

Preparation of the anchored Bcl-xL Protein

Luis Garreta

June 3, 2022

Anchored Bcl-xL Protein

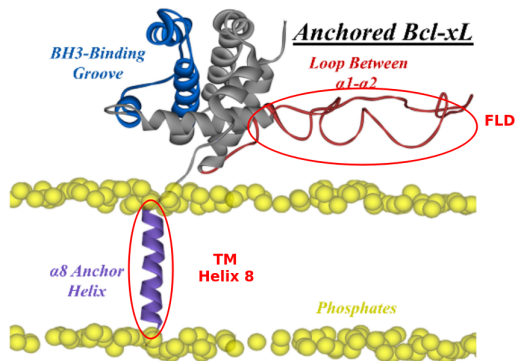
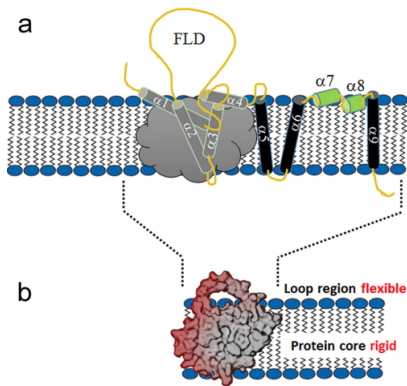


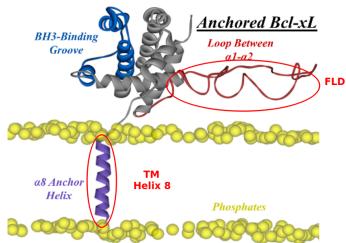
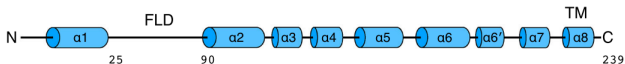
Figure: [Tyagi et al., 2021]

Bcl-2 is a Membrane-embedded

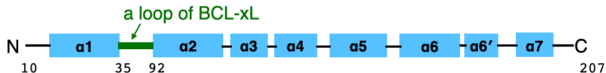


[Mushtaq et al., 2021]

Structure of full-length BCL-2

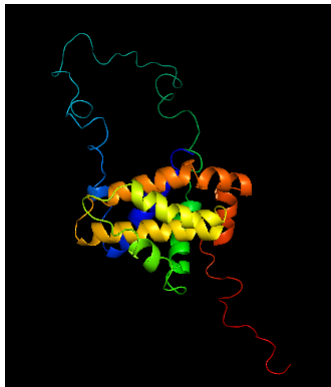


BCL-2- Δ TM/FLD (PDB: **2XA0**)

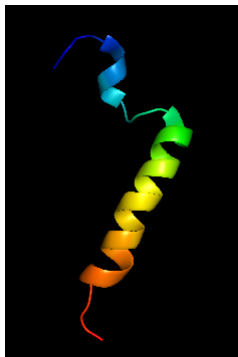


Head and Tail

PDB: 1lxl



PDB: 6f46

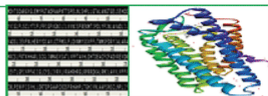


Homology Modelling

Basic Steps in Homology Modelling

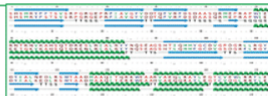
1

Sequence of Target &
Best Template Selection



2

Alignment of Target sequence &
Selected Template sequence



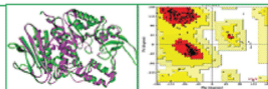
3

Homology Models Generation using
Modeller or other tool

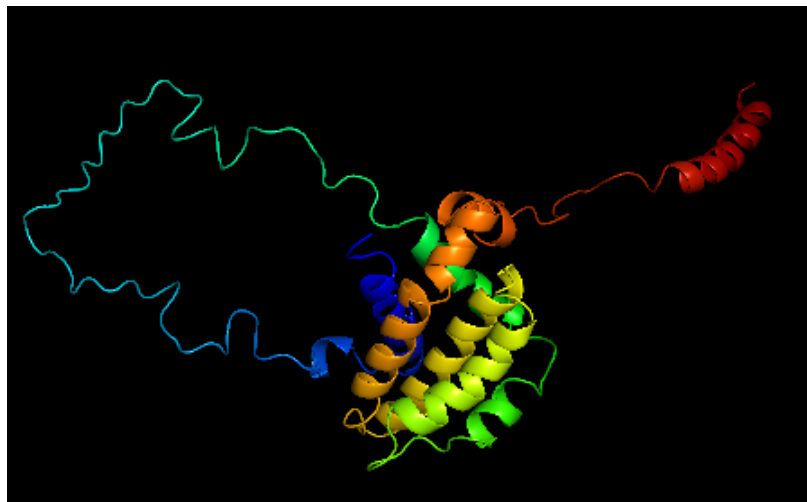


4

Selection, Assessment and
Refinement of Best Homology Model

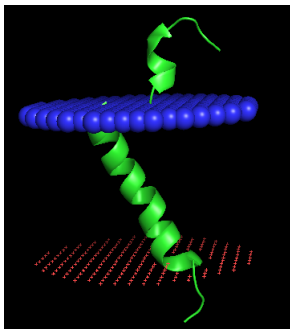


Bcl-xL Reconstructed

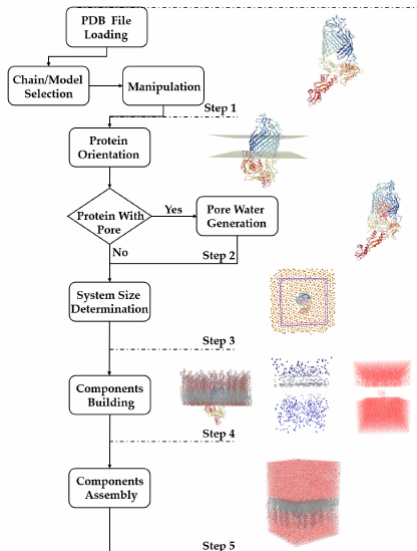


Orientation of Protein in Membrane

OPM Database: Orientations of Proteins in Membranes database



Preparing a membrane-protein system using CHARMM-GUI



System Parameters

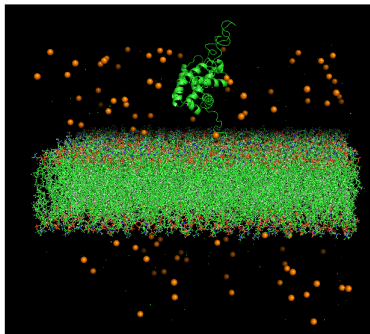
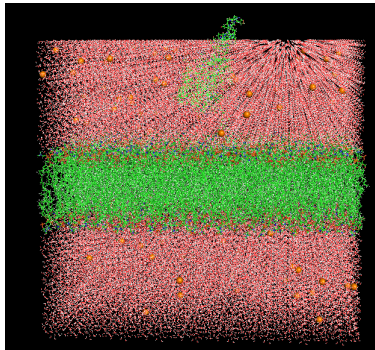
[Tyagi et al., 2021]^a

Table 1. Summary of microsecond-timescale simulations run on Anton2.

Simulated System	Protonation State	Membrane Composition
Bcl-xL with 50 mM NaCl	Protonated Bcl-xL	POPC
Bcl-xL with 50 mM NaCl	Unprotonated Bcl-xL	POPC
Bcl-xL with neutralizing NaCl	Protonated Bcl-xL	2:1 POPC:TOCL
Bcl-xL with neutralizing NaCl	Unprotonated Bcl-xL	2:1 POPC:TOCL

^aVivek Tyagi, Victor Vasquez-Montes, J A Freites, Alexander Kyrychenko, Douglas J Tobias, and Alexey S Ladokhin, "Effects of Cardiolipin on the Conformational Dynamics of Membrane-Anchored Bcl-xL" (2021).

Bcl-xl membrane-protein



System Size

Determined System Size:

# of Atoms	415756		
Crystal Type	TETRAGONAL		
System Size	A	168.264303	Dimension along the A (X) axis
	B	168.264303	Dimension along the B (Y) axis
	C	155.952	Dimension along the C (Z) axis
Crystal Angle	Alpha	90.0	Angle between the axis B and C
	Beta	90.0	Angle between the axis A and C
	Gamma	90.0	Angle between the axis A and B
# of Lipids	on Top	412	
	on Bottom	411	
# of Water	100580		
Z Center	0.0		Center of the system along the Z axis



Mushtaq, A. U., Ådén, J., Clifton, L. A., Wacklin-Knecht, H., Campana, M., Dingeldein, A. P. G., Persson, C., Sparrman, T., and Gröbner, G. (2021).

Neutron reflectometry and NMR spectroscopy of full-length Bcl-2 protein reveal its membrane localization and conformation.

Communications Biology, 4(1):507.



Tyagi, V., Vasquez-Montes, V., Freites, J. A., Kyrychenko, A., Tobias, D. J., and Ladokhin, A. S. (2021).

Effects of Cardiolipin on the Conformational Dynamics of Membrane-Anchored Bcl-xL.