http://flnph.jinr.ru/images/LifeSciencesBook.pdf

When nuclear physics applies to LIFE SCIENCES

at Frank Laboratory of Neutron Physics

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[2]Faculty of Pharmacy, Comenius University, Bratislava, Slovakia
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International Conference on Neutron Scattering
Buenos Aires, Argentina: August 25, 2022

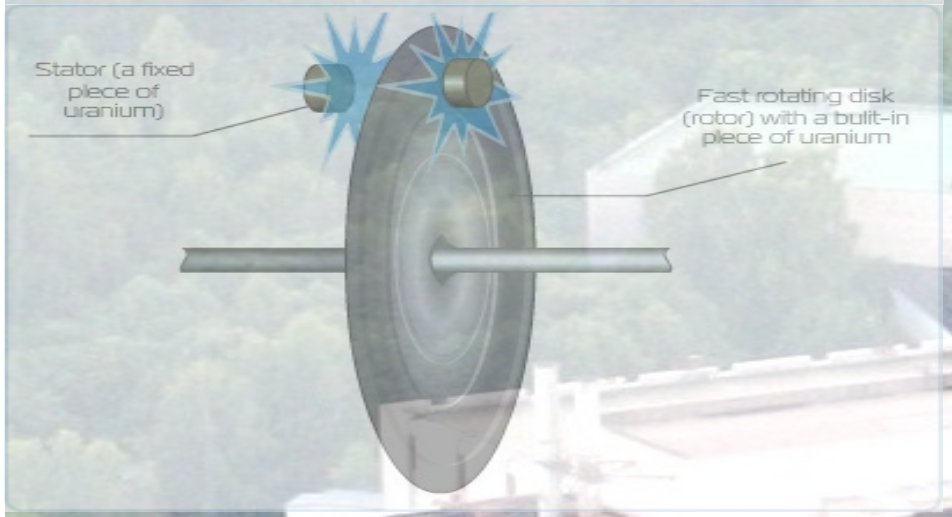
JOINT INSTITUTE FOR NUCLEAR RESEARCH

Outline

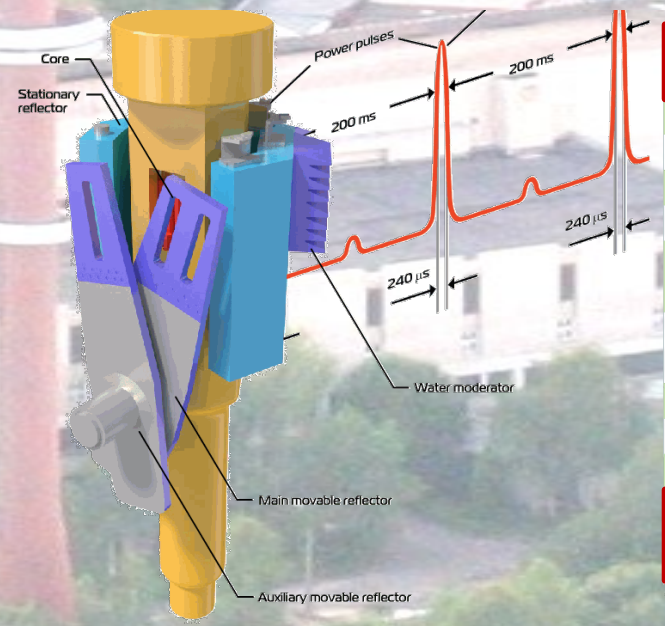
- **Pulsed reactor IBR-2**
- **Applications to Environmental Studies**
  - Monitoring the pollution in air, water, and soil
  - Protecting the plants
- **Fundamental Studies of Health and Medicine**
  - Crossing the membrane whilst defending the cell
  - Superstructures in signaling systems and behind the eye
  - Tracking the aging, challenging and curing diseases

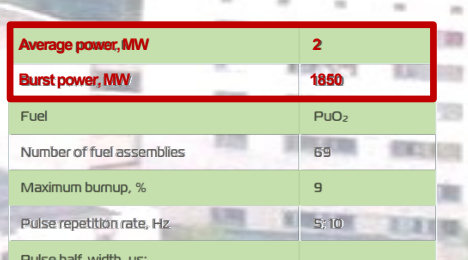
High Flux Pulsed Reactor IBR

Idea of IBR in 1955



- IBR-2 operating at 2 MW operates from 1984
- modernization of all components 2006-2010
- IBR-2 service life until 40th (additional refueling)

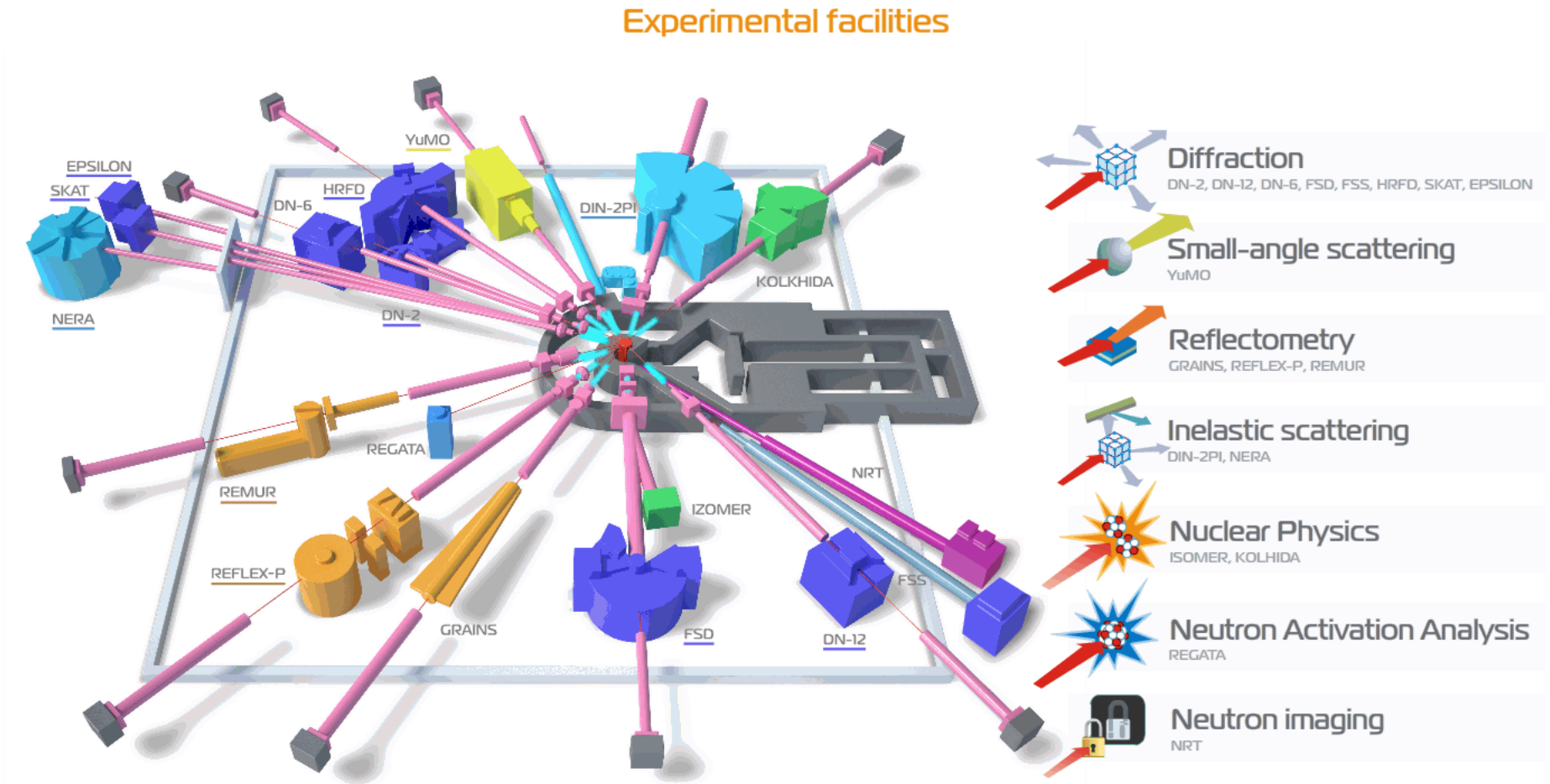




Average power, MW	2
Burst power, MW	1850
Fuel	PuO_2
Number of fuel assemblies	69
Maximum burnup, %	9
Pulse repetition rate, Hz	5; 10
Pulse half-width, μs: fast neutrons thermal neutrons	 240 320
Rotation rate, rev/min: main reflector auxiliary reflector	 600 300
MMR and AMR material	nickel + steel
MR service life, hours	55000
Background, %	7.5
Thermal neutron flux density from the surface of the moderator*: - time average - burst maximum	 ~10^{13} n/cm^{2}s ~10^{15} n/cm^{2}s

*Upgrade details on the thermal neutron flux density after the modernization will be available when the reactor operates at full power.

Suite of Spectrometers



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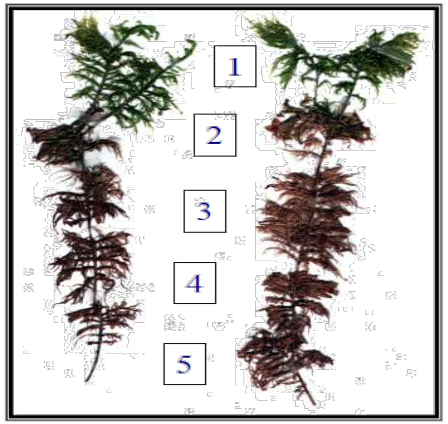
Atmospheric Deposition of Trace Elements

1993: Biomonitoring…

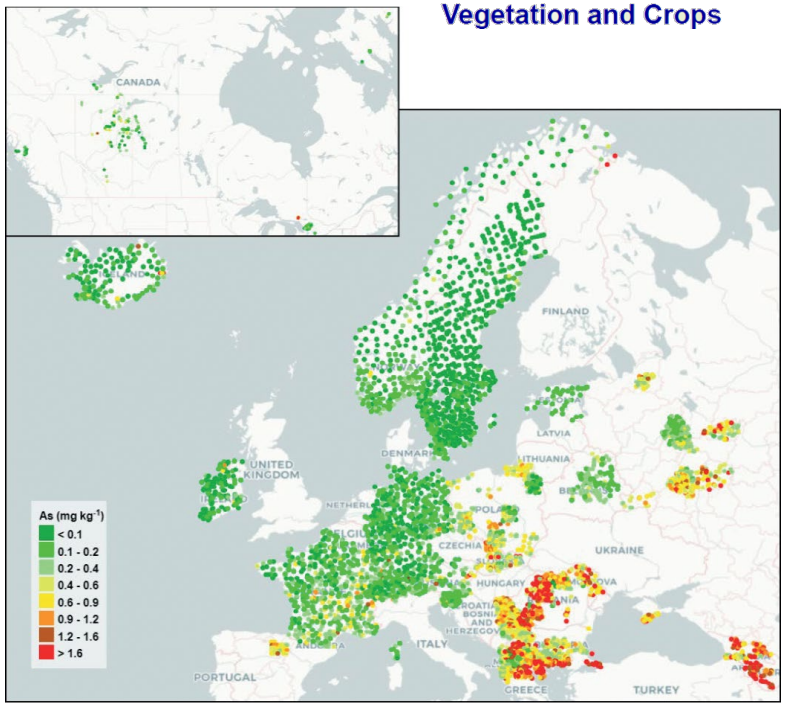
M.V. Frontasyeva, V.M. Nazarov and E. Steinnes. **Mosses as monitors of heavy metal deposition: Comparison of different multi-element analytical techniques.** In R.J. Allan and J.O. Nriagu, eds., *Heavy Metals in the Environment*, Vol.2, pp. 17-20. CEP Consultants, Edinburgh **1993**.



courtesy of Dr. M.V. Frontasyeva

- **Moss** is used as a monitor of **atmospheric pollution** determined using the **Neutron Activation Analysis** detecting **heavy metals** and other trace elements (up to **45** in total)

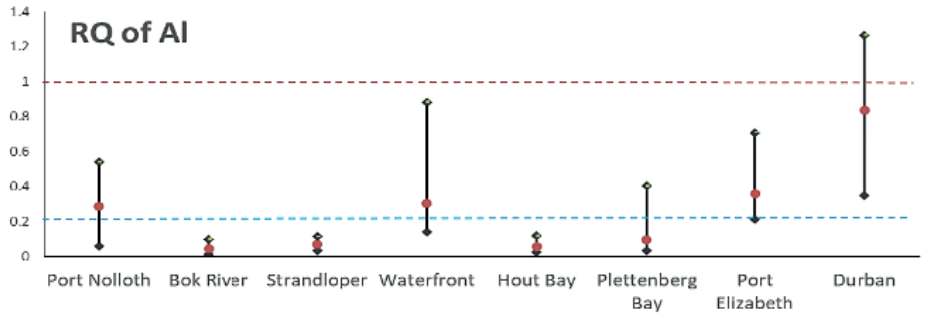
Map of arsenic distribution from the 2015-2016 report

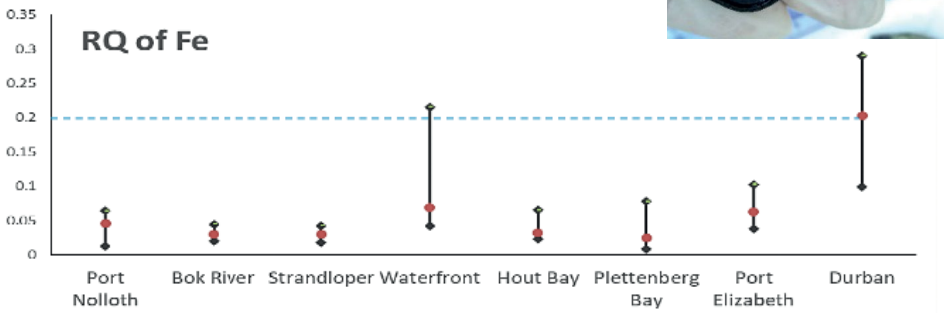


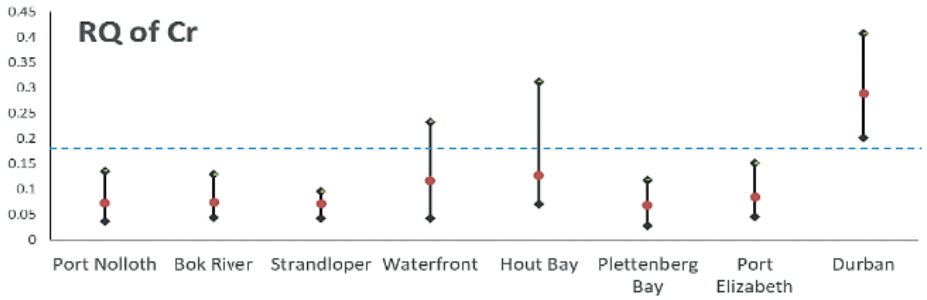
Frontasyeva M. et al., Report of the ICP Vegetation (2020)

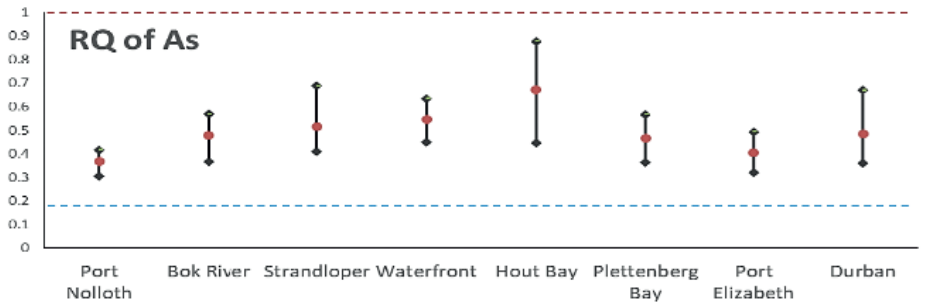
NAA in Safety of Seafood

- A natural bio-monitor for water pollution appear conveniently **molluscs**







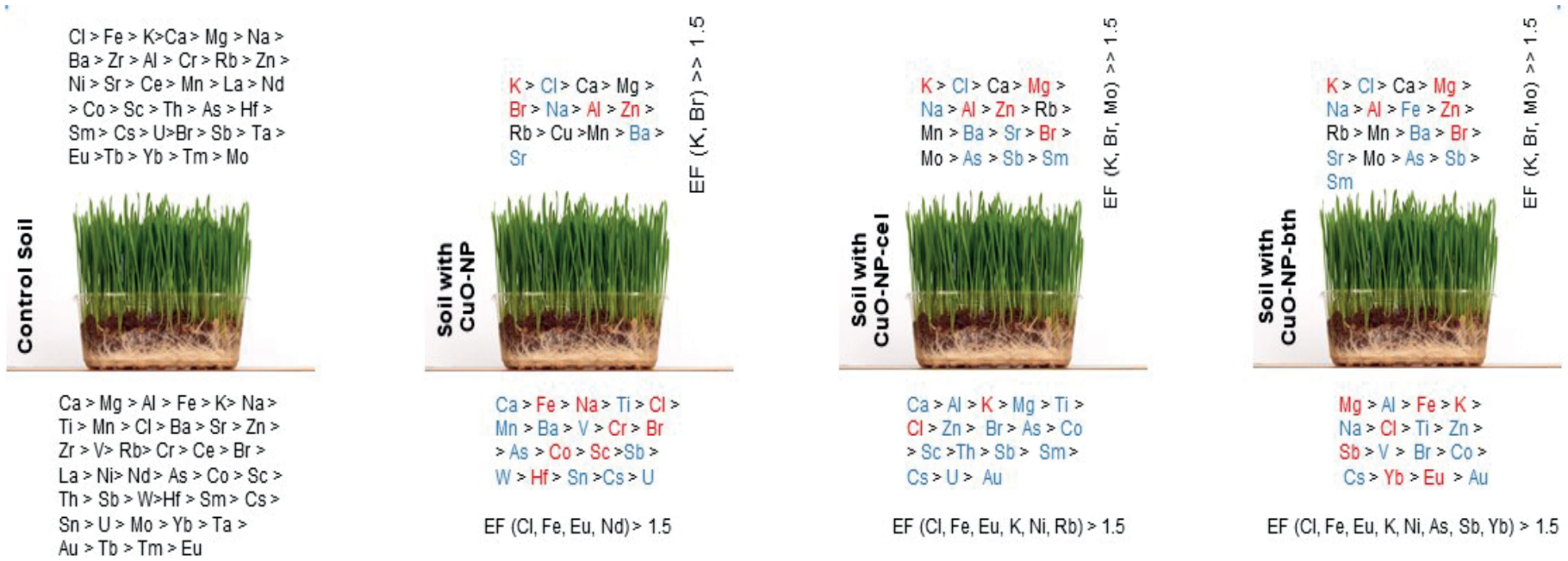


Risk Quotients of various pollutants when consuming mussel tissues at different places

Nekhoroshkov, P.S. et al., J. Food Compos. Anal., 98, p.103825 (2021)

NAA in Safety of Agricultural Plants

- NAA proved valuable also in monitoring the **soil pollution** and identifying the **effect of nanoparticles** (e.g., CuO-NP) on plants



Elements with a decrease/increase in concentration with regard to control value.
EF—enrichment factor with Al as reference element in soil

Lung I et al., Int. J. Environ. Res. Public Health 18(13), 6739 (2021)

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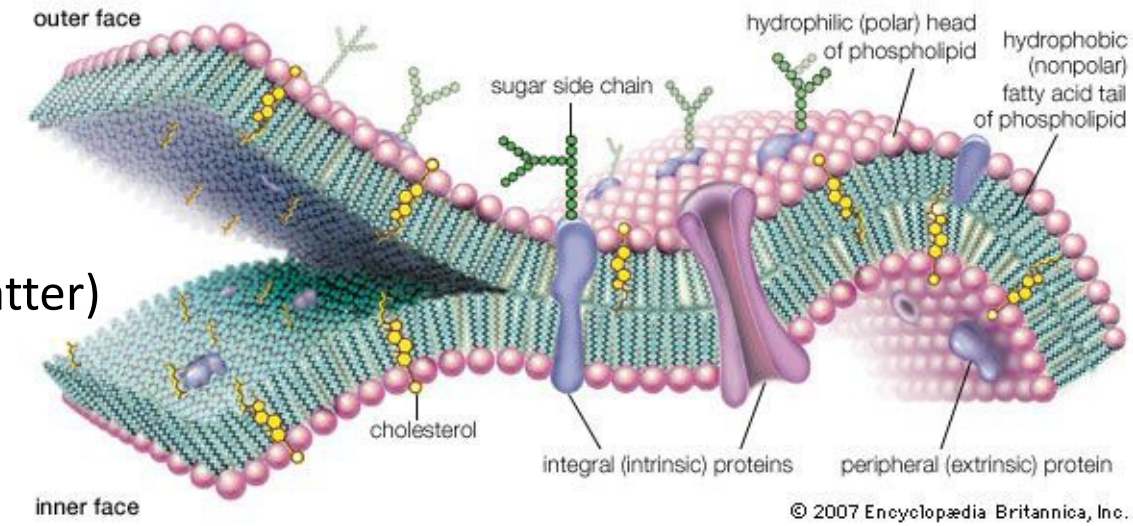
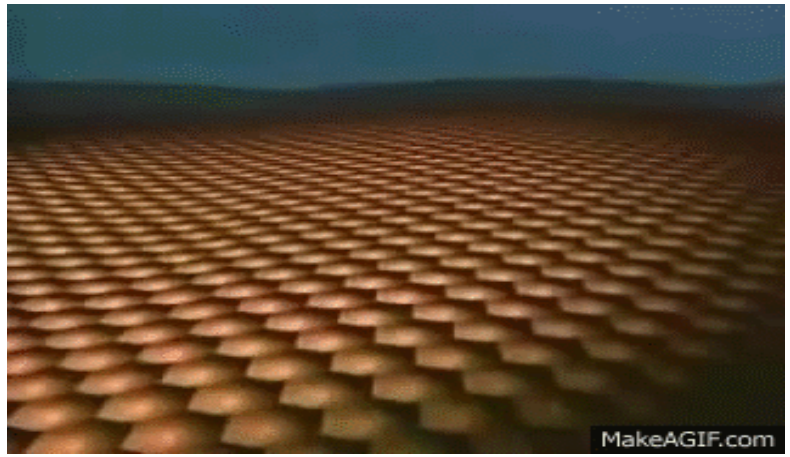
Biological Membranes

- Protection (separate cells)
- Signaling (transport of information)
- Selective permeability (transport of matter)

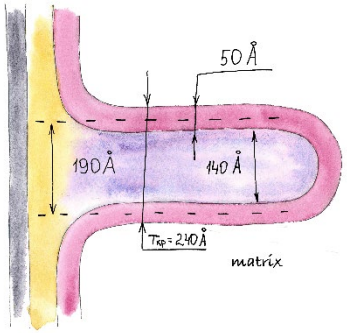


- Active functions are mainly provided by proteins
- However, overall functionality depends strongly on the structure of an underlying lipid matrix
- Lipid matrix is a 2D liquid, where:
  - lipids and proteins diffuse almost freely laterally
  - preserve a **robust structure vertically**

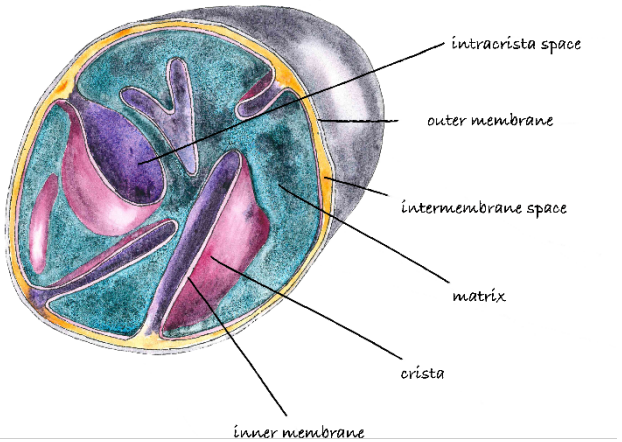


Membranes in “live” functioning mitochondria

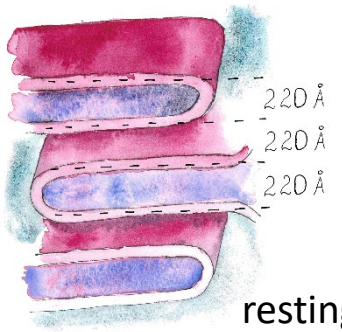
- First-time SANS structural analysis of live mitochondria



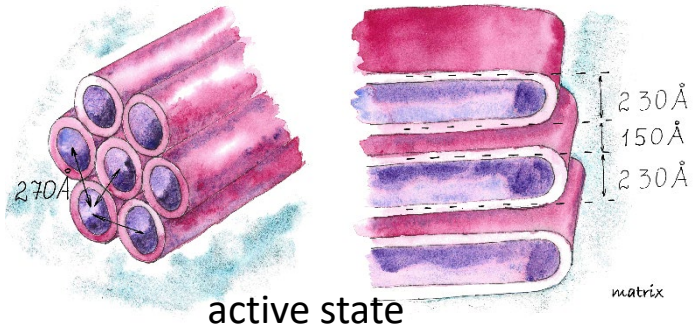
cristae of liver mitochondria form **double-membrane** structure at active state for improved energy efficiency



cristae of heart mitochondria form **highly ordered structures** under both resting and active states due to the high energy demand on the heart tissue



resting state

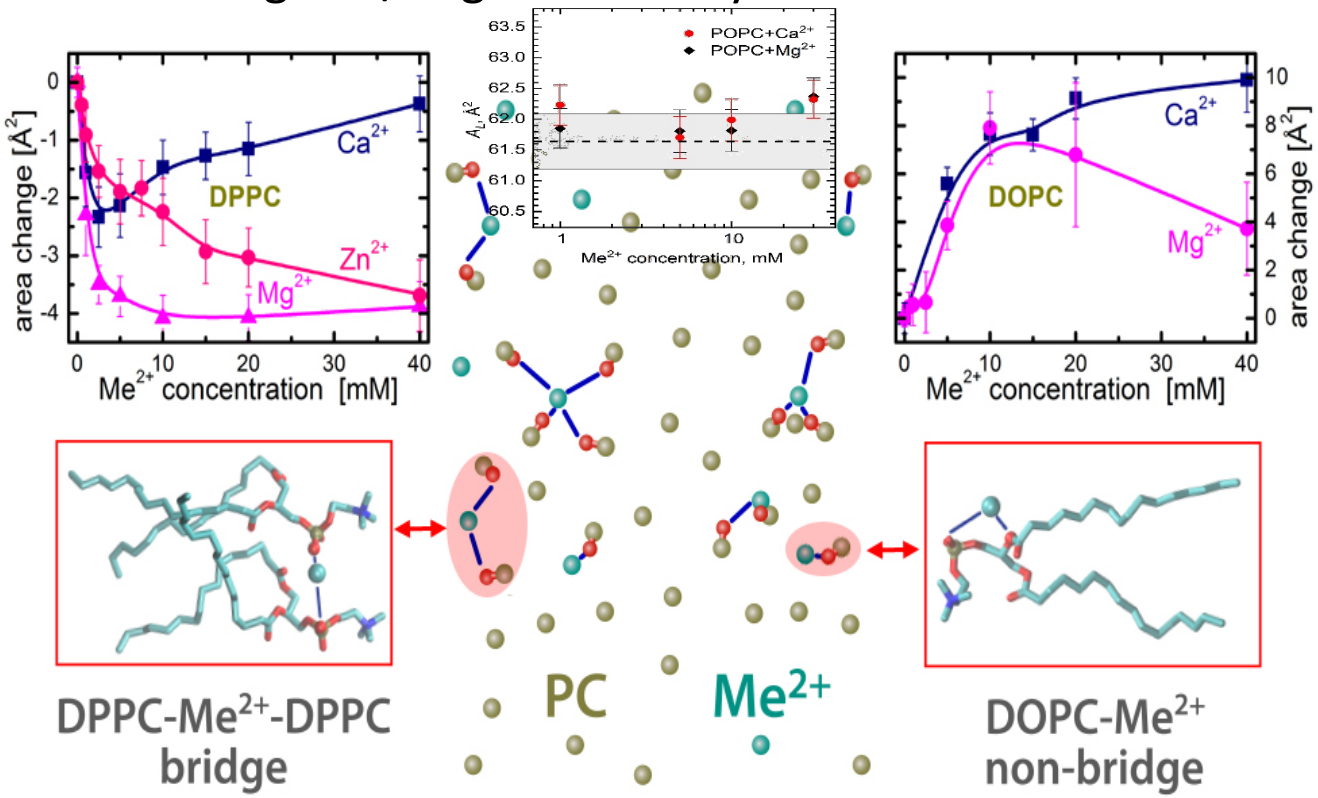


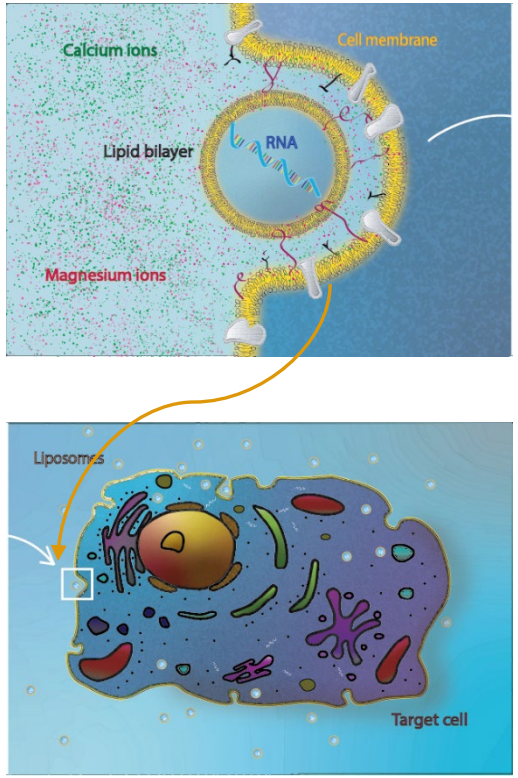
active state

Murugova, T. N., et al. Neutron News 22 (2011)
Moiseeva, V. S., et al. Biochem. Moscow Suppl. Ser. A 11 (2017).
Byvshev, I. M., et al. Biophysics 63 (2018)

Ion-Lipid Interactions in Drug Delivery

- **Lipid-ion interactions** become increasingly important when functionalizing membrane systems with specific applications such as drug and/or gene delivery

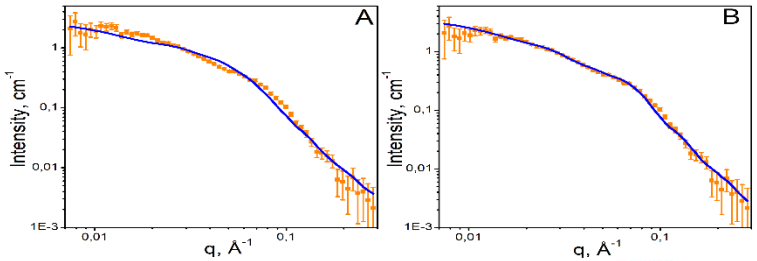


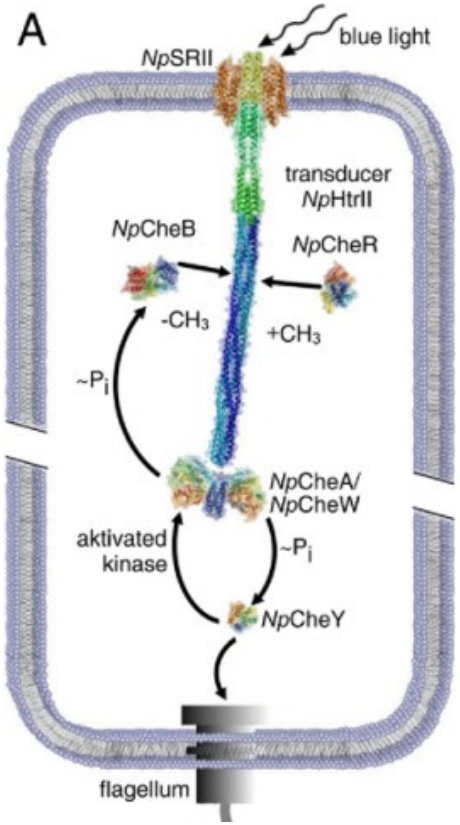


Kučerka, et al. ***Calcium and zinc differentially affect the structure of lipid membranes.*** *Langmuir (2017)*
Kučerka, et al. ***Cation-zwitterionic lipid interactions are affected by the lateral area per lipid.*** *Langmuir (2021)*
Kurakin, et al. ***Cations do not alter the membrane structure of POPC.*** *Frontiers in Mol. Biosc. (2022)*

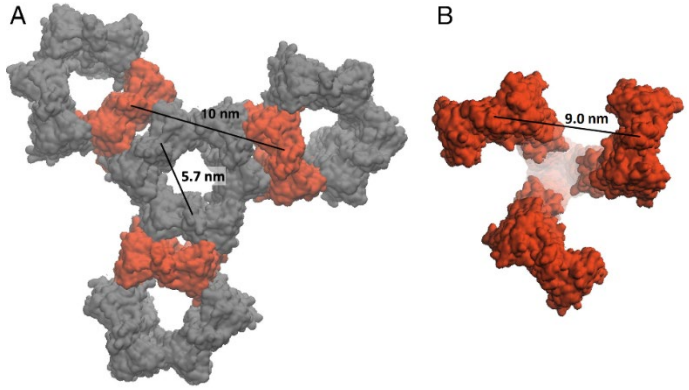
Superstructure of Signaling Systems

- **Two-component systems** (transmembrane proteins in general) are responsible for the communication of microorganisms with their environment

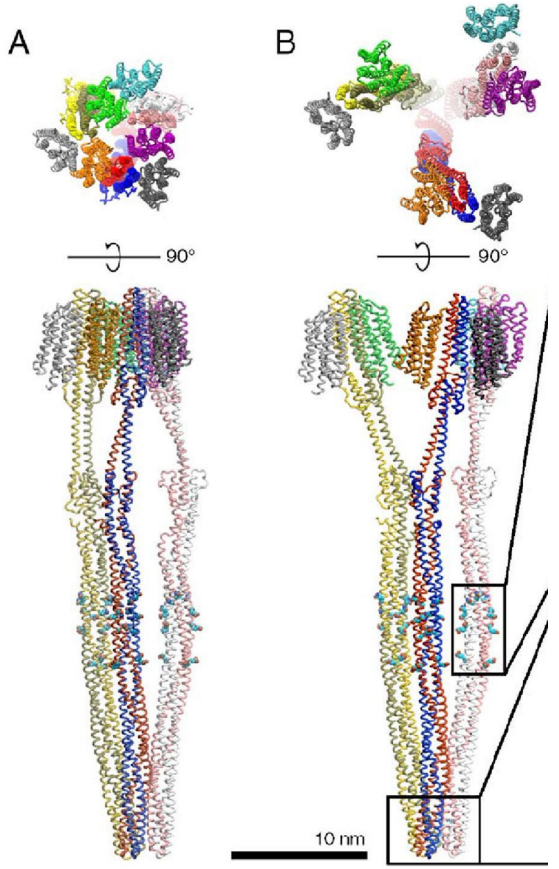




SANS revealed the formation of **trimers of dimers** – that form further the 2D signaling arrays (compact membrane supercomplexes) responsible for amplifying the incoming stimulus



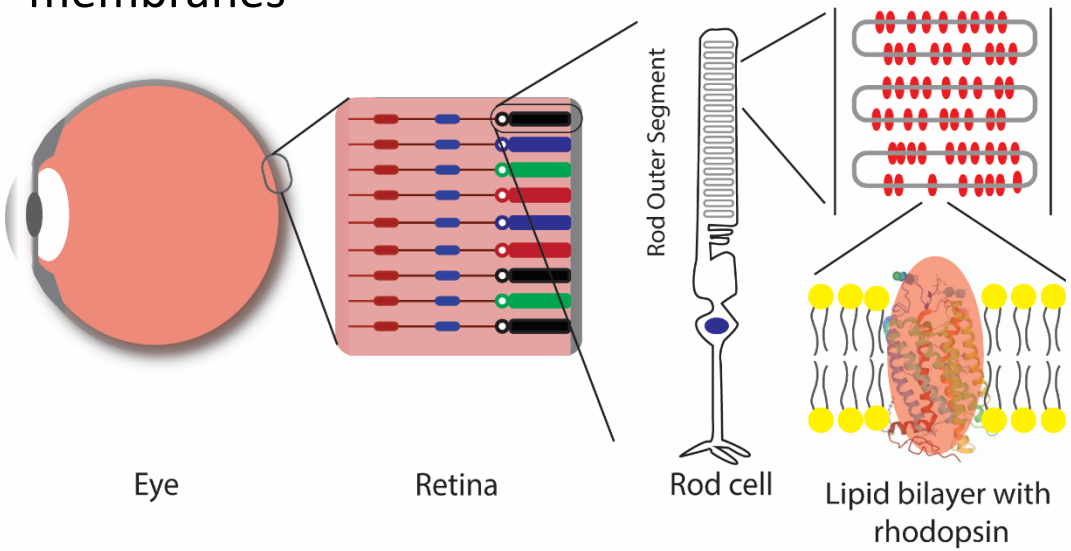
"O"-shaped or **"tripod"-shaped**

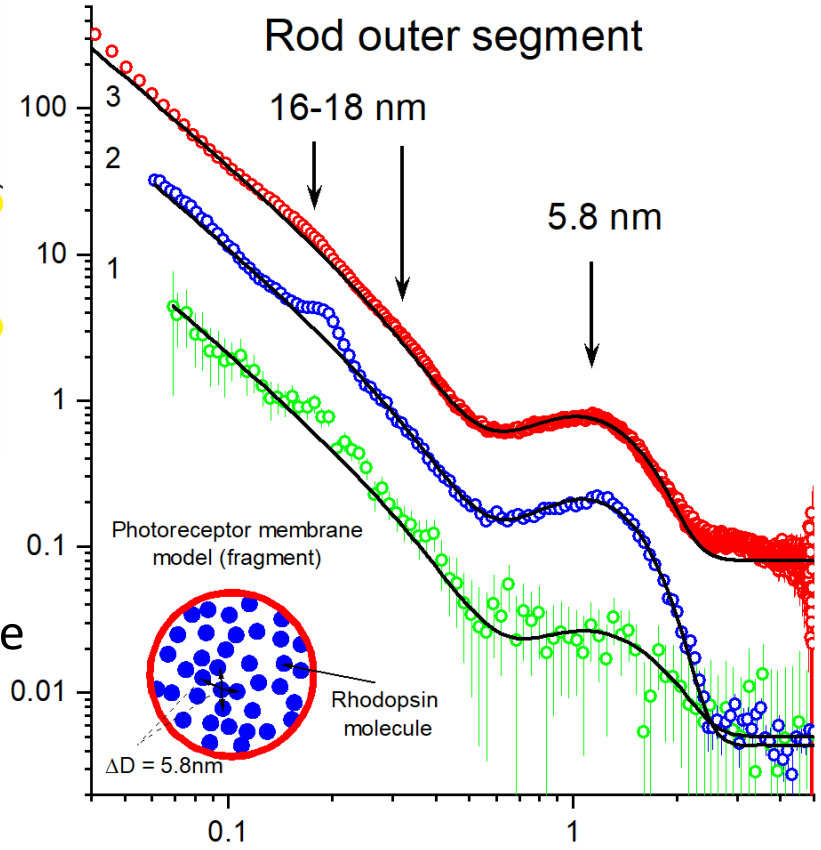


Ryzhykau, et al. Sci Rep 11, 10774 (2021)

Supermolecular Organization of Rhodopsin

- **Visual pigment rhodopsin** is a G-protein coupled receptor in photoreceptor membranes



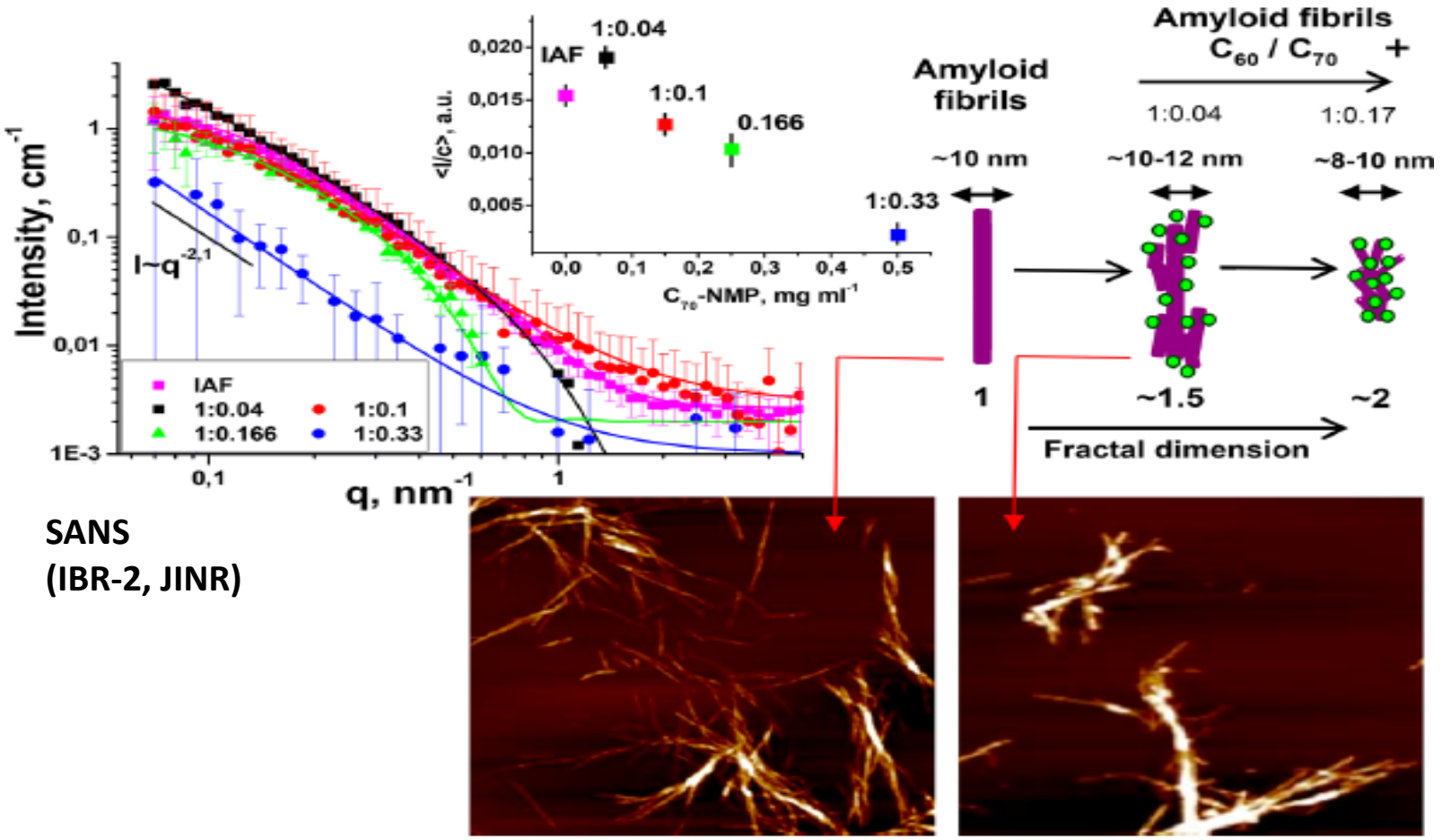


SANS data document a high packing density of rhodopsin molecules, however the average distance between neighbouring molecules suggests their **monomeric state**

Feldman, et al. BBA-Biomembranes 1861 (2019)

Fullerene Nanoparticles against Amyloid Fibrils

- Neutron scattering revealed a **disaggregating impact** of fullerenes on the **amyloid fibrils**.

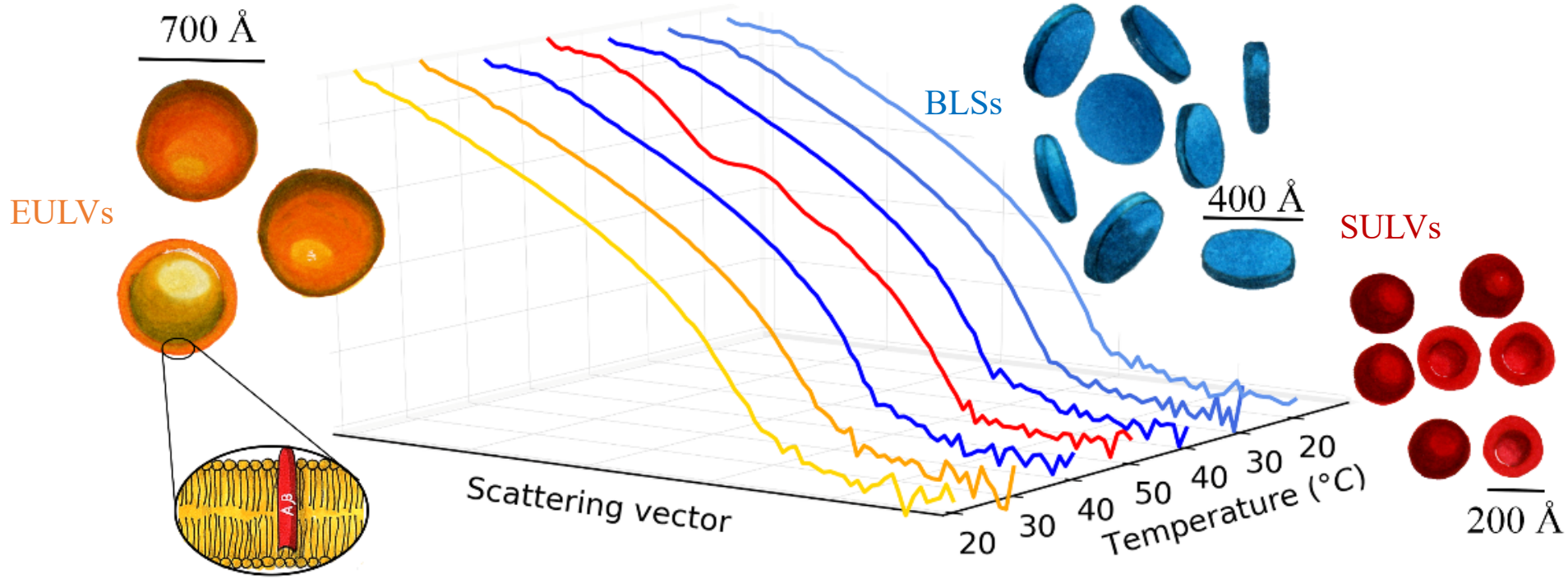


SANS
(IBR-2, JINR)

Nagorna et al., J Mol Liquids (2018)
Šipošová et al., ACS Applied Materials and Interfaces (2020)

Understanding the Mechanism of Alzheimer's Disease

- Neutron scattering allows to study model membranes that replicate **pre-clinical** stage of AD



Changes in the membrane self-organization happen during the thermodynamic phase transitions of lipids and are interpreted as the **peptide driven membrane breakage**.

Oleksandr Ivankov: Amyloid-beta peptide triggers a reorganization of lipid membranes driven by temperature changes

Tatiana Murugova: To the root of mechanism for a structural reorganization of lipid membranes triggered by Aβ-peptide

Ivankov, Murugova, Ermakova, Kondela, Badreeva, Soloviov, Kuklin, Kučerka, Sci Rep 11, 21990 (2021)

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THANK YOU FOR YOUR ATTENTION

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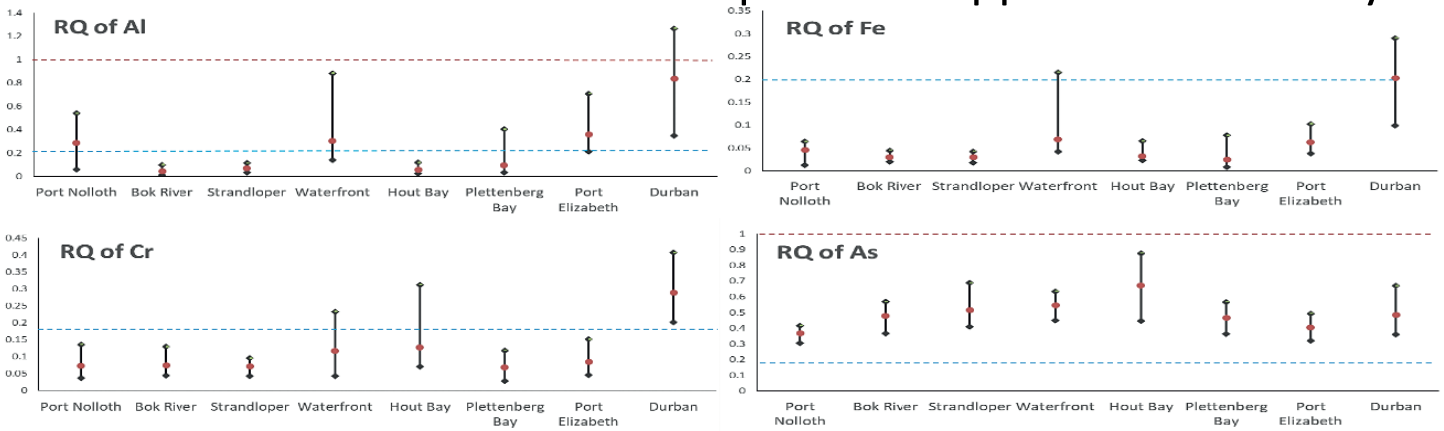

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Nekhoroshkov, P.S. et al., J. Food Compos. Anal., 98, p.103825 (2021)

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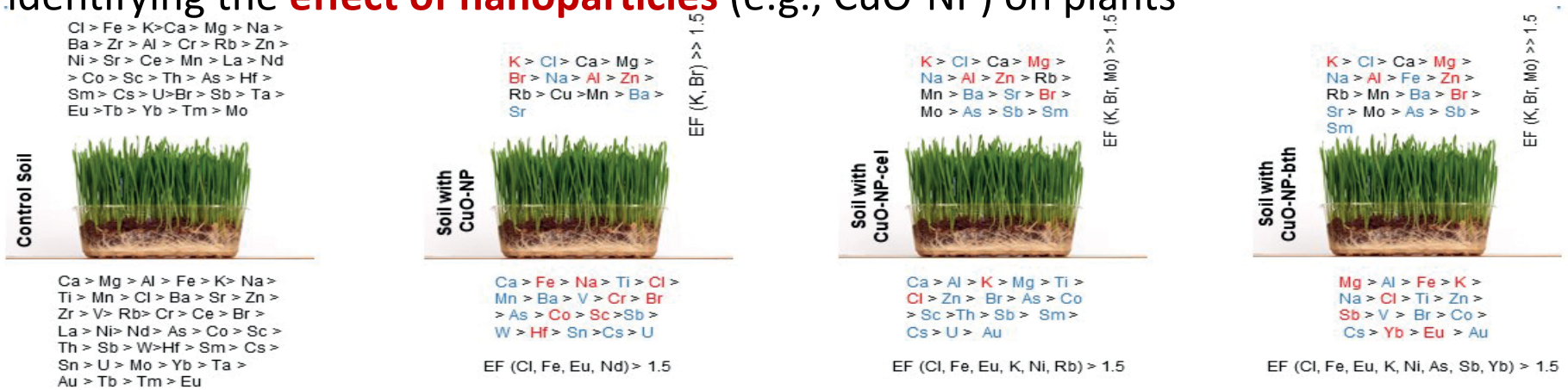
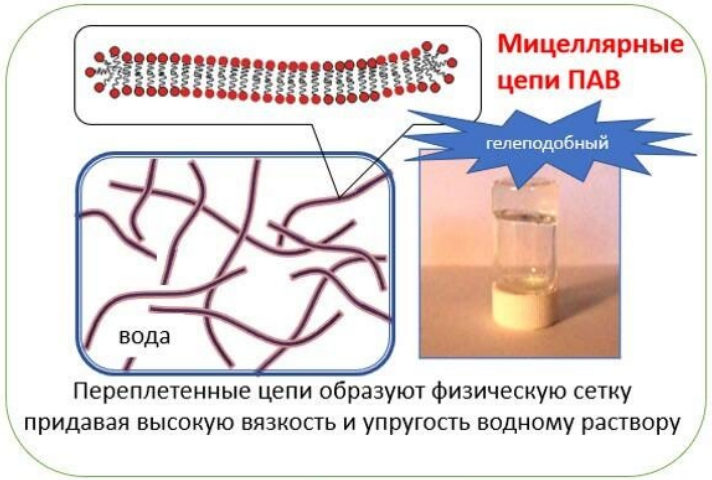
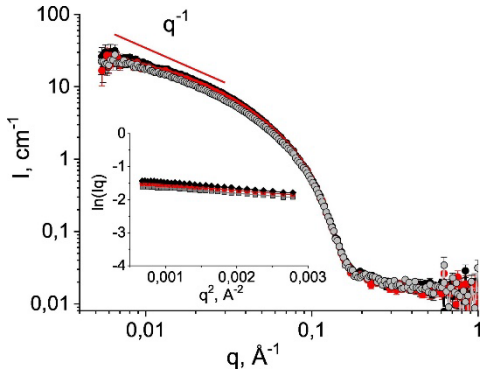


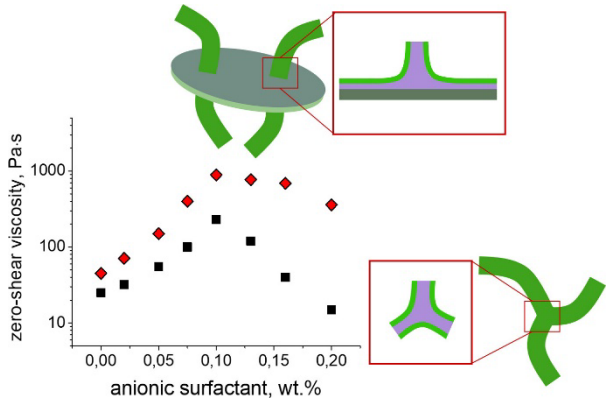
Lung I et al., Int. J. Environ. Res. Public Health 18(13), 6739 (2021)

Plant Protection Products in Agriculture

- A

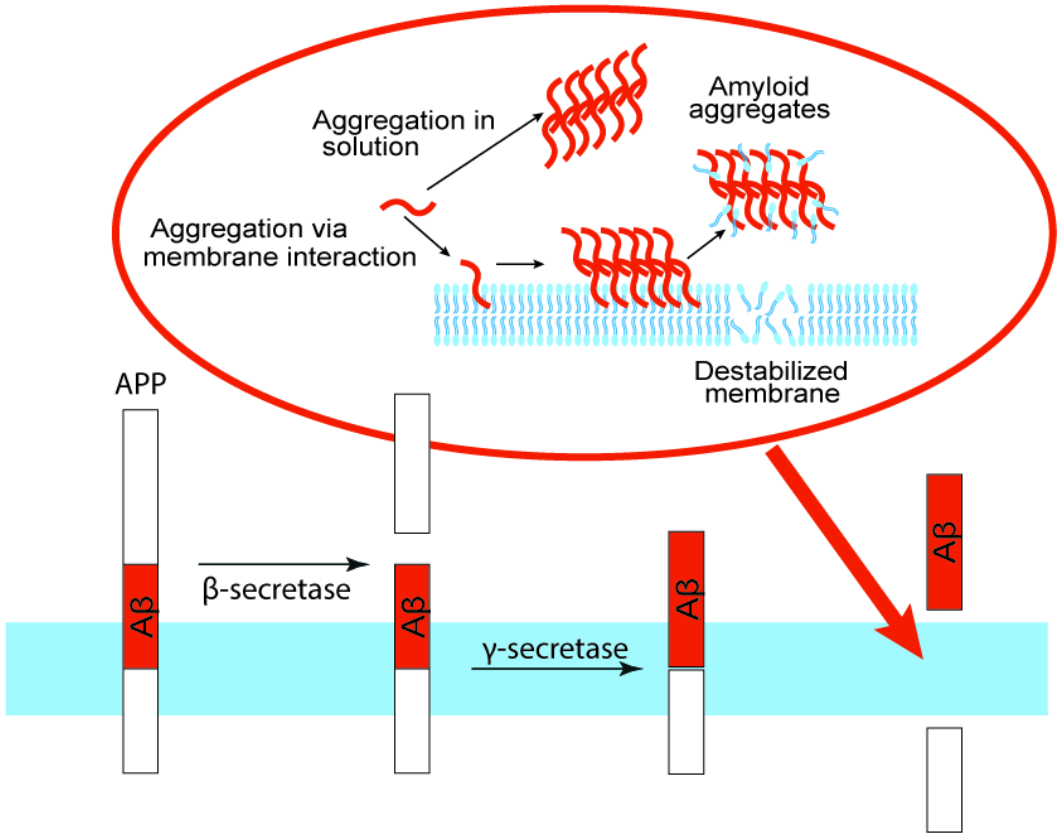


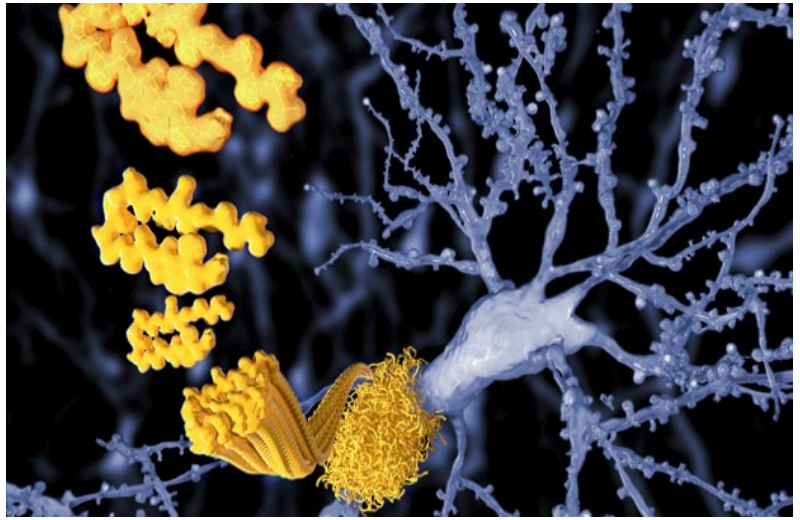




Molchanov V.S. et al., J Mol Liq 314 (2020)

Alzheimer's Disease





Amyloid fibrils are a fingerprint characteristic to AD

The main role in the **initiation of fibrils** may however be played by **membrane-peptide interactions**

User Program