KØBENHAVNS UNIVERSITET

TS2CG

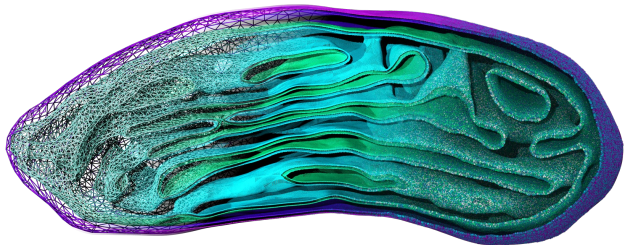
Backmapping tool or input builder?

Weria Pezeshkian

August 2025

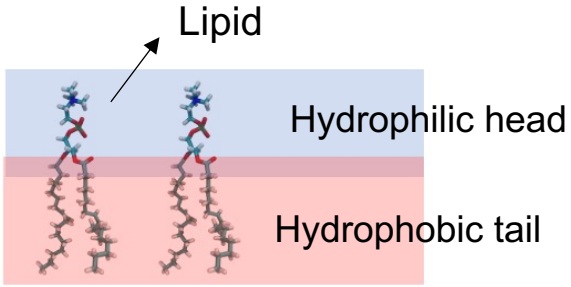
Groningen, Netherlands

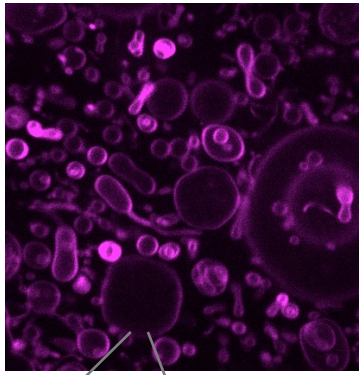
Martini workshop 2025

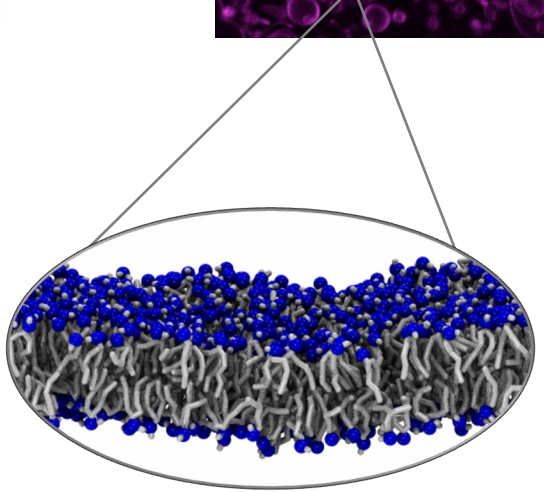


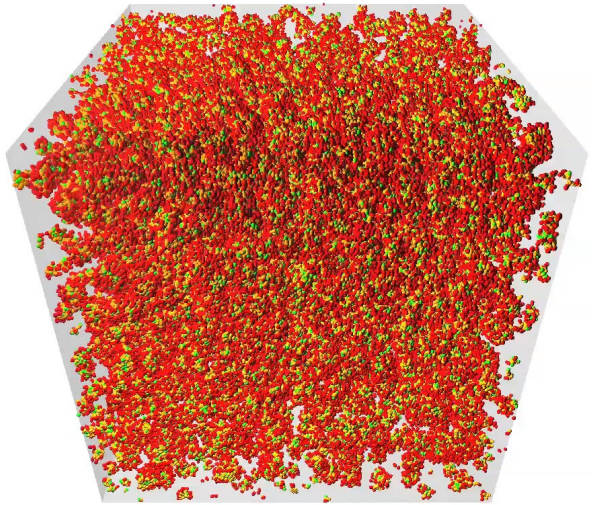
https://commicgroup.ku.dk

Lipid bilayers

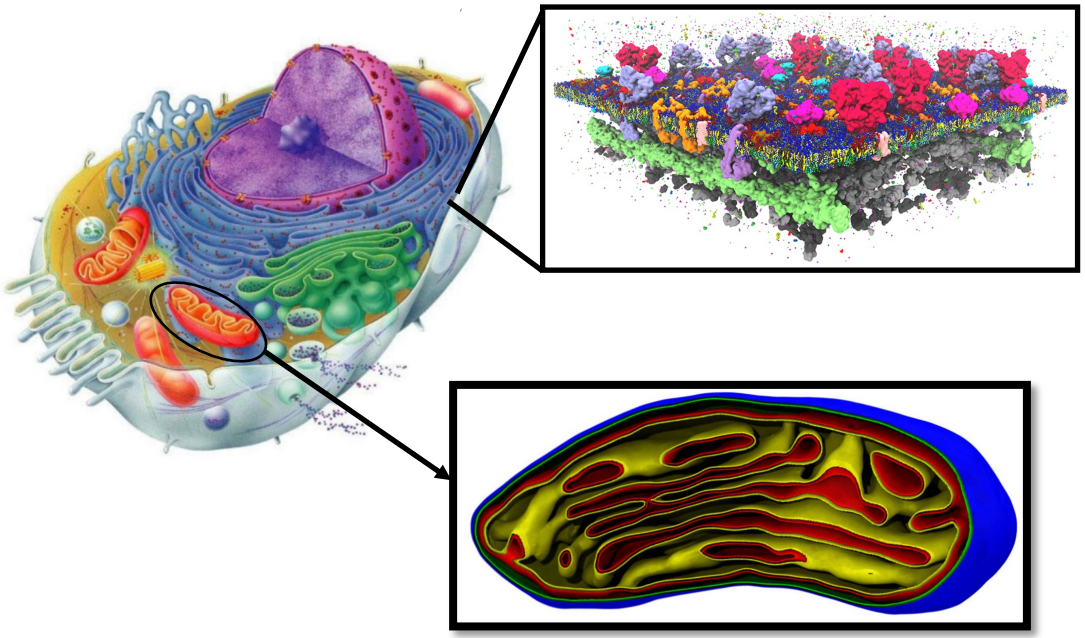




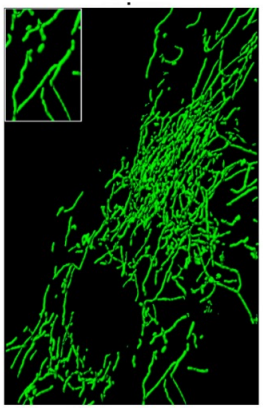




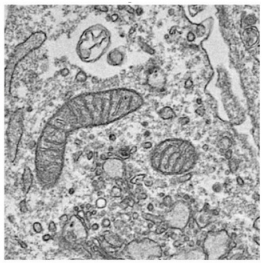
Biomembranes



cellular scale



ultrastructure

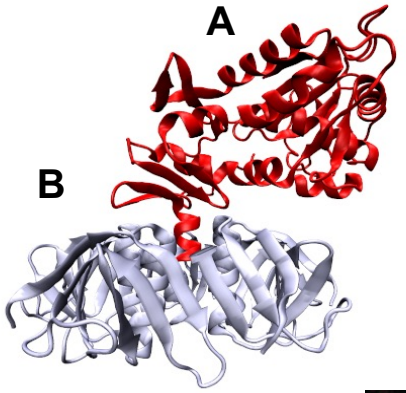


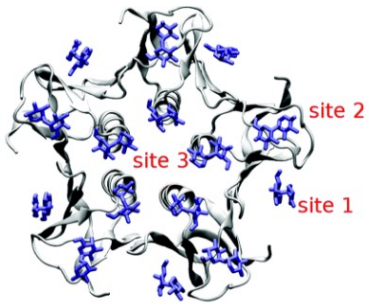
multiscale shape organization of mitochondria

Pezeshkian, et al, Nat. Commun (2020); Marrink, et al, Chemical Reviews(2018), Antonella Izzo et al, Hum Mol Genet (2017)

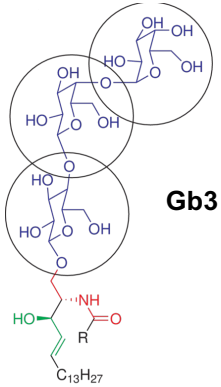
Initial stage of Shiga toxin internalization

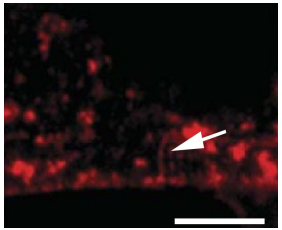
Shiga toxin creates its own route to enter the cell



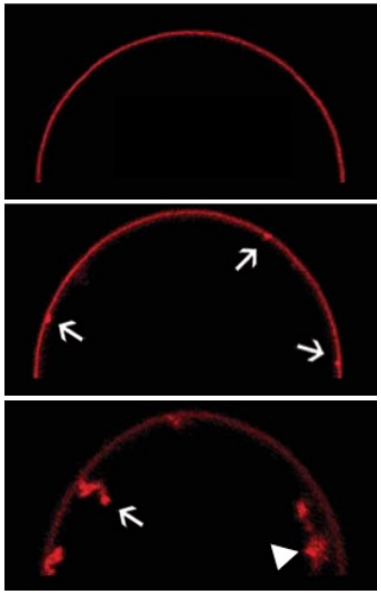


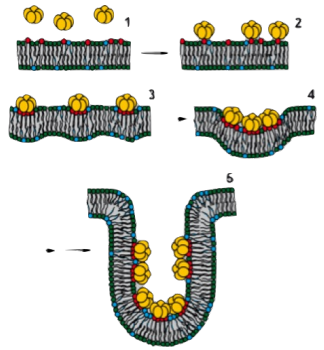
B subunit





without the complexity of the cell





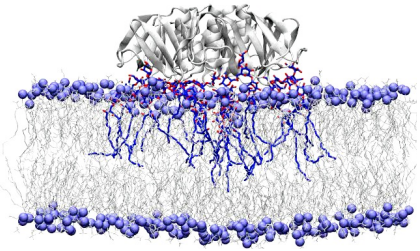
Speculative mechanism

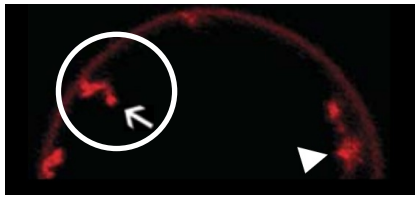
W. Romer et al, *Nature* (2007); H. Ling et al, Biochemistry, (1998).

all-atom

Coarse-grained

mesoscale

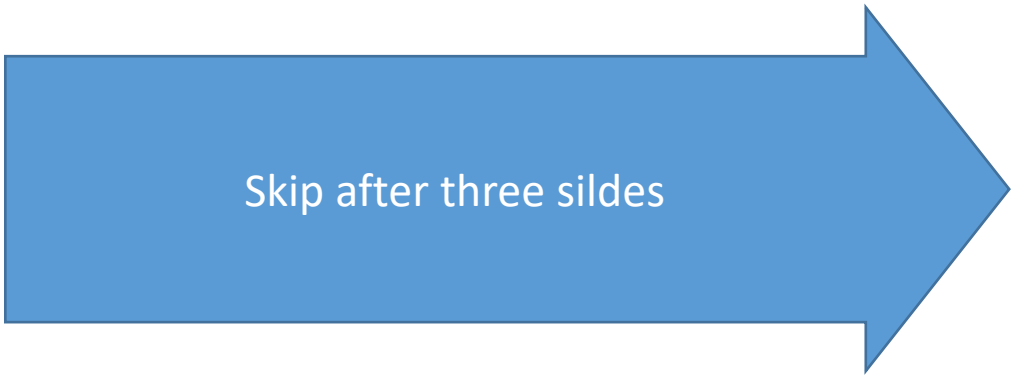




Scale

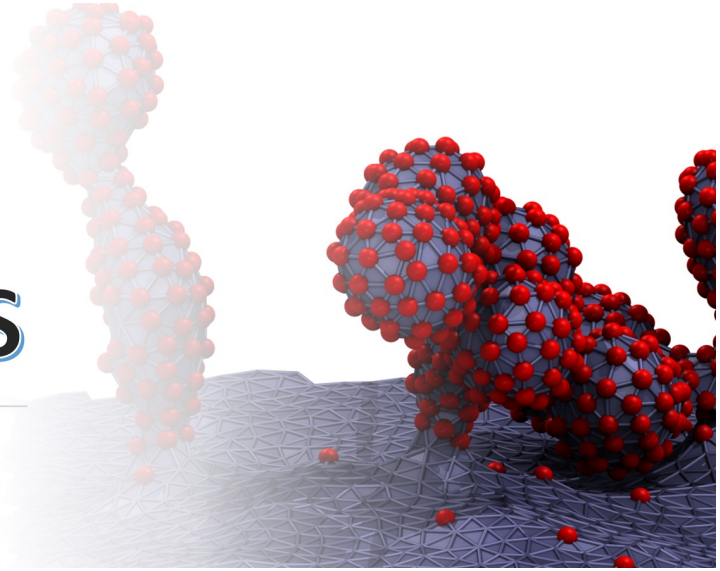
Pezeshkian, et al*, ACS Nano*, (2017); Pezeshkian et al, Soft Matter (2016); Pezeshkian, et al, Nat. Commun 11, 2296 (2024).

Commercial break



Mesoscale modeling of biomembranes

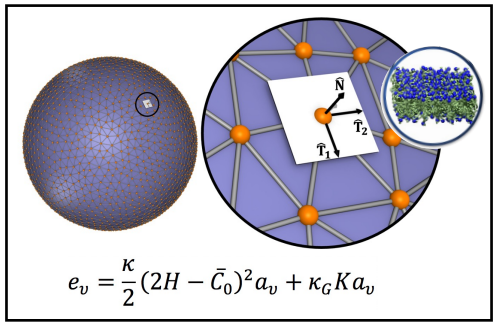
FreeDTS



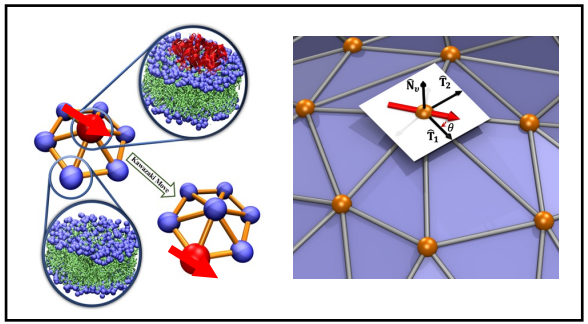
https://github.com/weria-pezeshkian/FreeDTS/
Pezeshkian et. al. Nat. Commun. (2024)

FreeDTS Force field

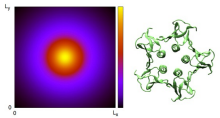
Membrane



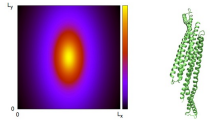
Proteins



Proteins-Membrane interaction



$[\bar{c}_0, \Delta\kappa, \Delta\kappa_G]$

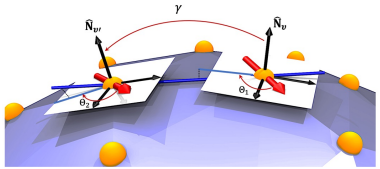


$[k_{\parallel}, C_0^{\parallel}, k_{\perp}, C_0^{\perp}]$

Membrane FF

$[\kappa, \kappa_G, \bar{C}_0]$

Proteins-protein interaction

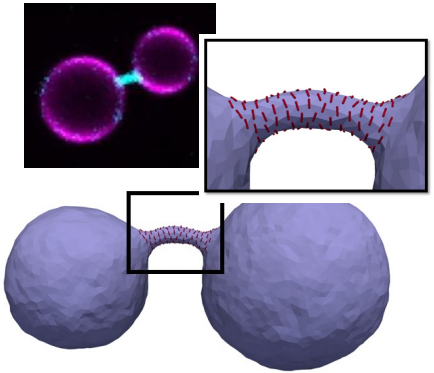


$$e_{inc,inc} = -A_{i,j} - B_{i,j}\cos[N(\Theta - \Theta_0)] - C_{i,j}\cos[\gamma - \gamma_0]$$

https://github.com/weria-pezeshkian/FreeDTS/

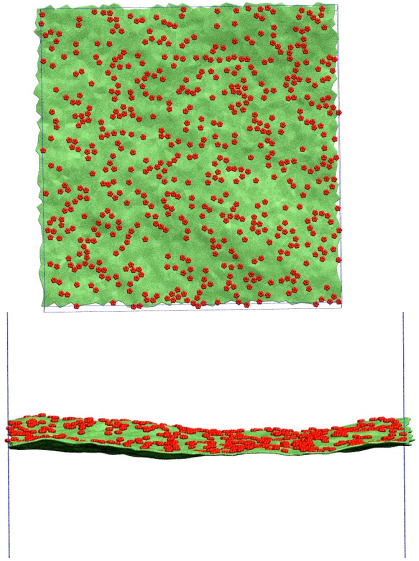
Pezeshkian et. al. Nature Communications (2024)

FreeDTS applications

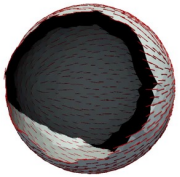


Protein induced neck constriction

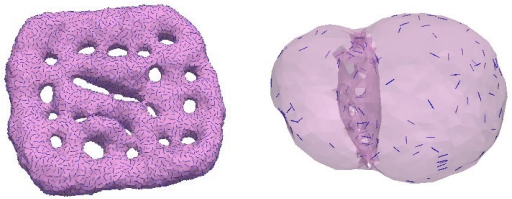
Tube pulling



endocytosis



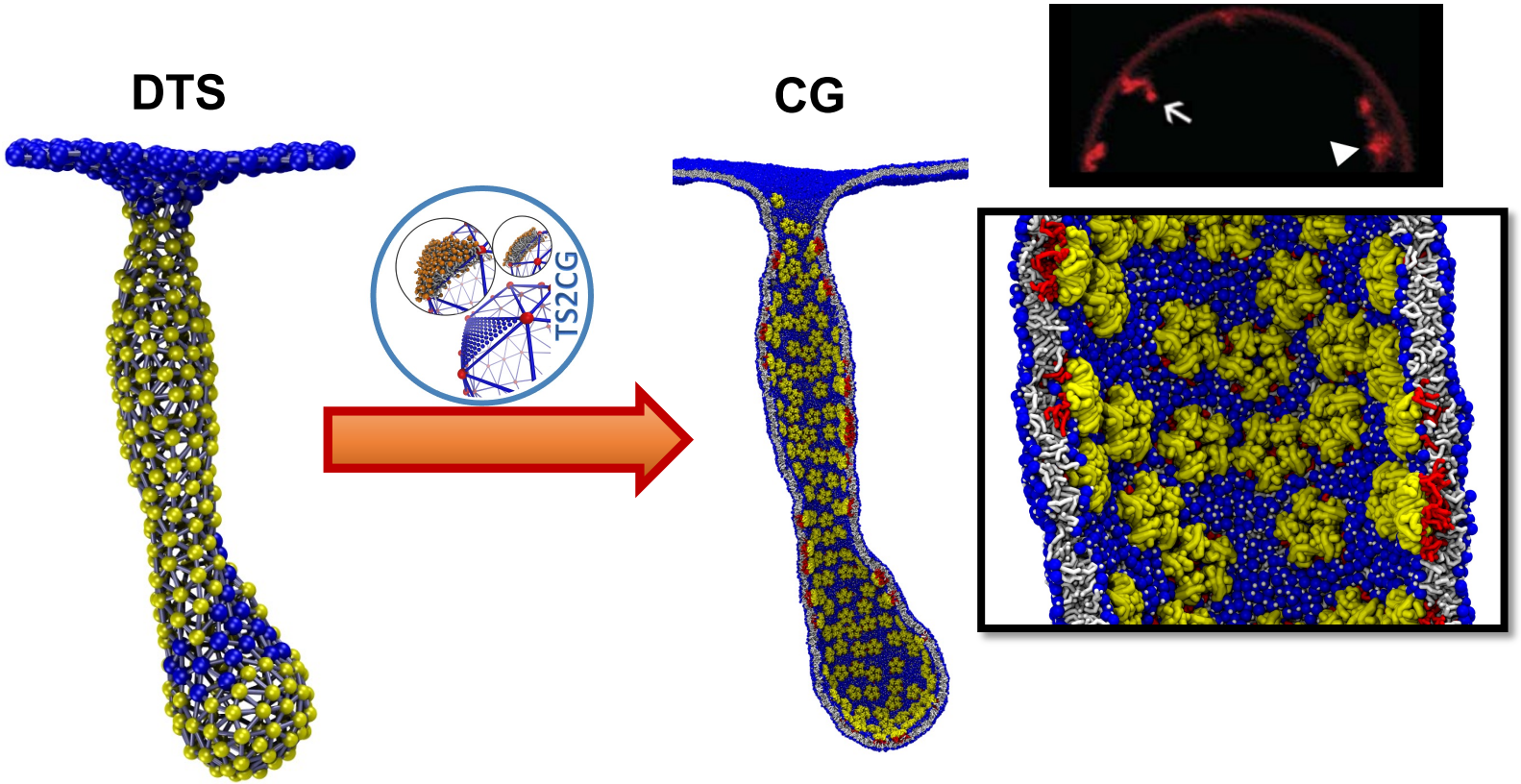
membrane repair



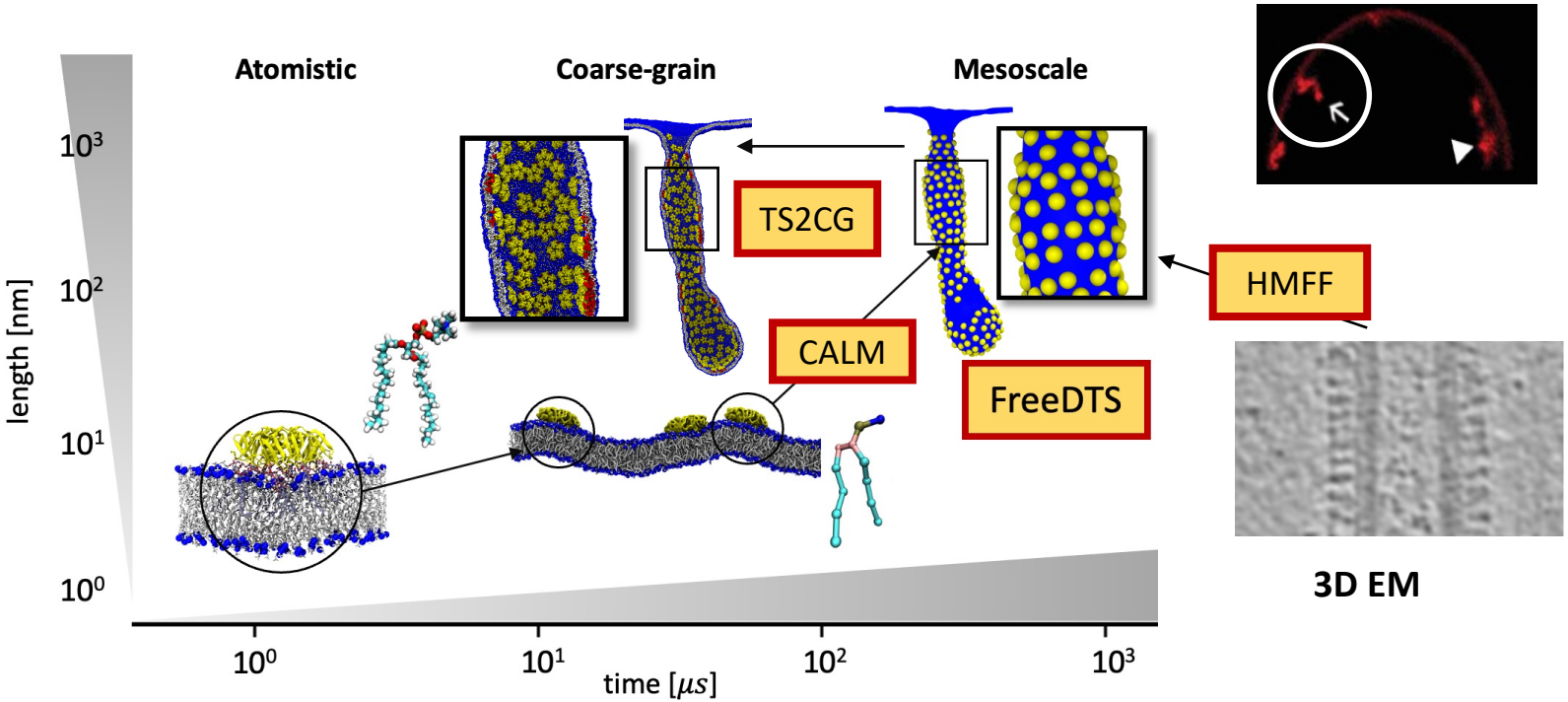
organelle shapes

Pezeshkian et. al. Nature Communications (2024)
Cornet et al, Soft matter, 20, 4998 (2024)
Pezeshkian et al, Structure 31, 492 (2023)
De Franceschi et al, ACS Nano 17, 966 (2023)

Molecular architecture of the tube

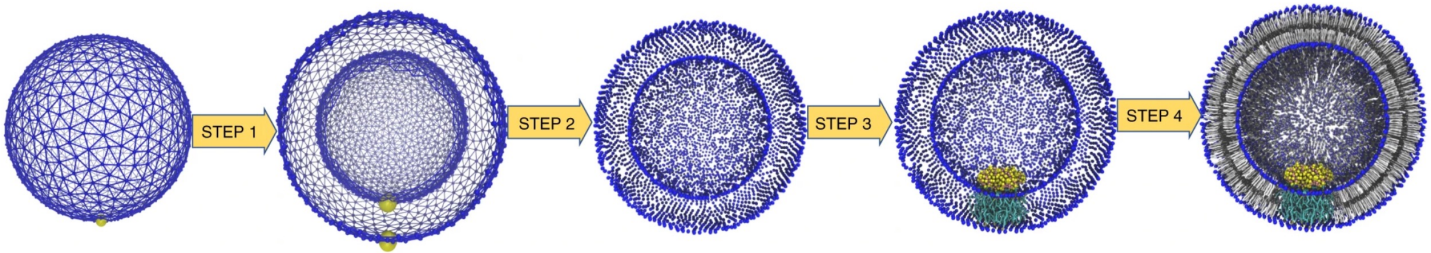


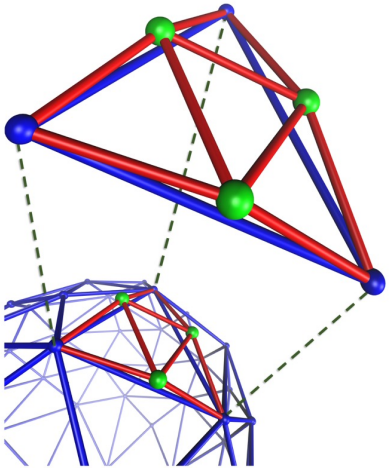
Multiscale simulation at a glance

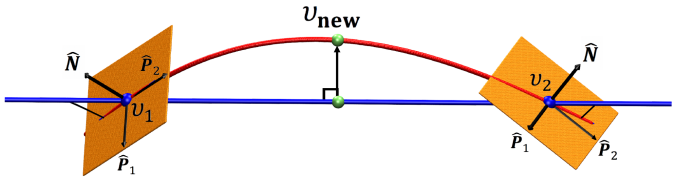


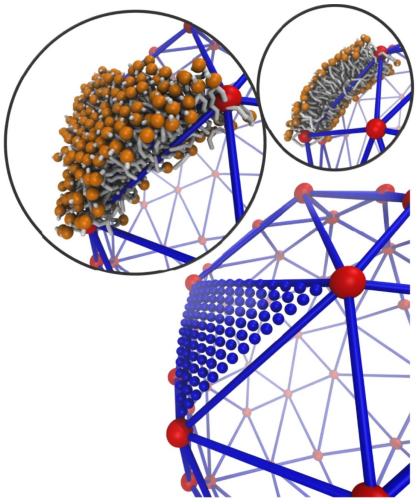
Pezeshkian et al, Nat. Commun; (2024), Pezeshkian et al, Nat. Commun; (2020), Pezeshkian et al, Curr. Opin. Cell Biol. (2021), Maurer et al (2025), Schuhmann, Angew. Chem. (2025).

Basic idea of TS2CG









https://github.com/weria-pezeshkian/TS2CG-v2.0

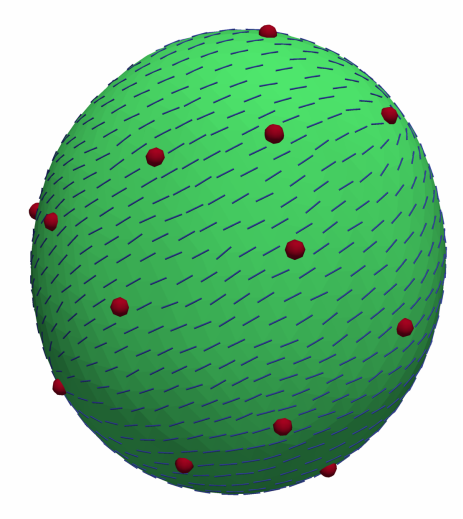
W. Pezeshkian, et al, Nature Communications **11**, 2296 (2020)

SARS-CoV-2 envelope

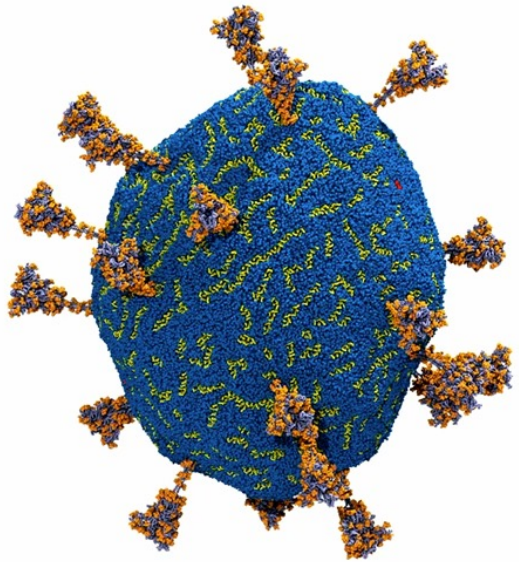
Spike protein (25)

M dimer (1000)

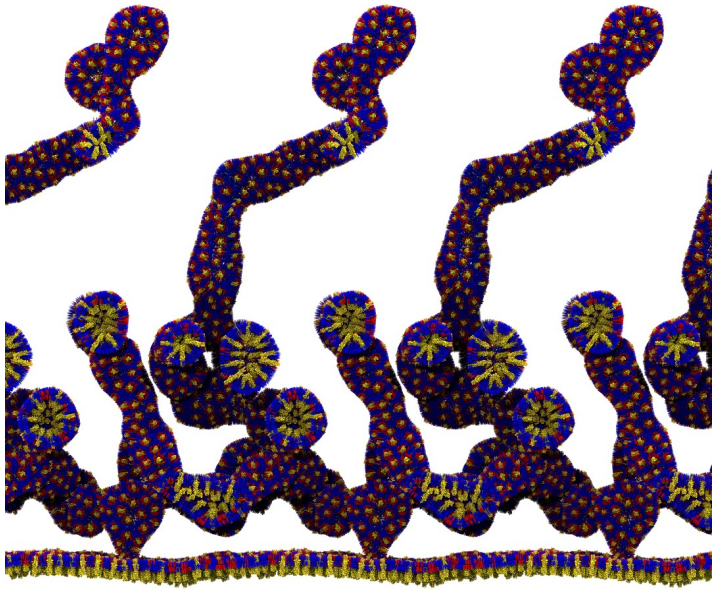
E pentamer (3)

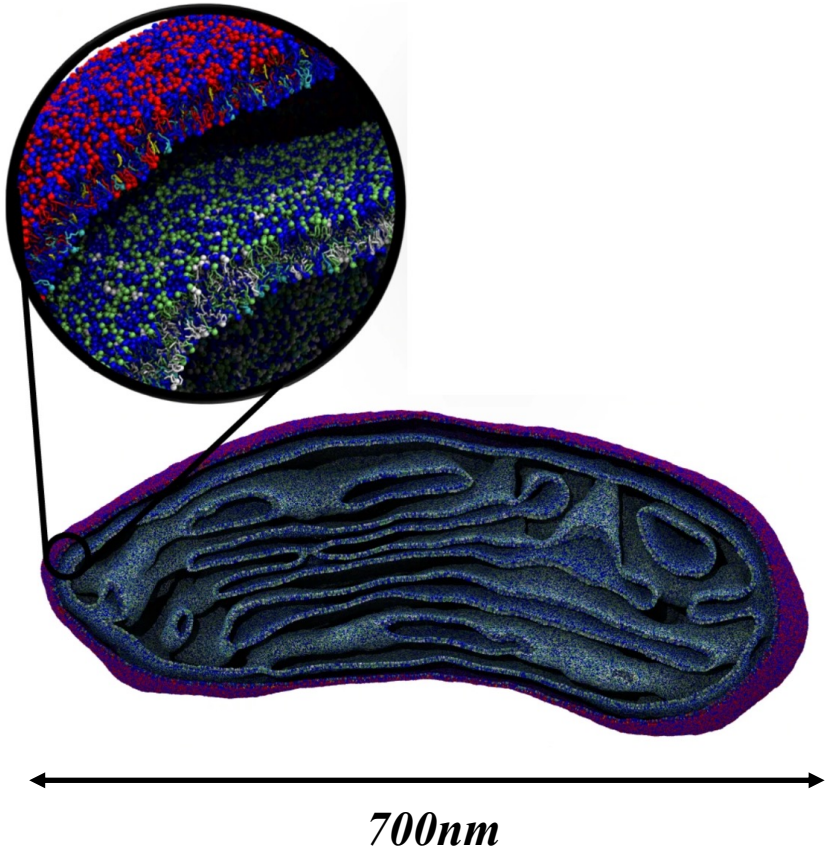


TS2CG



Pezeshkian, et al, Structure 31, 492-503(2023)



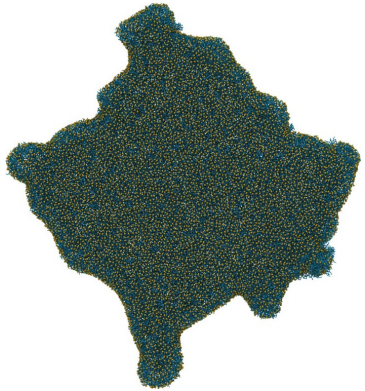


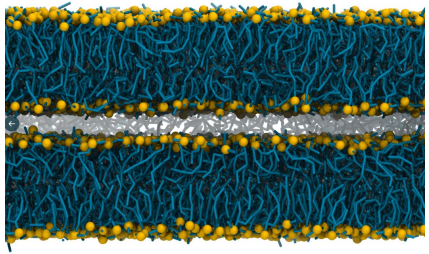
Pezeshkian, et al, Nat. Commun **11**, 2296 (2020

Martini Exhibition

Martini bunny

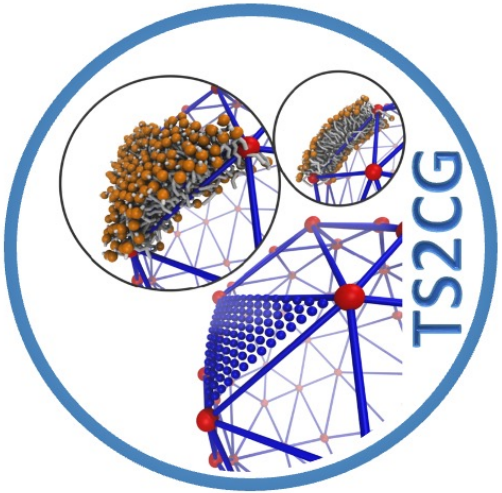
Martini Kosovo





Martini Glass

Credit: Matthieu Chavent and others on Twitter whose names I cannot recall.



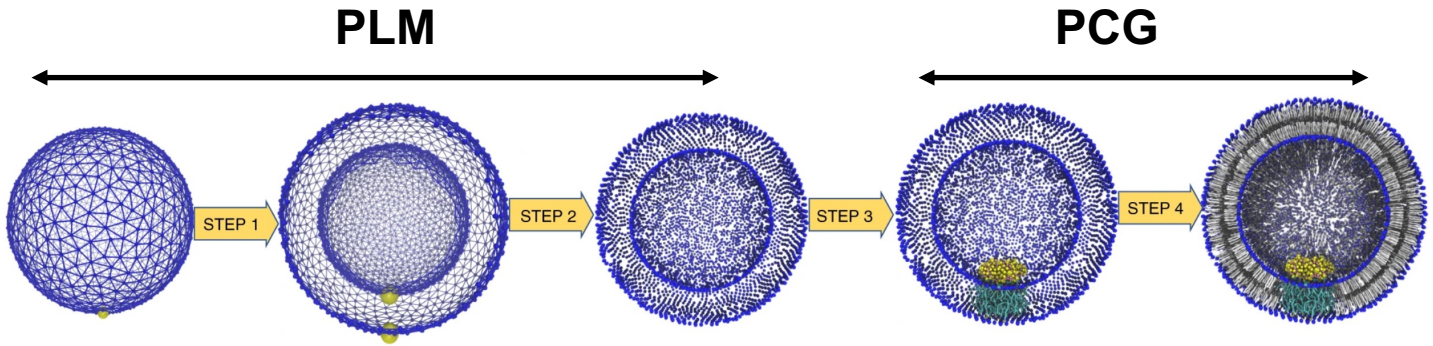
Version 1.x

C++

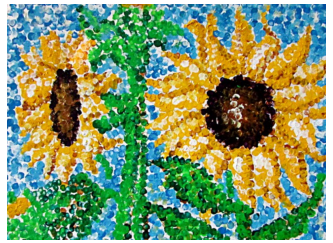
PLM: Pointillism

PCG: Point-to-Coarse-Grained Model

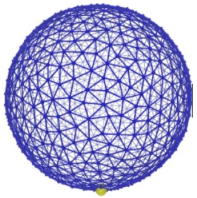
SOL: Fast solvation



Pointillism: PLM



INPUT



Triangulated Mesh

OUTPU

Domain

Domain

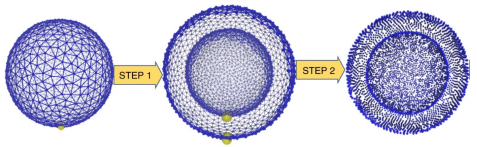
Domain

point

point

point

- position
- area
- local coordinate (normal/tangent plane)
- curvature
- inclsuion/exclusion/nothing



Membrane Builder: PCG

INPUT

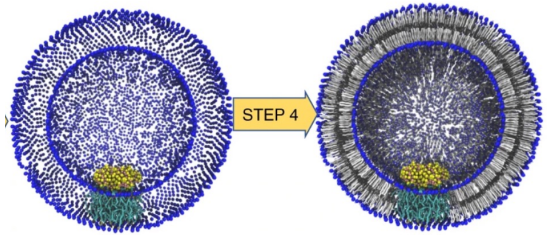
- Lipid composition for each domain.
- A protein structure for each inclusion type.
- Lipid map file

STEP

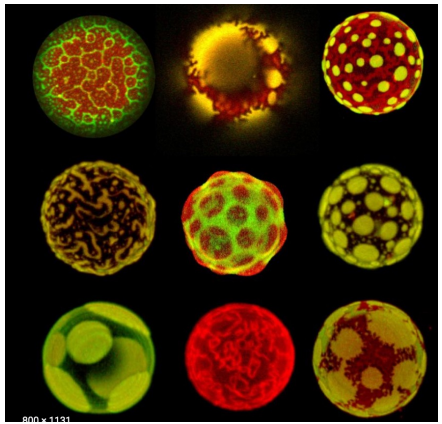
- Place the protein in the inclusion location.
- Remove points within the exclusion. zone and those overlapping with proteins.
- Randomly place lipids with the defined composition.

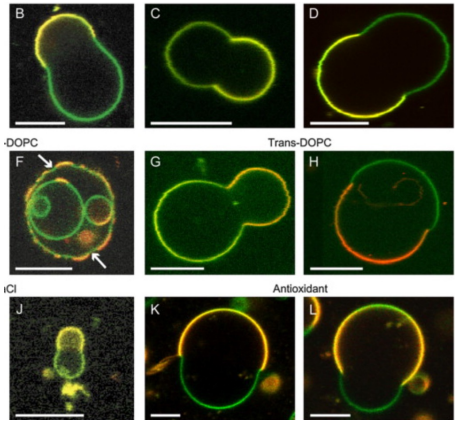
OUPUT

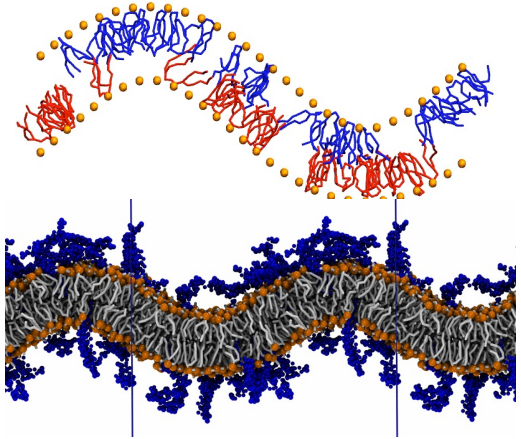
Coordinate file of the full system.



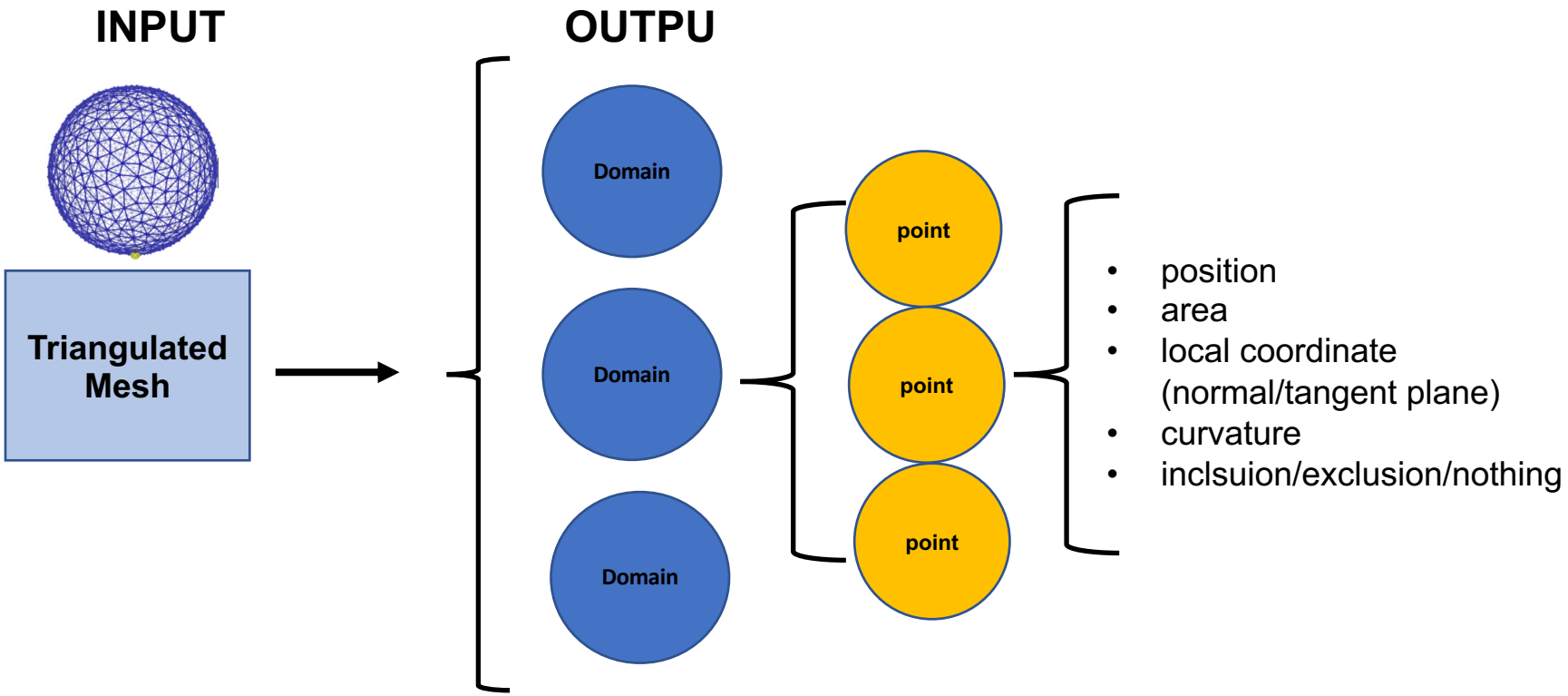
Membrane shape and lateral organization are coupled



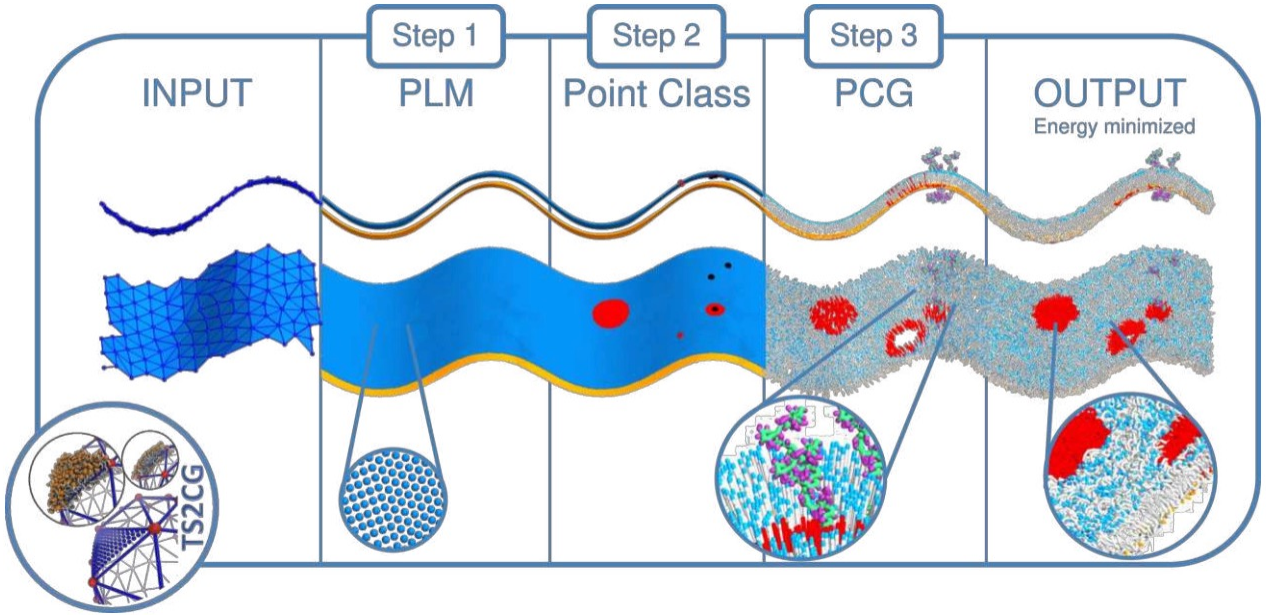




Pointillism: PLM



TS2CG v2.x



Pezeshkian, et al, Nat. Commun **11**, 2296 (2020).
Fabian Schuhmann, et al, JCTC (2025) doi: https://doi.org/10.1101/2025.04.16.649160
https://github.com/weria-pezeshkian/TS2CG-v2.0;

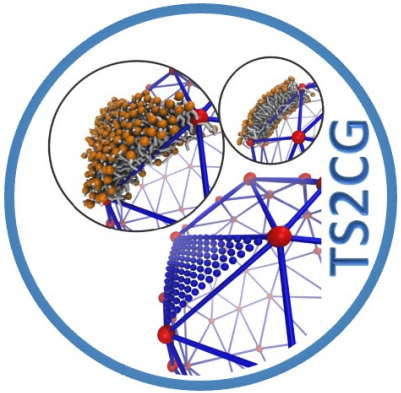
TS2CG 2.0 Adds “The Point Class API”

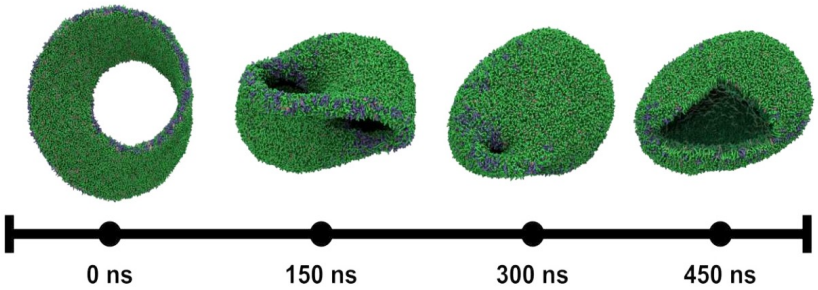
TS2CG 2.0 is distributed through PyPI, so install via pip.

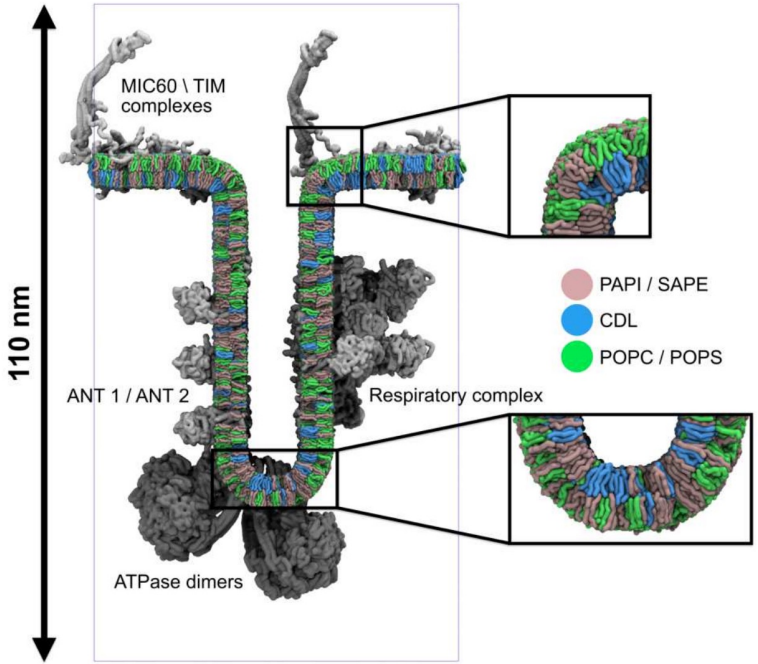
DAI (**D**omains **A**round **I**nclusions): circular lipid domains around proteins or around any arbitrary point (DAI).

DOP (**D**istribution-based **O**ptimized **P**lacement): assigning lipids based on curvature preference.

INU (**IN**clusion **U**pdater): inserting membrane proteins based on curvature preference.



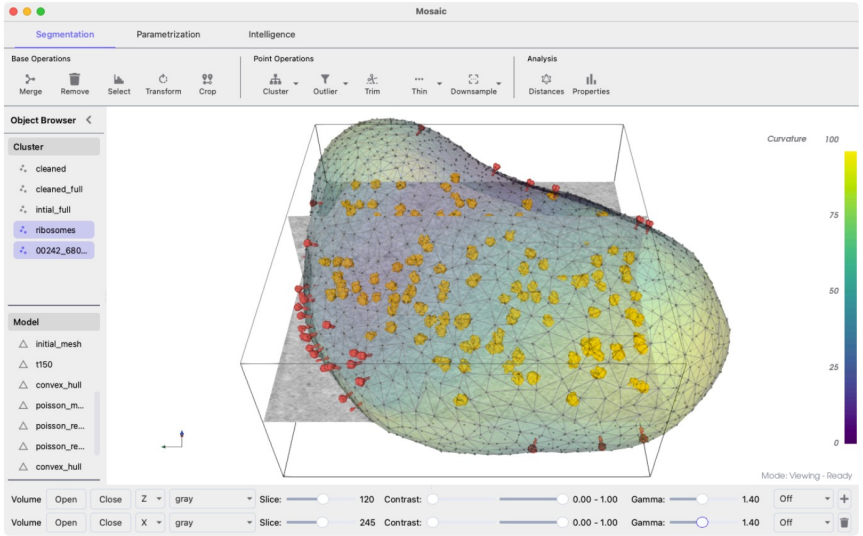




Pezeshkian, et al, Nat. Commun **11**, 2296 (2020).
Fabian Schuhmann, et al, (2025) doi: https://doi.org/10.1101/2025.04.16.649160
https://github.com/weria-pezeshkian/TS2CG-v2.0;

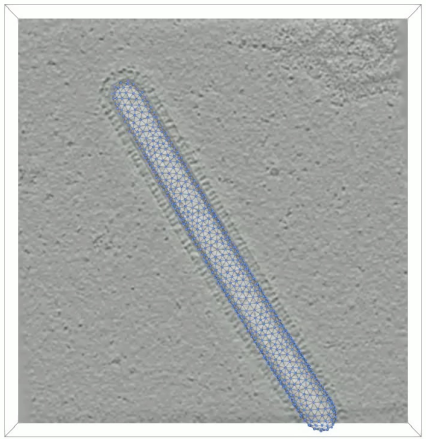
If you are dealing with cryo-ET data

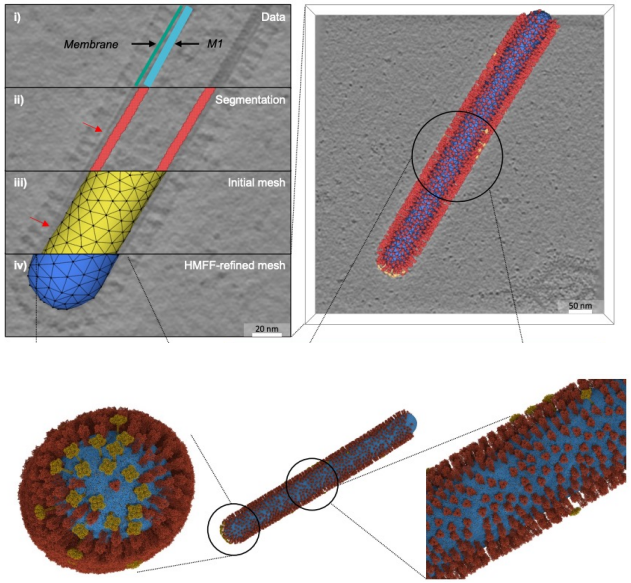
mosaic



V, Maurer, et al, (2025) doi: https://doi.org/10.1101/2025.05.24.655915
Helfrich Monte Carlo Flexible Fitting: physics-based, data-driven cell-scale simulations;

Influenza A virus particles





V, Maurer, et al, (2025) doi: https://doi.org/10.1101/2025.05.24.655915
Helfrich Monte Carlo Flexible Fitting: physics-based, data-driven cell-scale simulations;

Any ideas for future development?

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MARIE CURIE ACTIONS
DANMARKS FRIE FORSKNINGSFOND
INDEPENDENT RESEARCH FUND DENMARK
novo nordisk fonden

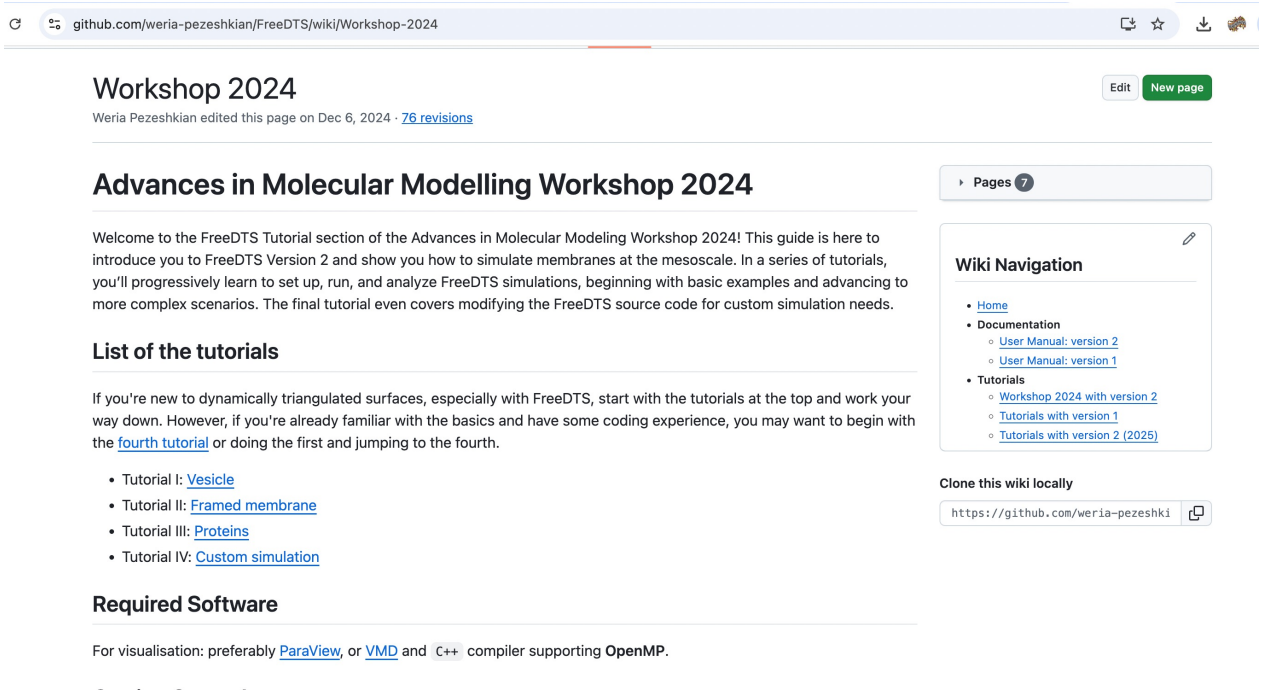
```
include protein.gro
[Lipids List]
;LipidName  RatioUp RatioDown   Area/Lipid
Domain 0
POPC        0.5     0.5         0.63
POPE        0.5     0.5         0.64
End
Domain 1
POPC        0.5     0.5         0.63
POPE        0.5     0.5         0.64
End
[Shape Data]
ShapeType    Flat
Box    40    40    40
Density      2     2
Thickness    3.8
WallRange    0     1    0    1
End
[Protein List]
;ProteinName    Incl.Id     Surface_Coverage    0   0   z-position
STxB            1           0.5                 0   0   -1.1
end Protein
```

```
Description Martini Map CG
Version Martini 3
;Martini 3 lipid library for TS2CG 2.0
;Made by Reinier de Vries on 31-03-2021. Last updated: 04-05-2021
;NOTE: Bead atom names don't match current Martini 3 bead atom names, use -maxwarn in GROMACS

[DAPC]
1 NC3 0 0    1
2 PO4 0 0    0
3 GL1 0 0   -1
4 GL2 0 0.5 -1
5 D1A 0 0 -2
6 D2A 0 0 -3
7 D3A 0 0 -4
8 D4A 0 0 -5
9 C5A 0 0 -6
10 D1B 1 0 -2
11 D2B 1 0 -3
12 D3B 1 0 -4
13 D4B 1 0 -5
14 C5B 1 0 -6

[POPC]
1 NC3 0 0    1
2 PO4 0 0    0
3 GL1 0 0   -1
4 GL2 0 0.5 -1
5 C1A   0     0   -2
6 D2A   0     0   -3
7 C3A   0     0   -4
8 C4A   0     0   -5
9 C1B   1     0   -2
10 C2B  1     0   -3
11 C3B  1     0   -4
12 C4B  1     0   -5
```

Useful links

Source code: https://github.com/weria-pezeshkian/TS2CG-v2.0
Tutorials: https://github.com/weria-pezeshkian/TS2CG-v2.0/wiki/Tutorial
PointClass Documentation:
https://weria-pezeshkian.github.io/TS2CG_python_documentation/

Tutorials and the manual



If you are interested, you can follow tutorials to learn how to perform simulations using FreeDTS and conduct research on biomembranes.

https://github.com/weria-pezeshkian/FreeDTS/wiki/Workshop-2024