Fine mapping of biomolecular surfaces using the new Molecular Surface Topography (MST) web tool

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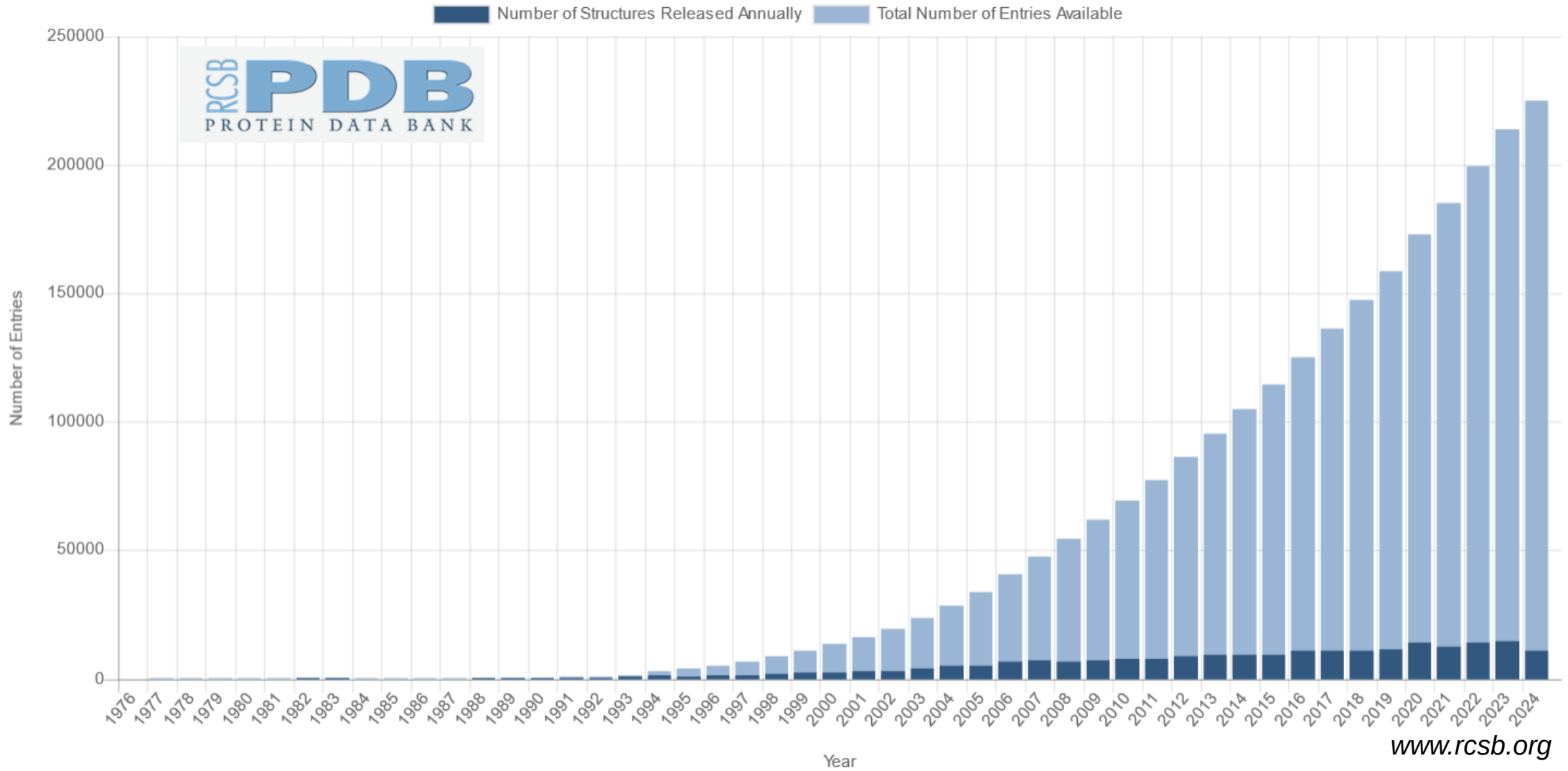
BCADD-2024, 16 September 2024

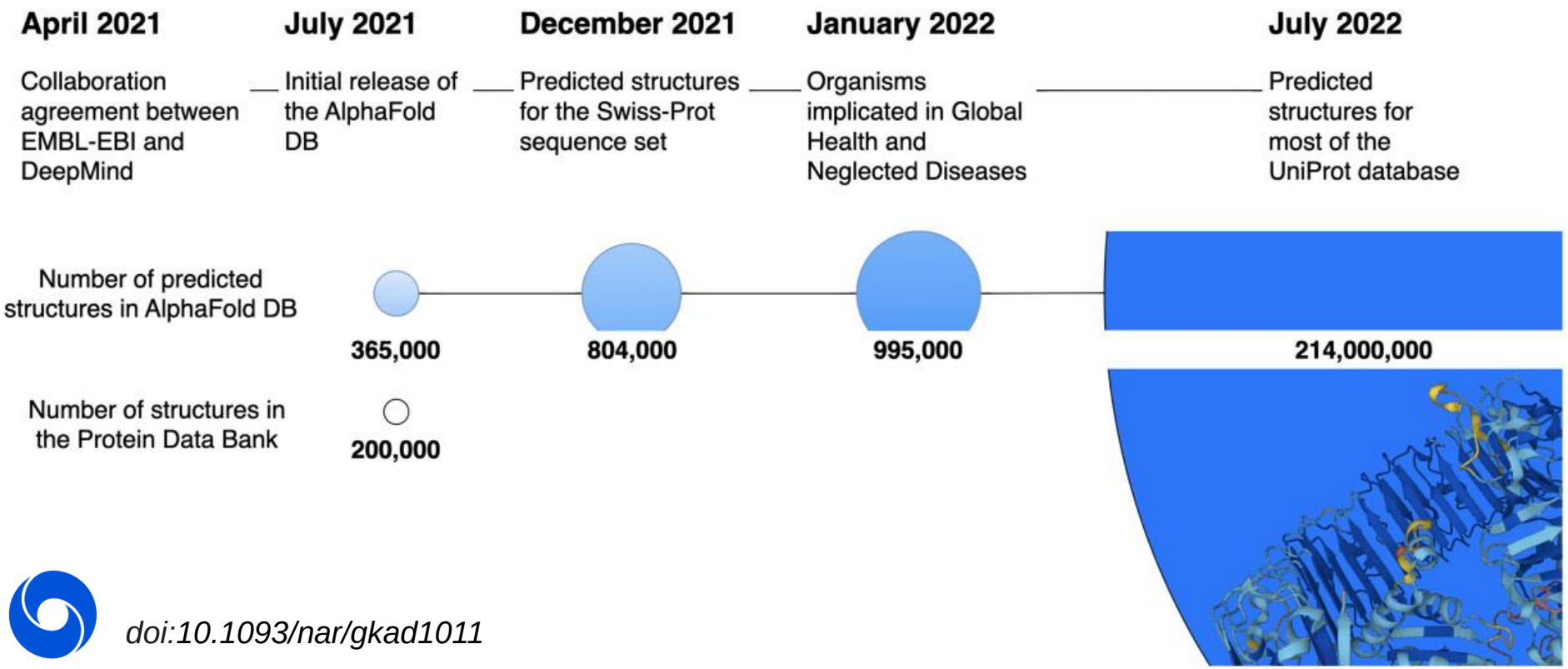
Experimental biomolecular structures



PDB Statistics: Overall Growth of Released Structures Per Year

AI generated structural data

Not only AlphaFold!



doi:10.1093/nar/gkad1011

The expansion of AlphaFold Protein Structure Database

RoseTTAFold

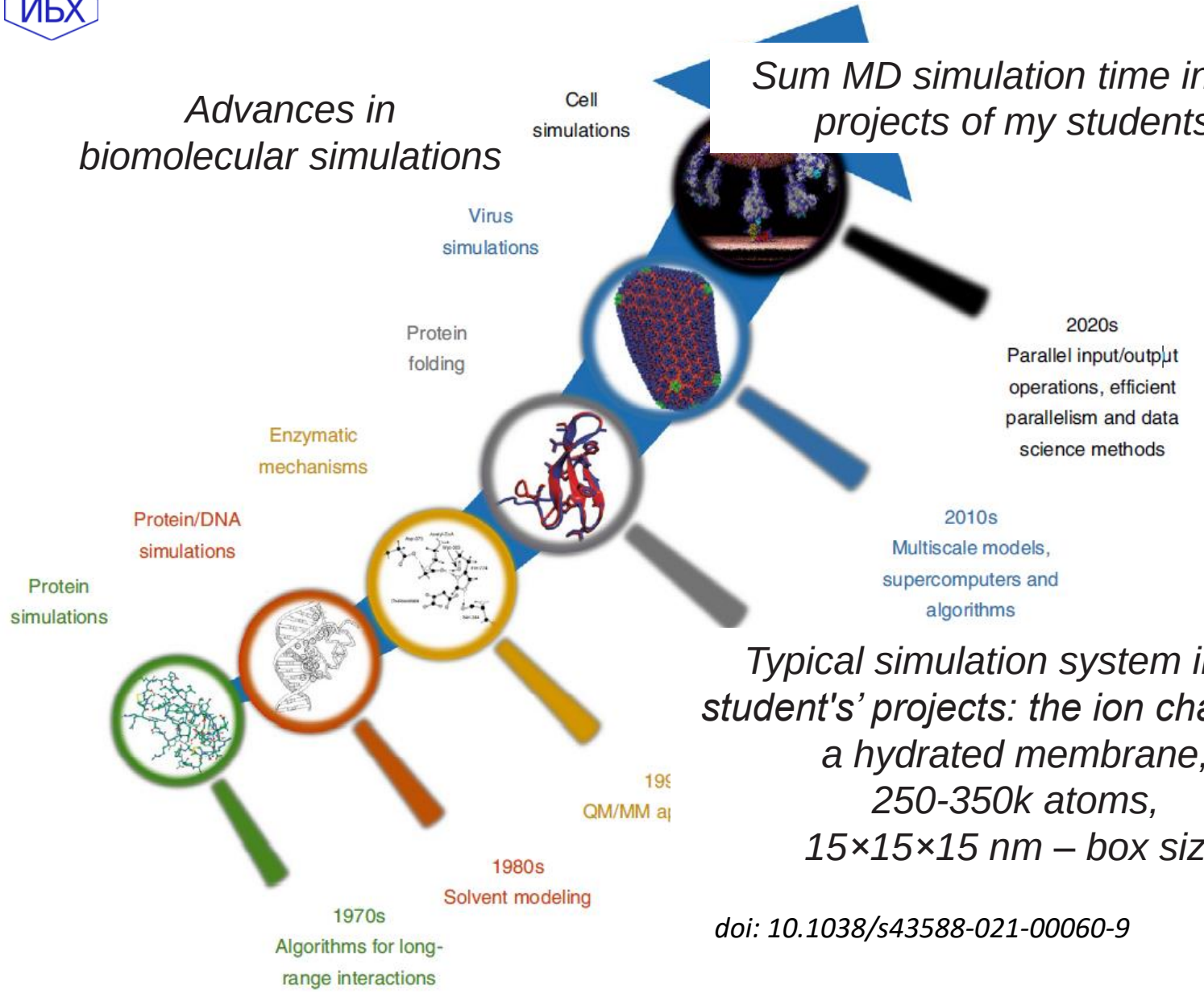
ESM Fold
>600M protein structures

ProteinMPNN
Protein sequence design

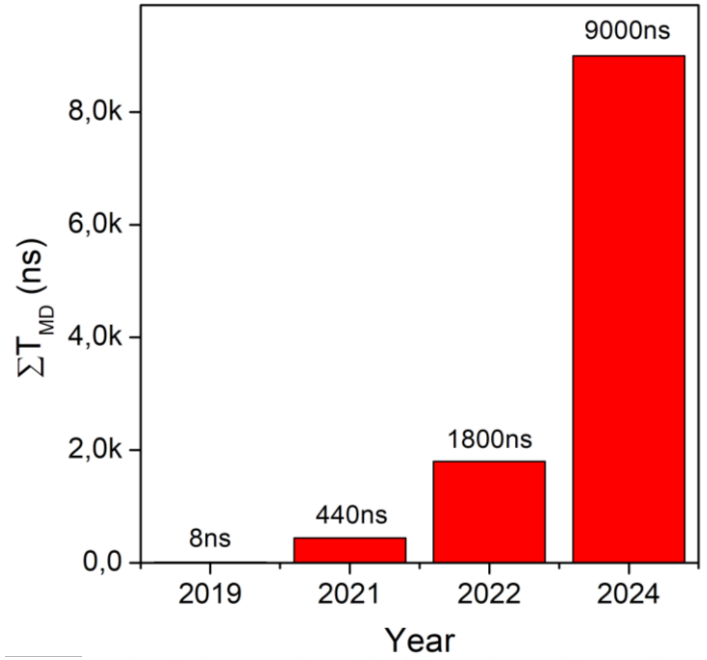
and so on…

Biomolecular modeling

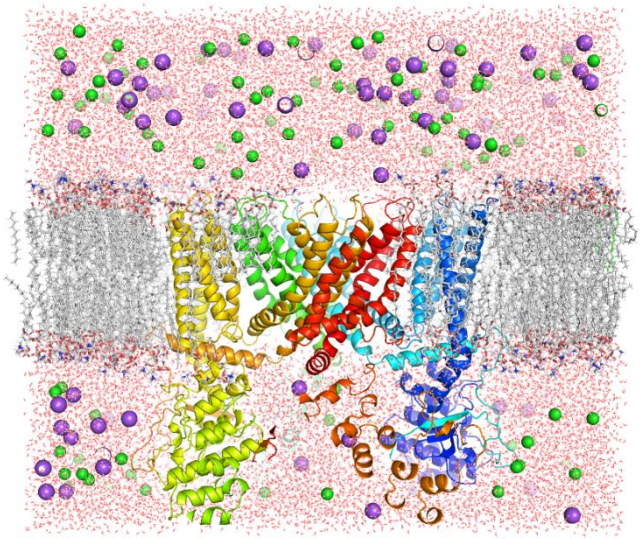
Advances in biomolecular simulations



Sum MD simulation time in the projects of my students



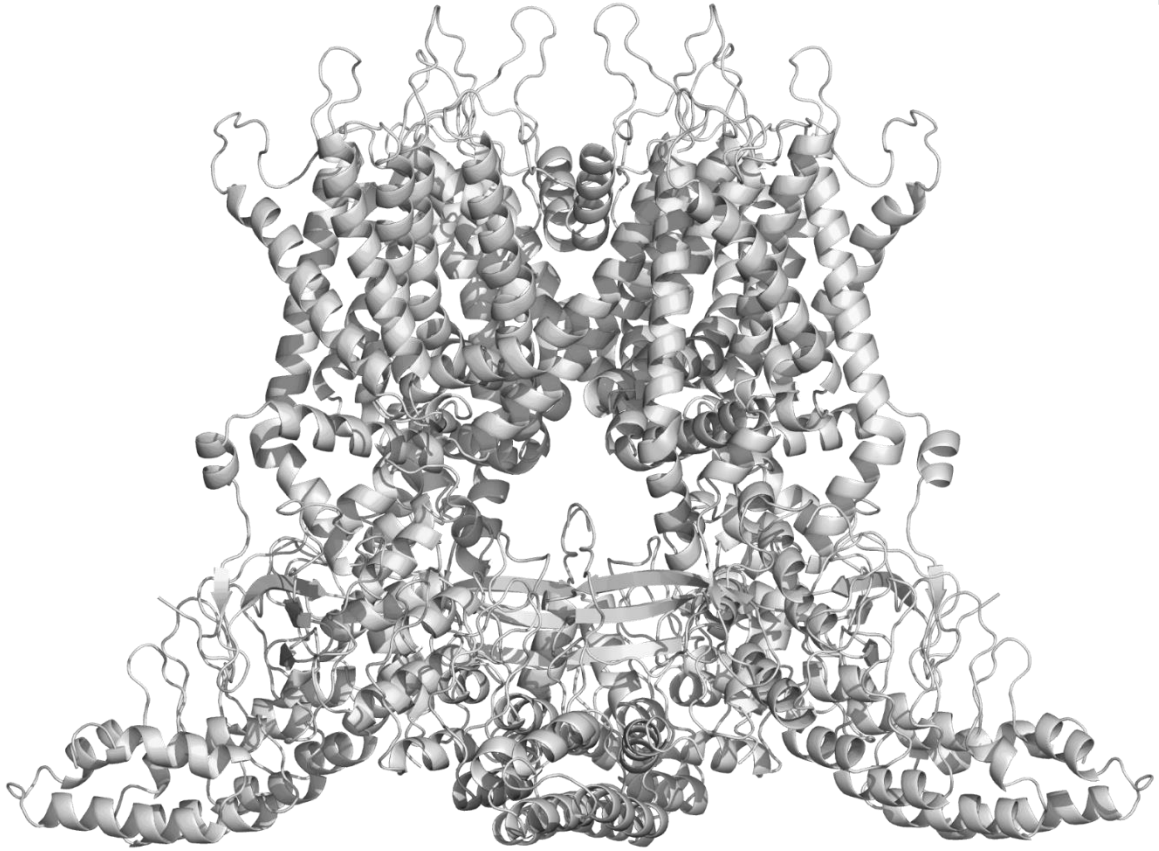
Typical simulation system in the student's' projects: the ion channel in a hydrated membrane, 250-350k atoms, 15×15×15 nm – box size



doi: 10.1038/s43588-021-00060-9

Structural data is not enough

Atomic structure of the macromolecule or molecular complex



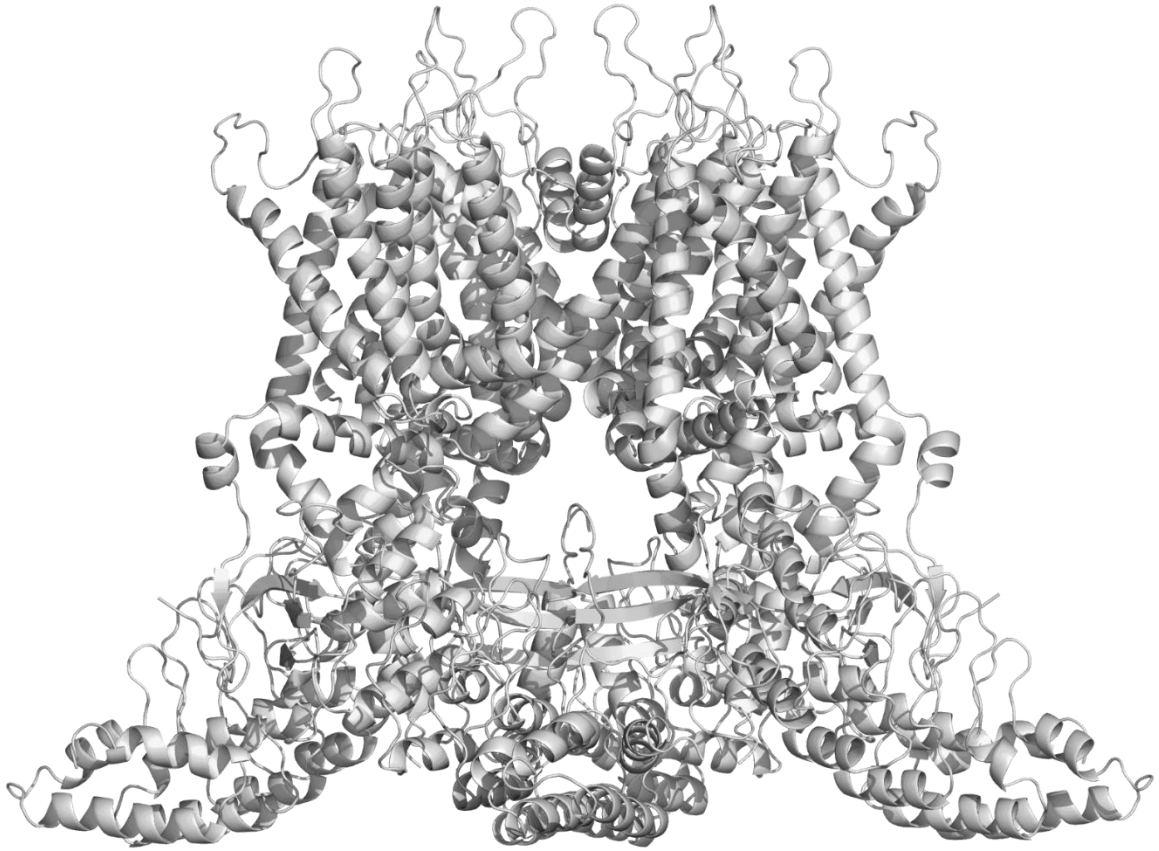
Functional state of the molecule conformation

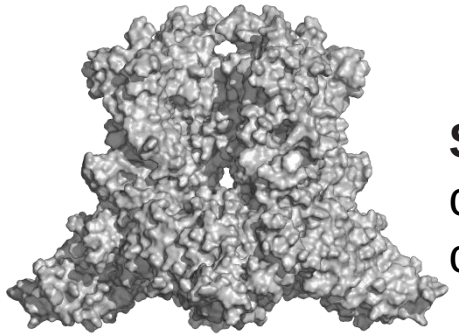
Properties and energetics of iner- and intramolecular interactions

Physicochemical properties of the molecular surface

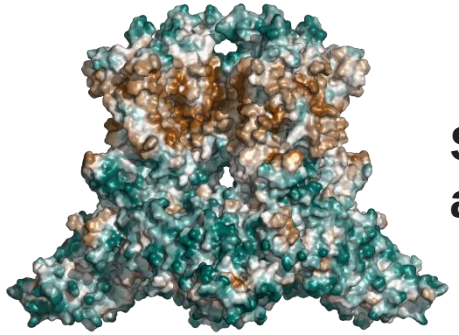
What kind of the surface properties?

Atomic structure of the macromolecule or molecular complex

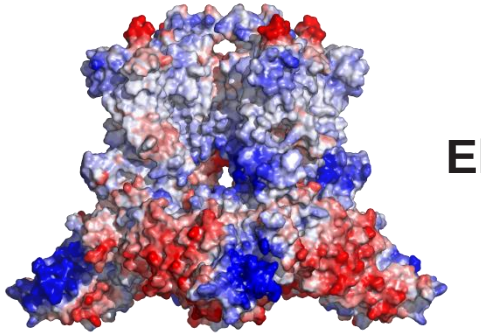




Surface geometry
convexities and concavities



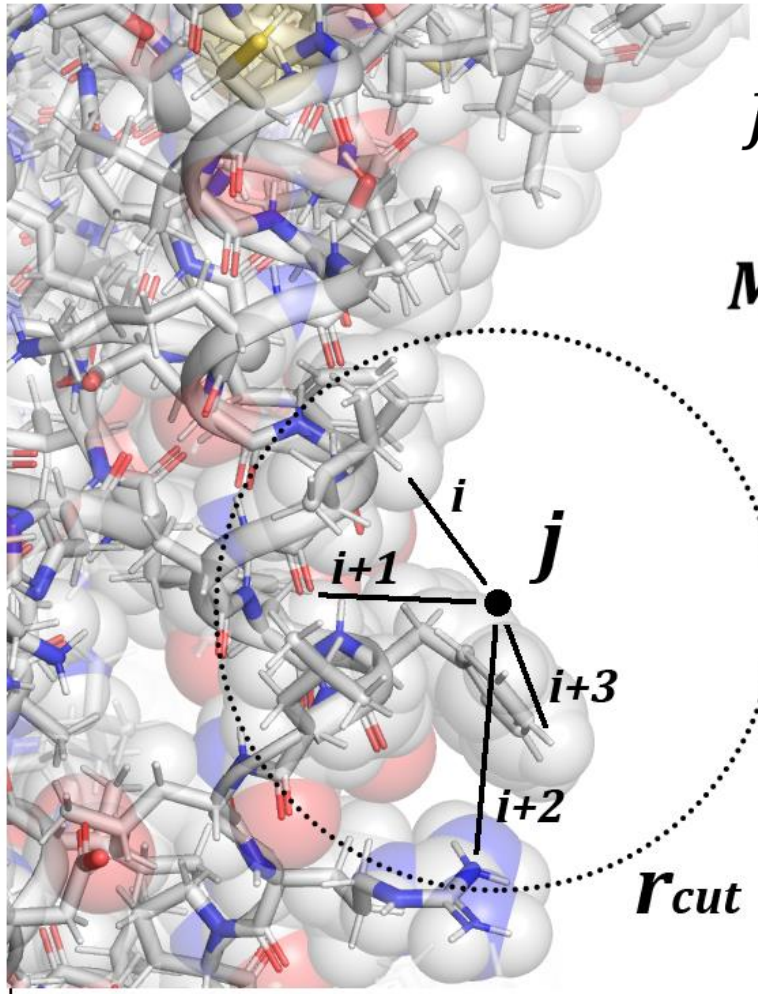
Surface hydrophobicity and hydrophilicity



Electrostatic potential

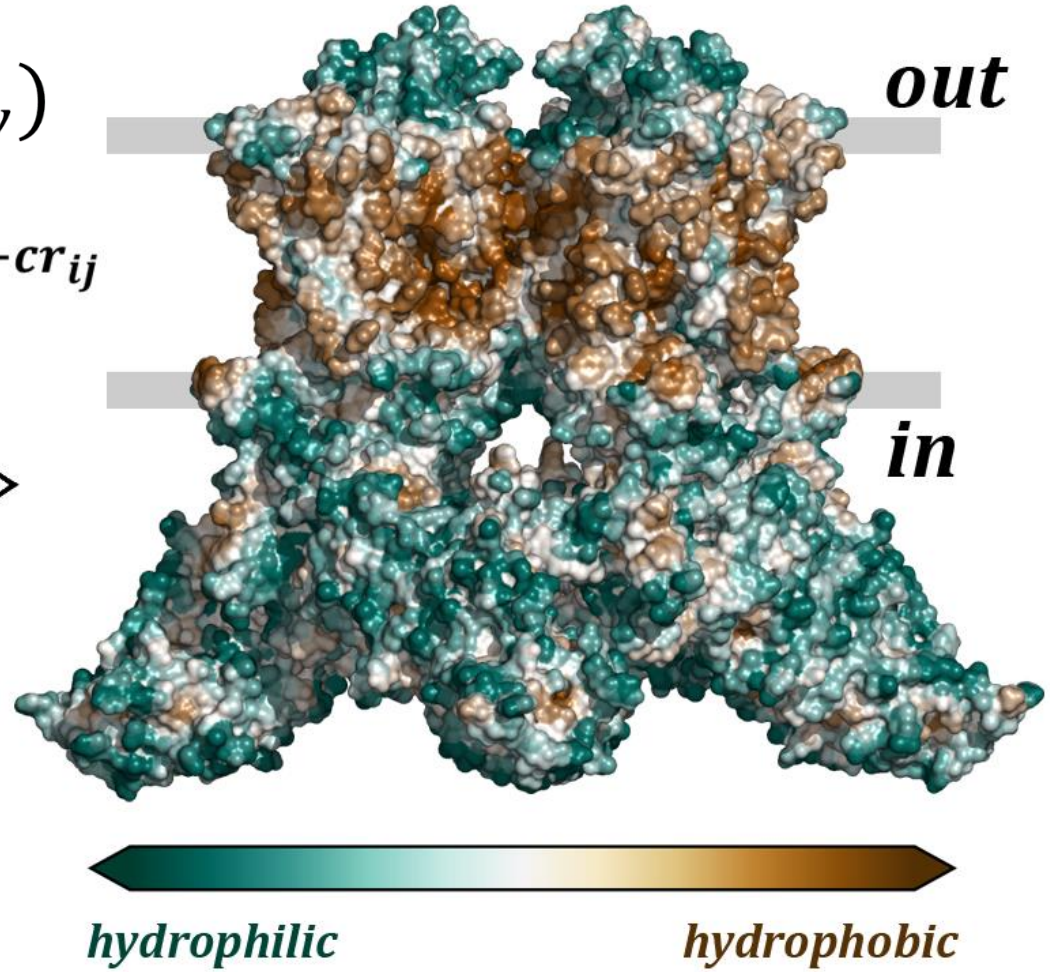
Molecular Hydrophobic Potential (MHP)

Experimentally measured n-octanol/water partition coefficients ($P_{o/w}$) as "hydrophobic charges" of the atoms or atomic groups



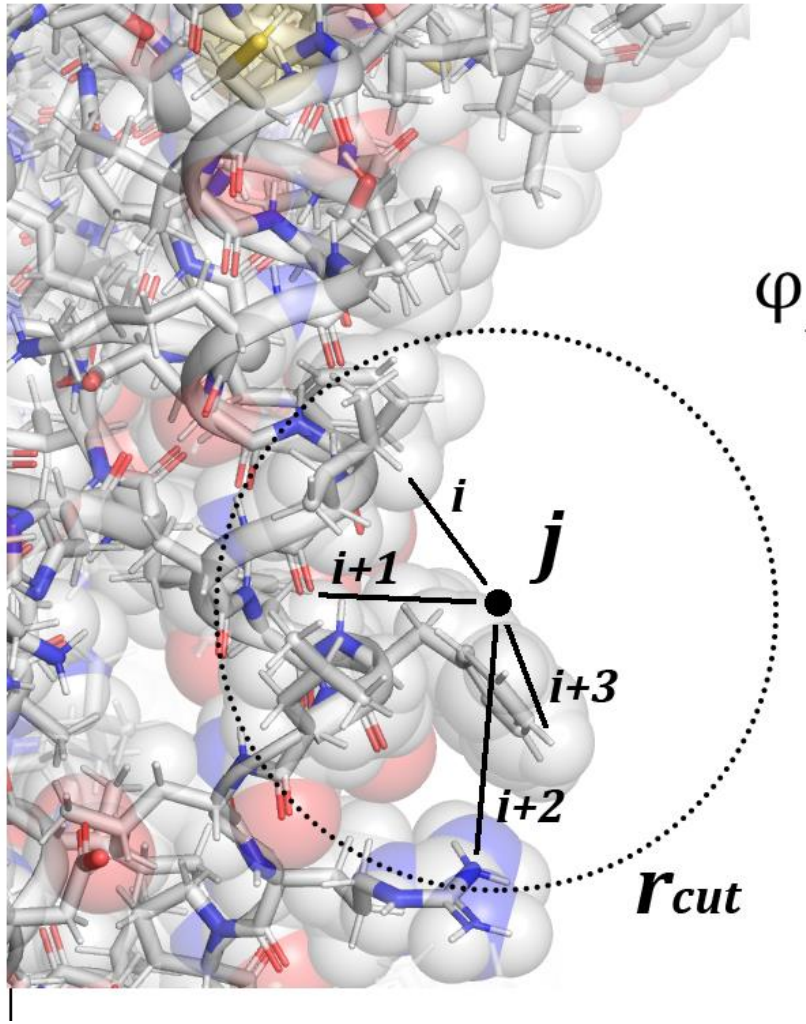
$$f_i = Log(P_{o/w})$$

$$MHP_j = \sum_i f_i e^{-cr_{ij}}$$

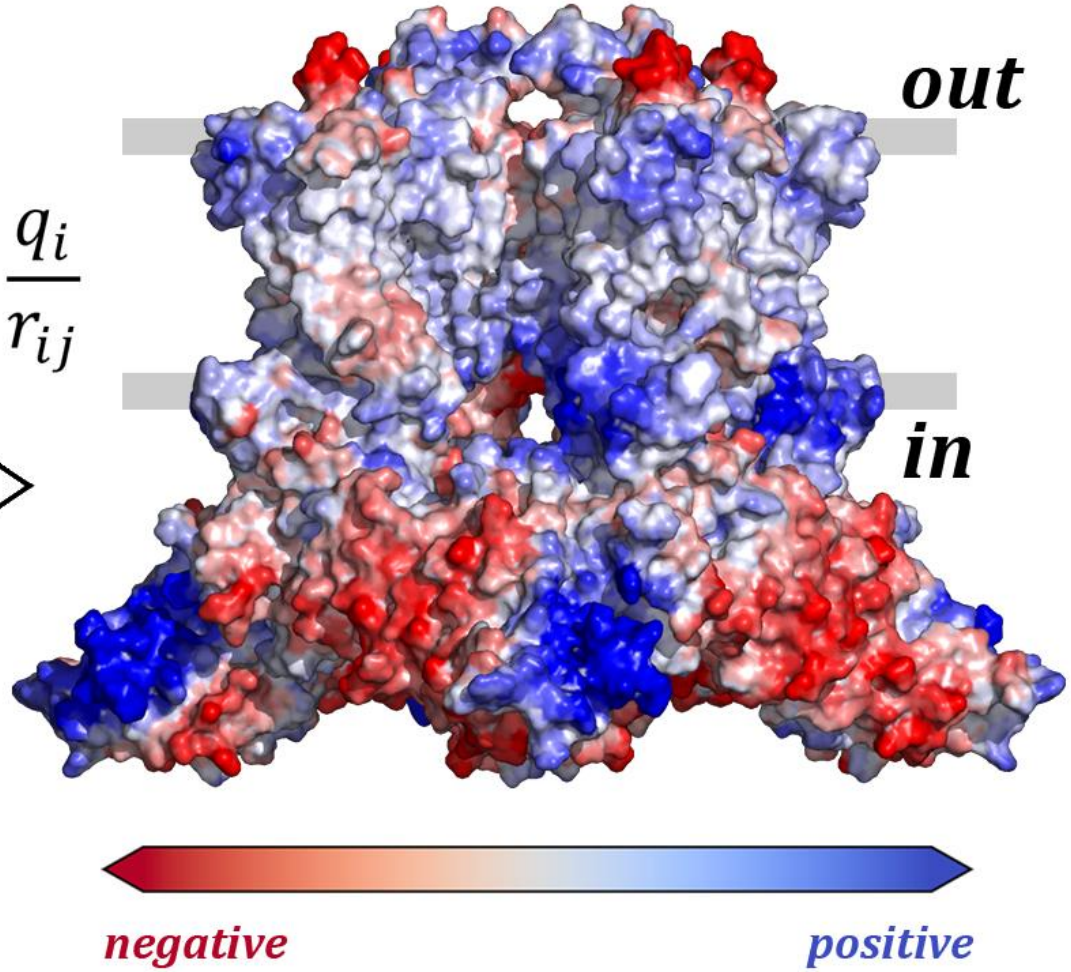


Electrostatic Potential (ESP)

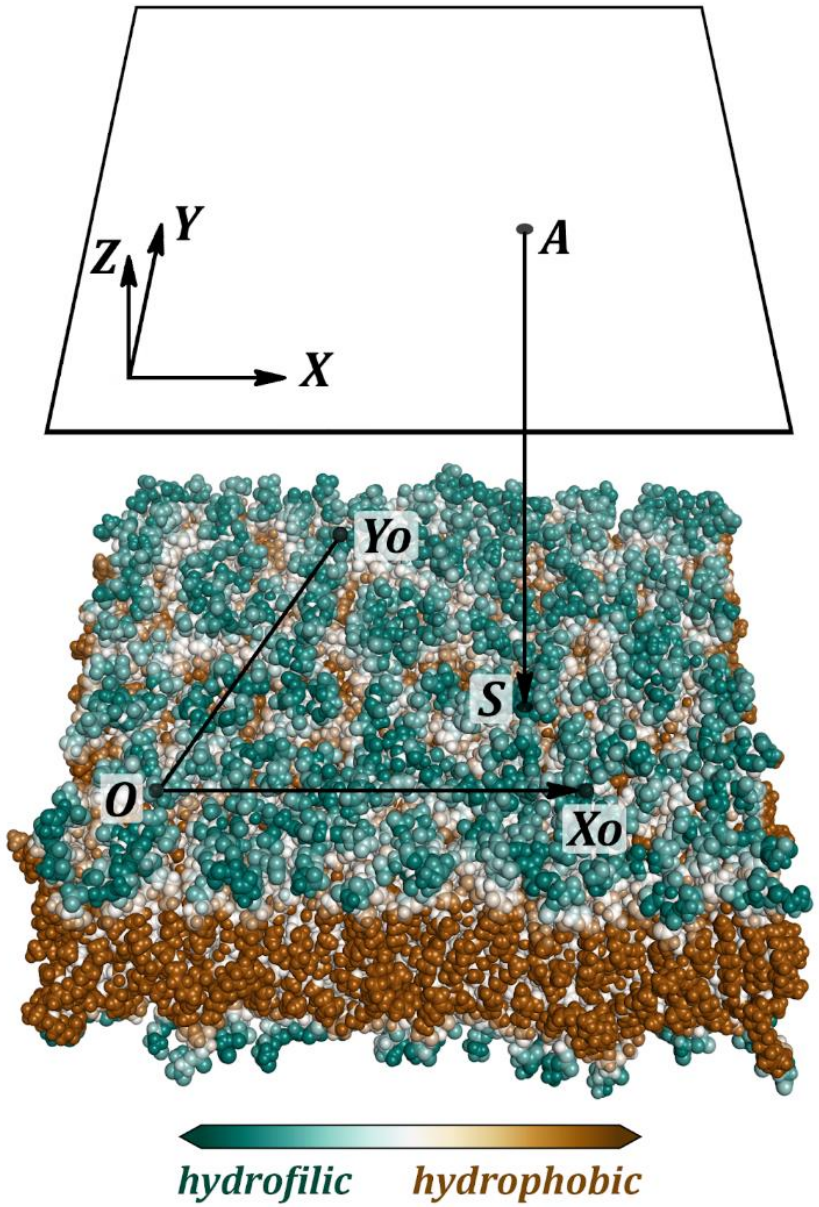
Partial atomic charges (q_i) as an electric potential source

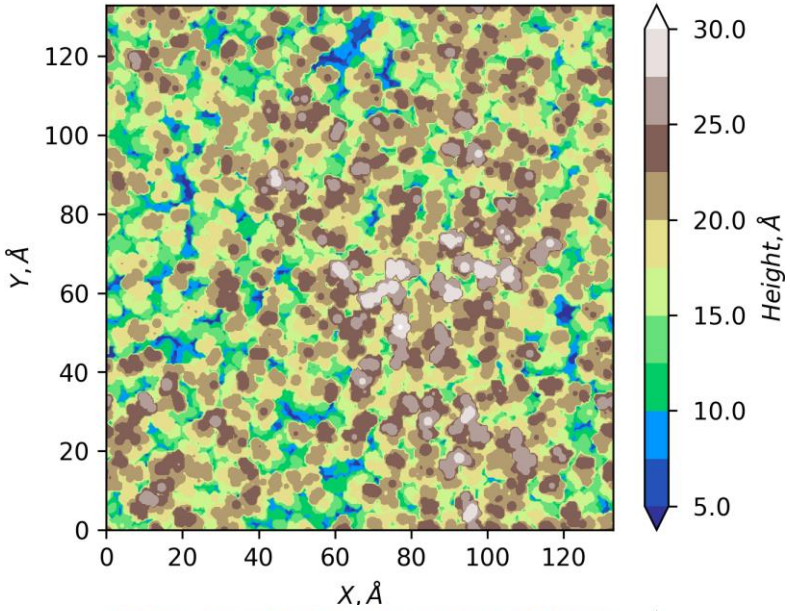


$$\varphi_j = \frac{1}{4\pi\varepsilon\varepsilon_0}\sum_i \frac{q_i}{r_{ij}}$$

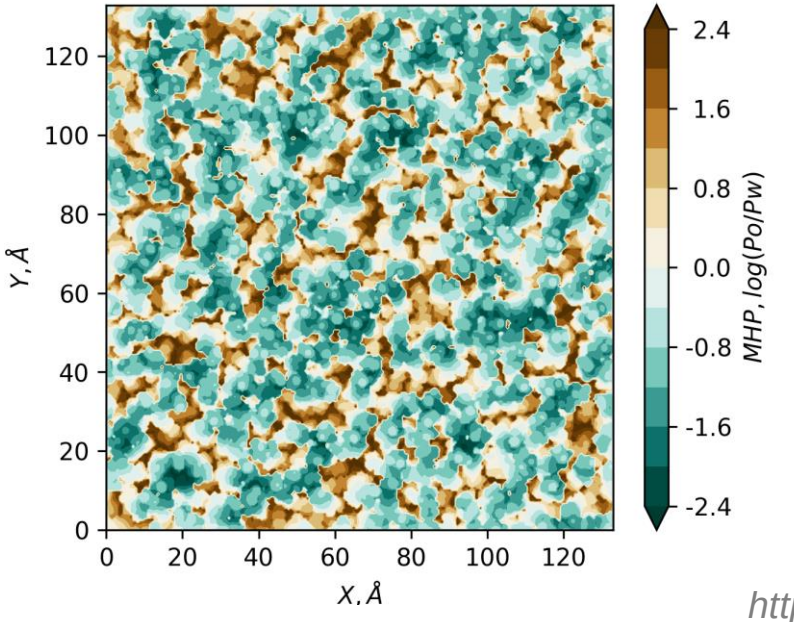


Planar projecting (membrane surface)



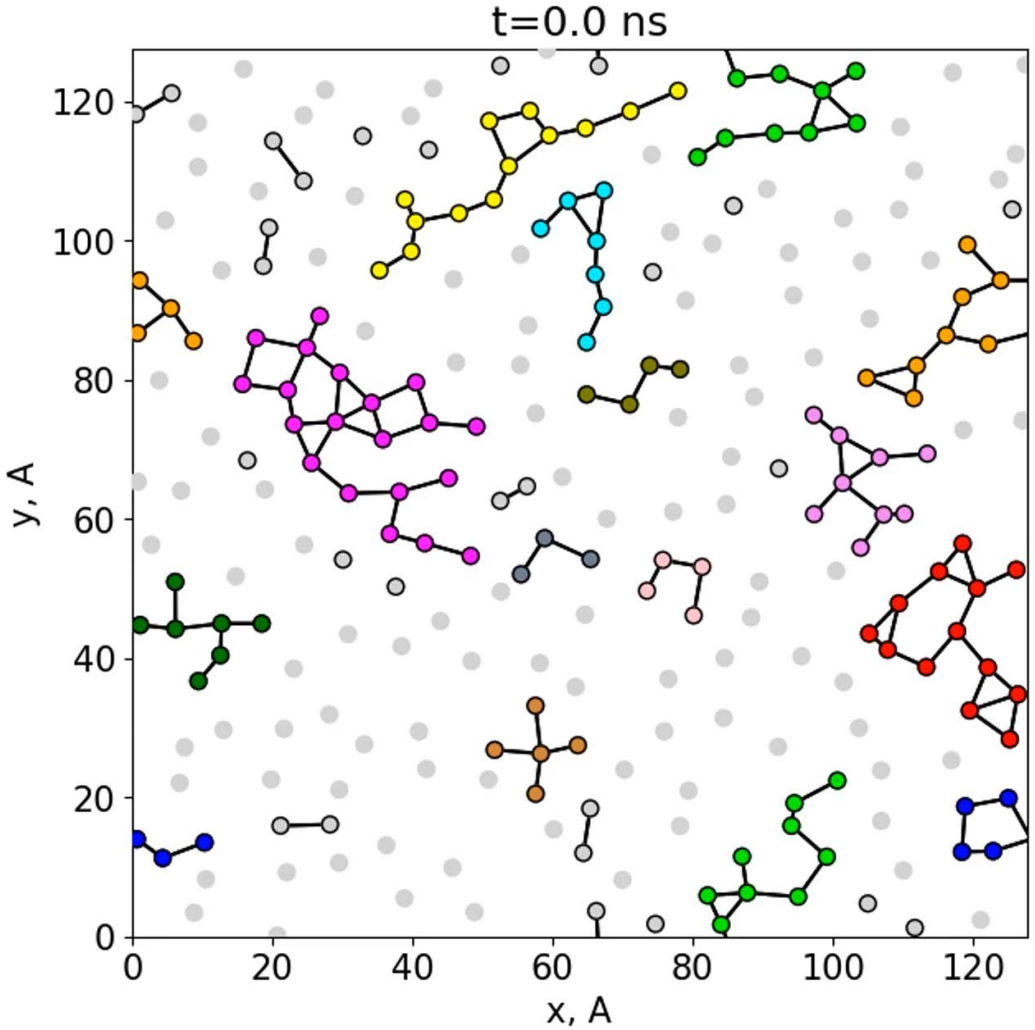


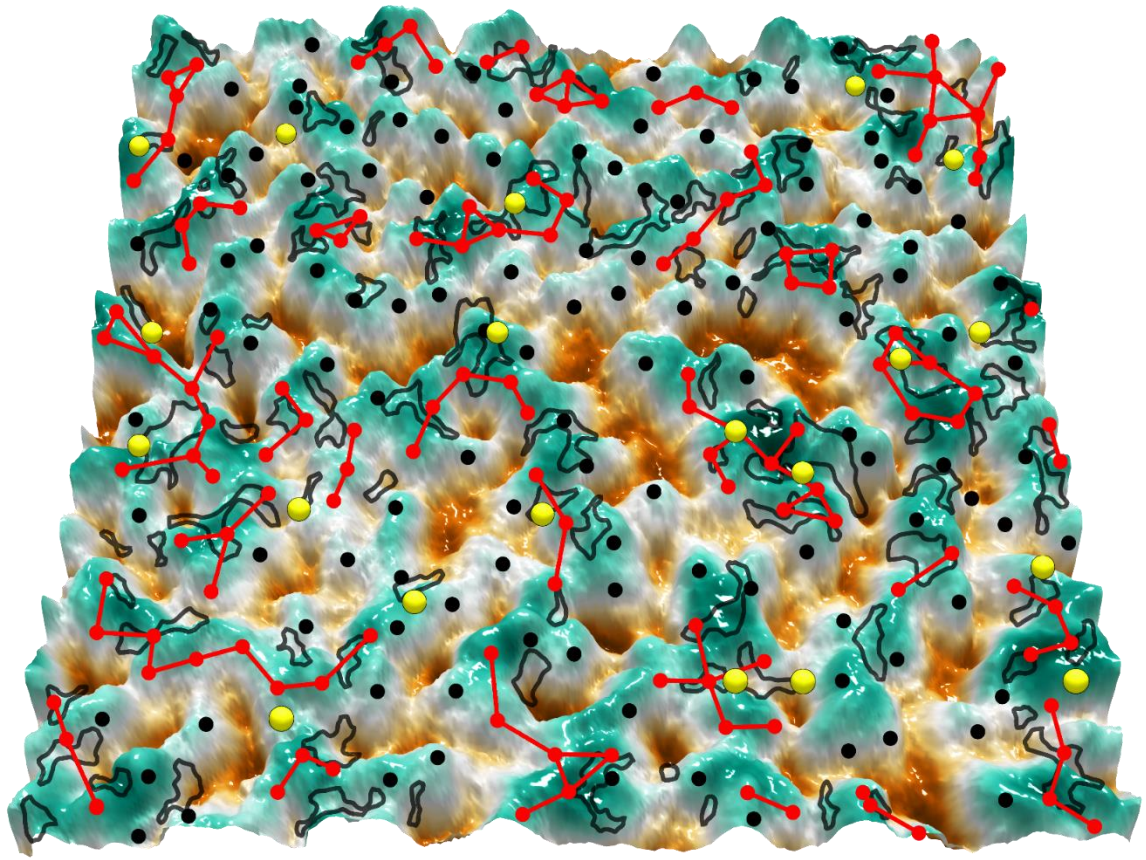
Landscape map



MHP map

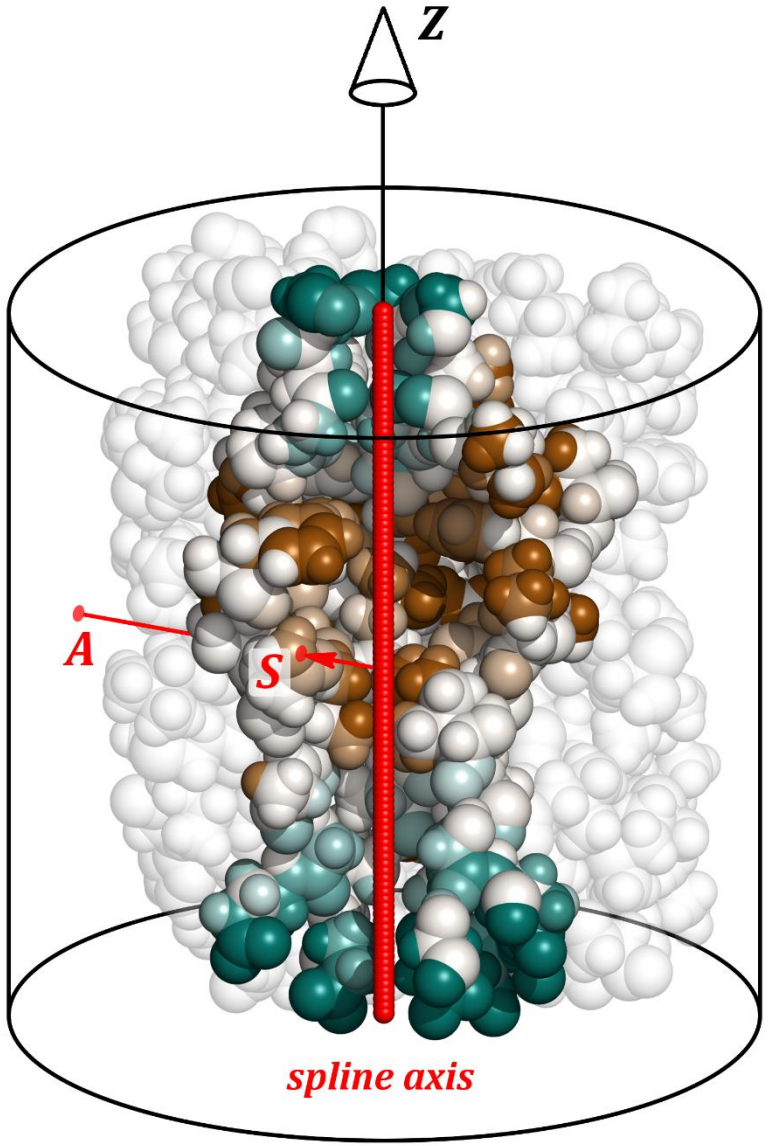
Dynamic molecular portrait of DOPS lipid bilayer

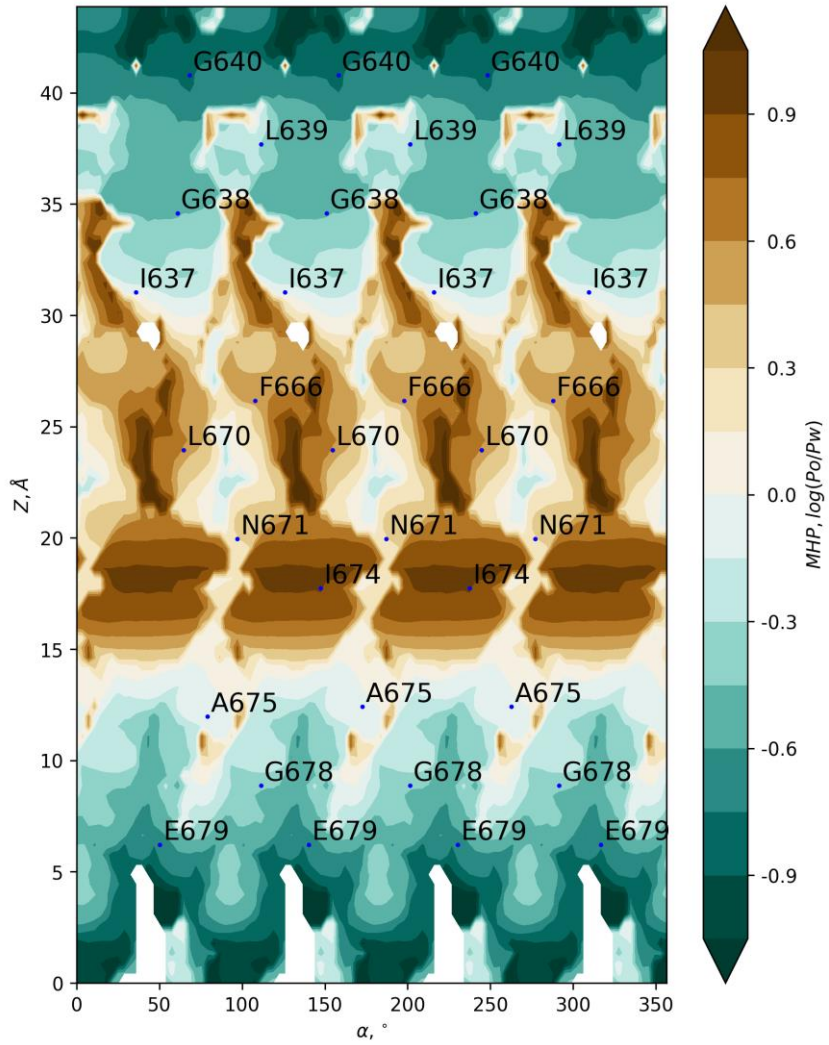




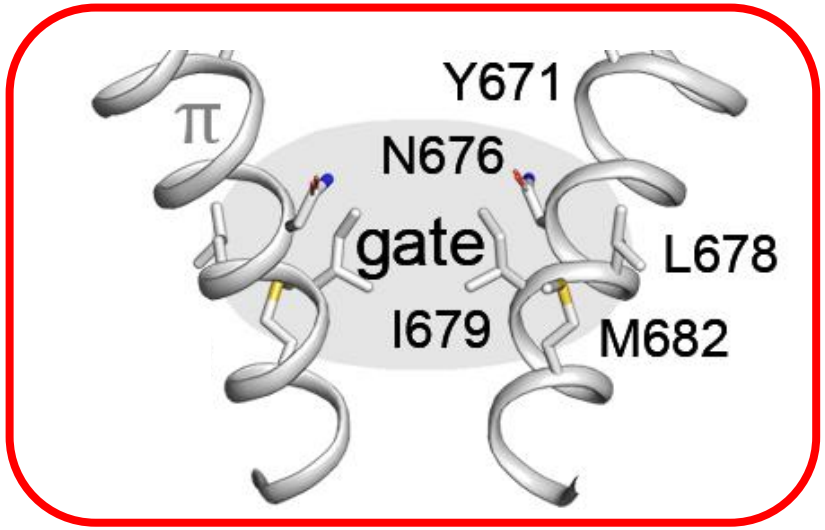
Veretenenko et al. (2024)
doi: 10.1016/j.bbamem.2024.184376

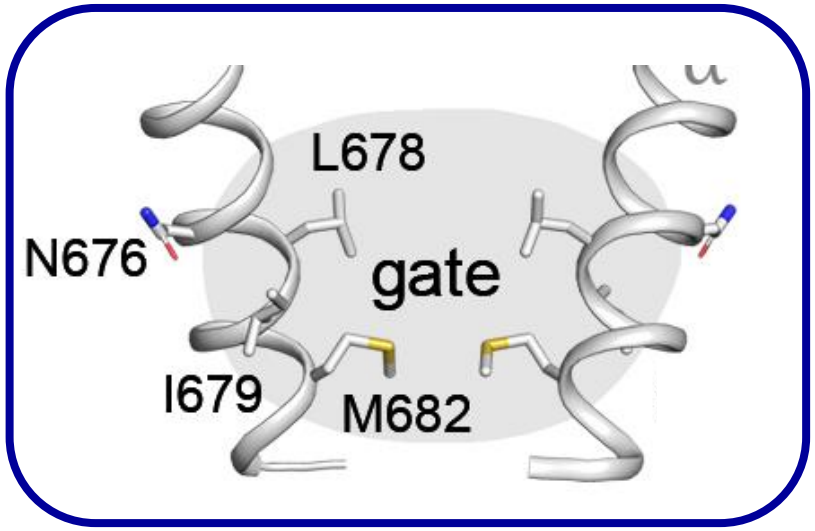
Cylindrical projecting (ion channel pore)

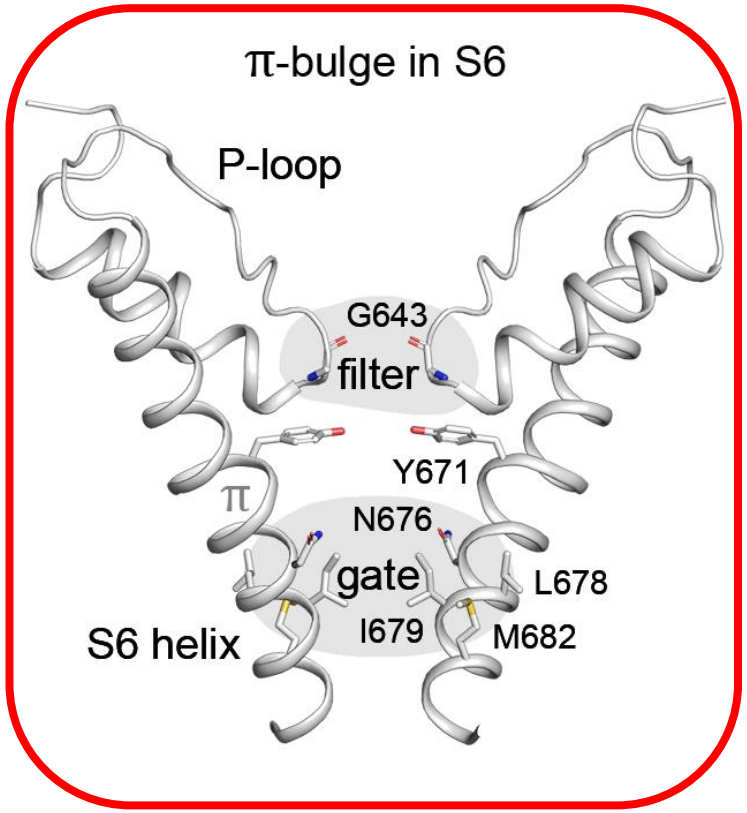




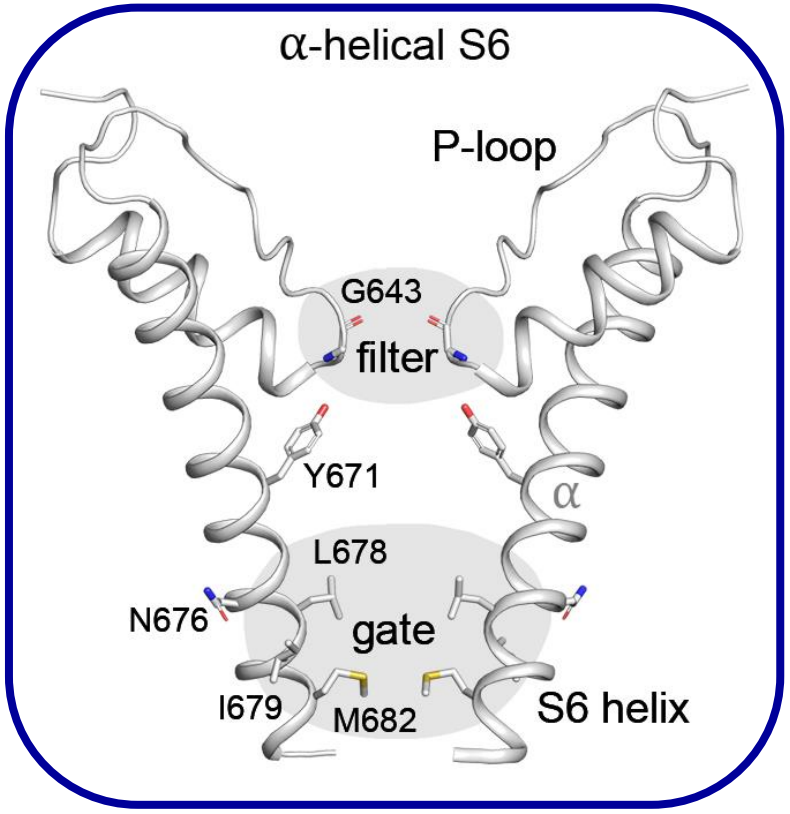
Conductive pores of TRPV ion channels







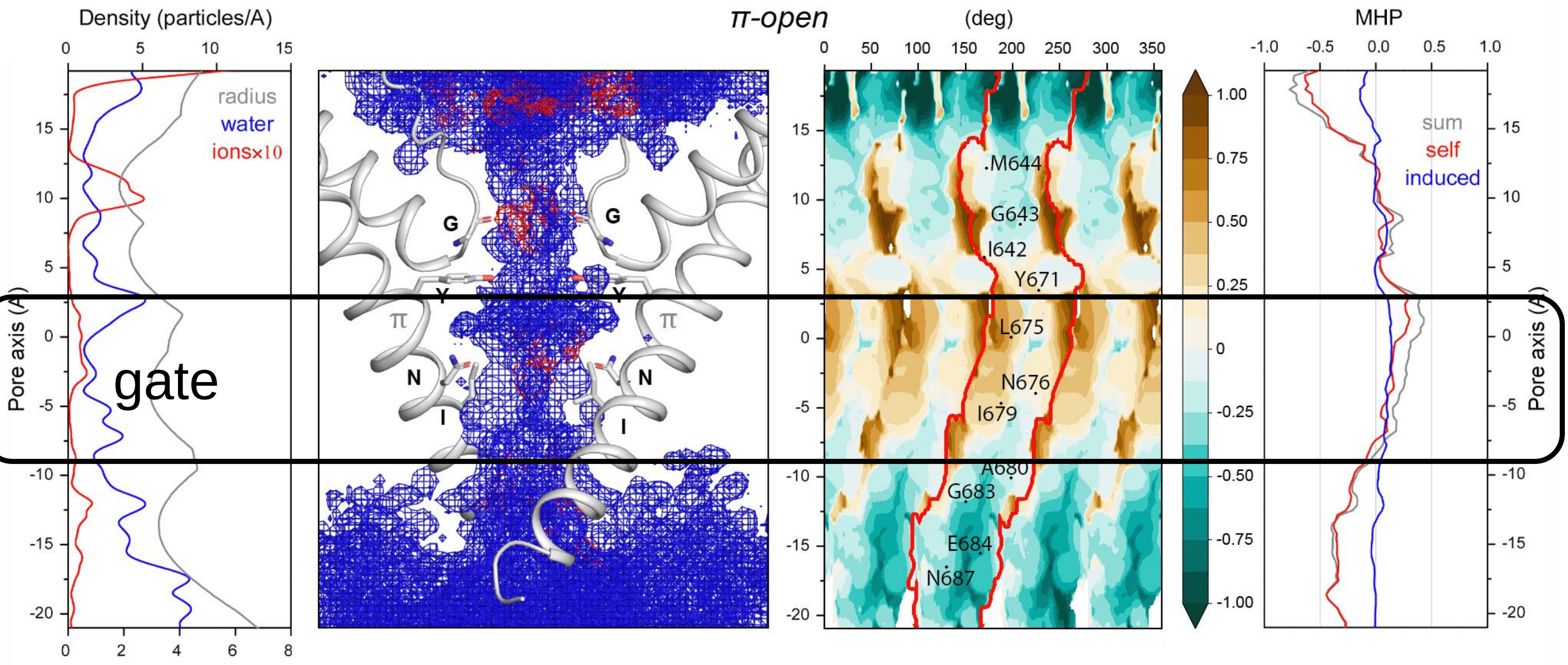
π-bulge state of S6-helix



α-helical state of S6-helix

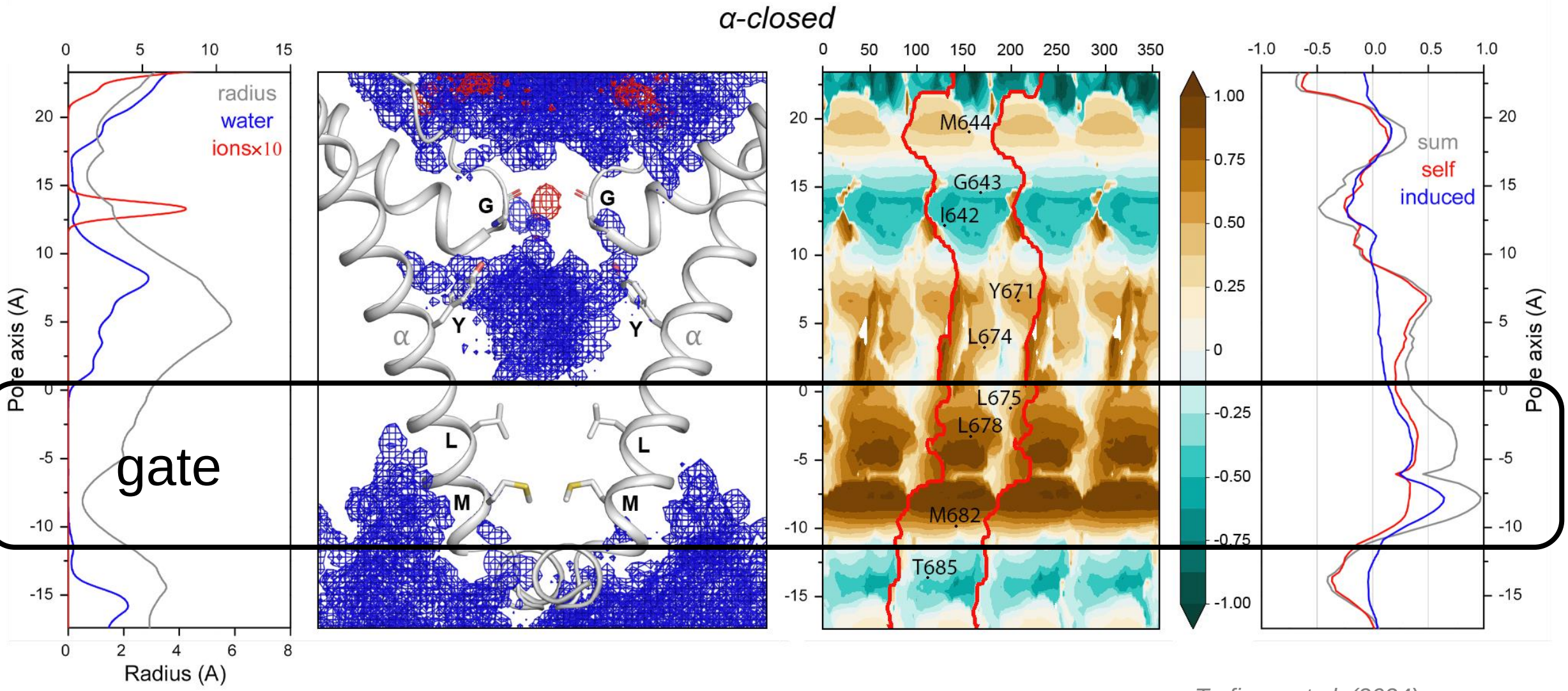
Trofimov et al. (2024)
doi: 10.1038/s42004-024-01198-z

π-open state of the TRPV1 pore



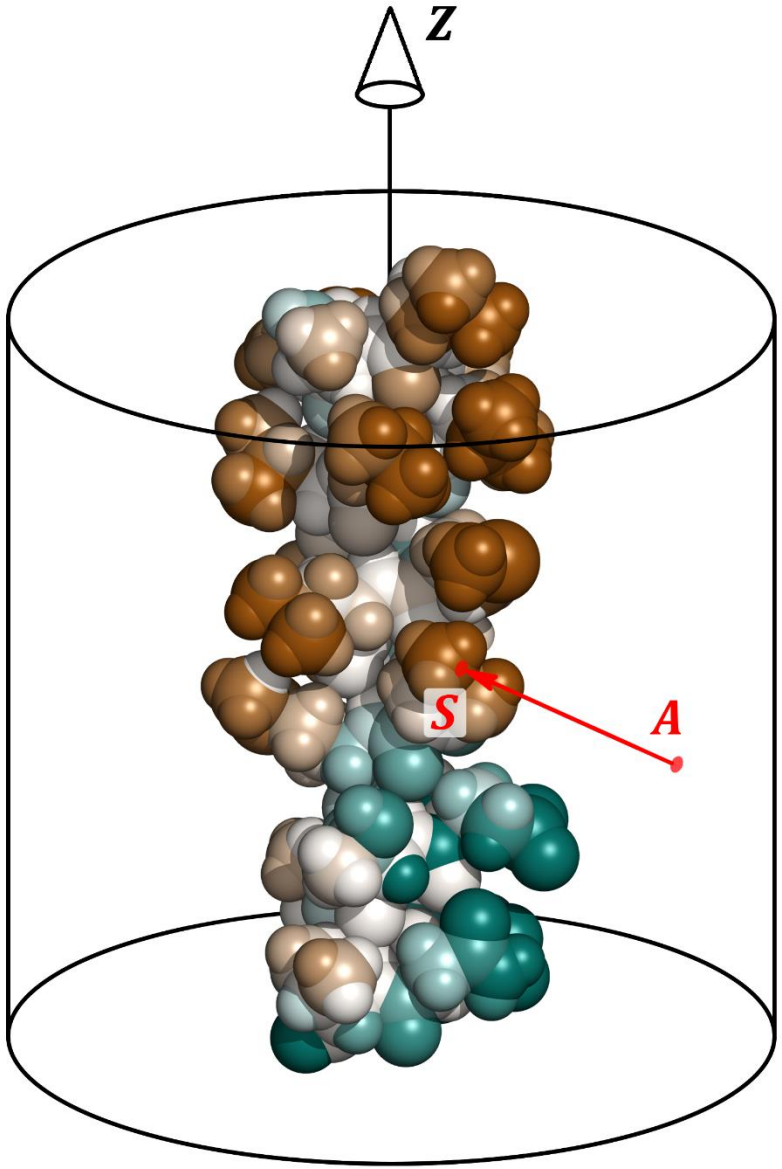
Trofimov et al. (2024)
doi: 10.1038/s42004-024-01198-z

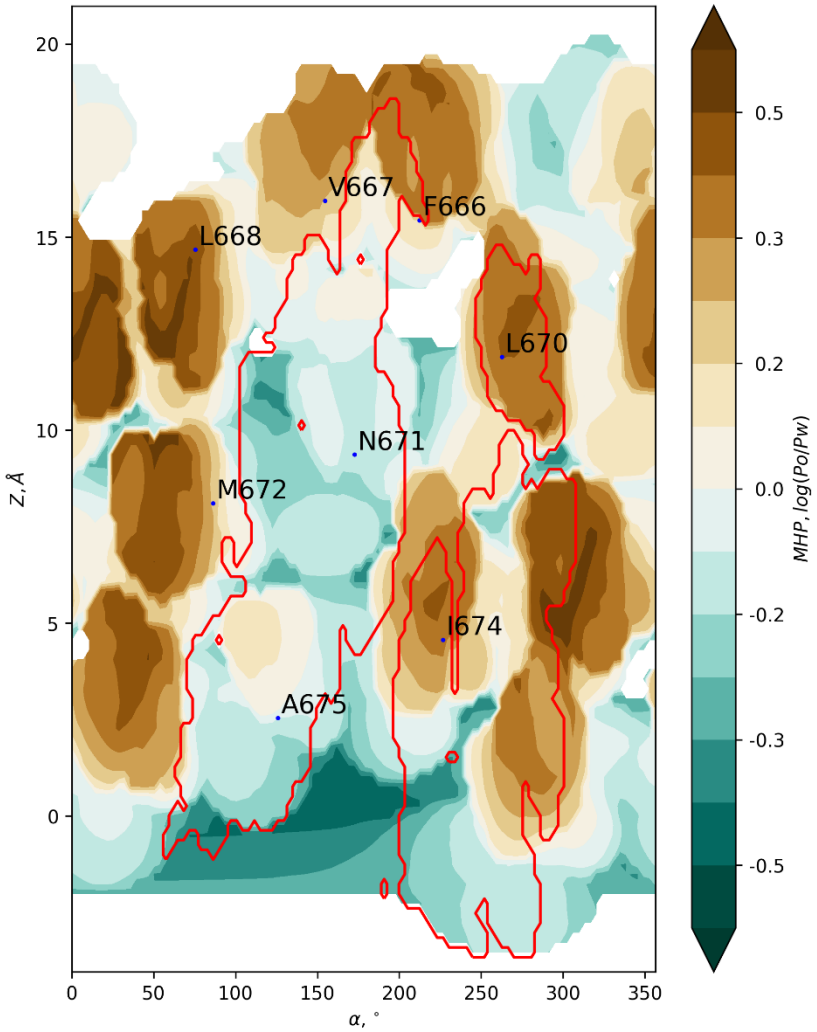
α-closed состояние поры TRPV1



Trofimov et al. (2024)
doi: 10.1038/s42004-024-01198-z

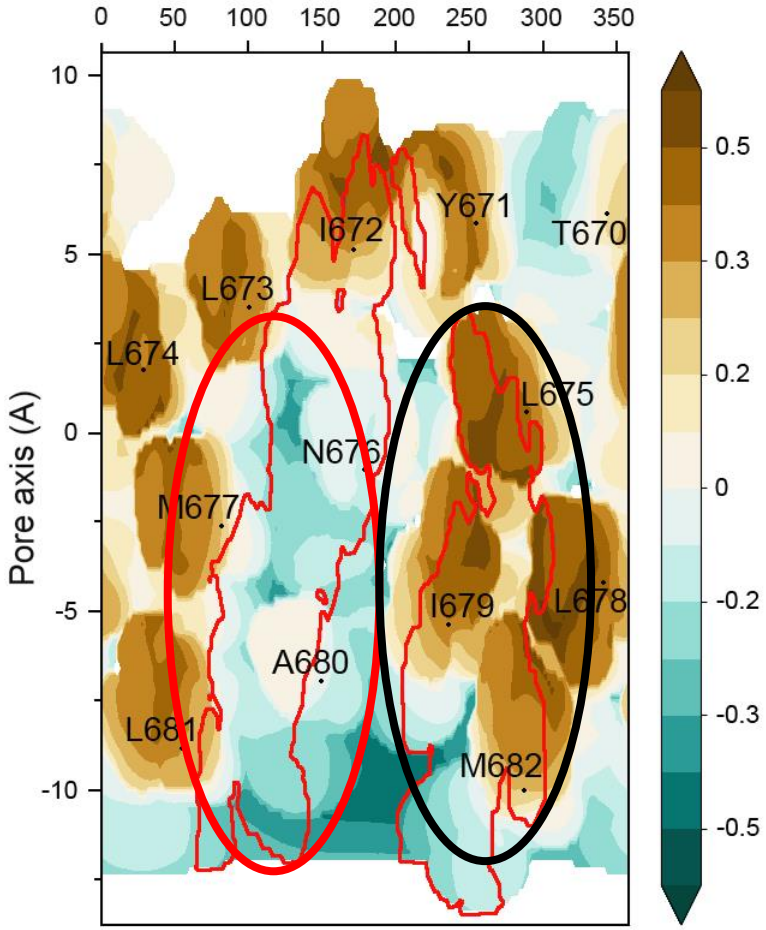
Cylindrical projecting (helix)





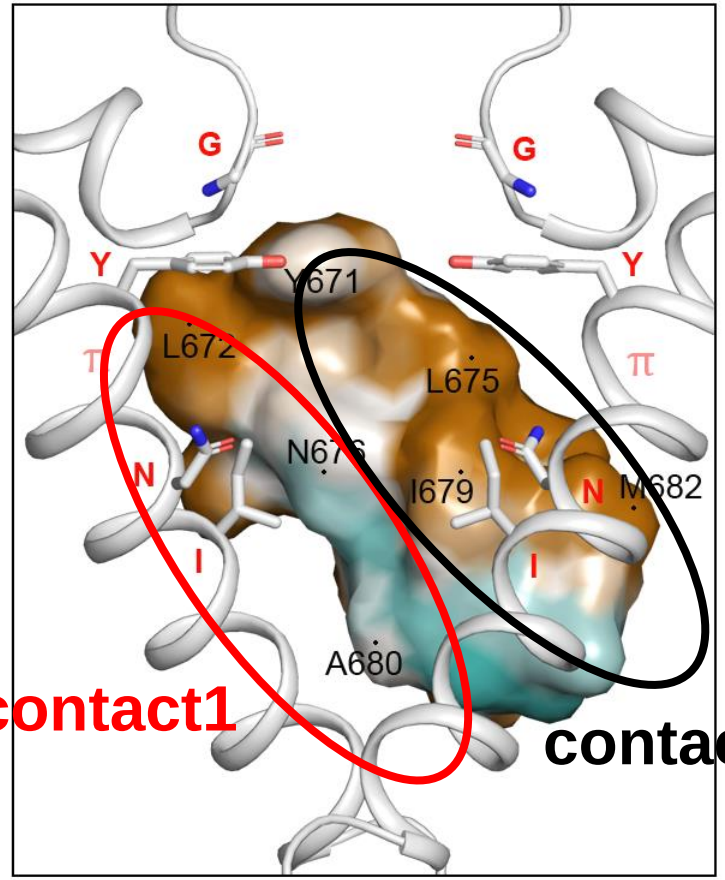
π-open TRPV1 interhelix contacts at the gate region

MHP map of S6 helix

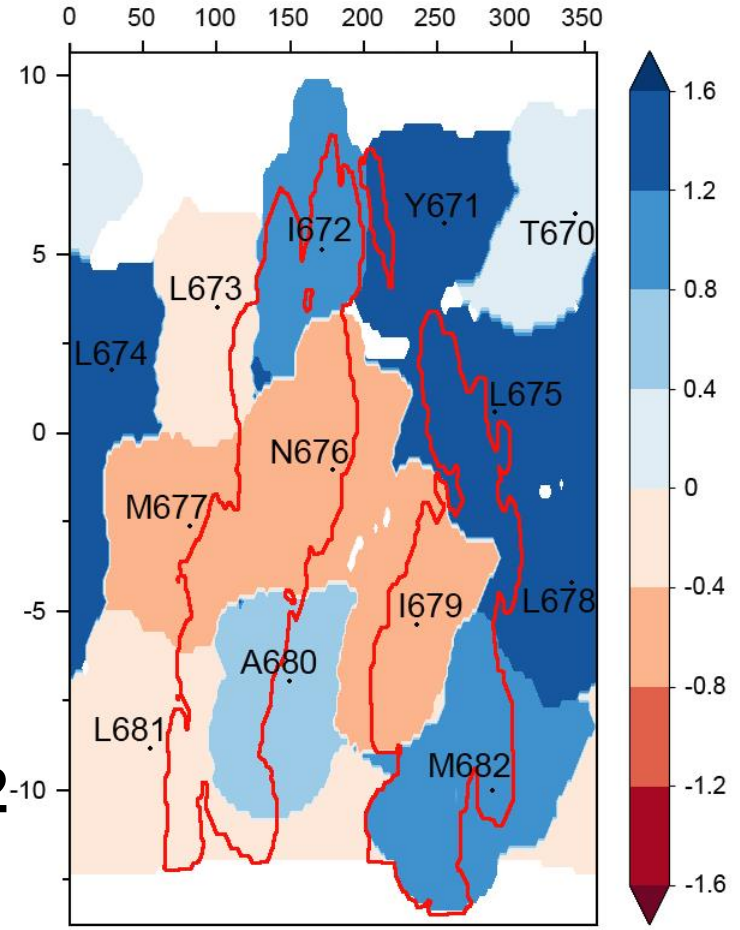


contact1 **contact2**

π-open



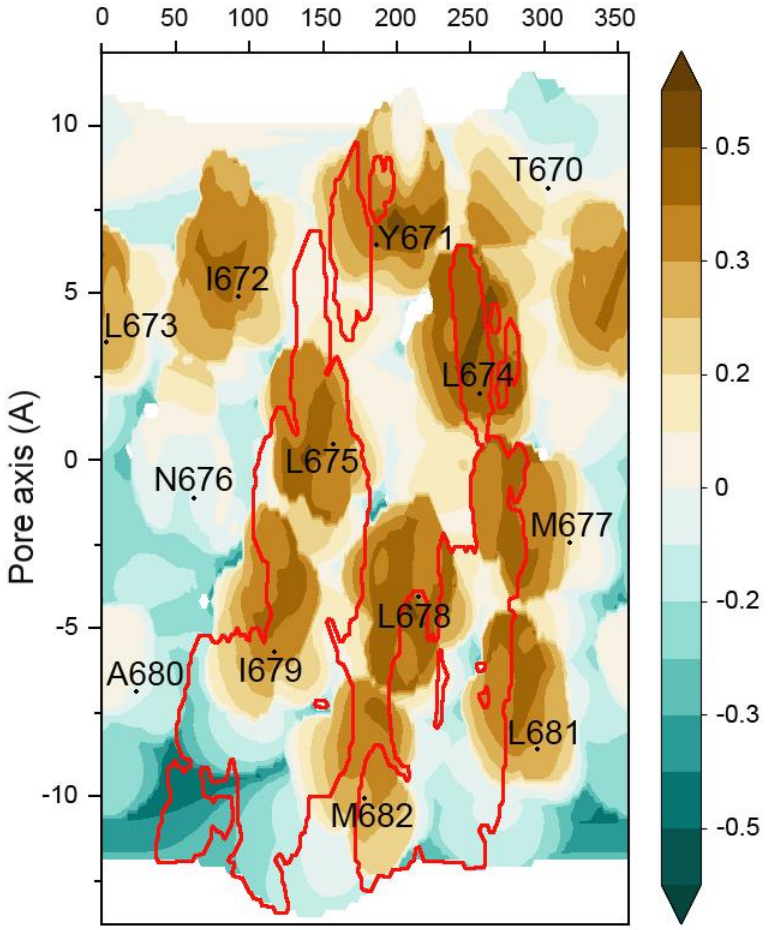
3d-1d score or residue packing quality



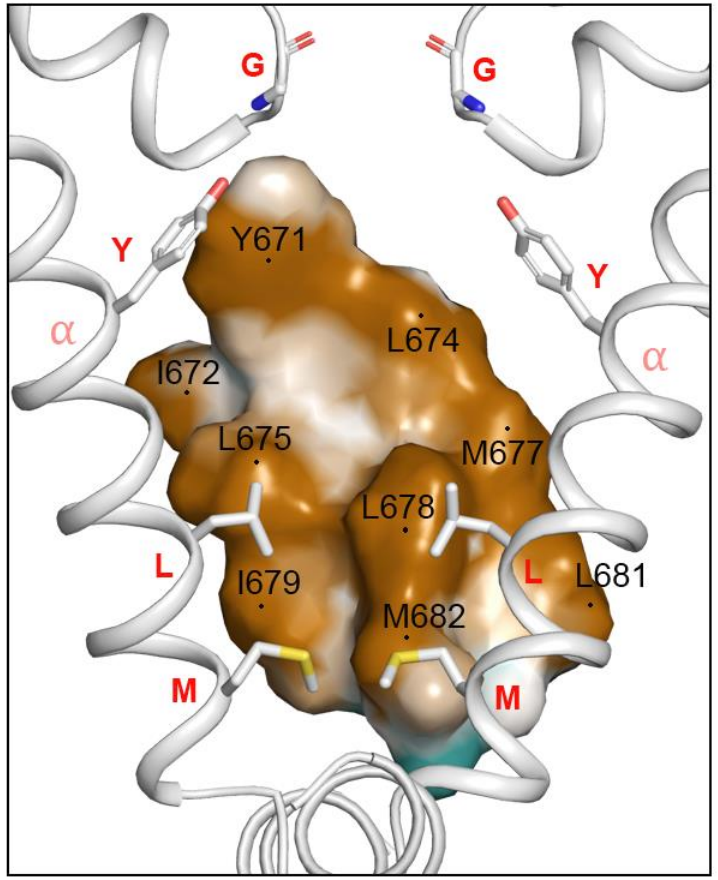
Trofimov et al. (2024)
doi: 10.1038/s42004-024-01198-z

α-closed TRPV1 interhelix contacts at the gate region

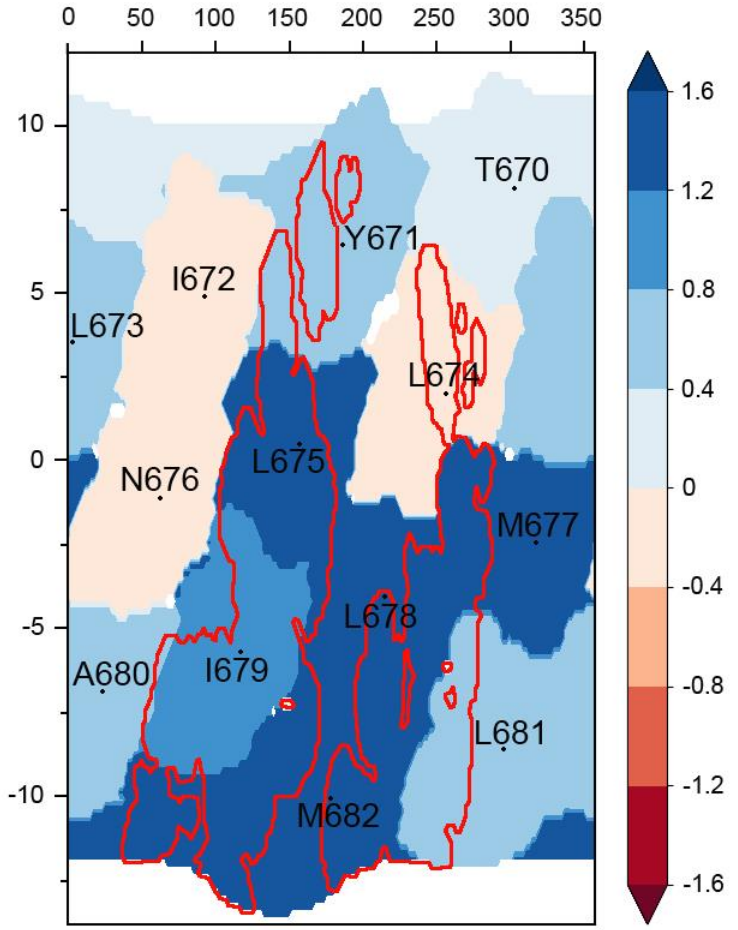
MHP map of S6 helix



α-closed



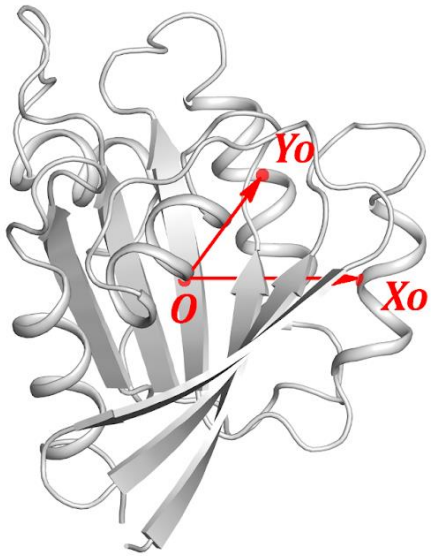
3d-1d score or residue packing quality



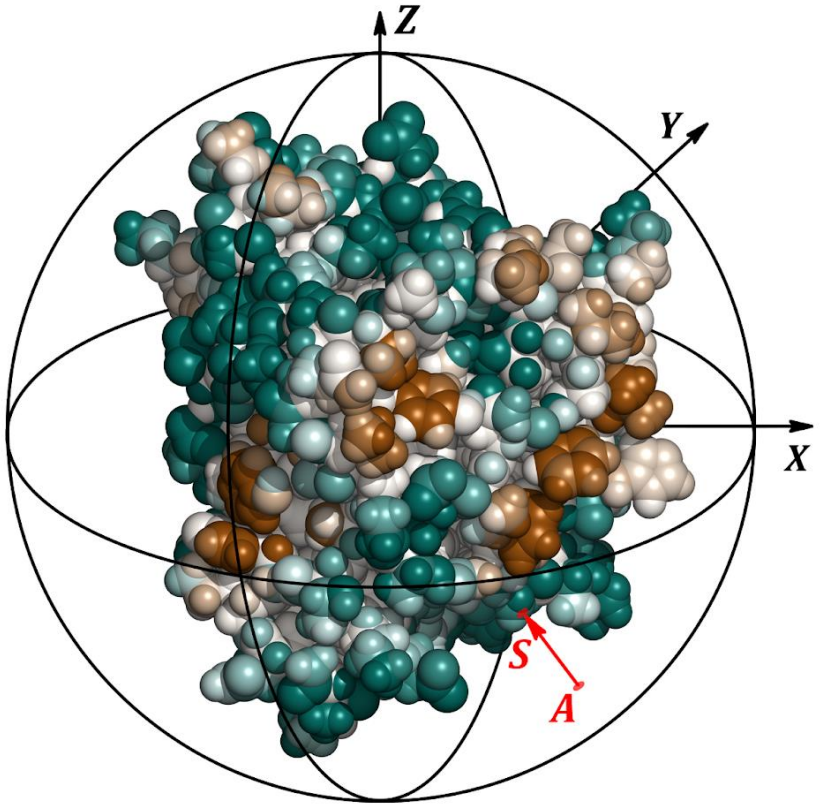
Trofimov et al. (2024)
doi: 10.1038/s42004-024-01198-z

Spherical projecting (peptide)

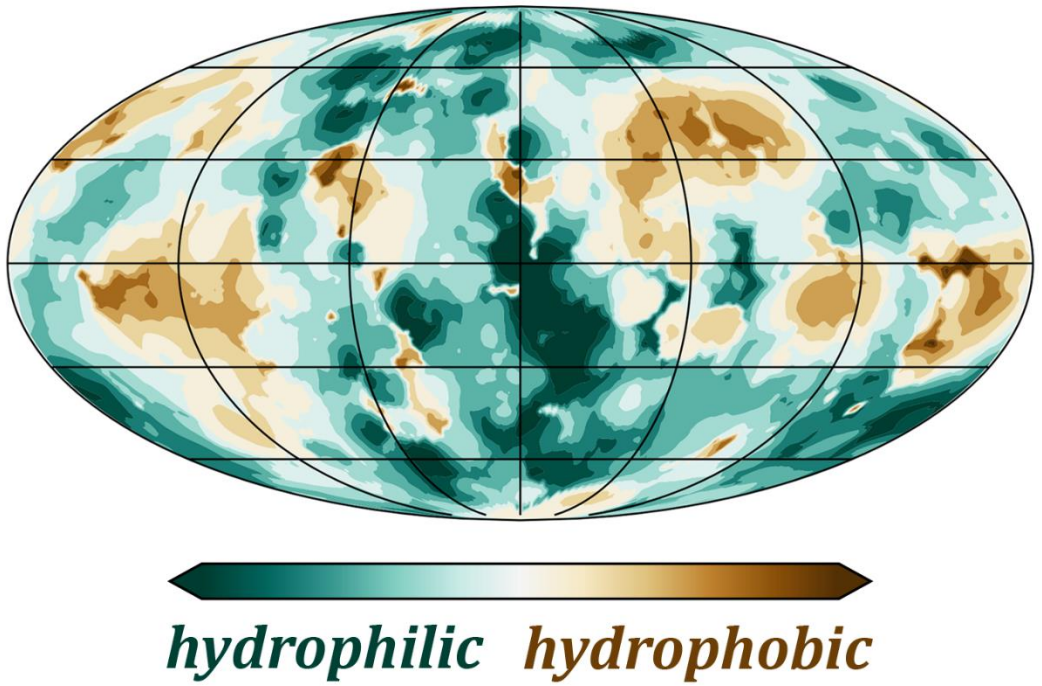
AFR6 peptide structure



MHP calculated on the peptide surface



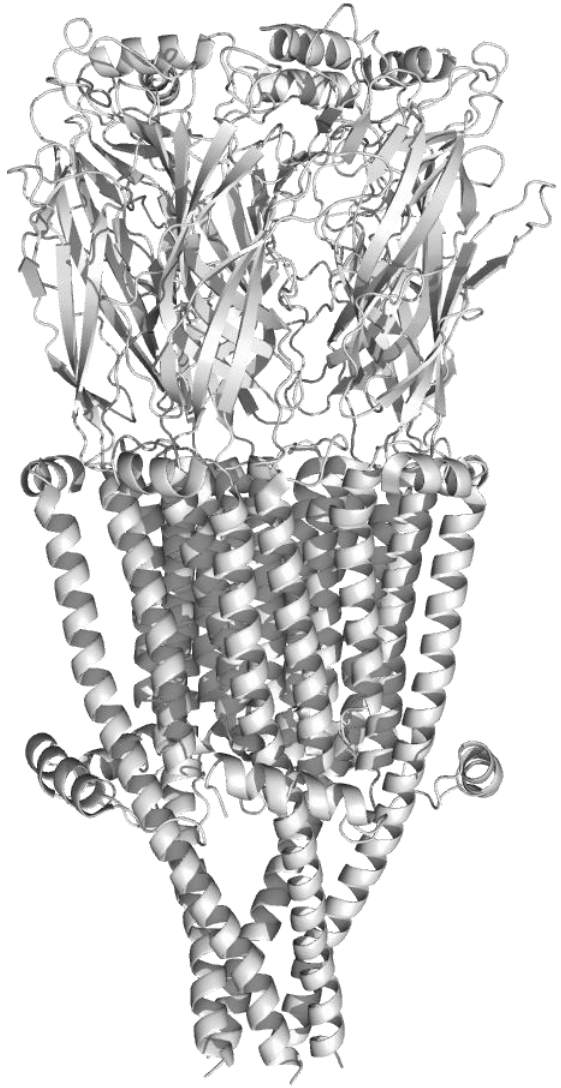
Mollweide projection of the MHP distribution



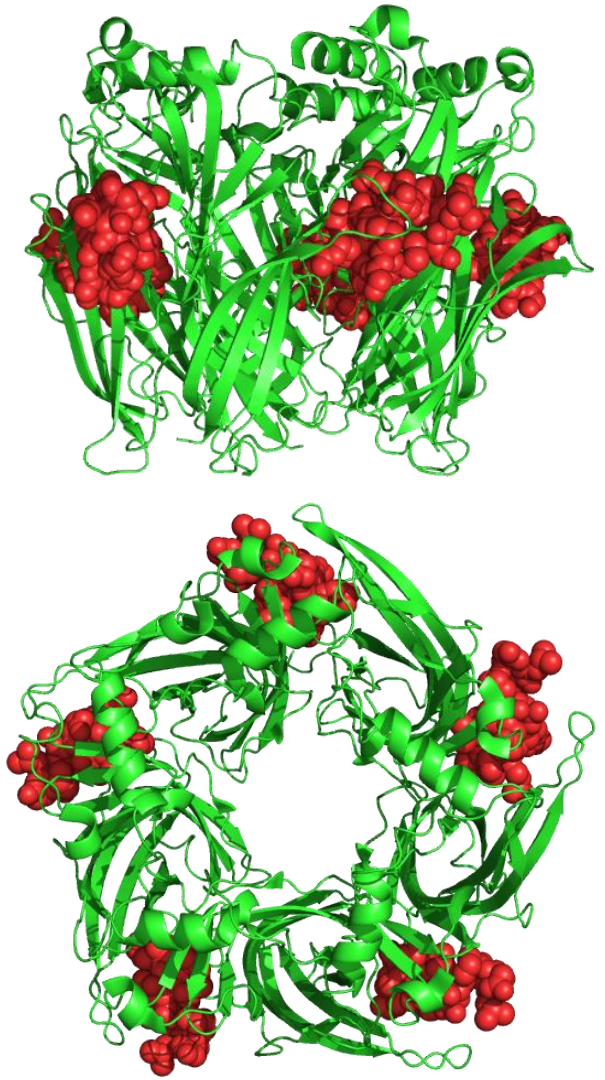
Complex of Acetylcholine binding protein (AChBP) with α-conotoxin

ligand-binding domain

Trans membrane domain



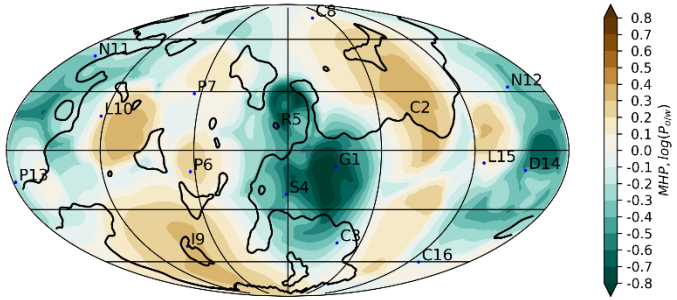
Alpha7-nicotinic acetylcholine receptor (nAchR) PDB ID: 8V89



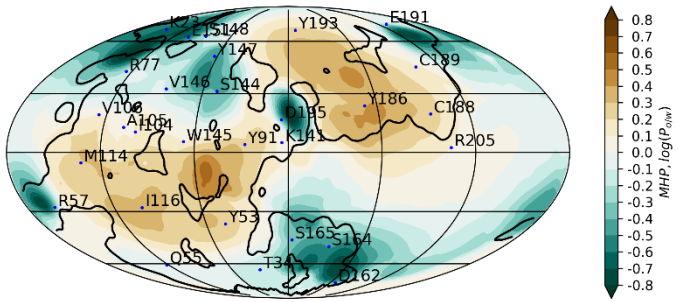
Acetylcholine binding protein (AChBP) complex with a-conotoxin TxIA10 PDB ID: 2UZ6

Match of surface properties at AchBP-Conotoxin (TxIA) interface

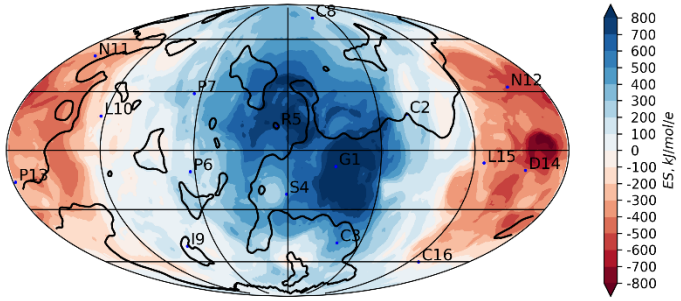
TxIA MHP



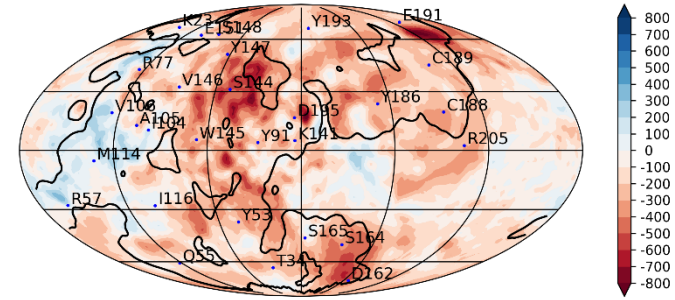
AchBP MHP



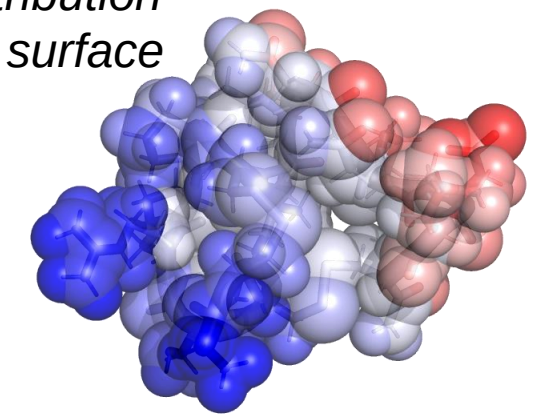
TxIA ESP



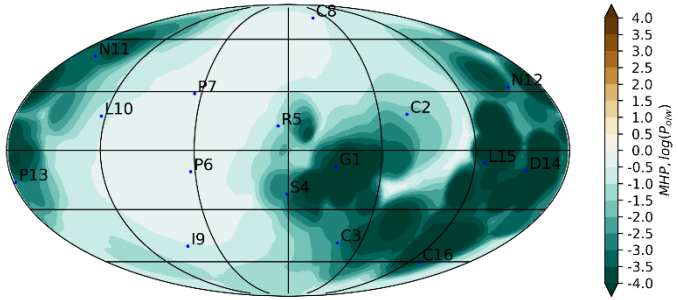
AchBP ESP

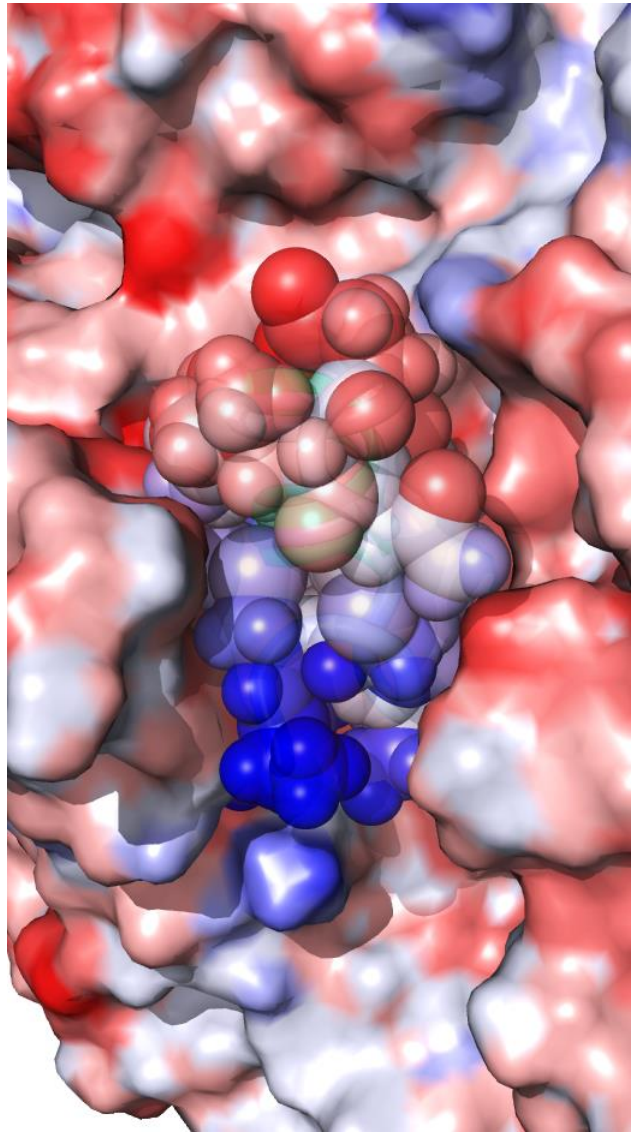


ESP distribution over the surface



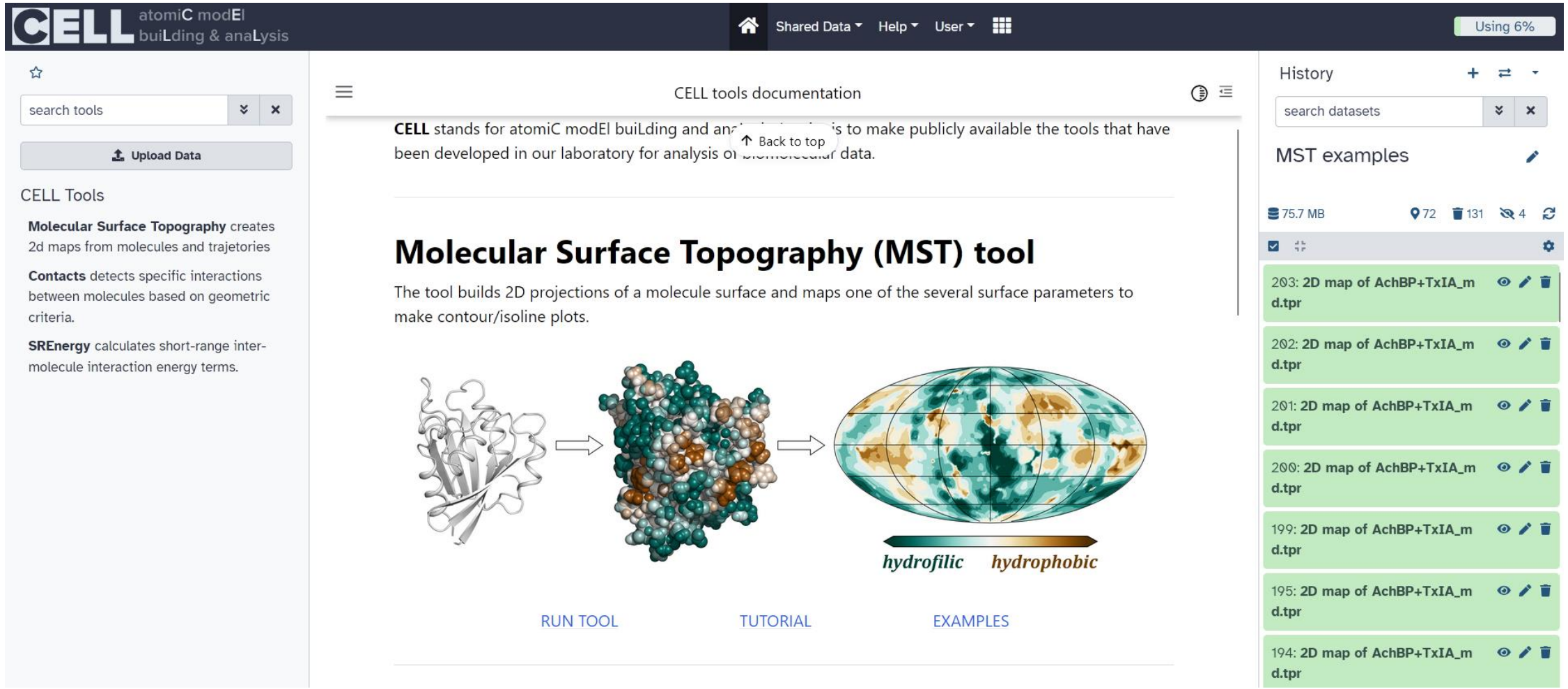
water MHP





Koromyslova et al. (2014)
doi: 10.1021/ci500158y

CELL virtual laboratory



model.nmr.ru/cell

Thank you for your attention!