OPTICA
Advancing Optics and Photonics Worldwide
Formerly OSA

Molecular Probes and Nanobio-Optics Technical Group

Molecular Understanding of Electromagnetic Field-Biomatter Interaction

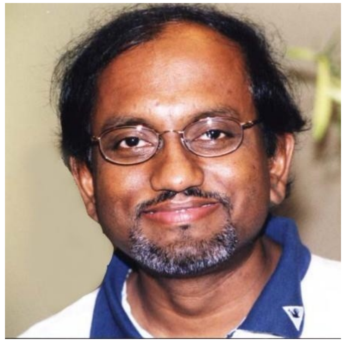
Michal Cifra, Institute of Photonics and Electronics of the Czech Academy of Sciences

29 October 2021

Technical Group Executive Committee

Chair
Girija Gaur, Ph.D.
University of California, Irvine

Vice Chair
Prof. Michel Meunier
Polytechnique Montreal, Canada
Co-founder Vega BioImaging

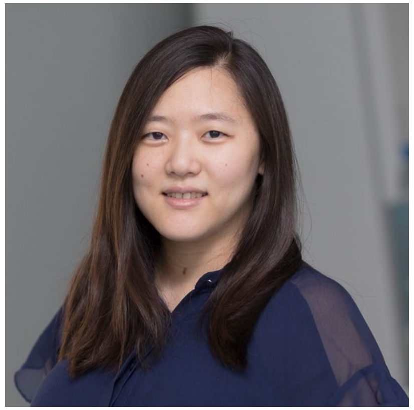


Conference Chair
Achyut Dutta, Ph.D.
CEO, Banpil Photonics

Global Events Officer
Shuren Hu, Ph.D.
Lidar System Architect, Aurora

Planning & Social Media Officer
Atrouli Chatterjee
University of California, Irvine

Technical Group Executive Committee



Events-Asia Pacific
Assistant Prof. Hyeon Jeong Lee
Zhejiang University, China

Events Officer
Assistant Prof. Lucien Weiss
Polytechnique Montreal, Canada

Events Officer
Assistant Prof. Aniruddha Ray
University of Toledo

About Our Technical Group

Our technical group focuses on using novel nano-probes such as QDs, fluorescent proteins, and plasmonic nanoparticles, to deepen our understanding of biological tissues. Applications span novel therapeutics, tissue imaging, and point-of-care diagnostics.

Our mission is to accelerate the development of the state-of-the-art technologies and connect the 1000+ members of our community through technical events, webinars, networking events, and social media.

Past & Upcoming Webinars:

- Medical Hyperspectral Imaging: Artificial Intelligence and Image-Guided Surgery by Prof. Baowei Fei in January 2021.
- Minimally instrumented SHERLOCK for CRISPR-based point-of-care diagnosis of SARS-Cov-2 and emerging variants, November 10, 2021, at 10 AM PDT.

Connect With Our Technical Group

Join our online community to stay up to date on our group's activities. You also can share your ideas for technical group events or let us know if you're interested in presenting your research.

Ways to connect with us:

- Our website at www.optica.org/BP
- On LinkedIn at www.linkedin.com/groups/12561256/
- On Facebook at www.facebook.com/groups/opticamolecularprobestg
- Email us at TGactivities@optica.org

Today's Speaker

Michal Cifra

Head of Bioelectrodynamics Team and Senior Scientist
Institute of Photonics and Electronics of the Czech Academy of Sciences

Dr. Michal Cifra (OSA & IEEE Senior member, chair of EMB chapter of the IEEE Czechoslovakia section, SPIE Life member) is head of Bioelectrodynamics research team and senior scientist at the Institute of Photonics and Electronics of the Czech Academy of Sciences. He obtained MSc. (2006) in Biomedical Engineering (University of Žilina, Slovakia) and PhD (2009) in Radioelectronics (Czech Technical University in Prague, Czechia). Apart from ~1 year biophotonics research experience from Germany (RWTH, Aachen / IIB, Neuss), he also gained experience with high-frequency bioelectronic interfaces (8 months, University of Chicago, USA). His research focus is on understanding and engineering electromagnetic field-biomatter interaction.

Molecular Understanding of Electromagnetic Field-Biomatter Interaction

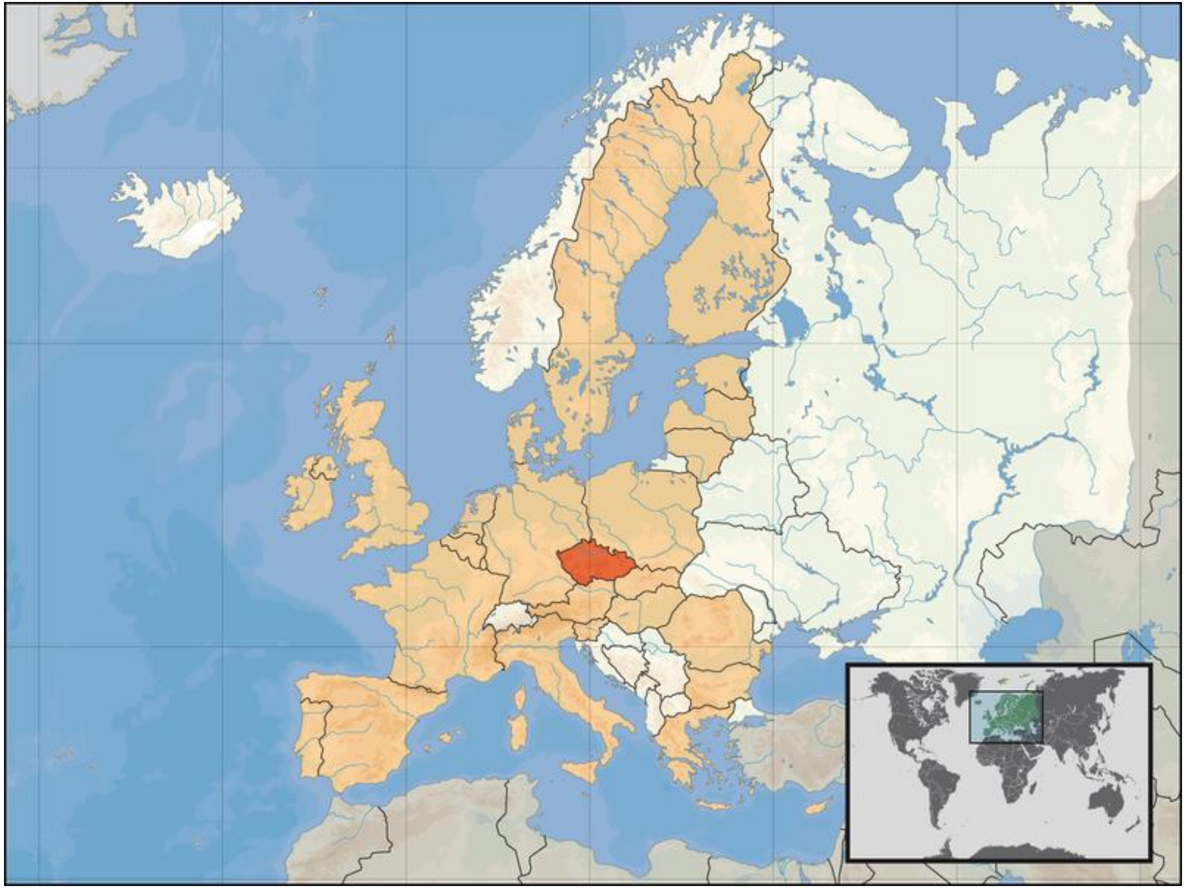
Michal Cifra

Institute of Photonics and Electronics of the Czech Academy of Sciences

Optica webinar - Molecular Probes and Nanobio-optics Technical Group

October 29, 2021

Czech Republic (Czechia)



Czech Academy of Sciences

- established 1890
- 54 research institutes
- 10 000 employees
- 2 500 PhD students
- ranks as 14th most productive governmental research organization in the world (*Nature index*)

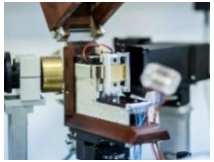
FUN FACT: CAS houses most intense laser in the world

eli | beamlines

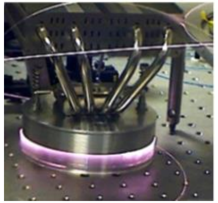
Institute of Photonics and Electronics of the Czech Academy of Sciences

RESEARCH UNITS

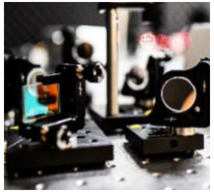
- Optical Biosensors



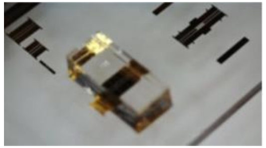
- Fiber Lasers and Non-linear Optics



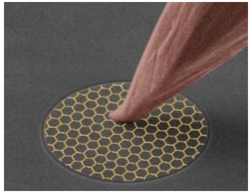
- Nano-optics



- **Bioelectrodynamics**

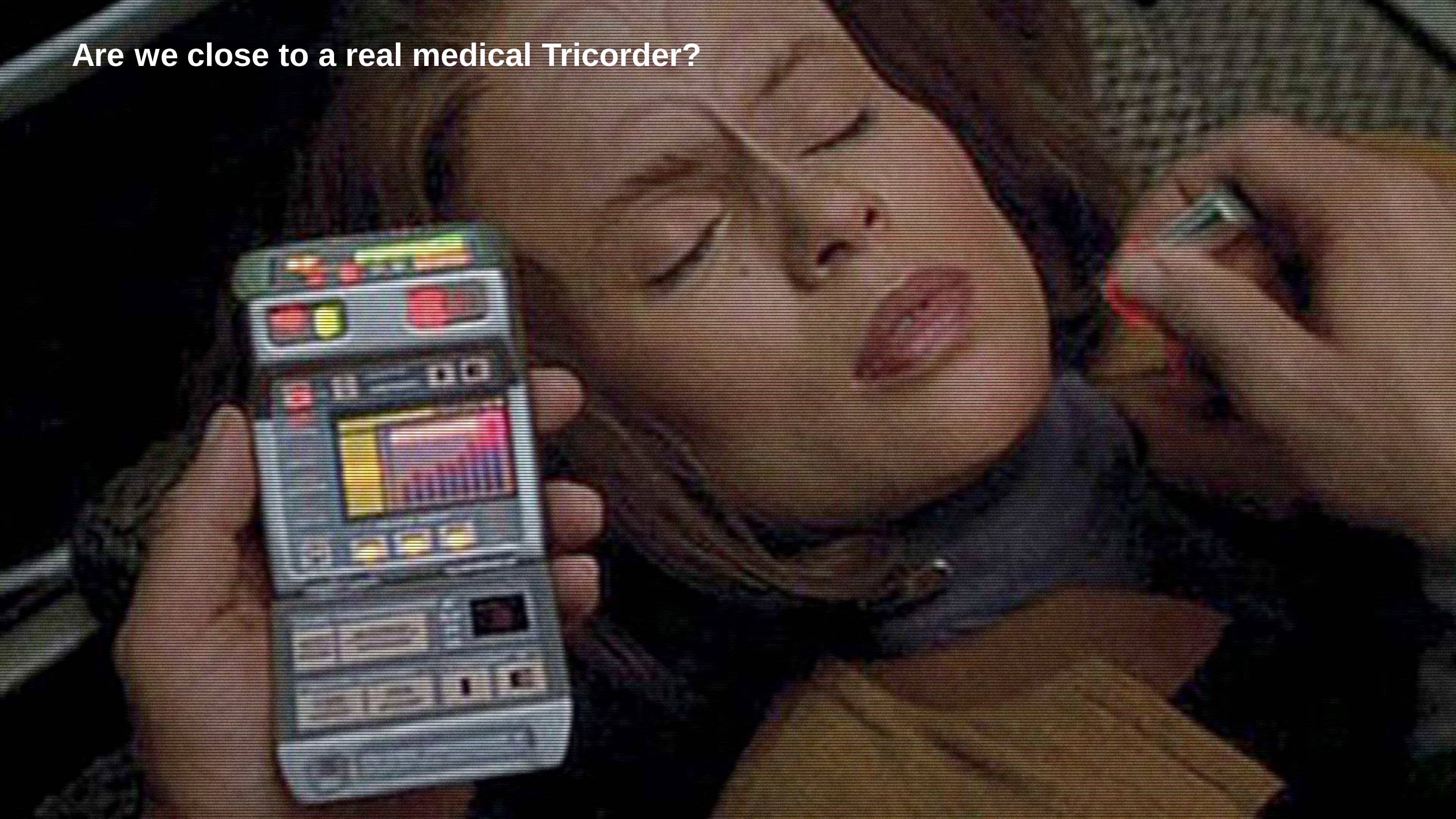


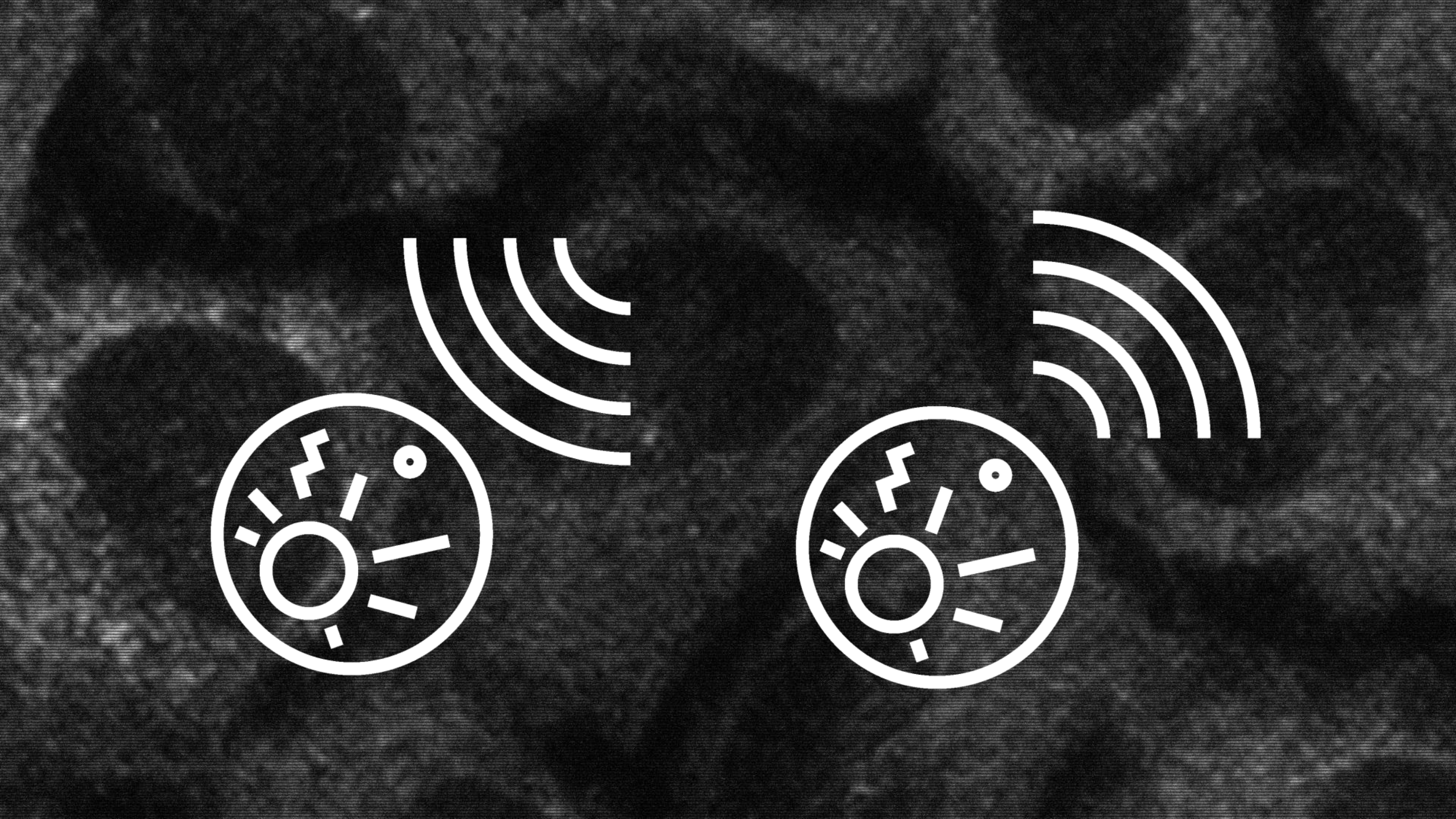
- Preparation and Characterization of Nanomaterials



- Laboratory of State Etalon of Time and Frequency

Are we close to a real medical Tricorder?





Mission

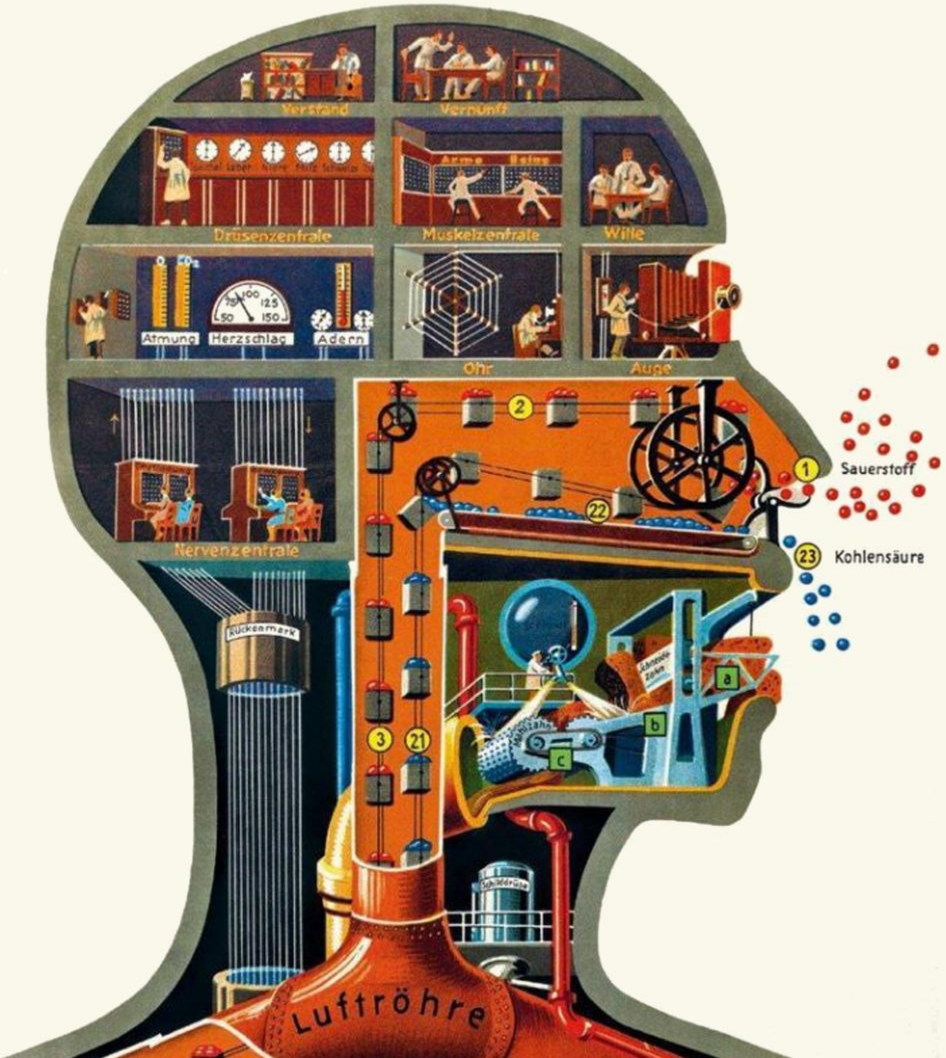
Probing and influencing bio(molecular) systems using an electromagnetic field

Vision

Novel electromagnetic methods for gentler and more efficient bio-nanotechnology and medicine

Tools

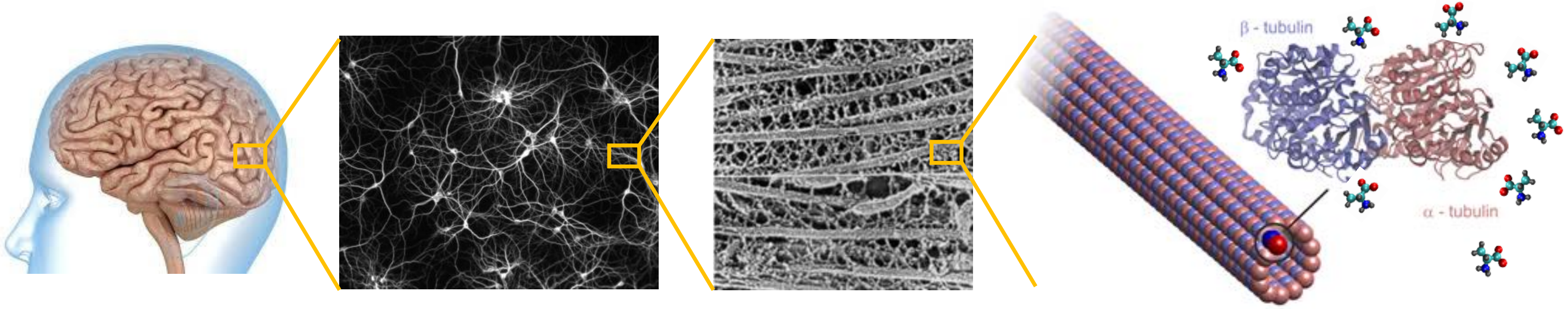
- **advanced electromagnetic concepts**
- **micro/nanotechnology enabled tools**
- **computational methods**


Verstand
Vernunft
Drüsenzentrale
Muskelzentrale
Wille
Atmung
Herzschlag
Adern
Ohr
Auge
Nervenzentrale
Rückenmark
Sauerstoff
Kohlensäure
Luftröhre

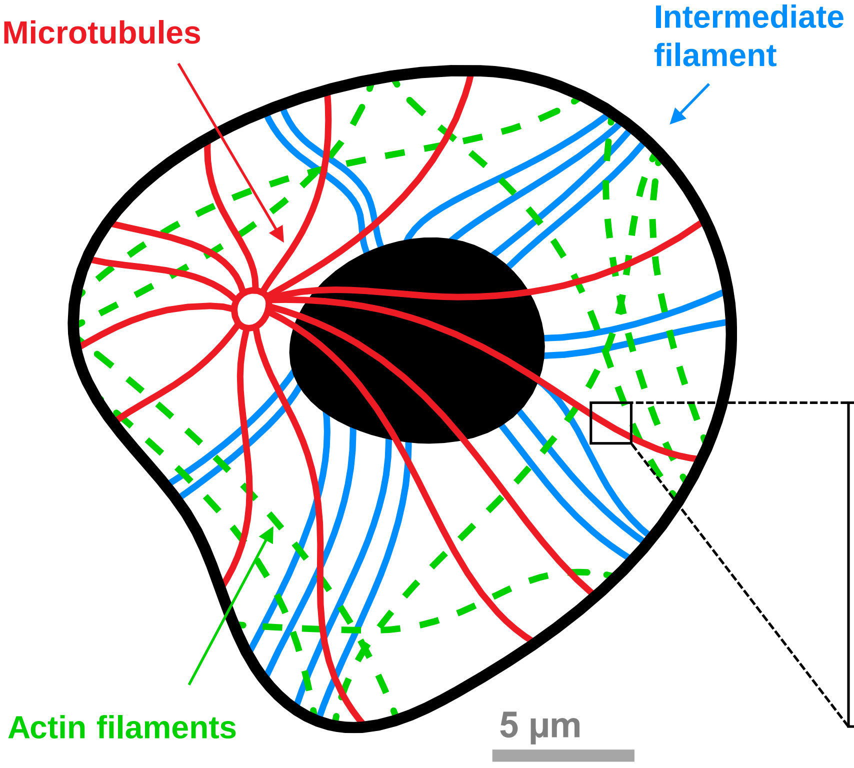
Mechanistic and integrative science philosophy

understand the parts and their interactions to understand the whole...

understand how biomolecular components and their interactions respond to electromagnetic field…

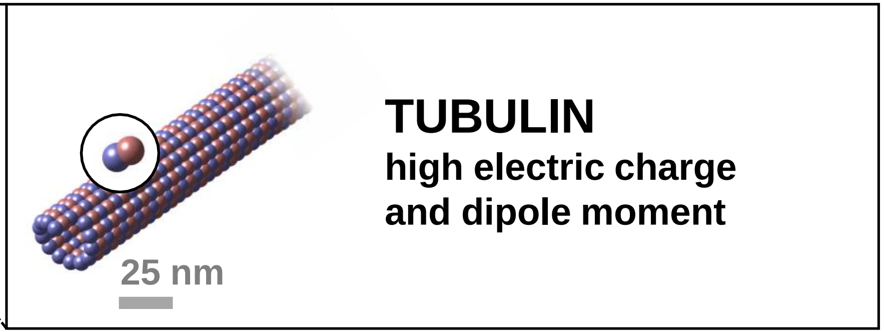


Why microtubules ?

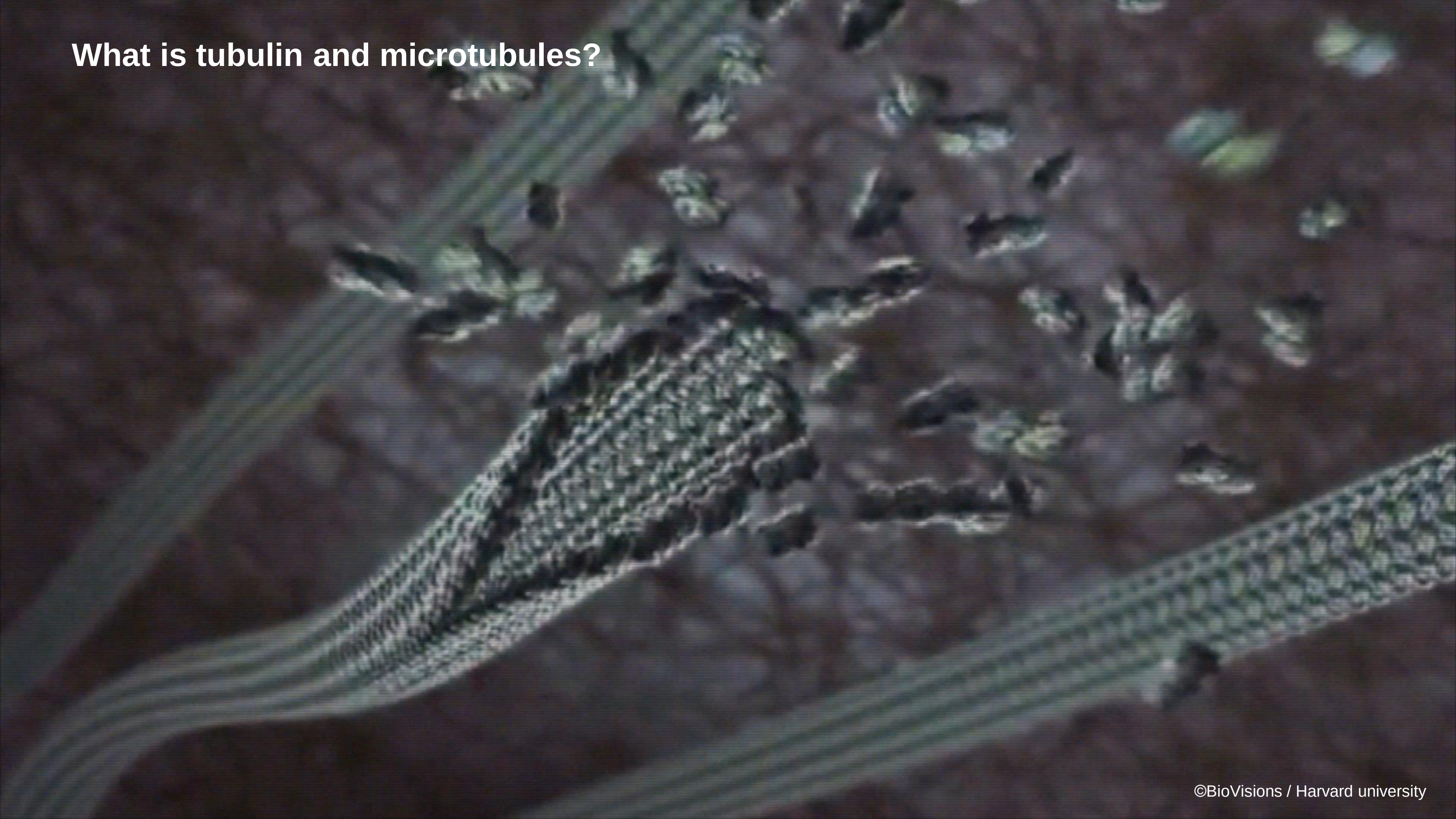


Biological cell

- cell division
- intracellular transport
- intracellular signaling

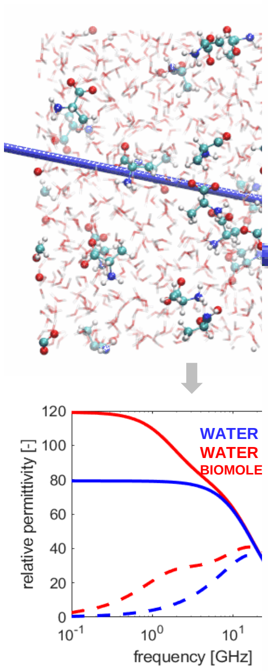


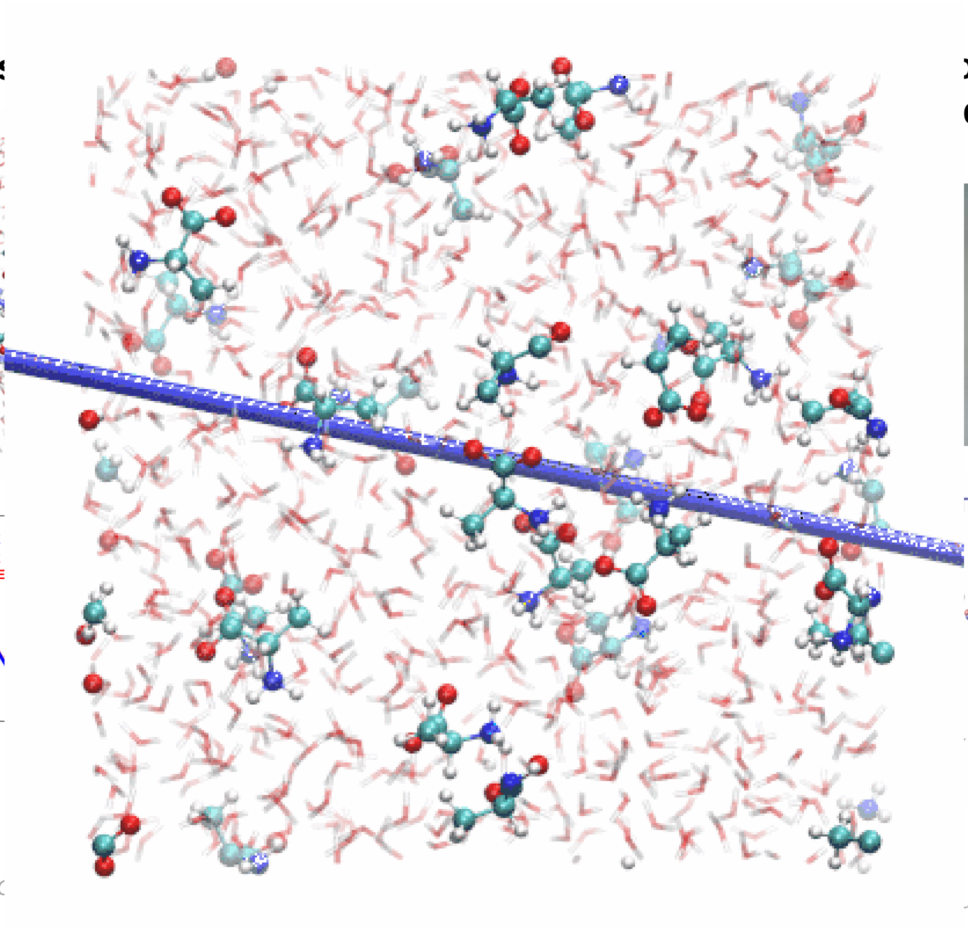
What is tubulin and microtubules?



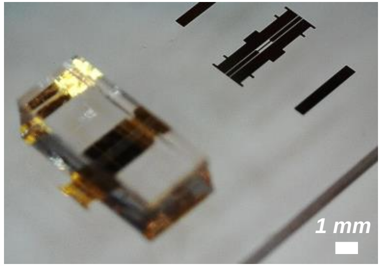
Response of biomolecular systems to electromagnetic field

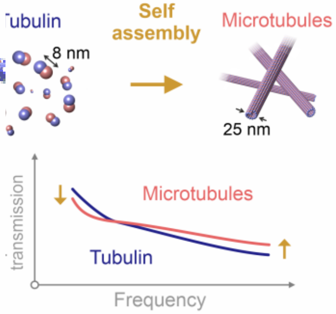
Molecular simulation





sample analysis of d sensing



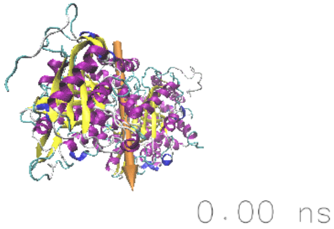


Průša et al. *J Mol Liquids* ***2020*** 112613
Cifra et al. *IEEE JERM*, 97–104, **2019**
Cifra, et al. *In Proc. IEEE/MTT-S IMBio*

ıdský et al. *Sens. Act. B*, ***2021***, *129068, 328*

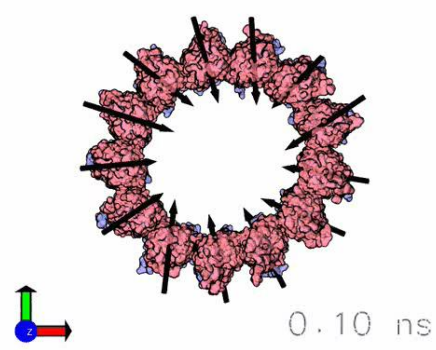
Response of biomolecular systems to electromagnetic field

Molecular simulations: proteins in electric field



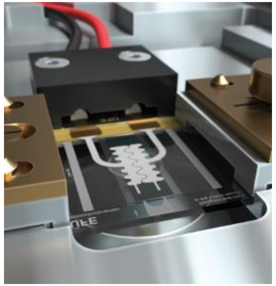
Marracino et al. *Sci Rep,* **2019**, 9:10477

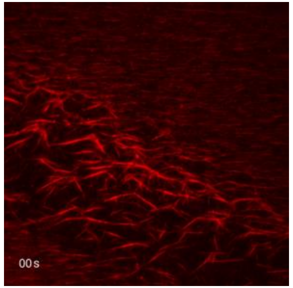
100 MV/m



Průša et al. *Comp Struct Biotech J,* **2021**, 19:1488-96

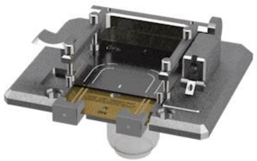
Chips for on-microscope imaging

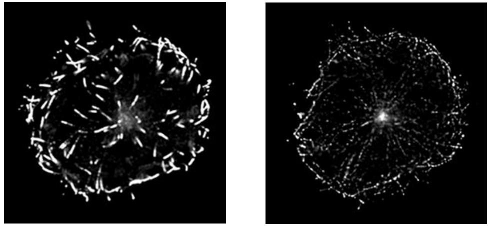




Havelka et al. *submitted*

Microtubules actuation by electric pulses

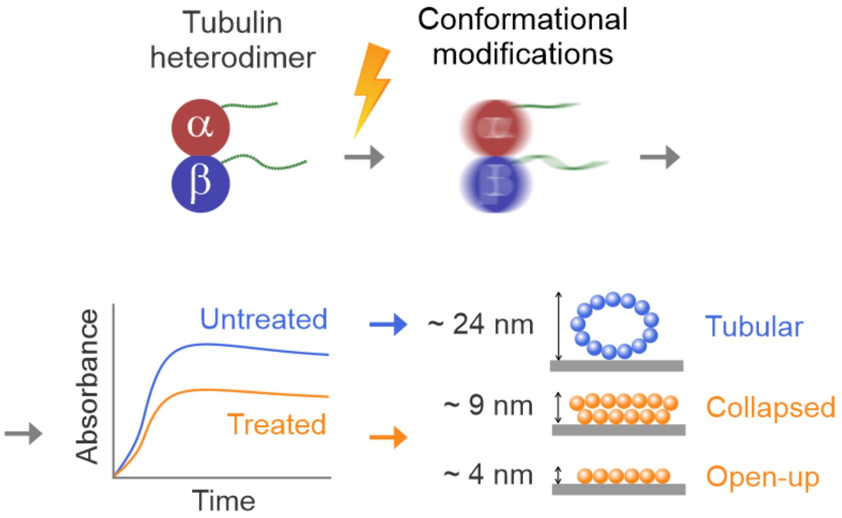


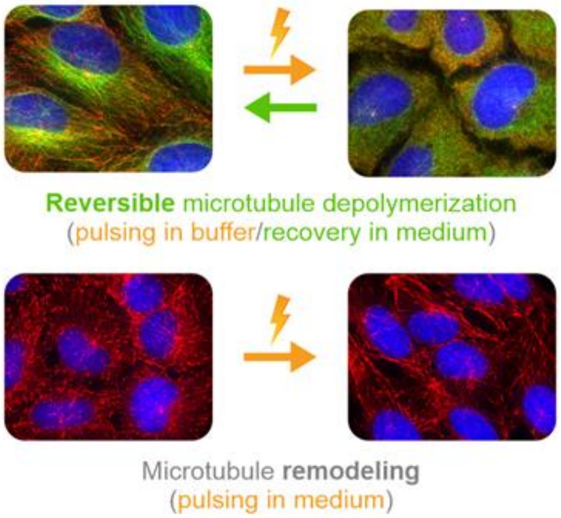


Havelka et al. *Adv Mat Tech,* **2020**, 5:1900669

Control vs. treated cell

Response of biomolecular systems to electromagnetic field: experiments

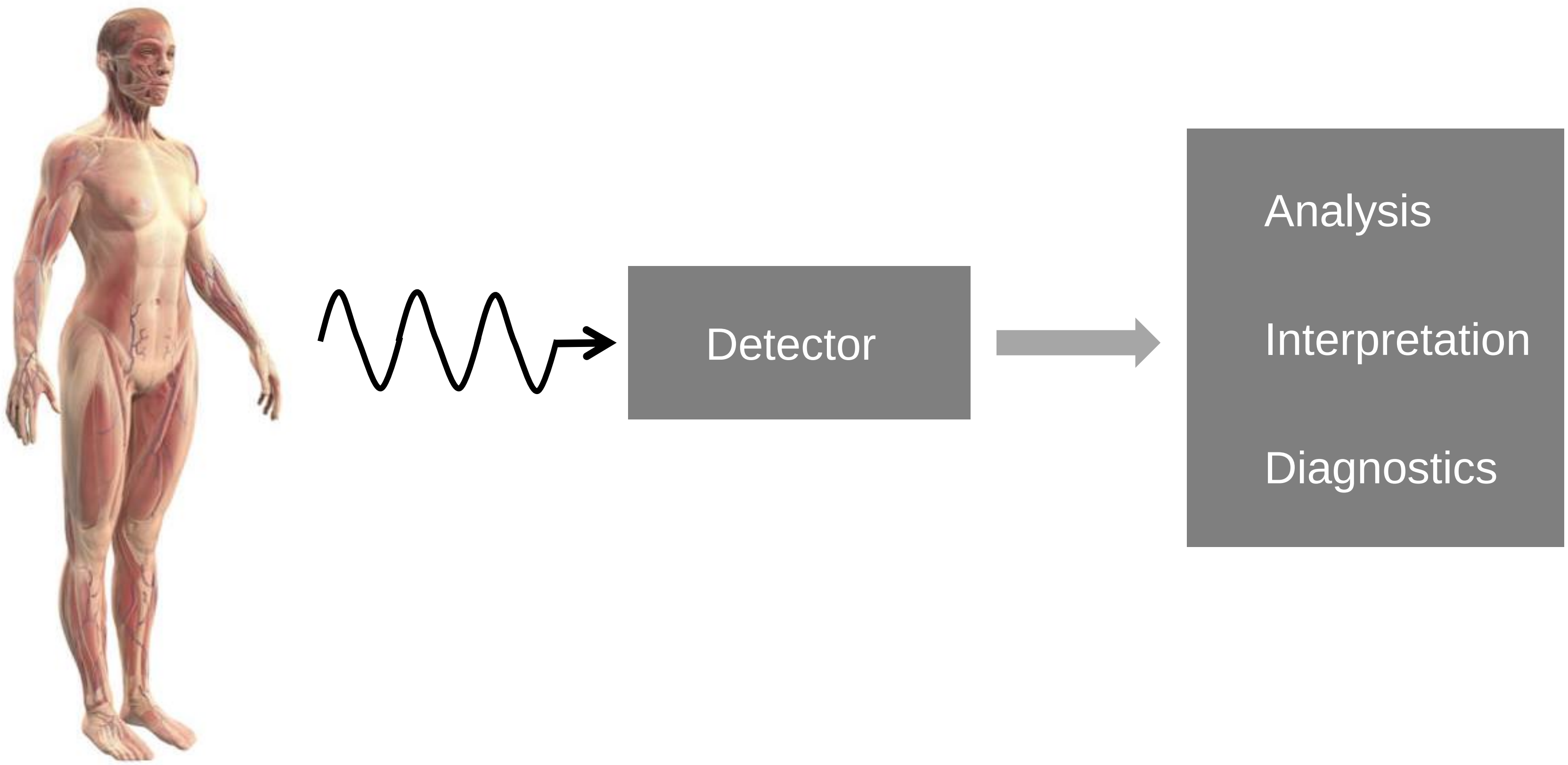




Chafai et al. *Adv Mat* **2019**, 31: 1903636

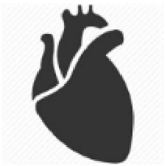
Chafai et al. *Adv Biosys* **2020**, 7:2000070

Electrodynamic activity of organisms: route to novel diagnostics methods



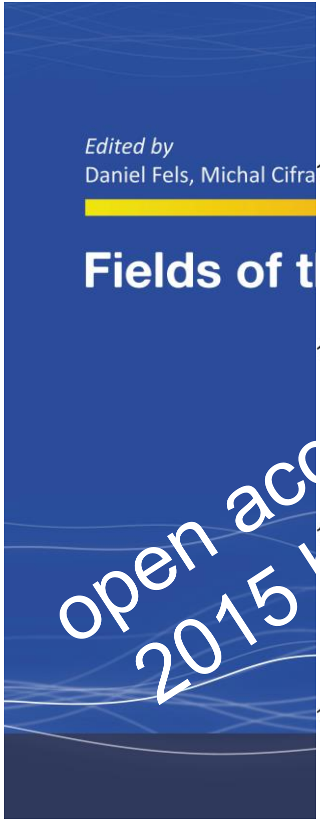
ELECTROMAGNETIC SPECTRUM

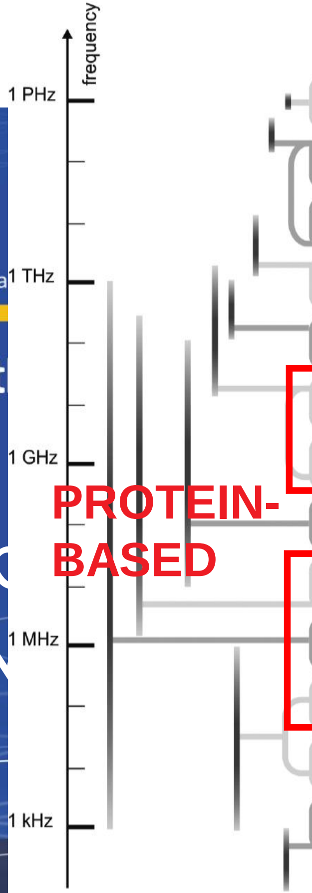
low-frequency



classical
electrophysiology

Pokorny *et al*. Integrative Biology, 2013, 12, 1419-510





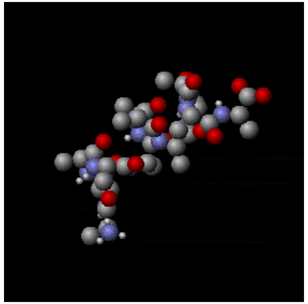
PROTEIN-BASED

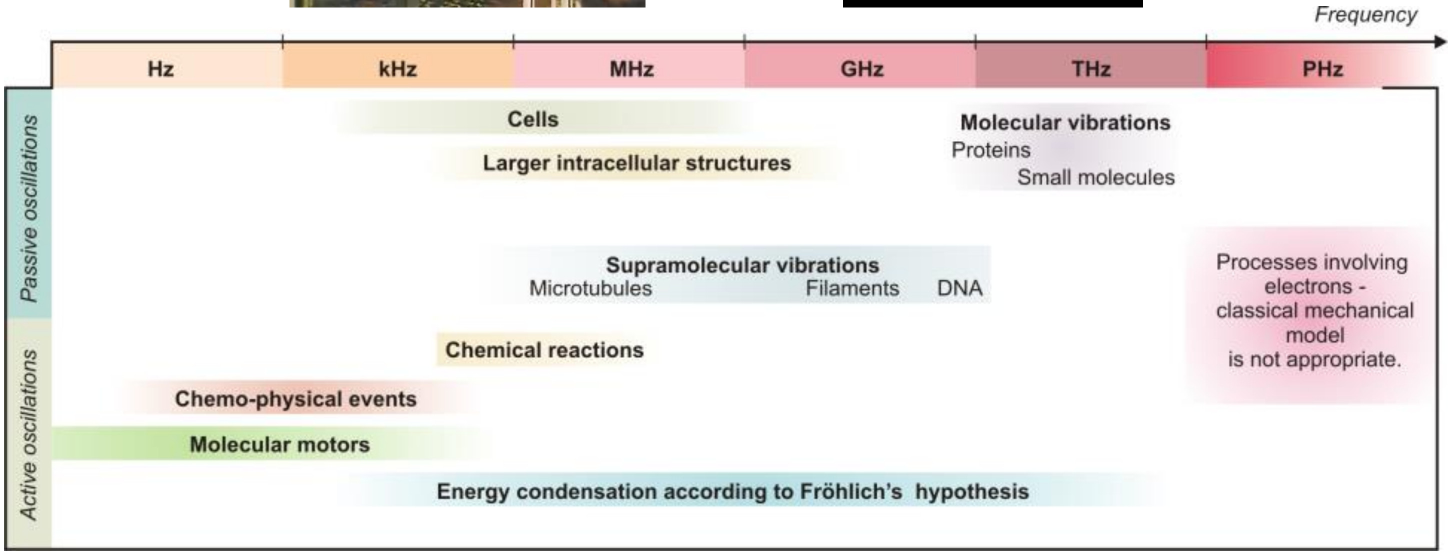
PHENOMENOM	THEORY	EXPERIMENT	REFERENCES
high energy (MID - UV) auto-luminescence	✕	?	[96]
auto-luminescence from oxidative chemical reactions	?	✓	[142]
bio-luminescence from specialized protein/enzyme complexes	✓	✓	textbooks
thermal movement of electric charge, peak of thermal radiation (Planck's law)	✓	✓	textbooks
THz radiation from electroexcitable tissues	✕	?	[90,91]
coherent longitudinal vibrations of electrically polar cellular structures (Fröhlich)	?	?	[21,34,35]
electrosolitons in proteins	?	✕	[47,48]
acousto-electrical waves generated in cellular membranes	?	✕	[37,38,143]
polar vibrations of microtubules	?	✕	[35,40,42]
electron oscillations in protein structures	✕	✕	✕
inverse process to electroconformational coupling in enzymatic systems	?	✕	[19]
coupling of oscillating chemical reactions with mobile ions	?	✕	[3,4]
classical electrophysiology: ionic currents related to membrane depolarization	✓	✓	textbooks

LEGEND	✓	?	✕
THEORY	broadly accepted	proposed, but not generally accepted/known	not known
EXPERIMENT	available, broadly accepted	pioneering experiments, not reproduced or accepted	not known

Microtubule microwave fluctations

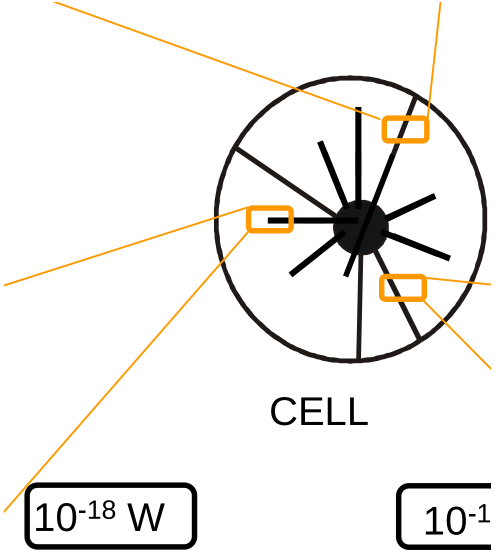
Mechanical vibrations in cells





Kučera, O. and Havelka, D. "Mechano-electrical vibrations of microtubules—Link to subcellular morphology." *Biosystems* 109.3 (2012): 346-355.

Energy supply to microtubule vibrations: power rates for the whole cellular MT network

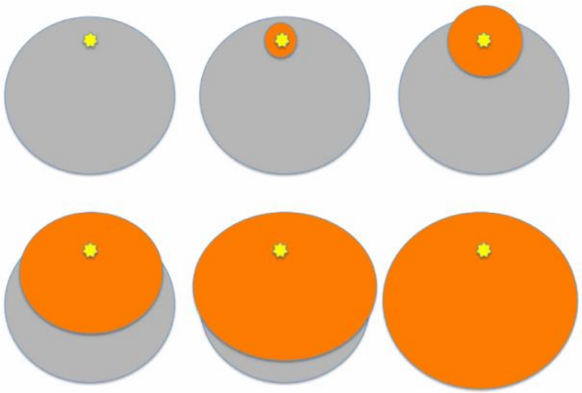


Jelinek *et al*. *Electromagnetic Biology and Medicine*, 2009, 28, 223-32 Cifra *et al*. *Biosystems*, 2010, 100, 122-31

Energy supply to microtubule vibrations

Hypothesis: GTP hydrolysis in tubulin generates acoustic pulses which excite the microtubule vibrations

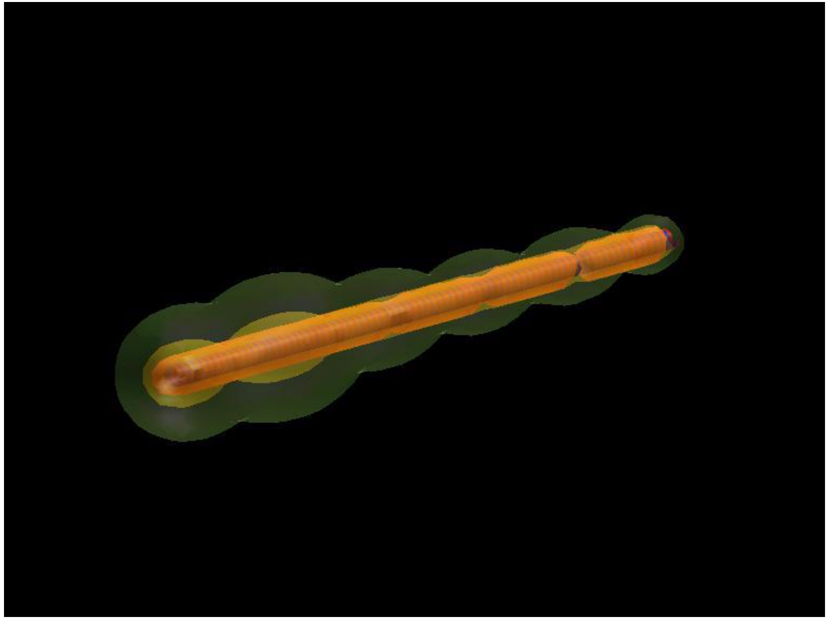
Exergonic enzymatic reactions generate acoustic wave (3 nm/ps) at the catalytic site of protein

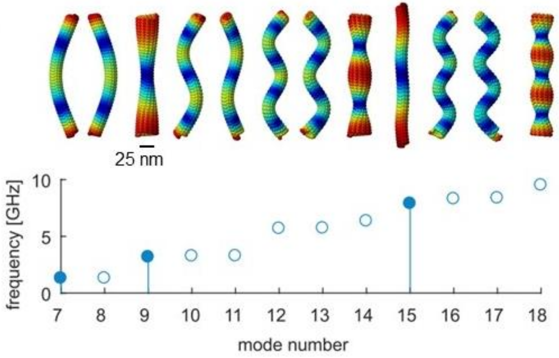


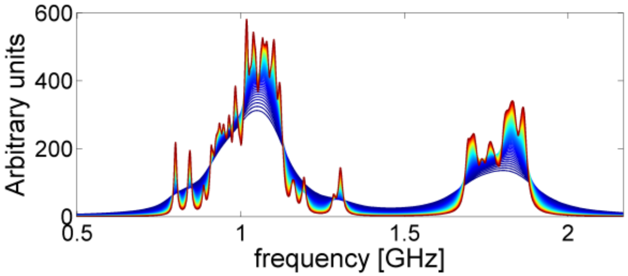
Riedel, C. *et al.* (2015) The heat released during catalytic turnover enhances the diffusion of an enzyme, *Nature,* 517, 227-230

Generation of electromagnetic field by biomolecular systems

Hypothesis: microwave vibrations/fluctuations of microtubules







Havelka et al. *App Phys Let*, **2014**, 104: 243702
Kučera and Havelka *Biosys* **2012** 109. 346-355
Havelka et al. *J Theor Biol* **2011** 286: 31-40
Cifra et al. *Biosys* **2010** 100. 122-131

Havelka et al. *Sci Rep* **2017** **7**: 4227
Havelka et al. *PLoS ONE* **2014** 9: e86501

All organisms glow:

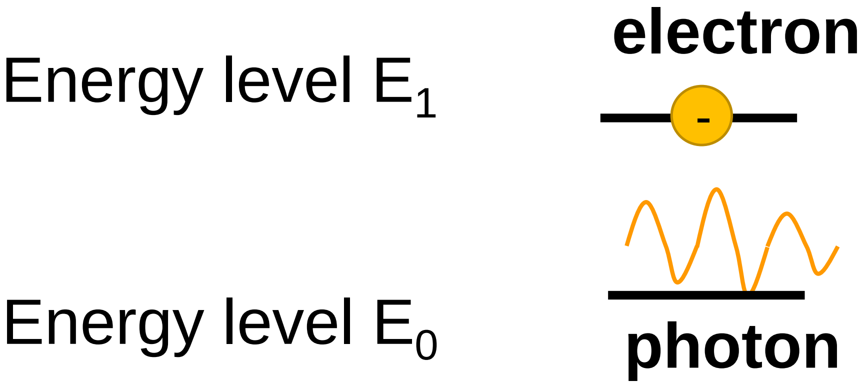
Biological autoluminescence

Biological autoluminescence (BAL)

"… is the luminescence from biosystems where electron excited species are formed due to energy from oxidation of endogenous biomolecules"

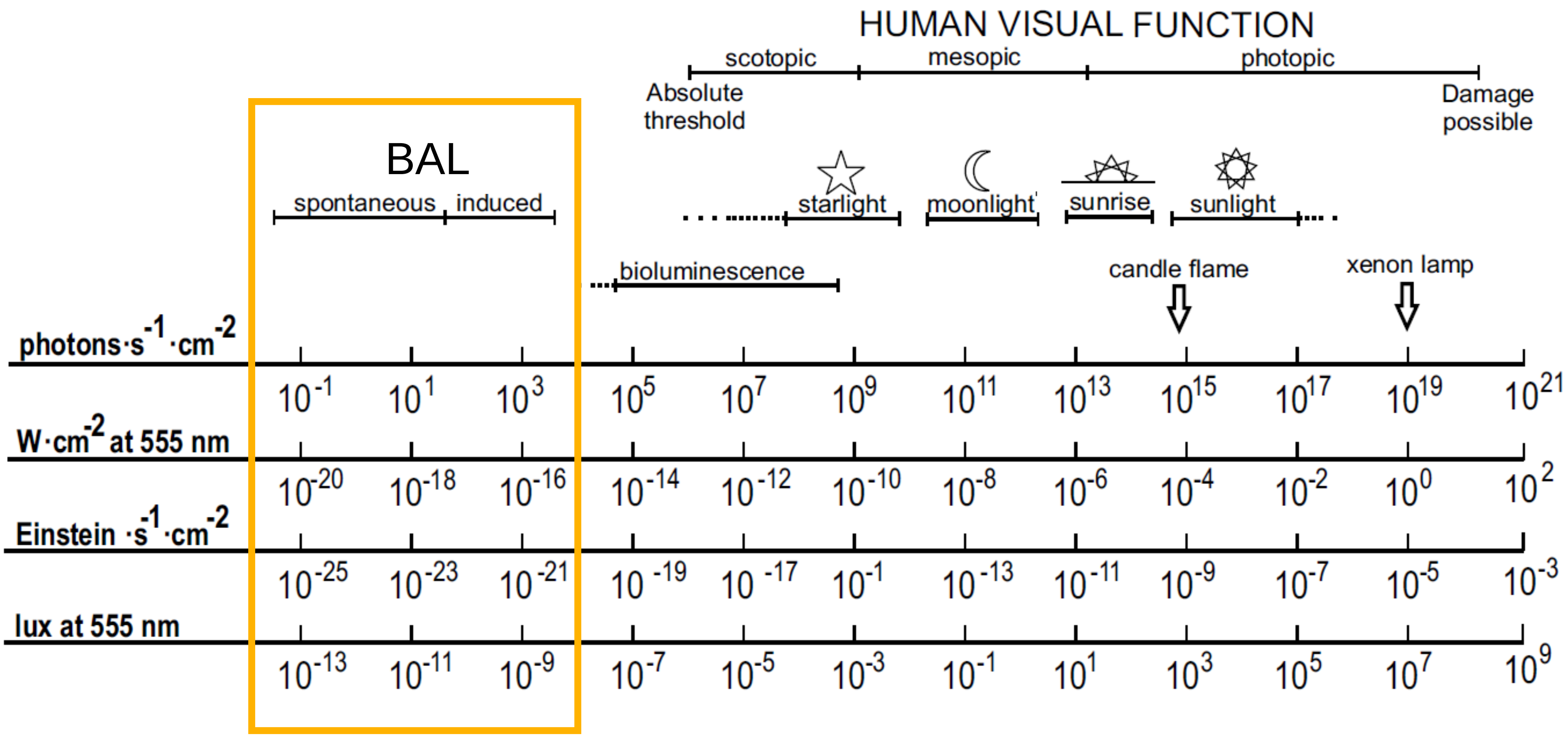
- wavelength range at least **350 – 700 nm**
- intensity **1-1000 photons cm^{-2} s^{-1}**
- **synonyma**: ultra-weak photon emission, weak bio/chemi-luminescence, biological autoluminescence, biophotons, photonic biosignals

$$[A] + [B] \rightarrow [P^*] \rightarrow [P] + \textbf{photon}$$



Cifra and Pospíšil *J Photochem & Photobiol B*, 2014, 139, 2-10

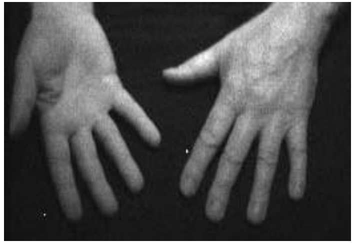
Biological autoluminescence (BAL)



Cifra and Pospíšil *J Photochem & Photobiol B*, 2014, 139, 2-10

Biological autoluminescence: detection methods

Object	Detector	Signal	



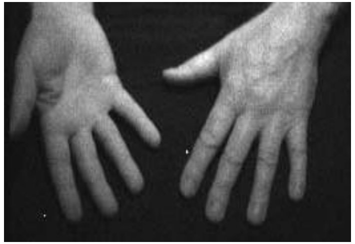
→

→

CCD

imaging

+ spatial resolution
+ higher quantum efficiency (60 %– 95 %)
- signal integration needed > 15 min



→

→

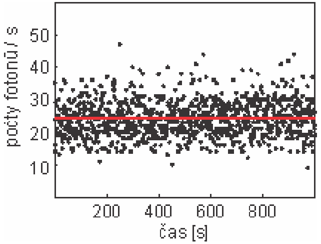
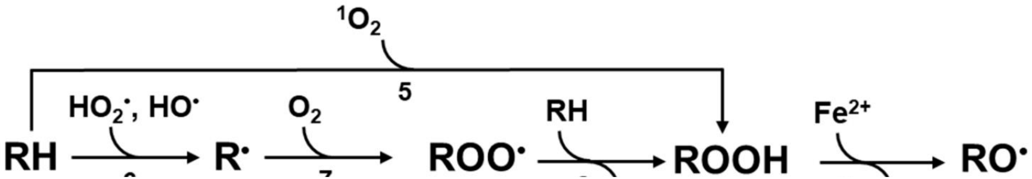


Photo multiplier

photon counting

+ high temporal resolution
- no spatial resolution (but there are 2D PMTs !)
- lower quantum efficiency (10 %– 40 %) than CCD camera

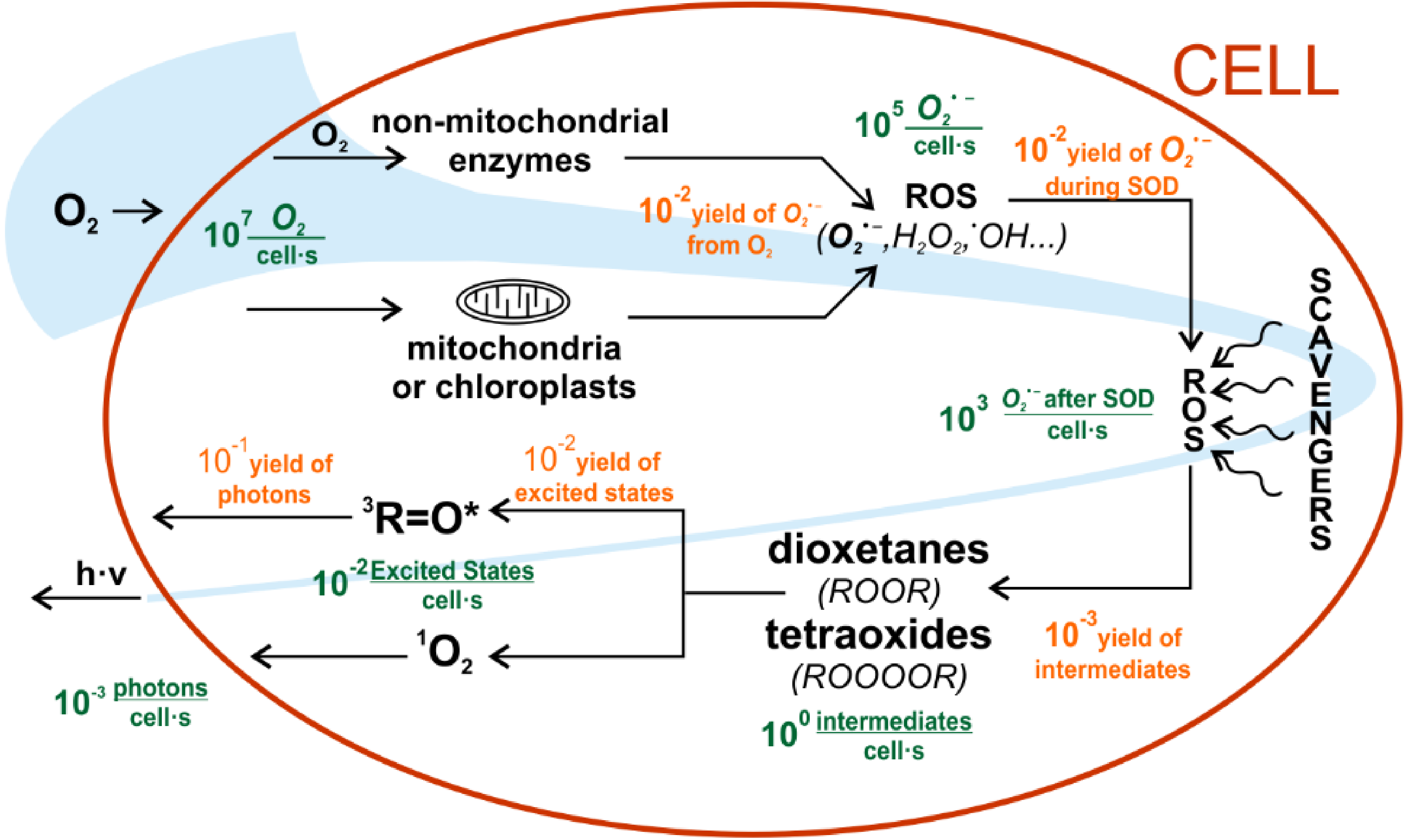
Biological autoluminescence: mechanisms & spectra



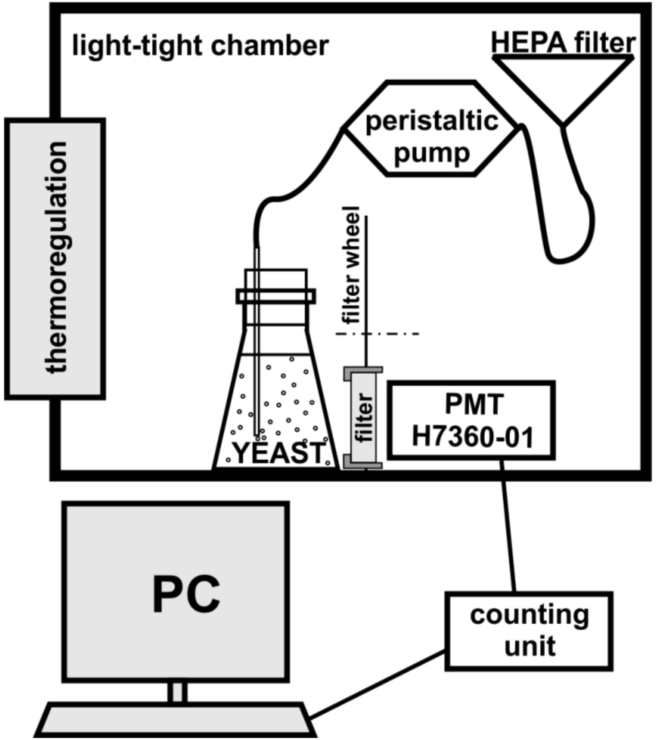
Electronically excited species	Wavelength
Triplet excited carbonyls	350 - 550 nm
Singlet excited pigments	360 - 560 nm melanin 680-740 nm chlorophyl
Triplet excited pigments	*870 – 1000 nm chlorophyll*
Dimolar singlet oxygen	634 nm, 703 nm
Monomolar singlet oxygen	*1270 nm*

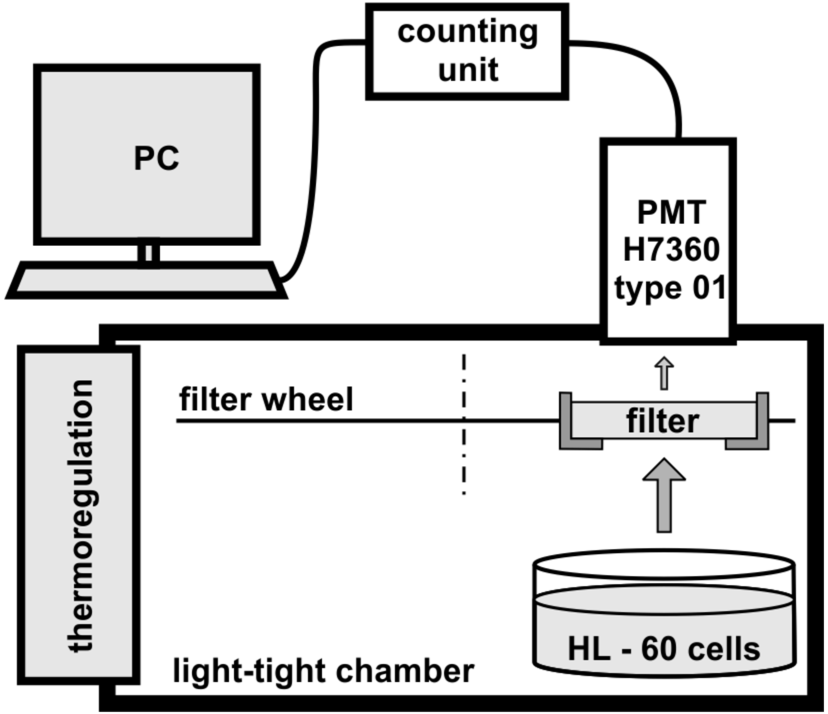
Pospíšil et al *Biomolecules*, 2019, 9, 258

Biological autoluminescence: quantitative

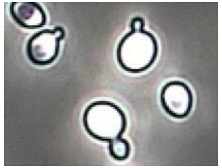


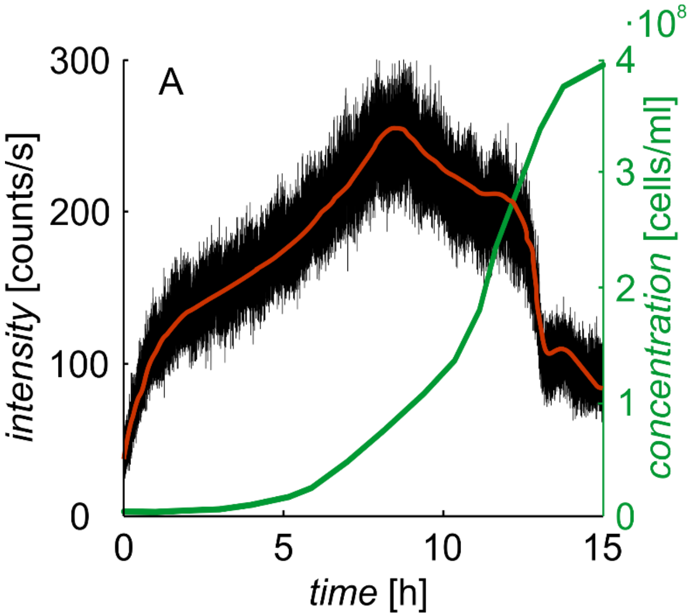
Biological autoluminescence: our detection systems





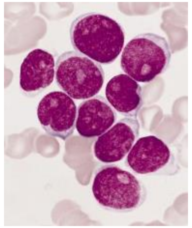
BAL is related to growth & metabolism

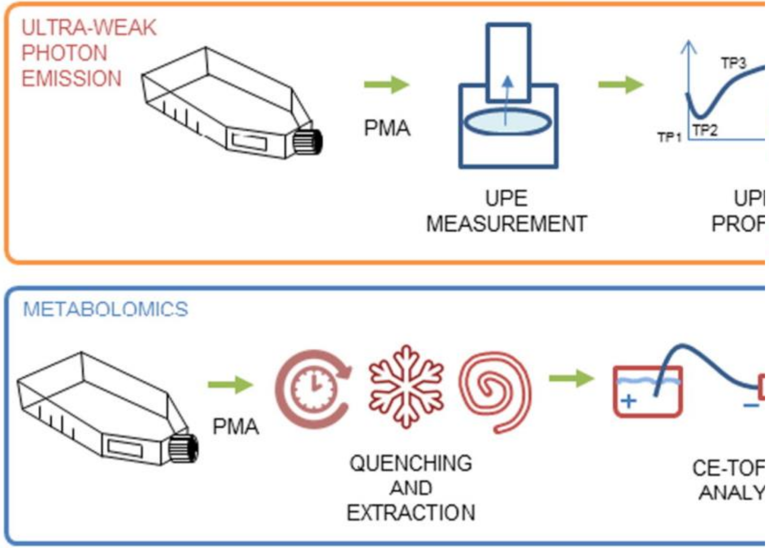


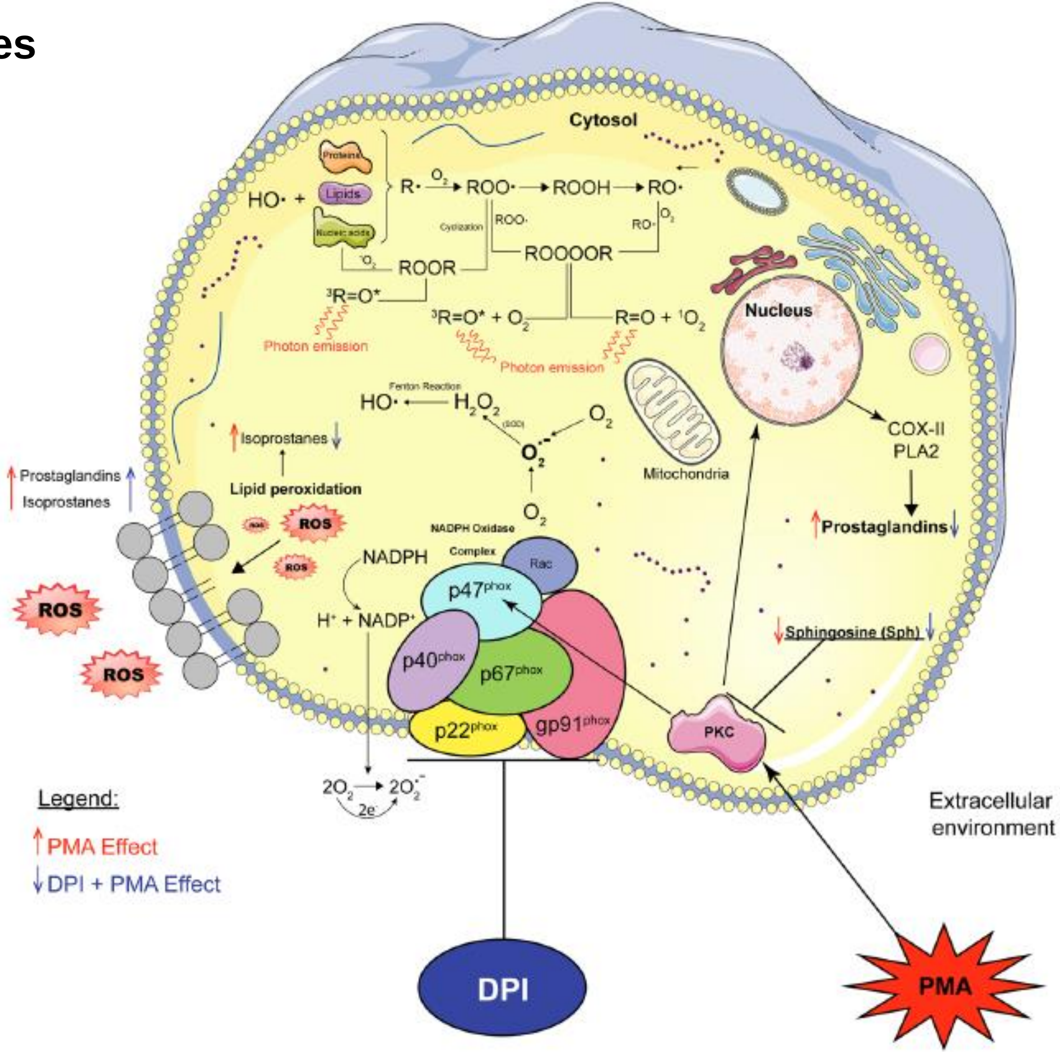


Vahalova et al *bioRxiv*, 2020.11.19.388801

BAL is related to oxidative metabolites

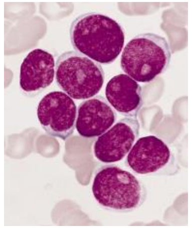


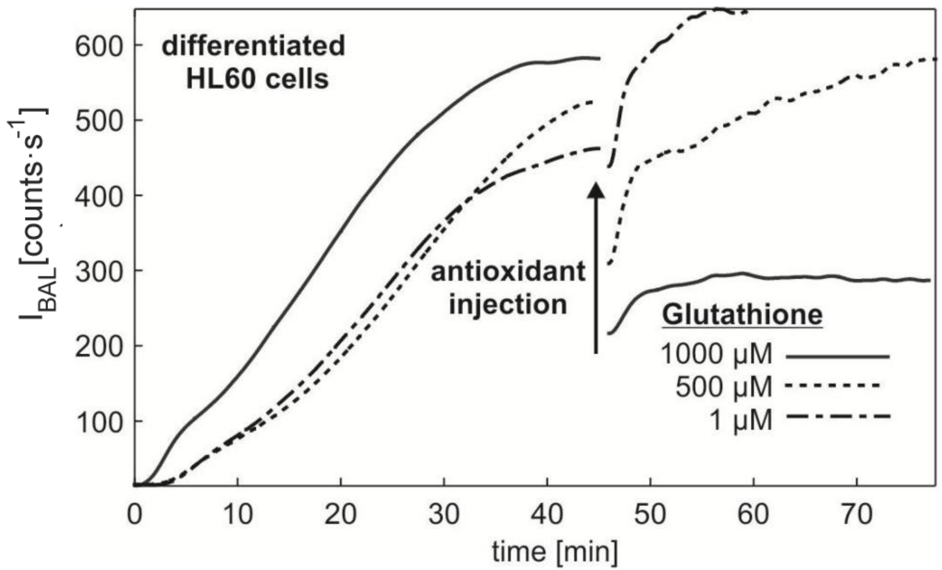


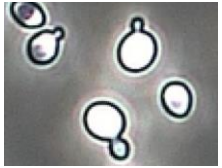


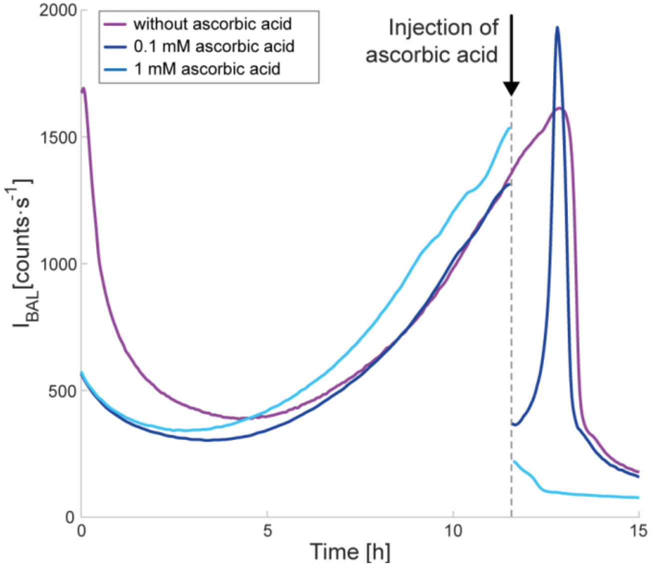
Burgos *et al. Sci Rep* **2017** 7: 1229.
Burgos *et al. JPPB:B,* **2016**, 163: 237-245

BAL is supressed by antioxidants





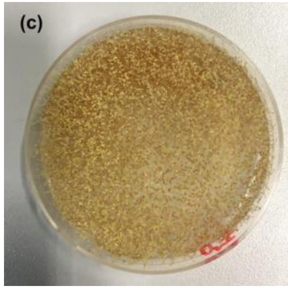




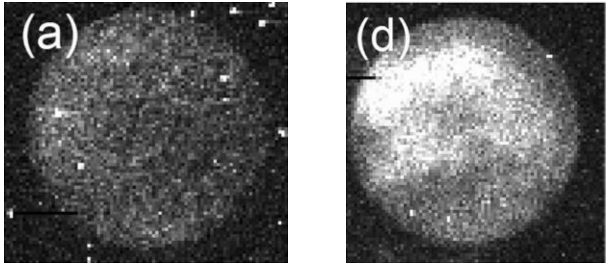
Červinková et al *SPIE Proceedings, 2015,* 10.1117/12.2070424

Vahalova et al *bioRxiv*, 2020.11.19.388801

BAL is enhanced by oxidants



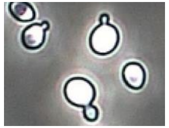
Arabidopsis thaliana

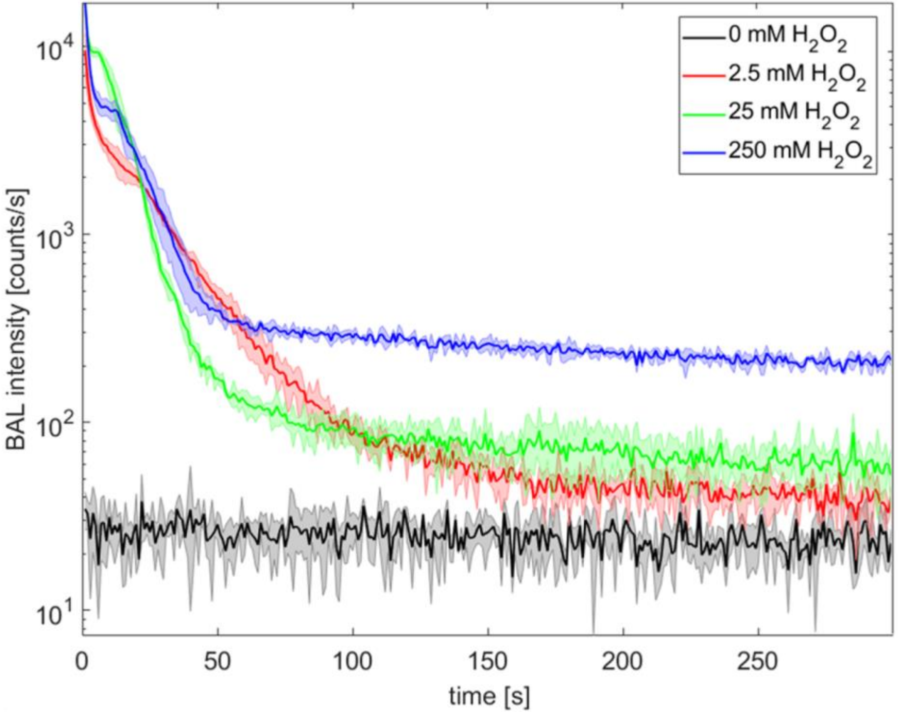


0 mM   6 mM

H_2O_2

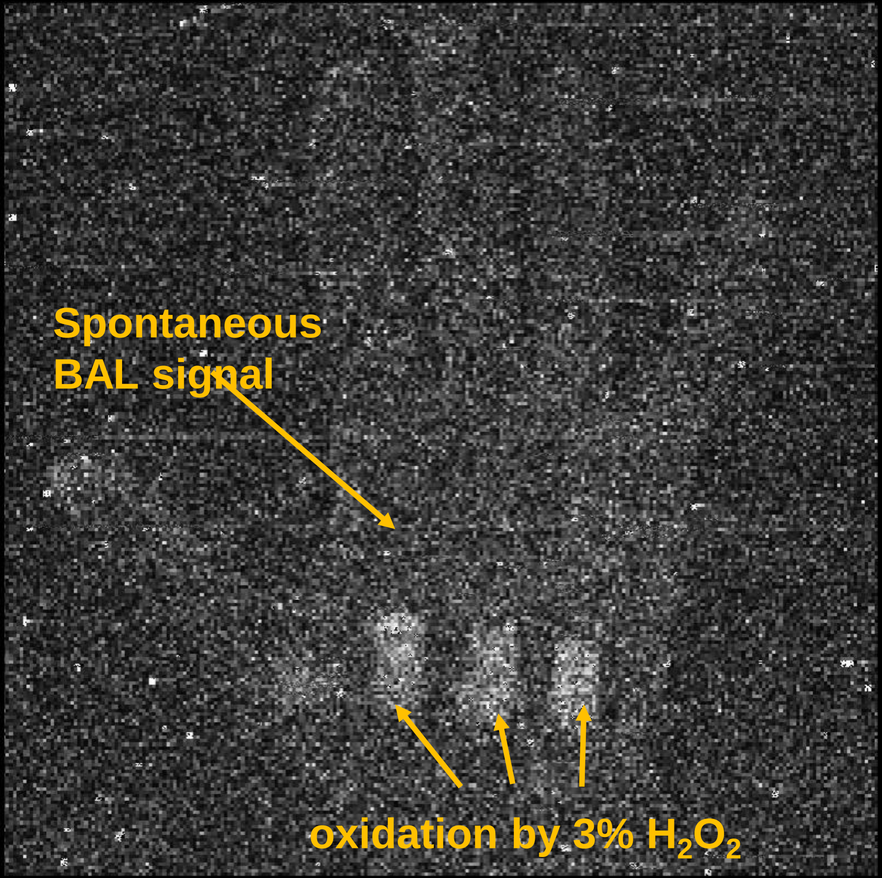
Saeidfirozeh et al *Scientific Reports*, 2018, 8, 16231





Bereta et al *Scientific Reports*, 2021,11, 328

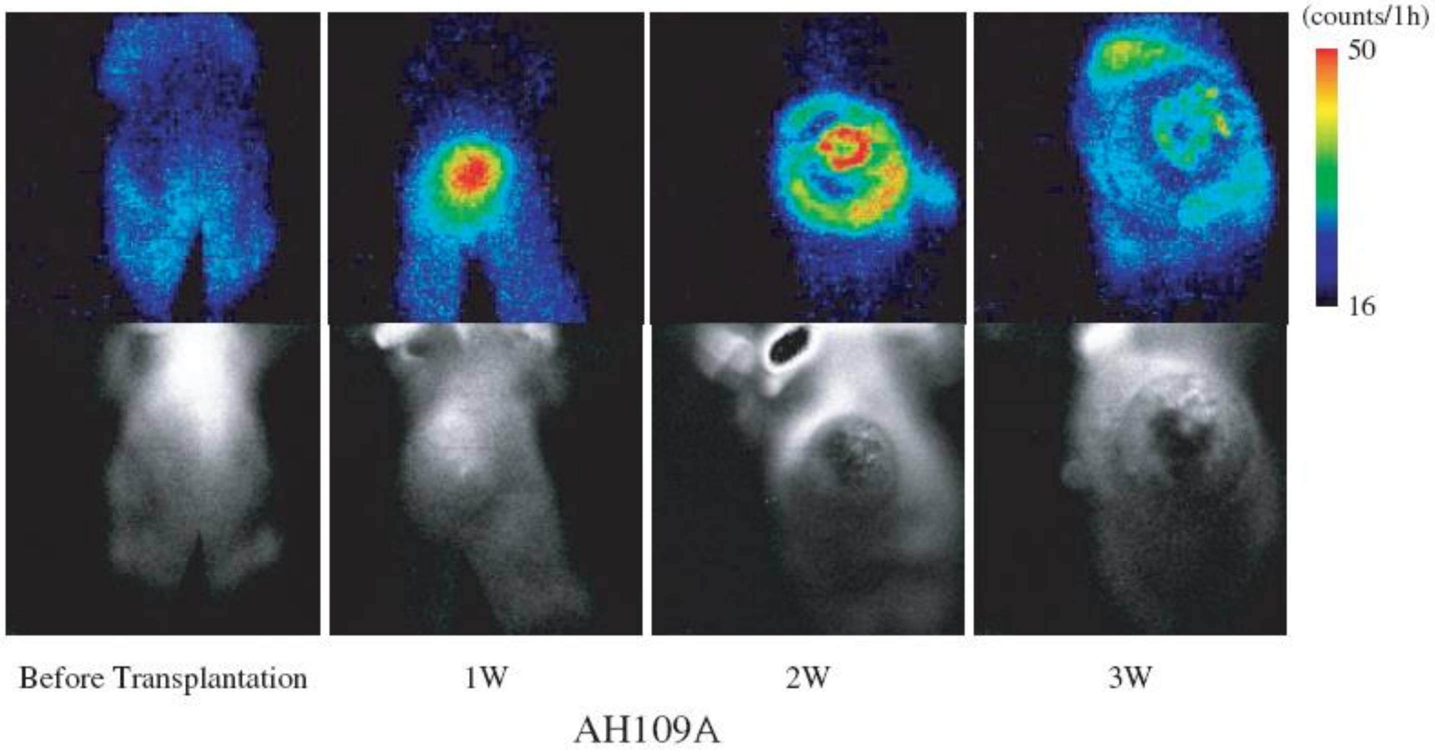
BAL is enhanced by oxidants



M. Poplová *et al., in preparation*

Biological autoluminescence: imaging & applications

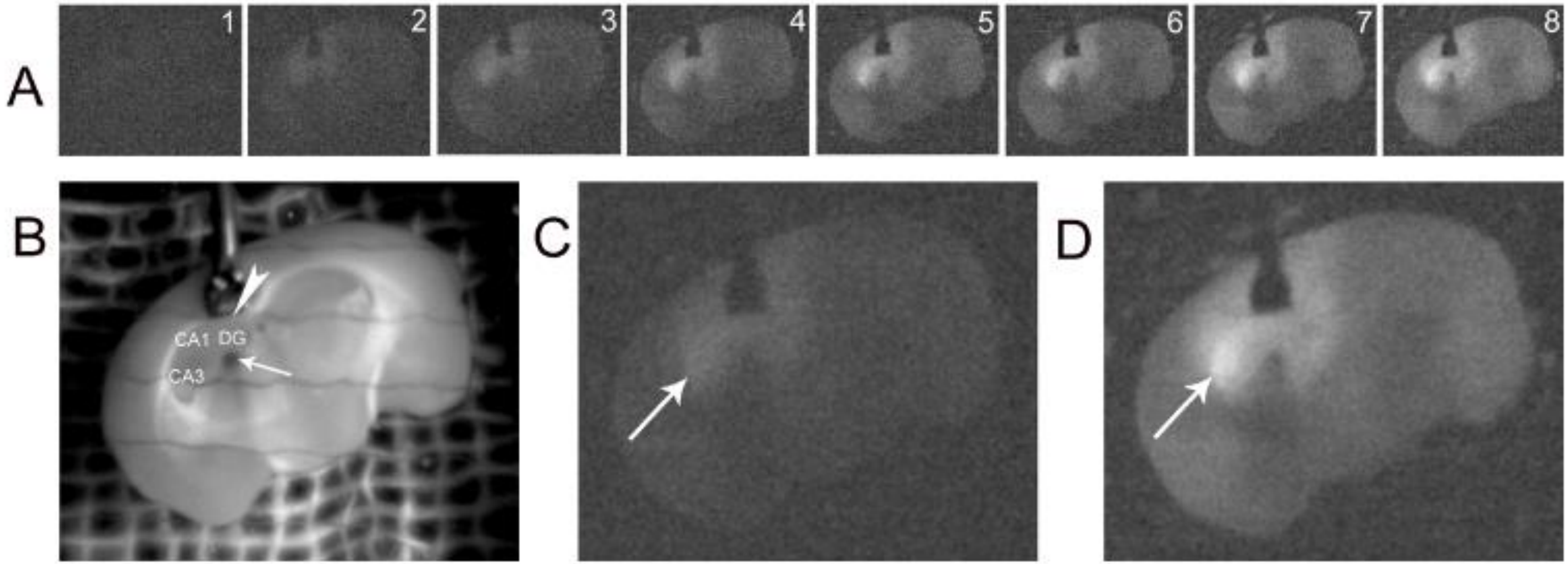
BAL from animals: cancer model



Takeda, Motohiro, et al. "Biophoton detection as a novel technique for cancer imaging." Cancer science 95.8 (2004): 656-661.

BAL from animals: neuroscience

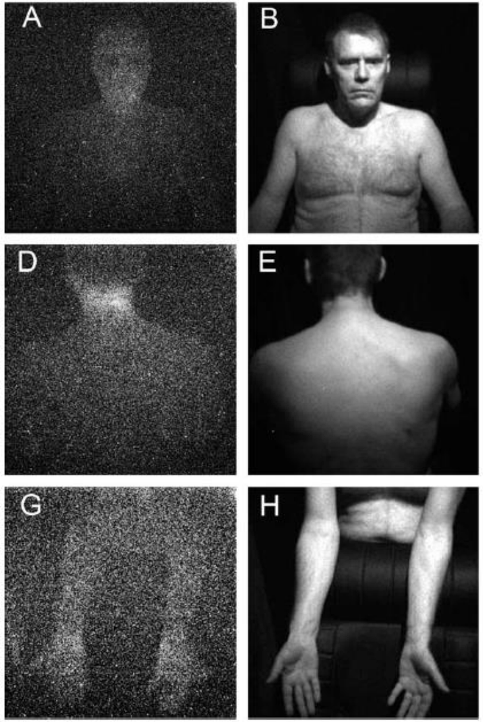
Brain slice – BAL intensity

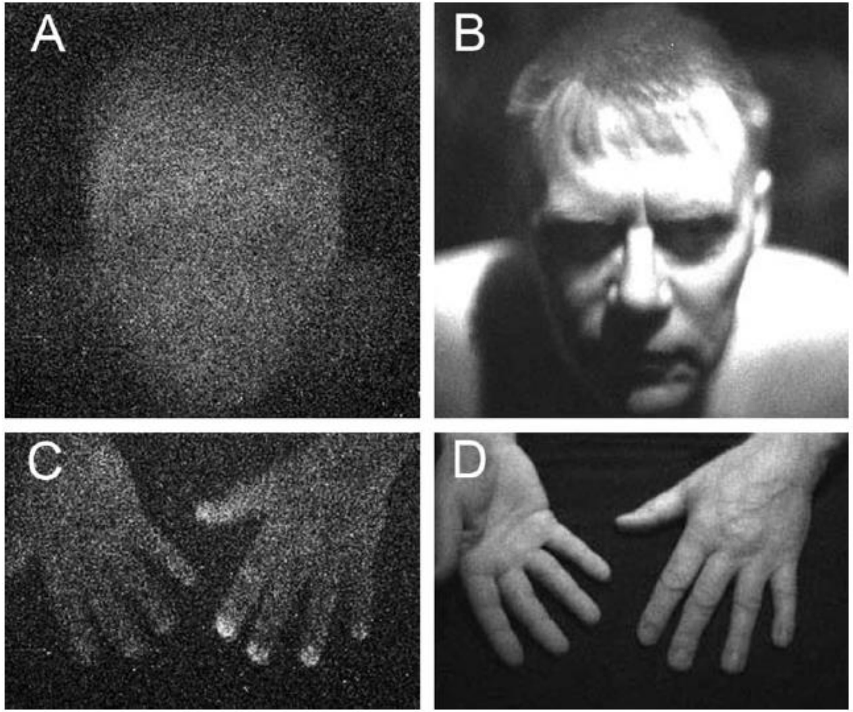


Brain - BW photography

Tang, Rendong, and Jiapei Dai. "Spatiotemporal imaging of glutamate-induced biophotonic activities and transmission in neural circuits." PloS one 9.1 (2014).

Human body BAL: first systematic imaging studies

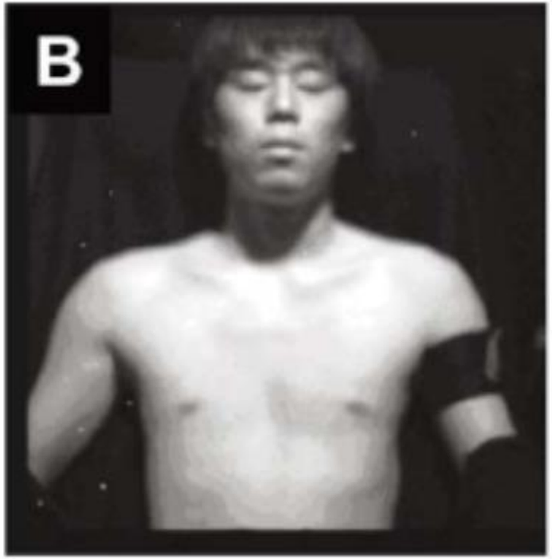




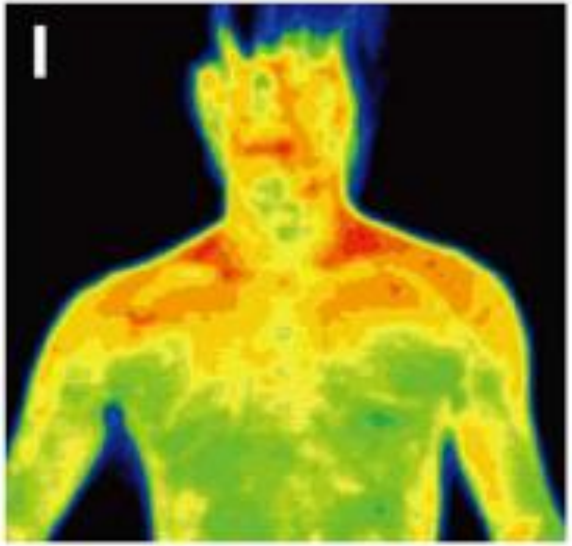
R. Van Wijk, *et al.* " Anatomic characterization of human ultra-weak photon emission with a moveable photomultiplier and CCD imaging " *Journal of Photochemistry and Photobiology B: Biology* 83 (2006): 69-76.

Human body BAL: first systematic imaging studies

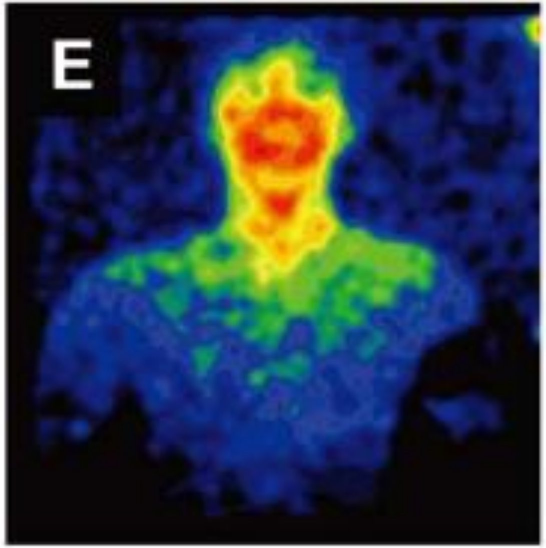
photo



IR emission (3.5 - 5 μm)

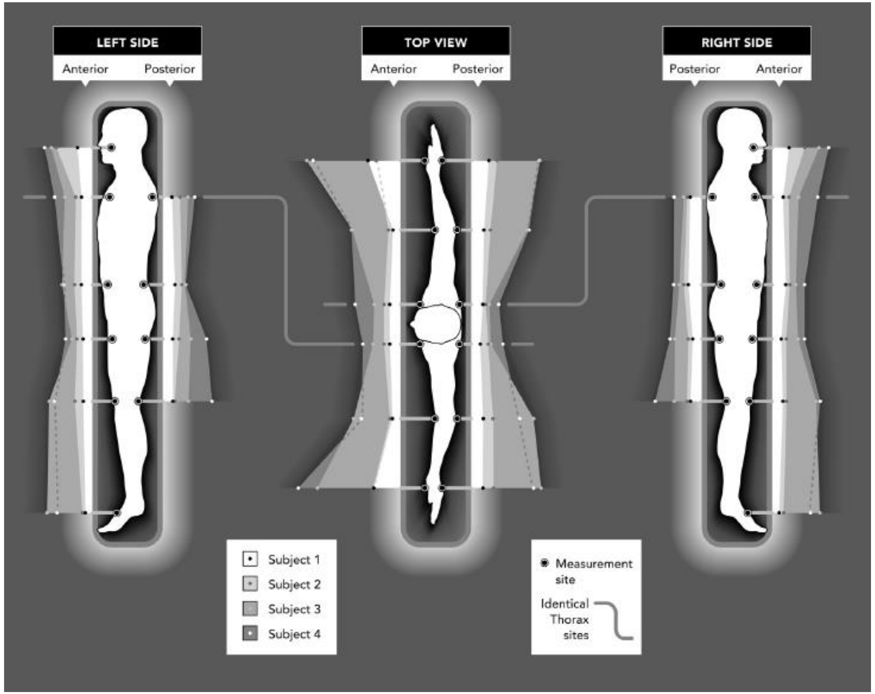


BAL



Kobayashi, Masaki, Daisuke Kikuchi, and Hitoshi Okamura. "Imaging of ultraweak spontaneous photon emiassion from human body displaying diurnal rhythm." *PLoS one* 4.7 (2009): e6256.

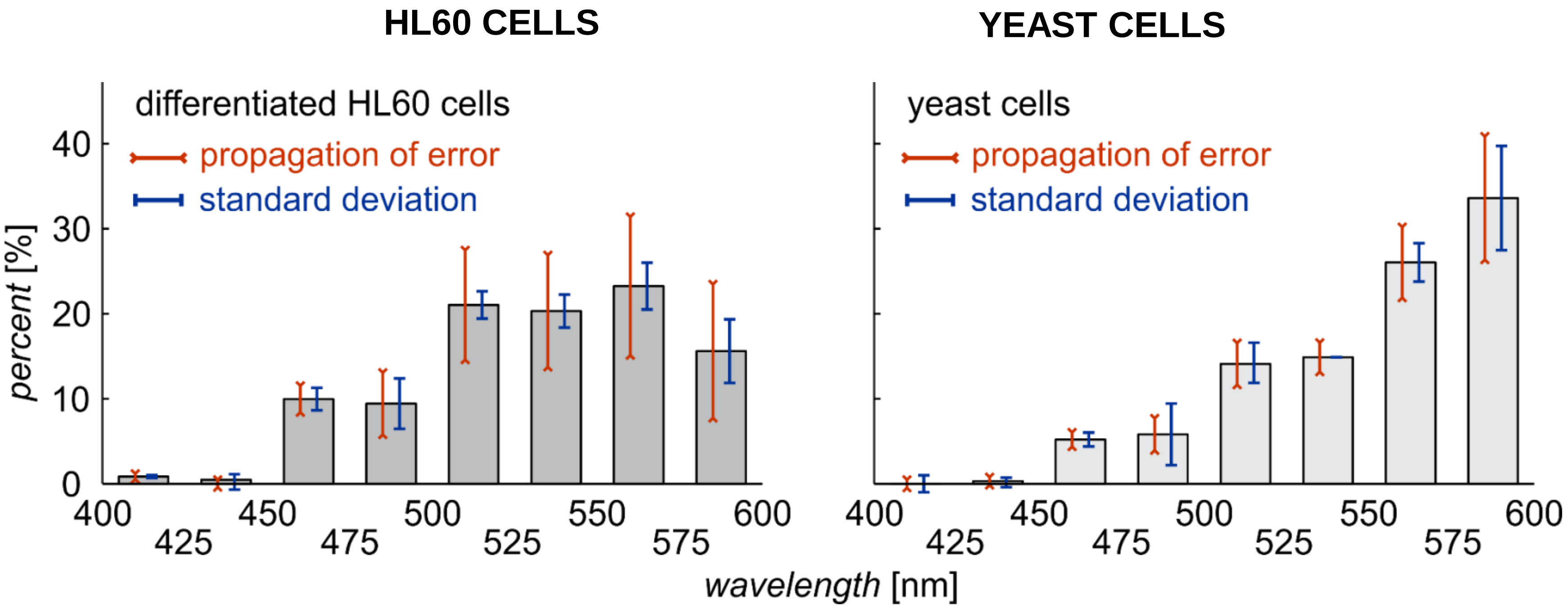
Human body BAL: first systematic imaging studies



Van Wijk, Roeland, et al. "Towards whole-body ultra-weak photon counting and imaging with a focus on human beings: A review." Journal of Photochemistry and Photobiology B: Biology 139 (2014): 39-46.

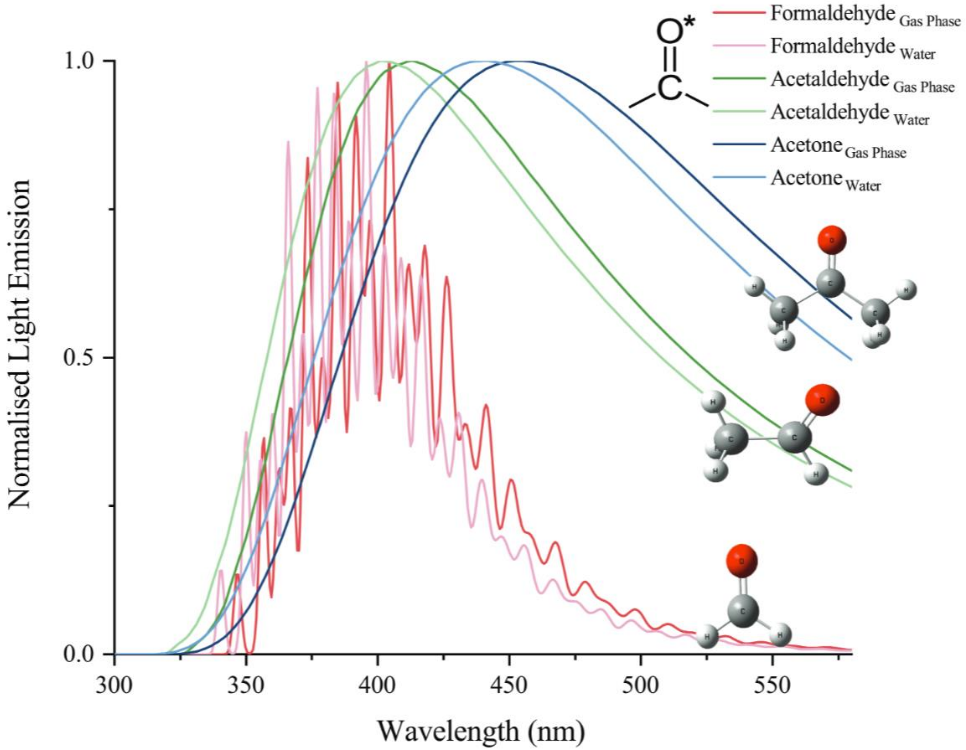
Biological autoluminescence: wavelength spectrum

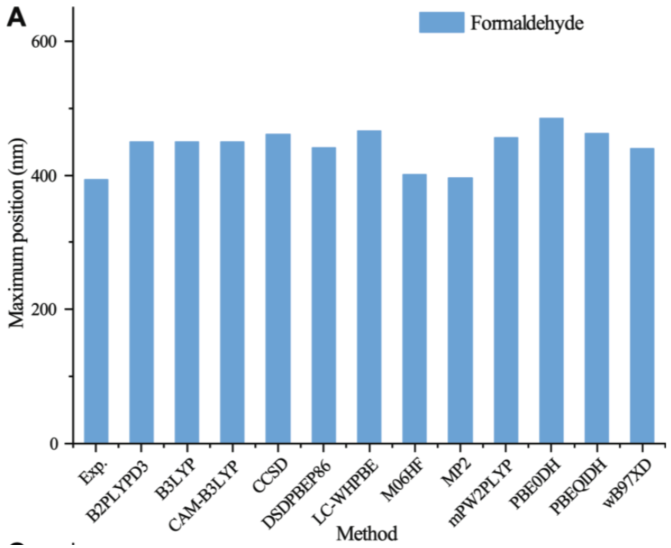
Different organisms emit BAL of different color



M. Nerudová *et al.*, Optical spectral analysis of ultra-weak photon emission from tissue culture and yeast cells, *Proc. of SPIE Vol. 9450, 94500O, 2015*

Quantum chemical modelling of BAL emitters spectra





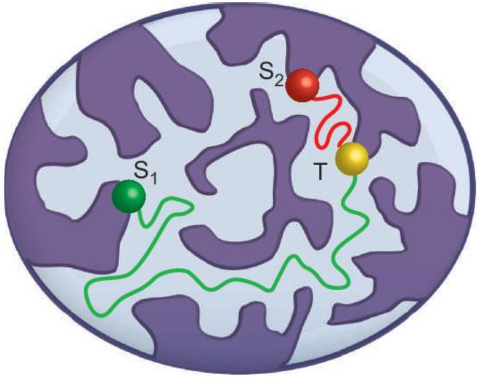
Saeidfirozeh et al. 2021, accepted, “*book on BAL*”

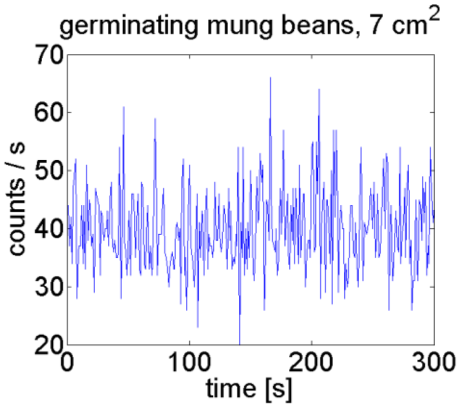
Biological autoluminescence: statistical signal properties

BAL signal properties

- BAL photocount distribution ? Physical interpretation ?
- Analysis of the photon count time series – fractal, chaotic properties, …

Intracellular environment (proteins, organelles) surfaces exhibit fractal geometry → Chemical reaction events form fractal time series



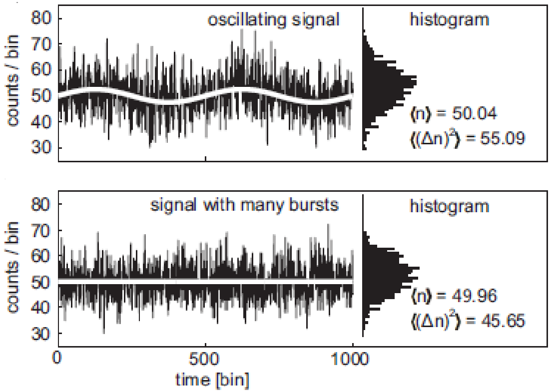


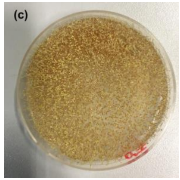
Bénichou et al. *Nature Chemistry* 2, no. 6 (2010): 472–77.

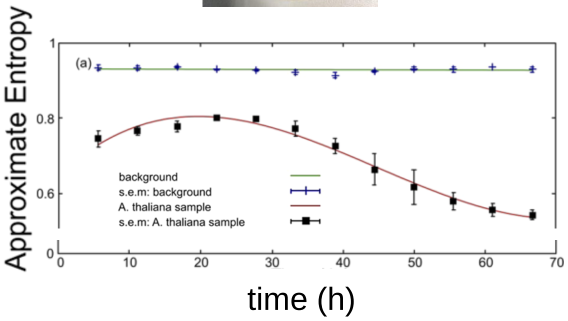
Kopelman, *Science* 241, no. 4873 (1988): 1620–26.

BAL signal properties

- BAL photocount distribution ? Physical interpretation ?
- Analysis of the photon count time series – fractal, chaotic properties, …







Hurst exponent lower than ref -> antipersistent behavior

Cifra et al. *J Lumin* **2015** 164: 38-51.
Rafieolhosseini *et al. JPPB:B*, **2016**, 162: 50-55
Poplová et al. *PLOS ONE* **2017** 12:e0188622.

Saeidfirozeh et al. *Sci Rep* **2018** 8:16231

Dlask et al. *PLOS ONE* **2019** 14: e0214427

Perspective: physical enhancement of biological autoluminescence

intense electric pulses

BAL: enhancement by electric pulses

Oxidation of biomolecules → BAL

BAL: enhancement by electric pulses

Maccarrone, *et al. Biochem Biophys Res Comm* **206** (1995): 238-245.

Maccarrone, *et al. Biochem Biophys Res Comm* **209** (1995): 417-425.

Gabriel and Teissie, *Eur J Biochem,* **223** (1994), 25-33

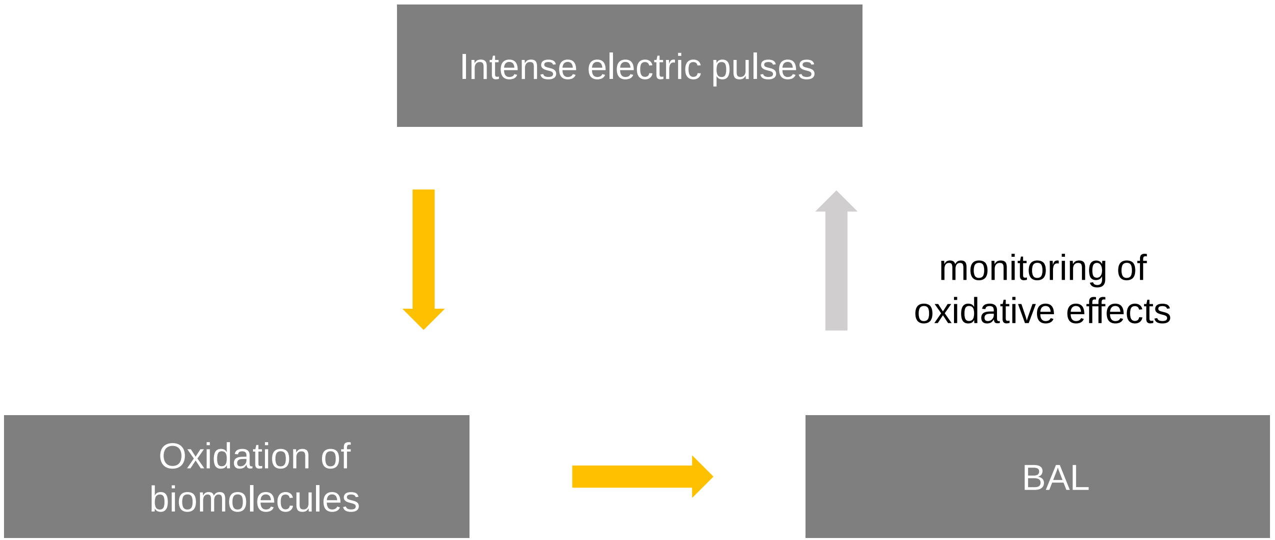
Pakhomova *et al.*, *Arch Biochem Biophys,* **527** (2012), 55-64

Intense electric pulses

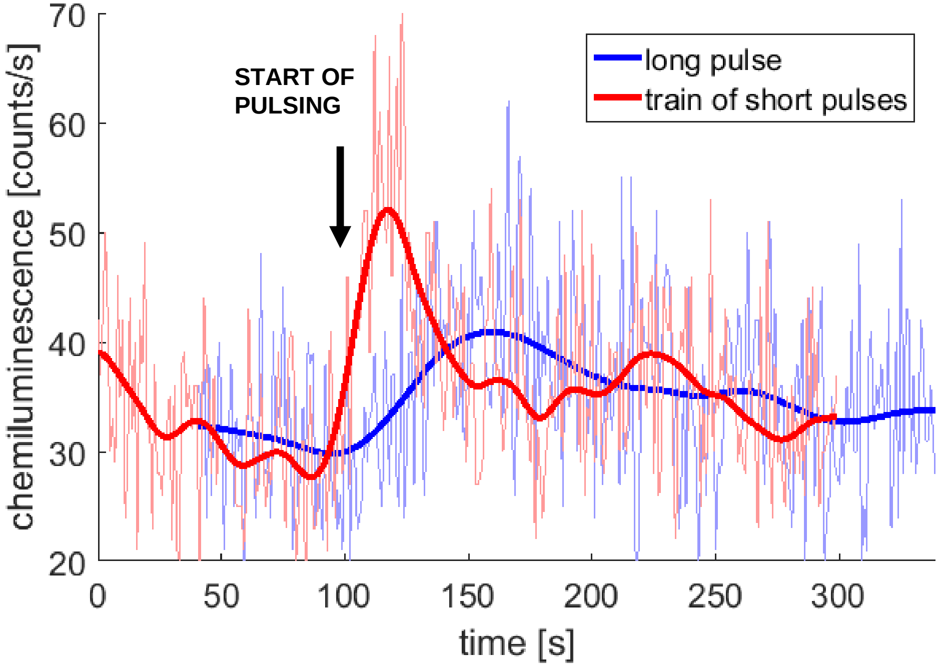
↓

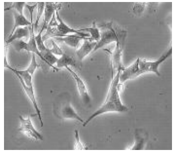
Oxidation of biomolecules

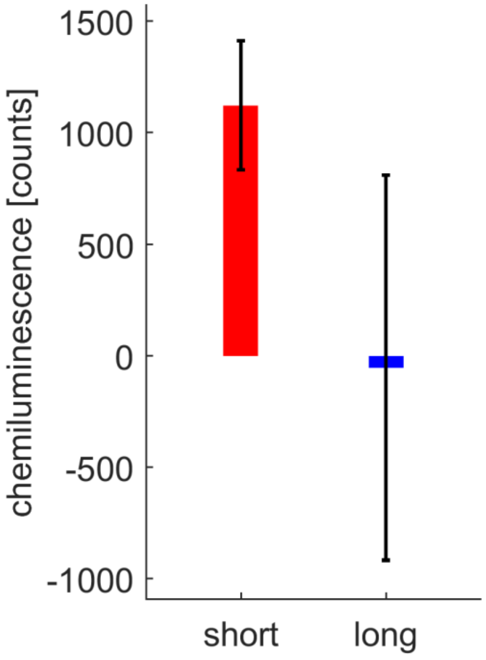
BAL: enhancement by electric pulses



Any difference for treatment with single long pulse vs. several shorter pulses (total duration is same) ?







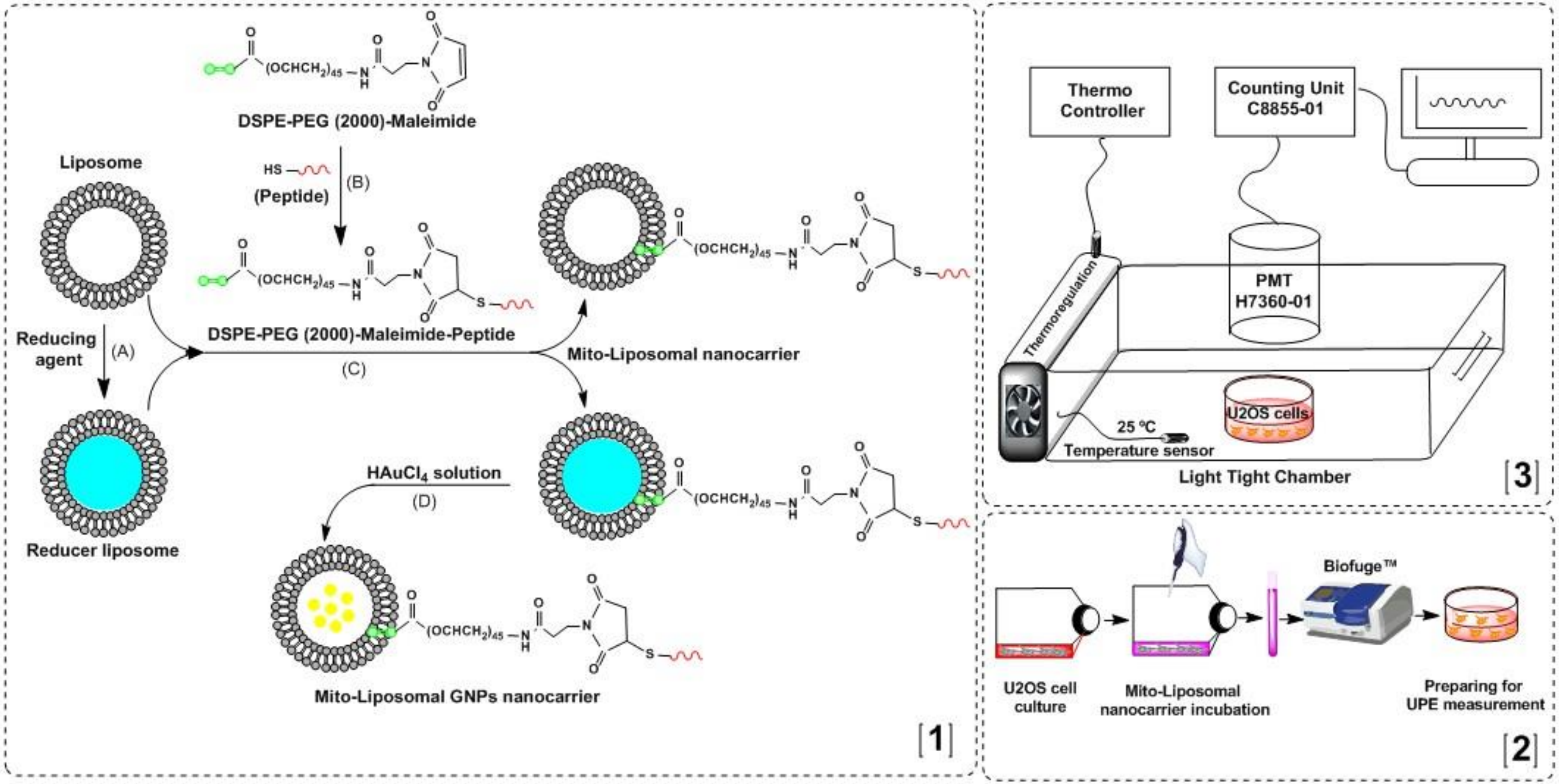
20x 200 kV/m 250 us 1Hz (experiment 129) pulses vs. single 200 kV/m 5 ms pulse (experiment 63)

Chemiluminescence (area under curve), N=3, error bars are standard deviation

Perspective: physical enhacement of biological autoluminescence

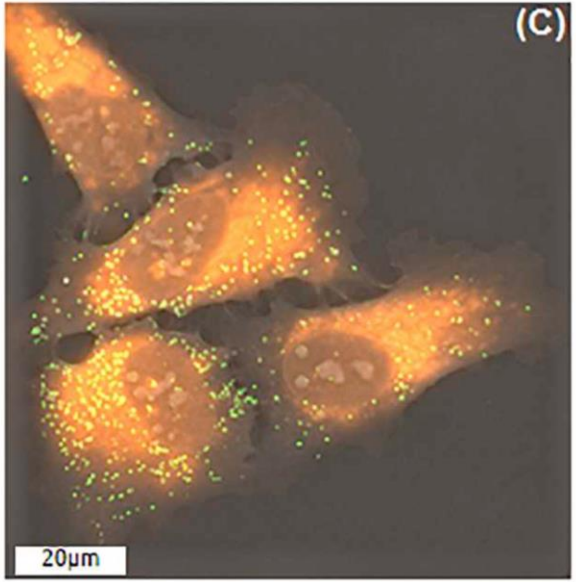
nanoparticles

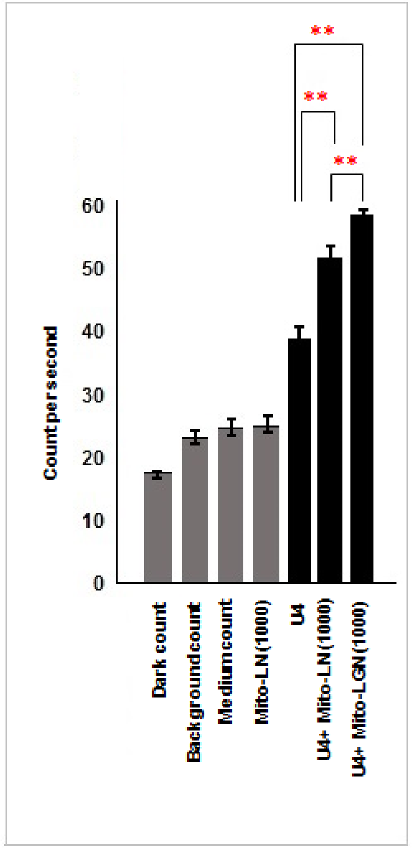
BAL: enhancement by nanoparticles



Sardarabadi *et al., Journal of Photochemistry and Photobiology B, 2020,* 204, 111812

Nanoparticles delivery and BAL signal enhancement in osteosarcoma cells





Orange – mitochondria

Green – gold nanoparticles

Sardarabadi *et al., Journal of Photochemistry and Photobiology B, 2020,* 204, 111812

Take-home message

BIOLOGICAL AUTOLUMINESCENCE

- relaxation of excited electron states of bio/molecules generated endogenously in biosystems

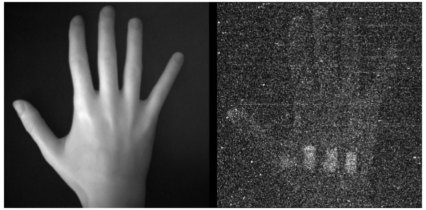
- excitation energy from oxidative reactions with biomolecules

$[A] + [B] \rightarrow [P^*] \rightarrow [P]$ + **photon**

PERSPECTIVE DIAGNOSTICS OF OXIDATIVE STRESS/ PROCESSES

- applications in biomedicine (and beyond)
- fingerprints: intensity, spectra, signal properties ?
- physical enhancement of the signal

- non-invasive
- almost real-time
- low operation costs
- label-free



Springer book on biological autoluminescence

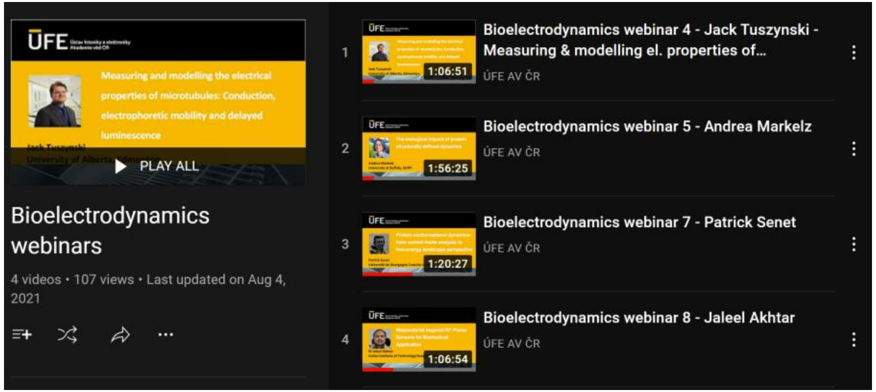
Springer

Covering topics from quantum & physical chemistry to applications, potential biological significance, and history

Editors I. Volodyaev, Yu. Vladimirov, E. Van Wijk, M. Cifra

Bioelectrodynamics webinars

- every second week - typically Mondays
- electromagnetics & biophysics
- follow our social media to register and to get to an emailing list
- Youtube channel of ÚFE AV ČR



Make science fiction a reality

twitter.com/BioED_IPE

www.facebook.com/bioedIPE

www.linkedin.com/company/bioelectrodynamics

bioed.ufe.cz

cifra@ufe.cz