Using cryo-EM maps to determine protein transmembrane regions

The MemBlob database and server

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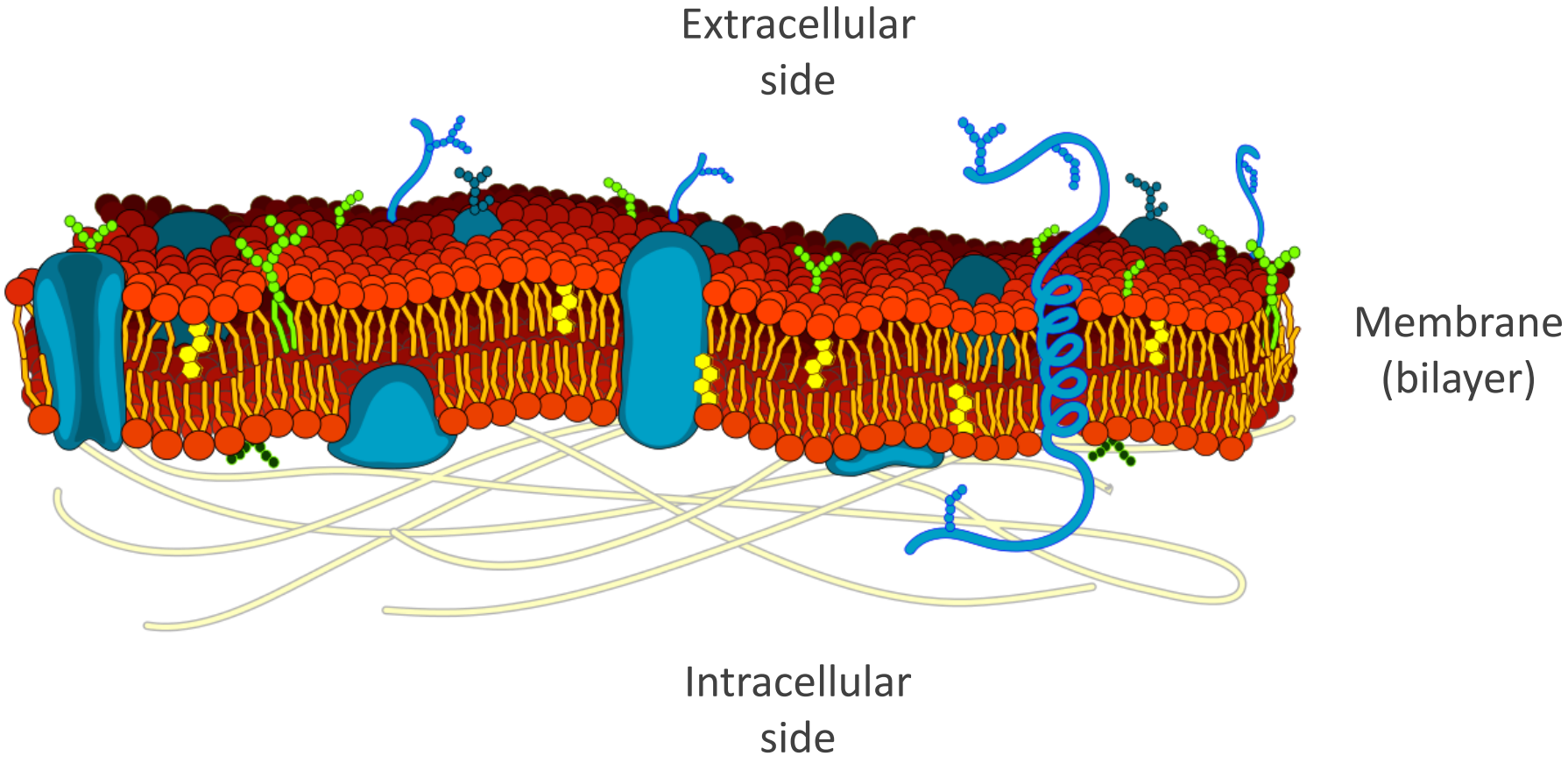
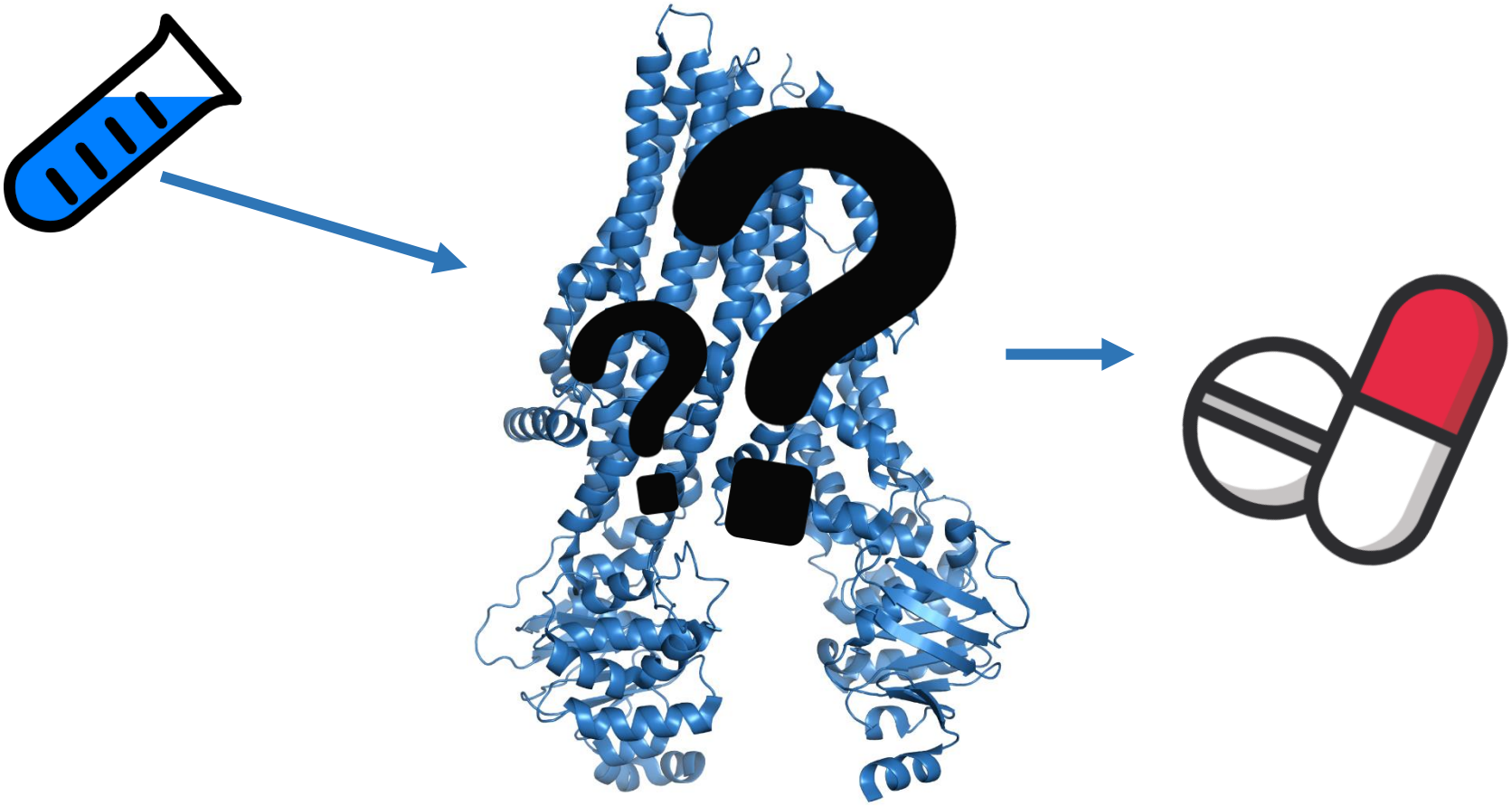
GPU Day 2019

Transmembrane proteins are significant drug targets



Experimental data on the bilayer boundaries is sparse

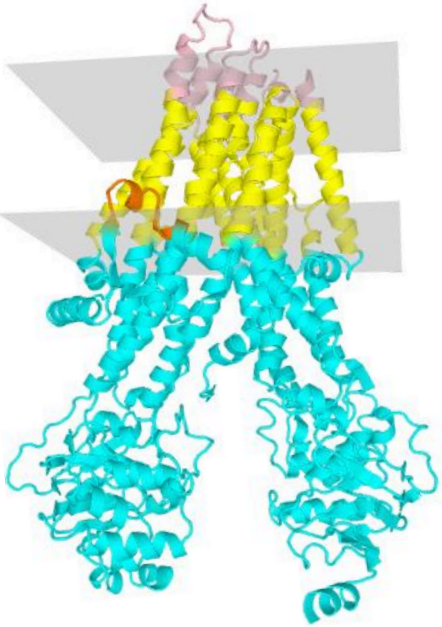


CFTR (PDBID: 5UAK)

In silico methods are predictions

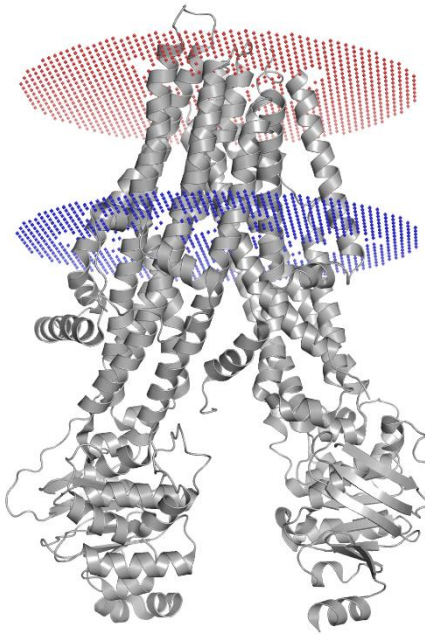
CFTR (PDBID: 5UAK)

TMDET



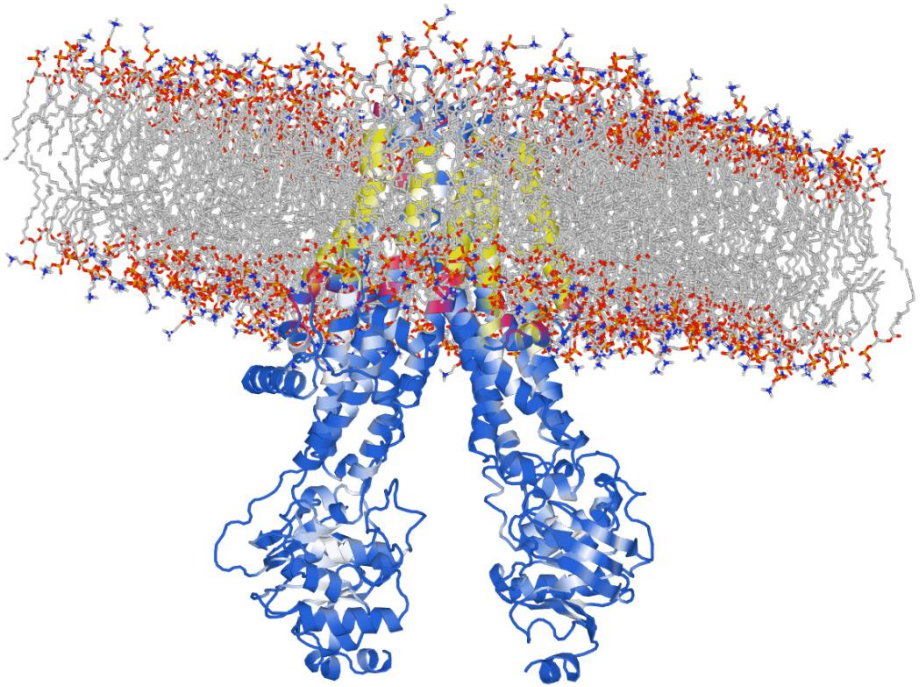
pdbtm.enzim.hu

PPM



opm.phar.umich.edu

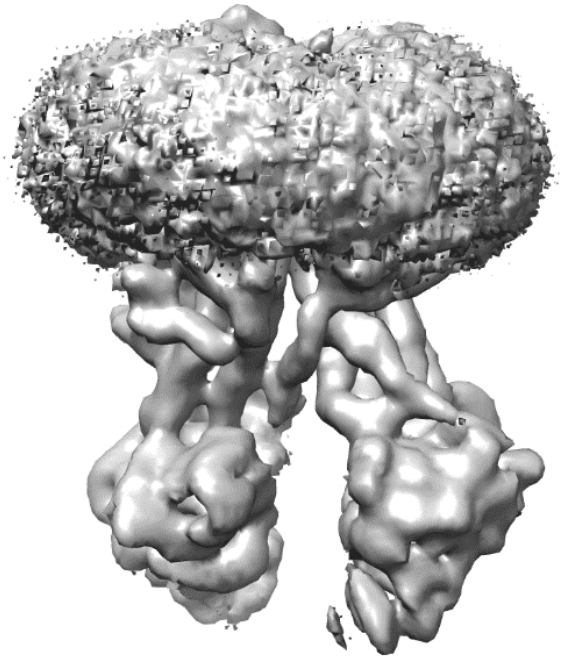
MemProtMD



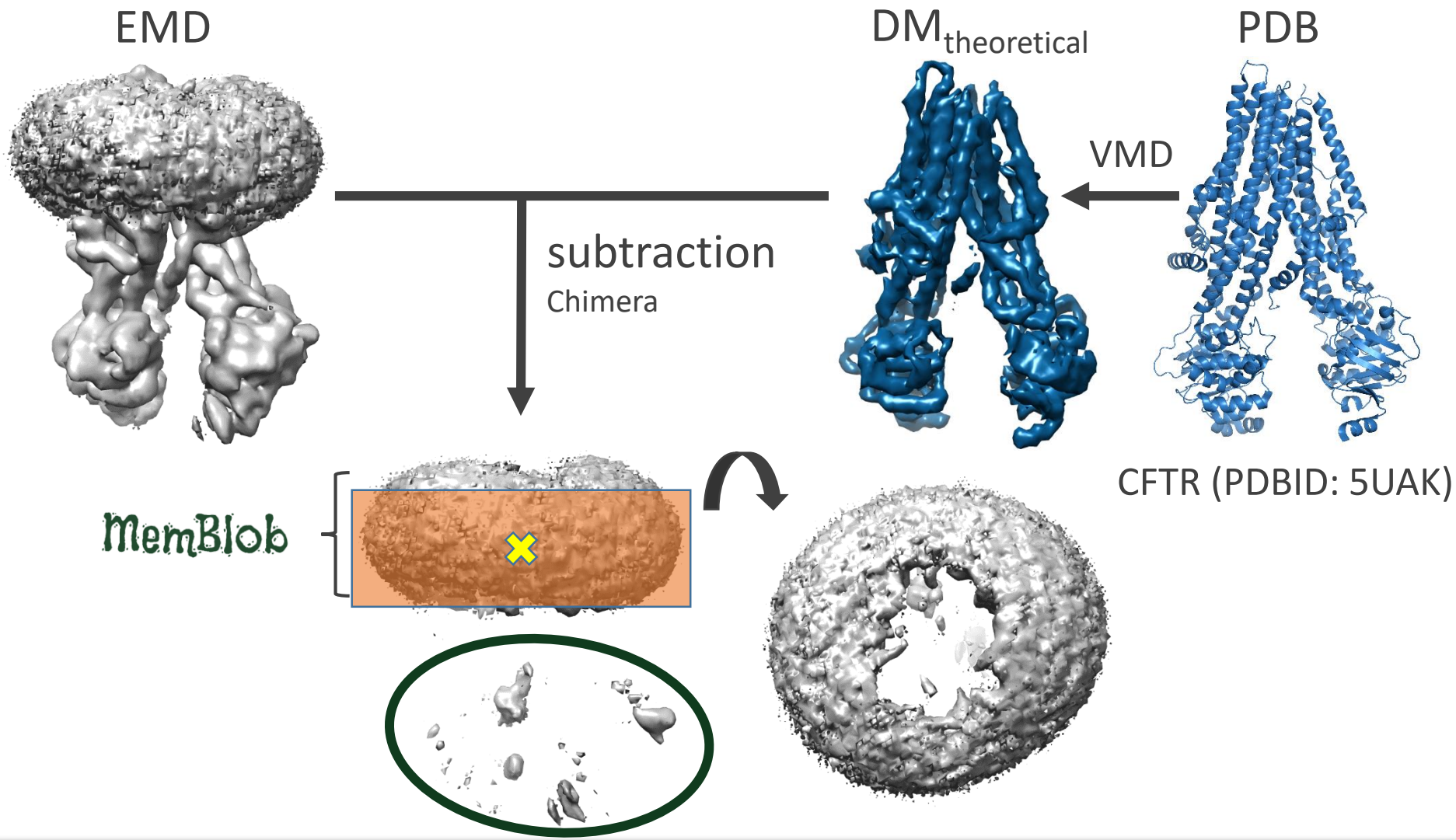
memprotmd.bioch.ox.ac.uk

Membrane embedment data is a blob in the EMD maps

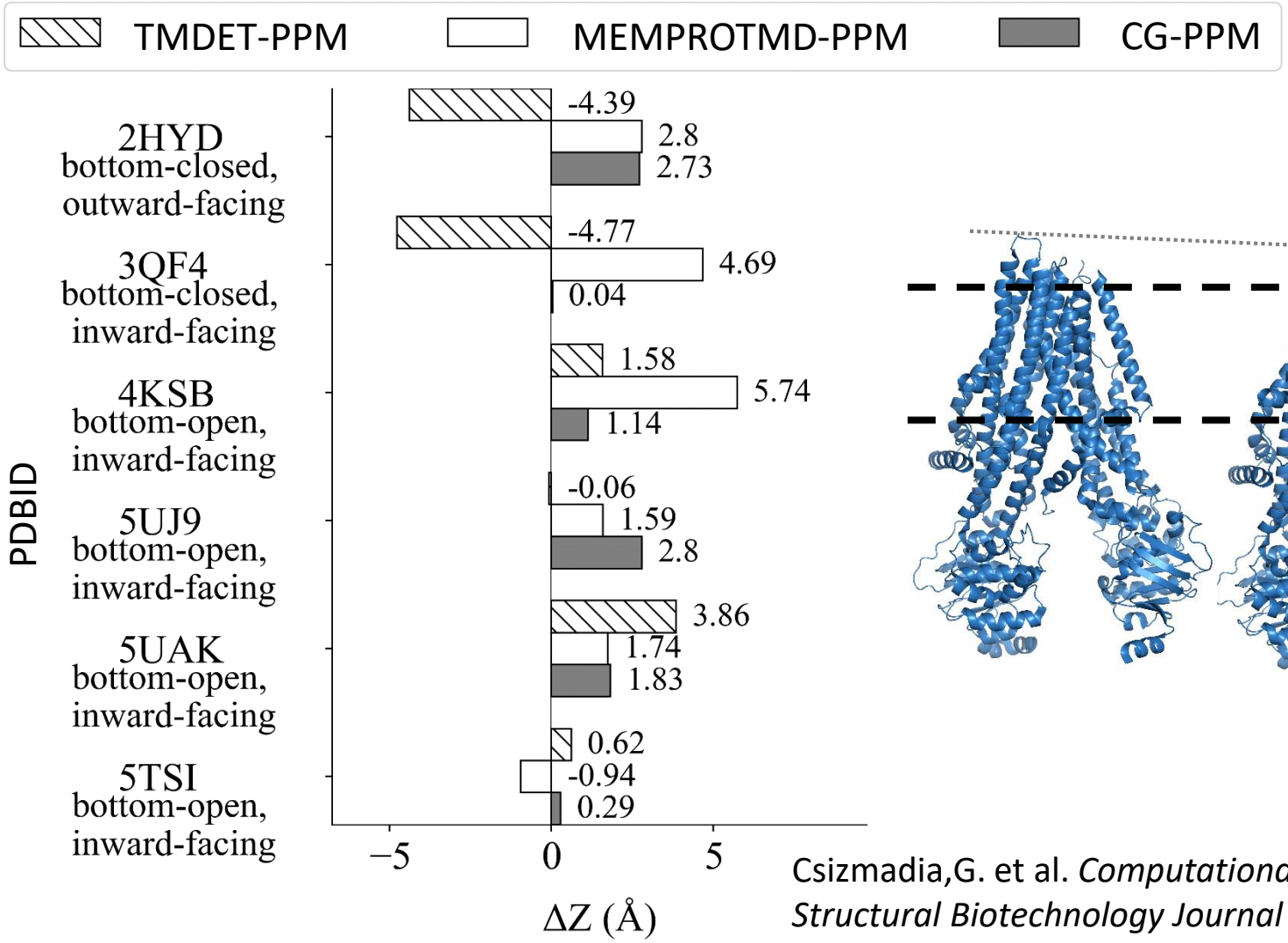
CFTR (PDBID: 5UAK, EMD-8516)

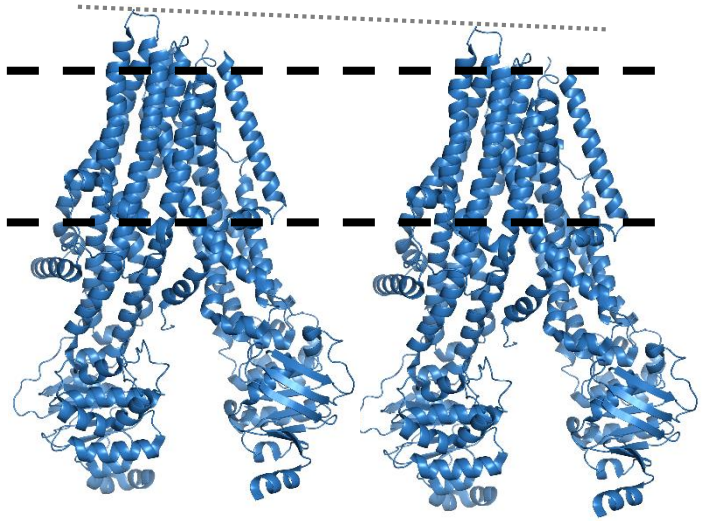


We extract the MemBlob from the EMD map



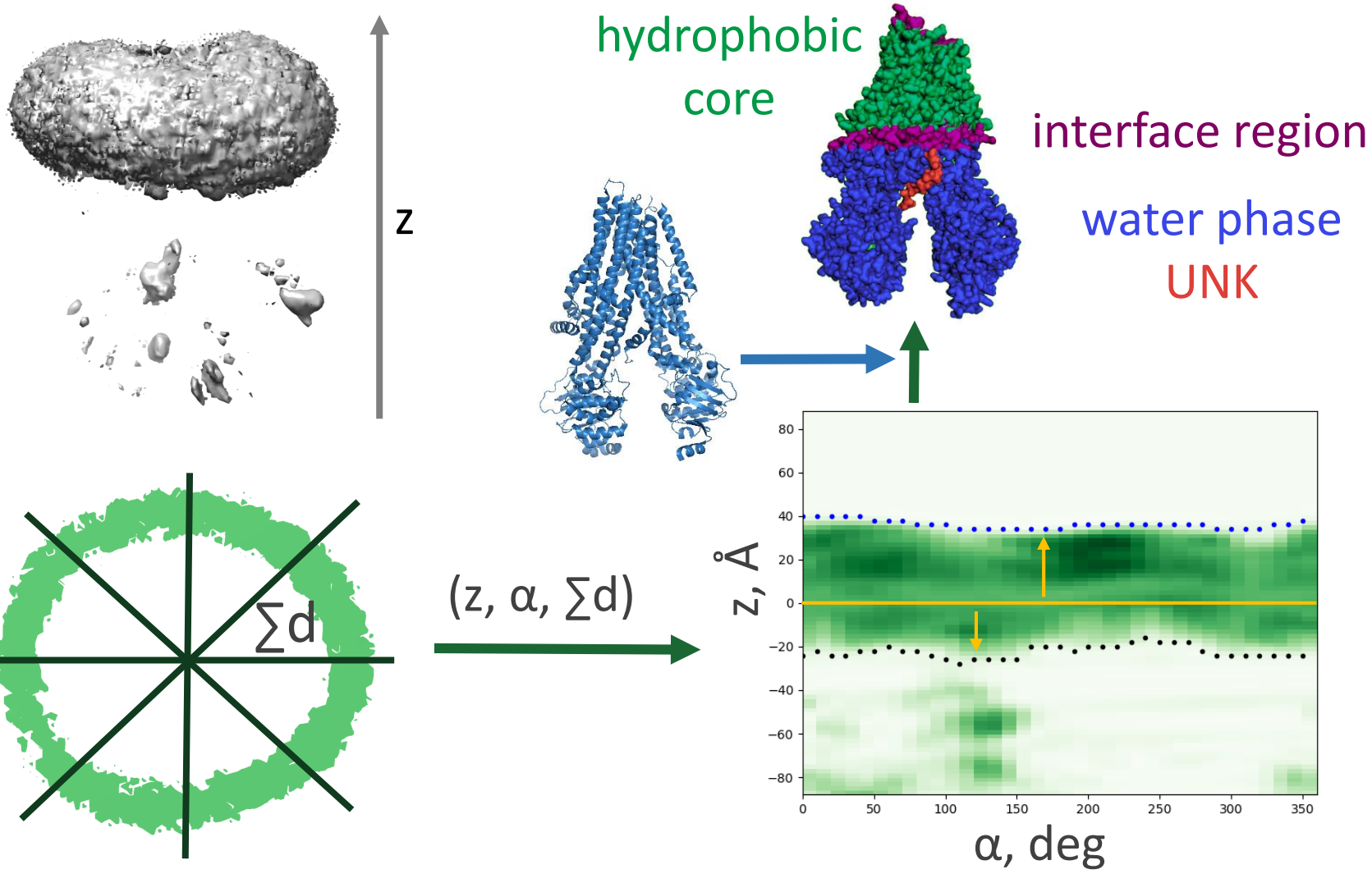
In silico methods have similar results



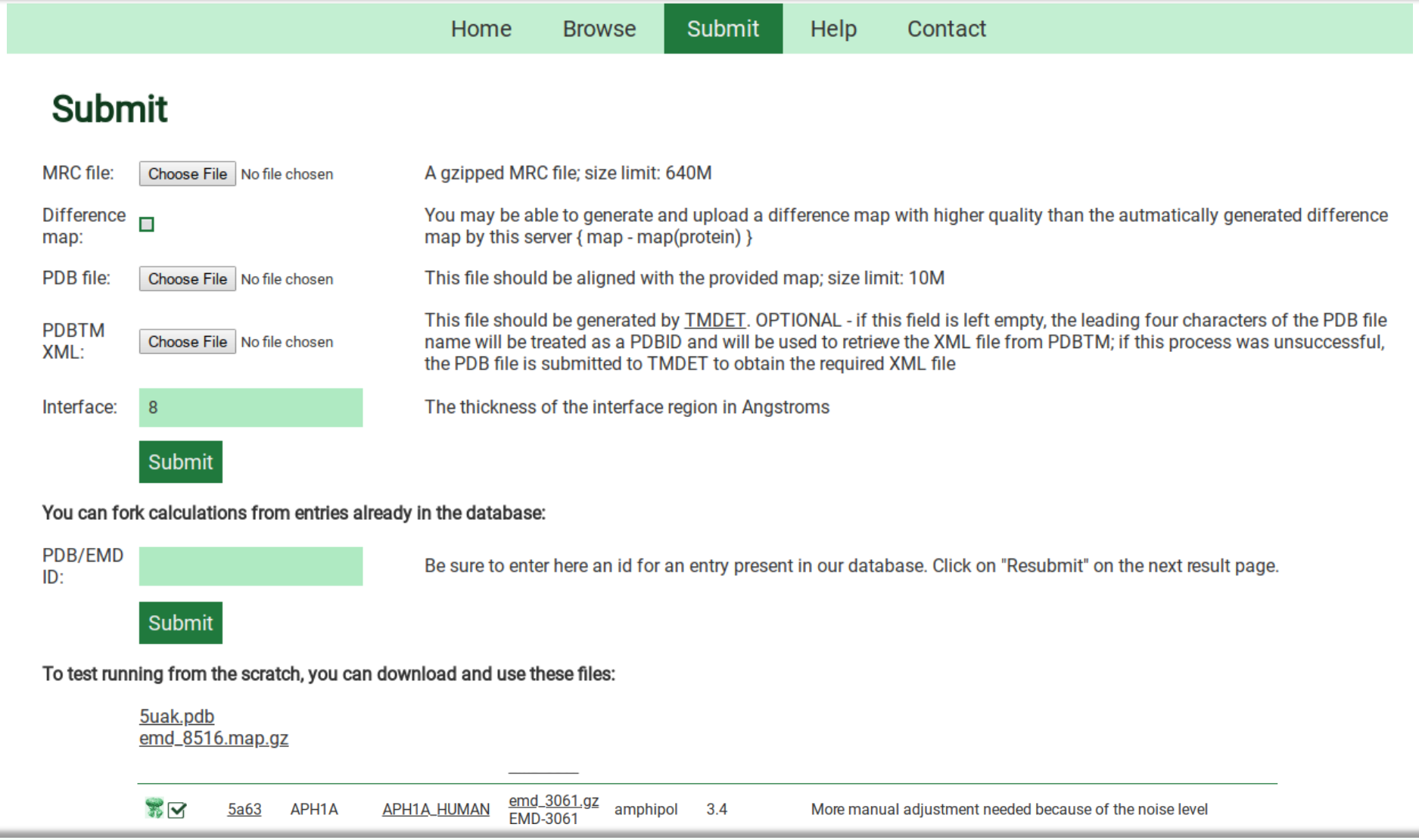


Csizmadia,G. et al. *Computational and Structural Biotechnology Journal* (2018)

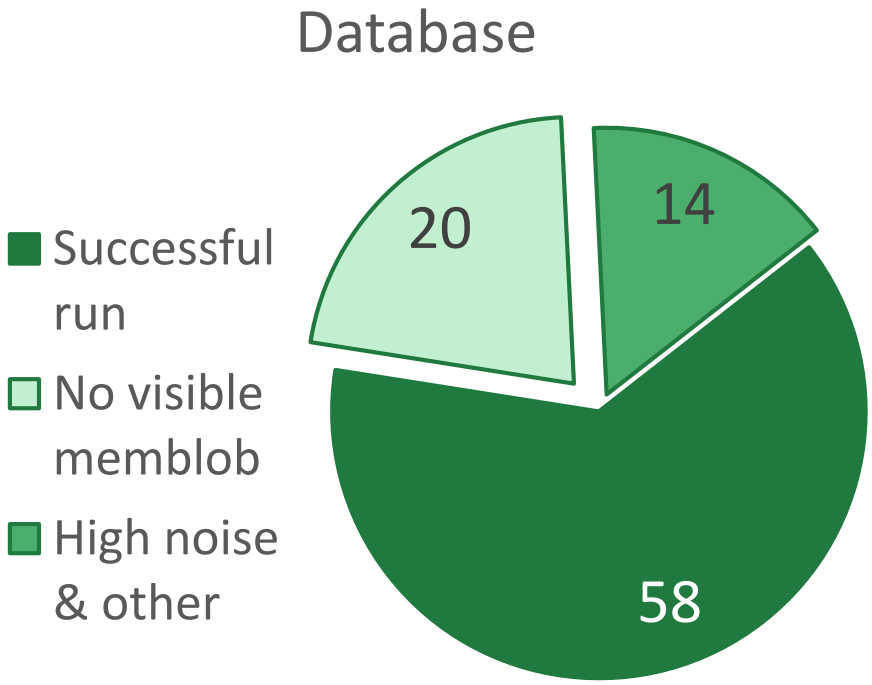
We convert the membrane blob to membrane boundaries



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

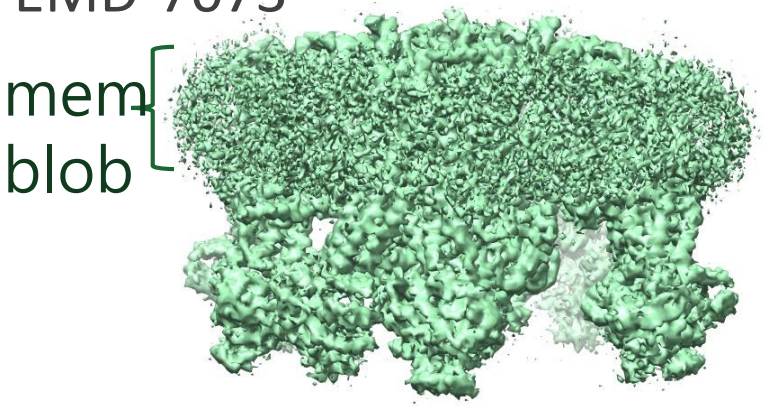


Some EMD maps lack blobs

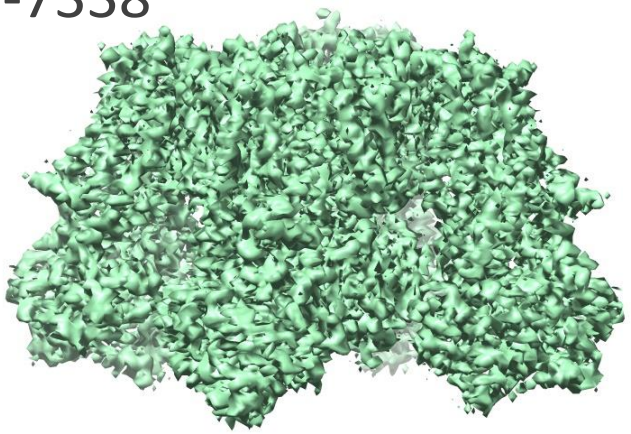


ABCC8/Kir6.2 complex

EMD-7073

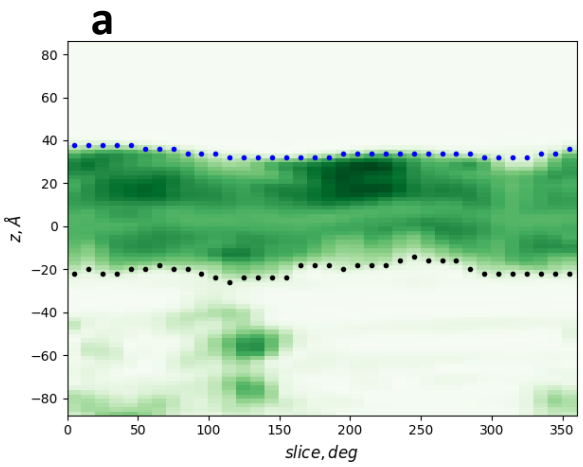


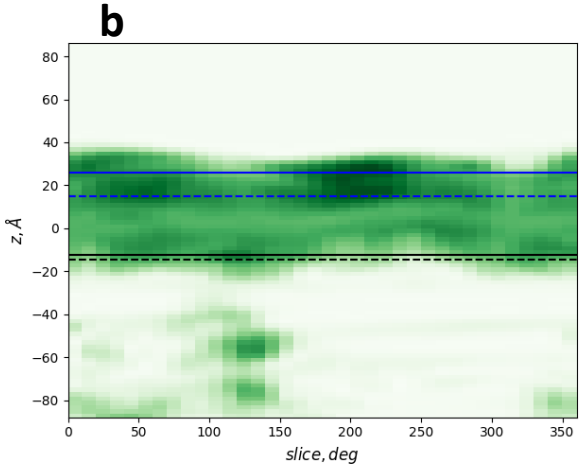
EMD-7338



Some of the experimental membrane blobs are thicker than expected

Membrane boundaries

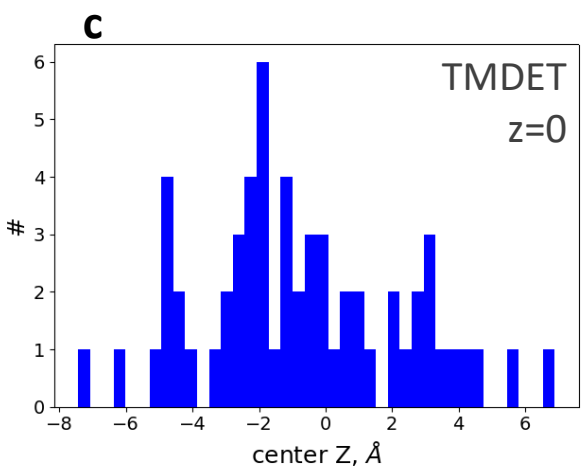


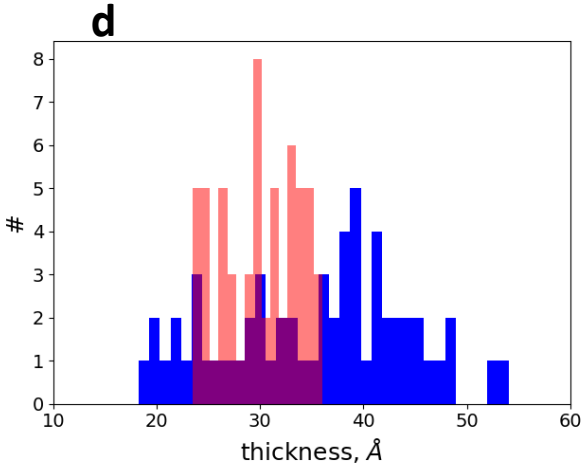


MemBlob: solid lines

TMDET: dashed lines

Distribution of bilayer centres



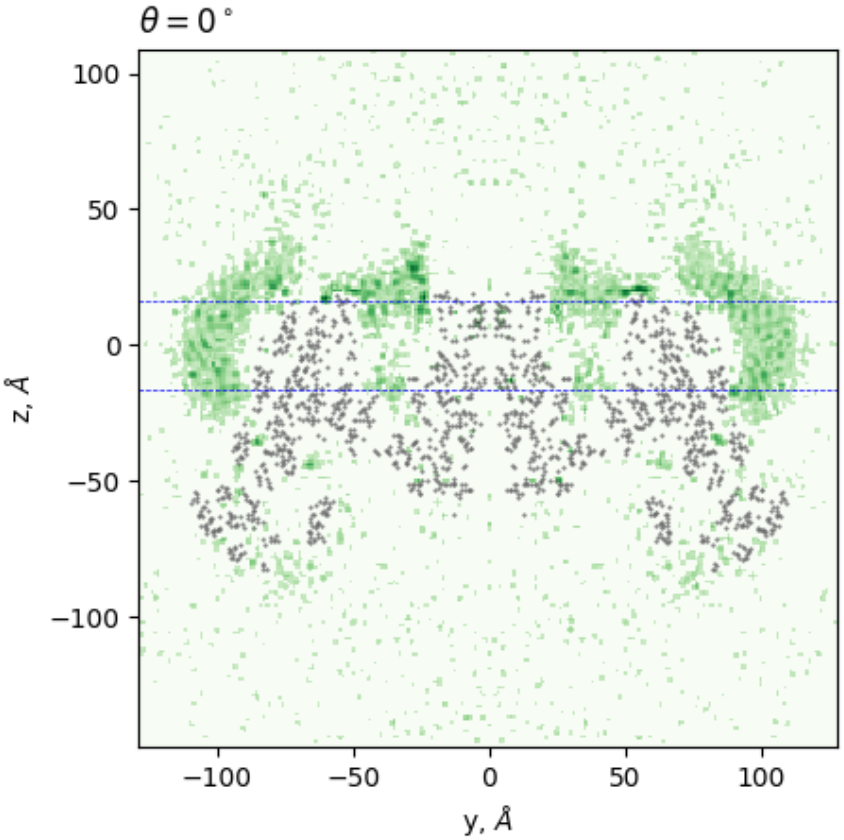


Distribution of bilayer Thickness

TMDET

MemBlob

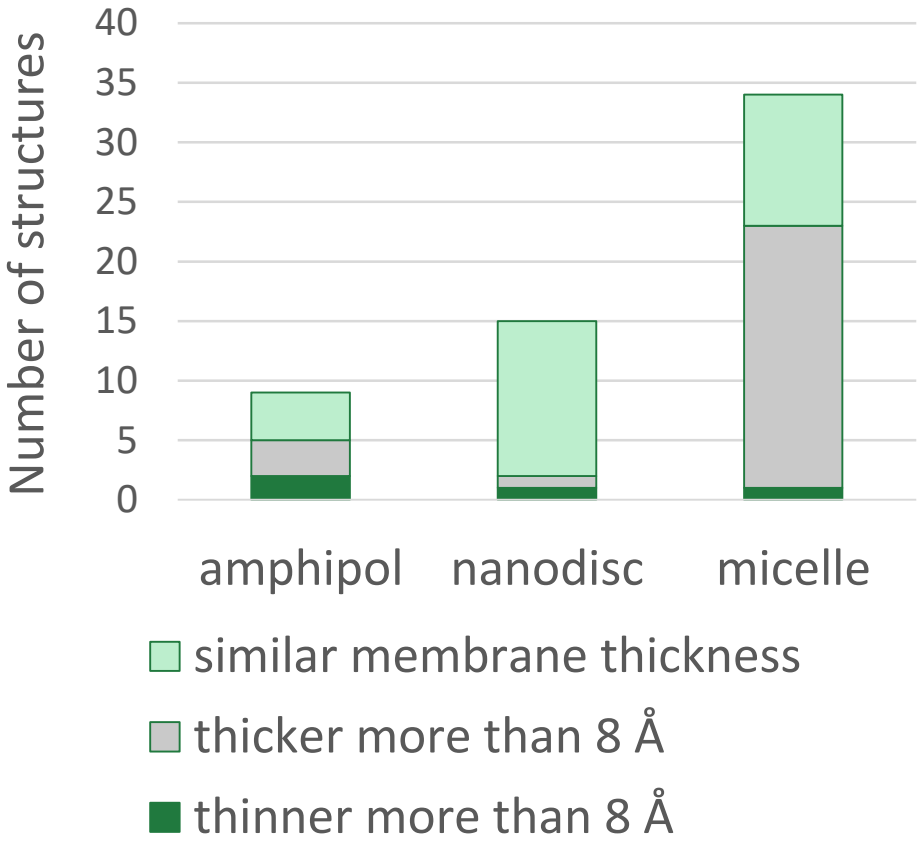
Some proteins sit deep in the lipids



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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