

When nuclear physics applies to **LIFE** SCIENCES

at Frank Laboratory of Neutron Physics



Norbert Kučerka,^{1,2} **Otilia Culicov**,^{1,3} **Dorota Chudoba**,¹ **Mikhail Avdeev**,¹
Valery Shvetsov¹

¹Frank Laboratory of Neutron Physics, JINR, Dubna

²Faculty of Pharmacy, Comenius University, Bratislava, Slovakia

³INCDIE ICPE – CA (ICPE – Advanced Researches), Bucharest, Romania

International Conference on Neutron Scattering
Buenos Aires, Argentina: August 25, 2022



JOINT INSTITUTE
FOR NUCLEAR RESEARCH

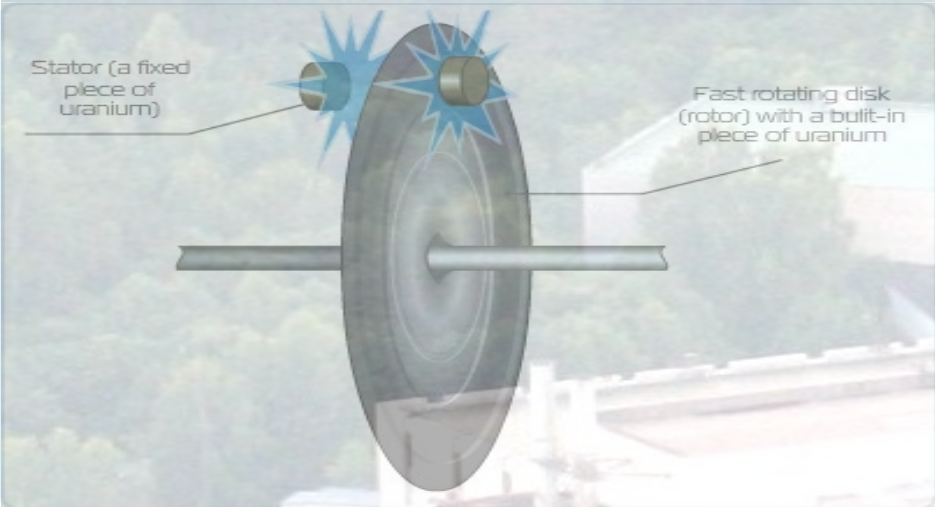


Outline

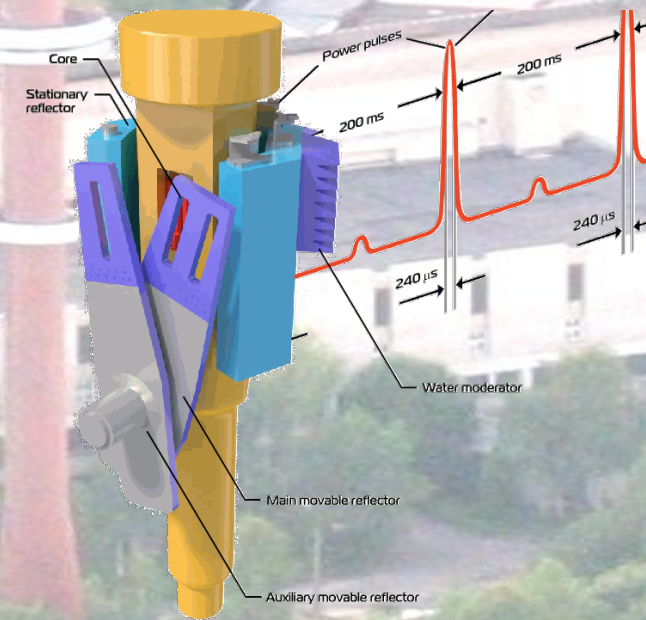
- **Pulsed reactor IBR-2**
- **Applications to Environmental Studies**
 - Monitoring the pollution in air, water, and soil
 - Protecting the plants
- **Fundamental Studies of Health and Medicine**
 - Crossing the membrane whilst defending the cell
 - Superstructures in signaling systems and behind the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

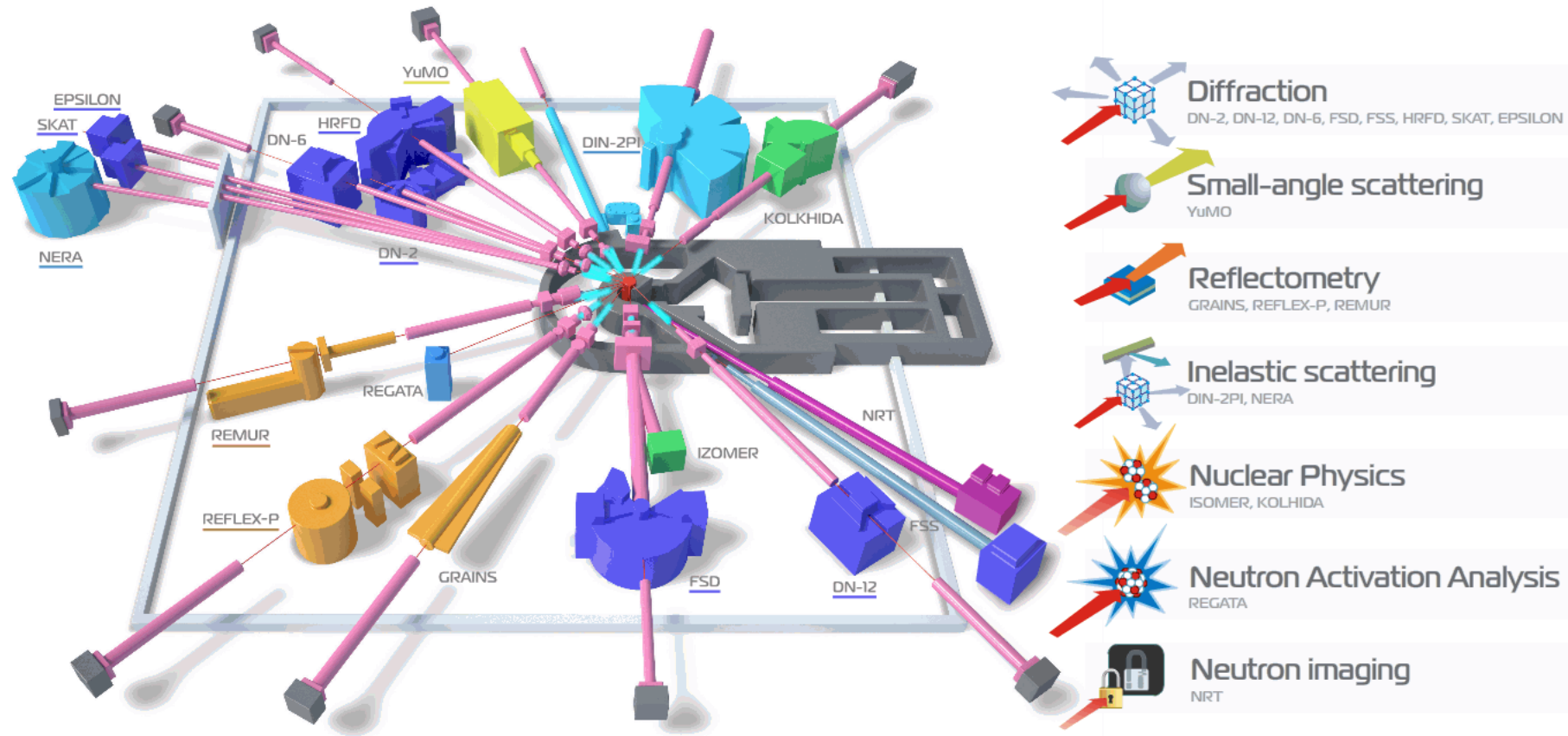


Average power, MW	2
Burst power, MW	1880
Fuel	PuO ₂
Number of fuel assemblies	69
Maximum burnup, %	9
Pulse repetition rate, Hz	5:10
Pulse half-width, μs: fast neutrons thermal neutrons	240 320
Rotation rate, rev/min: main reflector auxiliary reflector	600 300
MMR and AMR material	nickel + steel
MR service life, hours	55000
Background, %	7.5
Thermal neutron flux density from the surface of the moderator ² : - time average - burst maximum	~10 ¹² n/cm ² ·s ~10 ¹⁸ n/cm ² ·s

²More precise values for the thermal neutron flux density from the moderator will be available in the future.

Suite of Spectrometers

Experimental facilities





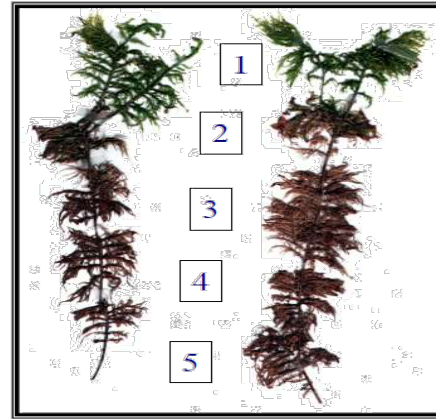
Outline

- 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

Atmospheric Deposition of Trace Elements

1993: Biomonitoring...

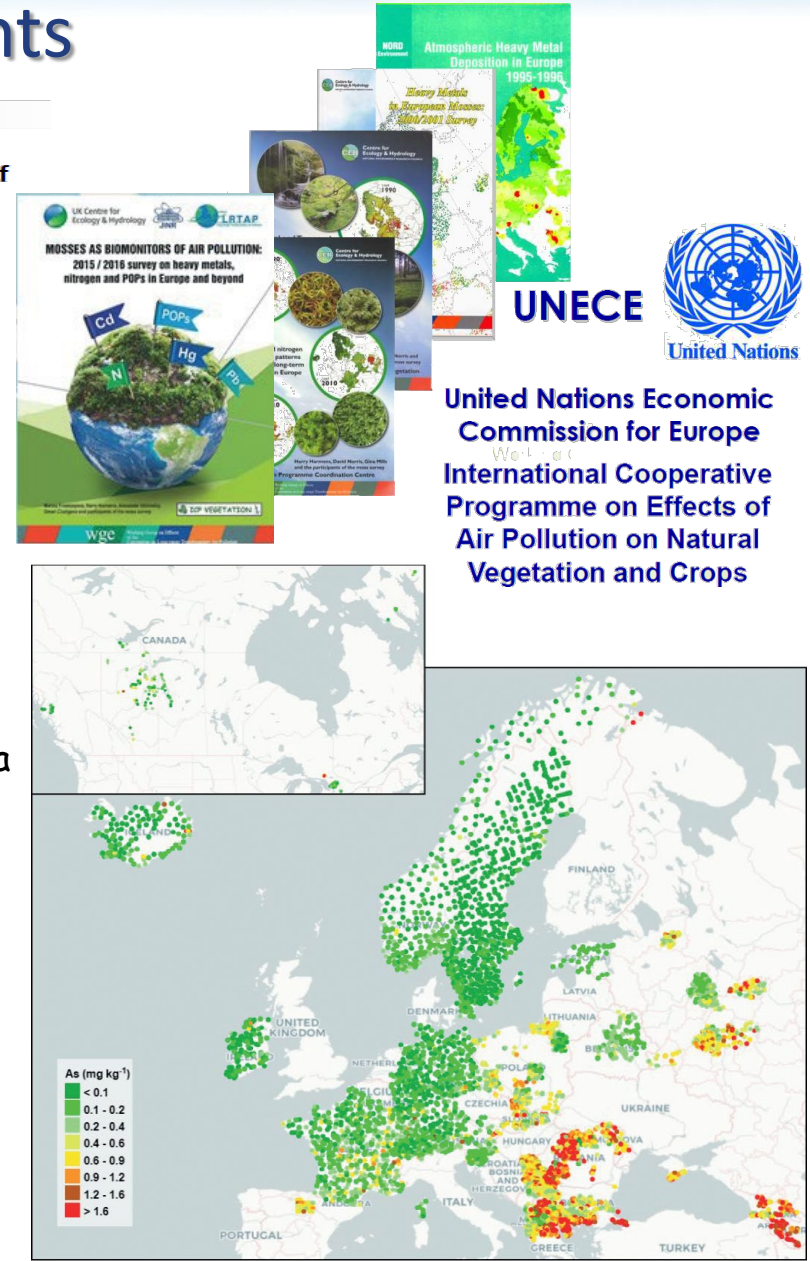
M.V. Frontasyeva, V.M. Nazarov and E. Steinnes. **Mosses as monitors of heavy metal deposition: Comparison of different multi-element analytical techniques.** In R.J. Allan and J.O. Nriagu, eds., *Heavy Metals in the Environment*, Vol.2, pp. 17-20. CEP Consultants, Edinburgh **1993**.



courtesy of Dr. M.V. Frontasyeva

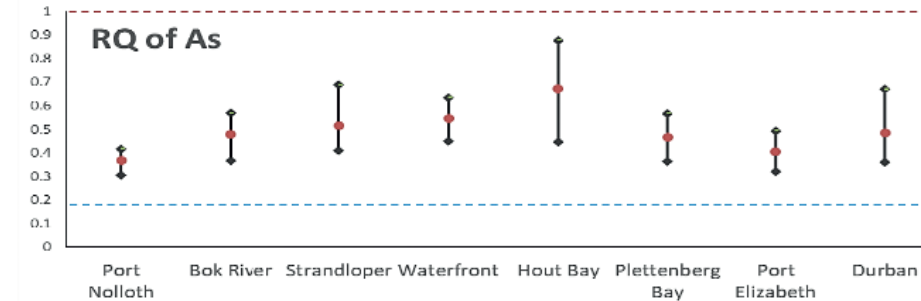
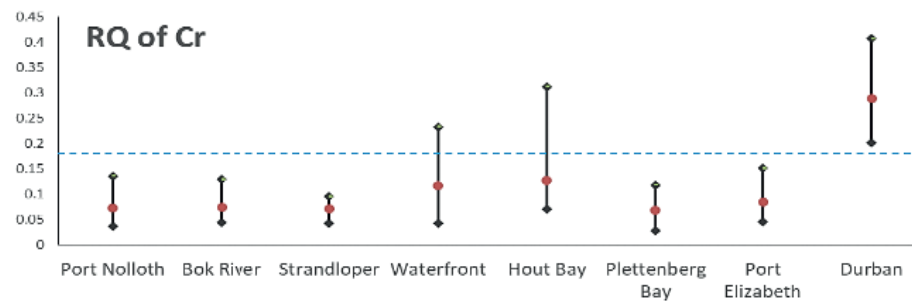
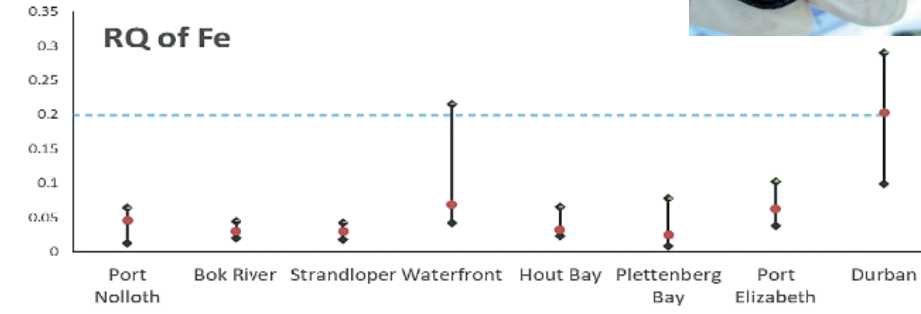
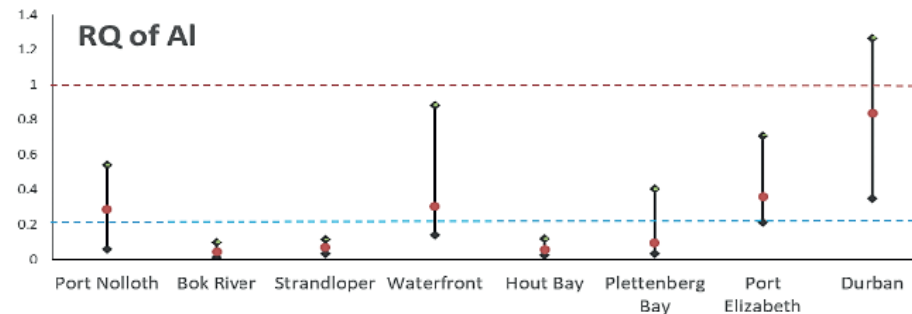
- Moss is used as a monitor of **atmospheric pollution** determined using the **Neutron Activation Analysis** detecting **heavy metals** and other trace elements (up to **45** in total)

Map of arsenic distribution from the 2015-2016 report



NAA in Safety of Seafood

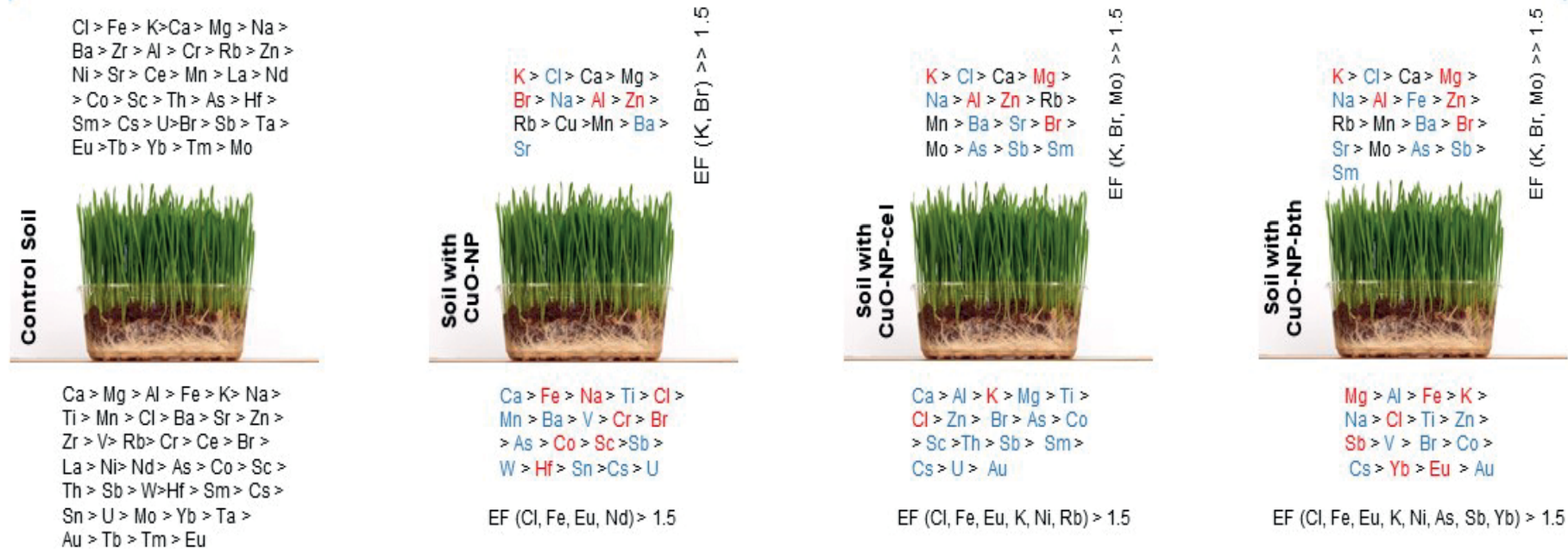
- A natural bio-monitor for water pollution appear conveniently **molluscs**



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

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

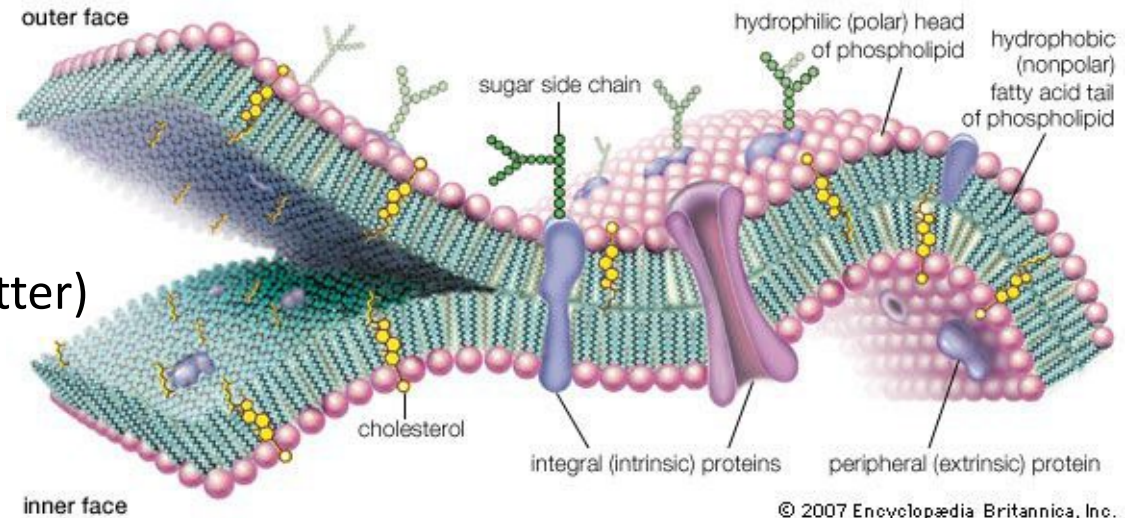


Outline

- 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

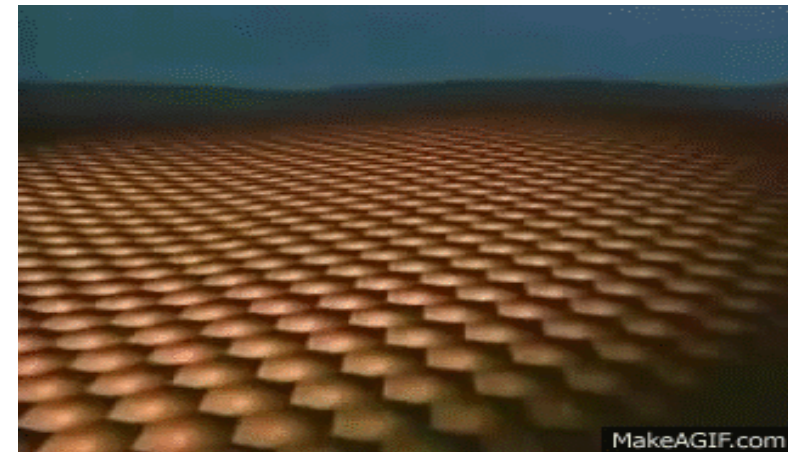
Biological Membranes

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



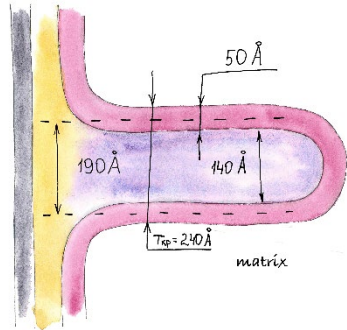
© 2007 Encyclopædia Britannica, Inc.

- 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**

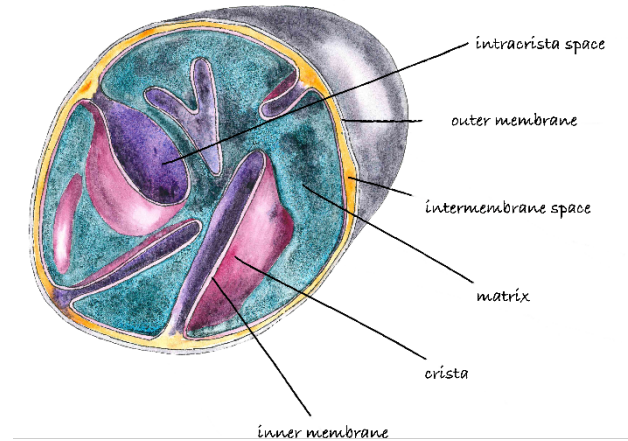


Membranes in “live” functioning mitochondria

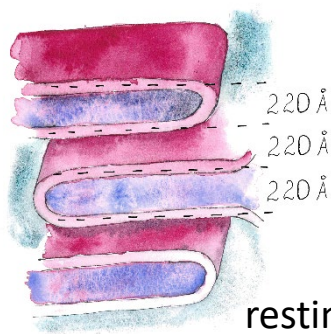
- First-time SANS structural analysis of live mitochondria



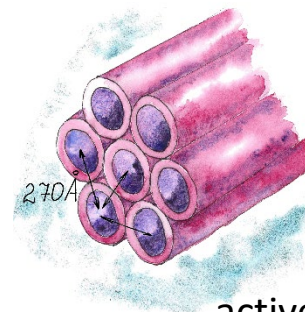
cristae of liver mitochondria form **double-membrane** structure at active state for improved energy efficiency



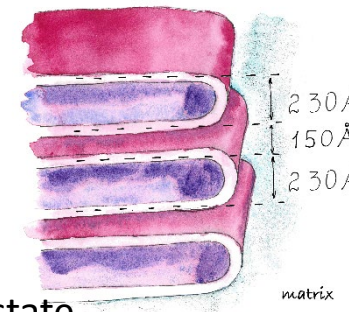
cristae of heart mitochondria form **highly ordered structures** under both resting and active states due to the high energy demand on the heart tissue



resting state



active state



matrix

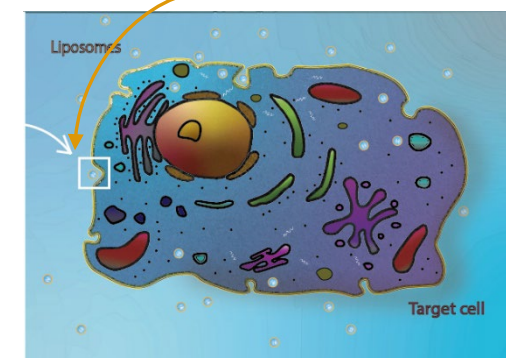
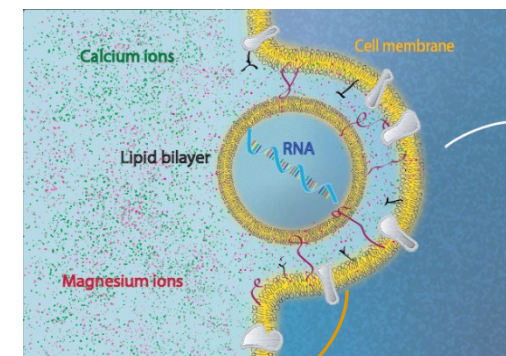
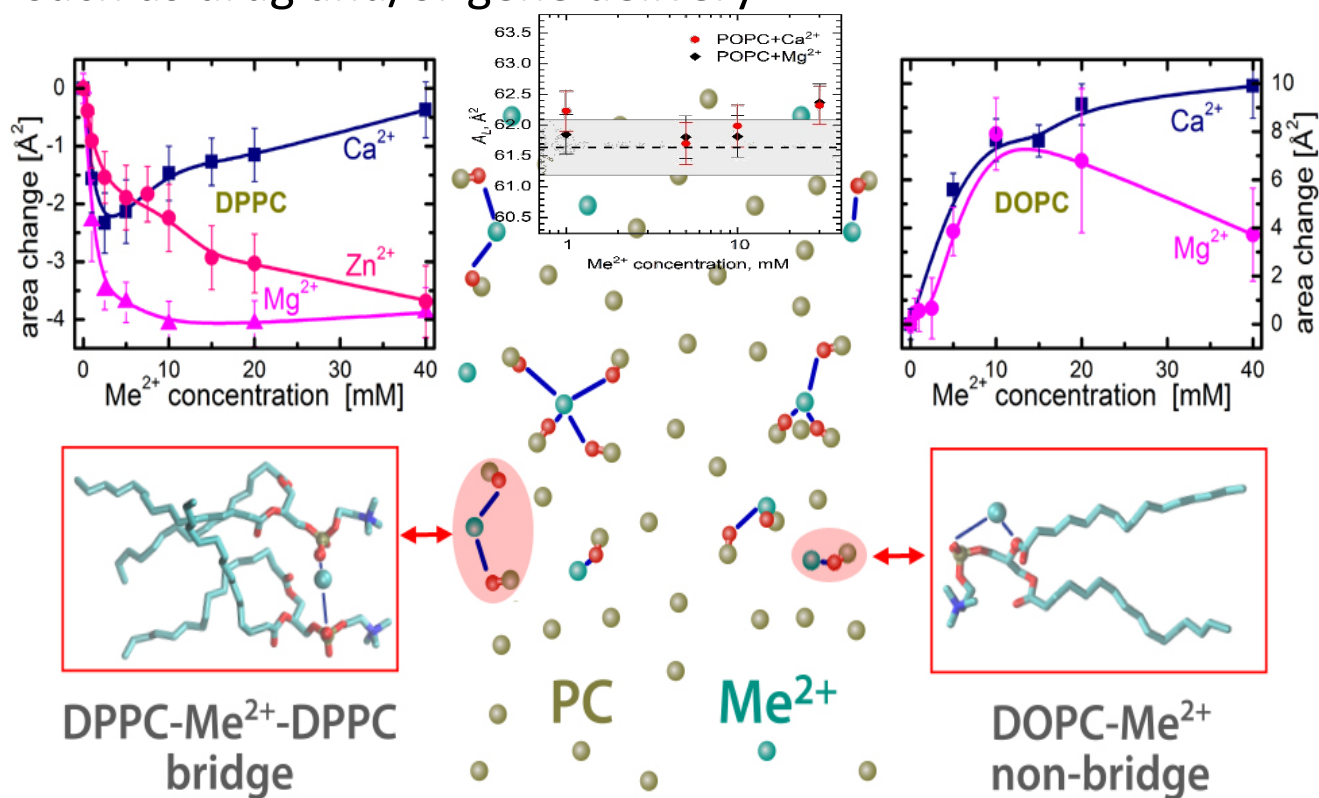
Murugova, T. N., et al. Neutron News 22 (2011)

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

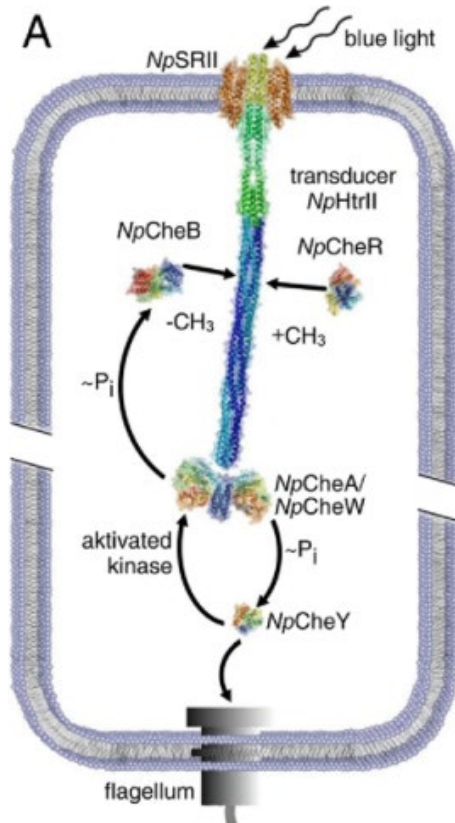
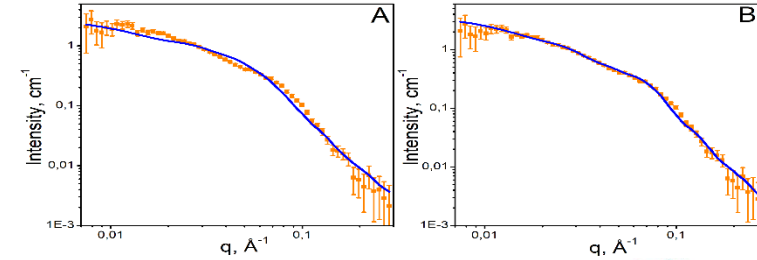
- **Lipid-ion interactions** become increasingly important when functionalizing membrane systems with specific applications such as drug and/or gene delivery



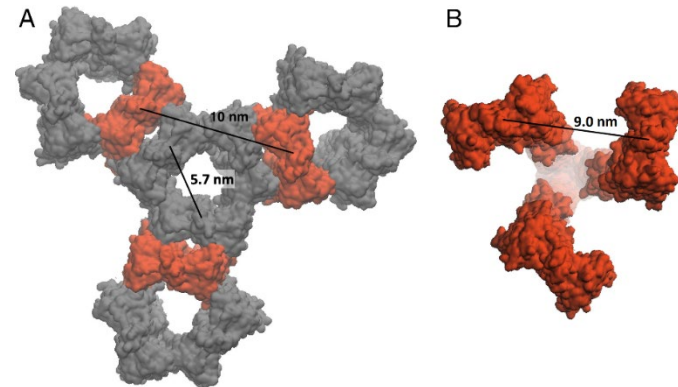
Kučerka, et al. **Calcium and zinc differentially affect the structure of lipid membranes.** *Langmuir* (2017)
 Kučerka, et al. **Cation-zwitterionic lipid interactions are affected by the lateral area per lipid.** *Langmuir* (2021)
 Kurakin, et al. **Cations do not alter the membrane structure of POPC.**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

Superstructure of Signaling Systems

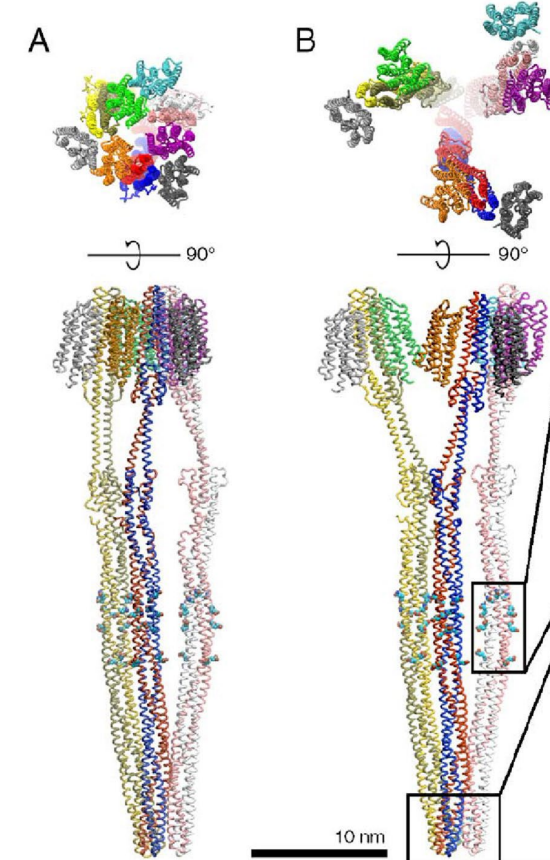
- **Two-component systems** (transmembrane proteins in general) are responsible for the communication of microorganisms with their environment



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

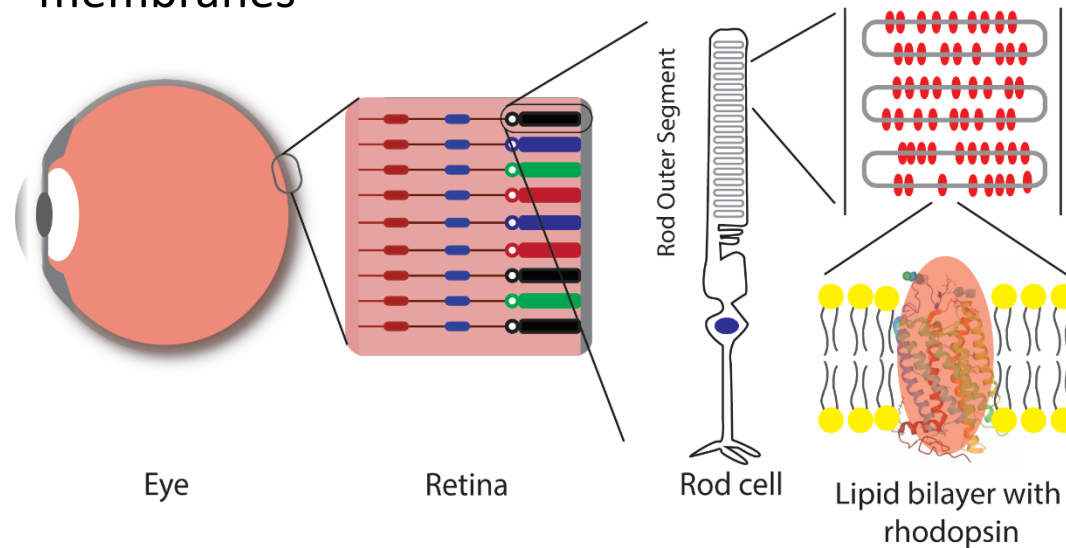


“O”-shaped or **“tripod”-shaped**

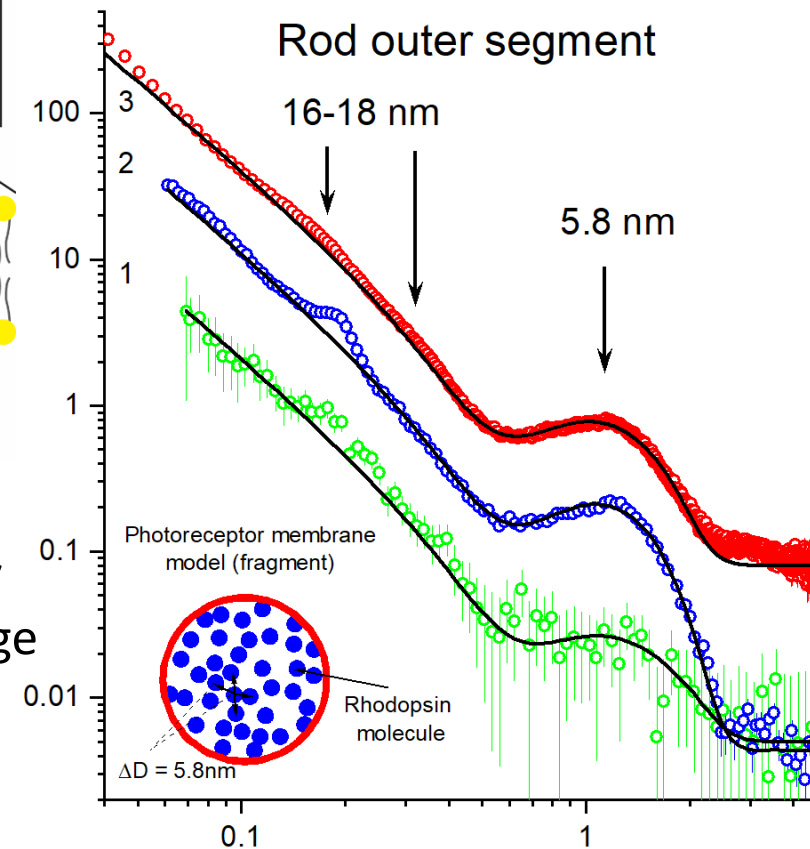


Supramolecular Organization of Rhodopsin

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

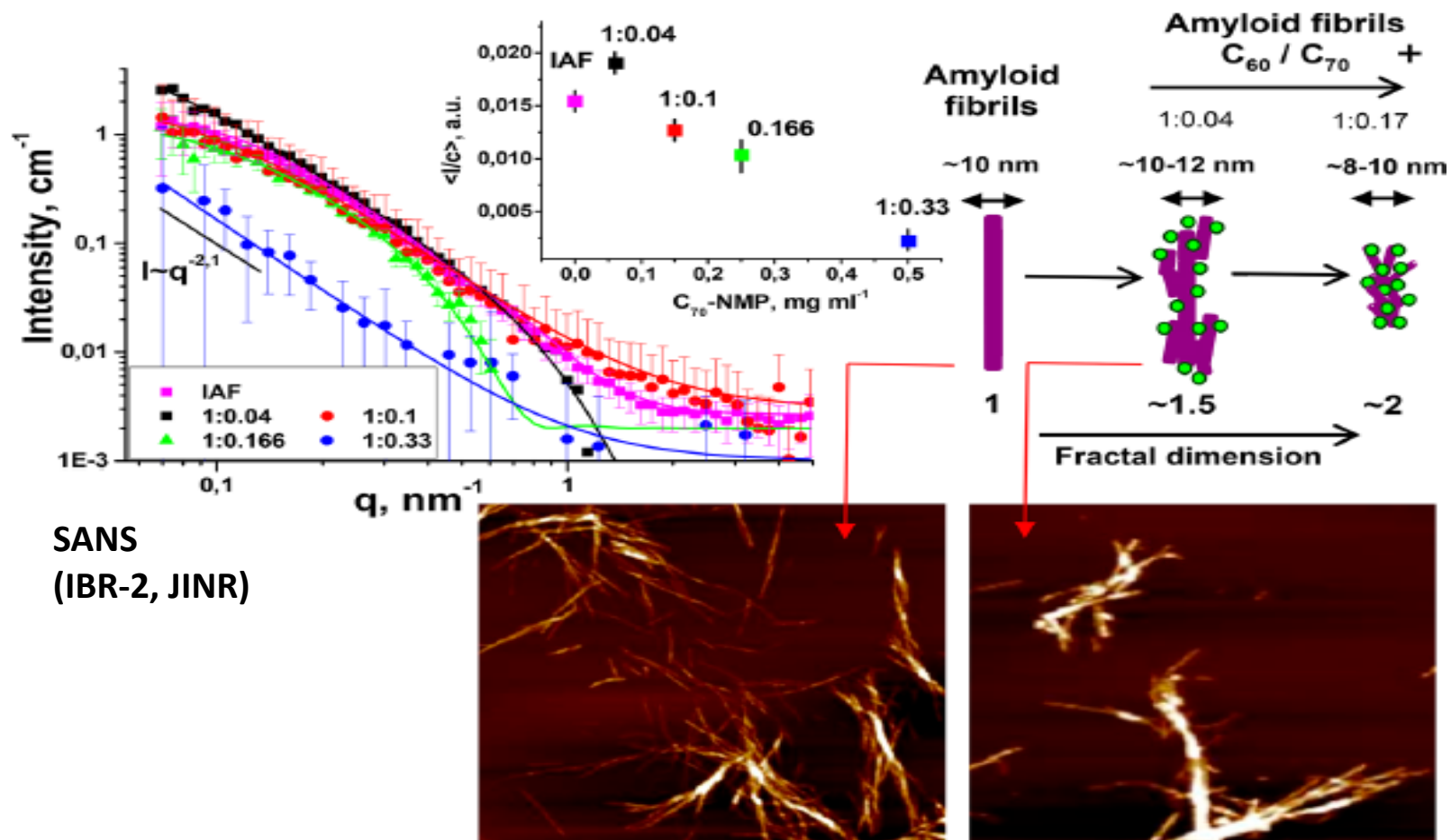


SANS data document a high packing density of rhodopsin molecules, however the average distance between neighbouring molecules suggests their **monomeric state**



Fullerene Nanoparticles against Amyloid Fibrils

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

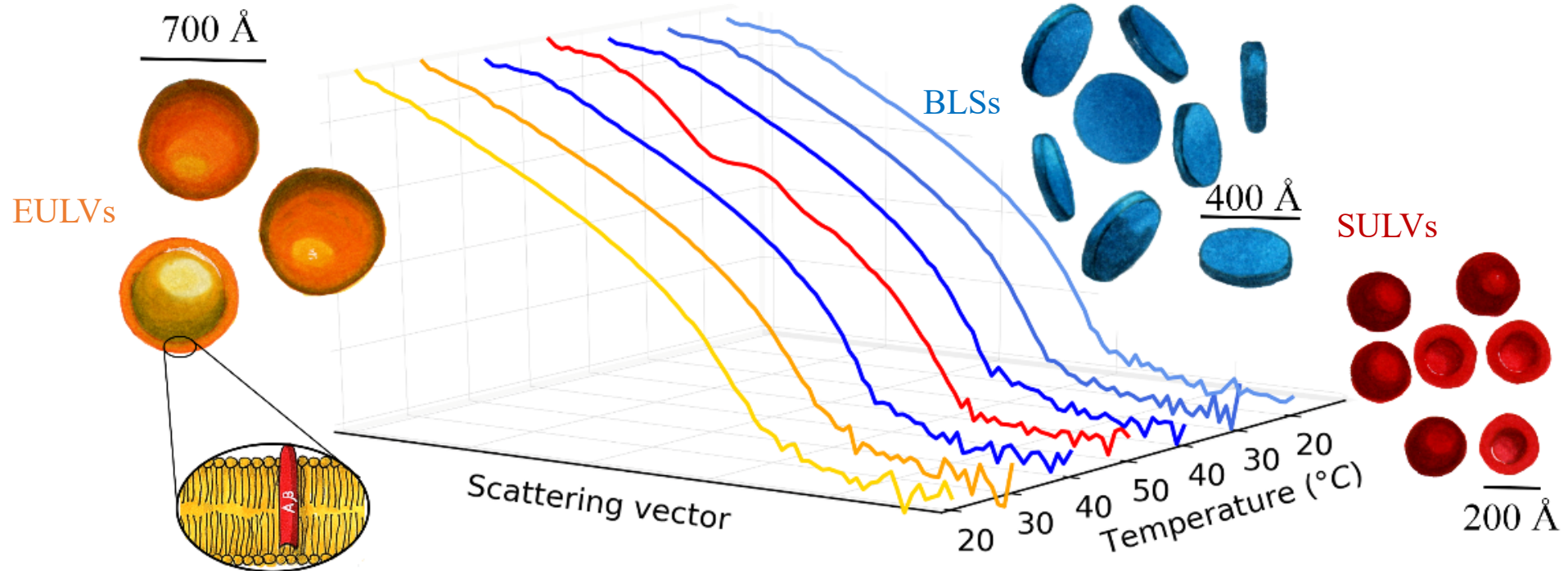


Nagorna et al., *J Mol Liquids* (2018)

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 A β -peptide

THANK YOU FOR YOUR ATTENTION



Norbert Kučerka,^{1,2} Otilia Culicov,^{1,3} Dorota Chudoba,¹ Mikhail Avdeev,¹
Valery Shvetsov¹

¹Frank Laboratory of Neutron Physics, JINR, Dubna

²Faculty of Pharmacy, Comenius University, Bratislava, Slovakia

³INCDIE ICPE – CA (ICPE – Advanced Researches), Bucharest, Romania

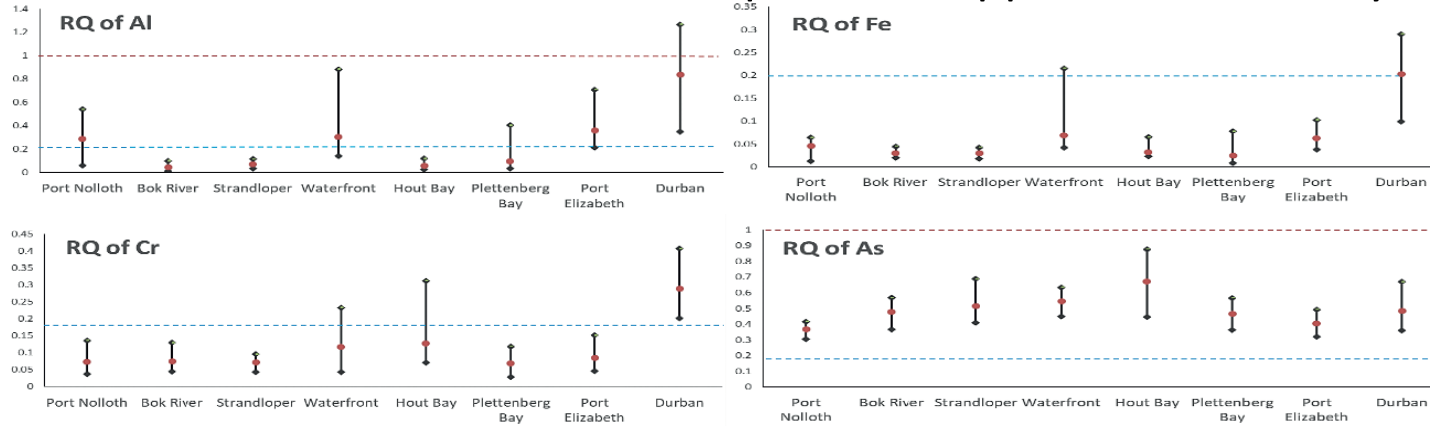
International Conference on Neutron Scattering
Buenos Aires, Argentina: August 25, 2022



JOINT INSTITUTE
FOR NUCLEAR RESEARCH

NAA in Safety of Seafood and Agricultural Plants

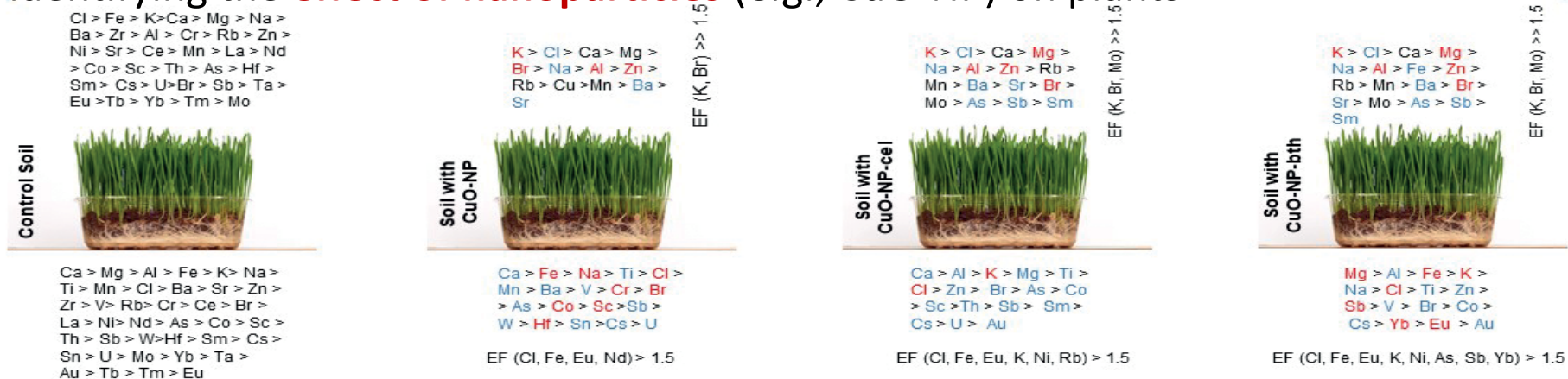
- A natural bio-monitor for water pollution appear conveniently **molluscs**



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)

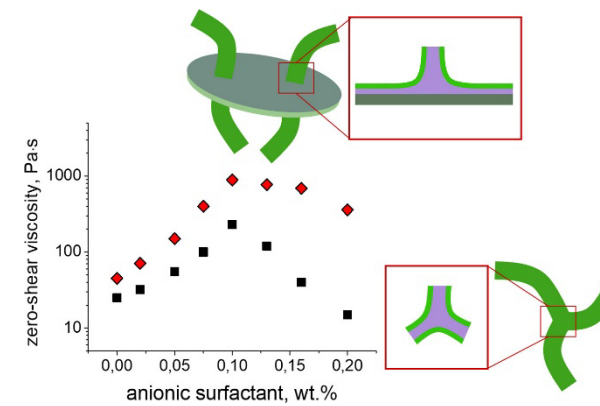
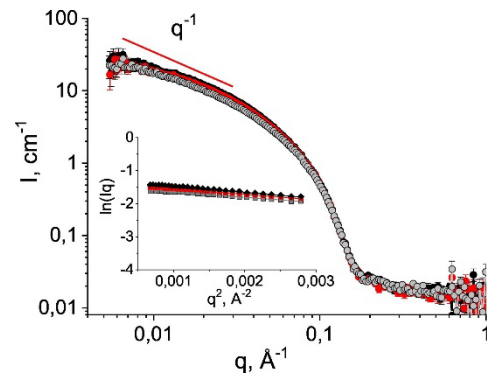
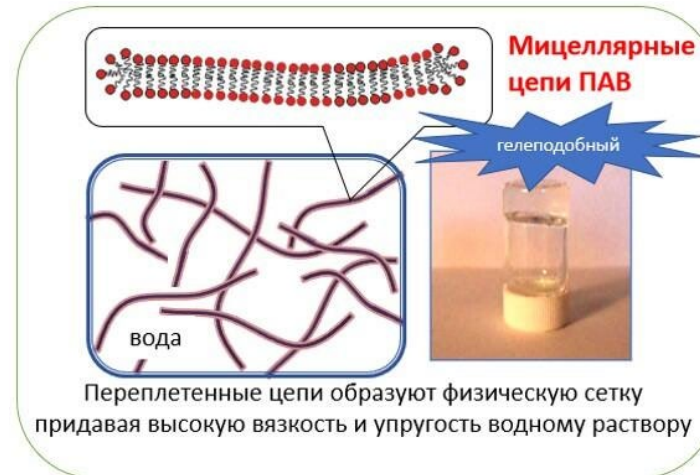
- NAA proved valuable also in monitoring the **soil pollution** and identifying the **effect of nanoparticles** (e.g., CuO-NP) on plants



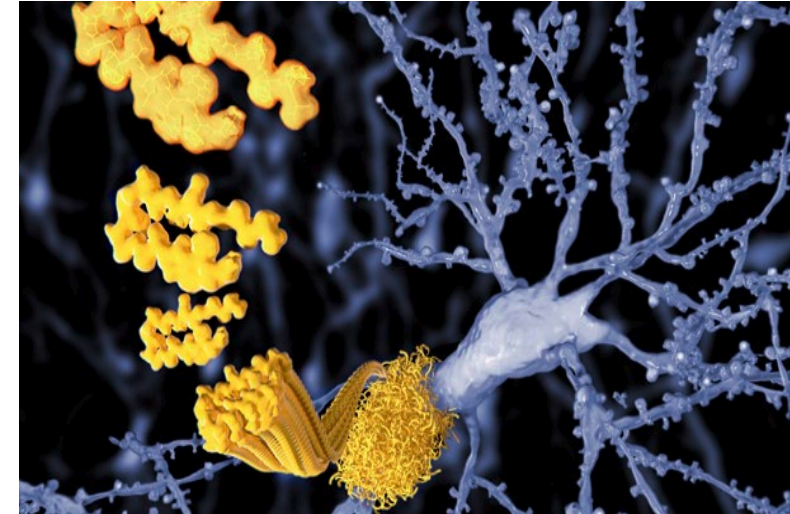
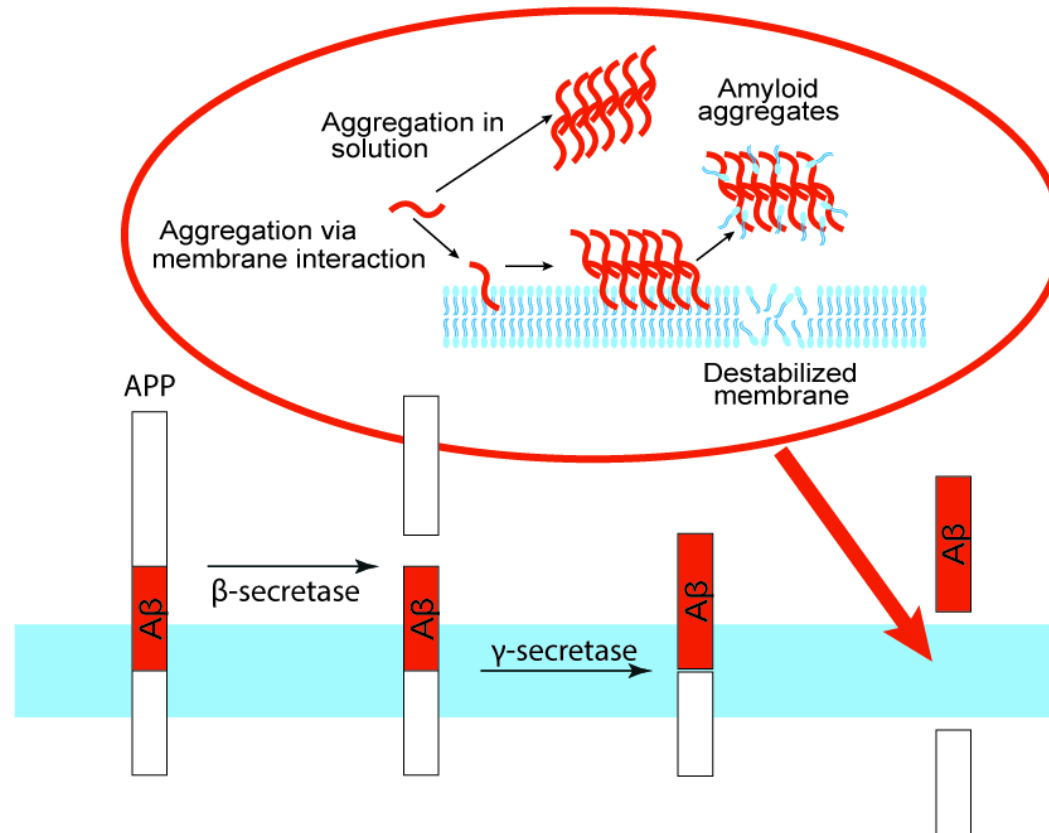
Lung I et al., *Int. J. Environ. Res. Public Health* 18(13), 6739 (2021)

Plant Protection Products in Agriculture

- A



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

Number of proposals

