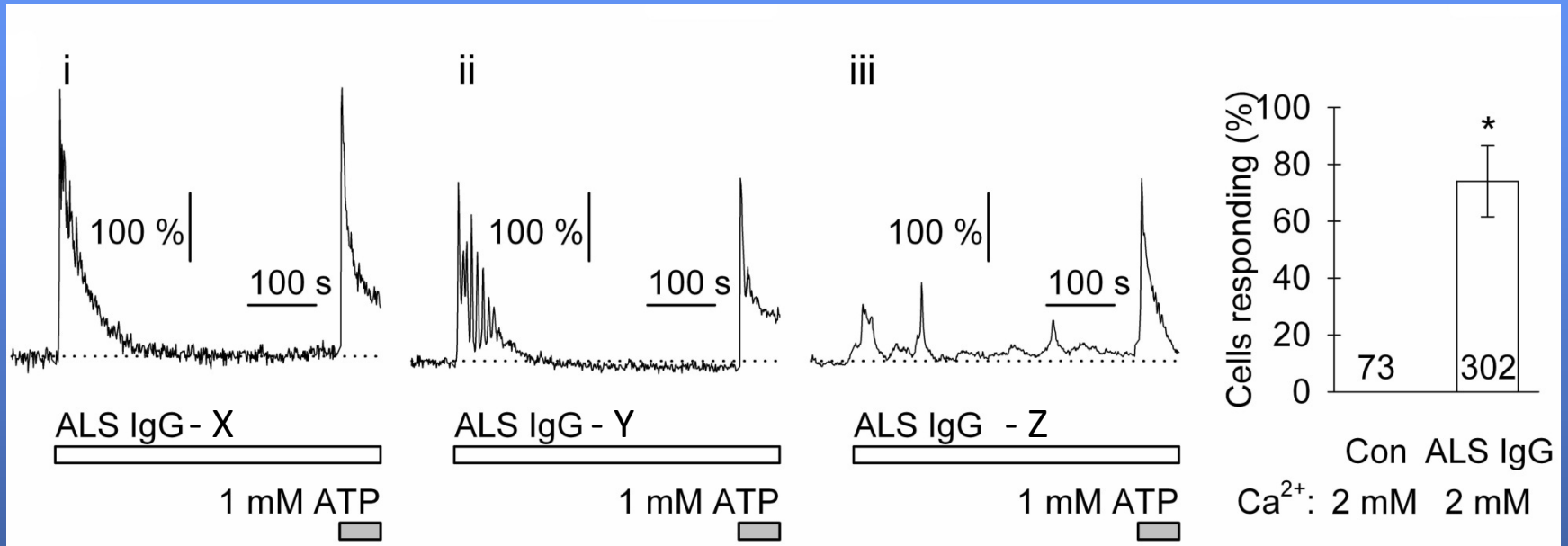
ALS IgG



Healthy
CTRL IgG



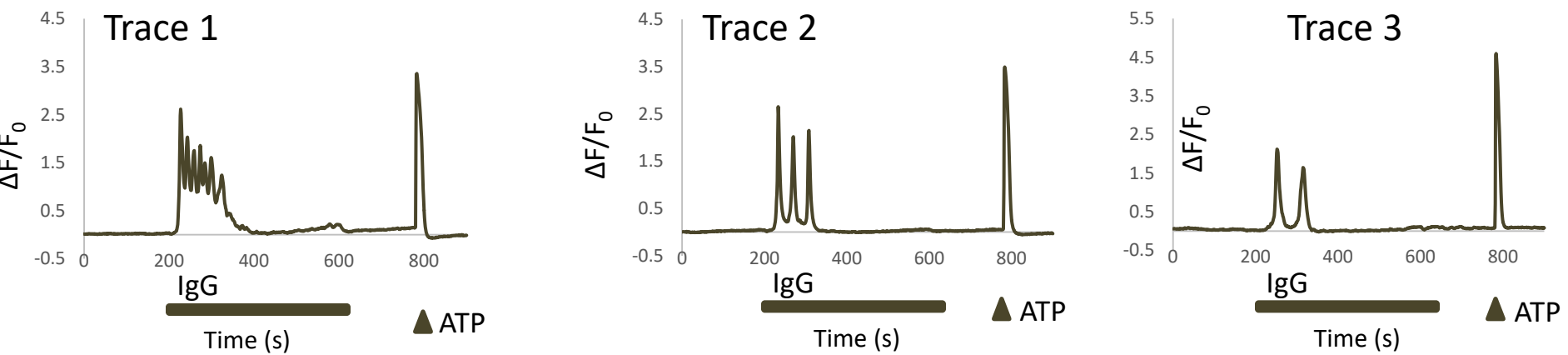
Diverse types of responses



Ca^{2+} -elevations:

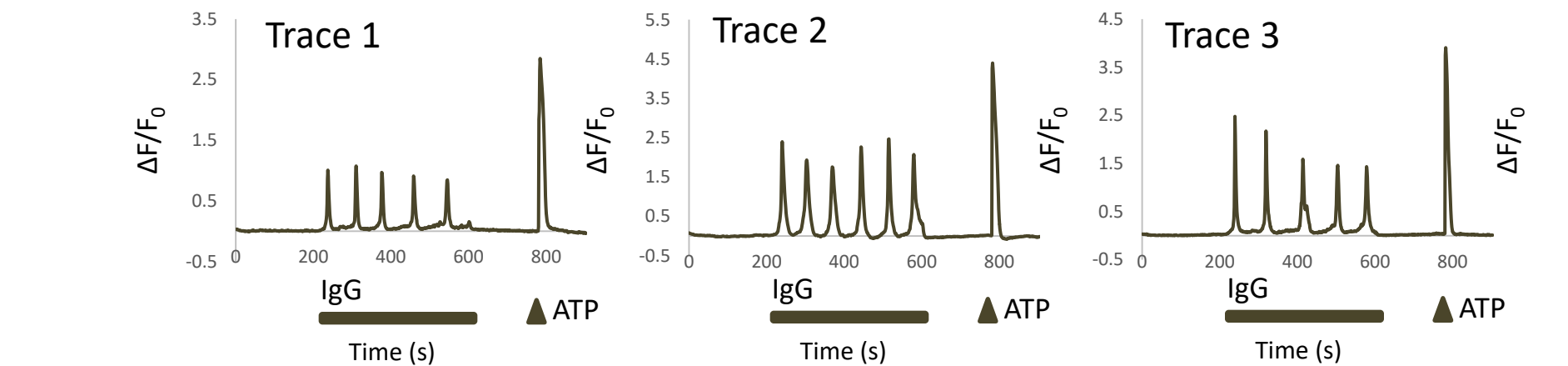
- single transients
- bursting transients
- long-lasting fluctuations

ALS IgG 1 Distinctive patterns in Ca signaling for different ALS IgGs in astrocytes



Dunja Bijelić

ALS IgG 2



Other physiological effects of ALS IgGs on the cellular level

 **frontiers**
in Immunology

ORIGINAL RESEARCH
published: 23 November 2017
doi: 10.3389/fimmu.2017.01619



Immunoglobulins G from Sera of Amyotrophic Lateral Sclerosis Patients Induce Oxidative Stress and Upregulation of Antioxidative System in BV-2 Microglial Cell Line

Milena Milošević^{1,4*}, Katarina Miličević^{1†}, Iva Božić², Irena Lavrnja², Ivana Stevanović³, Dunja Bijelić¹, Marija Dubaić¹, Irena Živković⁴, Zorica Stević⁵, Rashid Giniatullin^{6,7} and Pavle Andjus^{1*}

ACTA PHYSIOLOGICA

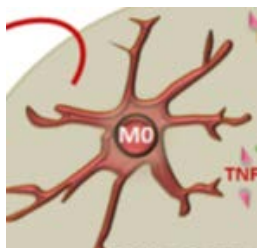
Acta Physiol 2011, 203, 457–471

Amyotrophic lateral sclerosis immunoglobulins G enhance the mobility of LysoTracker-labelled vesicles in cultured rat astrocytes

M. Stenovec,^{1,2*} M. Milošević,^{1,3*} V. Petrušić,⁴ M. Potokar,^{1,2} Z. Stević,⁵ M. Prebil,¹ M. Kreft,^{1,2} S. Trkov,^{1,2} P. R. Andjus³ and R. Zorec^{1,2}

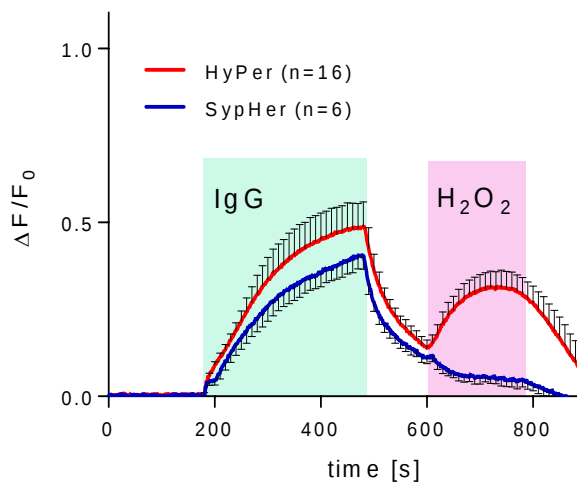


Katarina Milićević

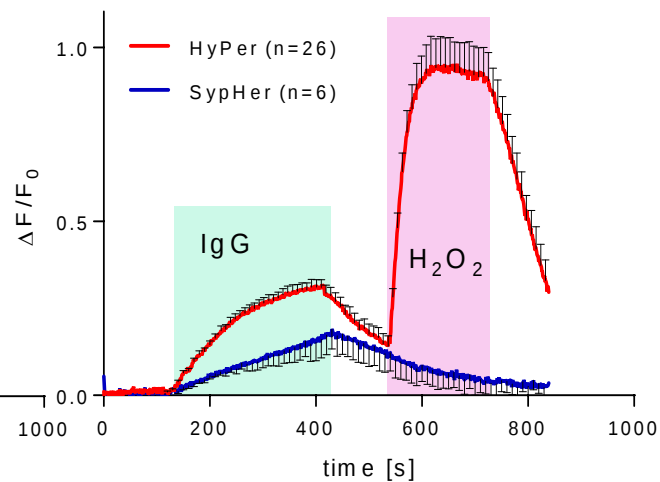


Microglia

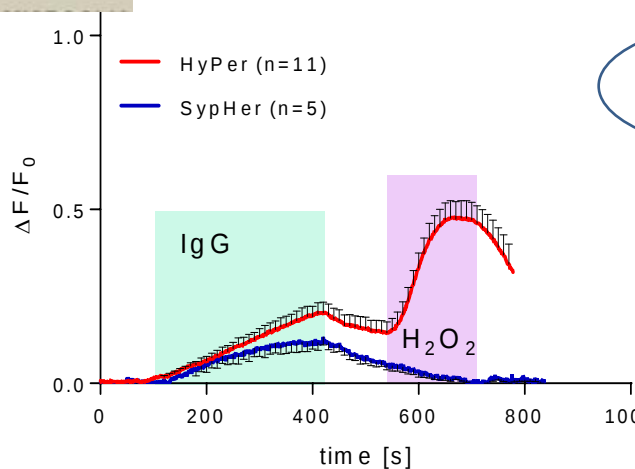
Patient #1 averaged data



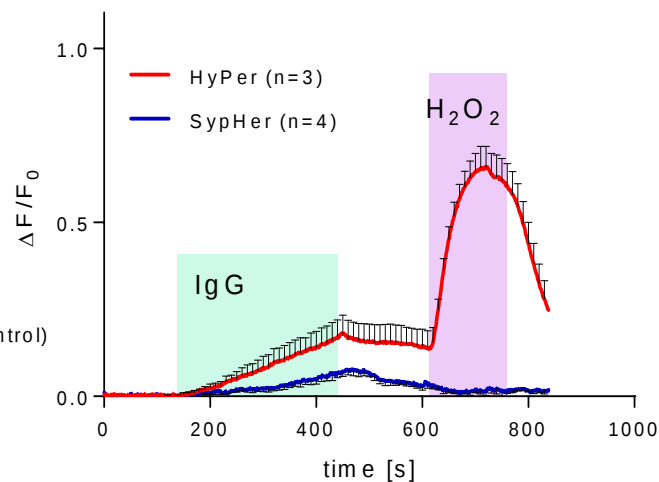
Patient #2 averaged data



Patient #3 averaged data



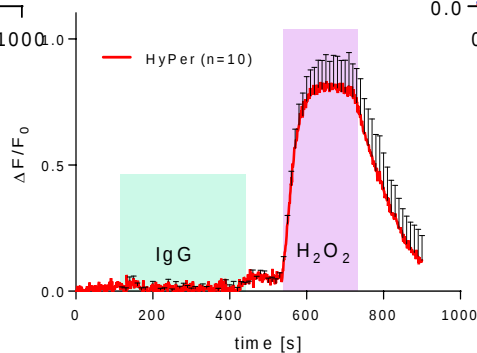
Patient #4 averaged data



ROS generation

Control

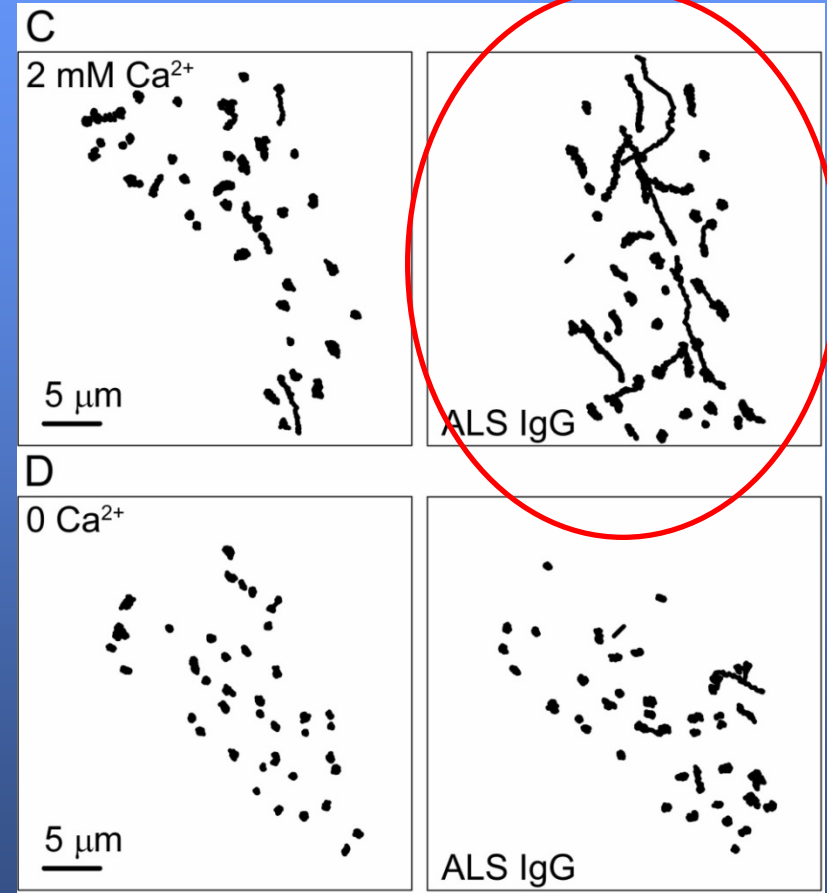
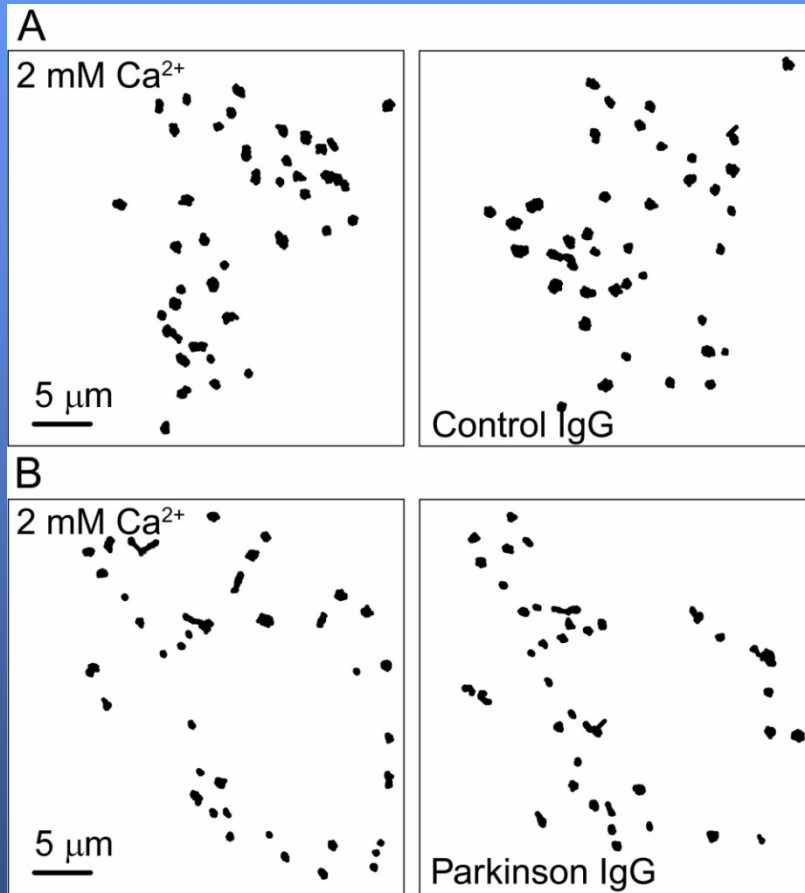
Patient #12 (disease control) averaged data



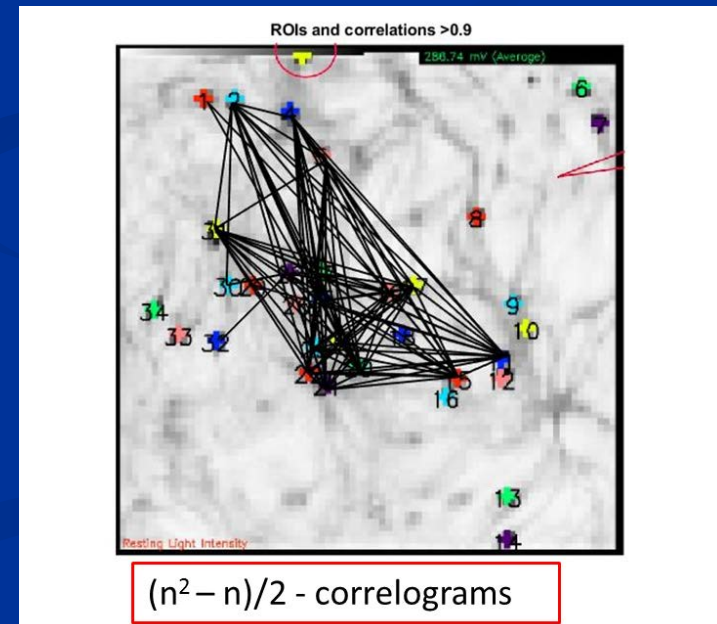
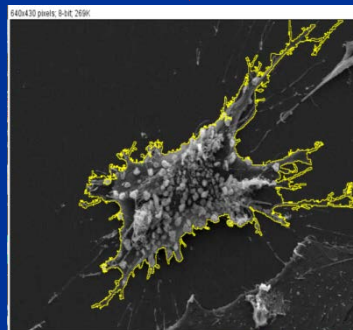
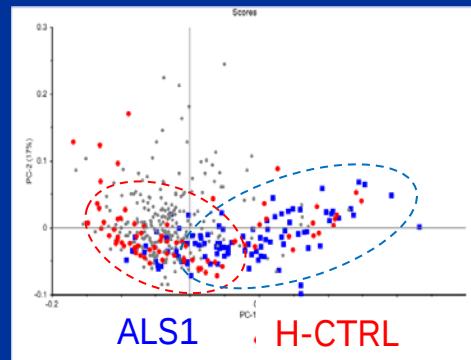
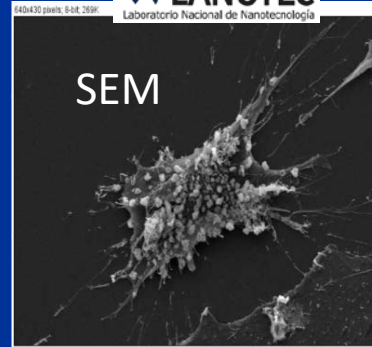
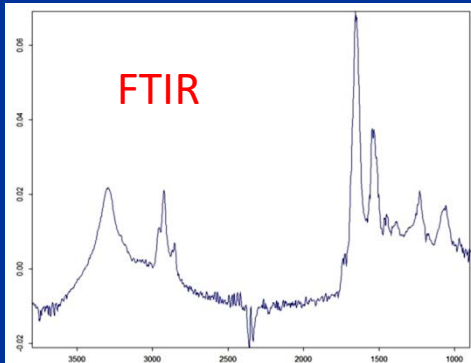
Intracellular vesicles tracking (astrocytes)



Milena
Milošević



ALS IgGs & cell biochemistry, surface texture, synchorinzed activity



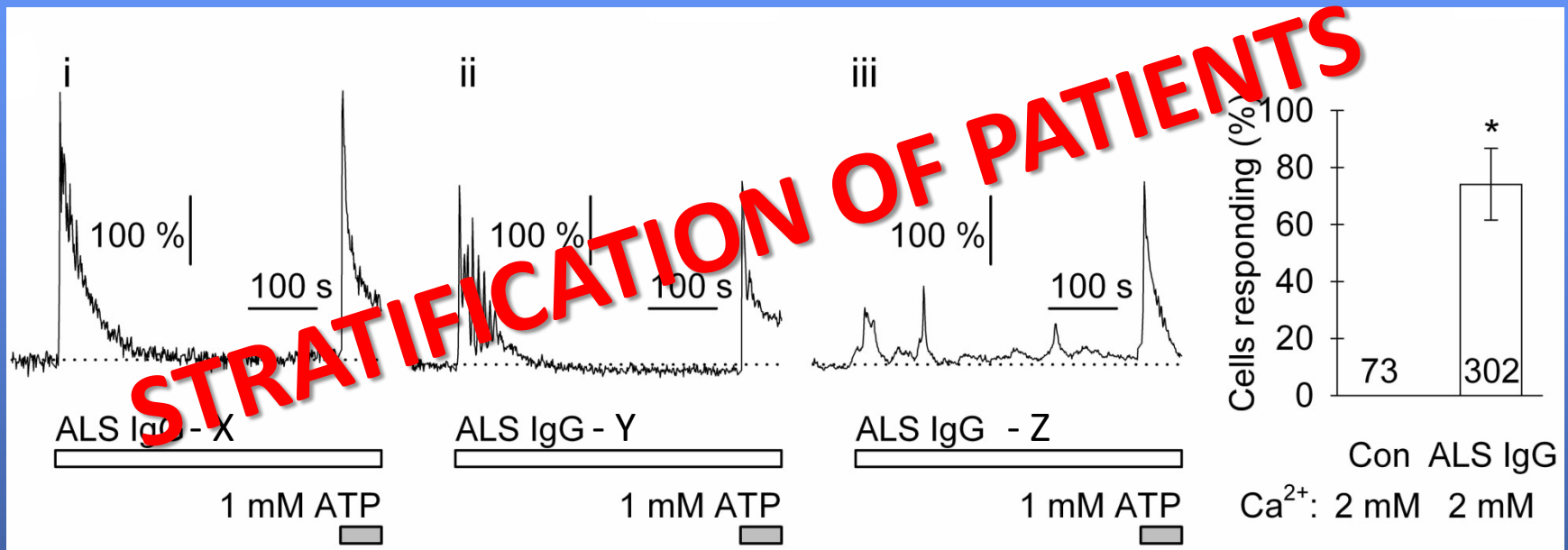
CAN WE BUILD A DEVICE ?

Requirements

- Early diagnosis
- **Use multiple markers**
- Stratification of patients
- Non-invasive
- Precise



Diverse types of responses

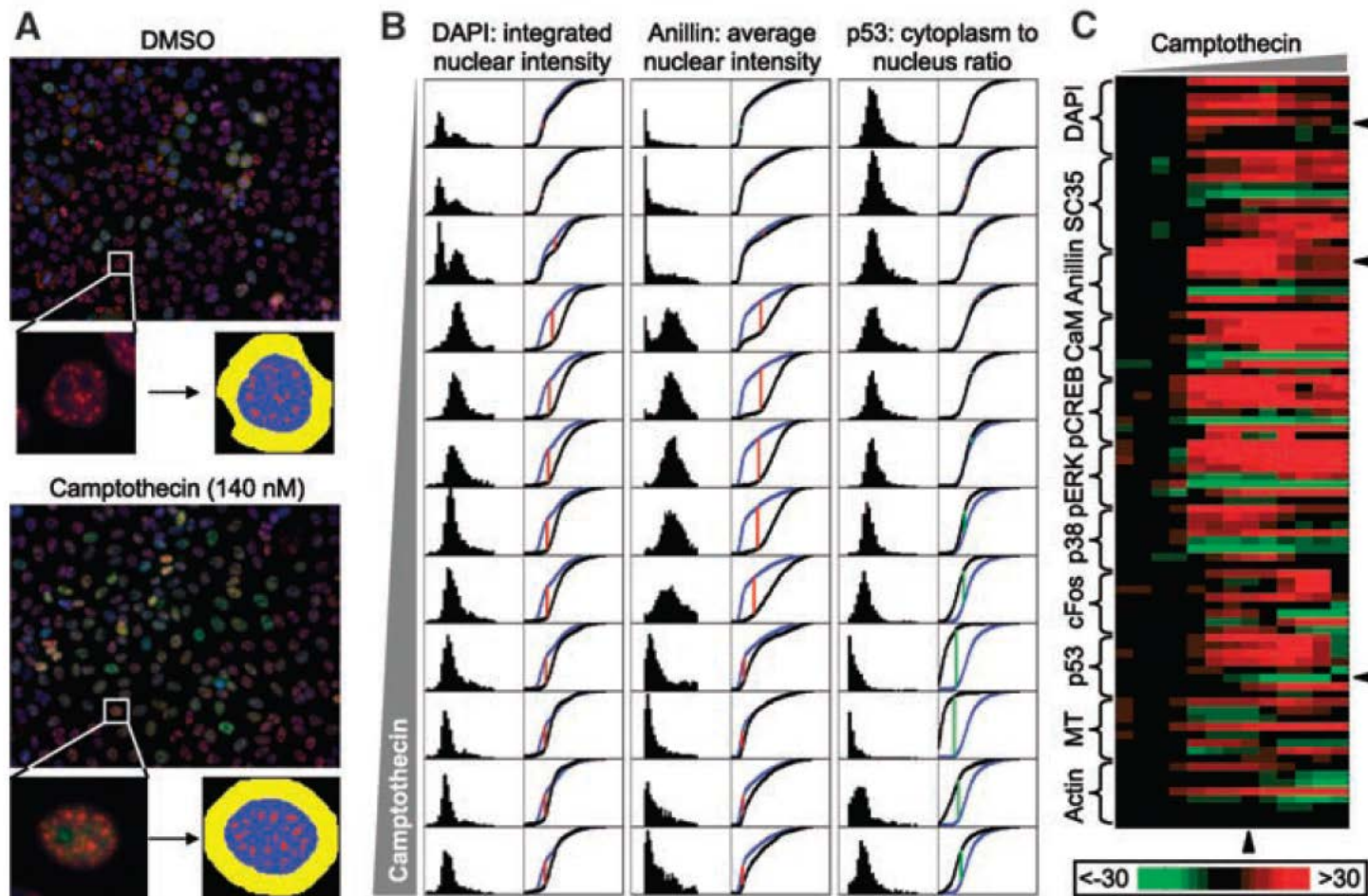


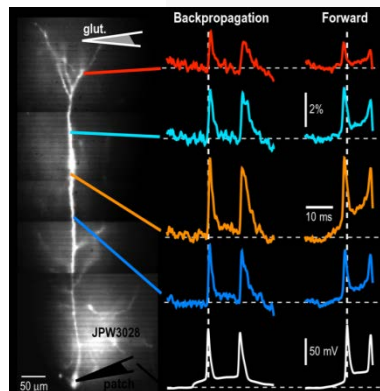
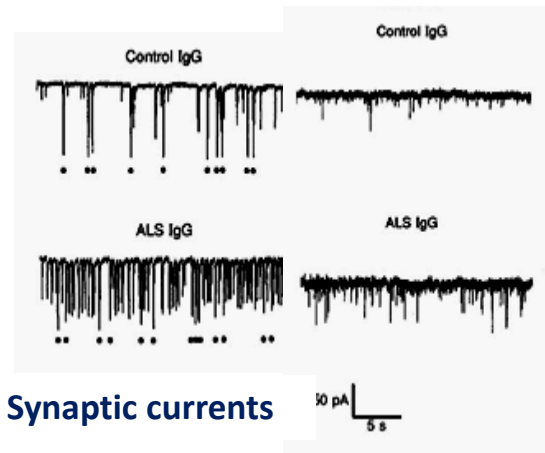
Ca²⁺ -elevations:

- single transients
- bursting transients
- long-lasting fluctuations

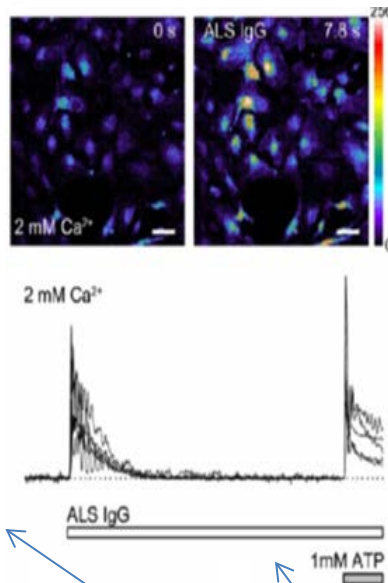
Multidimensional Drug Profiling By Automated Microscopy

Zachary E. Perlman,^{1,2*} Michael D. Slack,^{3*,†} Yan Feng,^{1*,‡}
Timothy J. Mitchison,^{1,2} Lani F. Wu,^{3§}
Steven J. Altschuler^{3§}

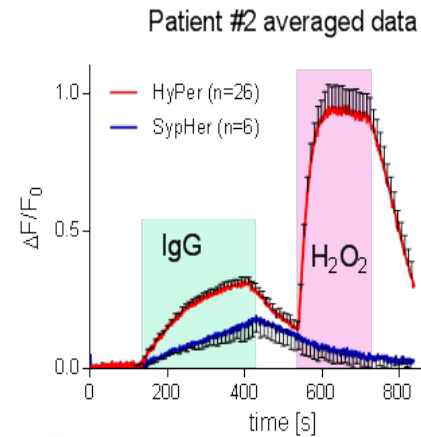




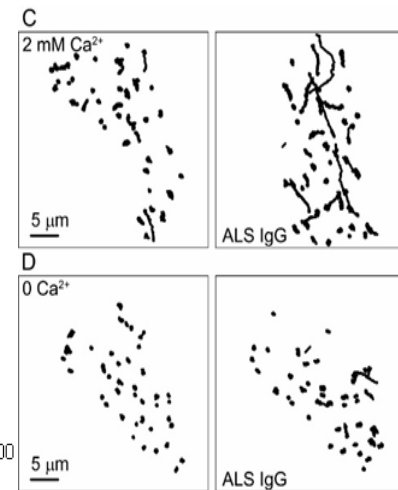
Calcium imaging



ROS and pH imaging

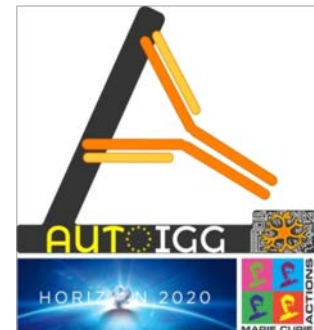
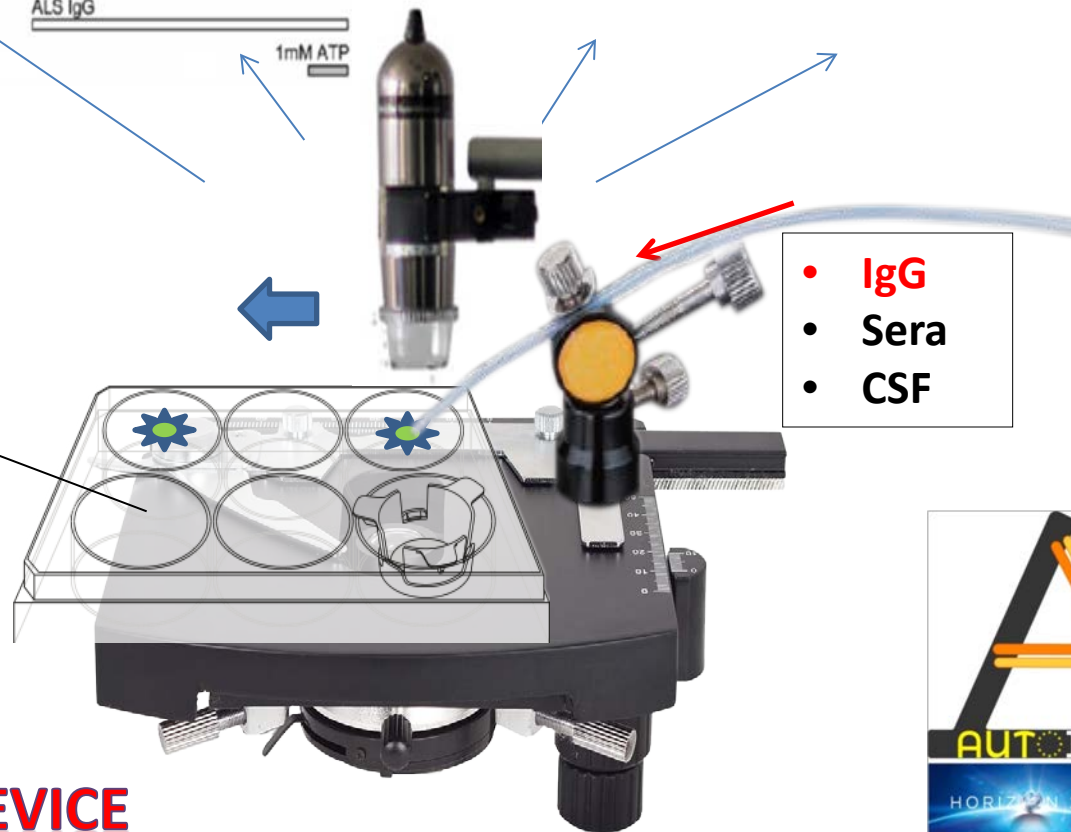


IC vesicle tracking



- Neurons
- Astrocytes
- Cell lines

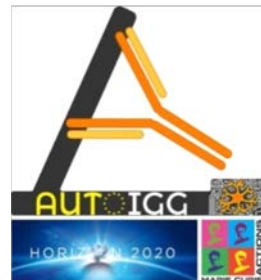
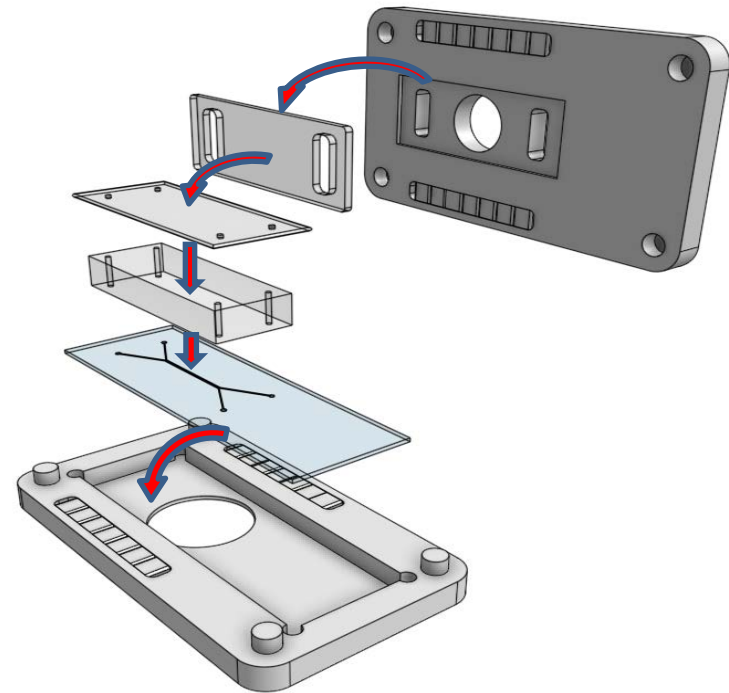
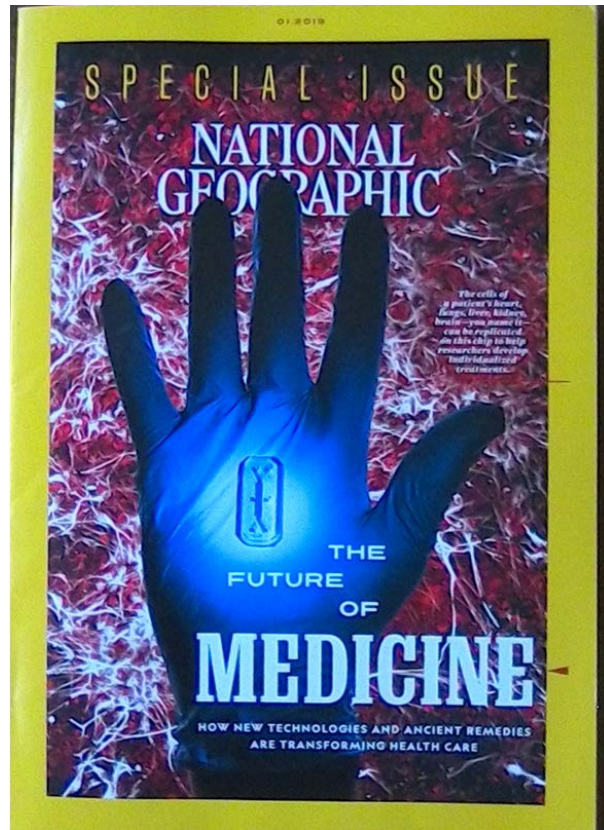
- IgG
- Sera
- CSF



INITIAL IDEA FOR THE DEVICE

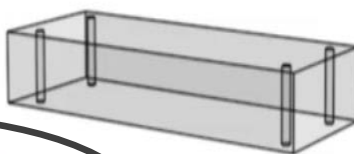
SOLUTION

Microfluidic chip – NIMOCHIP (NeuroIMmunOCHIP)

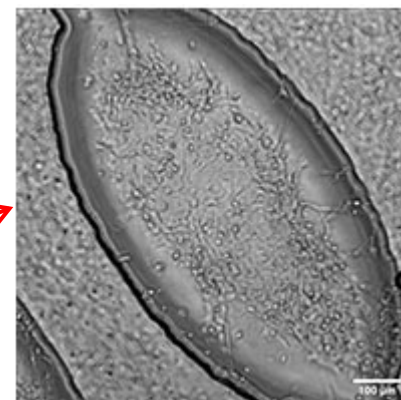
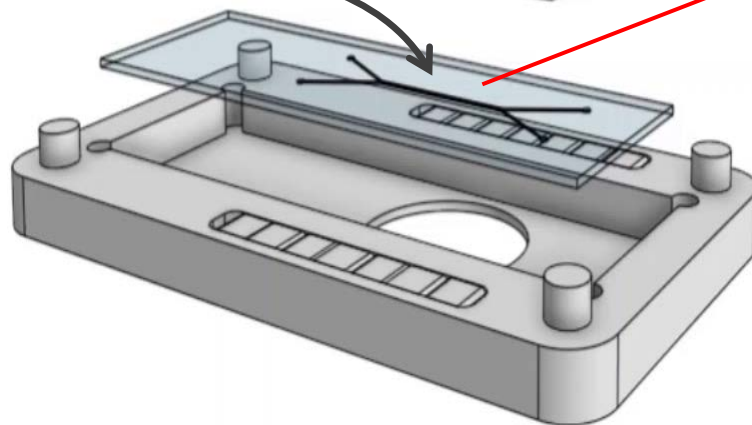


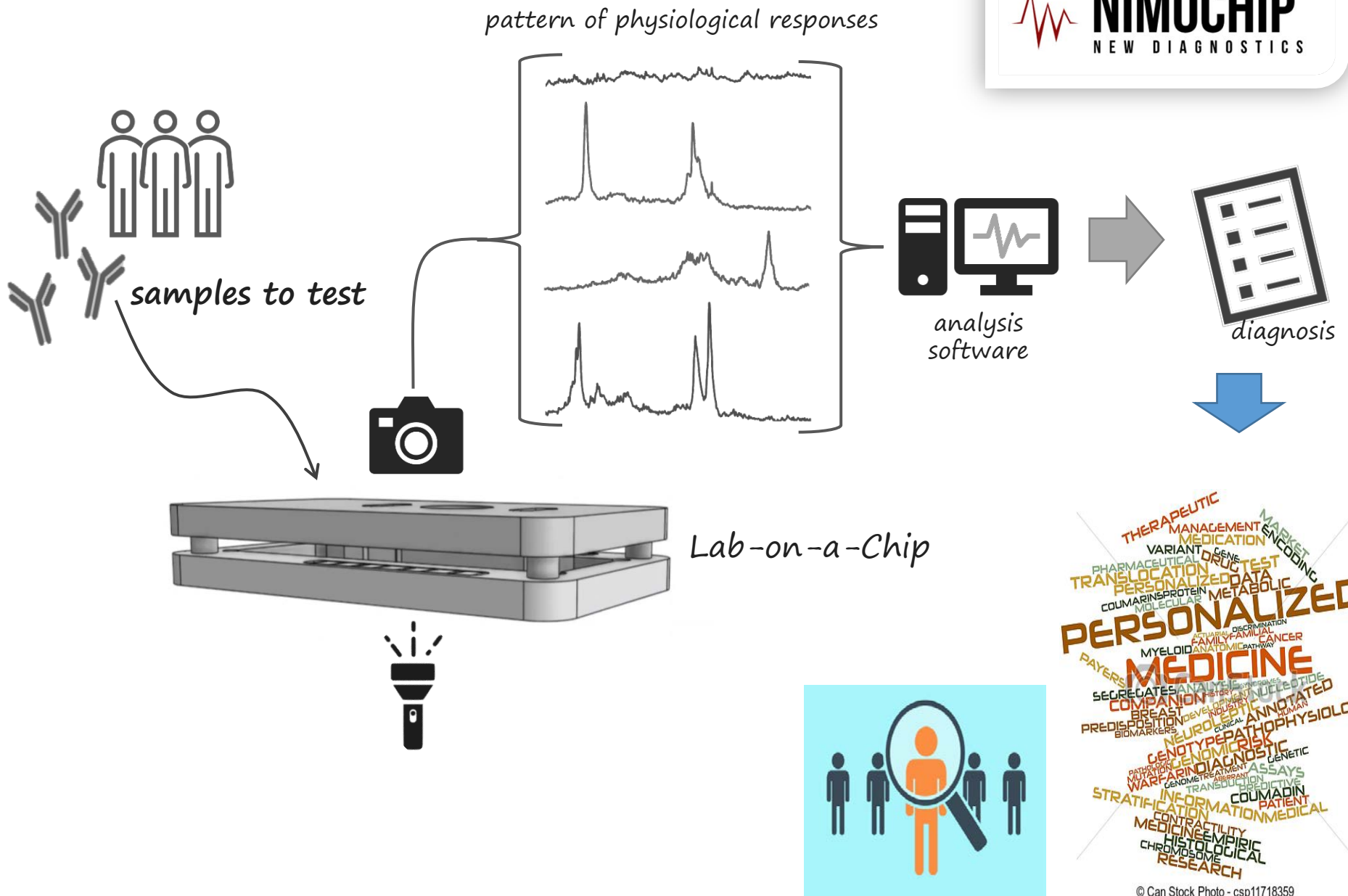


MAINFRAME ASSEMBLY



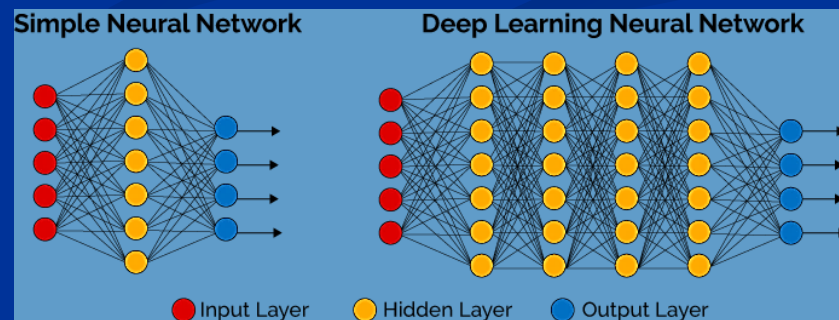
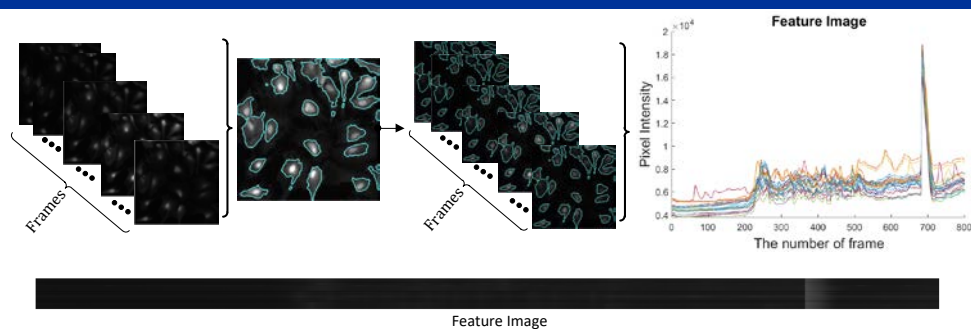
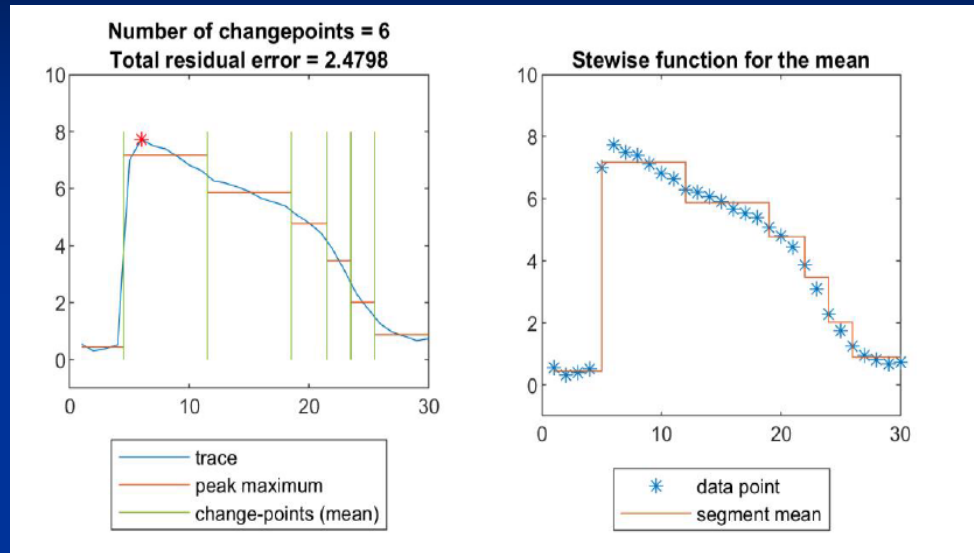
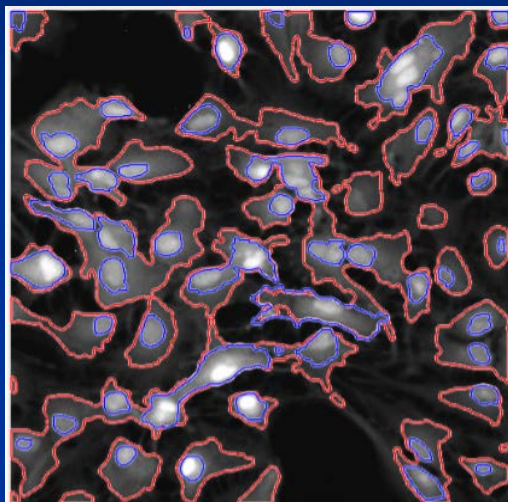
healthy
cells







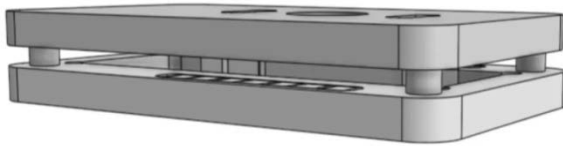
AUTOMATED TRACE ANALYSIS (Machine Learning)



Gizem Dursun, Ufuk Ozkaya, Abdulkarim Capar

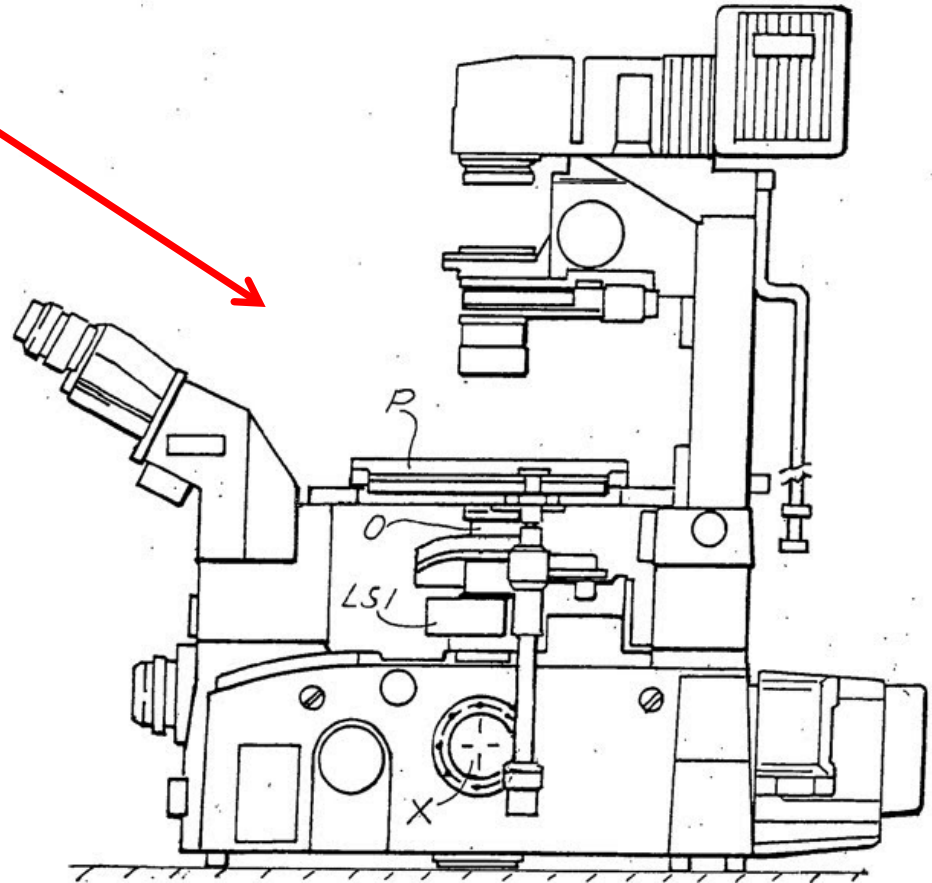
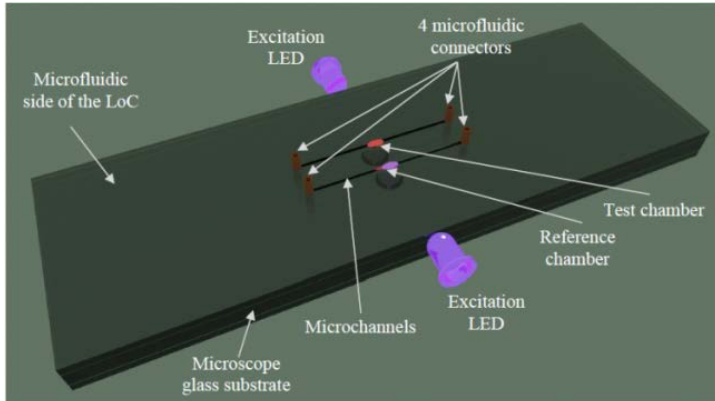
Andrej Korenić, Dunja Bijelić

Application



Lab frame

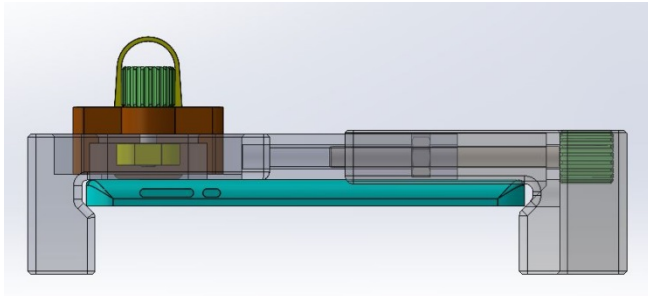
Standalone – integrated
optics-on-a-chip



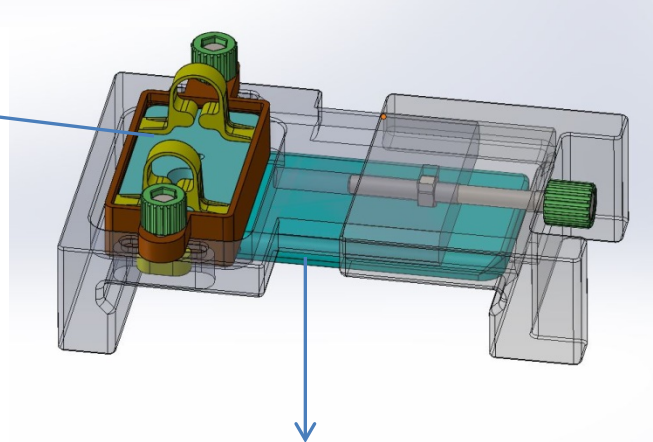
Application: standalone with mobile phone (camera) holder



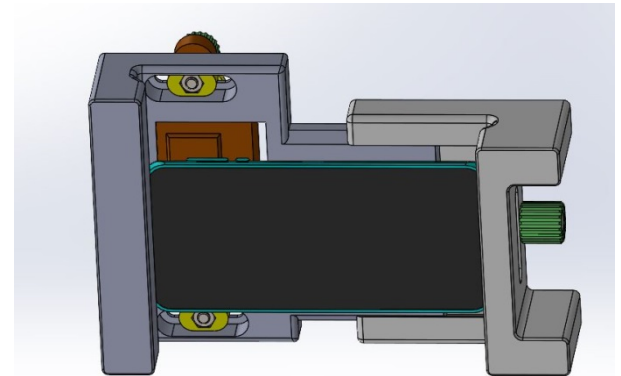
Dejan Pantelić

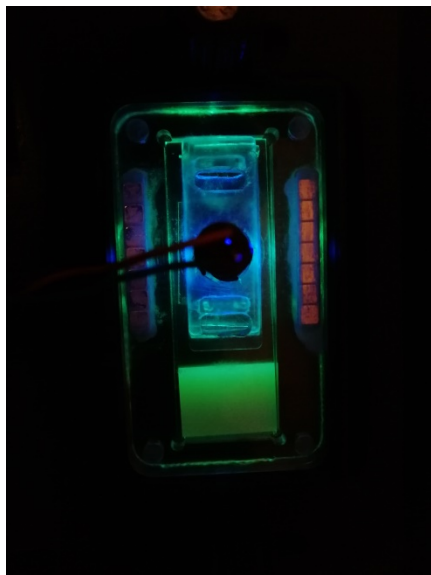
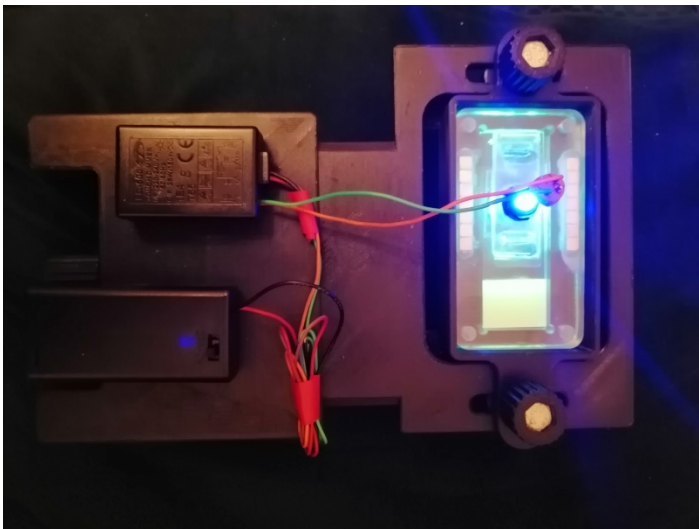
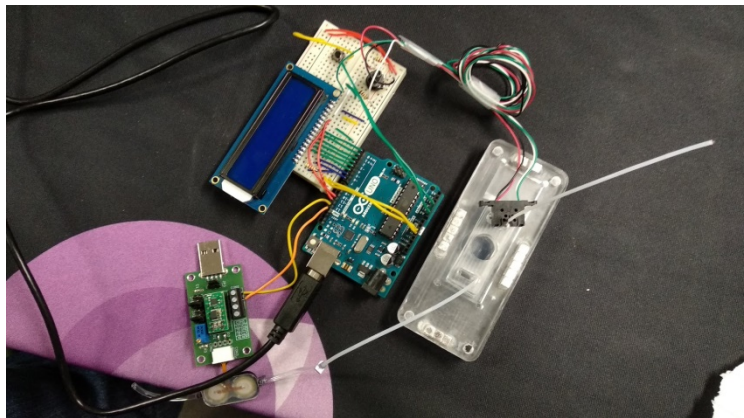
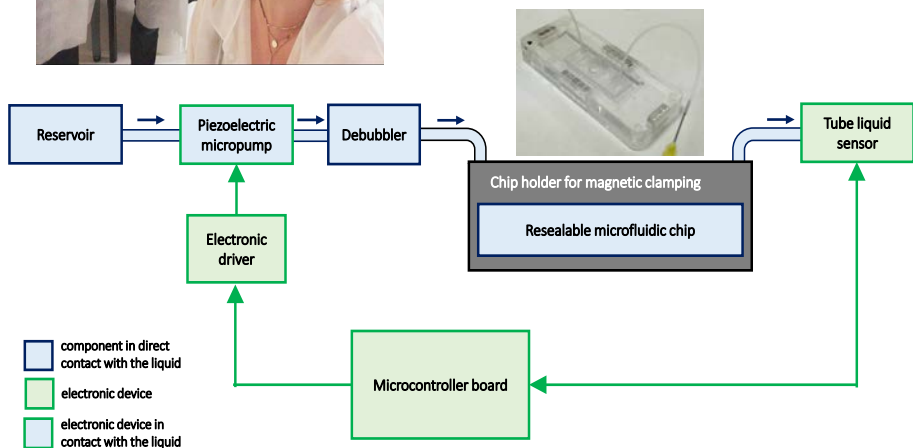


NIMOCHIP



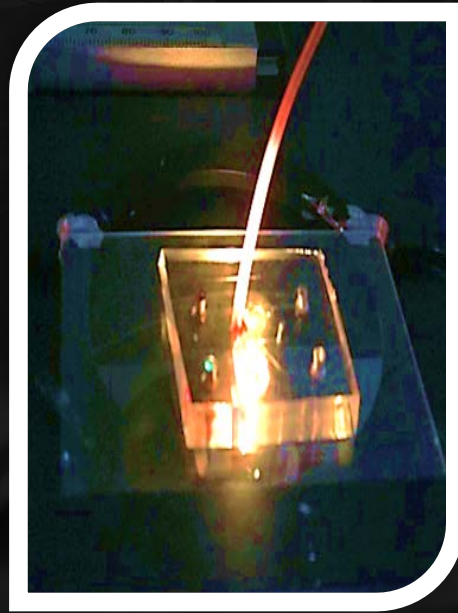
Mobile phone

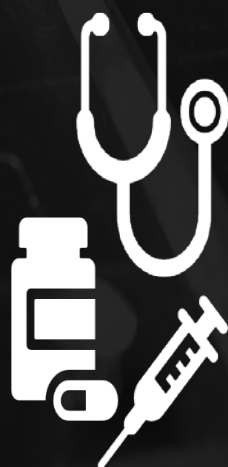


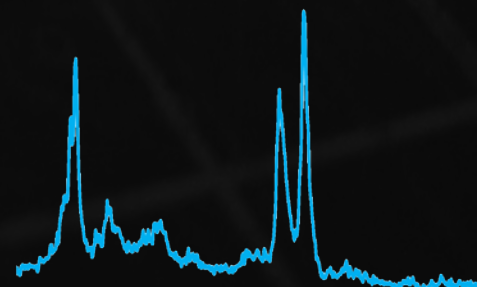
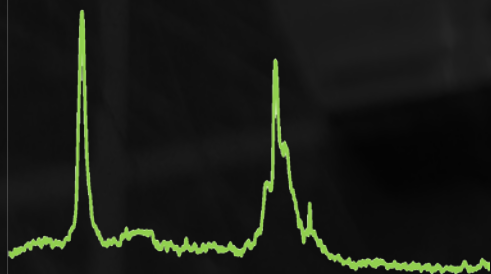
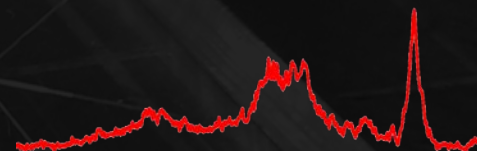
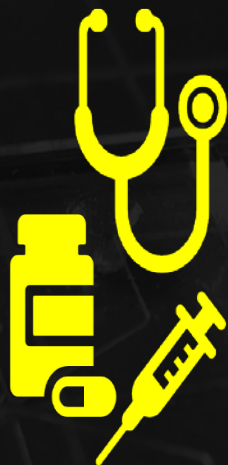


BENEFIT FOR PATIENTS

Personalized approach







PATIENT STRATIFICATION → BETTER THERAPY

Competitions and Accelerators



Funded by the
European Union



Innovation
FORUM

EIT Jumpstarter Online Pitch Day

Online event | Zoom platform | 13 June 2022 | All times are in CET.



Released on INTERNATIONAL TECHNOLOGY TRADE FAIR
ON ZGC FORUM 2022

03 SCI-Pavle Andjus

06-VEP/SEP-Erick-Past...

OBS - Jakob Gajšek

OBS-Aleksajs-Gromovs

ENT-Aija-Hermans-Sa...

ENT-MATEJ-PERETIN

OBS - Jakob Gaj...

01 Kristaps Jaudzems

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07 Josif Josifovski

08 Matijs Babris

09 Zoran Pučko

10 Tarik Selimovic

ARTIFICIAL SPIDER SILK: THE FUTURE BIOMATERIAL

NEXT GENERATION BIOPESTICIDES

NIMOCHIP: NEW DIAGNOSTICS

BIO-BASED VANILLIN FROM WOOD

MICROALGAE FOR FUTURE BIOECONOMY

ADDITIVE MANUFACTURING OF COMPOSITE MATERIALS

BIO.STAB: BIOPOLYMER STABILIZATION FOR A SAFE AND GREEN ENVIRONMENT

ACOUSTIC FURNITURE: ACOUSTICALLY ENGINEERED MODULAR PANELING SYSTEM FOR QUIETER WORKING ENVIRONMENTS

WATCHBUILT: INNOVATION FOR AUTOMATIC CONSTRUCTION PROGRESS MONITORING

TRS.INK: A NOVEL PLATFORM FOR ONLINE SUPPORT

A20TH IGNITION EVENT

NOV 11TH & 12TH 2022

REACTOR

LIAA

DEEP TECH ATELIER

altum

EIT

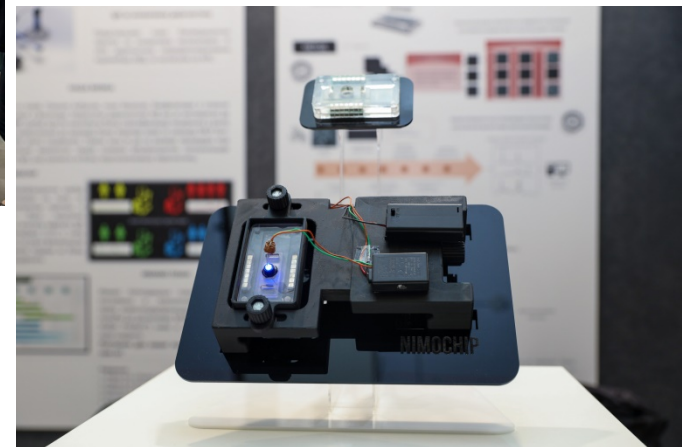
JUMPSTARTER

Funded by the European Union



65th International Technics Fair

Belgrade (May 16-19, 2023)



dAlignostics Ltd



Get in touch

contact@dalignostics.info

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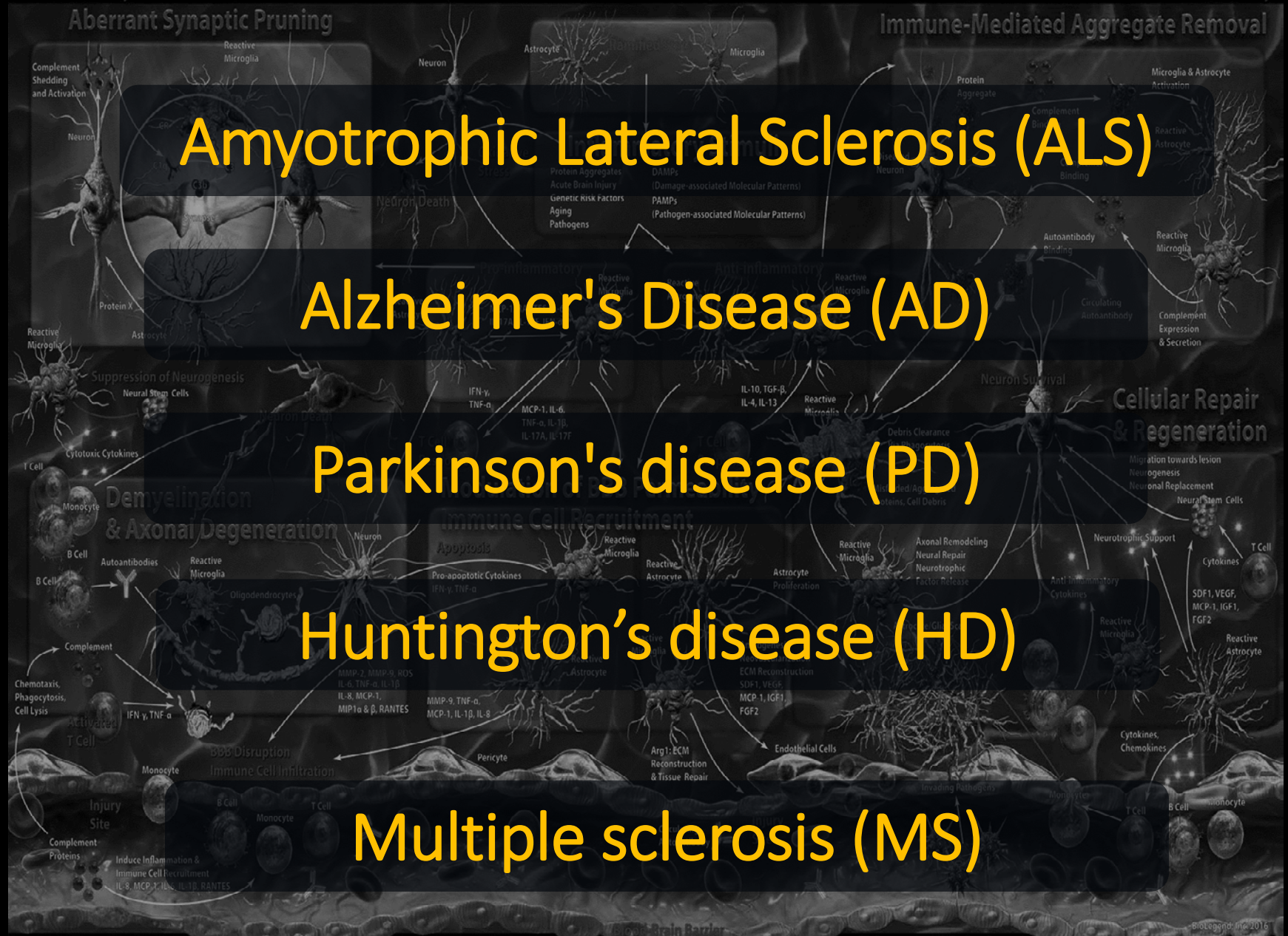
[Research partners](#)

[Contact](#)

Neurological disorders diagnostics powered by AI technology

Our inventive methodology is intended to diagnose neurological disorders, such as Amyotrophic Lateral Sclerosis (ALS), Parkinson's disease, Alzheimer's disease and Huntington's disease using specially designed apparatus and artificial intelligence powered data analysis.

Multiple sclerosis (MS)





Tanja Dučić



Wim van Drongelen



Reinaldo Pereira
Srajan Antić
Yendri Corales



Abdulkerim Capar

Enrico Cherubini Zorica Stević



REPUBLIC OF SERBIA
INNOVATION
FUND



- Milena Milošević
- Dunja Bijelić
- Katarina Milićević
- Andrej Korenić
- Lidija Radenović
- **Željko Janićijević**
- **Aleksa Marković**
- **Dejan Pantelić**

