



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

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Anton O. Chugunov, Roman G. Efremov

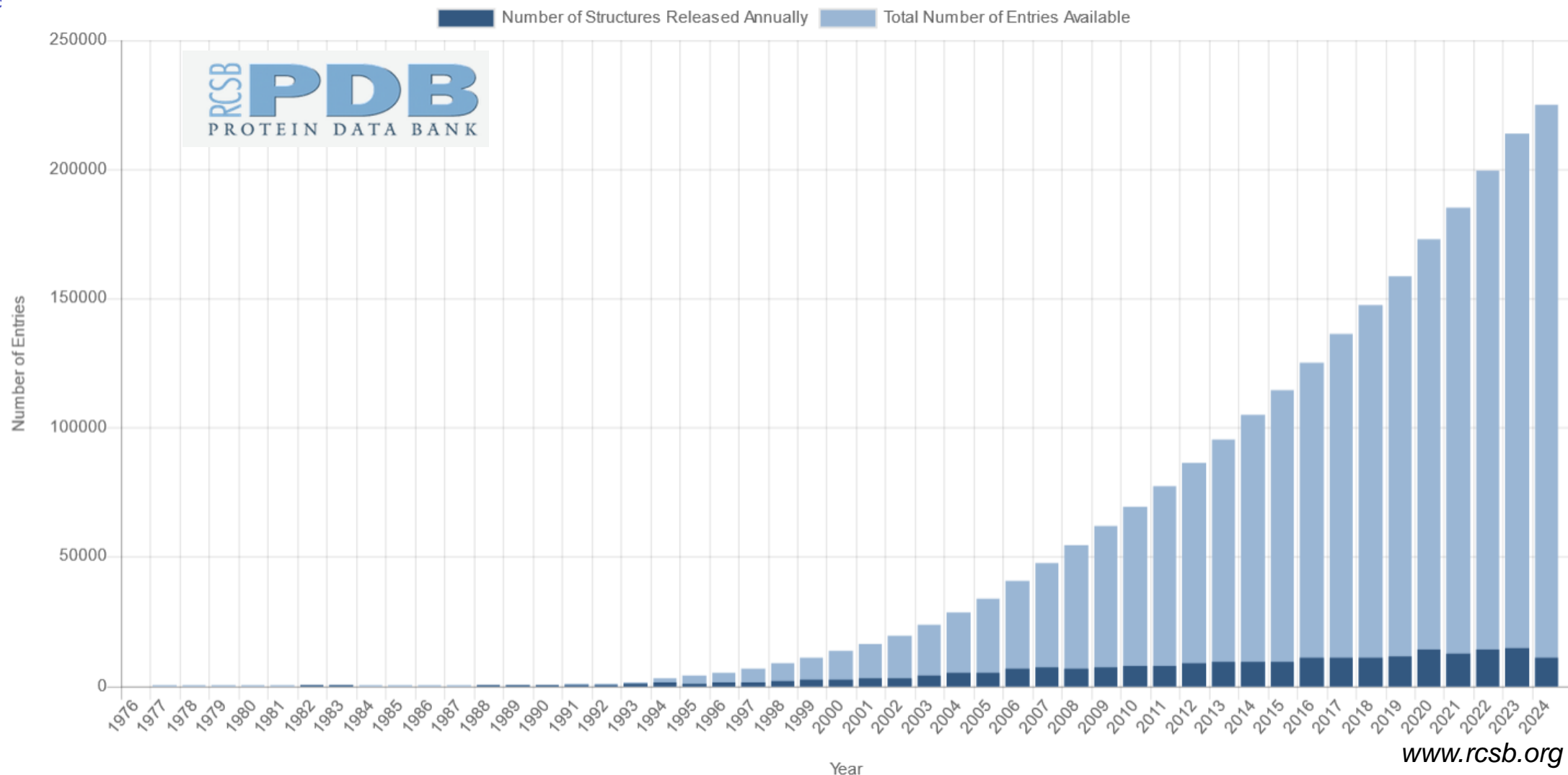
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BCADD-2024, 16 September 2024



Experimental biomolecular structures



www.rcsb.org

PDB Statistics: Overall Growth of Released Structures Per Year



AI generated structural data

Not only AlphaFold!

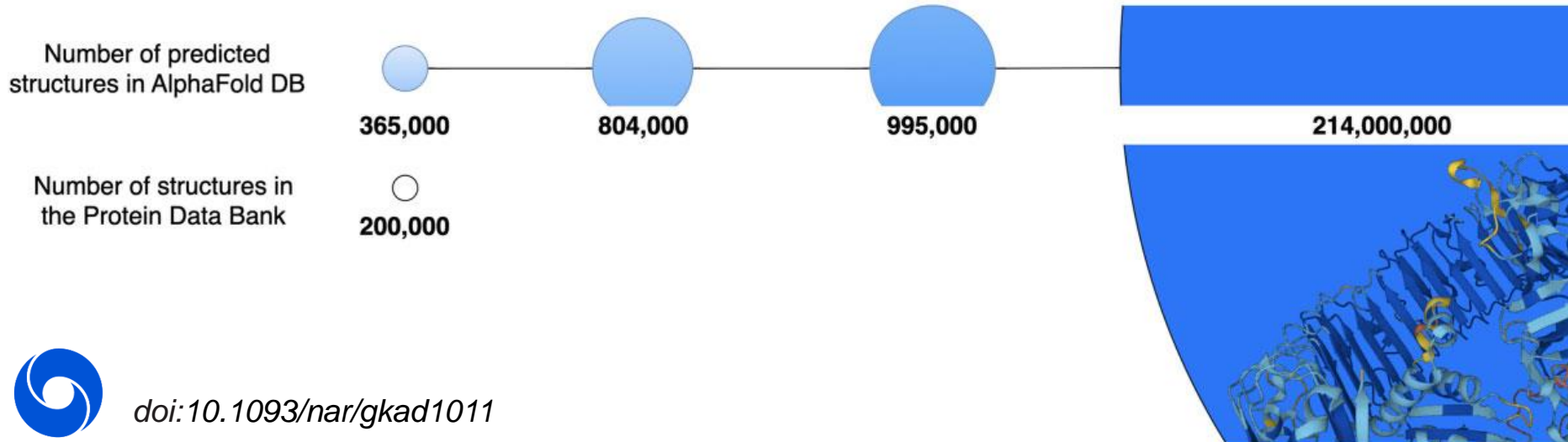
April 2021 Collaboration agreement between EMBL-EBI and DeepMind

July 2021 Initial release of the AlphaFold DB

December 2021 Predicted structures for the Swiss-Prot sequence set

January 2022 Organisms implicated in Global Health and Neglected Diseases

July 2022 Predicted structures for most of the UniProt database



RoseTTAFold

ESM Fold
>600M protein structures

ProteinMPNN
Protein sequence design

and so on...

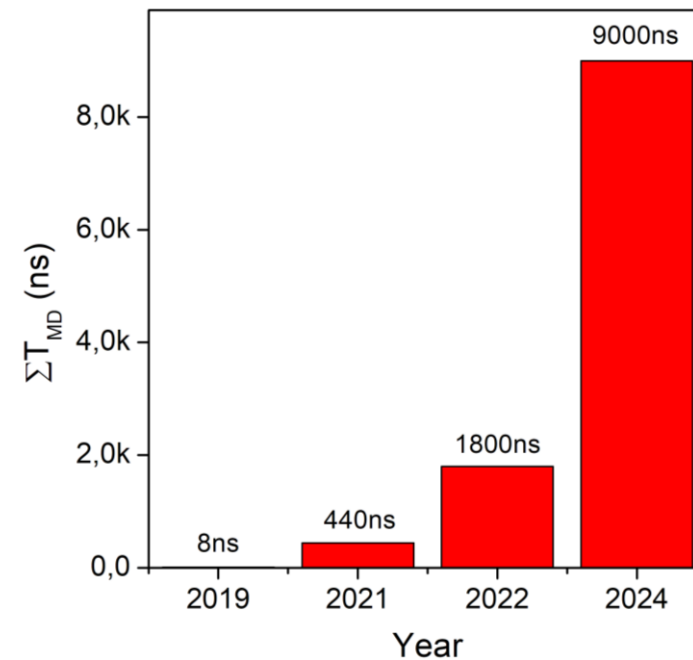
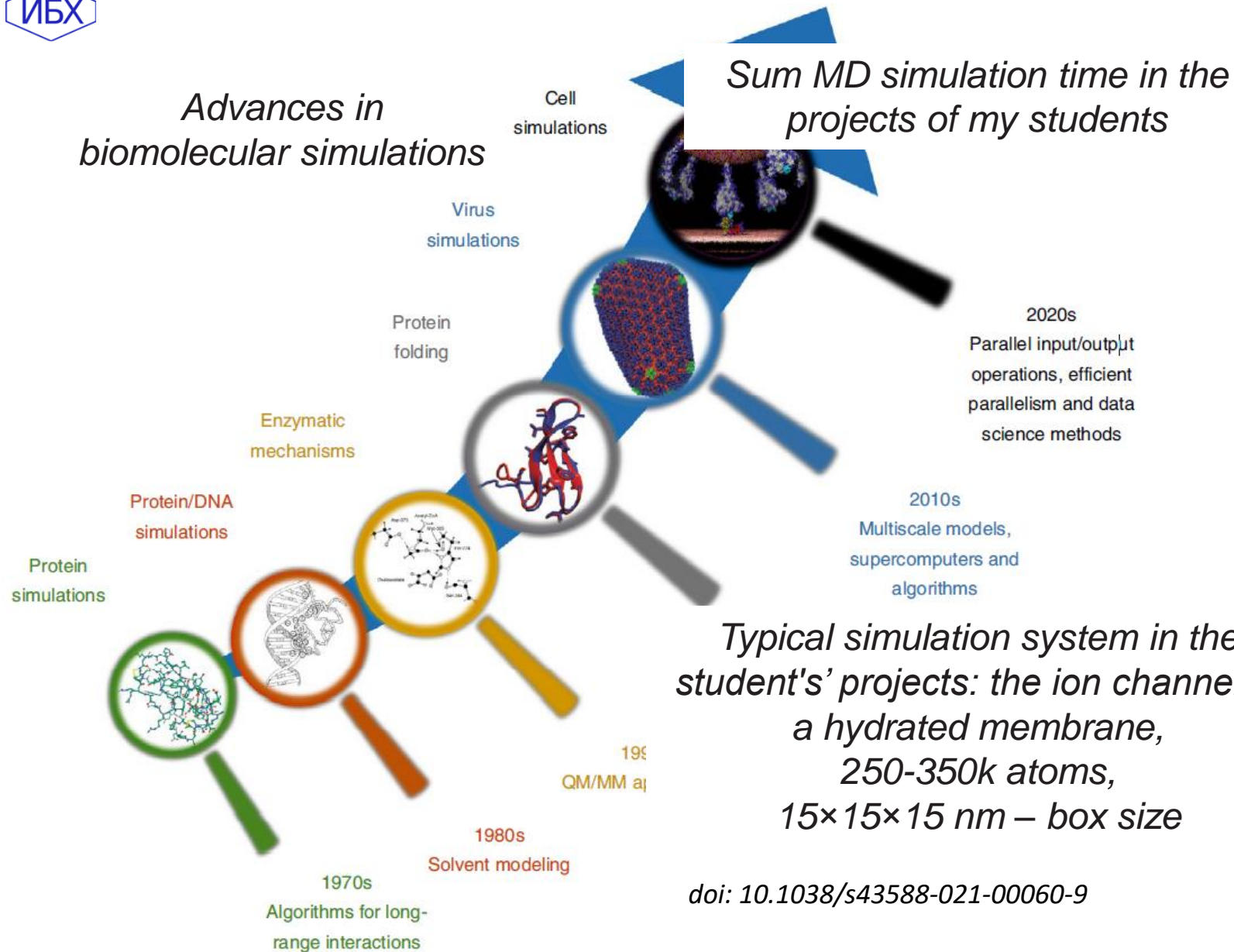


[doi:10.1093/nar/gkad1011](https://doi.org/10.1093/nar/gkad1011)

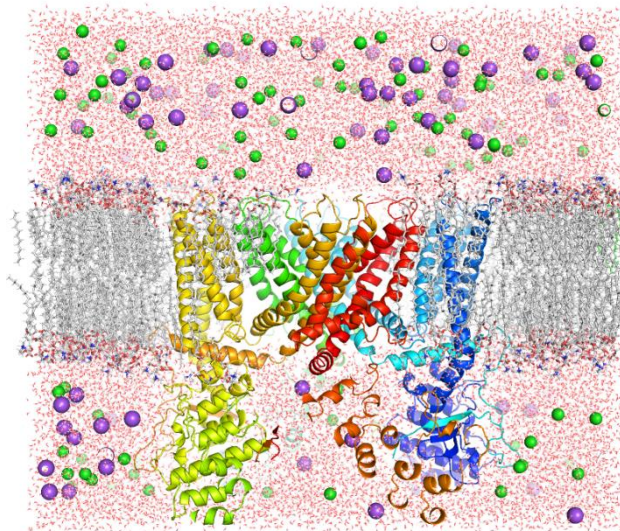
The expansion of AlphaFold Protein Structure Database

Biomolecular modeling

Advances in biomolecular simulations



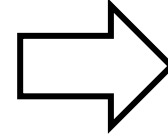
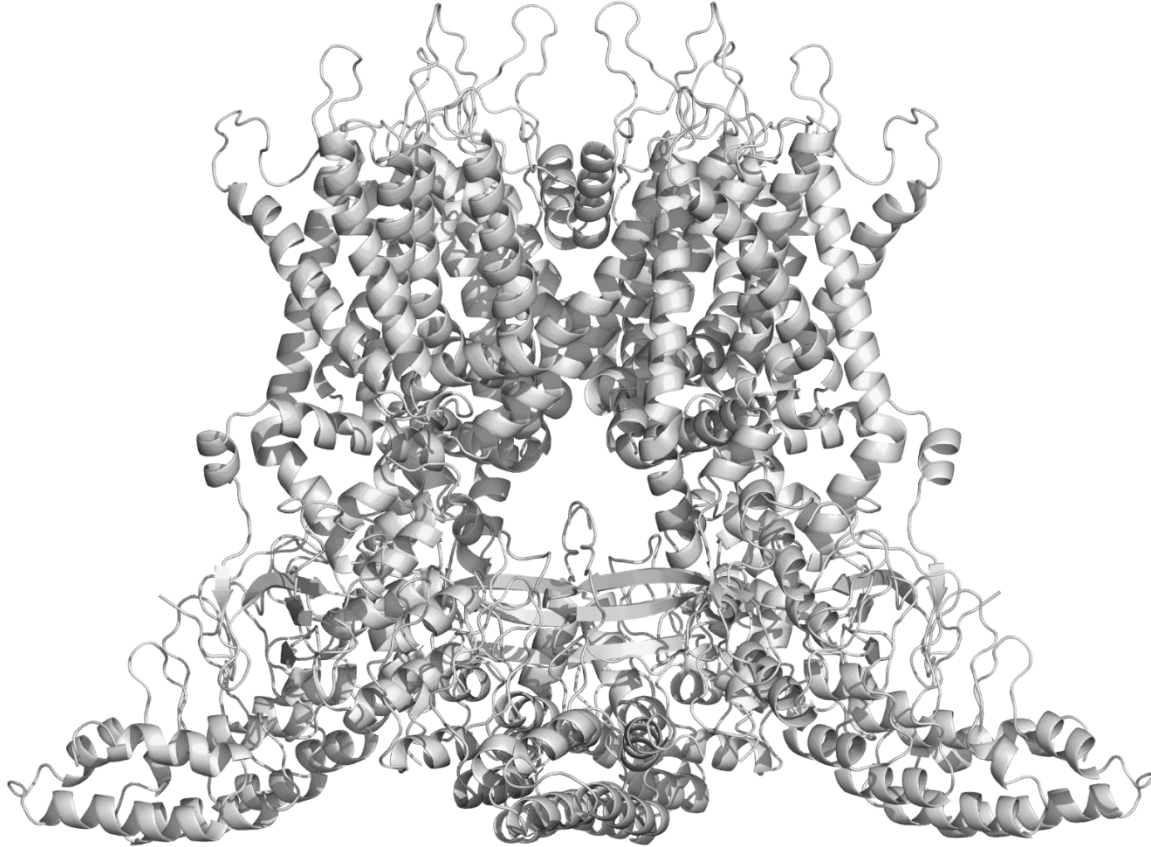
Typical simulation system in the student's' projects: the ion channel in a hydrated membrane, 250-350k atoms, 15×15×15 nm – box size



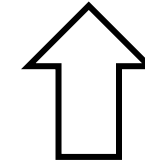
doi: 10.1038/s43588-021-00060-9

Structural data is not enough

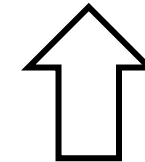
**Atomic structure of the
macromolecule or molecular complex**



**Functional state of the molecule
conformation**



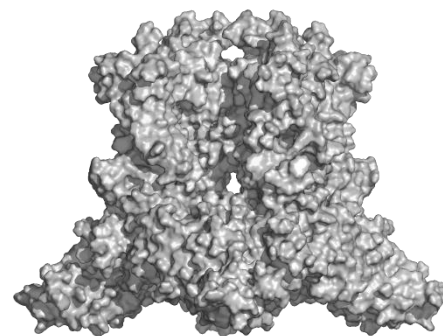
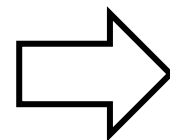
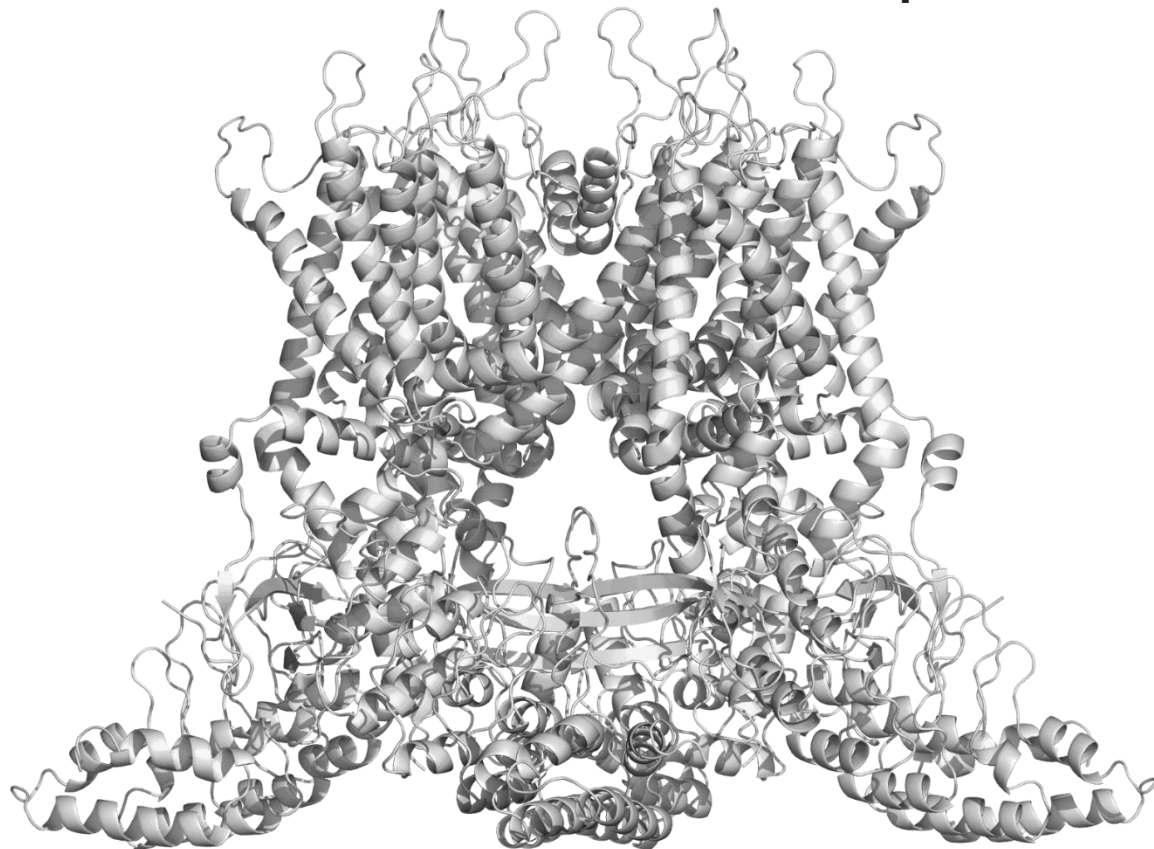
**Properties and energetics of inter-
and intramolecular interactions**



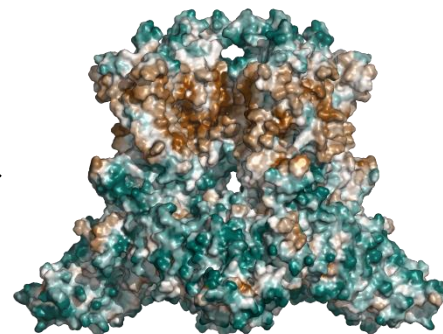
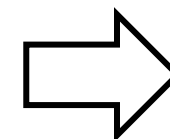
**Physicochemical properties of the
molecular surface**

What kind of the surface properties?

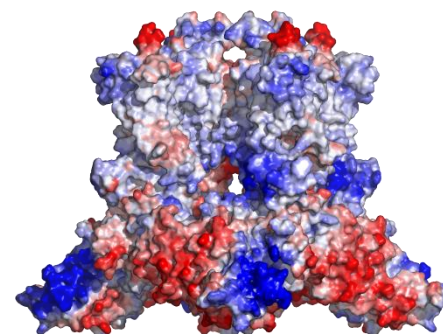
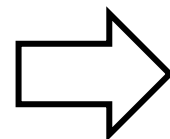
Atomic structure of the macromolecule or molecular complex



**Surface geometry
convexities and
concavities**



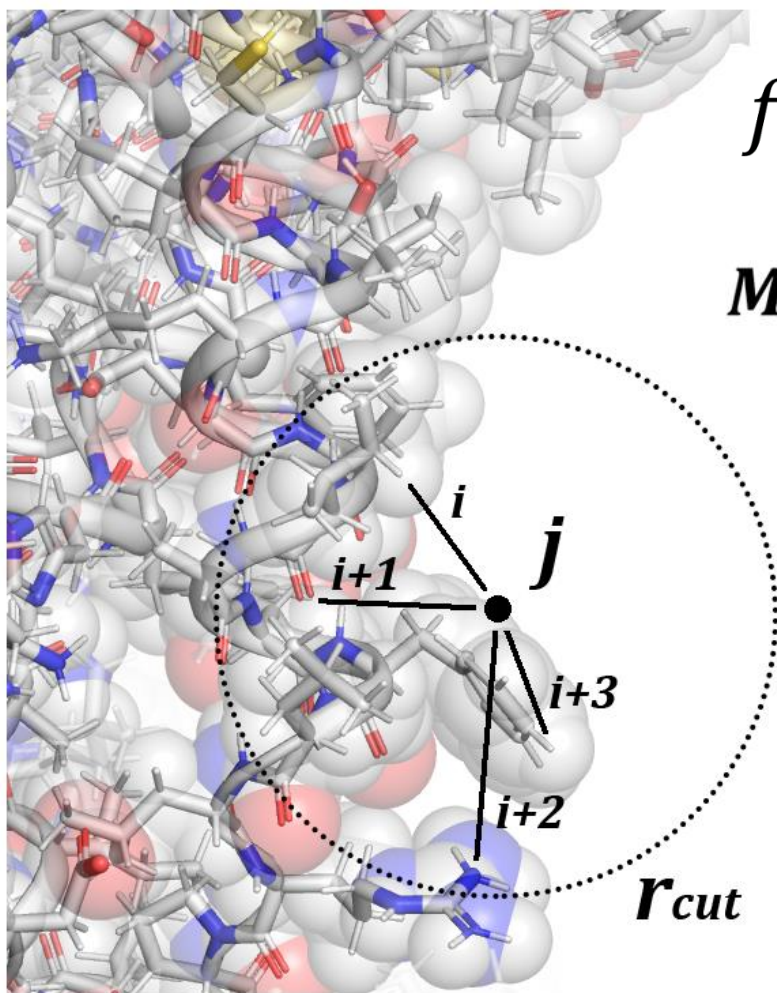
**Surface hydrophobicity
and hydrophilicity**



Electrostatic potential

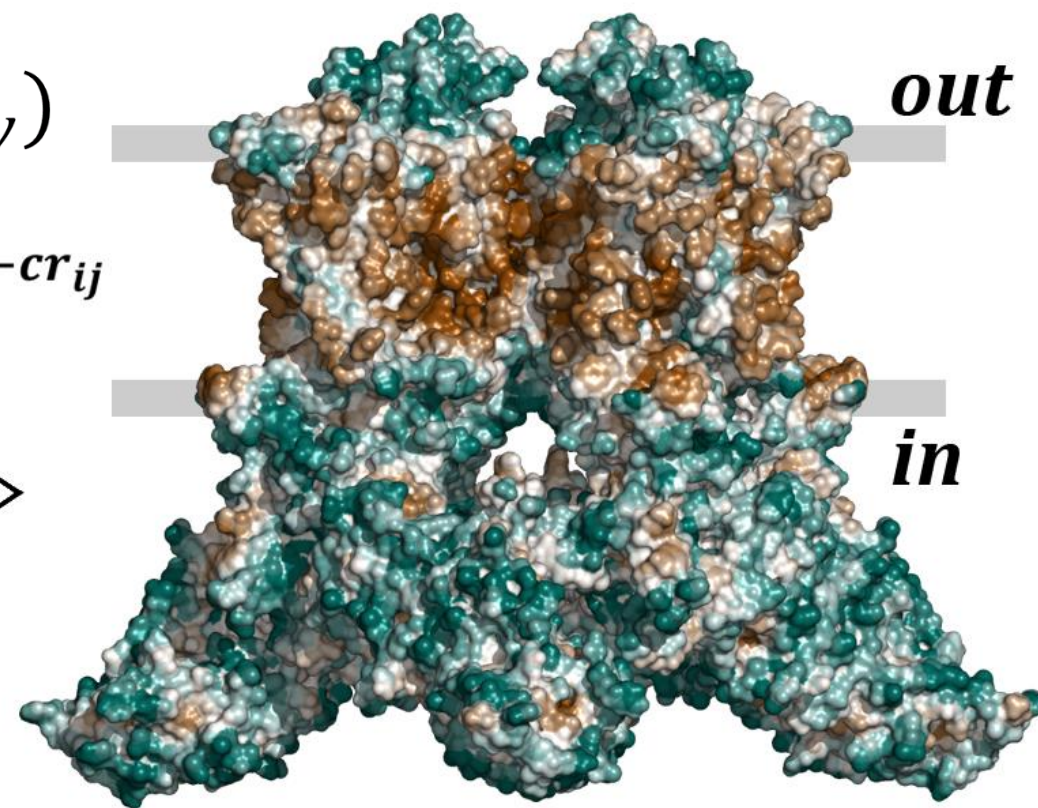
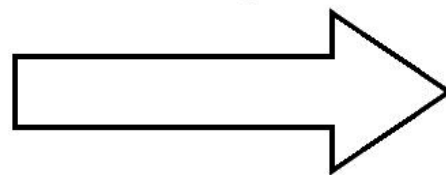
Molecular Hydrophobic Potential (MHP)

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



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

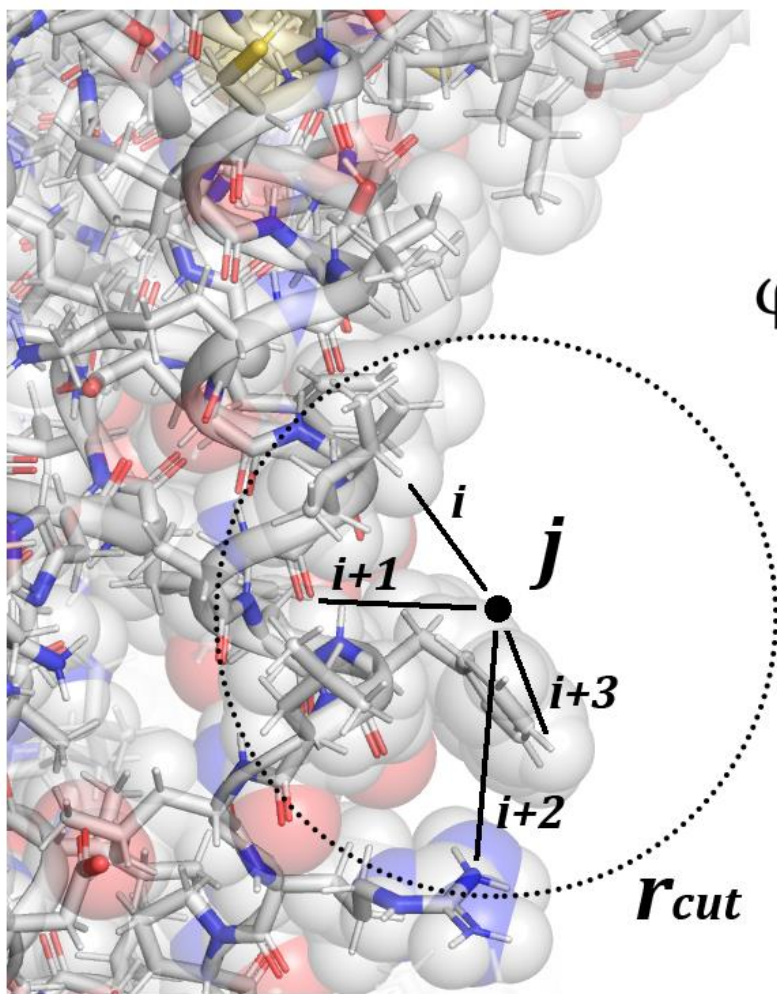
$$\text{MHP}_j = \sum_i f_i e^{-cr_{ij}}$$



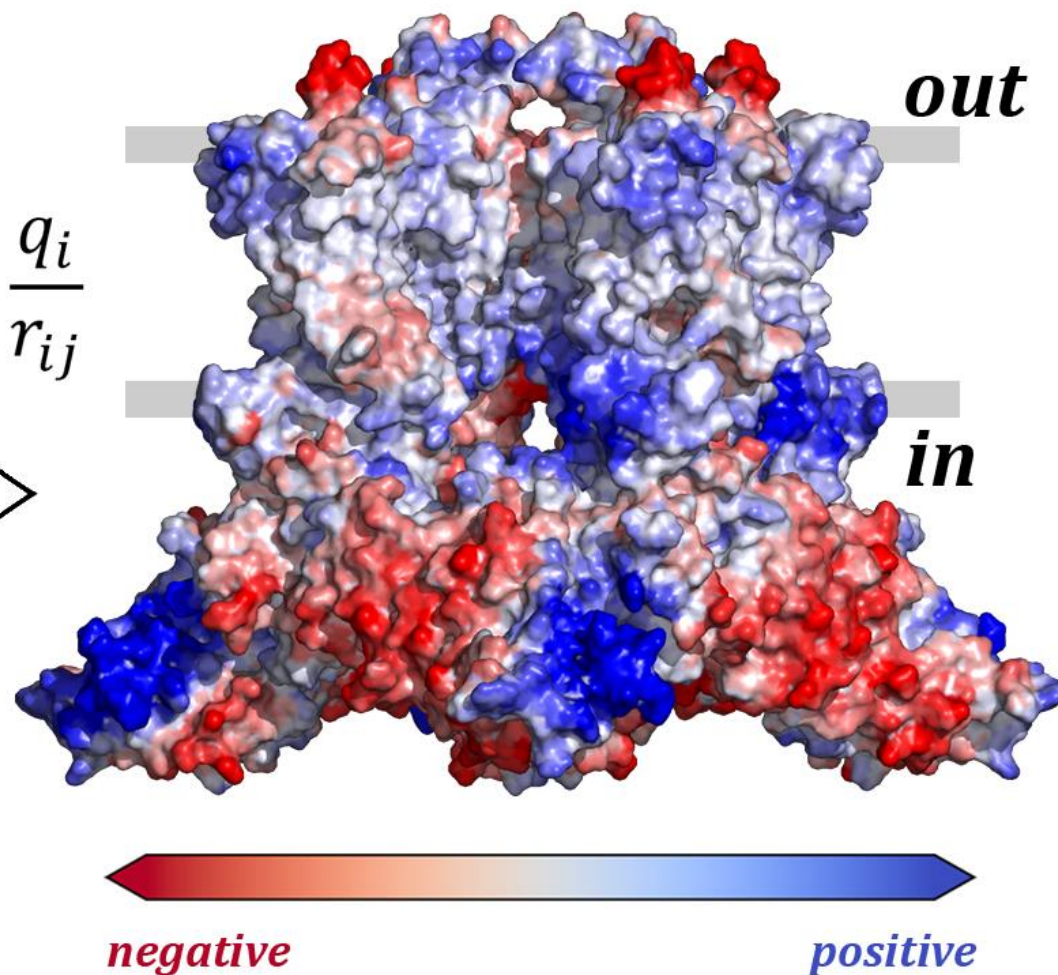
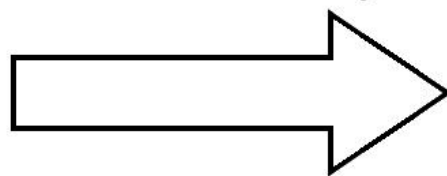
hydrophilic hydrophobic

Electrostatic Potential (ESP)

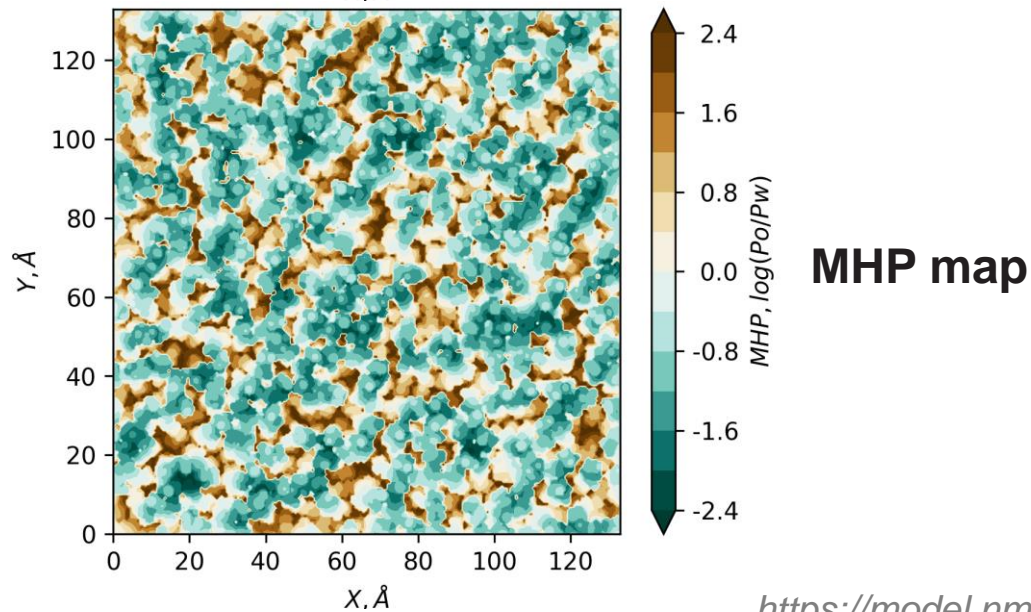
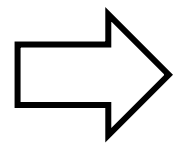
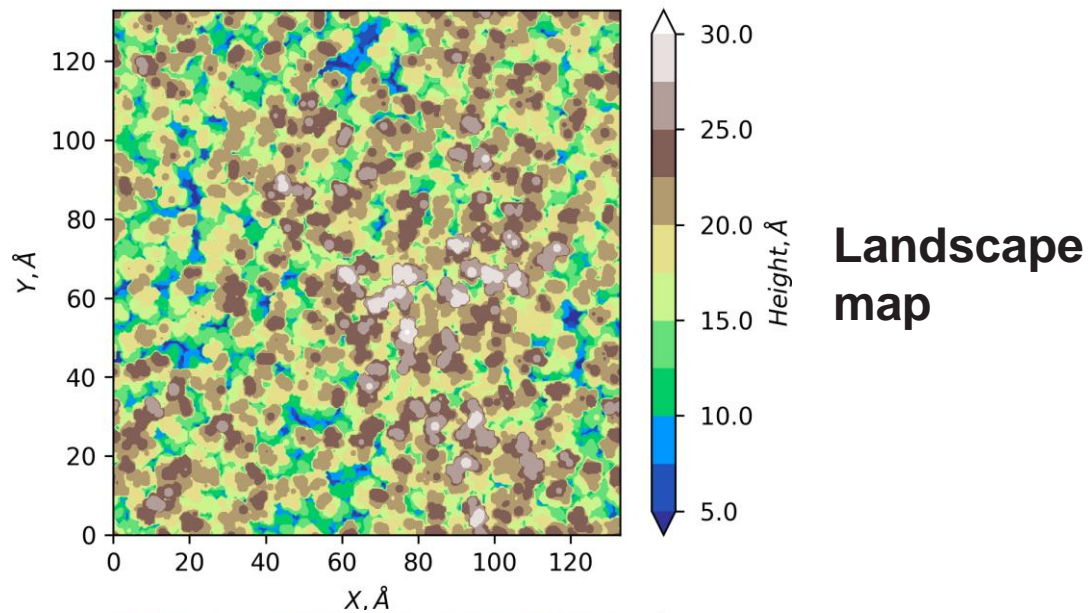
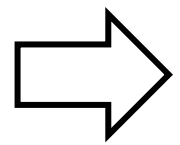
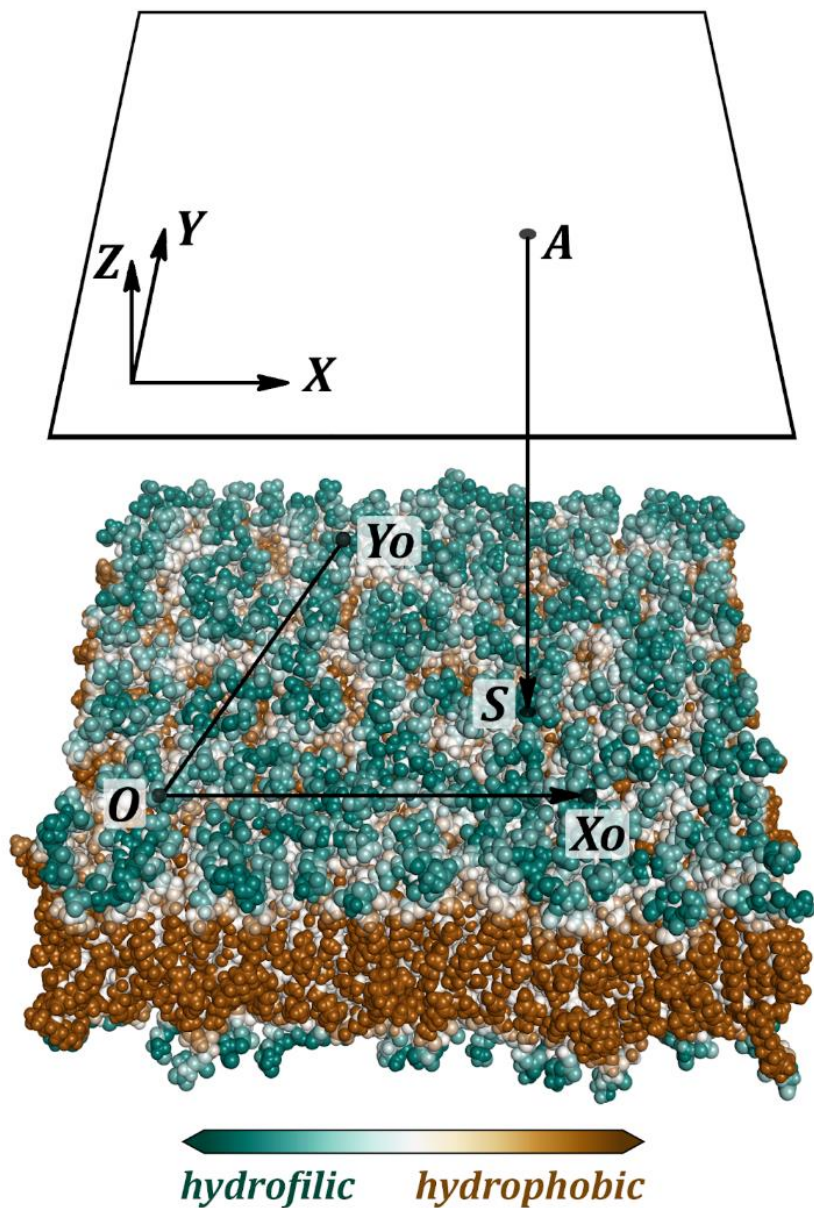
Partial atomic charges (q_i) as an electric potential source



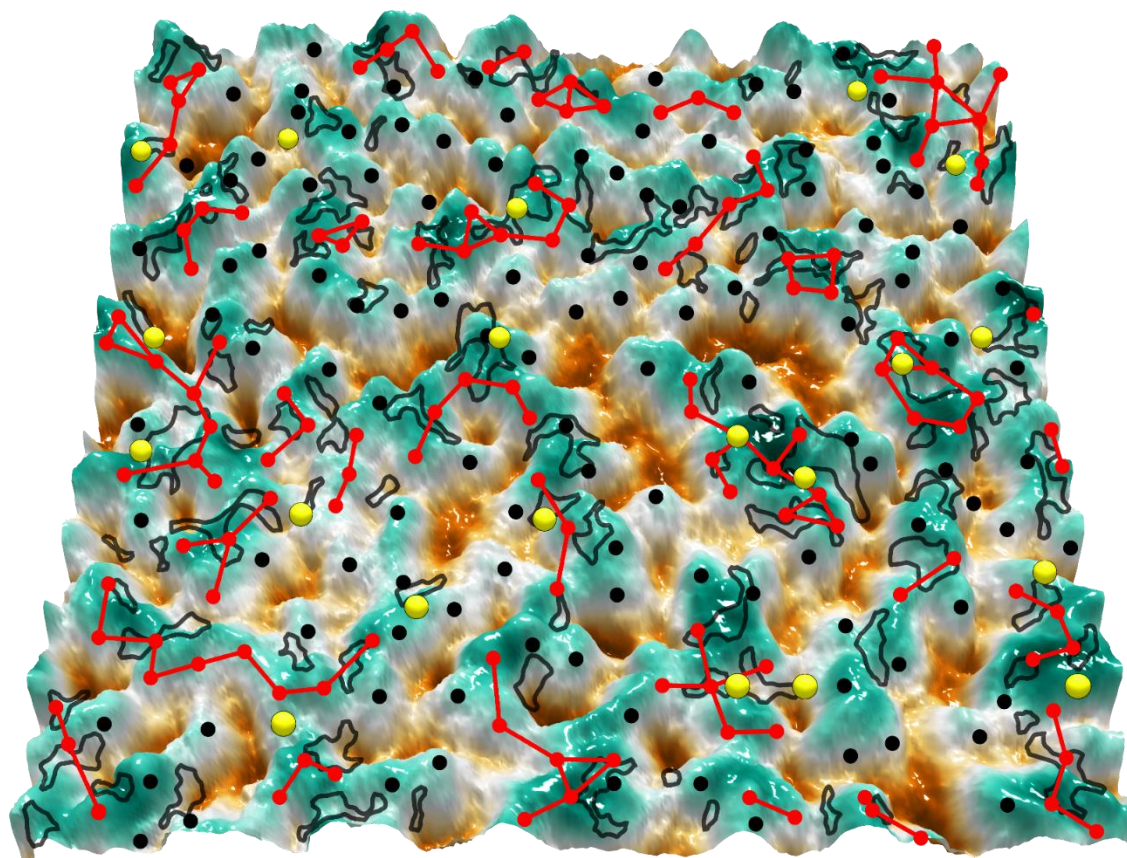
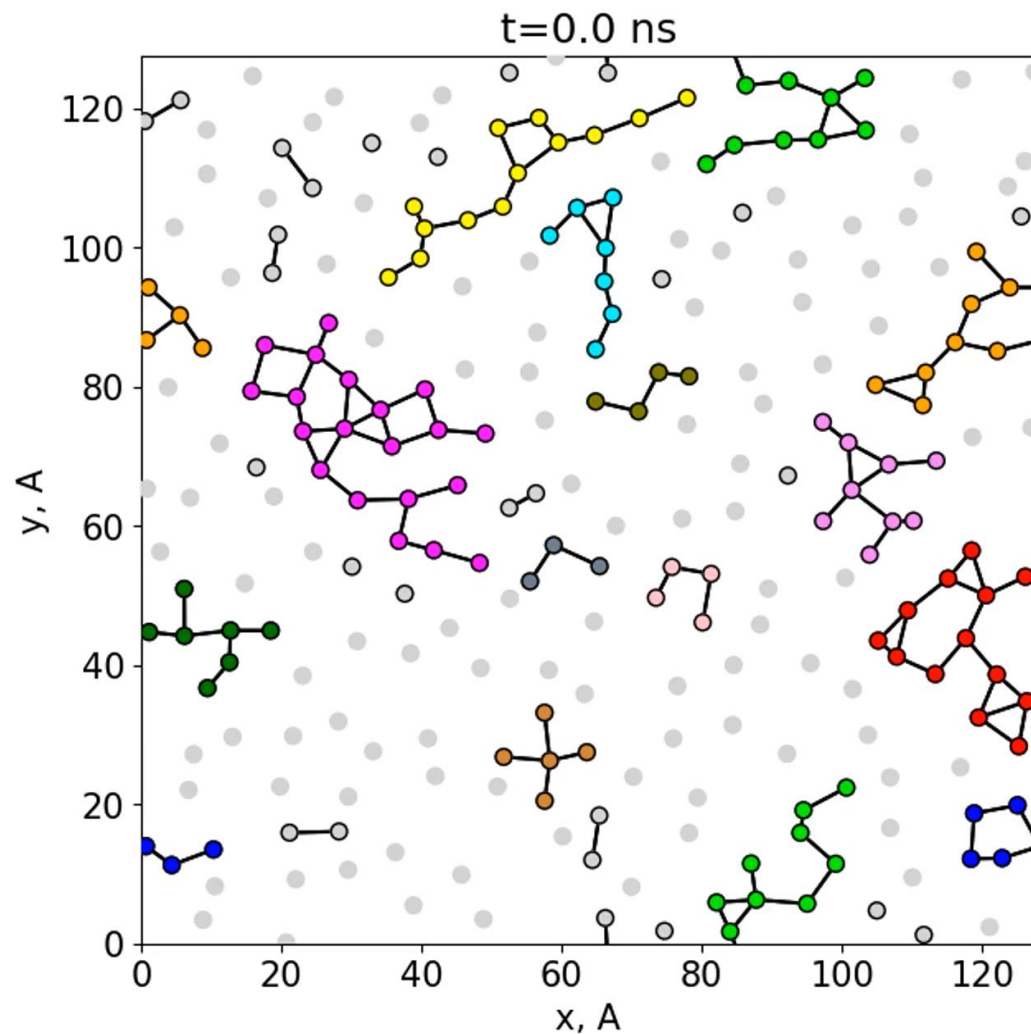
$$\varphi_j = \frac{1}{4\pi\epsilon\epsilon_0} \sum_i \frac{q_i}{r_{ij}}$$



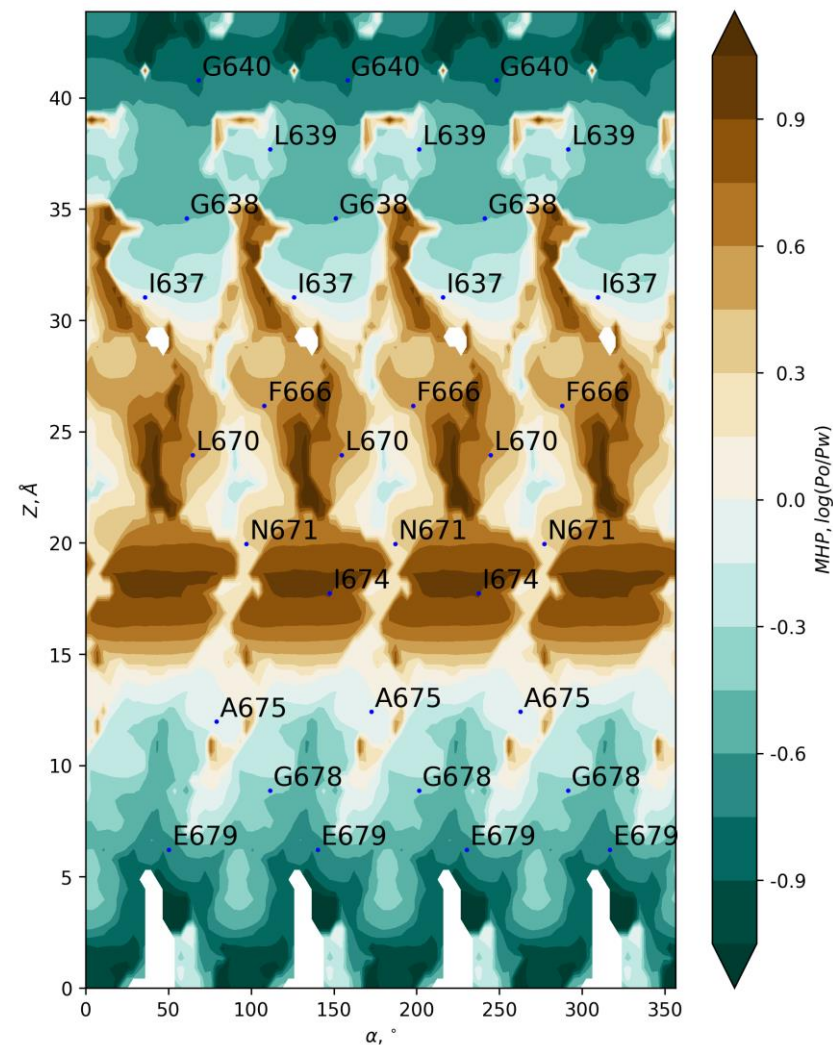
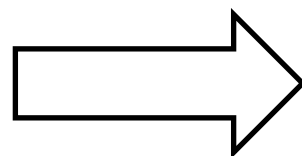
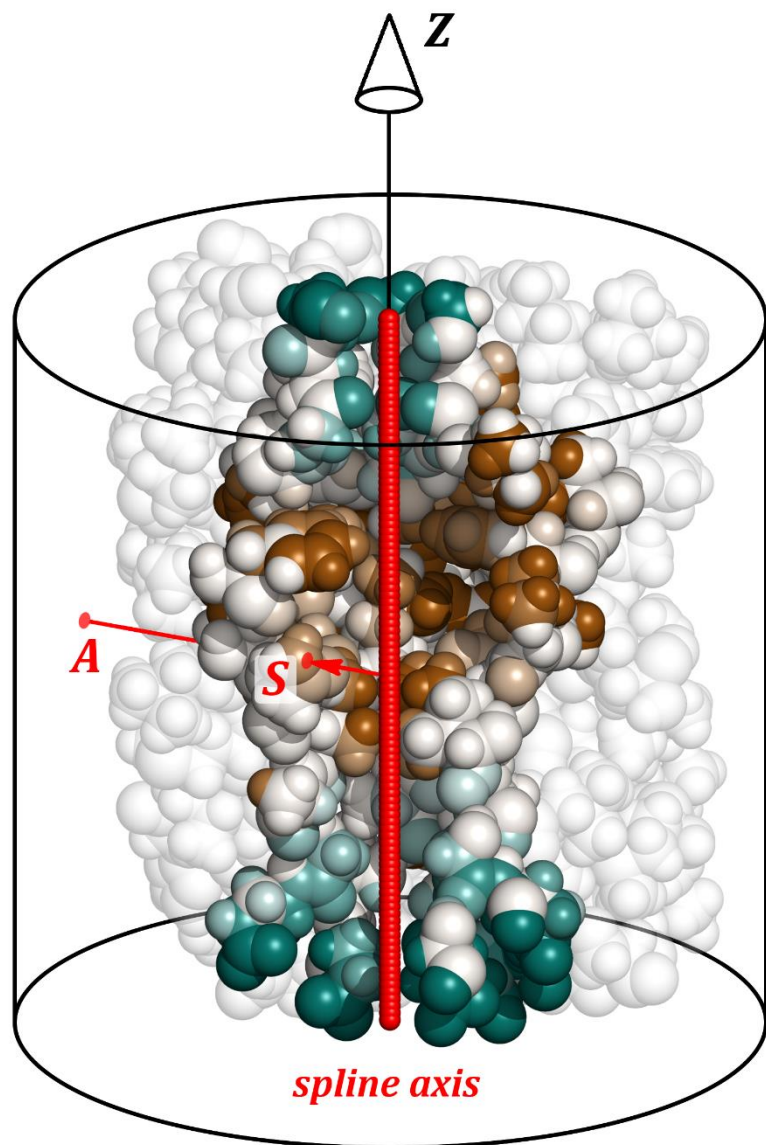
Planar projecting (membrane surface)



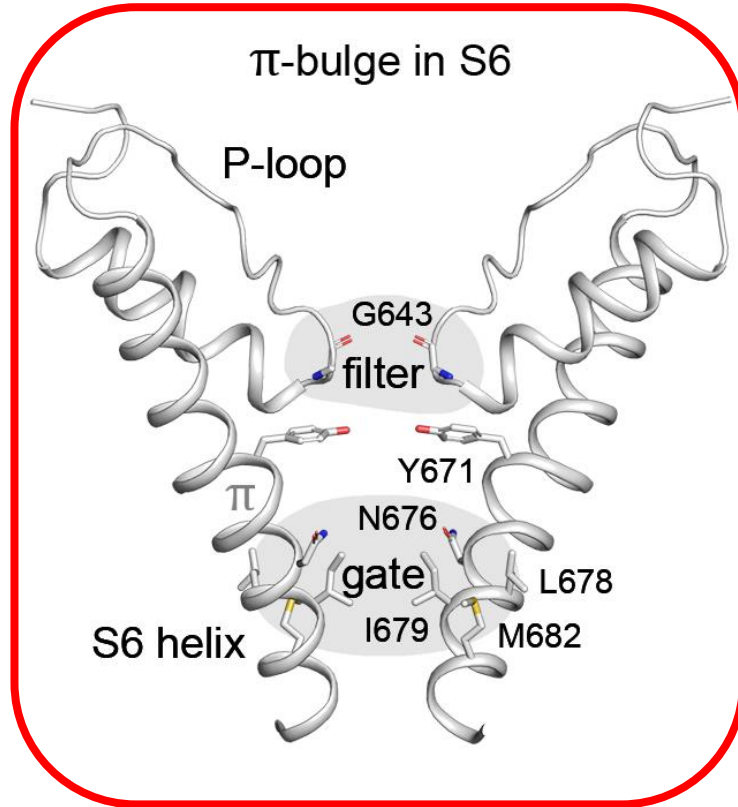
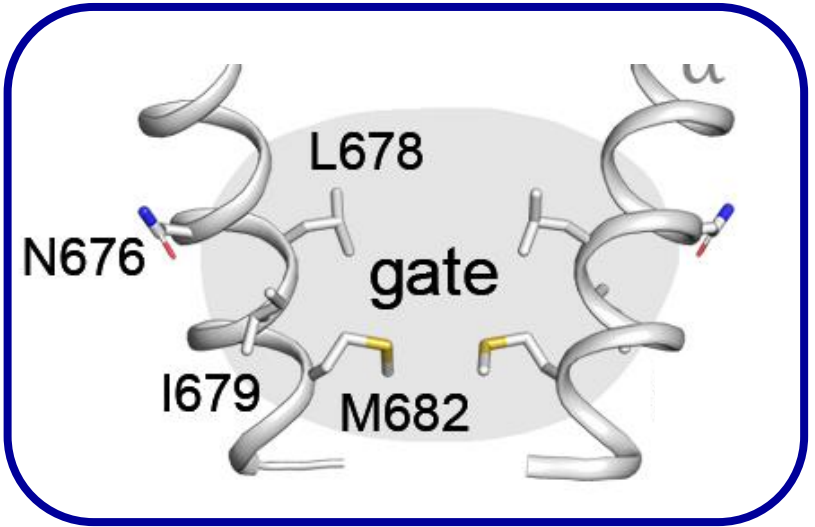
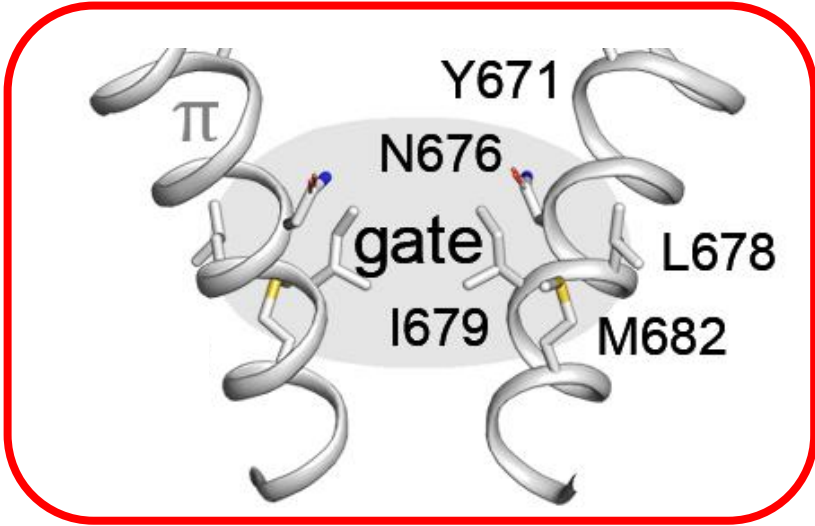
Dynamic molecular portrait of DOPS lipid bilayer



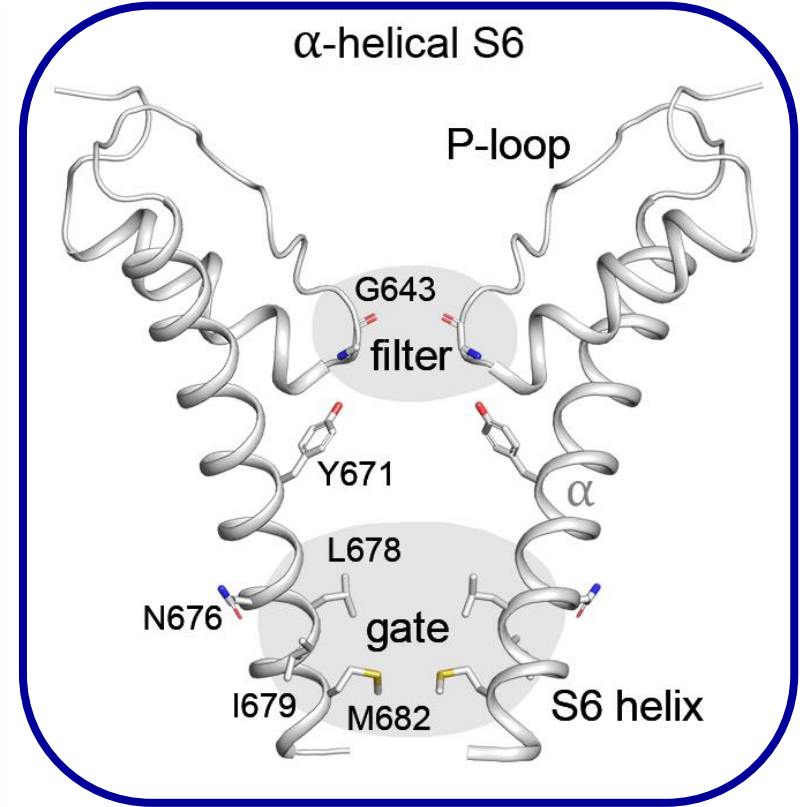
Cylindrical projecting (ion channel pore)



Conductive pores of TRPV ion channels



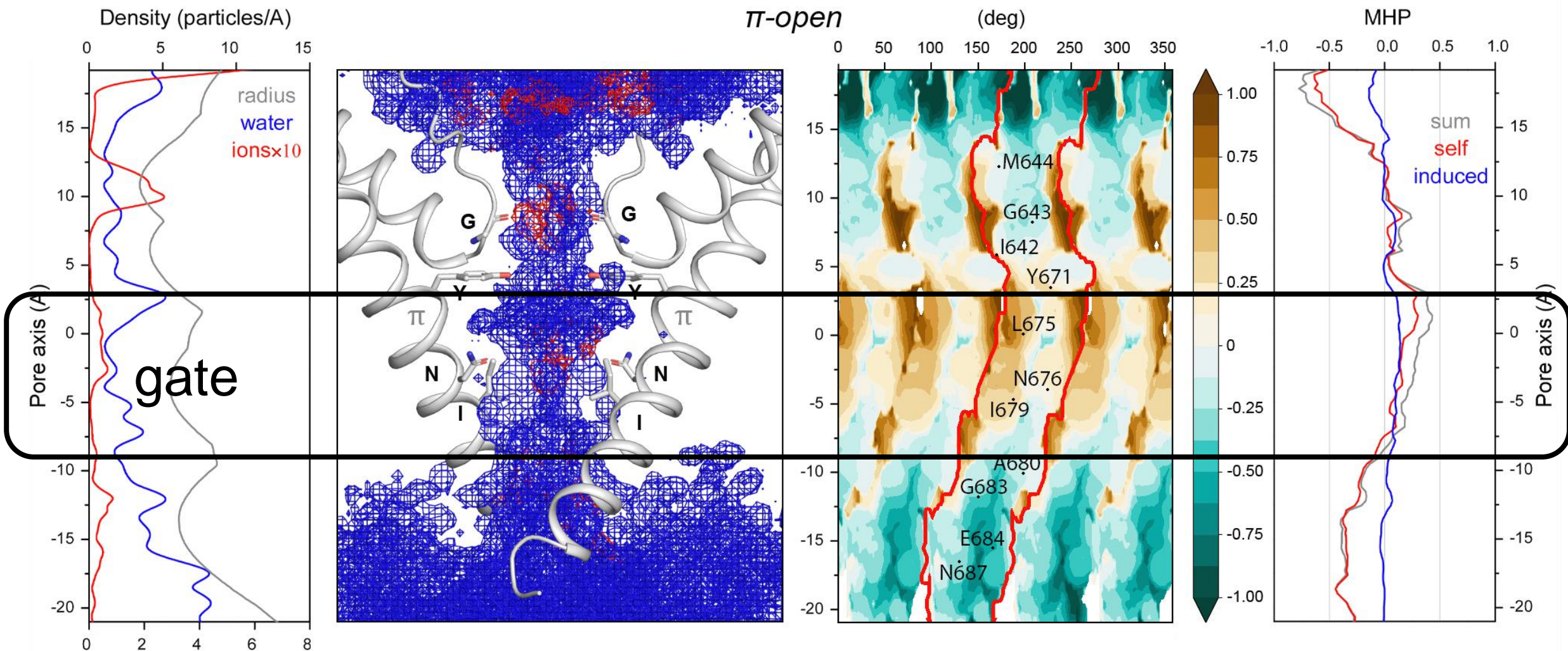
π -bulge state of S6-helix



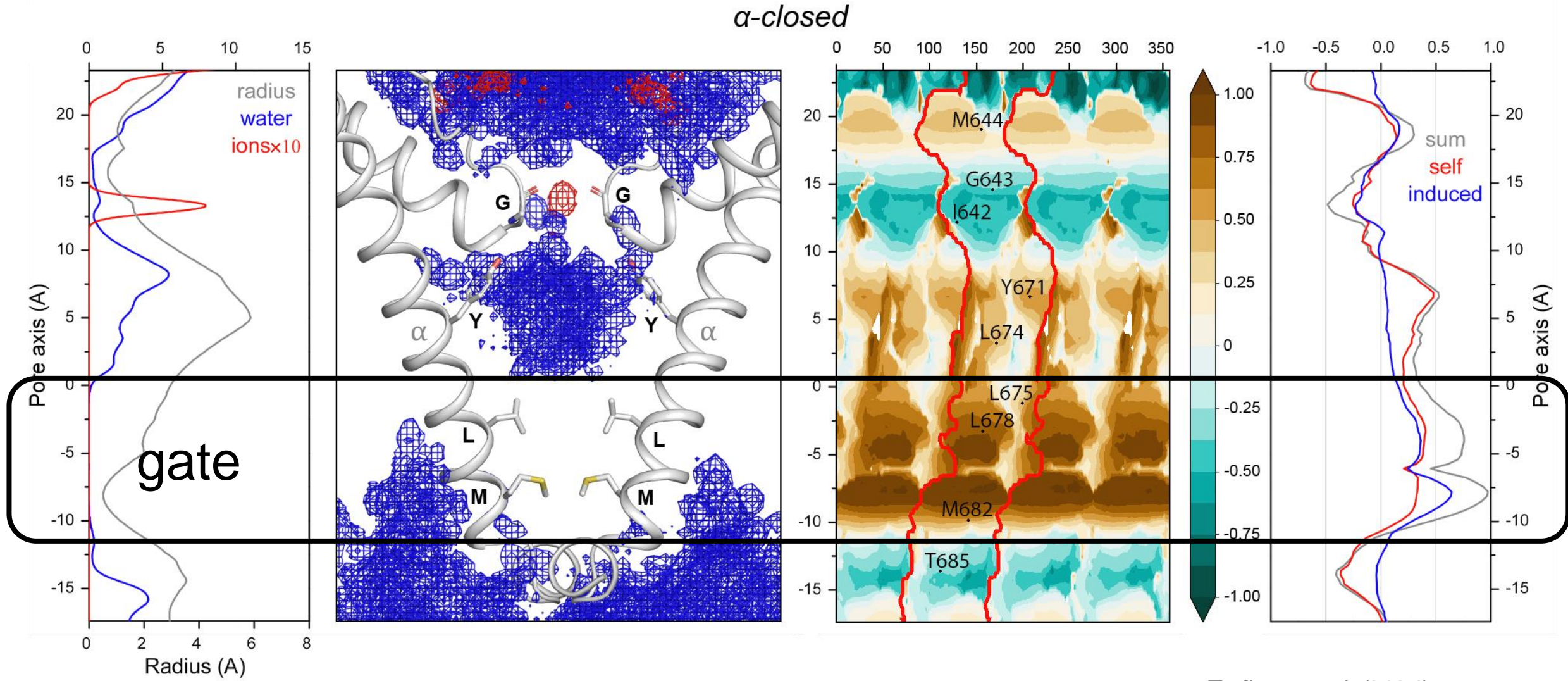
α -helical state of S6-helix



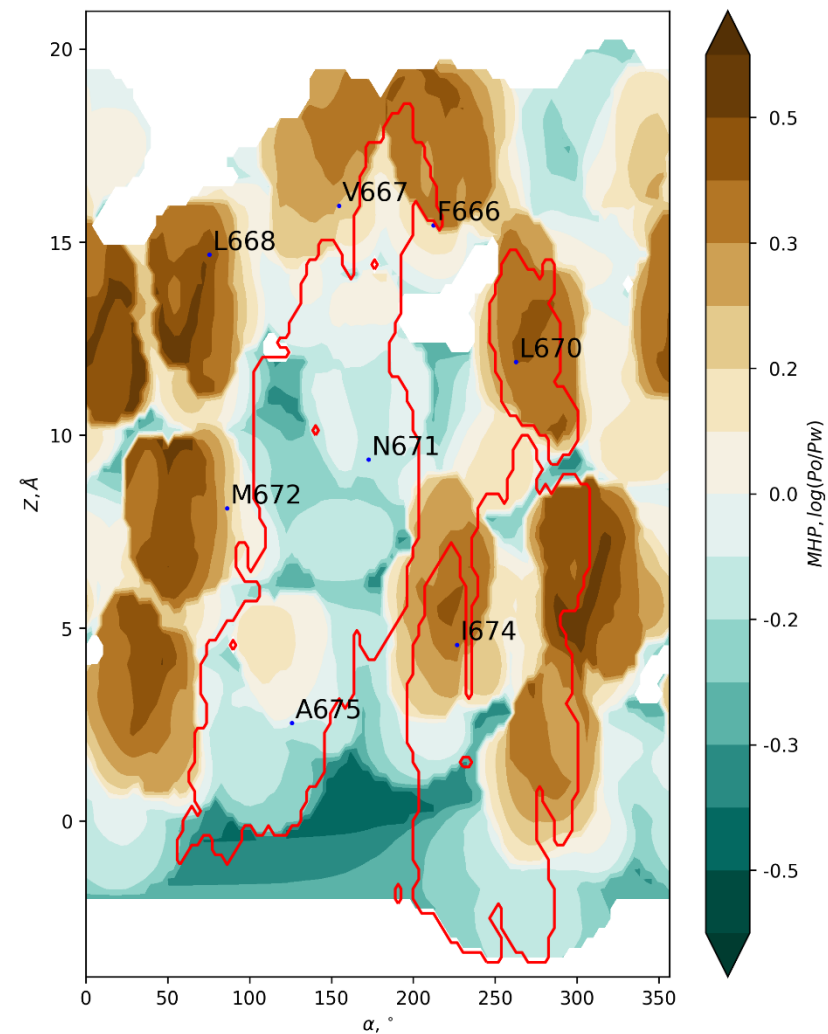
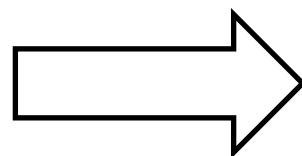
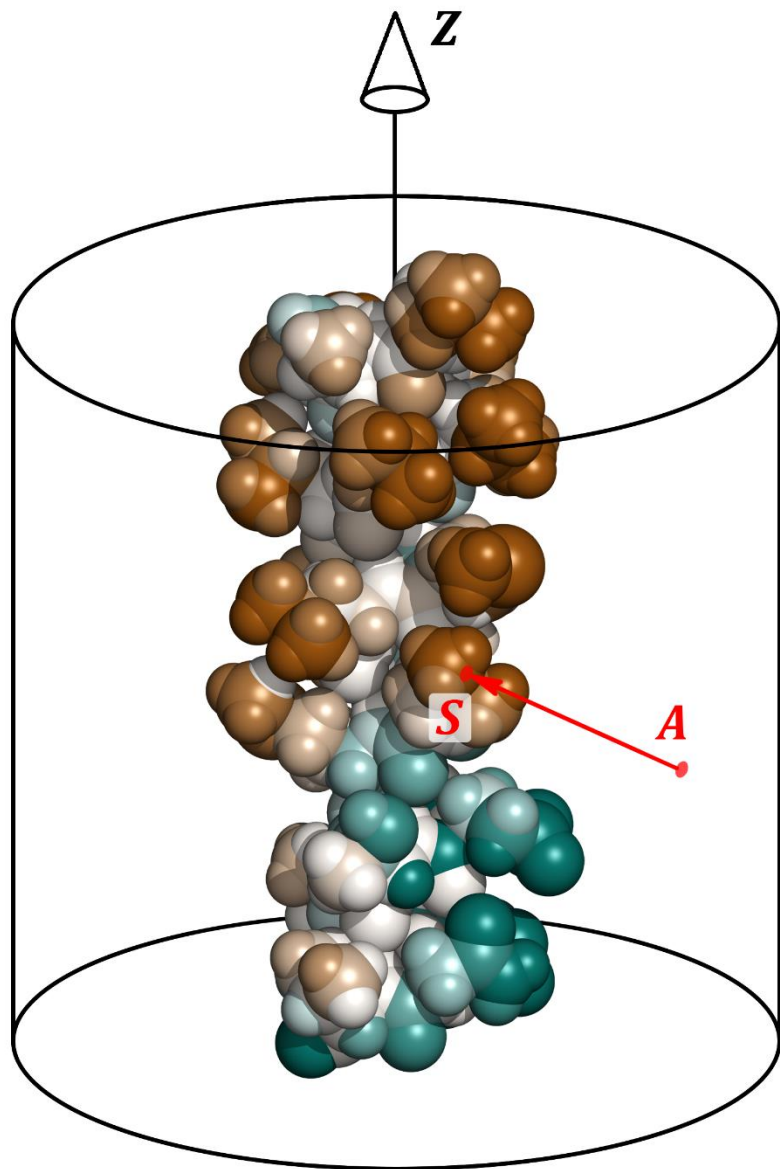
π -open state of the TRPV1 pore



α -closed состояние поры TRPV1

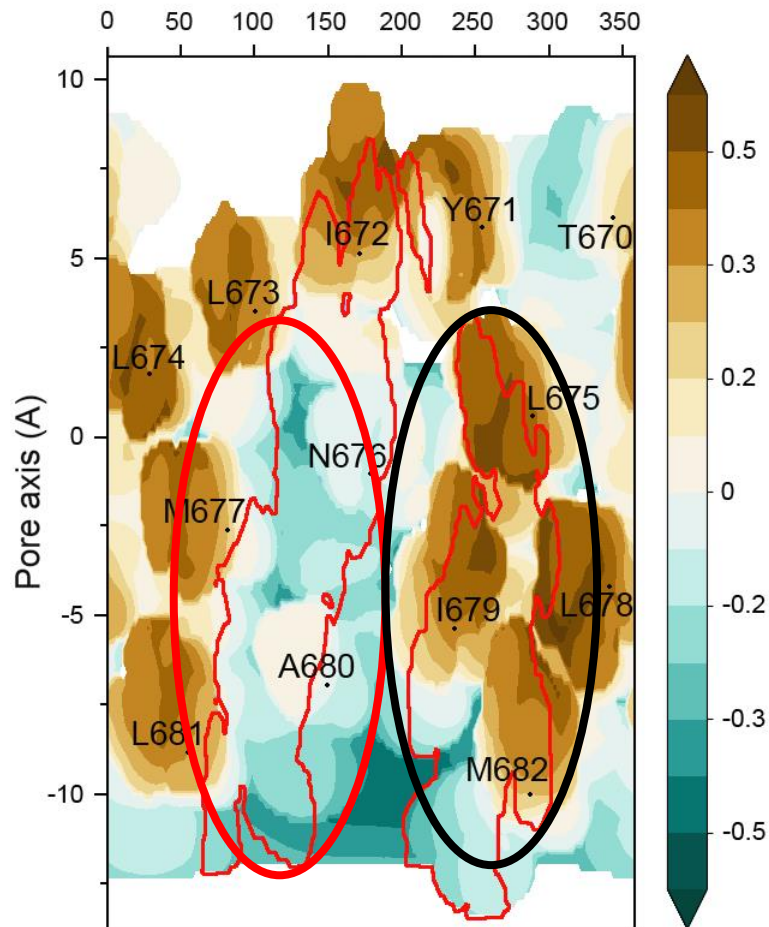


Cylindrical projecting (helix)



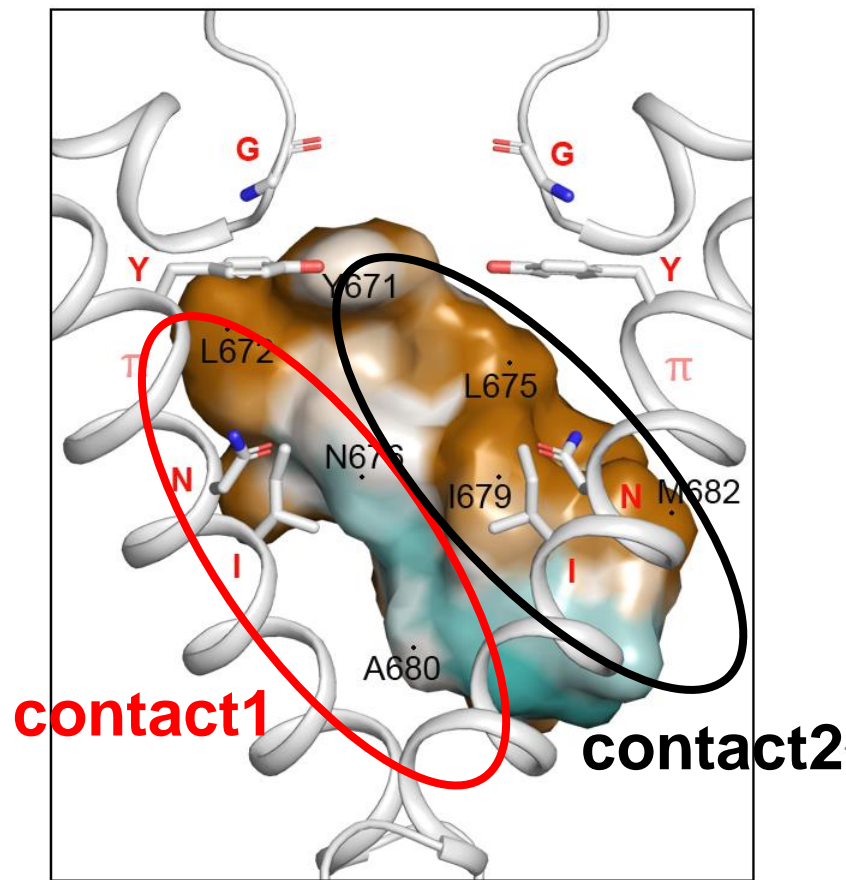
π -open TRPV1 interhelix contacts at the gate region

MHP map of
S6 helix



contact1 **contact2**

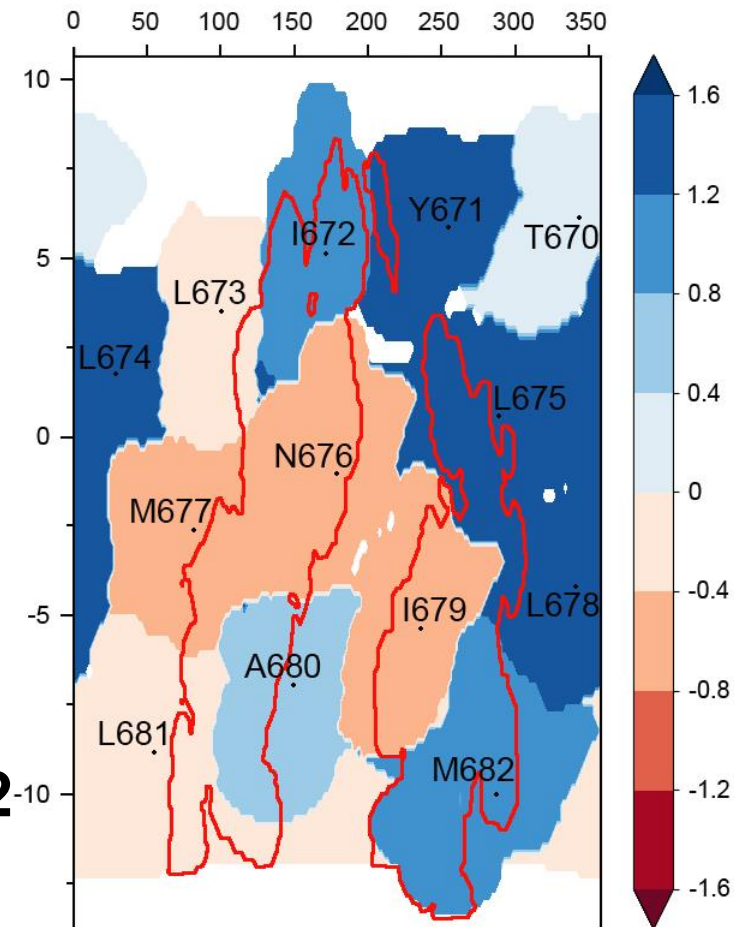
π -open



contact1

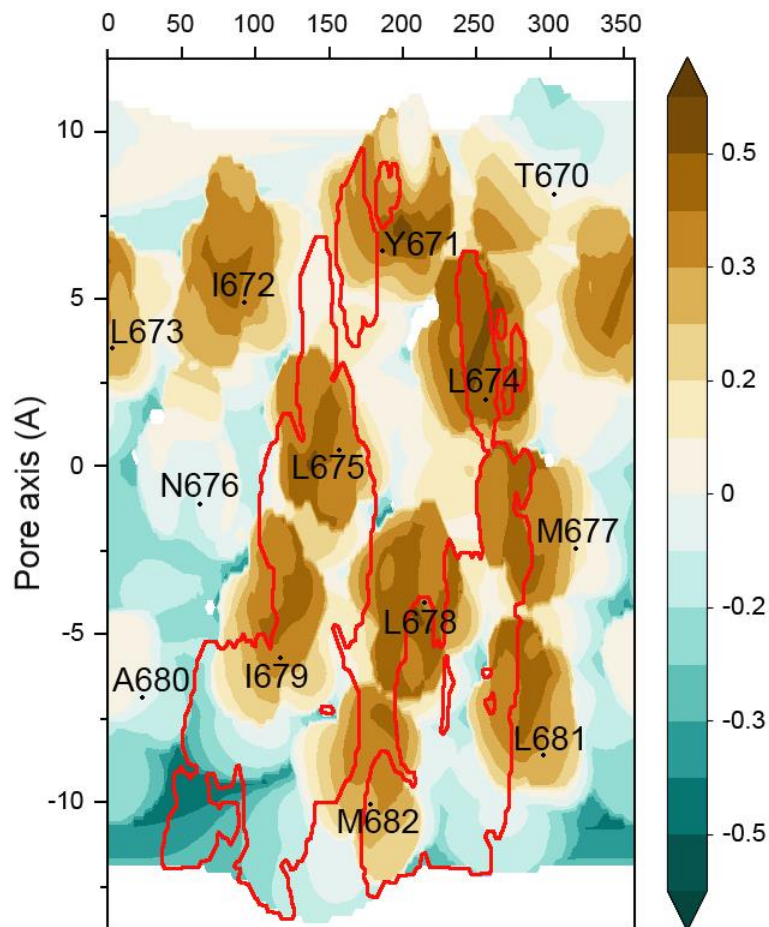
contact2

3d-1d score or
residue packing quality

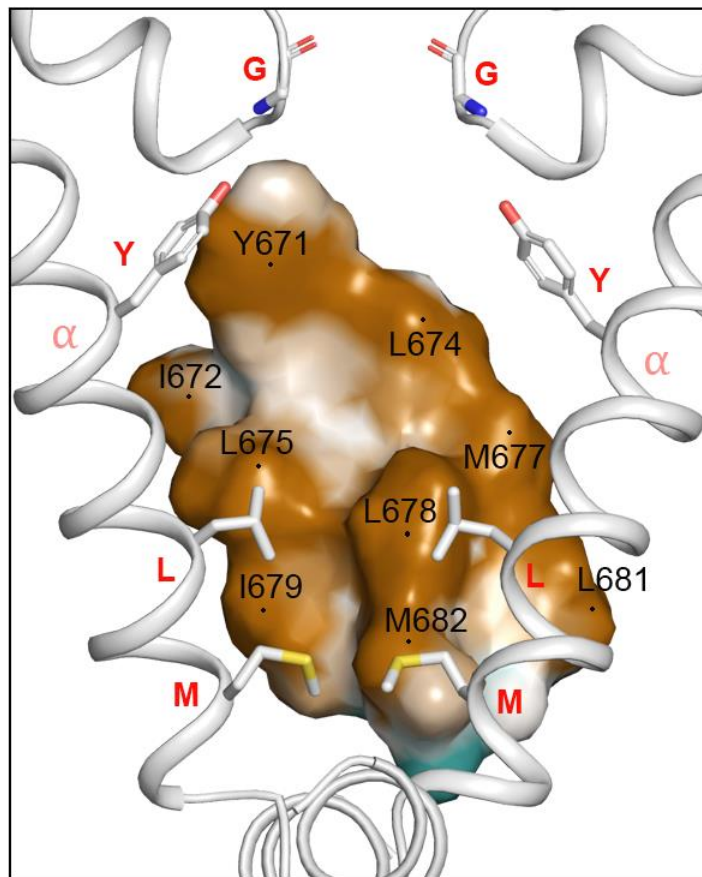


α -closed TRPV1 interhelix contacts at the gate region

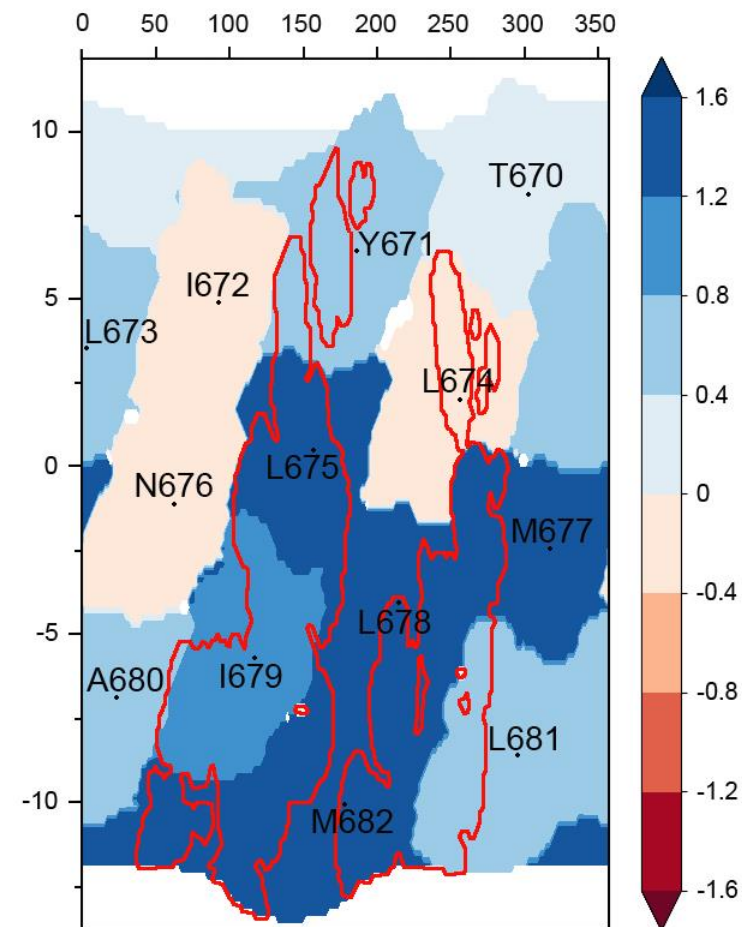
MHP map of
S6 helix



α -closed

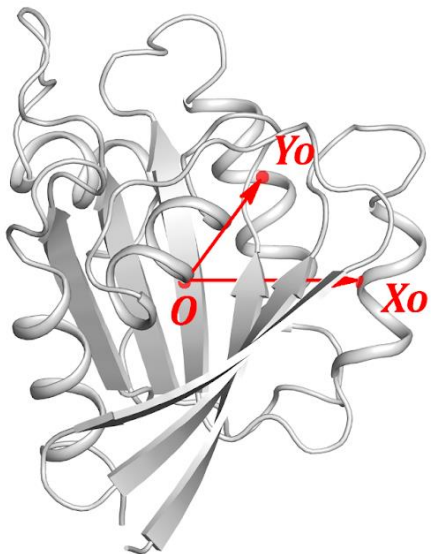


3d-1d score or
residue packing quality

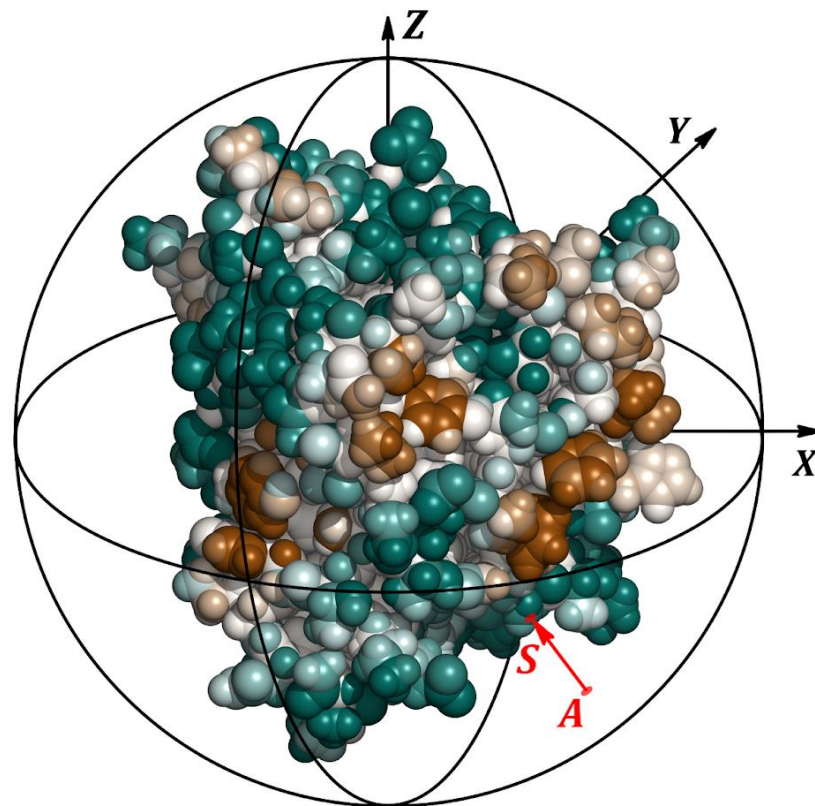


Spherical projecting (peptide)

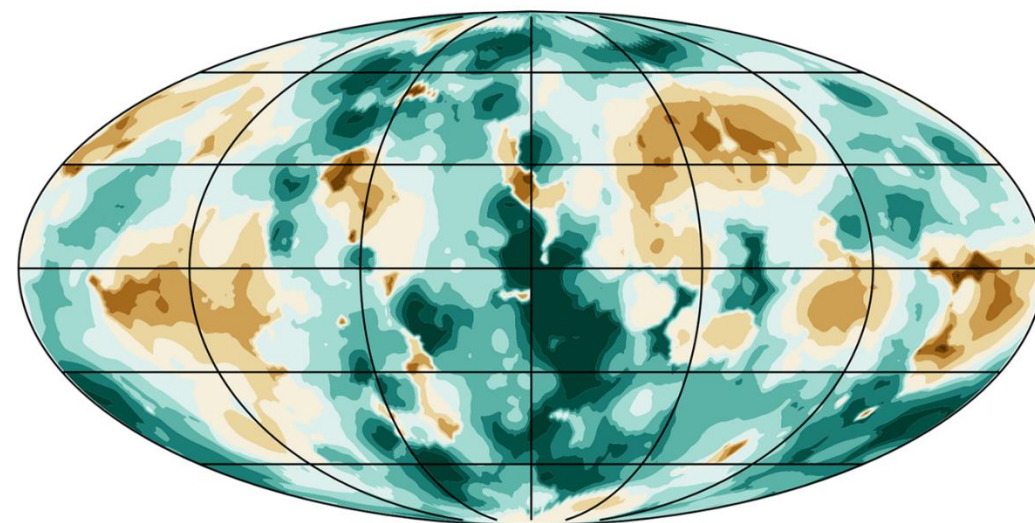
AFR6 peptide structure



MHP calculated on the peptide surface



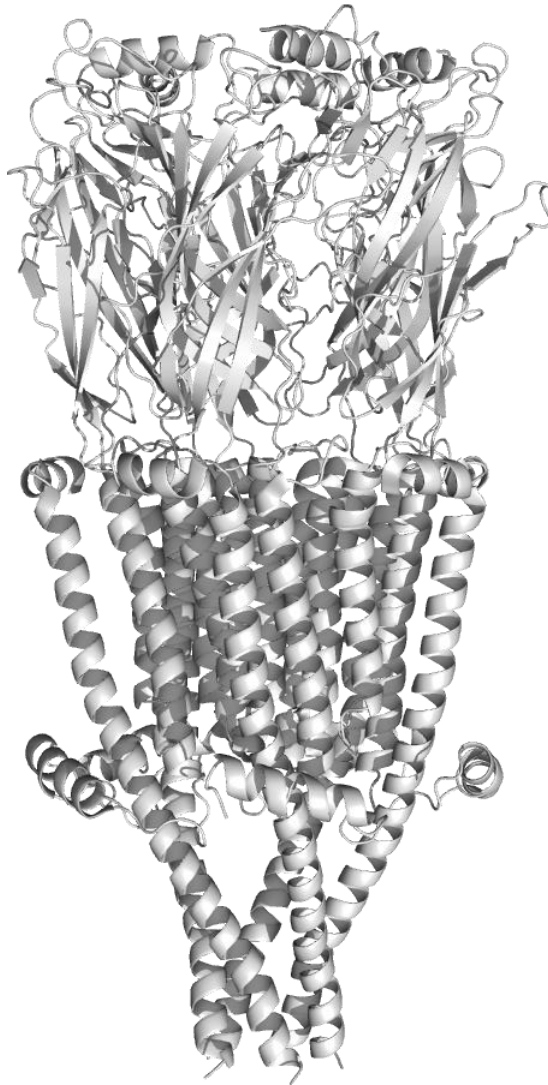
Mollweide projection of the MHP distribution





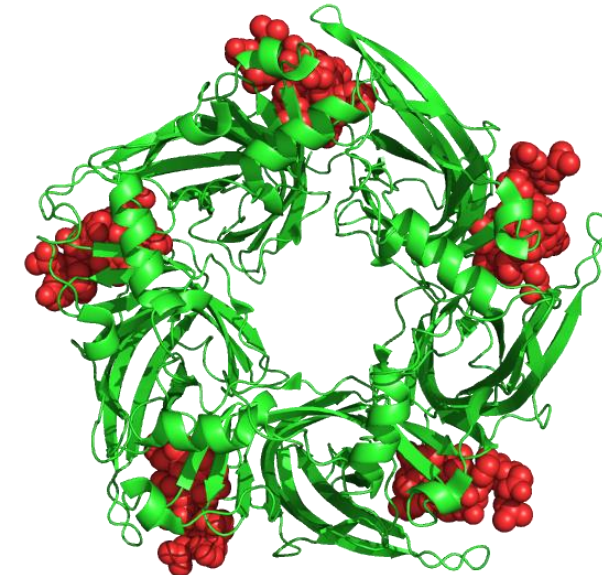
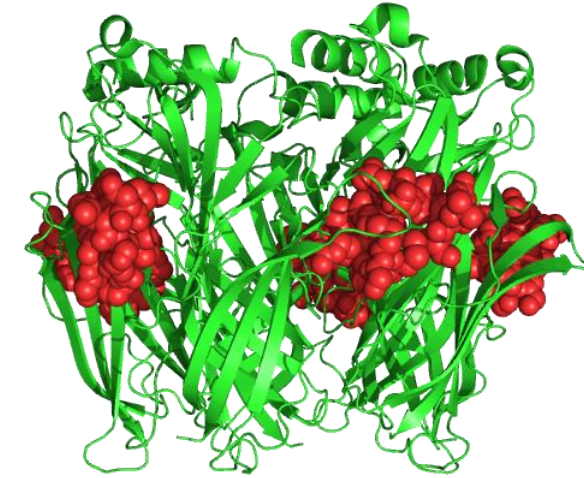
Complex of Acetylcholine binding protein (AChBP) with α -conotoxin

ligand-binding
domain



Trans membrane
domain

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

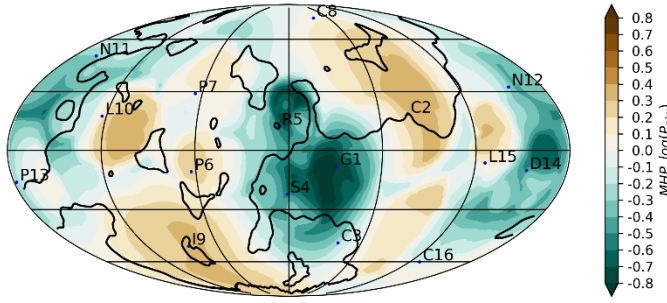


*Acetylcholine binding protein (AChBP) complex
with α -conotoxin Tx1A10* PDB ID: 2UZ6

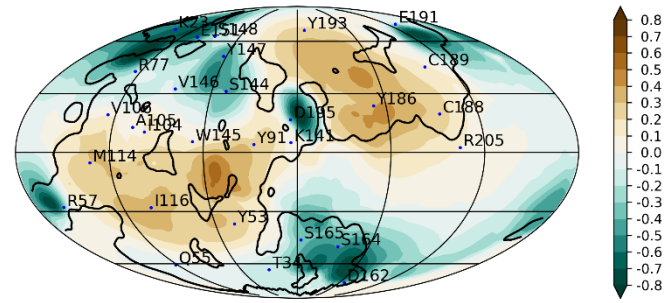


Match of surface properties at AchBP-Conotoxin (Tx1A) interface

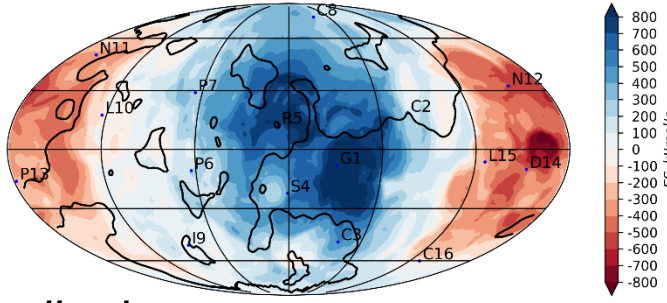
Tx1A MHP



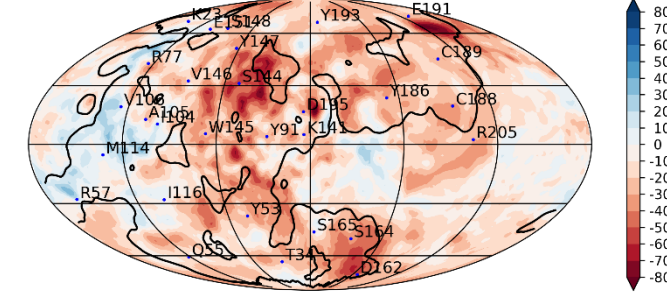
AchBP MHP



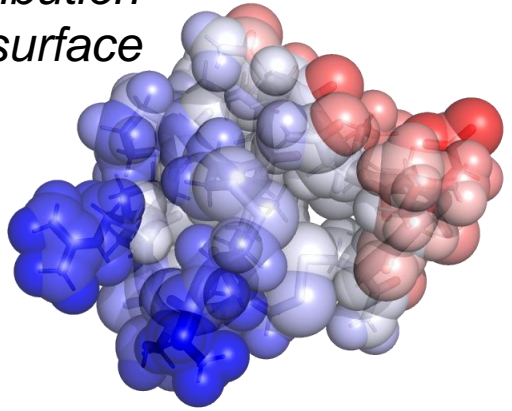
Tx1A ESP



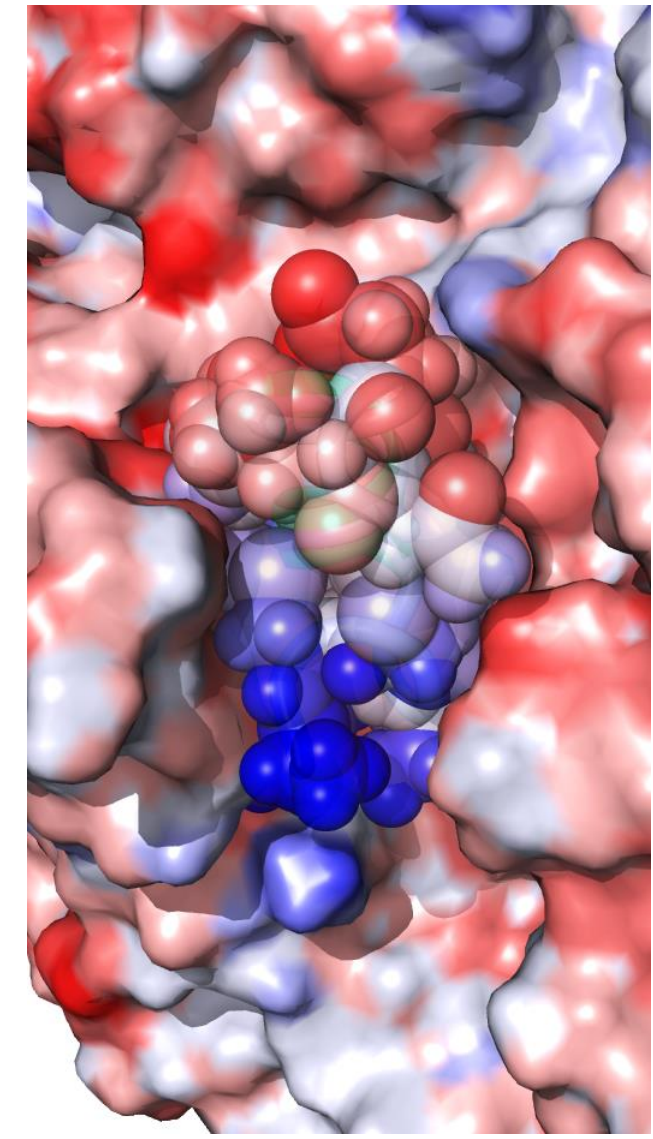
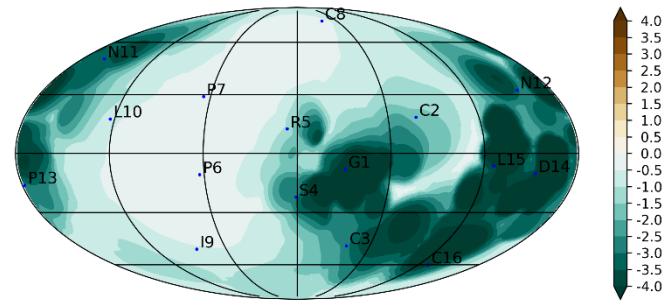
AchBP ESP



ESP distribution over the surface



water MHP



CELL atomiC modEl
buiLding & anaLysis

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Using 6%

CELL Tools

Molecular Surface Topography creates 2d maps from molecules and trajectories

Contacts detects specific interactions between molecules based on geometric criteria.

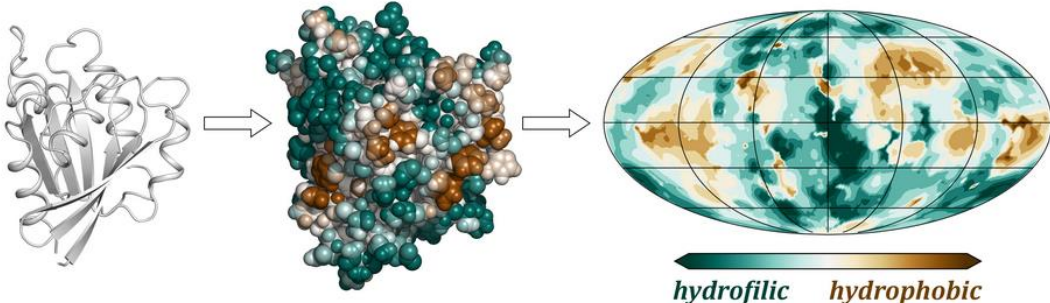
SREnergy calculates short-range inter-molecule interaction energy terms.

CELL tools documentation

CELL stands for atomiC modEl building and analysis tools to make publicly available the tools that have been developed in our laboratory for analysis of biomolecular data.

Molecular Surface Topography (MST) tool

The tool builds 2D projections of a molecule surface and maps one of the several surface parameters to make contour/isoline plots.



[RUN TOOL](#)
[TUTORIAL](#)
[EXAMPLES](#)

History

MST examples

75.7 MB 72 131 4

- 203: 2D map of AchBP+TxIA_m d.tpr
- 202: 2D map of AchBP+TxIA_m d.tpr
- 201: 2D map of AchBP+TxIA_m d.tpr
- 200: 2D map of AchBP+TxIA_m d.tpr
- 199: 2D map of AchBP+TxIA_m d.tpr
- 195: 2D map of AchBP+TxIA_m d.tpr
- 194: 2D map of AchBP+TxIA_m d.tpr

model.nmr.ru/cell

Thank you for your attention!

