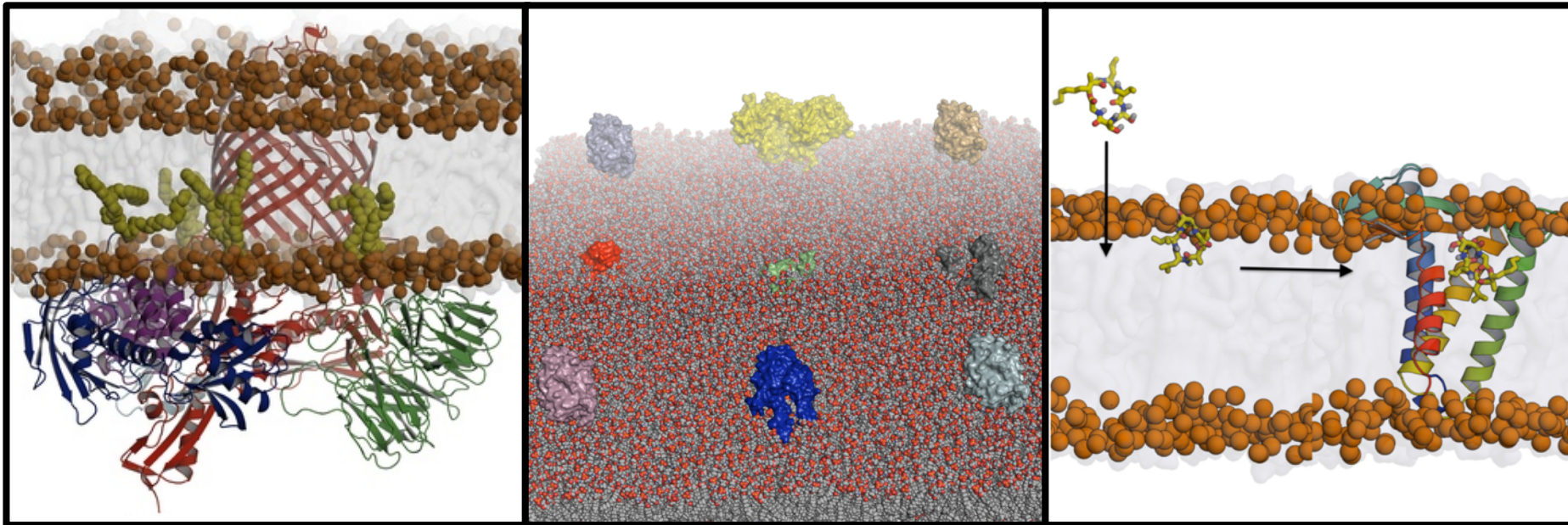




MemProtMD

A Resource for Membrane Proteins & their Lipid Interactions



DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF OXFORD



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University of Oxford
phillip.stansfeld@bioch.ox.ac.uk
<http://sbc.bioch.ox.ac.uk/stansfeld>

'Breathing Life' into Membrane Protein Structures

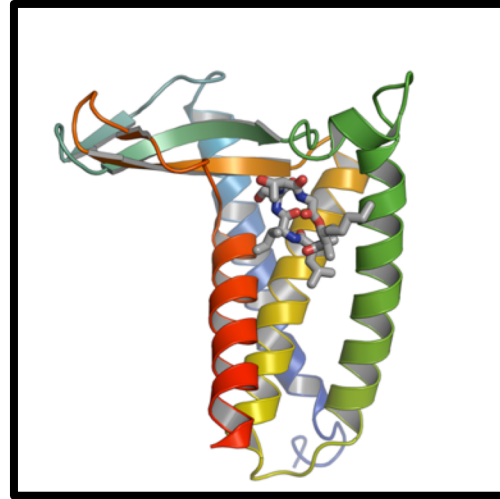
Function



Interactions



Dynamics



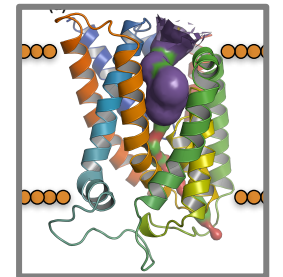
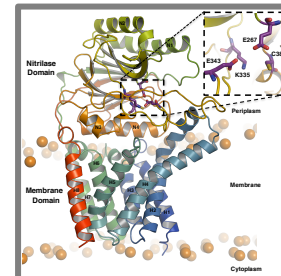
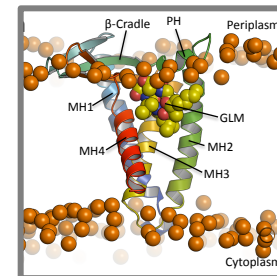
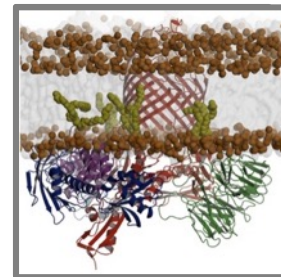
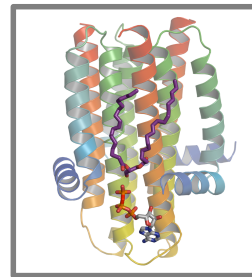
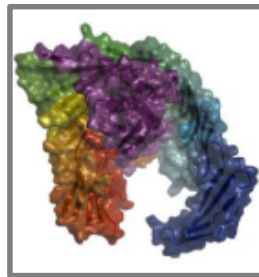
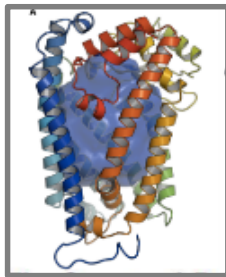
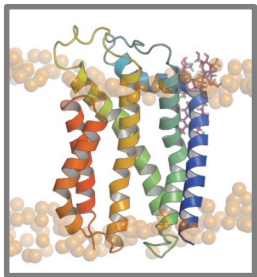
Cell



Structure



Simulation



2012

TatC
Nature

2013

ZMP
Science

2014

LptDE
Nature

2015

DgkA
Nat Com

2016

BAM
Nature

2016

LspA
Science

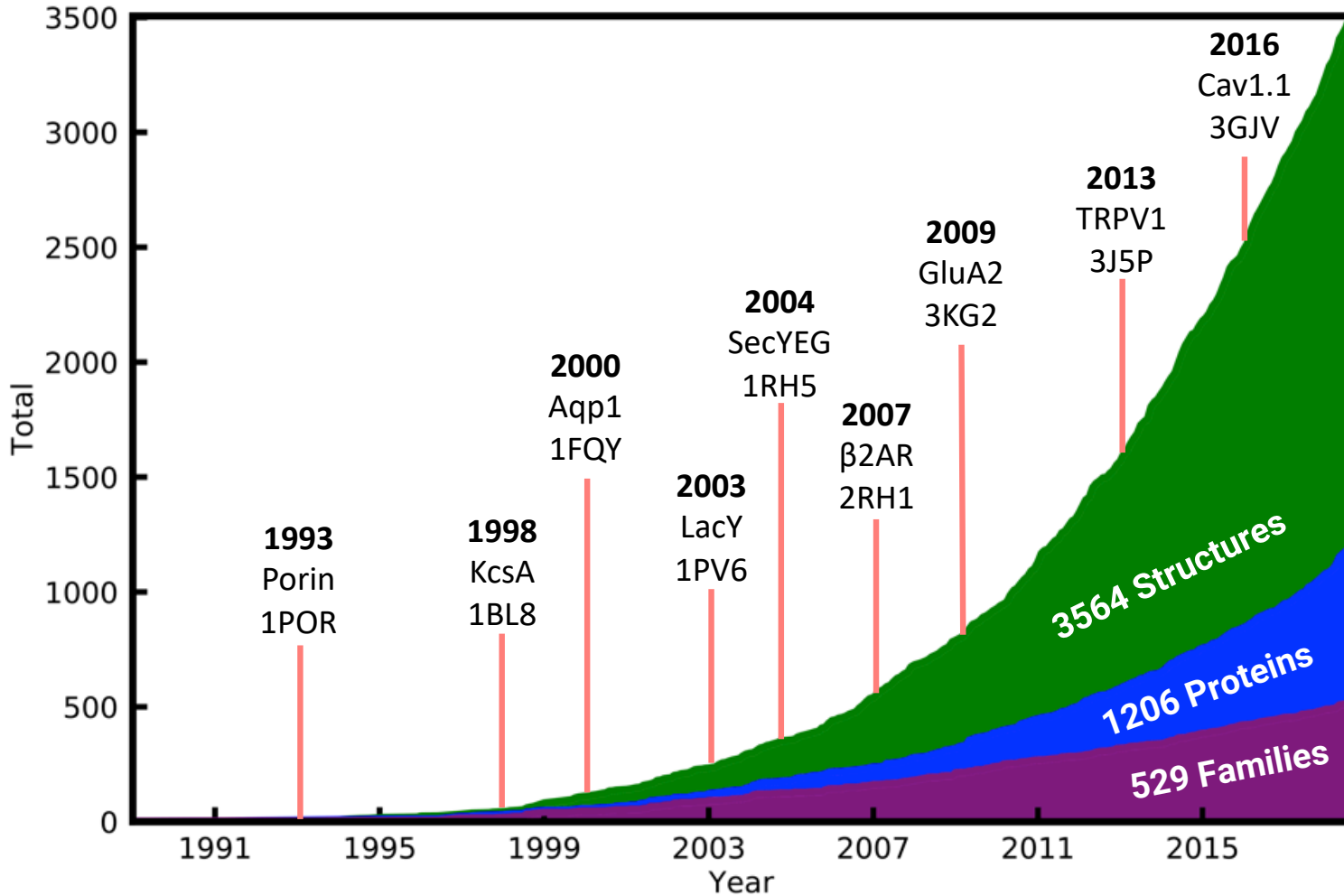
2017

Lnt
Nat Com

2018

UppP
Nat Com

How many Membrane Protein Structures are there?



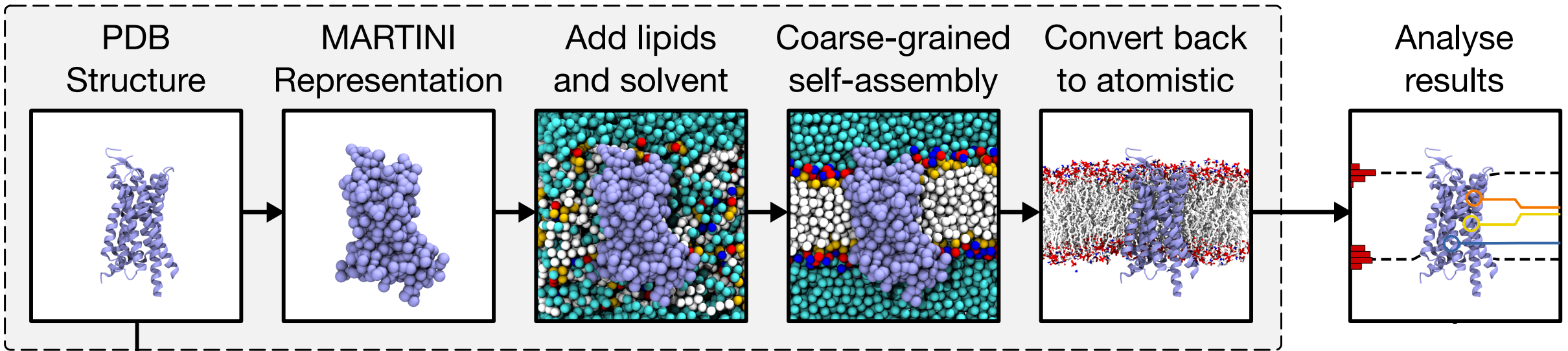
X-ray: 83%
 NMR: 6%
 Cryo EM: 11%

By 2028: ~10,500
 Membrane Protein Structures



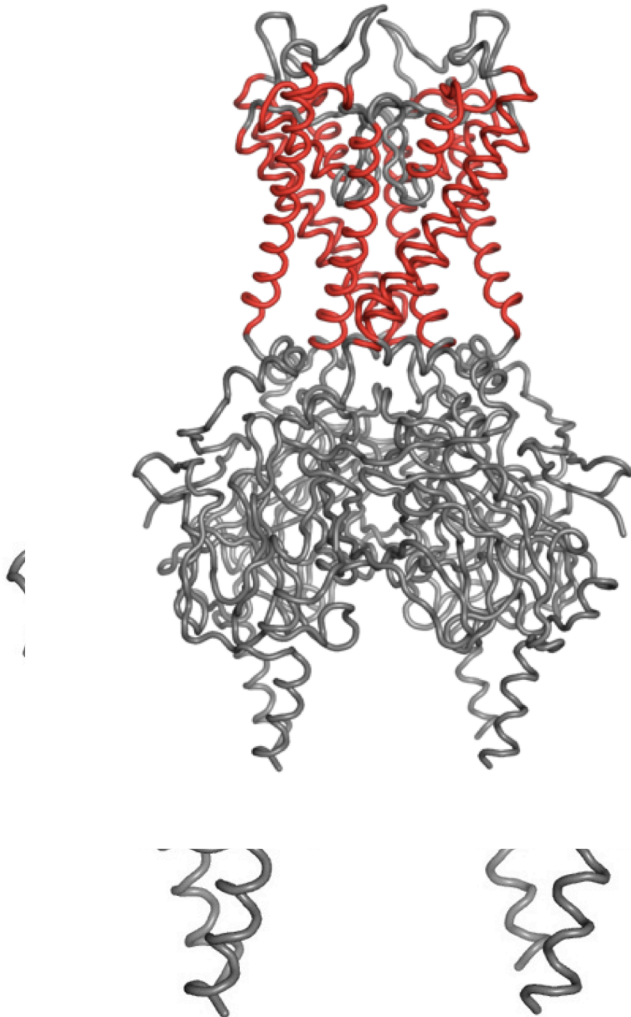
Automated Membrane Protein Simulations

MemProtMD Pipeline



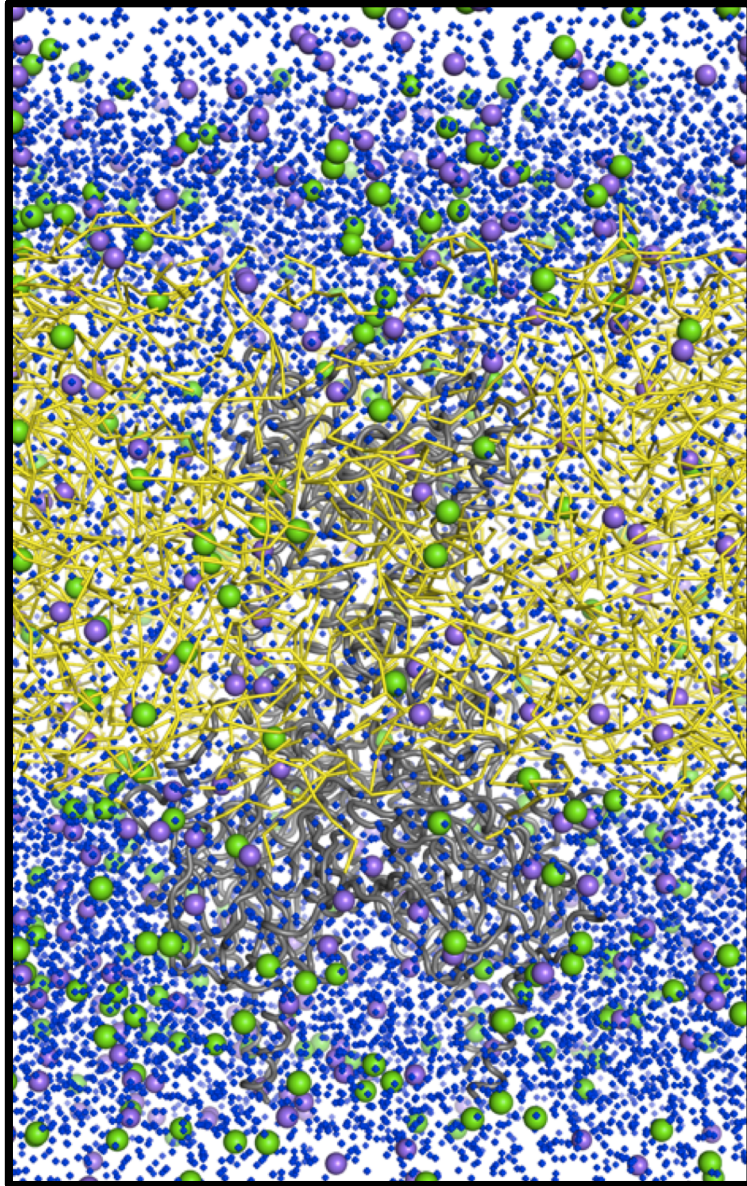
CG Self-assembly

- CG Protein
- Predict TM region and orient



Stansfeld PJ (2015) Structure.

CG Self-assembly

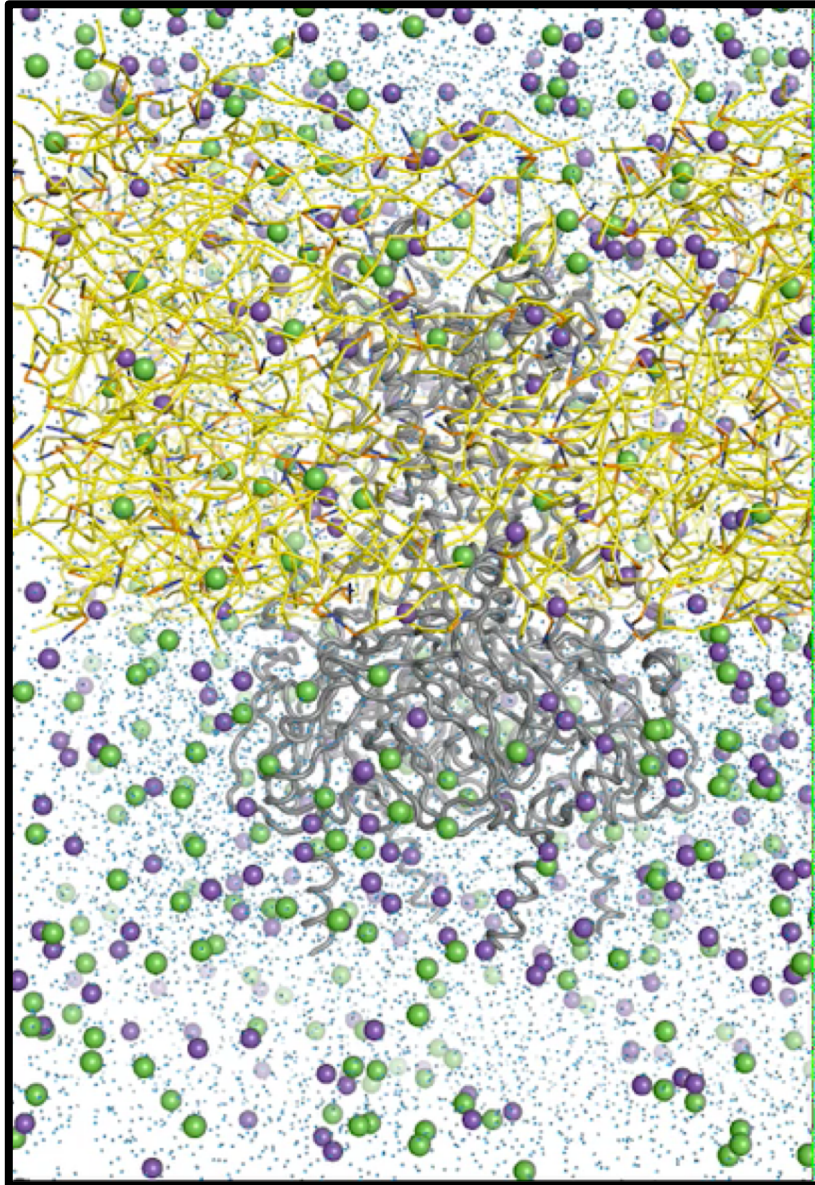


8 nm

- CG Protein
- Predict TM region and orient
- Add box of Lipids around TM domain.
- Extend box in the Z-axis
- Add Waters
- Add Ions

Stansfeld PJ (2015) Structure.

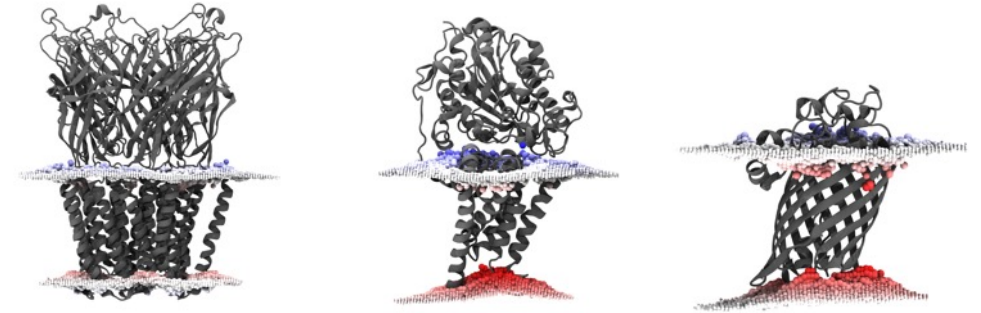
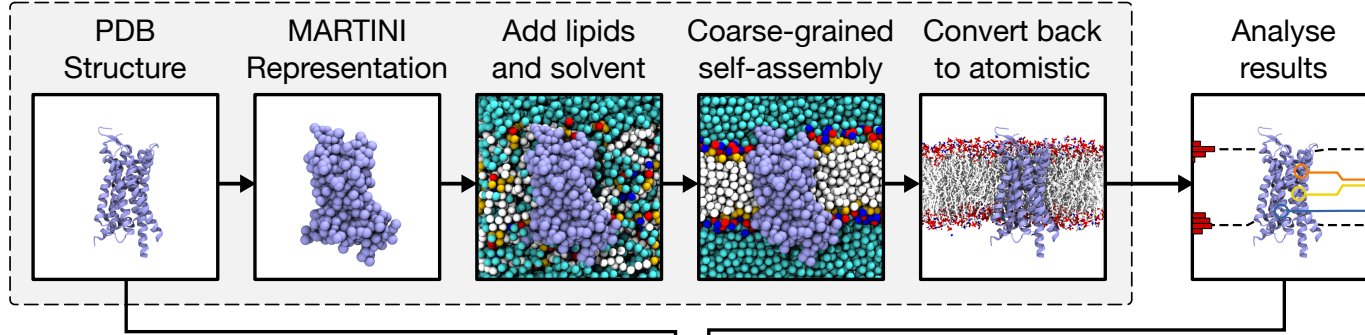
CG Self-assembly



- CG Protein
- Predict TM region and orient
- Add box of Lipids around TM domain.
- Extend box in the Z-axis
- Add Waters
- Add Ions
- 100 ns CGSA
- Followed by 900 ns

The MemProtMD Database

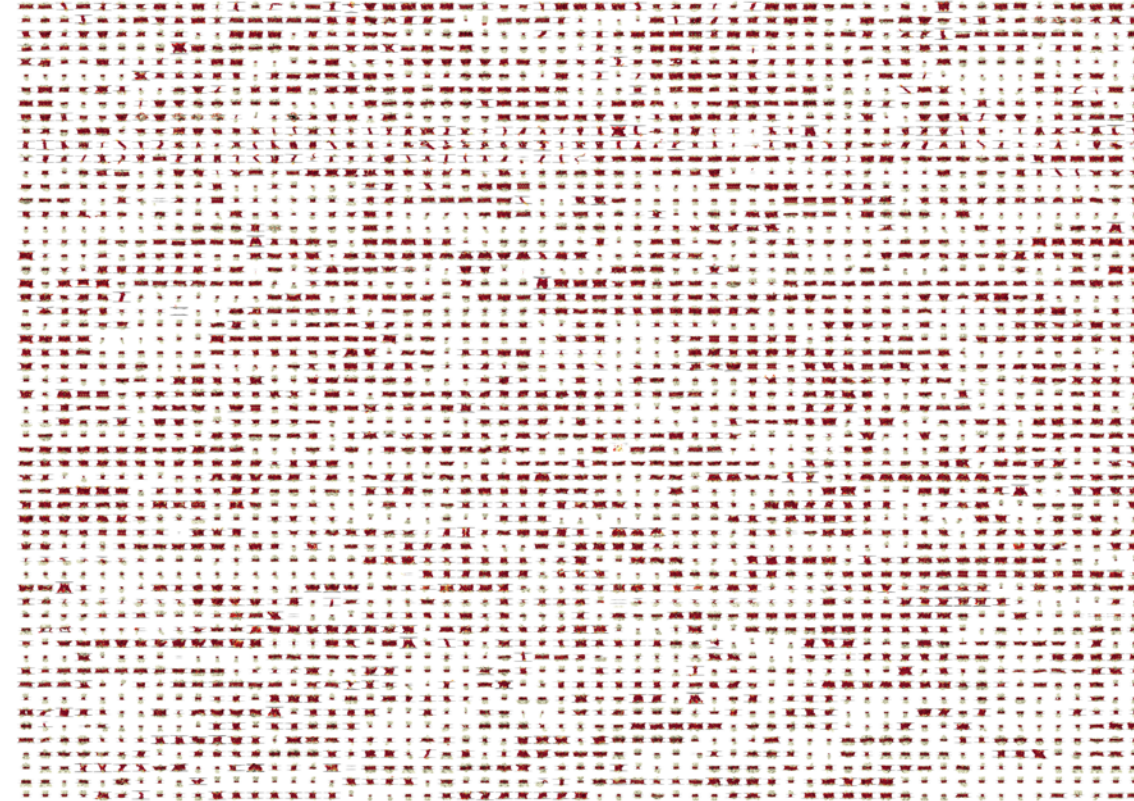
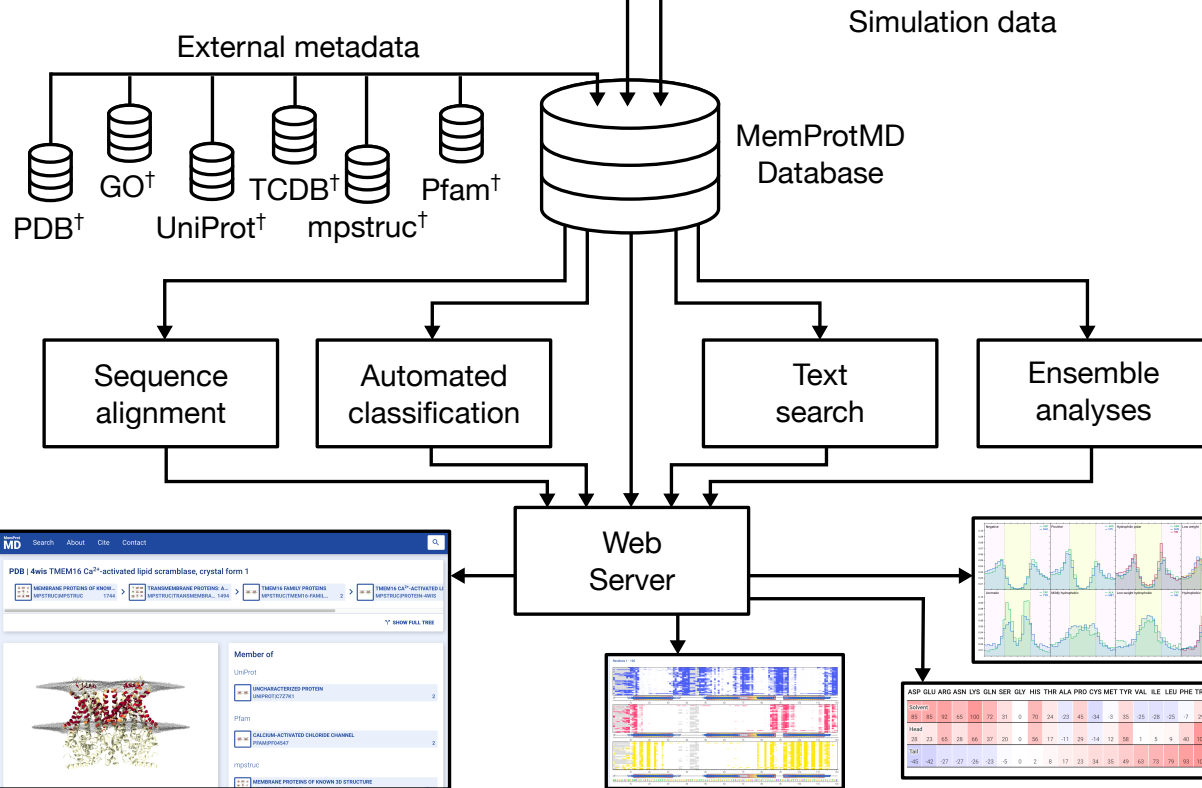
MemProtMD Pipeline



6EMX – Reba & Erik

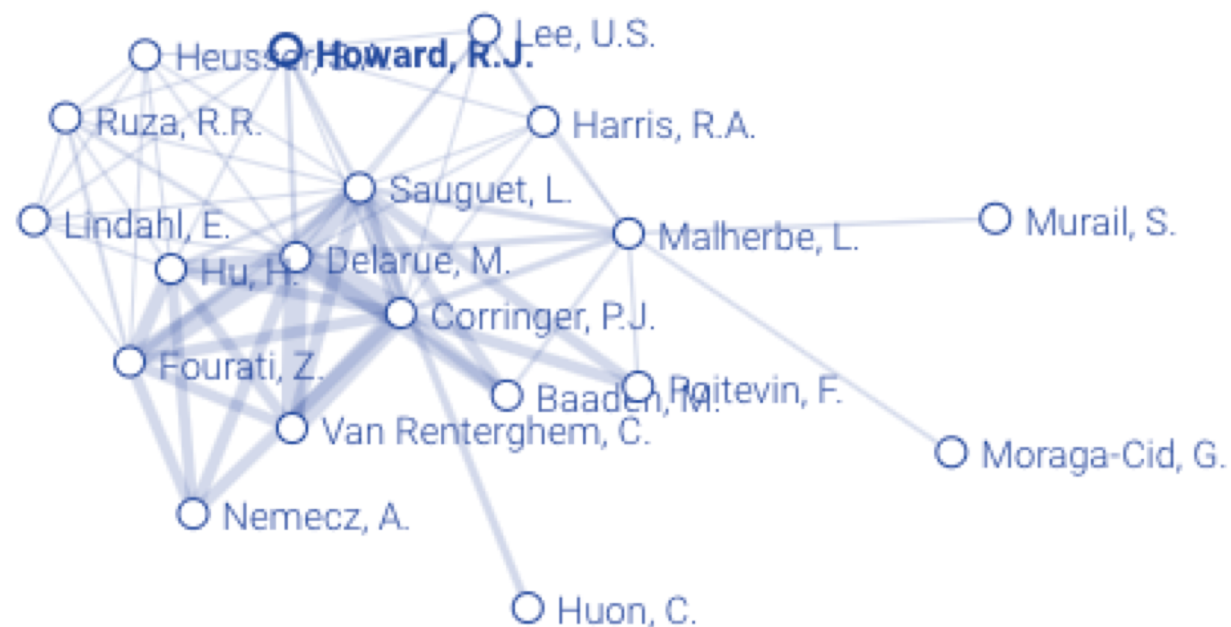
5FGN – Karmen

3FID – Alexandre



The MemProtMD Database

	N15'C mutant of GLIC X-RAY DIFFRACTION 3.2 Å	5 months ago PDB 6emx
	Prokaryotic pentameric ligand-gated ion channel (GLIC), H235... X-RAY DIFFRACTION 2.8 Å	9 months ago PDB 5mzq
	The GLIC pentameric Ligand-Gated Ion Channel F14'A ethanol-... X-RAY DIFFRACTION 2.75 Å	6 years ago PDB 4hfb
	The GLIC pentameric Ligand-Gated Ion Channel F14'A ethanol-... X-RAY DIFFRACTION 3.05 Å	6 years ago PDB 4hfc
	The GLIC pentameric Ligand-Gated Ion Channel F14'A ethanol-... X-RAY DIFFRACTION 3.1 Å	6 years ago PDB 4hfd
	The GLIC pentameric Ligand-Gated Ion Channel F14'A ethanol-... X-RAY DIFFRACTION 2.8 Å	6 years ago PDB 4hfe
	The GLIC pentameric Ligand-Gated Ion Channel (wild-type) co... X-RAY DIFFRACTION 2.65 Å	6 years ago PDB 4hfh
	Prokaryotic pentameric ligand-gated ion channel (ELIC) in com... X-RAY DIFFRACTION 3.649 Å	6 years ago PDB 3zkr

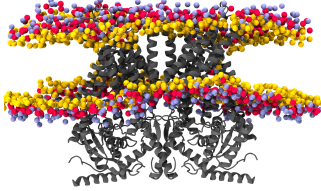


Molecular Imagery

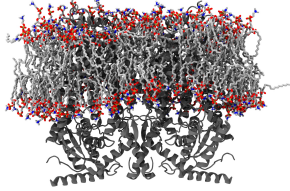
A Cartoon representation



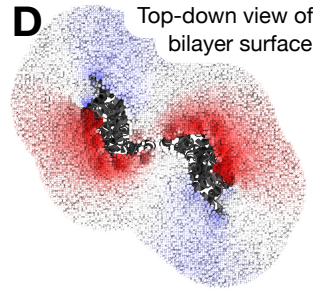
B Coarse-grained lipid head-groups



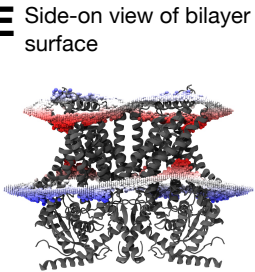
C Atomistic lipids



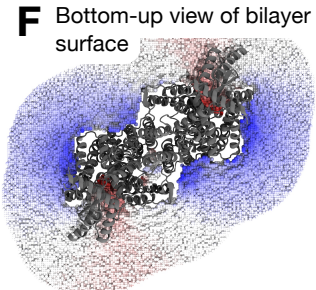
D Top-down view of bilayer surface



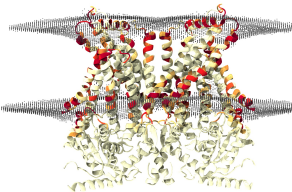
E Side-on view of bilayer surface



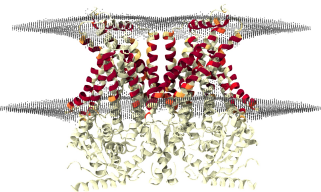
F Bottom-up view of bilayer surface



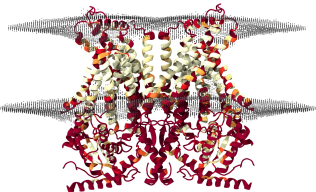
G Cartoon representation, shaded by head-group contacts



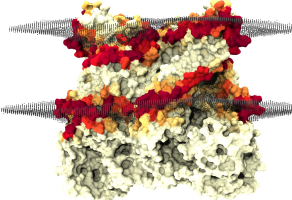
H Cartoon representation, shaded by acyl tail contacts



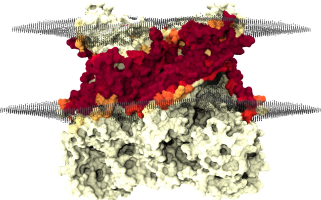
I Cartoon representation, shaded by solvent contacts



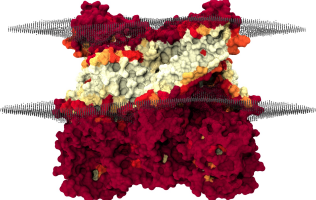
J Surface representation, shaded by head-group contacts



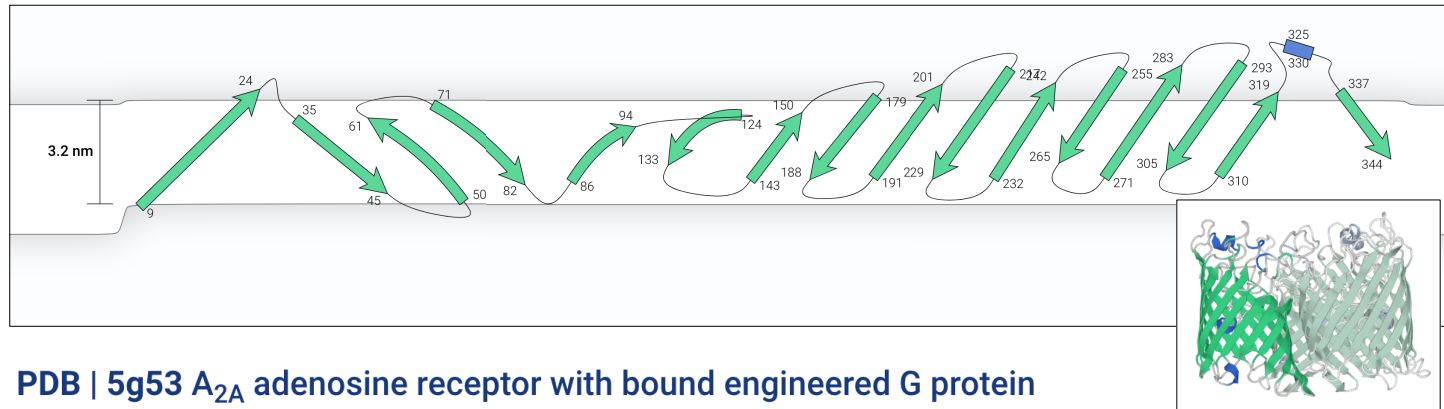
K Surface representation, shaded by acyl tail contacts



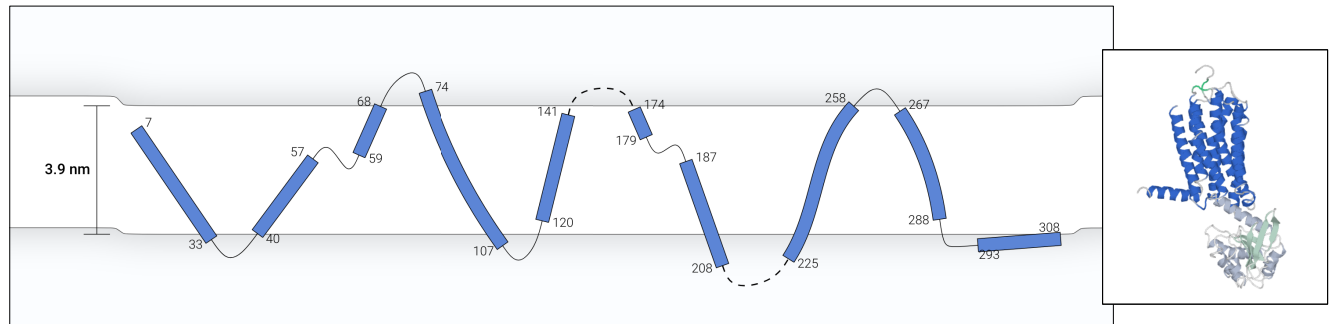
L Surface representation, shaded by solvent contacts



PDB | 2j1n OmpC Osmoporin

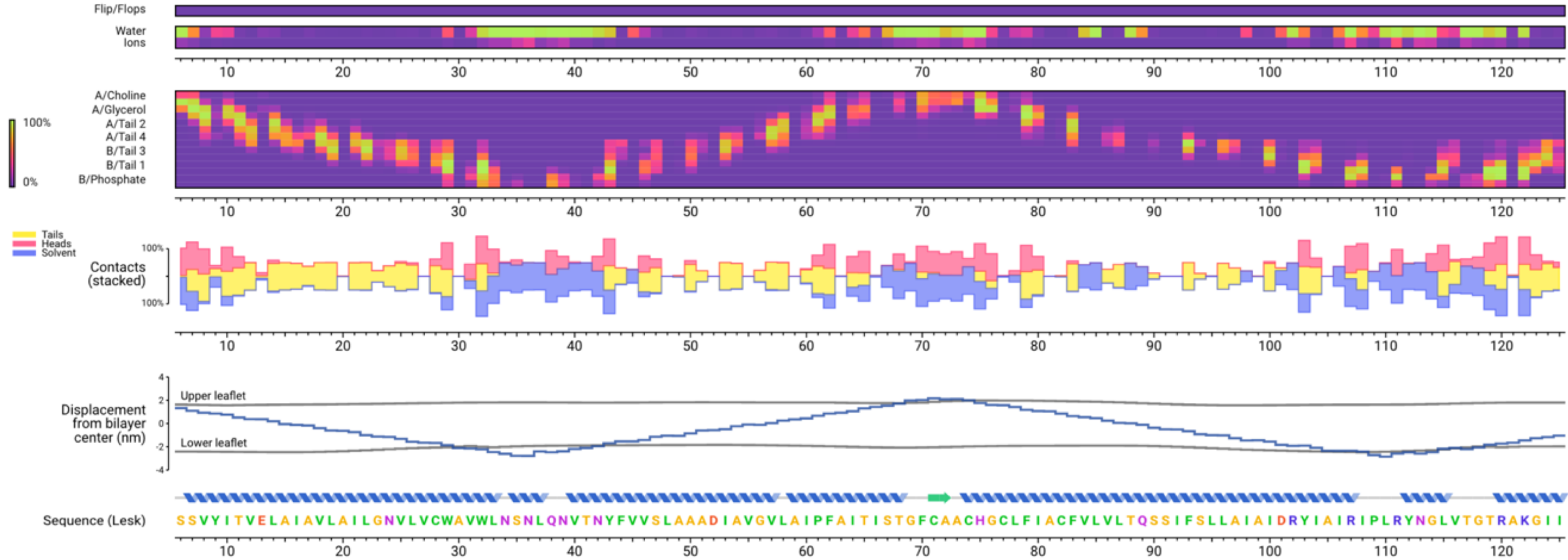


PDB | 5g53 A_{2A} adenosine receptor with bound engineered G protein



Lipid-Protein Interactions

E Chain A, Residues 6 - 125







A Comparison of Lipid Interactions: GPCRs

All 7TM Receptors (234)

MemProtMD Search About Cit

gpcrs

Quick search

-  G protein-coupled receptors (GPCRs) mpm gpcrs 175 simulations
-  G Protein-Coupled Receptors (GPCRs) mpstruc g-protein-coupled... 121 simulations
-  Beta2AR-T4L - CIM PDB 5d6l 1 simulation
-  Structure of the M3 muscarinic acetylcholine re

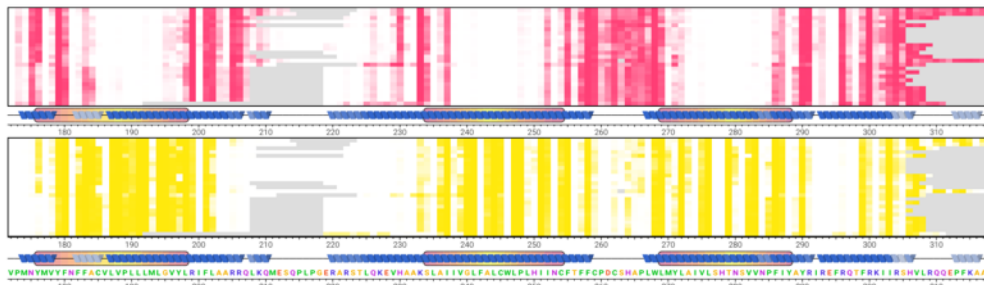
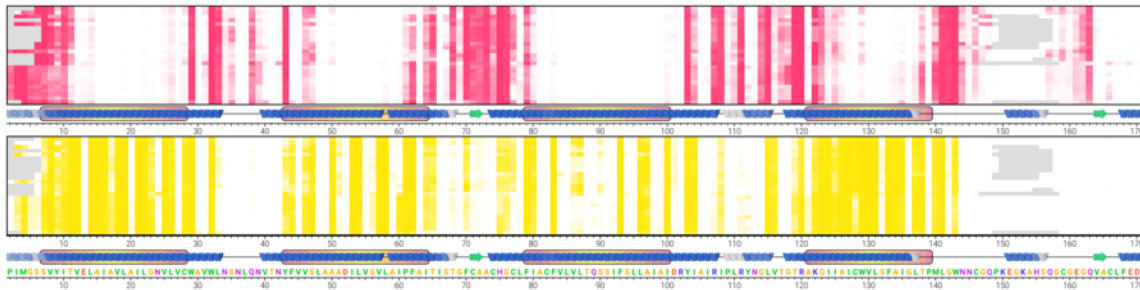
VIEW MORE RESULTS

MemProtMD

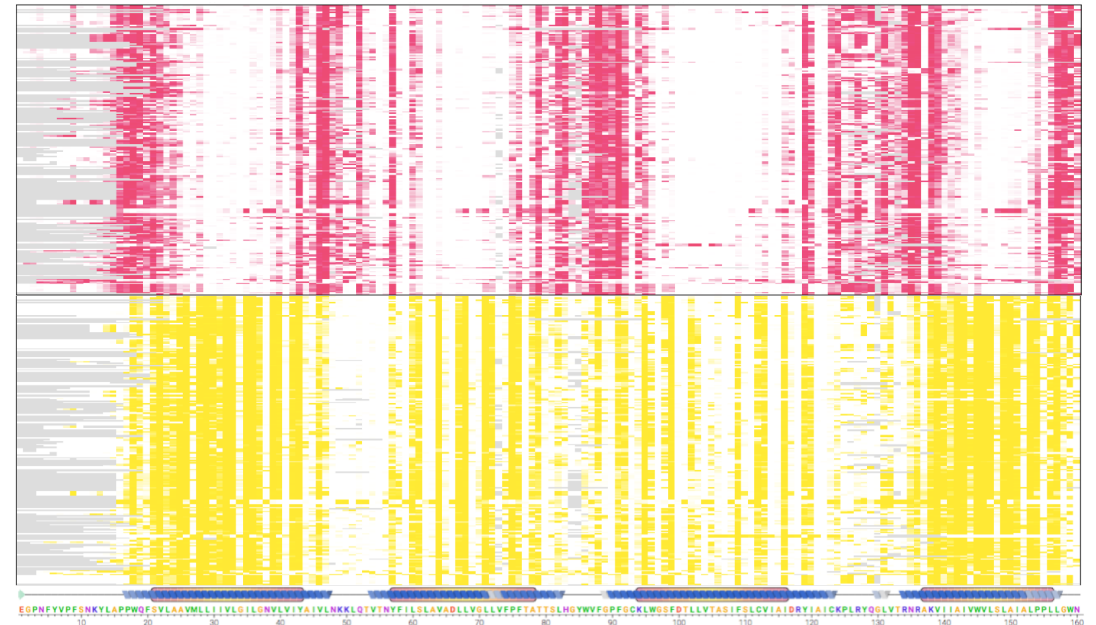
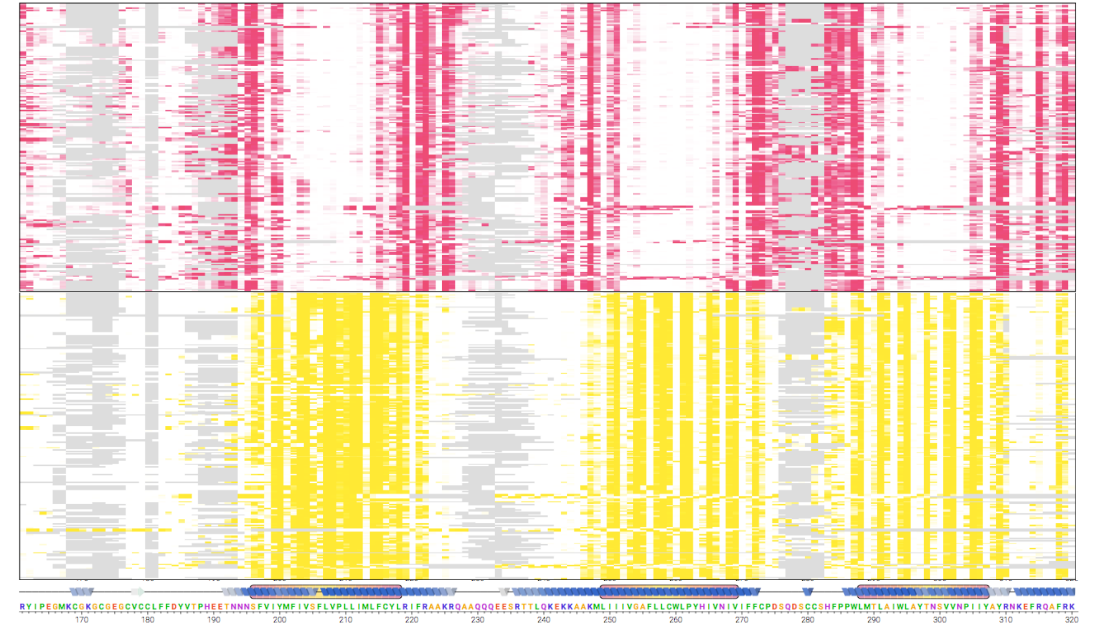
A database of membrane proteins

MemProtMD is a database of around 100,000 membrane proteins in the Protein Data Bank, inserted into a membrane and simulated in an Assembly Molecular Dynamics simulation, as well as resources for 100,000 simulations.

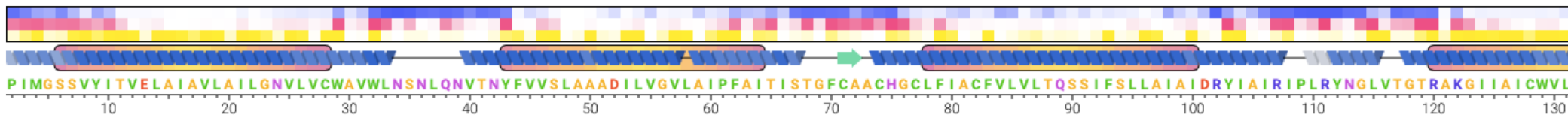
Latest Simulations



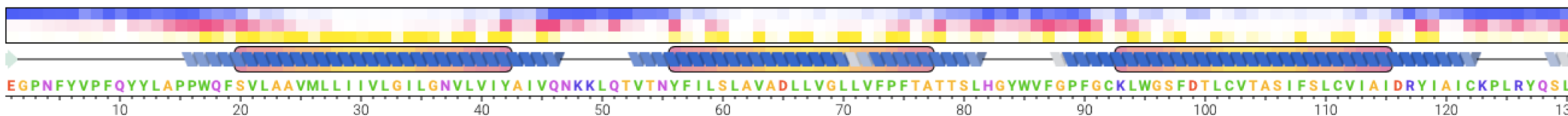
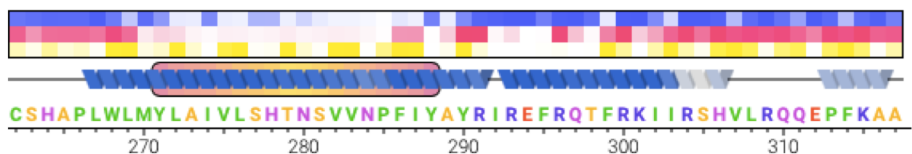
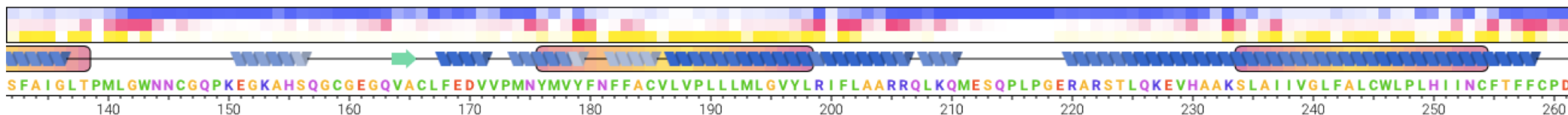
A2a (44)



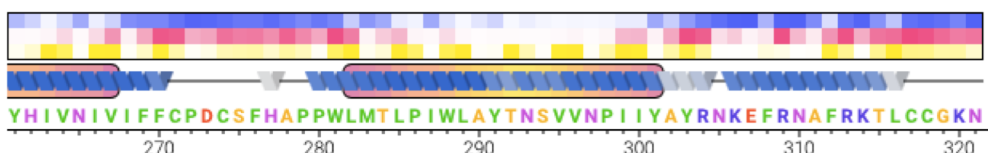
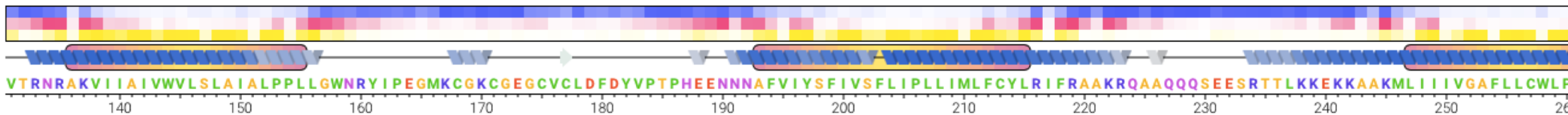
A Consensus of Lipid Interactions: GPCRs



A2a
(44)



All
7TM
Receptors
(234)



Amino Acid Interactions within the Membrane

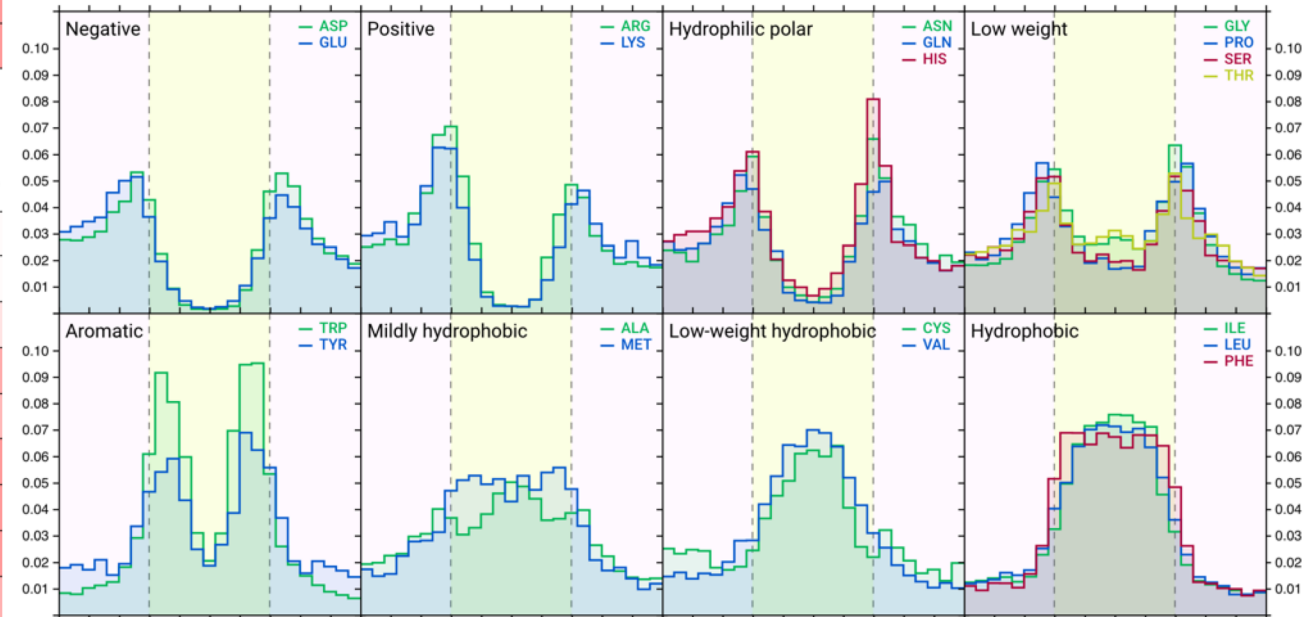
A

	ASP	GLU	ARG	ASN	LYS	GLN	SER	GLY	HIS	THR	ALA	PRO	CYS	MET	TYR	VAL	ILE	LEU	PHE	TRP
Solvent	85	84	91	65	100	71	31	0	69	24	-23	45	-35	-3	35	-25	-28	-25	-7	28
Head	28	24	66	28	67	38	20	0	57	17	-11	29	-16	12	59	1	6	9	39	100
Tail	-45	-42	-28	-27	-26	-23	-5	0	3	7	17	23	34	35	50	64	73	79	94	100

B

	ASP	GLU	ARG	LYS	ASN	GLN	SER	GLY	HIS	THR	ALA	PRO	CYS	MET	TYR	VAL	ILE	LEU	PHE	TRP
Chloride	0	3	95	100	20	29	14	0	33	9	-6	8	-6	2	9	-6	-7	-7	-2	5
Sodium	98	100	4	6	22	29	14	0	39	11	-8	9	-10	-4	8	-8	-9	-8	-3	5
Water	85	84	91	100	65	71	30	0	68	24	-22	45	-34	-3	34	-24	-27	-24	-6	28
Choline	97	87	65	61	53	75	29	0	100	19	-15	29	-22	4	52	-17	-16	-13	14	82
Phosphate	11	8	100	100	35	43	23	0	63	17	-13	15	-14	8	40	-12	-11	-10	11	69
Glycerol	-5	-6	47	45	11	15	13	0	40	15	-4	23	-2	19	58	13	17	20	48	100
Tail 1	-16	-15	-1	0	-4	0	5	0	21	10	5	28	14	27	56	35	42	45	70	100
Tail 2	-20	-19	-15	-14	-13	-11	-1	0	5	5	8	23	24	25	48	51	58	63	95	100
Tail 3	-23	-22	-21	-21	-17	-16	-3	0	-5	4	10	14	31	21	32	57	63	68	100	77
Tail 4	-30	-28	-27	-27	-22	-21	-5	0	-9	4	14	10	36	22	27	60	69	73	100	67

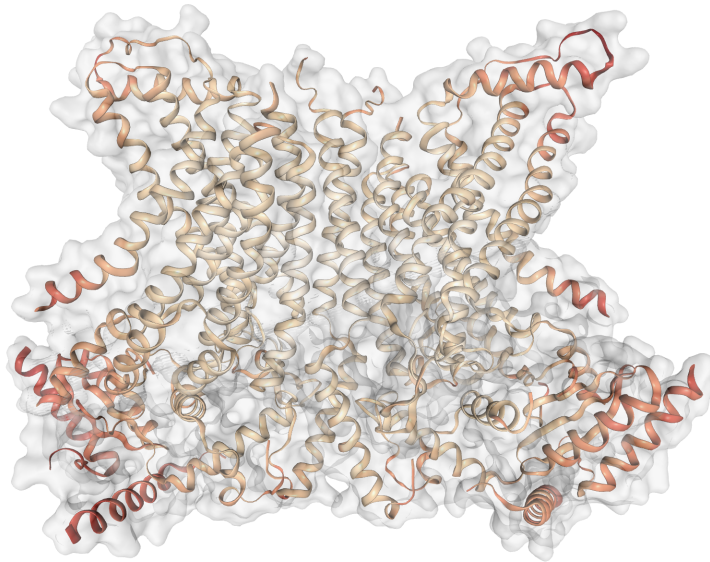
Scales of Interaction



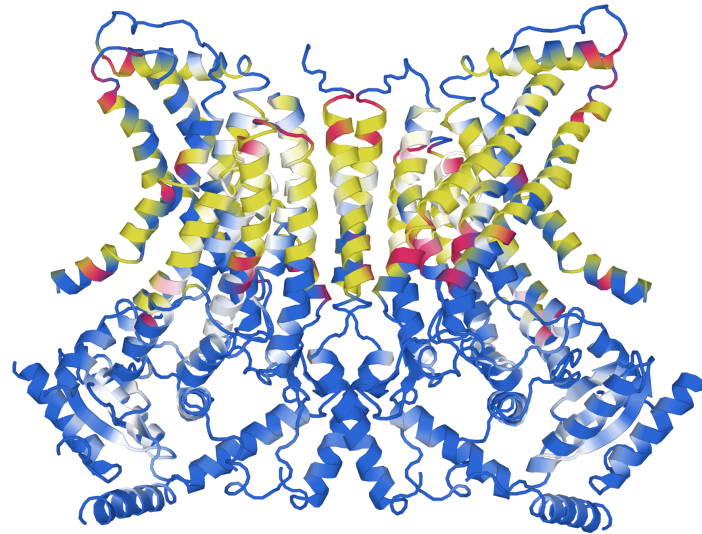
Residue Membrane Distribution

Which Molecular Viewer to use?

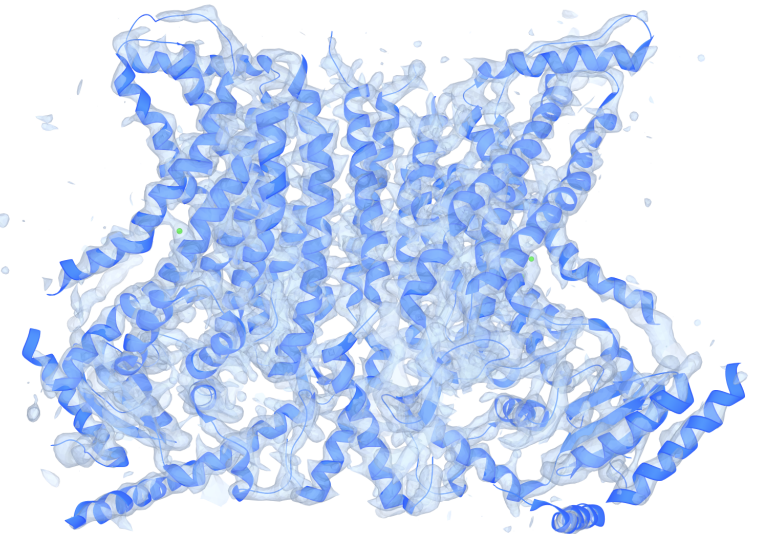
WebGL visualisations of PDB | 4wis Ca²⁺ activated lipid scramblase



NGL Viewer (RCSB PDB)
Coloured by temperature factor

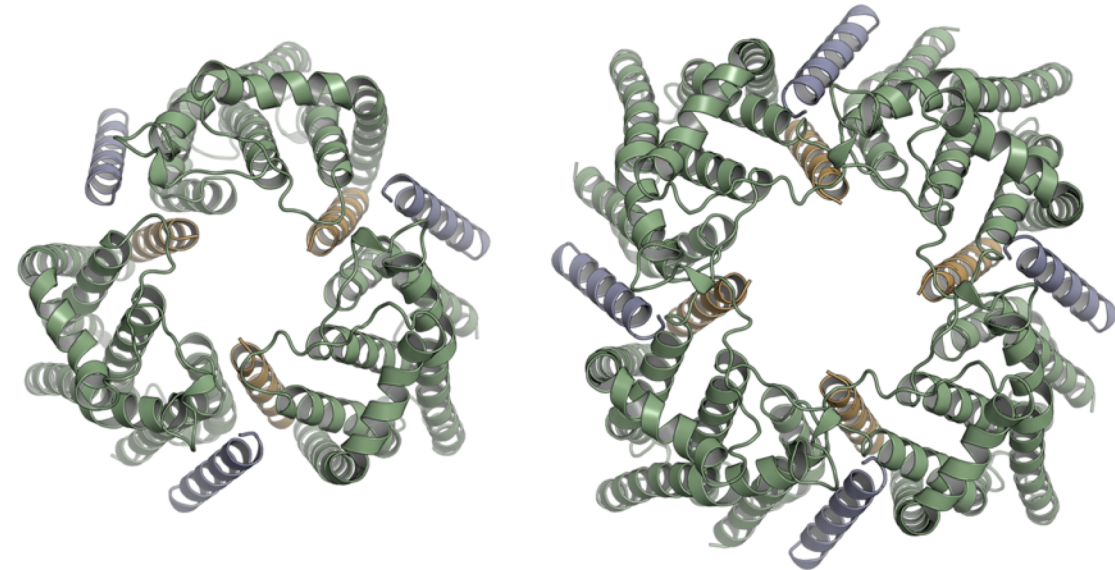
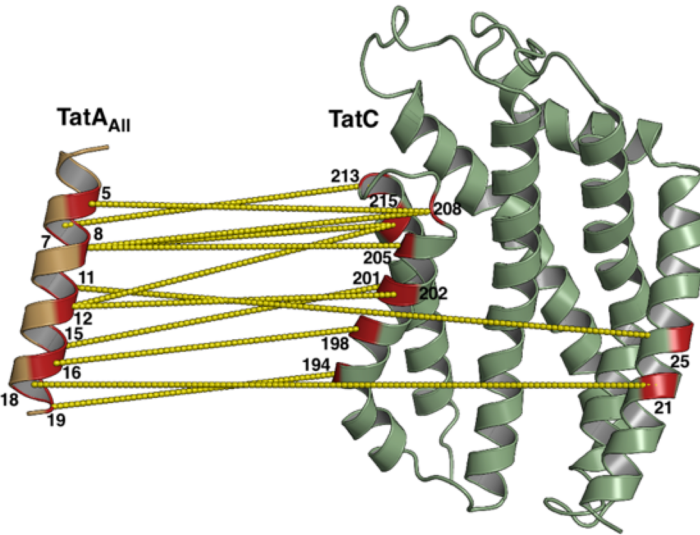
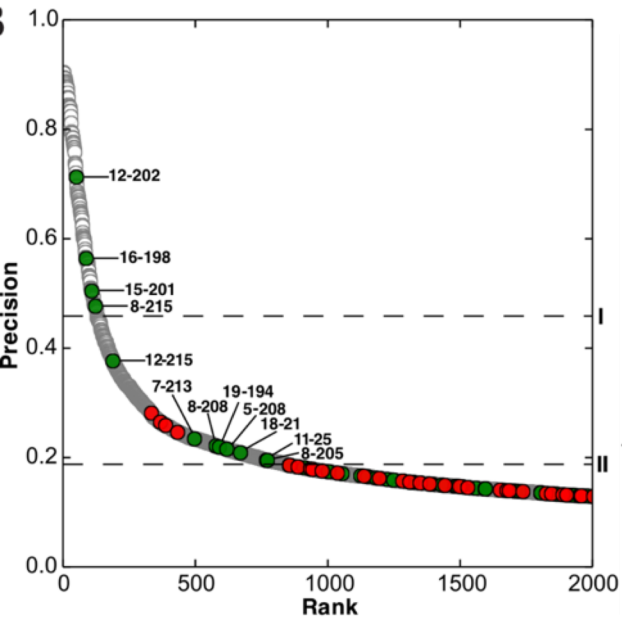
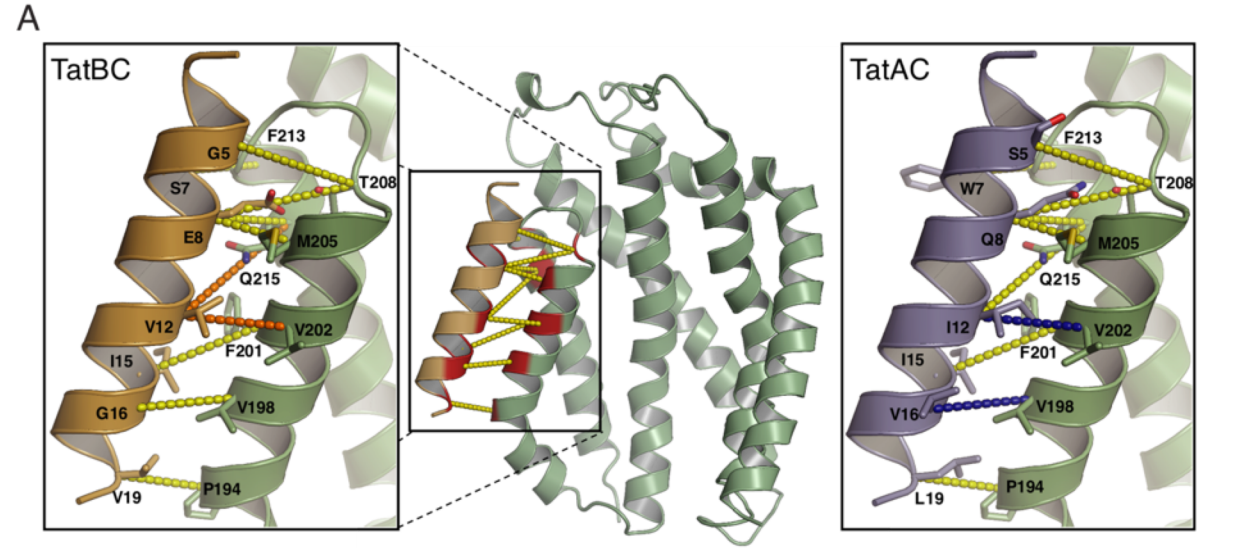
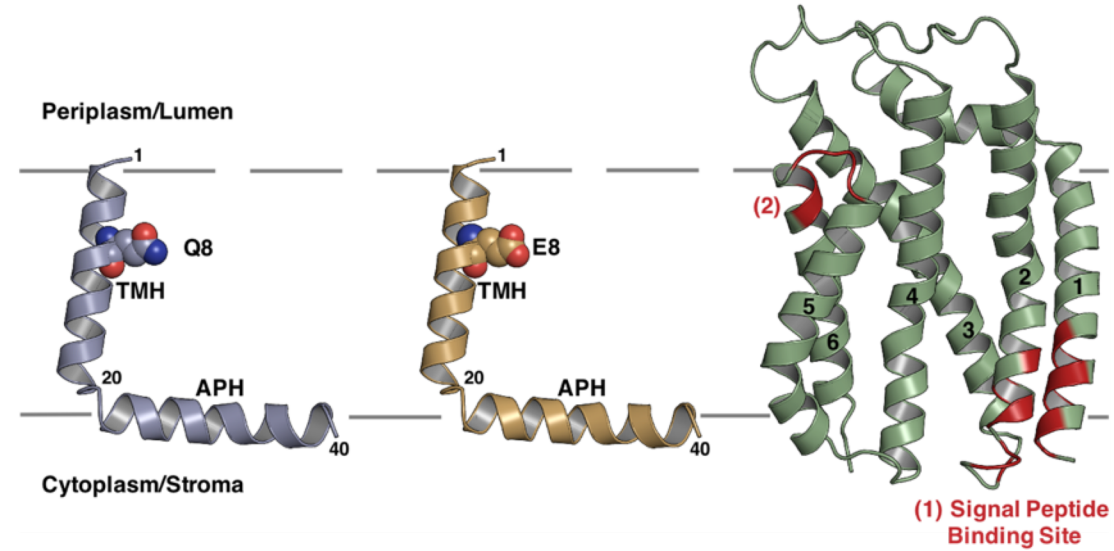


PV (MemProtMD web server)
Coloured by simulation lipid contacts



LiteMol (PDBe)
With 1.5 σ 2Fo - Fc isosurface

Assembling the Tat Subunits



People, Collaborations & Funding



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<http://sbc.bioch.ox.ac.uk/stansfeld>

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Nick Greene (Cambridge)

Elise Kaplan (Cambridge)

John Mitcheson (Leicester)

Tracy Palmer (Dundee)

Zara Sands (UCB)

Jiye Shi (UCB)

Jochen Zimmer (Virginia)

Fran Ashcroft (DPAG)

Tanmay Bharat (Pathology)

Liz Carpenter (SGC)

Rob Gilbert (Strubi)

Carol Robinson (Chemistry)

Paolo Tammara (Pharmacology)

Peijun Zhang (Strubi)

Ben Berks (Biochemistry)

Simon Newstead (Biochemistry)

Mark Sansom (Biochemistry)

John Vakonakis (Biochemistry)

Owen Vickery

Robin Corey

Keith Cassidy

Nick Michelarakis

Sophie Williams

Tom Dixon

Josh Sauer

Will Pipatpolkai

Michael Horrell

Patrick Simcock

Alissa Hummer

Callum Matthews

Ria Dinsdale

Jodie Ford

Andreas Kjaer

Dan Quetschlich

Alumni:

Ben Mynors-Wallis

Tom Dyer

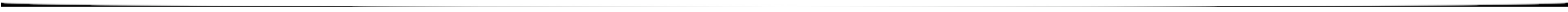
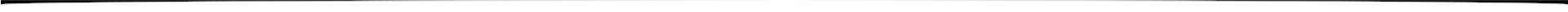
George Bates

Jan Domański

Tom Newport

Shanlin Rao

Mabel Wong



by Tom Newport

