

Using cryo-EM maps to determine protein transmembrane regions

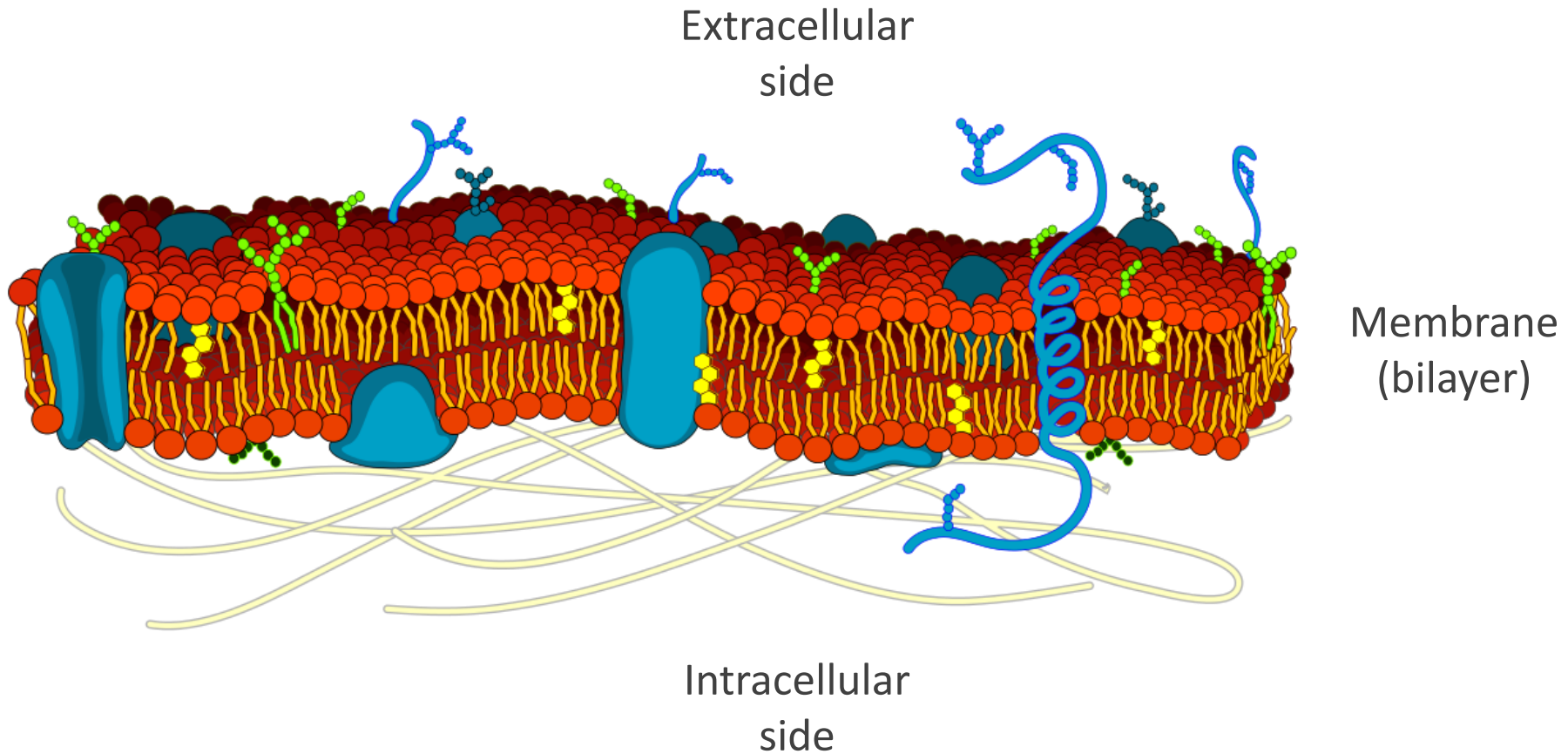
The MemBlob database and server

Georgina Csizmadia

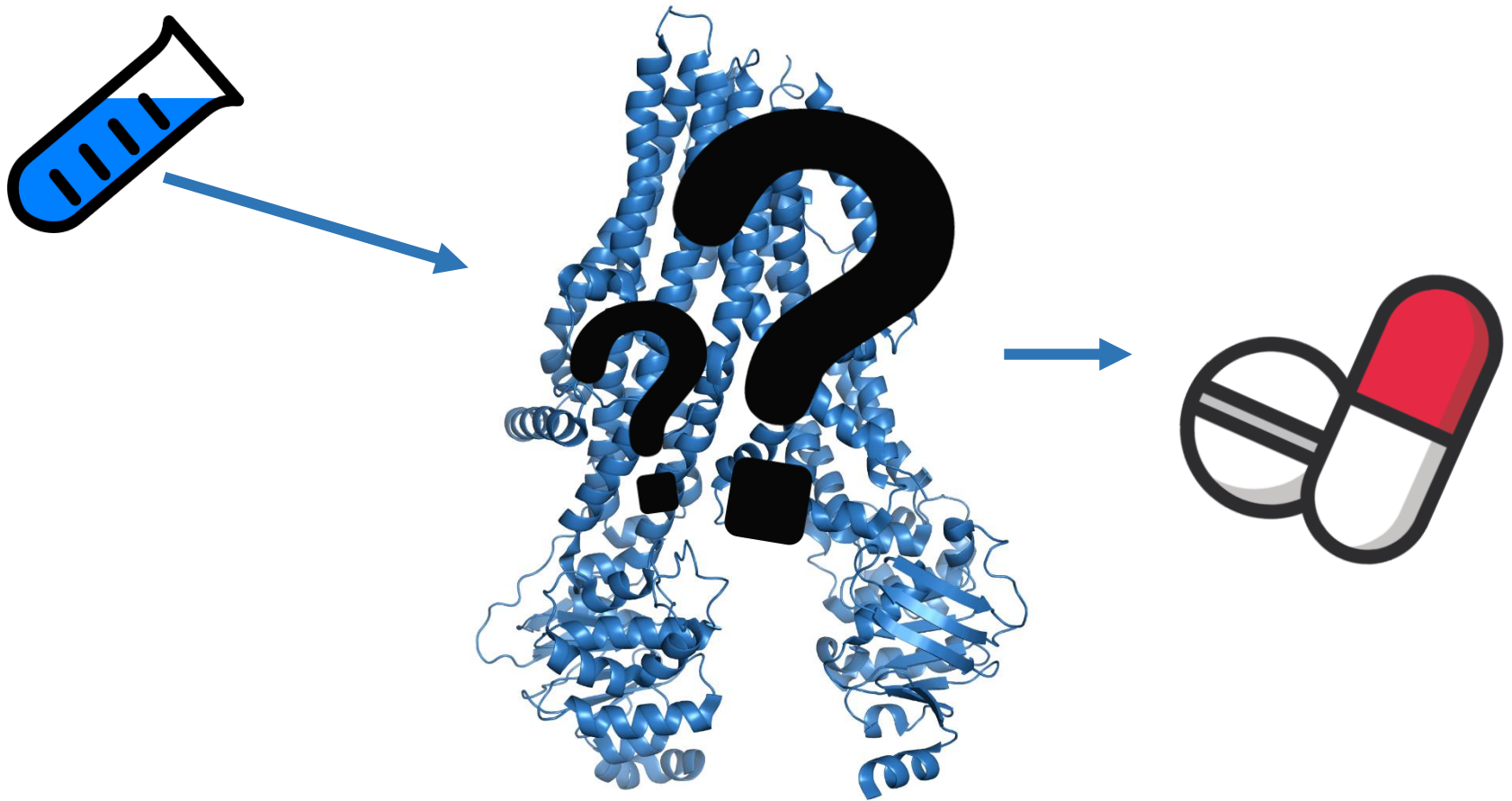


GPU Day 2019

Transmembrane proteins are significant drug targets



Experimental data on the bilayer boundaries is sparse

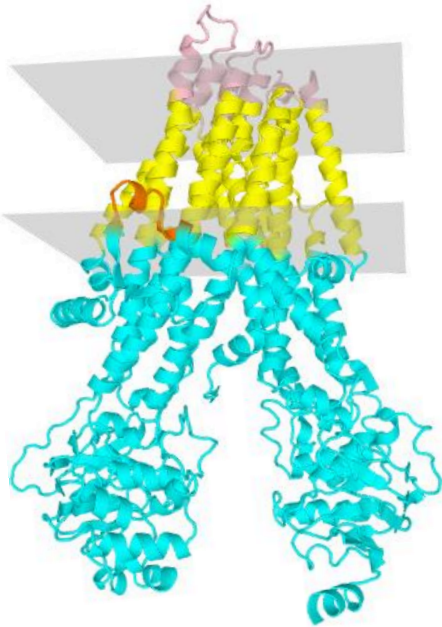


CFTR (PDBID: 5UAK)

In silico methods are predictions

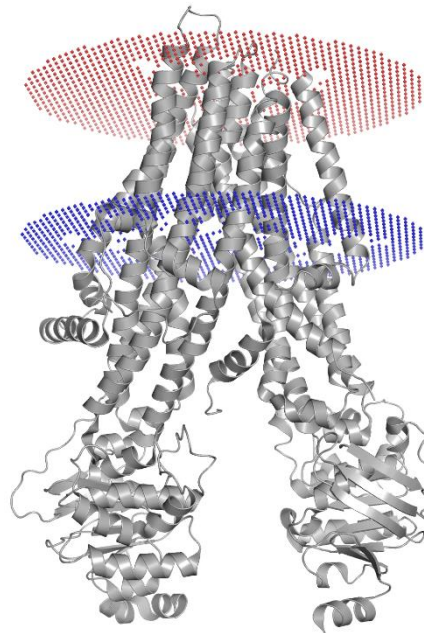
CFTR (PDBID: 5UAK)

TMDDET



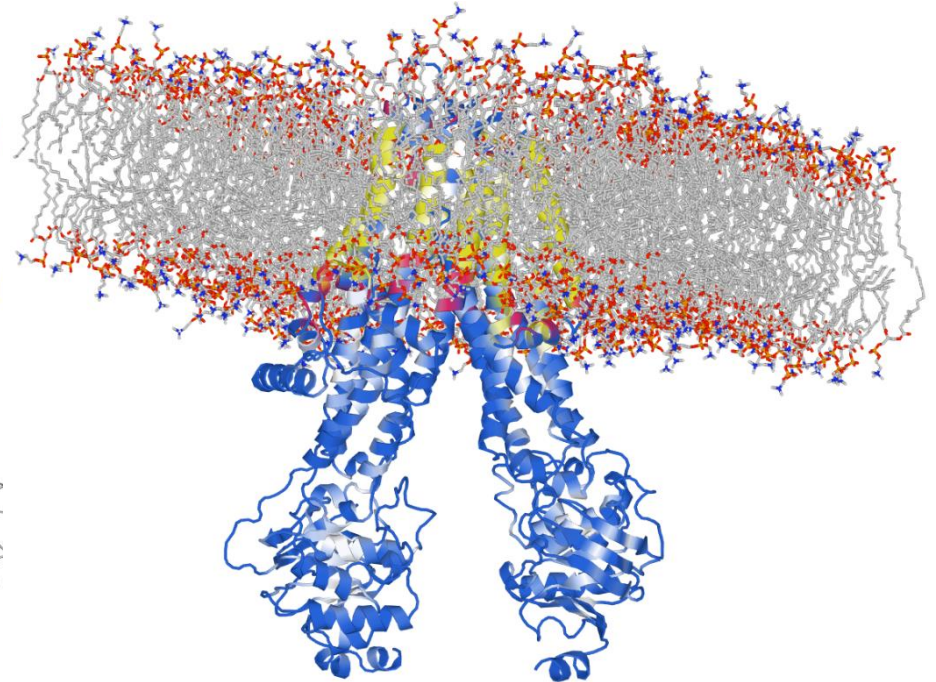
pdbtm.enzim.hu

PPM



opm.phar.umich.edu

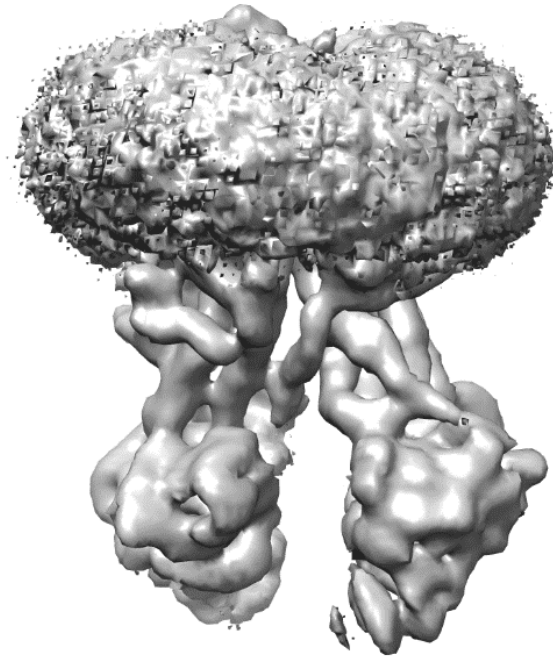
MemProtMD



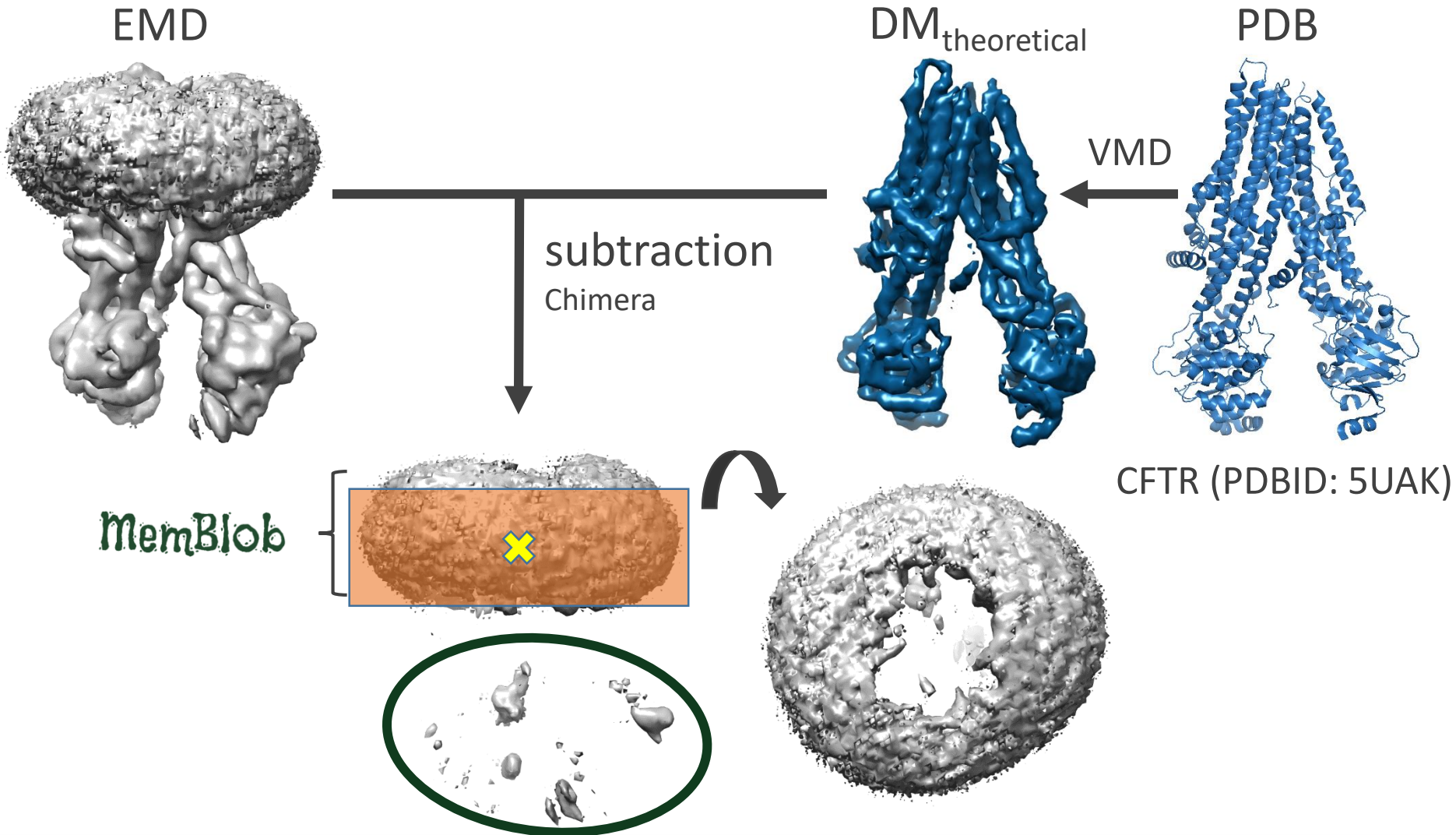
memprotmd.bioch.ox.ac.uk

Membrane embedding data is a blob in the EMD maps

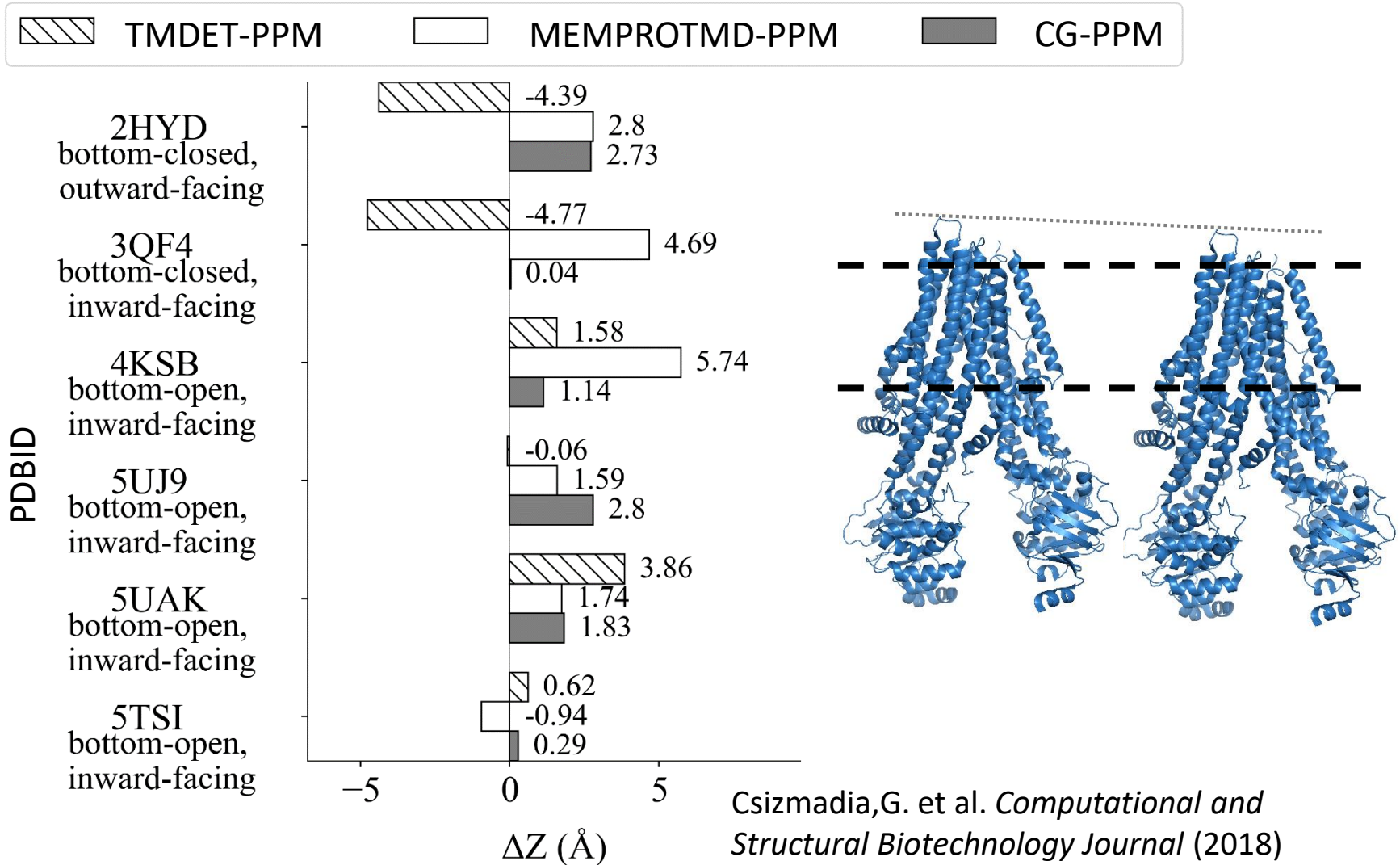
CFTR (PDBID: 5UAK, EMD-8516)



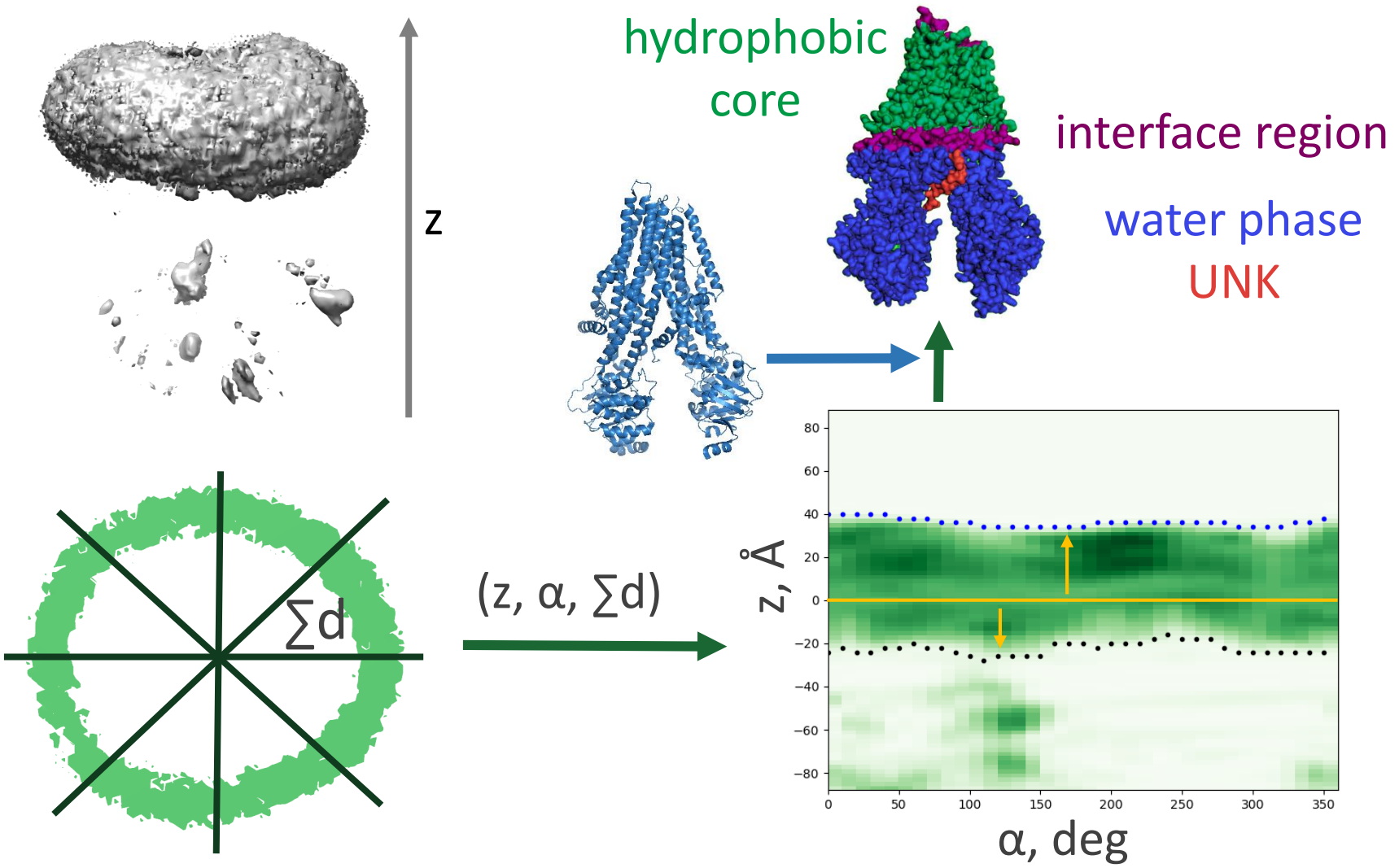
We extract the MemBlob from the EMD map



In silico methods have similar results



We convert the membrane blob to membrane boundaries



Our pipeline is available as a webserver on memblob.hegelab.org

[Home](#)[Browse](#)[Submit](#)[Help](#)[Contact](#)

Submit

MRC file: No file chosen

A gzipped MRC file; size limit: 640M

Difference map:

You may be able to generate and upload a difference map with higher quality than the automatically generated difference map by this server { map - map(protein) }

PDB file: No file chosen

This file should be aligned with the provided map; size limit: 10M

PDBTM XML: No file chosen

This file should be generated by [TMDET](#). OPTIONAL - if this field is left empty, the leading four characters of the PDB file name will be treated as a PDBID and will be used to retrieve the XML file from PDBTM; if this process was unsuccessful, the PDB file is submitted to TMDET to obtain the required XML file

Interface:

The thickness of the interface region in Angstroms

You can fork calculations from entries already in the database:

PDB/EMD ID:

Be sure to enter here an id for an entry present in our database. Click on "Resubmit" on the next result page.

To test running from the scratch, you can download and use these files:

[5uak.pdb](#)
[emd_8516.map.gz](#)



[5a63](#)

[APH1A](#)

[APH1A_HUMAN](#)

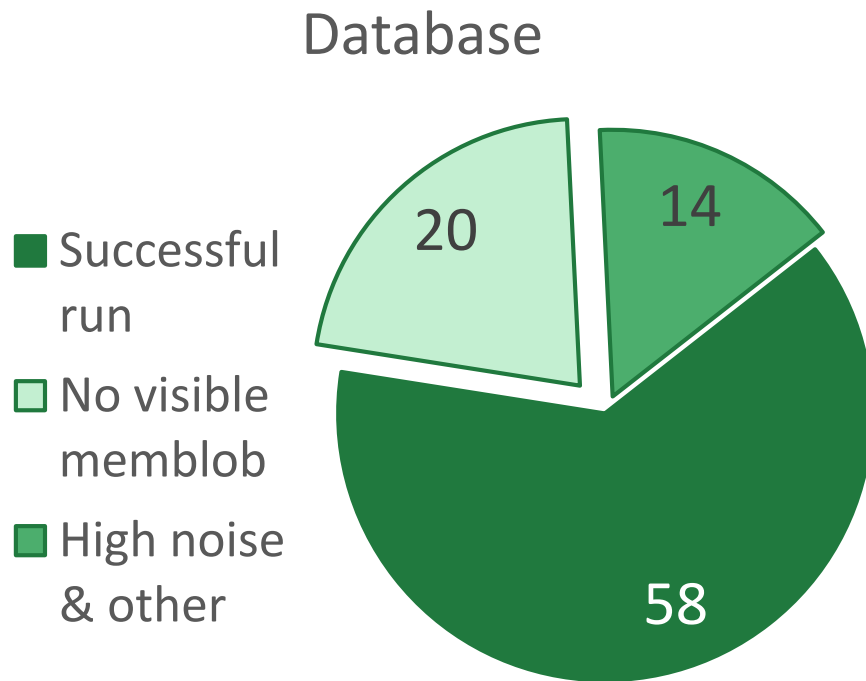
[emd_3061.gz](#)
[EMD-3061](#)

[amphipol](#)

3.4

More manual adjustment needed because of the noise level

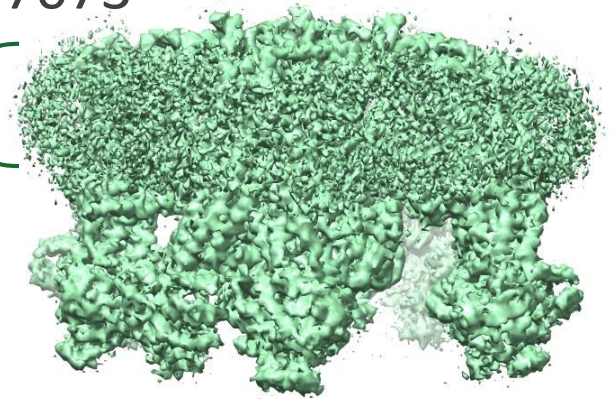
Some EMD maps lack blobs



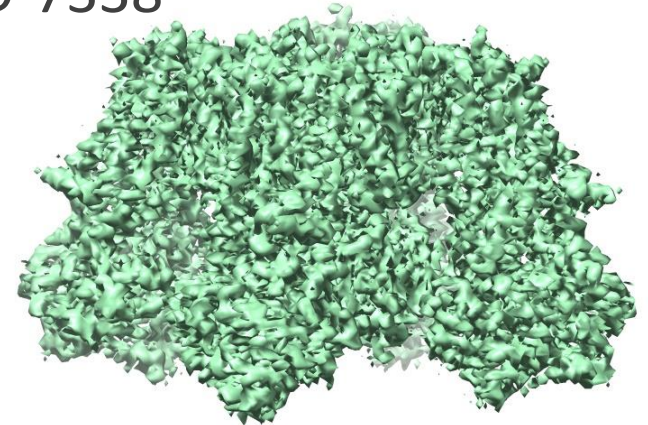
ABCC8/Kir6.2 complex

EMD-7073

memblob

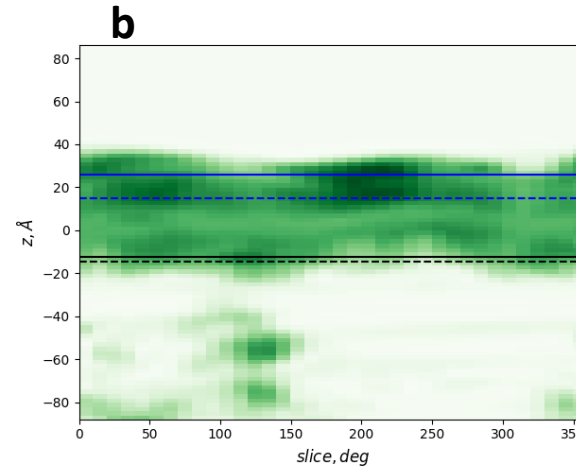
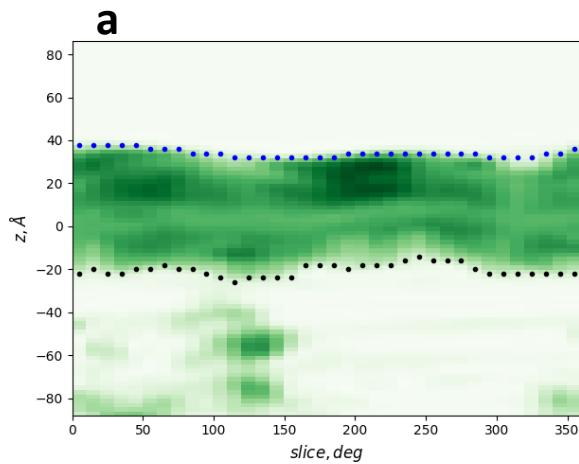


EMD-7338



Some of the experimental membrane blobs are thicker than expected

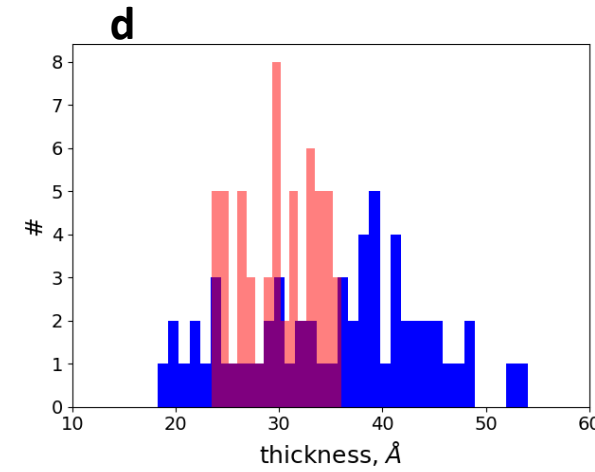
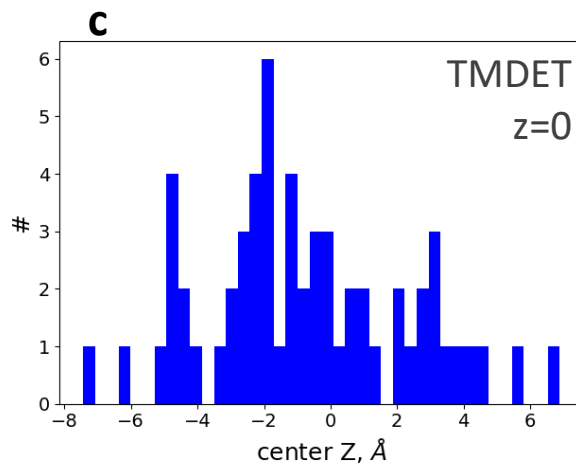
Membrane boundaries



MemBlob:
solid lines

TMDet:
dashed lines

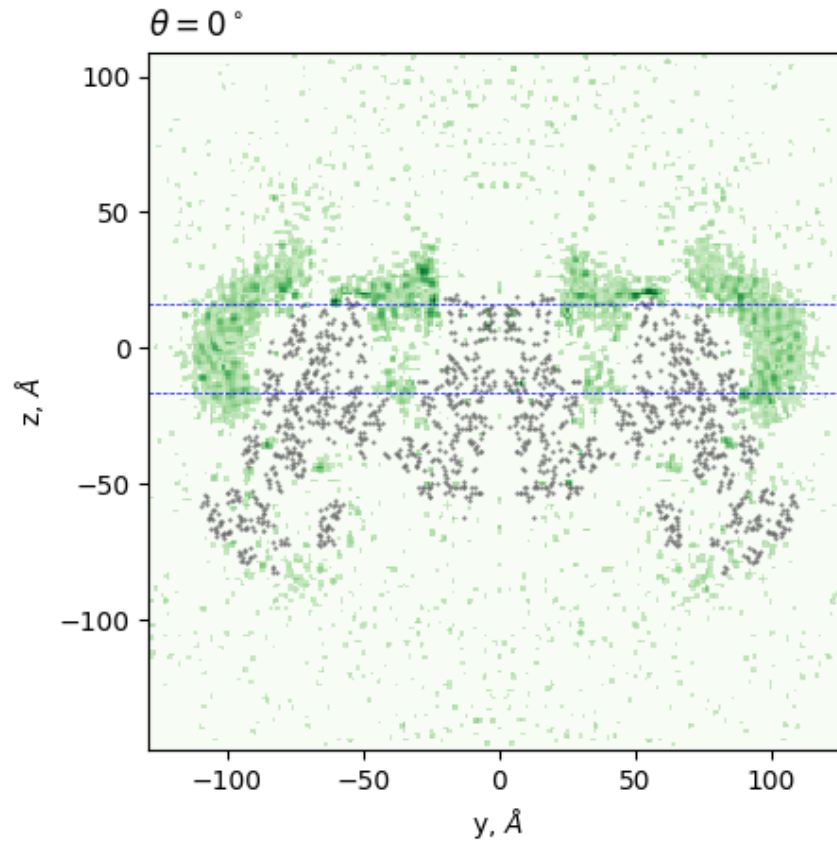
Distribution of bilayer centres



Distribution of bilayer Thickness

TMDet
MemBlob

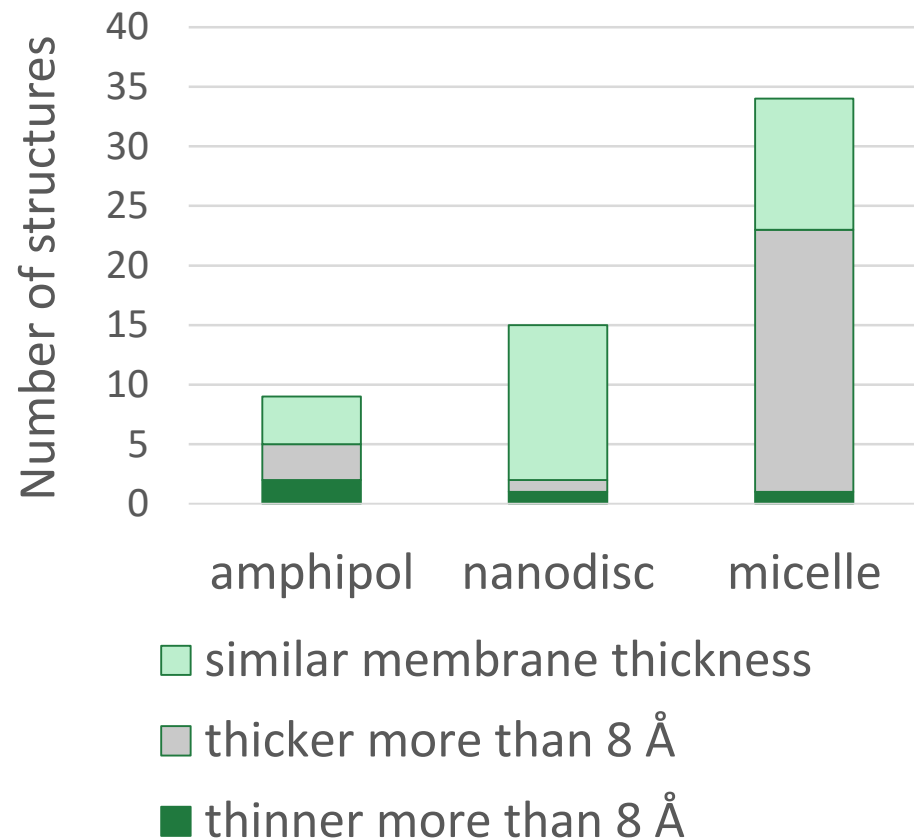
Some proteins sit deep in the lipids



Lipid densities
TMDet membrane
boundaries

ABCC8/Kir6.2 (PDBID: 6BAA, EMD-7073)

Does the membrane thickness depend on the type of membrane mimetics?



Conclusions

- EM density maps contain extra information
- MemBlob is a pipeline to extract transmembrane regions from EMD maps
- This provides high resolution experimental data on transmembrane regions

Acknowledgments

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