

Why 2D membrane protein crystals

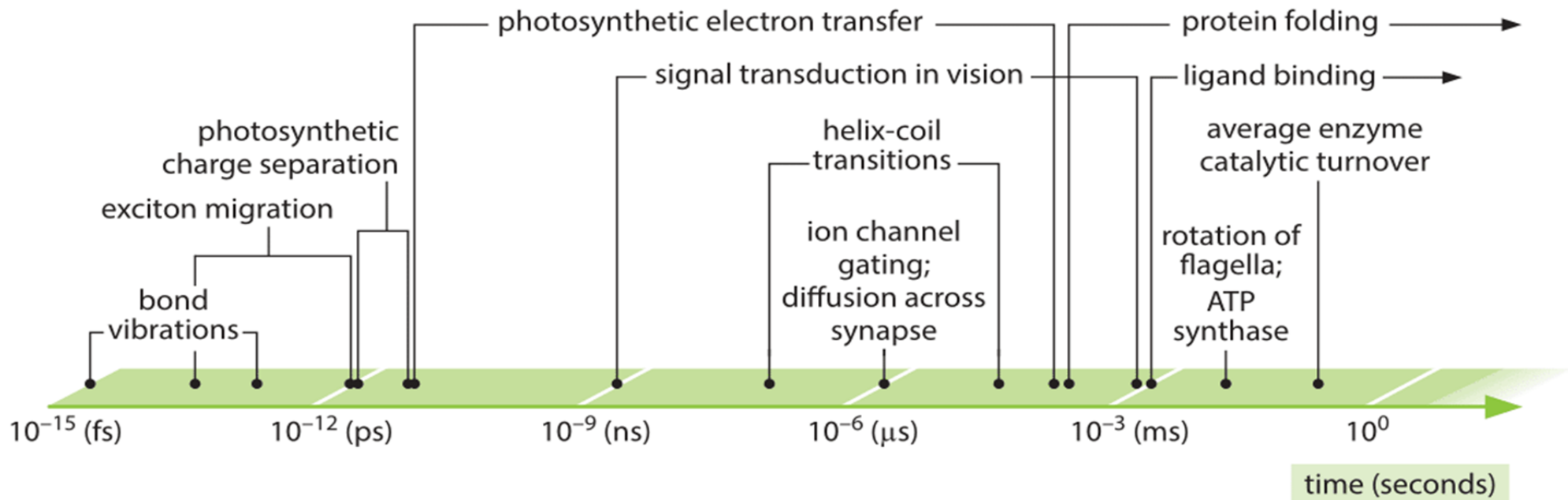
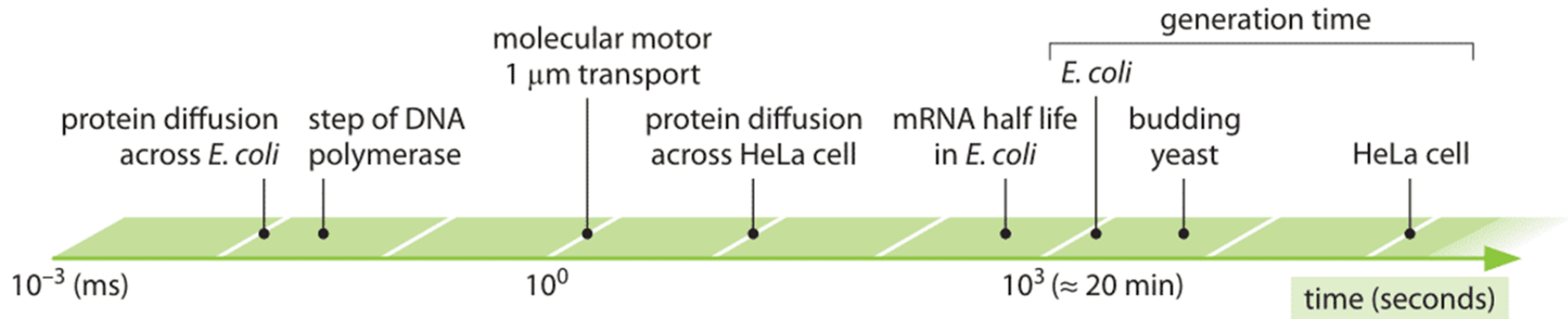
Xiaodan Li

Paul Scherrer Institute

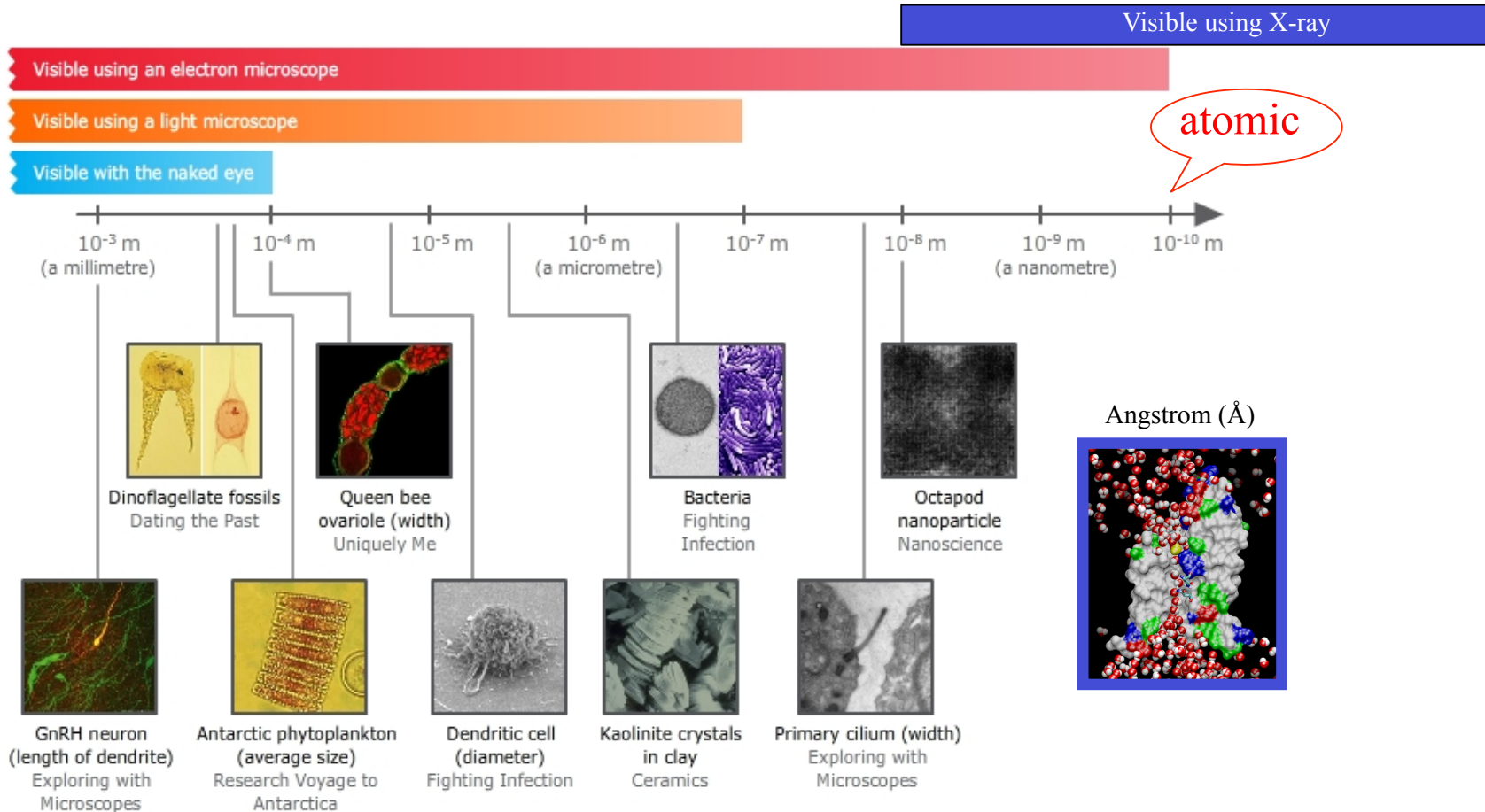
Scientific opportunities in protein 2D-crystallography at (Swiss)FELs

Jan 27, 2015

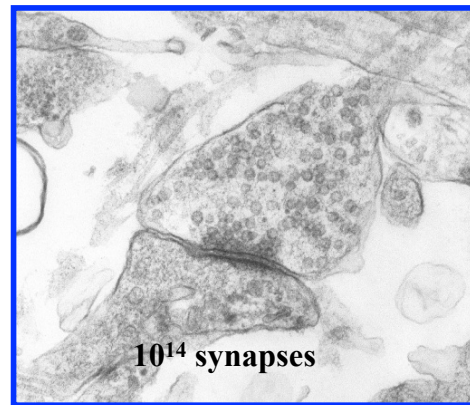
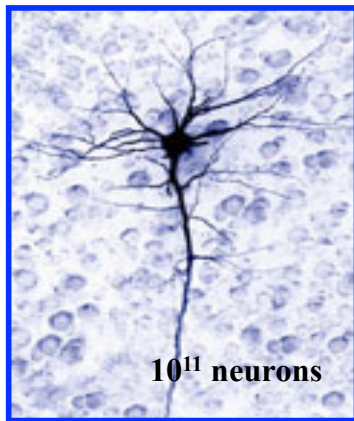
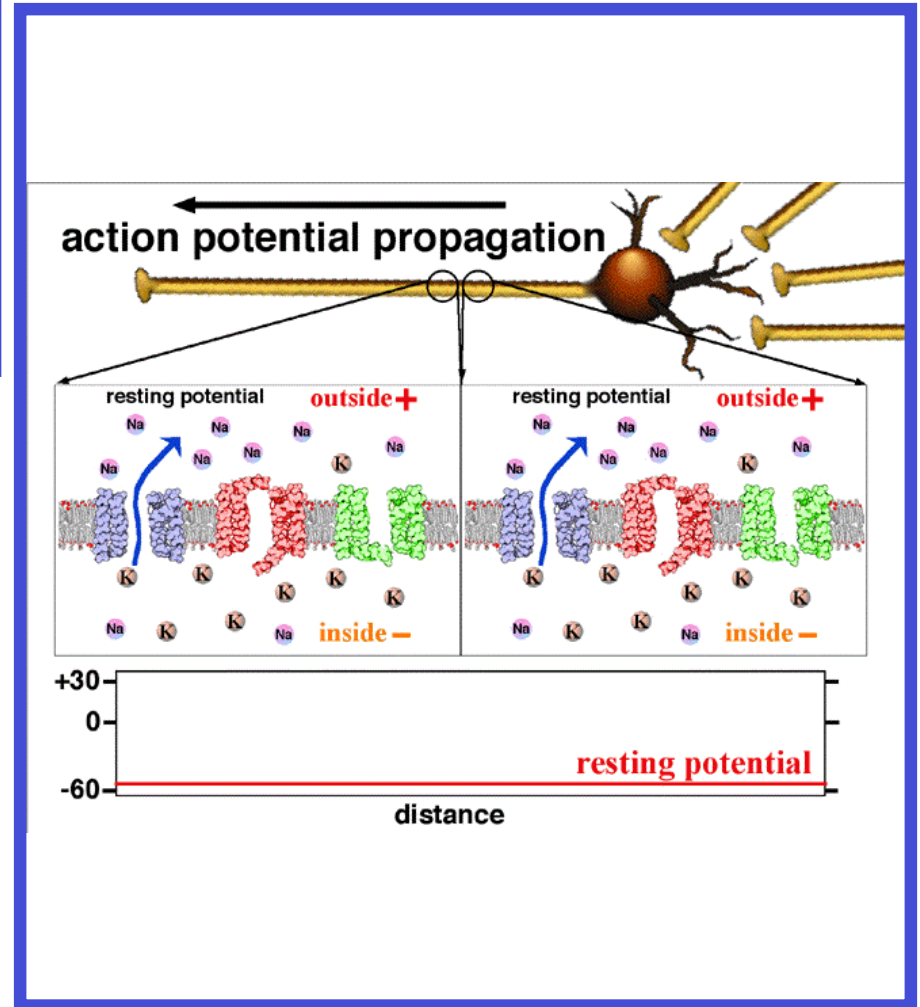
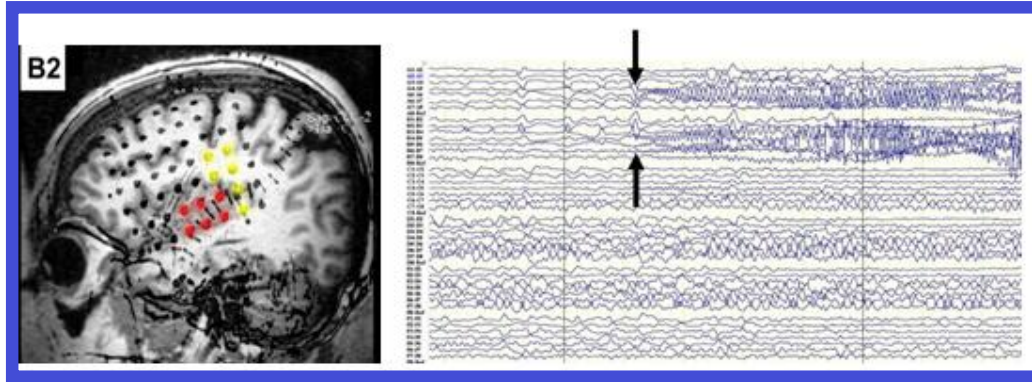
The time scale in biology



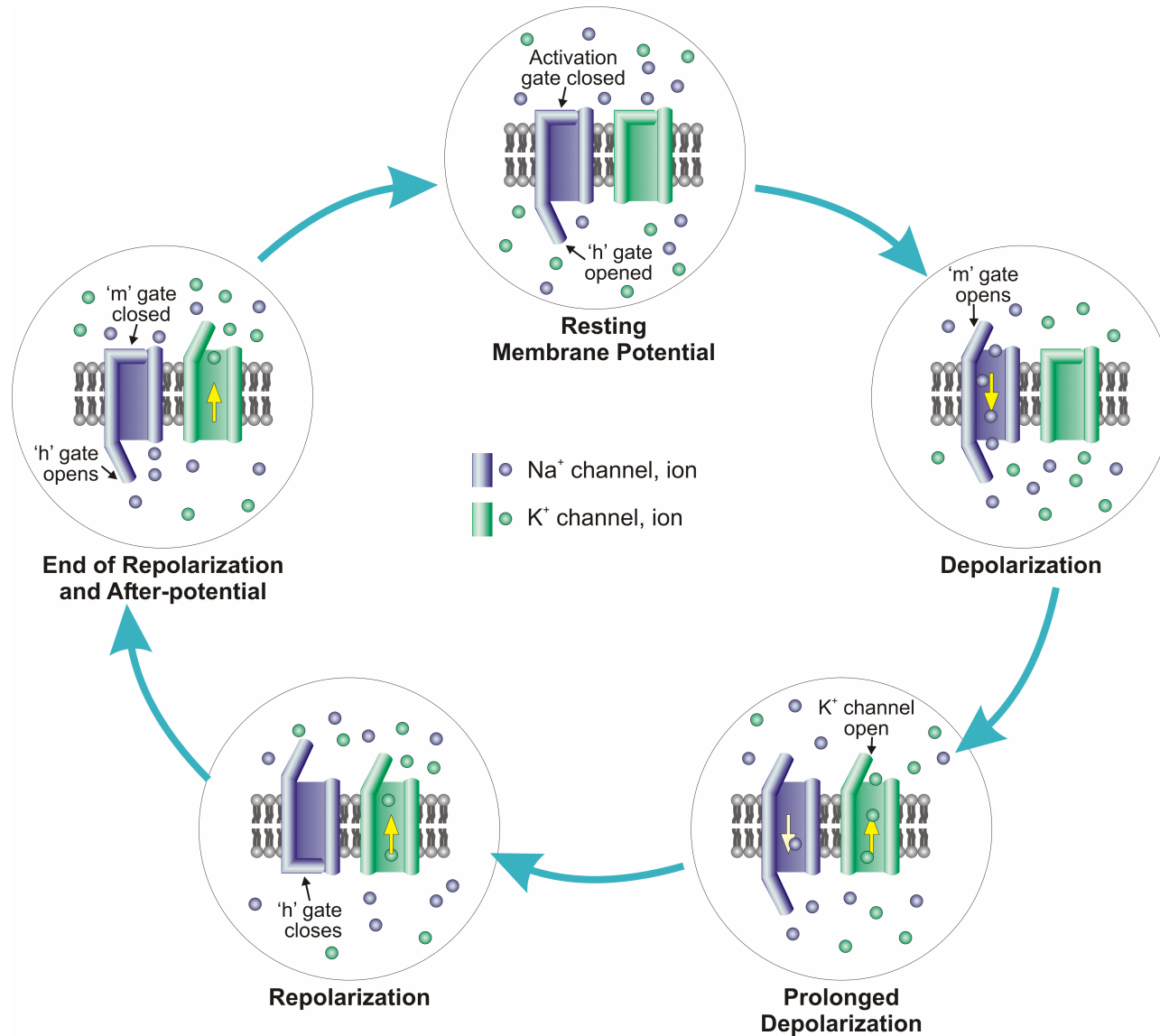
The space scale in biology

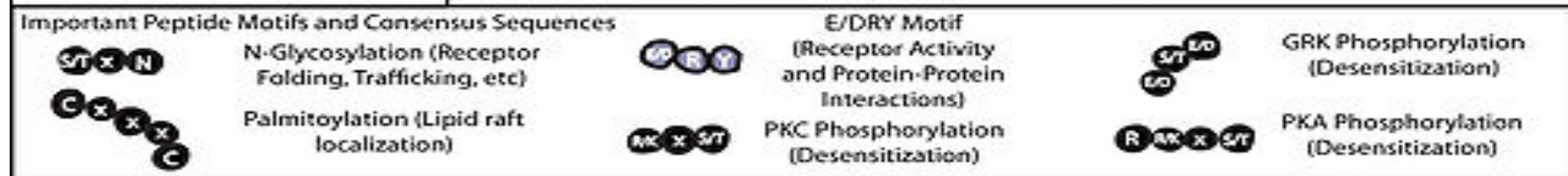
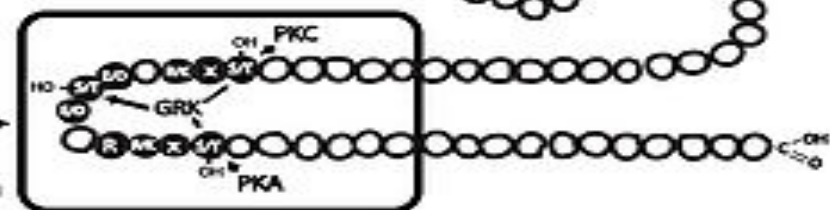
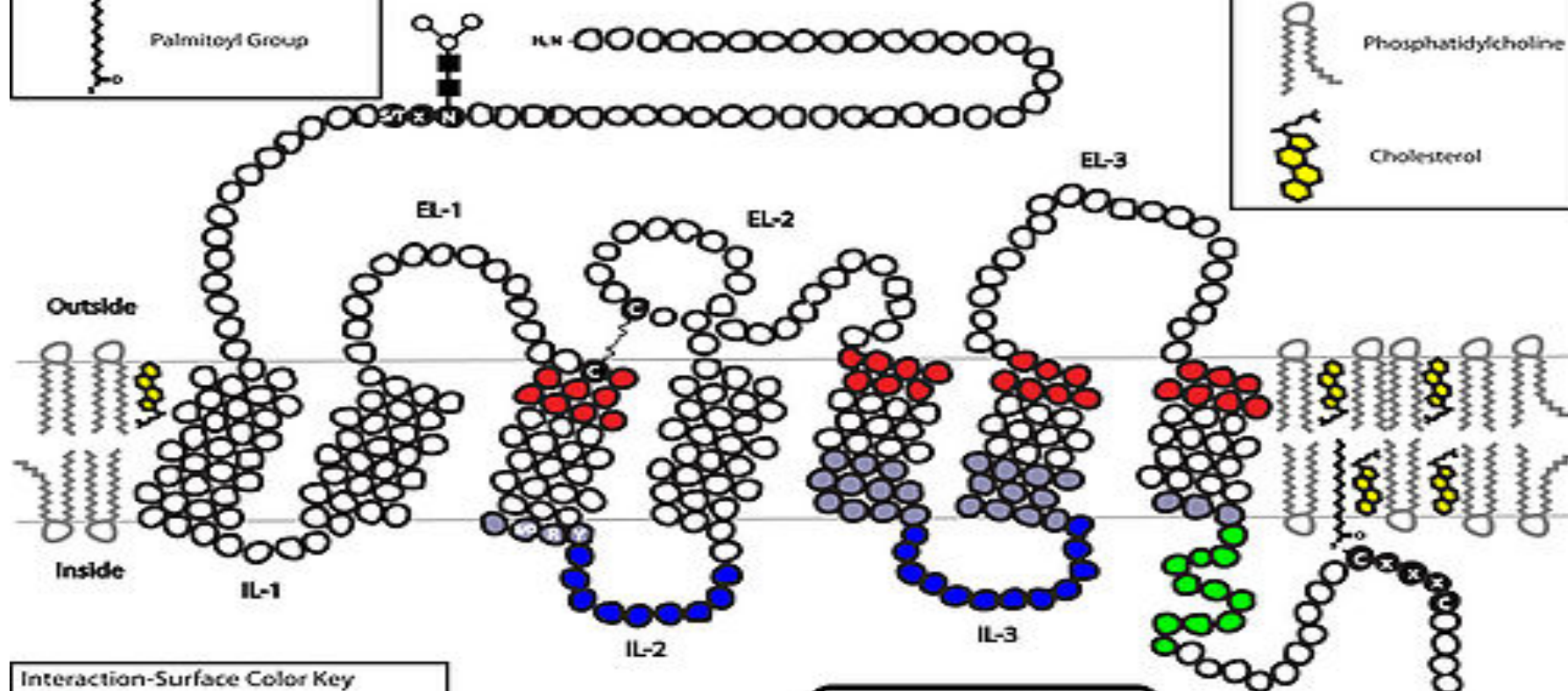
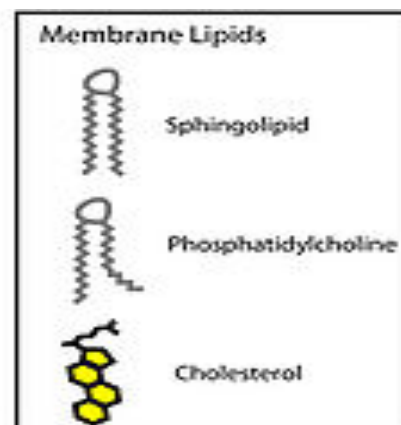
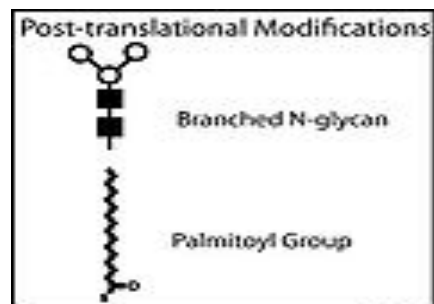


Ion channels control heart and brain electrical activity

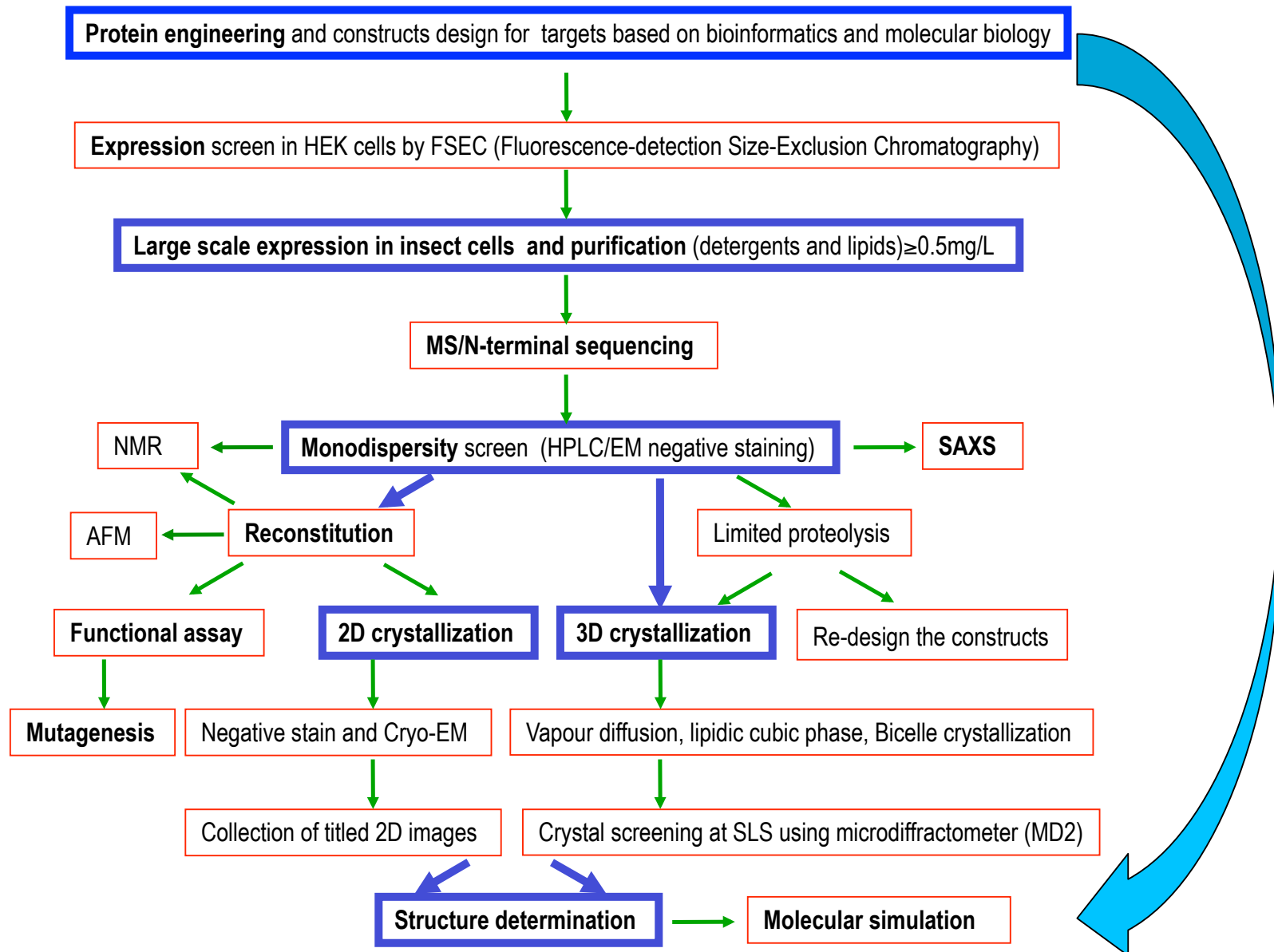


To understand how the membrane protein works across the space and time

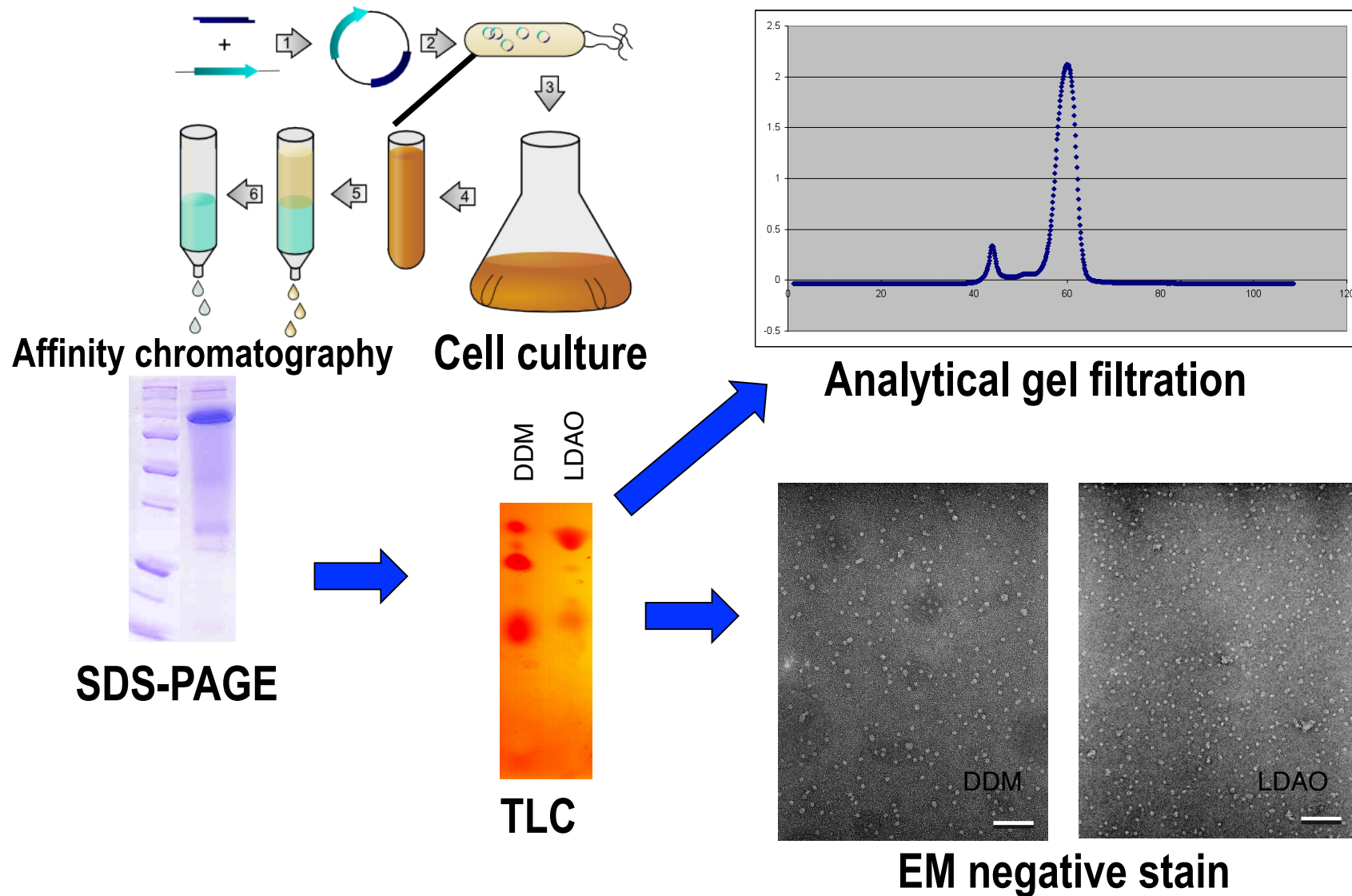




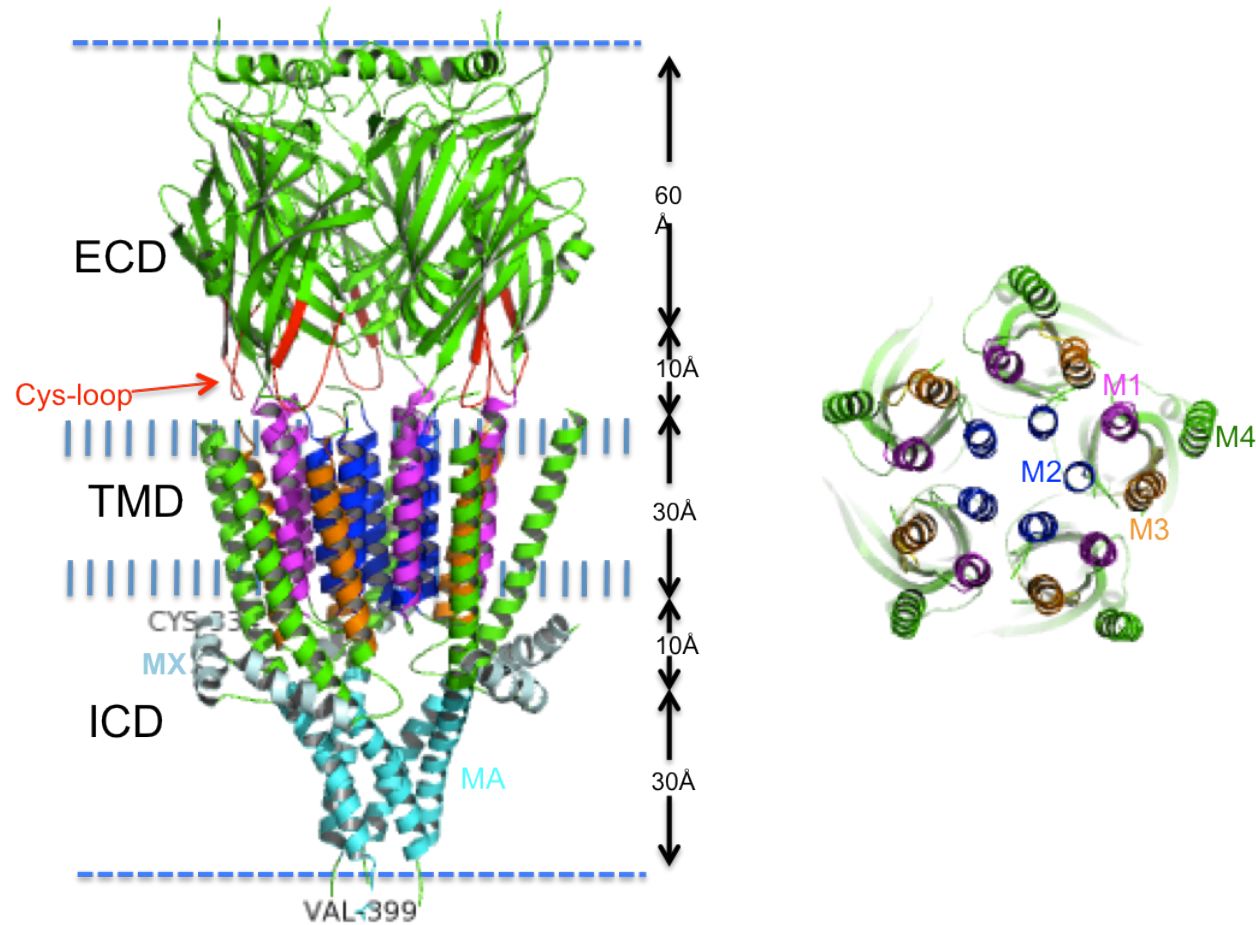
How to prepare membrane protein samples for structure determination



Sufficient amount of membrane proteins are expressed and purified for characterization

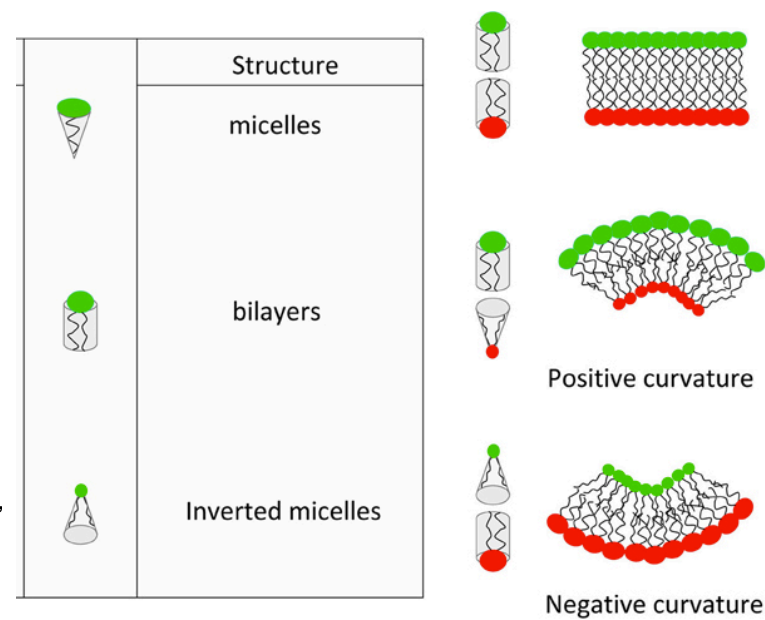
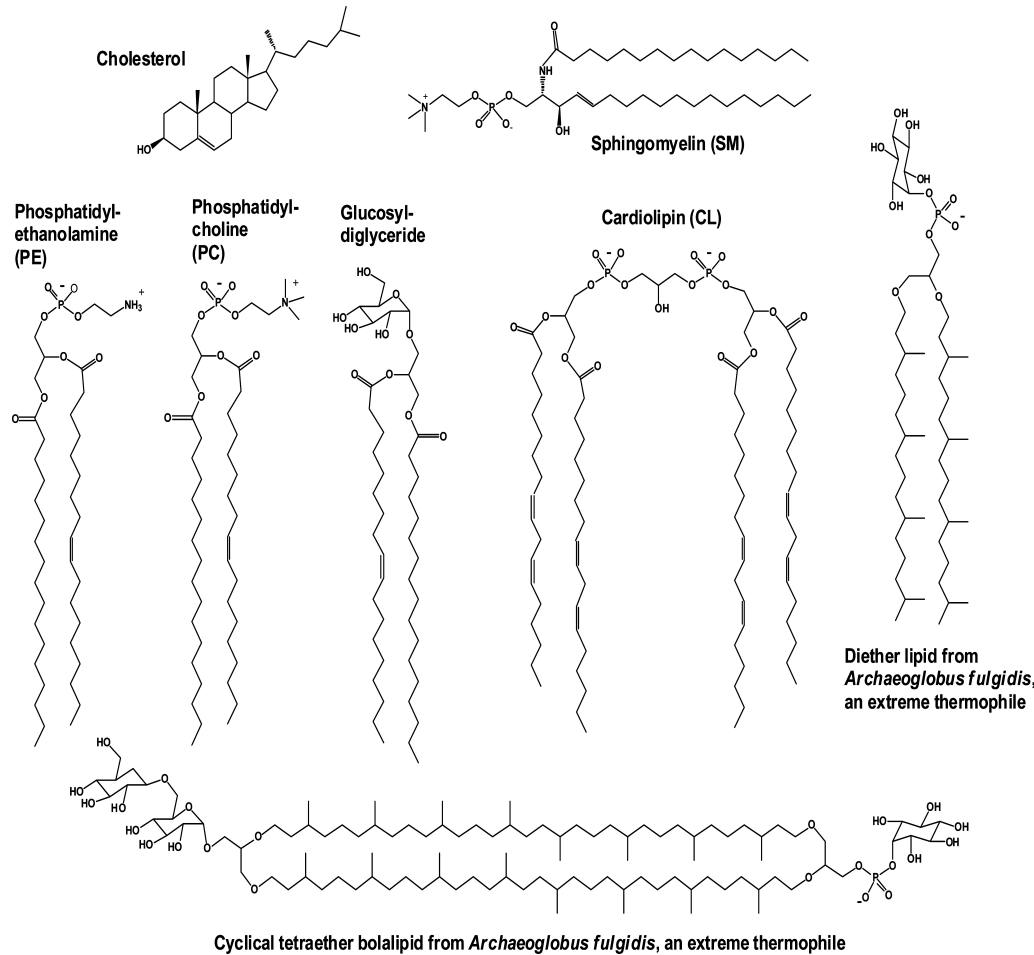


Structures of more than 95% membrane proteins are determined using X-ray

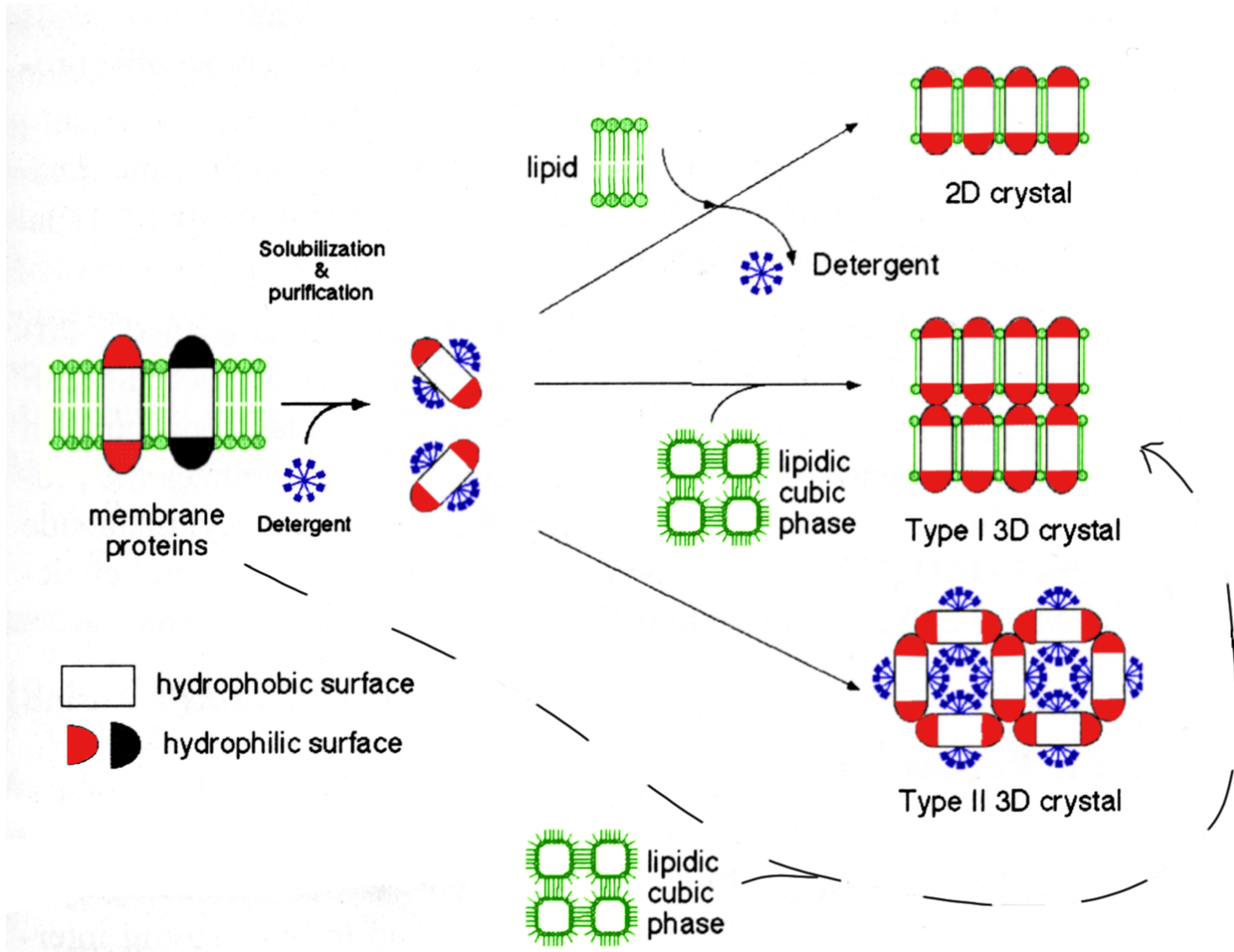


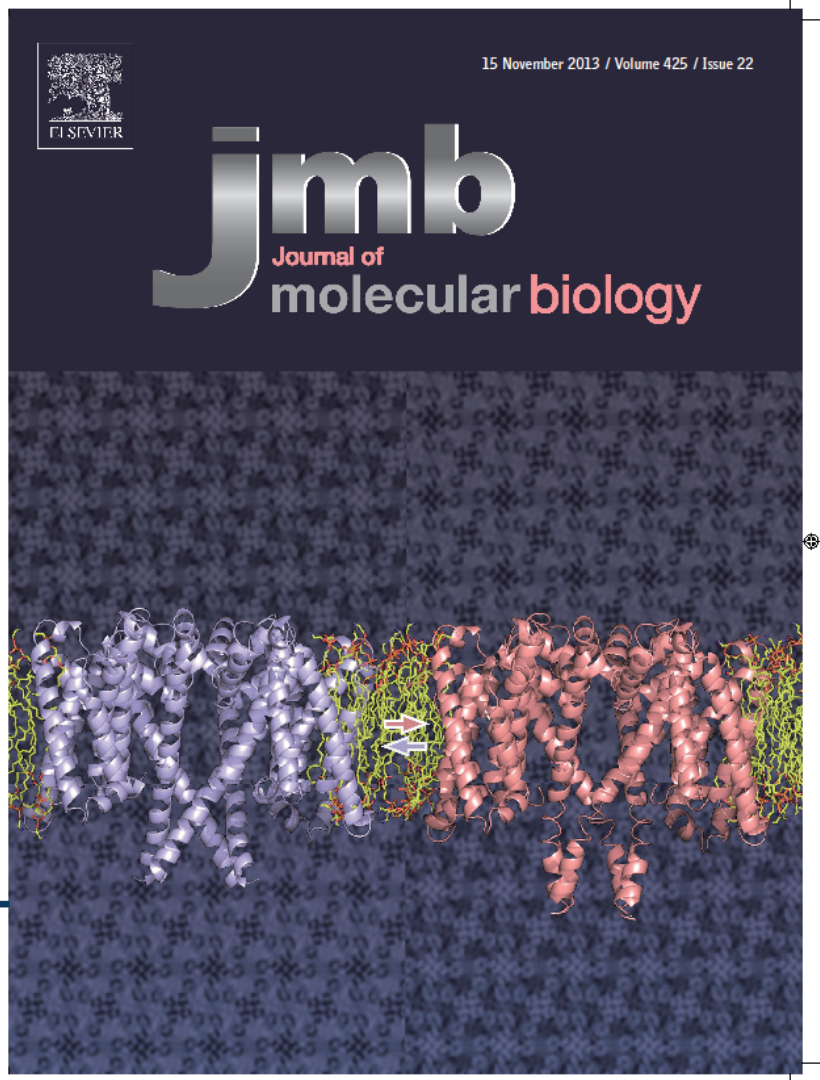
The X-ray structure of mouse serotonin receptor
Hassaine G et al Nature (2014) 512:276-281

Composition and curvature of lipid bilayer modulate the topology, structure, dynamic and function of membrane protein

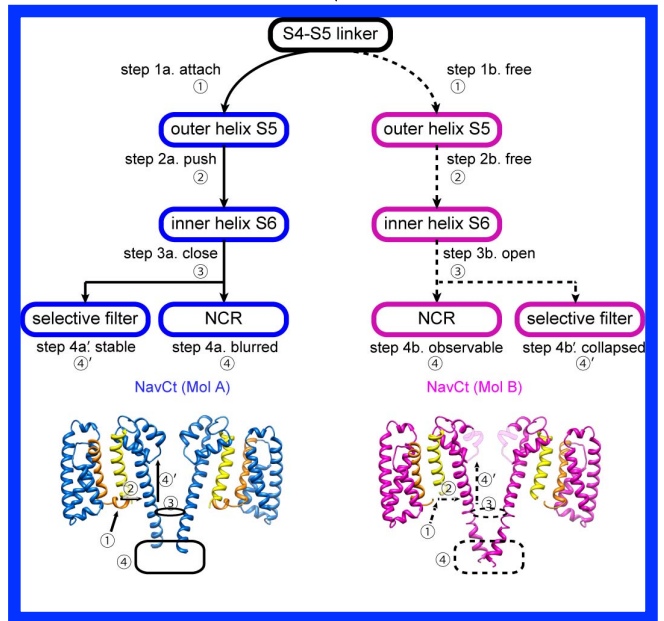
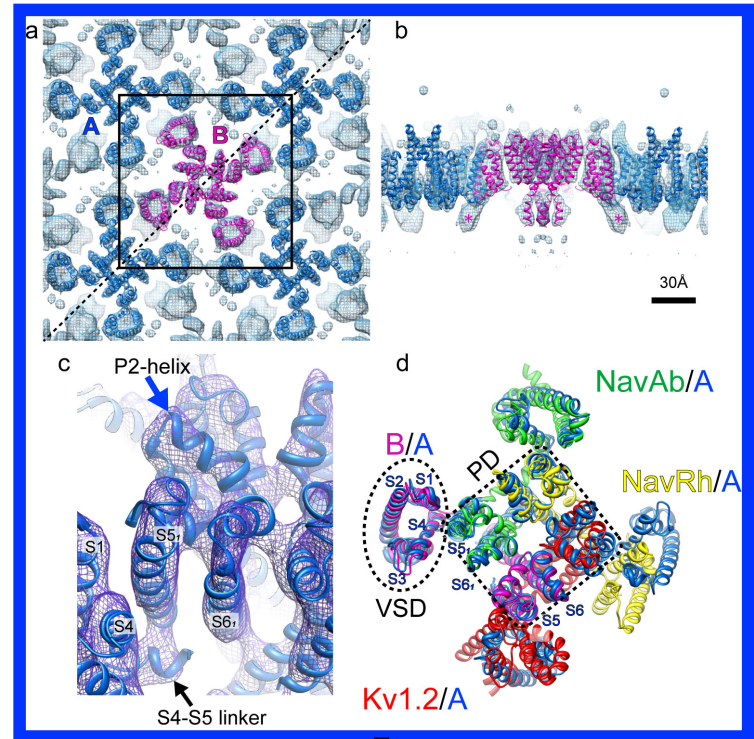


Membrane Protein crystallisation (reconstitution)

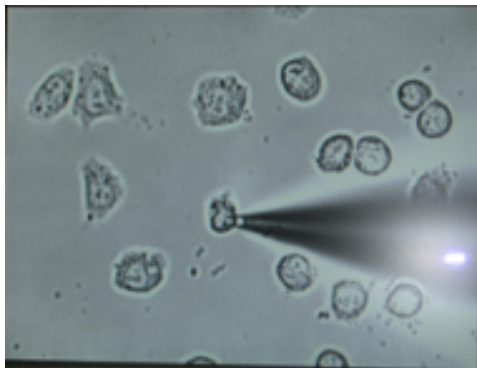
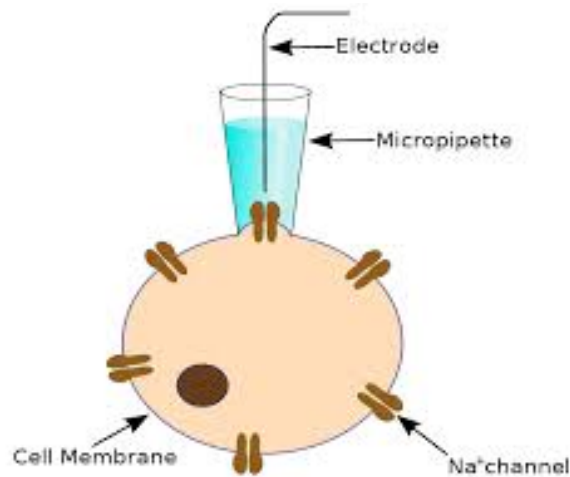




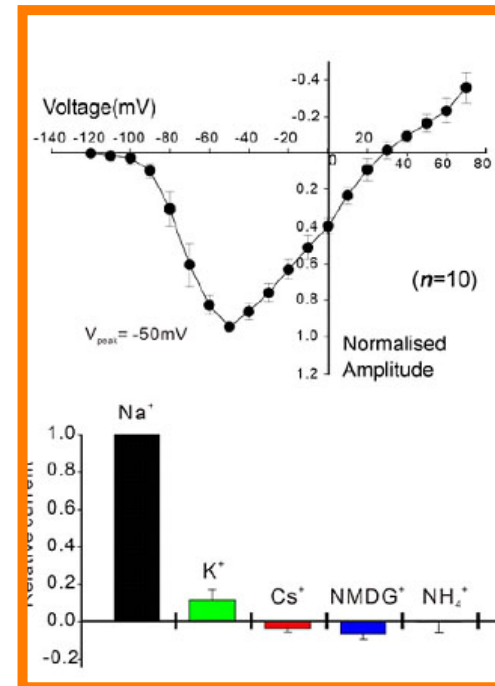
EM structure of NaV
Tsai et al (2013)JMB425(22):4074-88



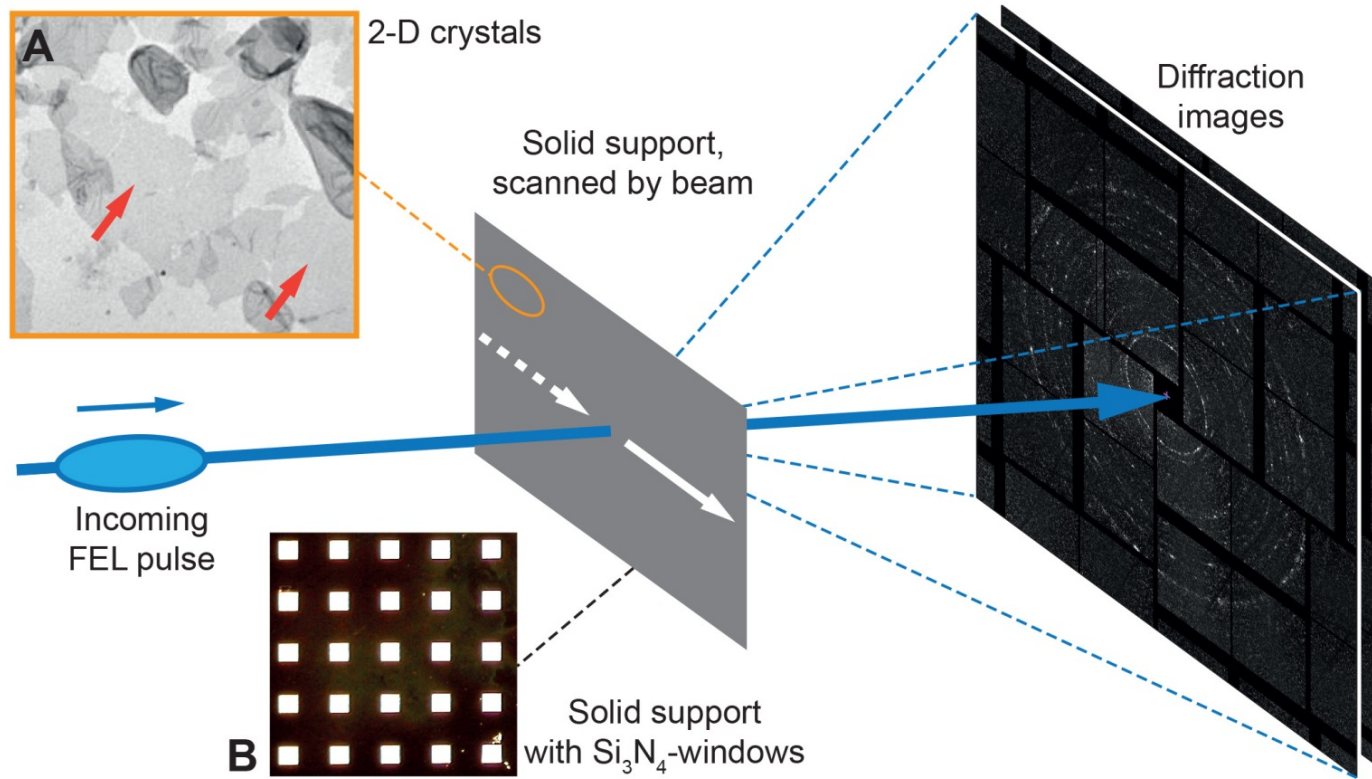
Patch clamping to measure the Na^+ conductance of the voltage-gated sodium channel



I/V curve of a bacterial voltage-gated sodium channel



XFEL opens a great opportunity to study dynamic of 2D membrane protein crystals-bR 2D crystals diffract to 4.5Å



Questions or remarks

- High quality 2D membrane proteins are rare (1-5%), can be improved to maximal 10-20%, make new lipids with different properties?
- It is easier to obtain 2D nanocrystals 100-300nm, SwissFEL nanofocus 100-200 useful at ES-C station and do we get enough photons for high resolution?
- What is the resolution limit of 2D nanocrystals at XFEL?
- How to ensure the flatness of the 2D crystals?
- Before diffraction, to measure the activity (ion flow, pH change or ligand-binding) of the 2D crystals are highly desirable, possibilities at ES-C?
- For radiation damage studies of 2D membrane protein crystals on fixed target, what will be the key experiments?
- The make-the-difference experiments of 2D crystals at XFEL?