Instituto de Física de Buenos Aires

Universidad de Buenos Aires

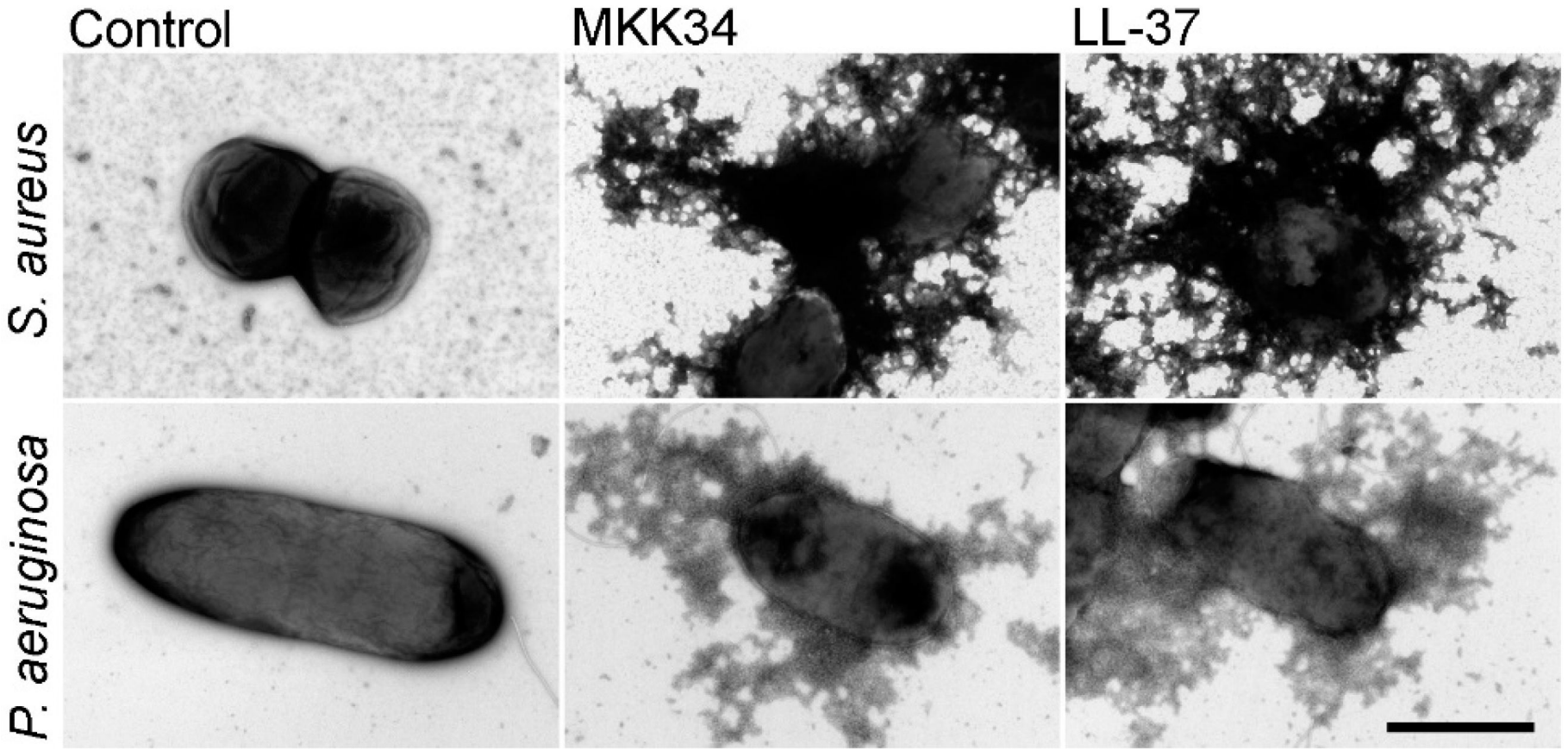
Interaction of antimicrobial peptides with POPC lipid structures modeled by molecular dynamics simulations

Advisor: Prof. Mónica Pickholz

Coadvisor: Dr. María Florencia Martini

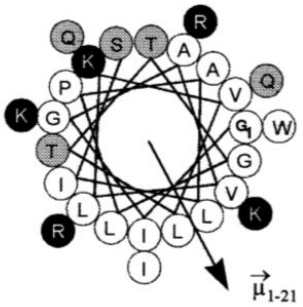
Lic. Galo Ezequiel Balatti

Antimicrobial Peptides



Exp. Dermatol. 2011, 20, 1004–1010

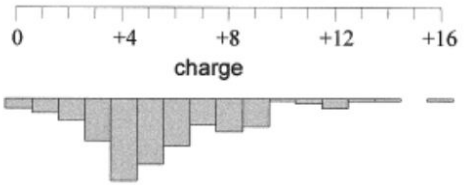
Helicoidal AMPs

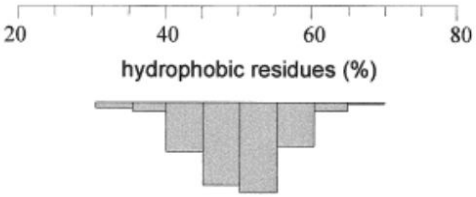


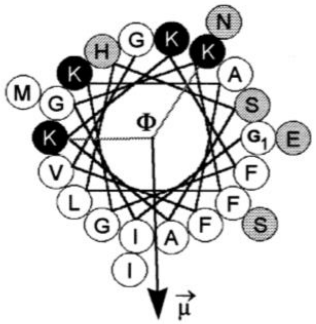
Melittin

GIGAV LKVLT TGLPA LISWI KRKRQ Q-NH_2

N= 26; Q= +6; $H_{1\text{-}21}$= 0.183; $|\mu|_{1\text{-}21}$= 0.266





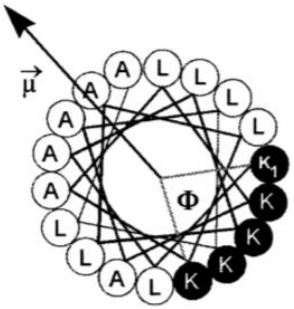


Magainin

GIGKF LHSAK KFGKA FVGEI MNS-NH_2

N= 23; Q= +4; H= -0.036; |μ|= 0.286; Φ= 120°

H_h= 0.331

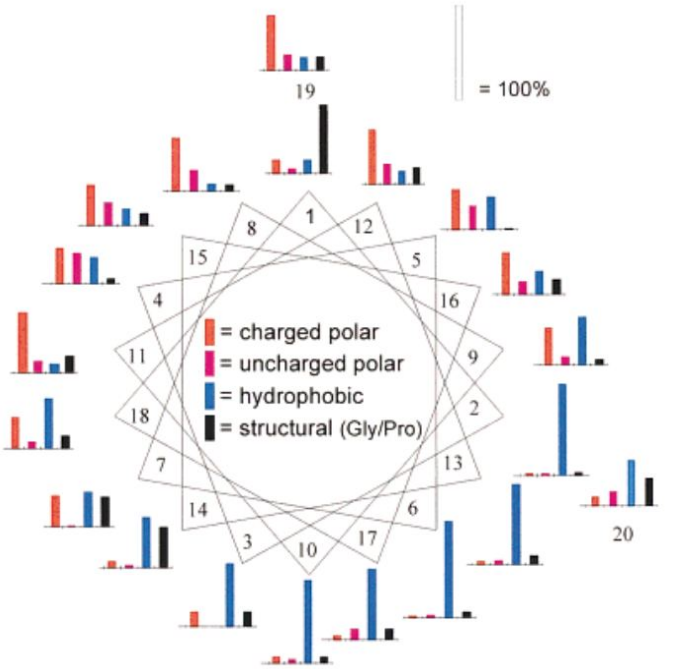


KLAL-Model

KLALK LALKA LKAAL KLA-NH_2

N= 18; Q= +5; H= -0.016; |μ| = 0.334; Φ= 80°

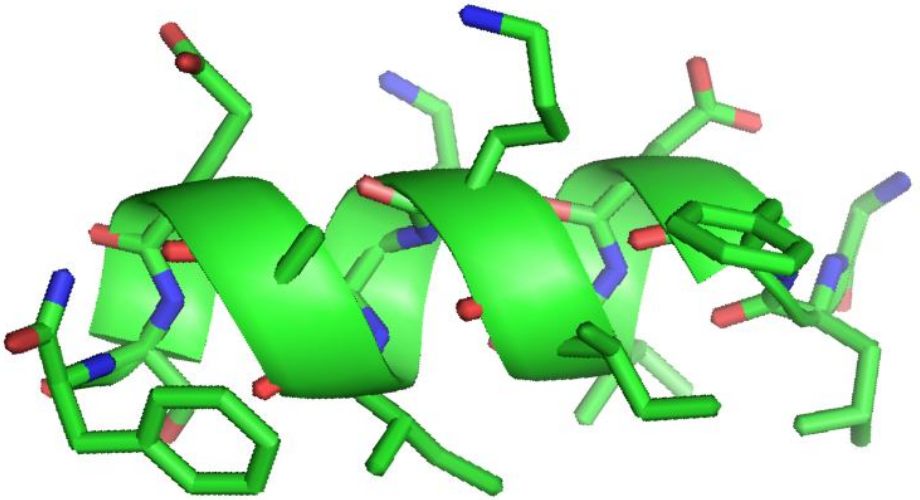
H_h= 0.401



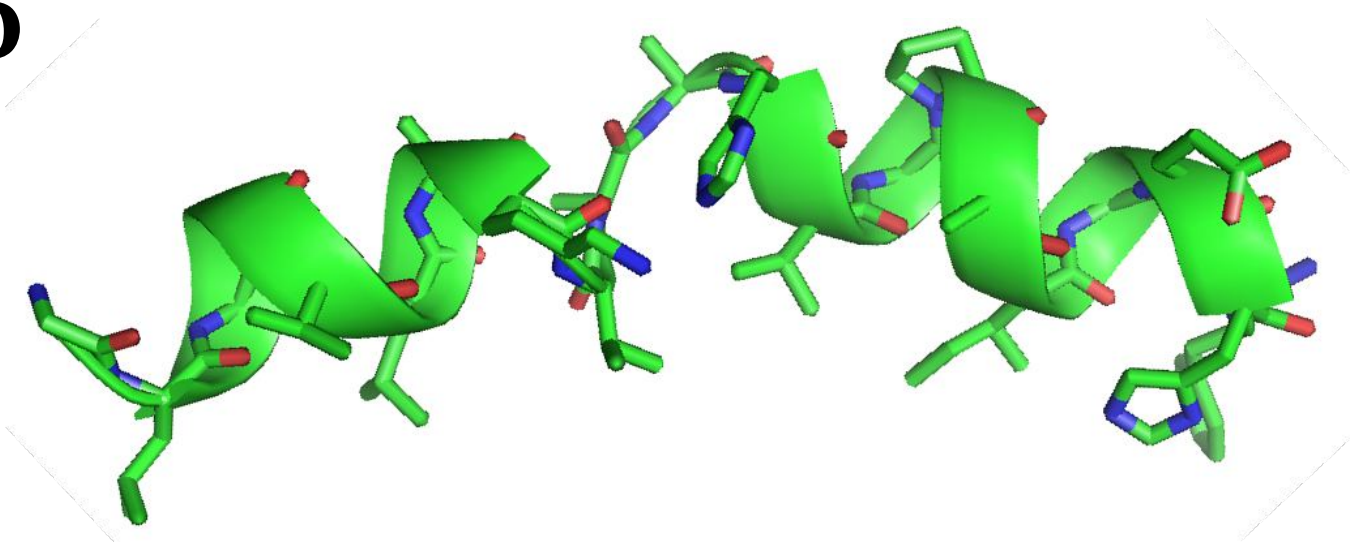
Biochimica et Biophysica Acta 1462 (1999) 71-87

Biopolymers (Peptide Science), Vol. 55, 4 –30 (2000)

Aurein 1.2

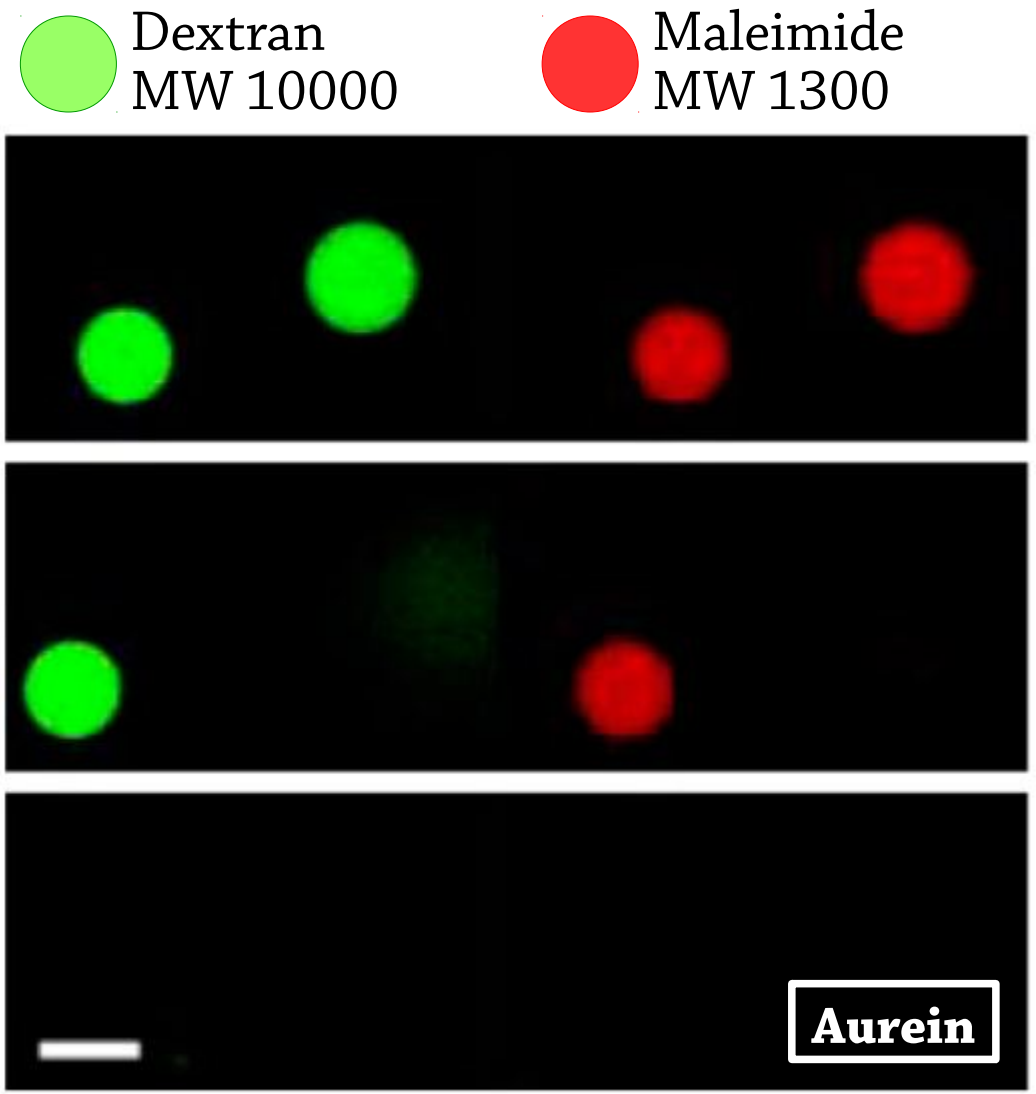


Maculatin-PRO

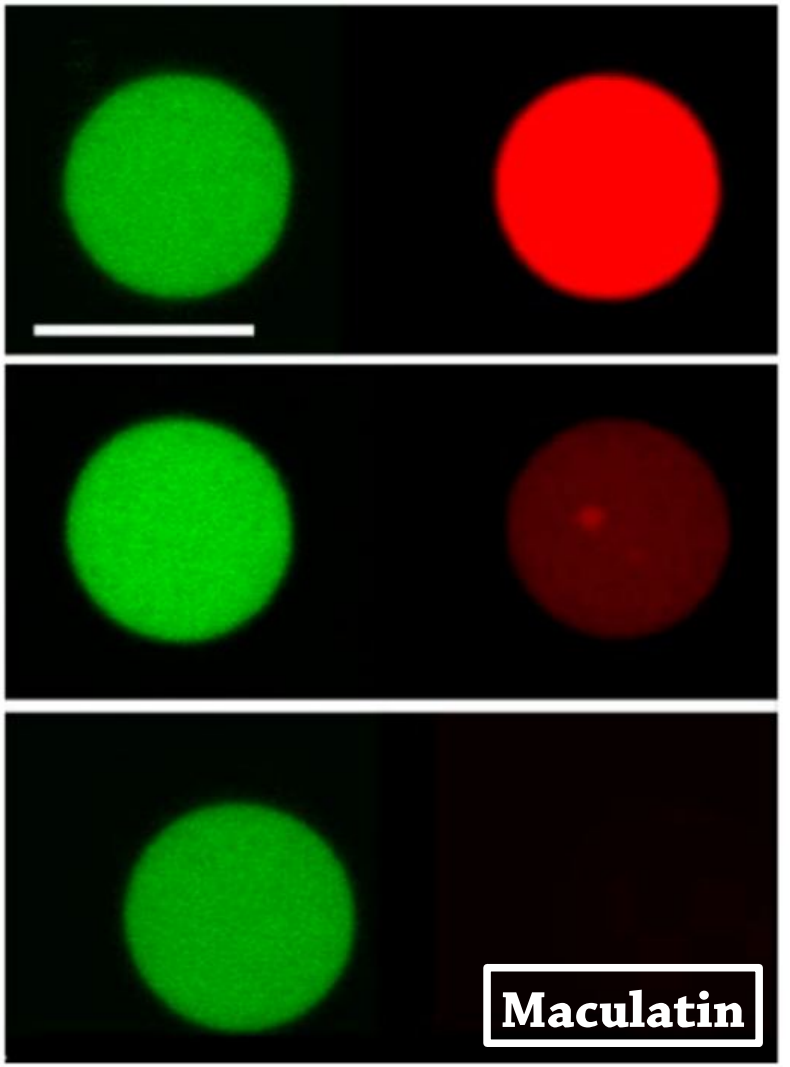


Helicoidal AMPs

Aurein and Maculatin in action



POPC GUVs filled with dextran (green) and maleimide (red) in presence of 5uM Aurein at times of 0s (up), 1162s, (middle) and 1191s (down)

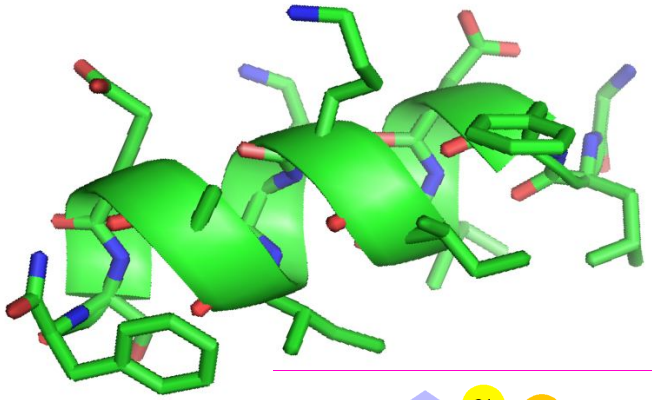


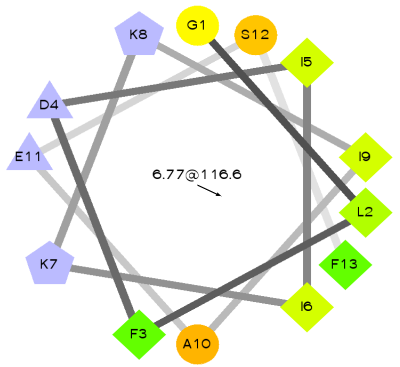
POPC GUVs filled with dextran (green) and maleimide (red) in presence of 5uM Macultin 1.1, at times of 0s (up), 580s, (middle) and 670s (down)

Biophysical Journal 89 September 2005 1874–1881

Aurein 1.2

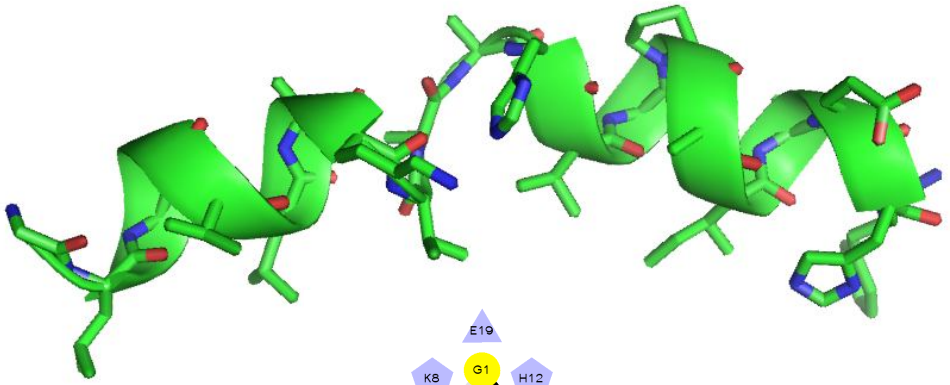
Residues: 13
Isoelectric Point: 9.9
Net charge: 1.0
Hydrofobicity: 0
$\%_{\text{Hydrofilical Residues}}$: 38%
Hydrofobic Moment: 6.77

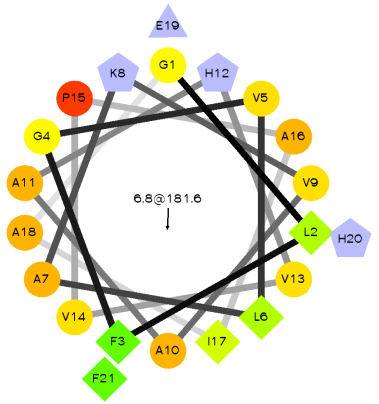




Maculatin-PRO

Residues: 21
Isoelectric Point: 10.1
Net charge: 1.2
Hydrofobicity: -0.7
$\%_{\text{Hydrofilical Residues}}$: 10%
Hydrofobic Moment: 6.8



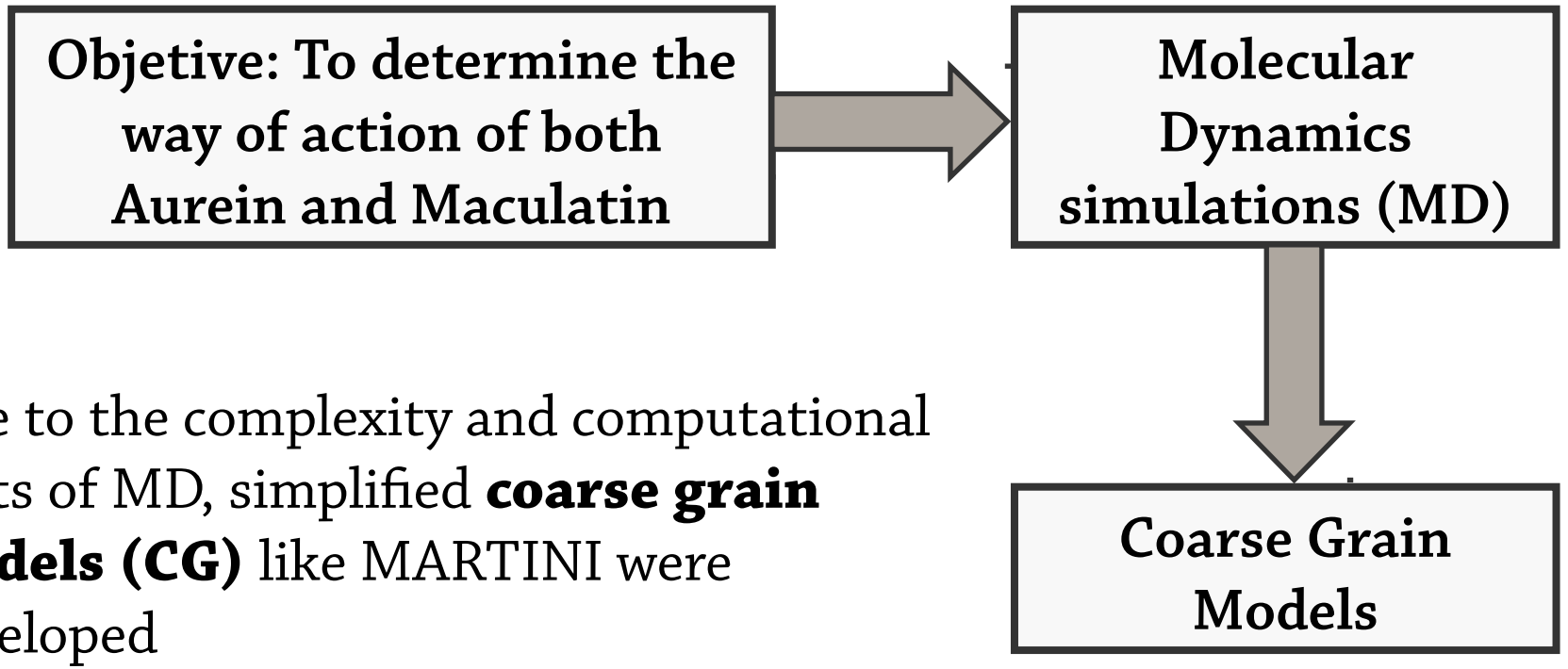


G	L	F	D	I	I	K	K	-	-	-	-	-	-	-	-	I	A	E	S	F	AUREIN
G	L	F	G	V	L	A	K	V	A	A	H	V	V	P	A	I	A	E	H	F	MACULATIN

BLOSUM62
GP: 10
EP: 0.05

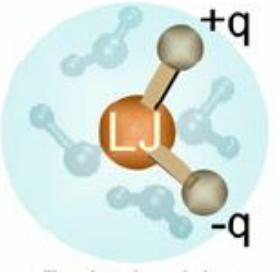
Molecular Dynamics

Molecular Dynamics Simulations can gives us a **molecular detailed point of view** of the AMPs behavior

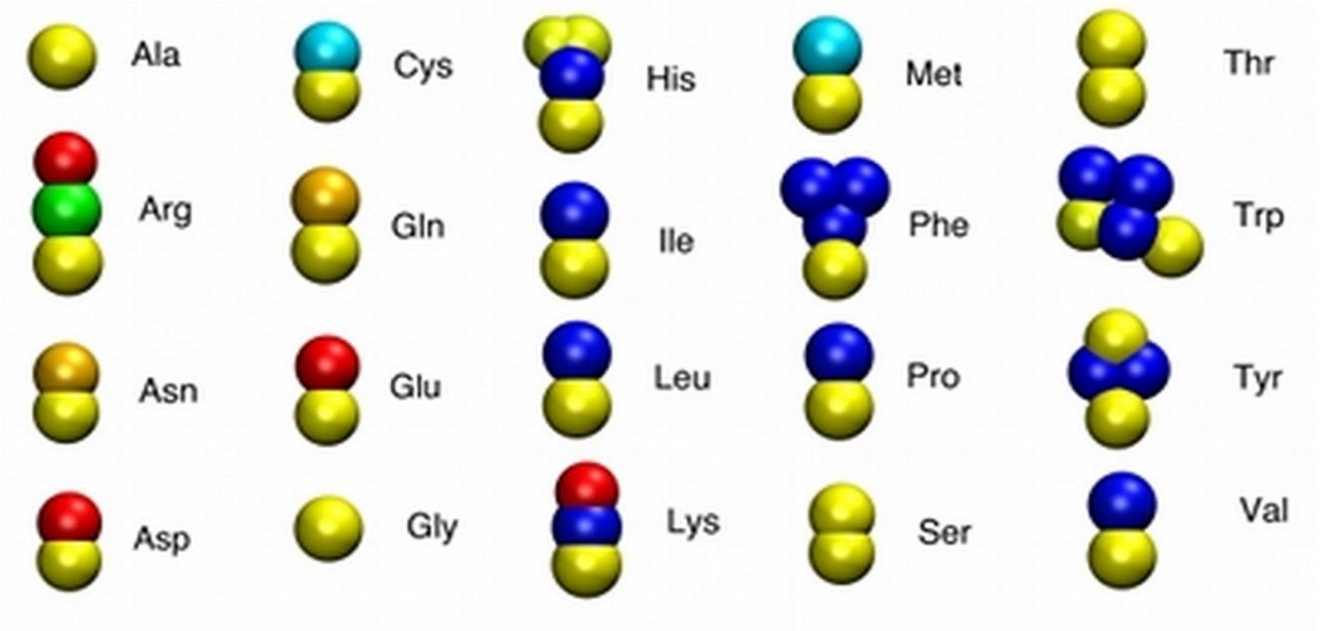


Due to the complexity and computational costs of MD, simplified **coarse grain models (CG)** like MARTINI were developed

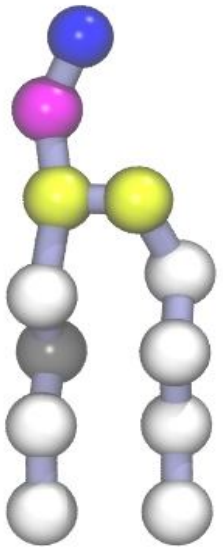
Coarse grain model: MARTINI



H20

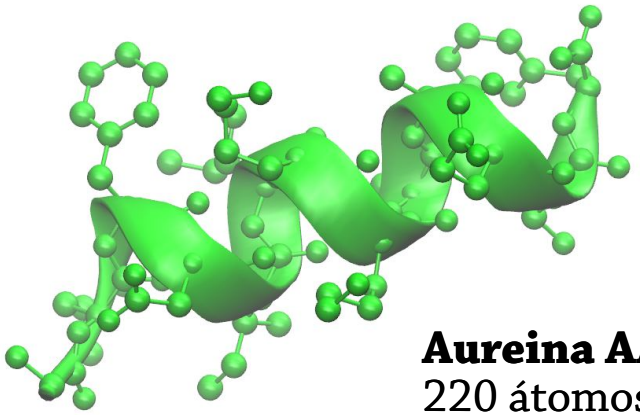


AMINOACIDS

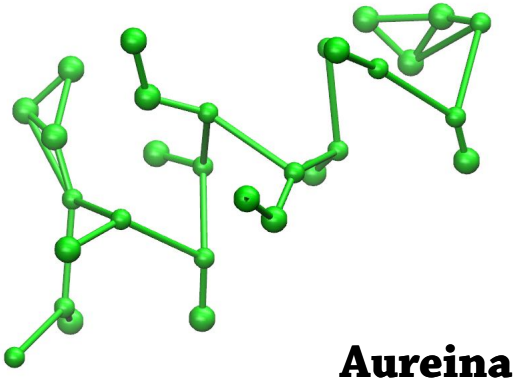


POPC

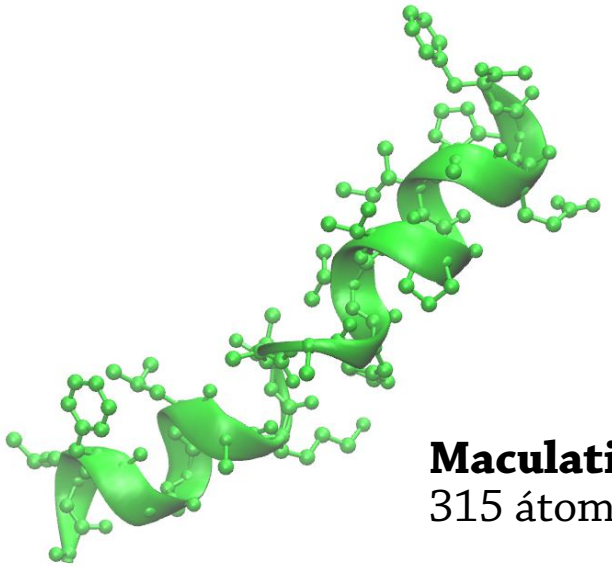
Coarse grain model: MARTINI



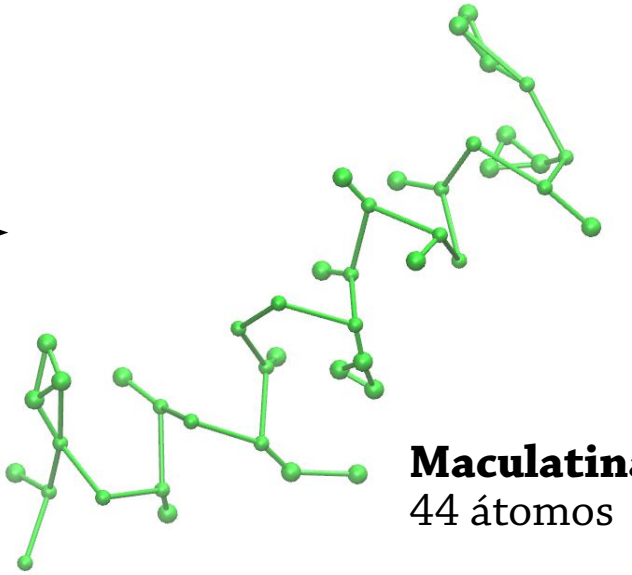
Aureina AA
220 átomos



Aureina CG
30 átomos



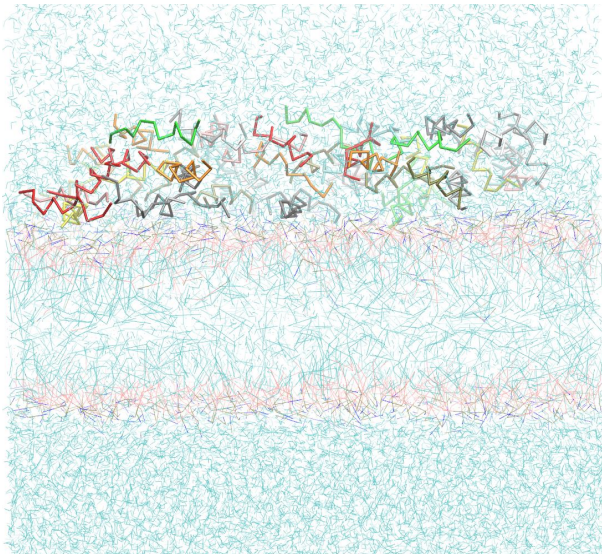
Maculatina AA
315 átomos



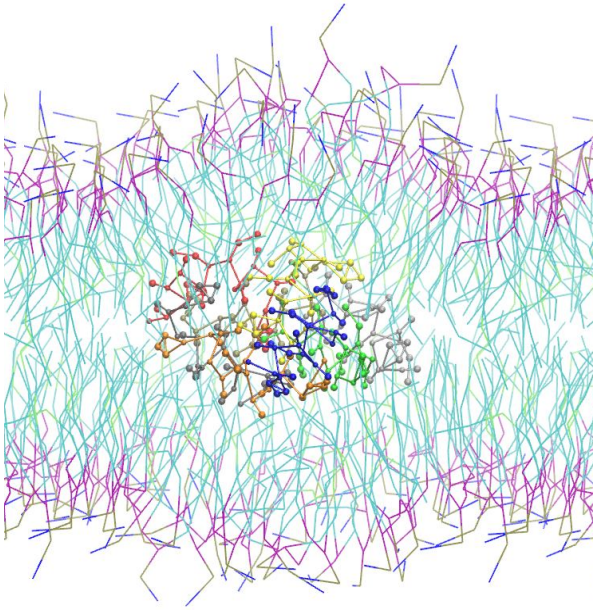
Maculatina CG
44 átomos

Strategy: 3 != starting points

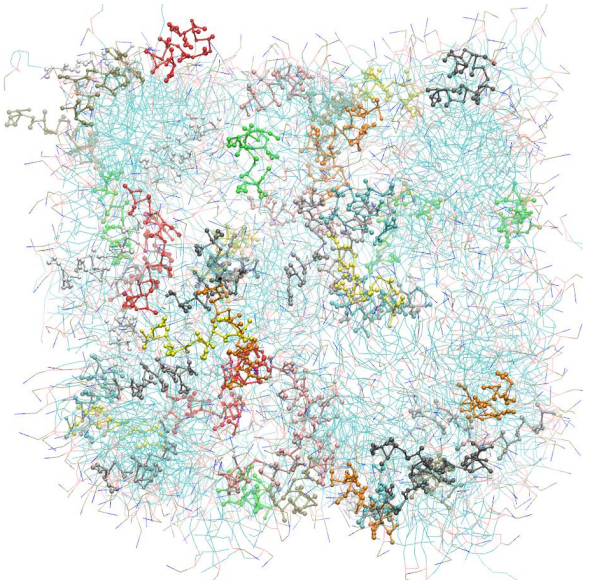
CASE A: peptides in aqueous solution near to a planar POPC bilayer



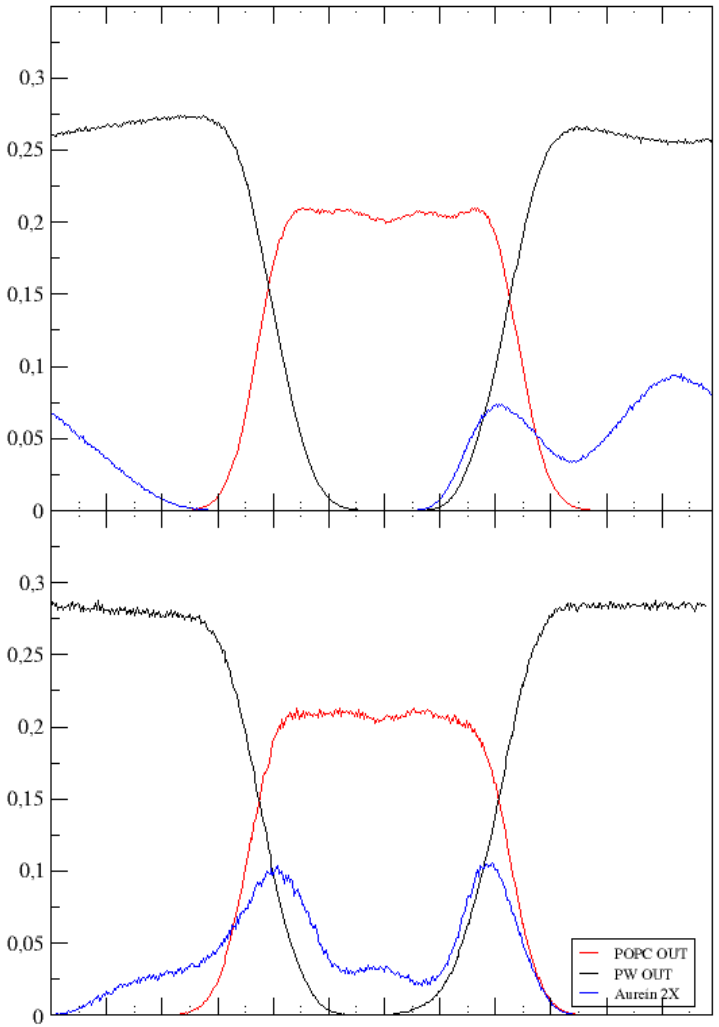
CASE B: peptides placed inside the hydrofobic core of the bilayer

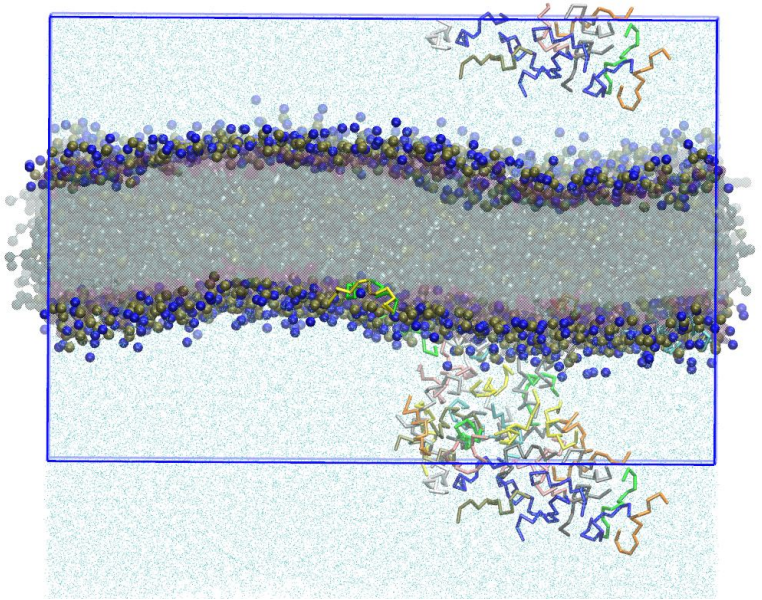


CASE C: molecules starting in a random position of the box

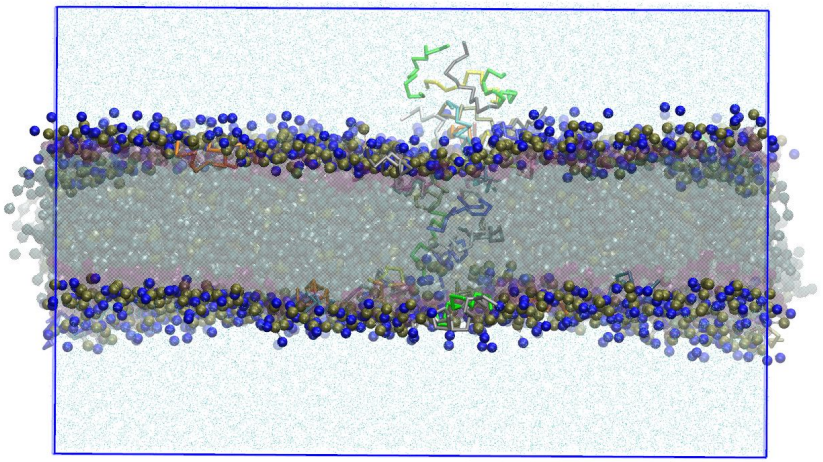


Aurein cases A (out) and B (in)





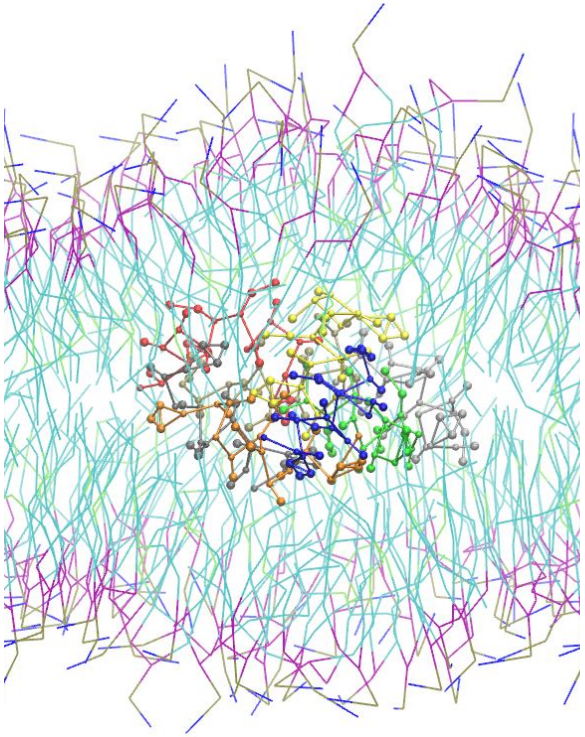
Case A: Starting from **outside**



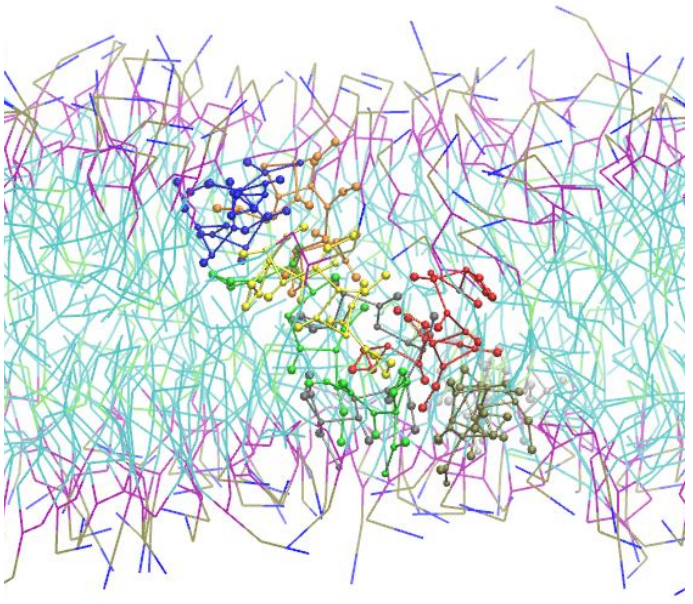
Case B: Starting from **inside**

CI: 50PP/1000LL/PW/NaCl 0,15M. 1500 ns. NPT ensamble, 323 K, 1 bar . Martini FF

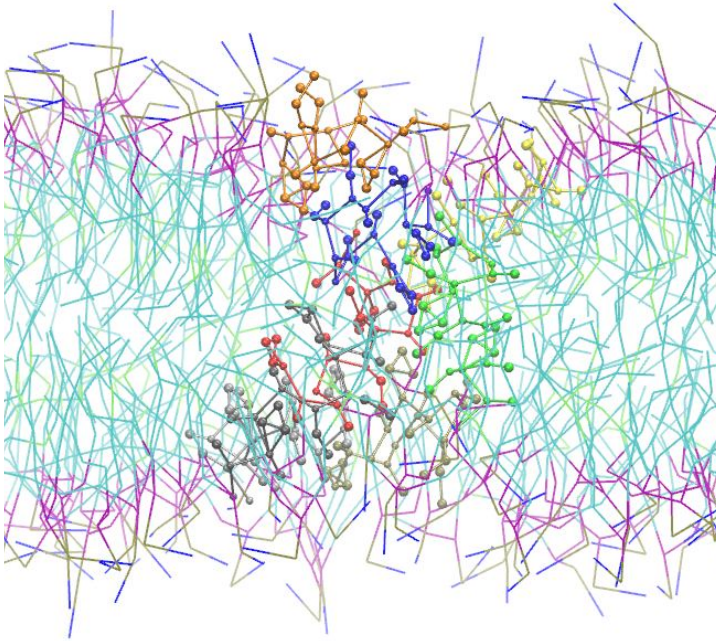
CASE B: Aurein pore formation



0 ns



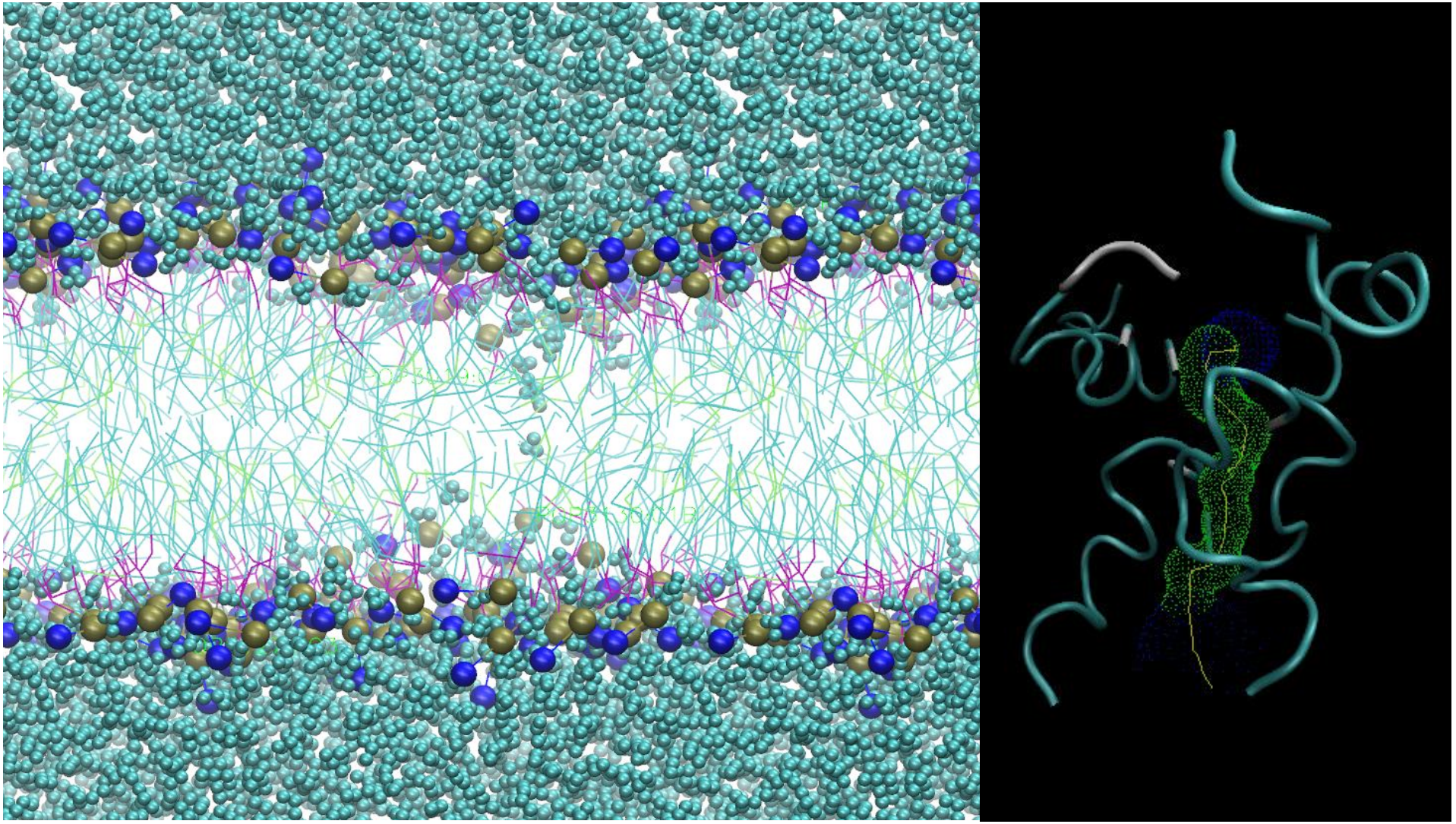
200 ns



1000 ns

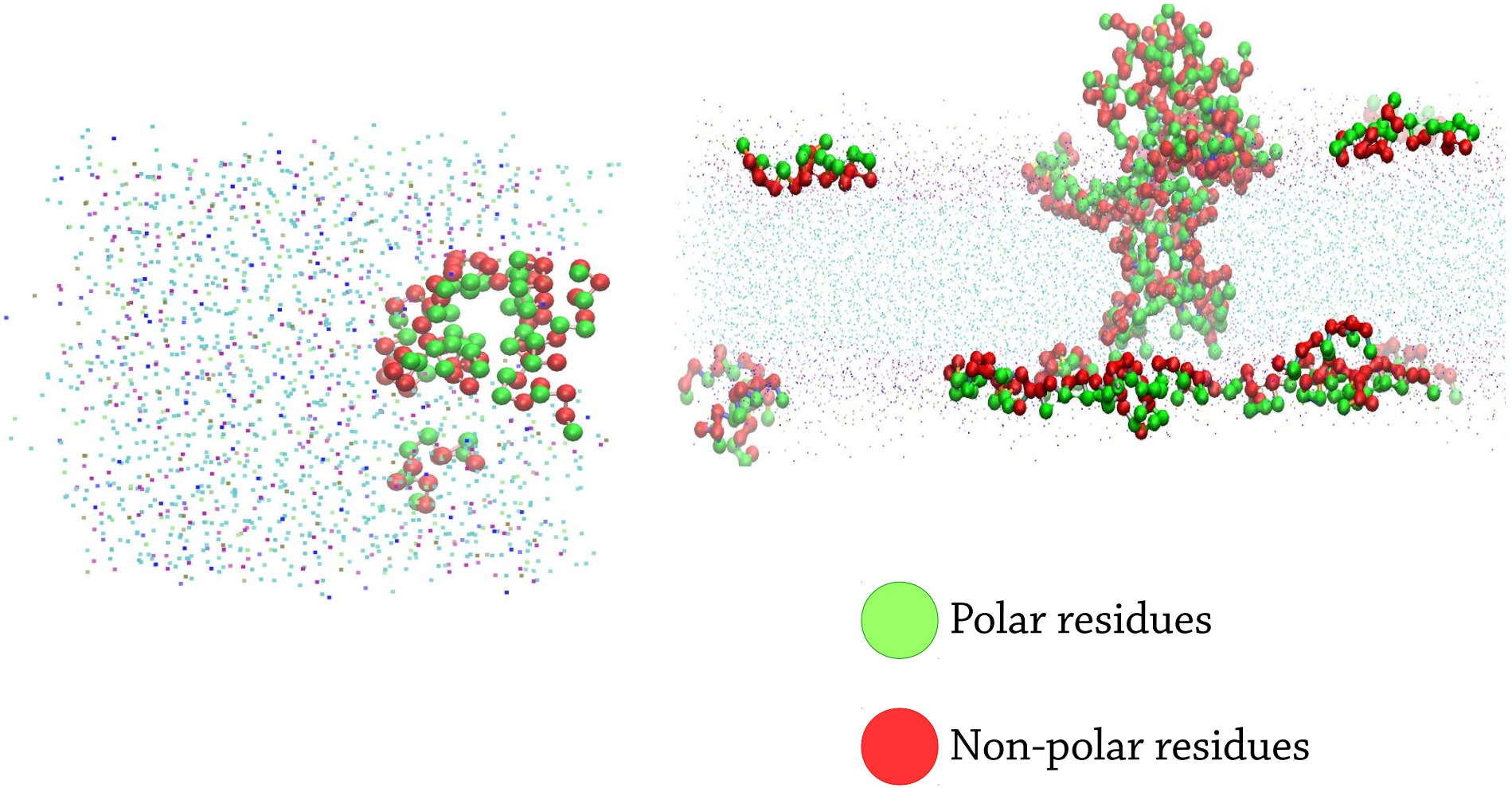
CI: 8PP/128 LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar .

CASE B: Aurein water channel



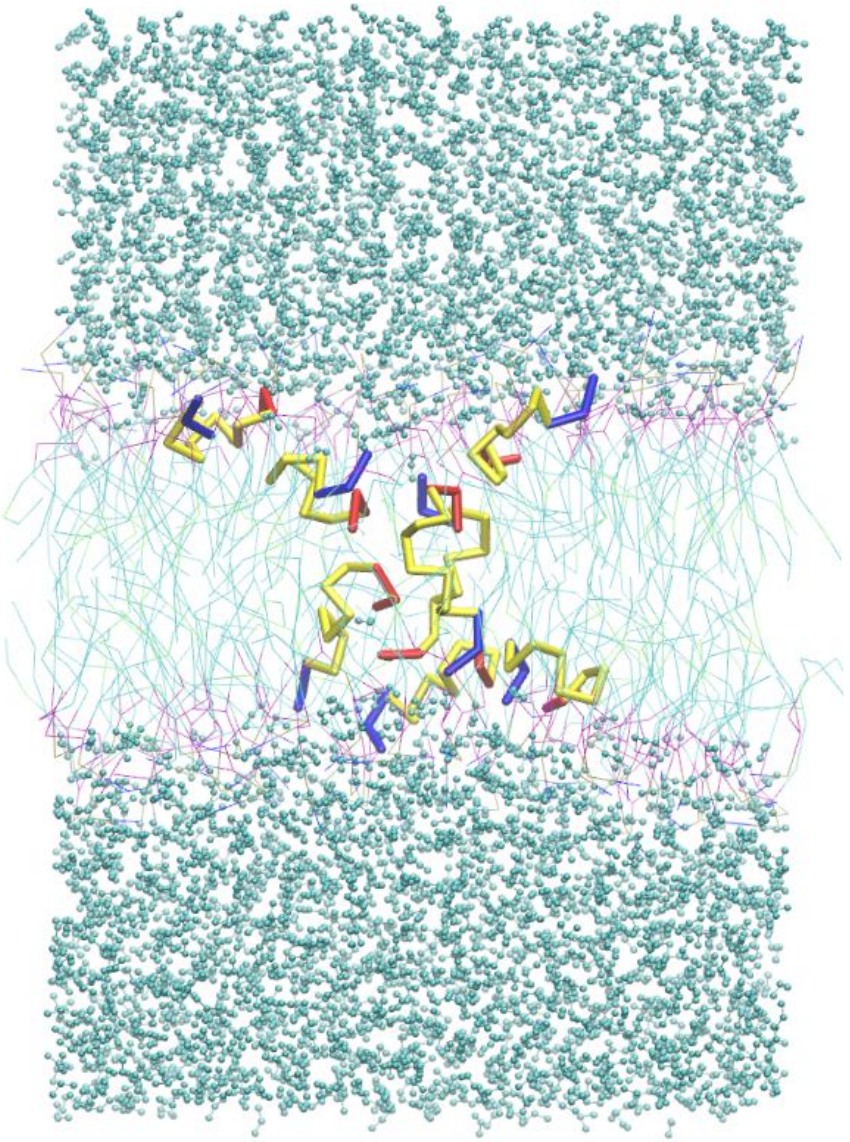
CI: 8PP/128 LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar .

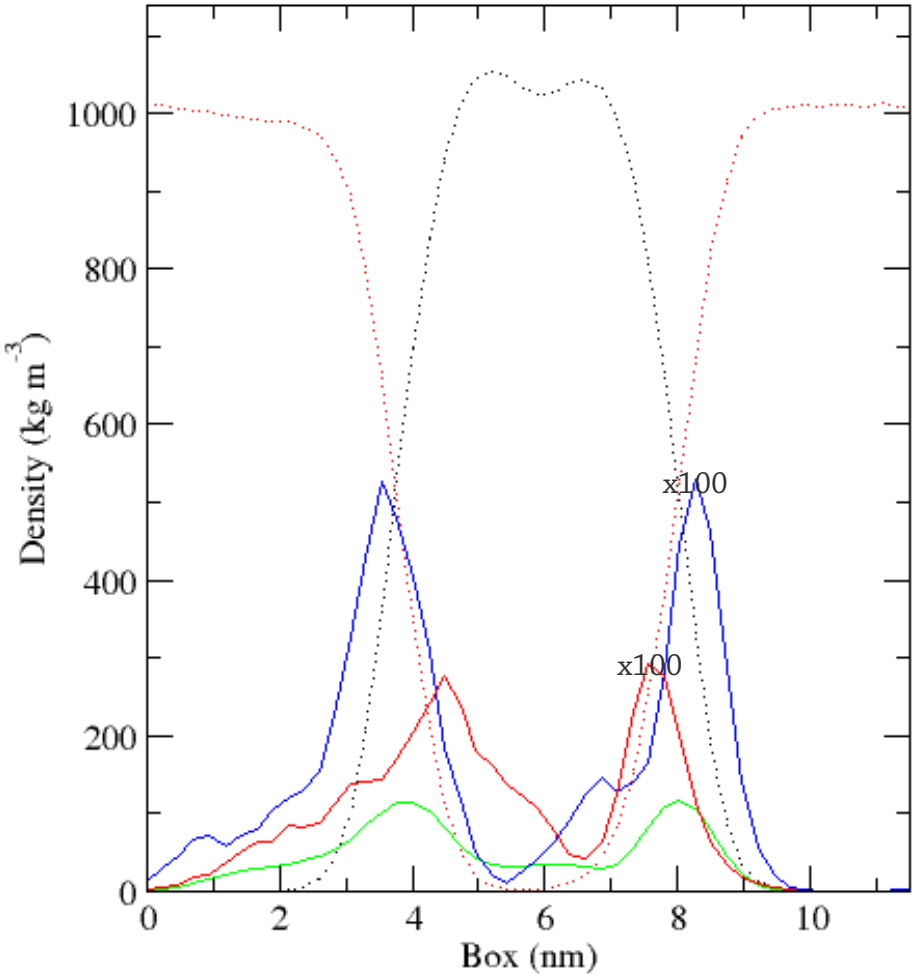
Aurein facial orientation



CI: 8PP/128LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar
CI: 50PP/1000LL/PW/NaCl 0,15M. 1500 ns. NPT ensamble, 323 K, 1 bar

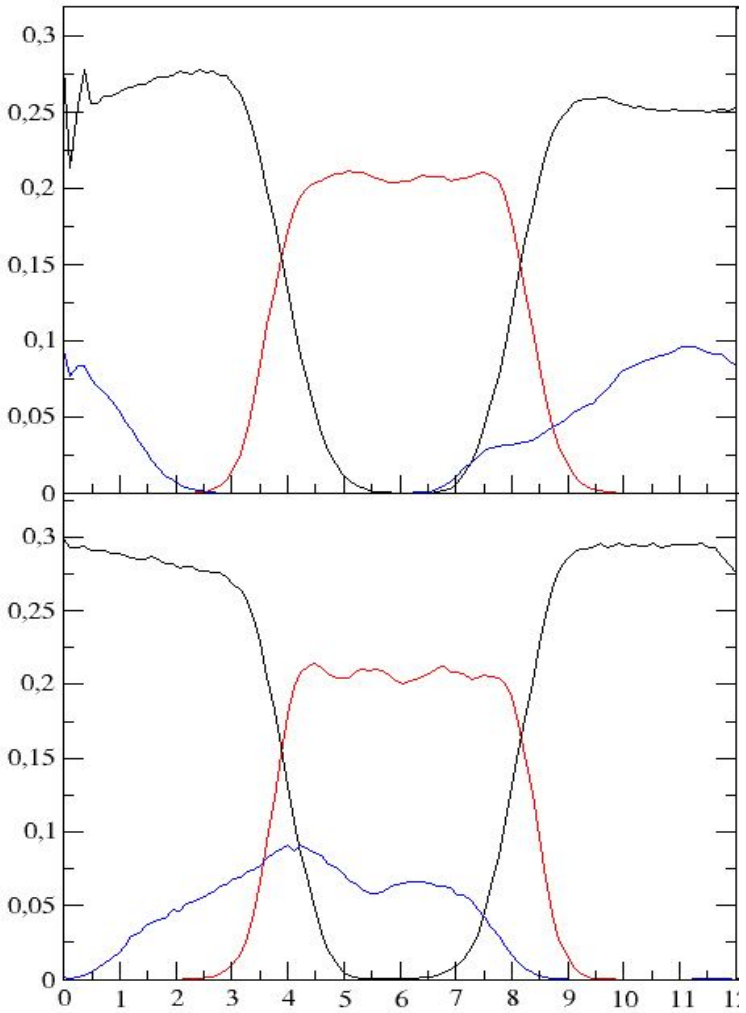
Aurein terminal orientation

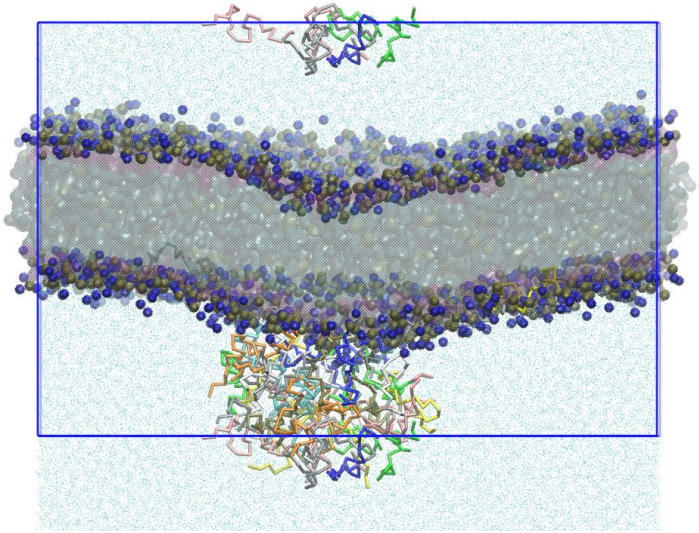




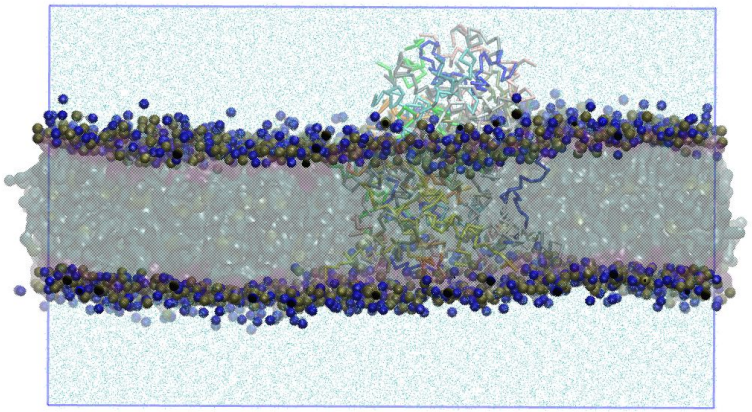
- CI: 8PP/128LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar .
  CI: 50PP/1000LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar

Maculatin cases A (out) and B (in)





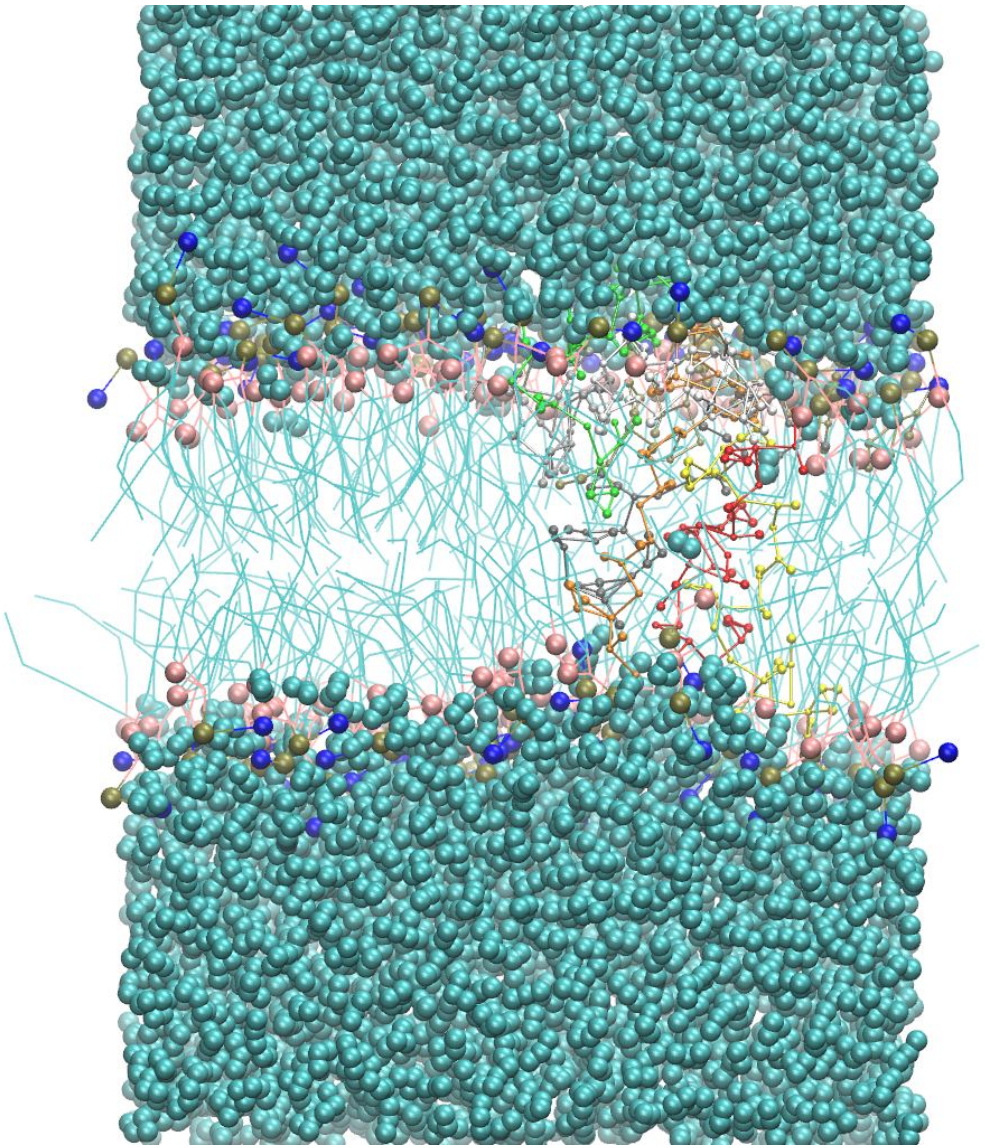
Case A: Starting from **outside**

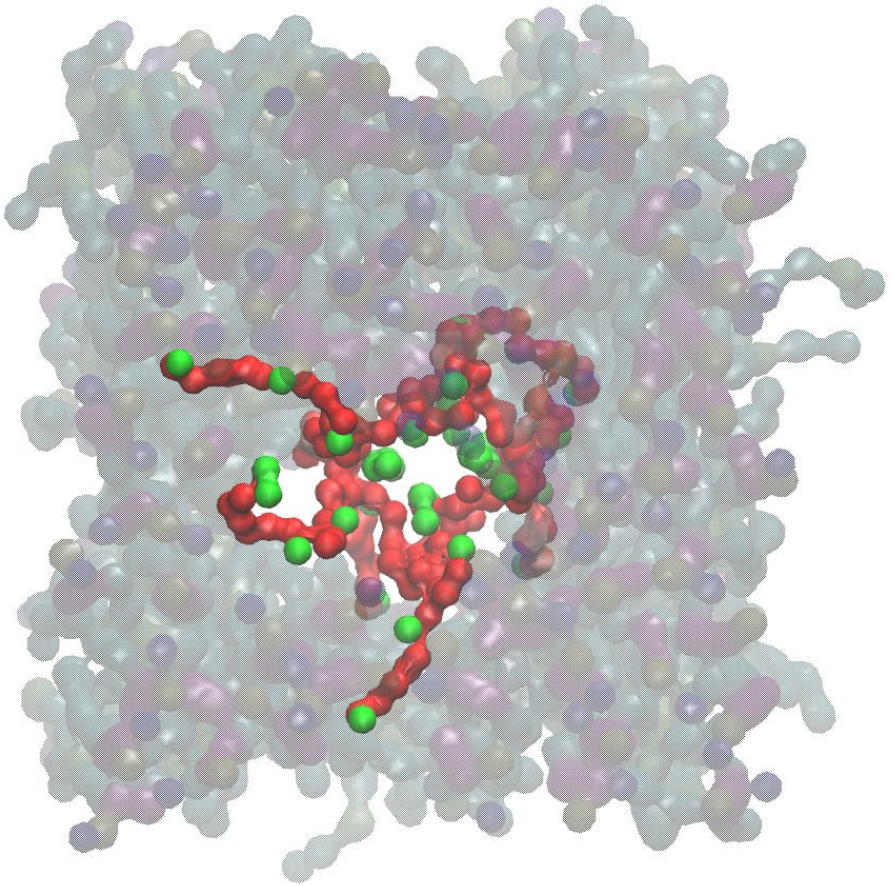


Case B: Starting from **inside**

CI: 50PP/1000LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar .

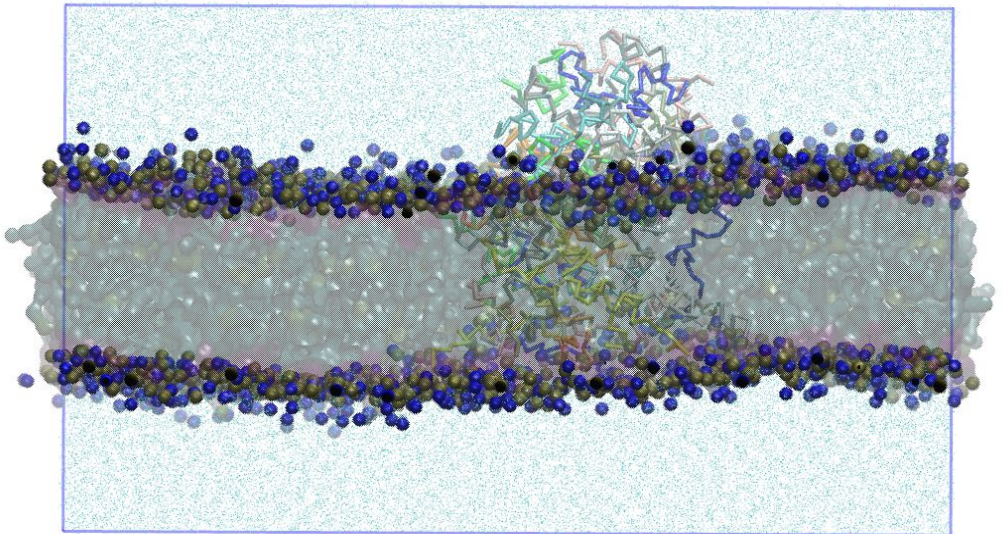
Maculatin water channel?



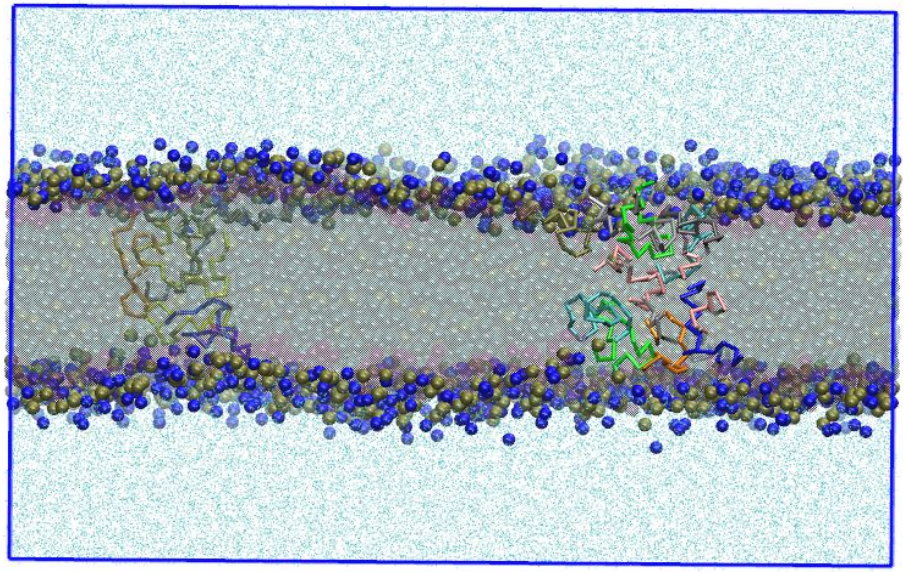


CI: 8PP/128 LL/PW/NaCl 0,15M. 200 ns. NPT ensamble, 323 K, 1 bar .

Maculatin clustering



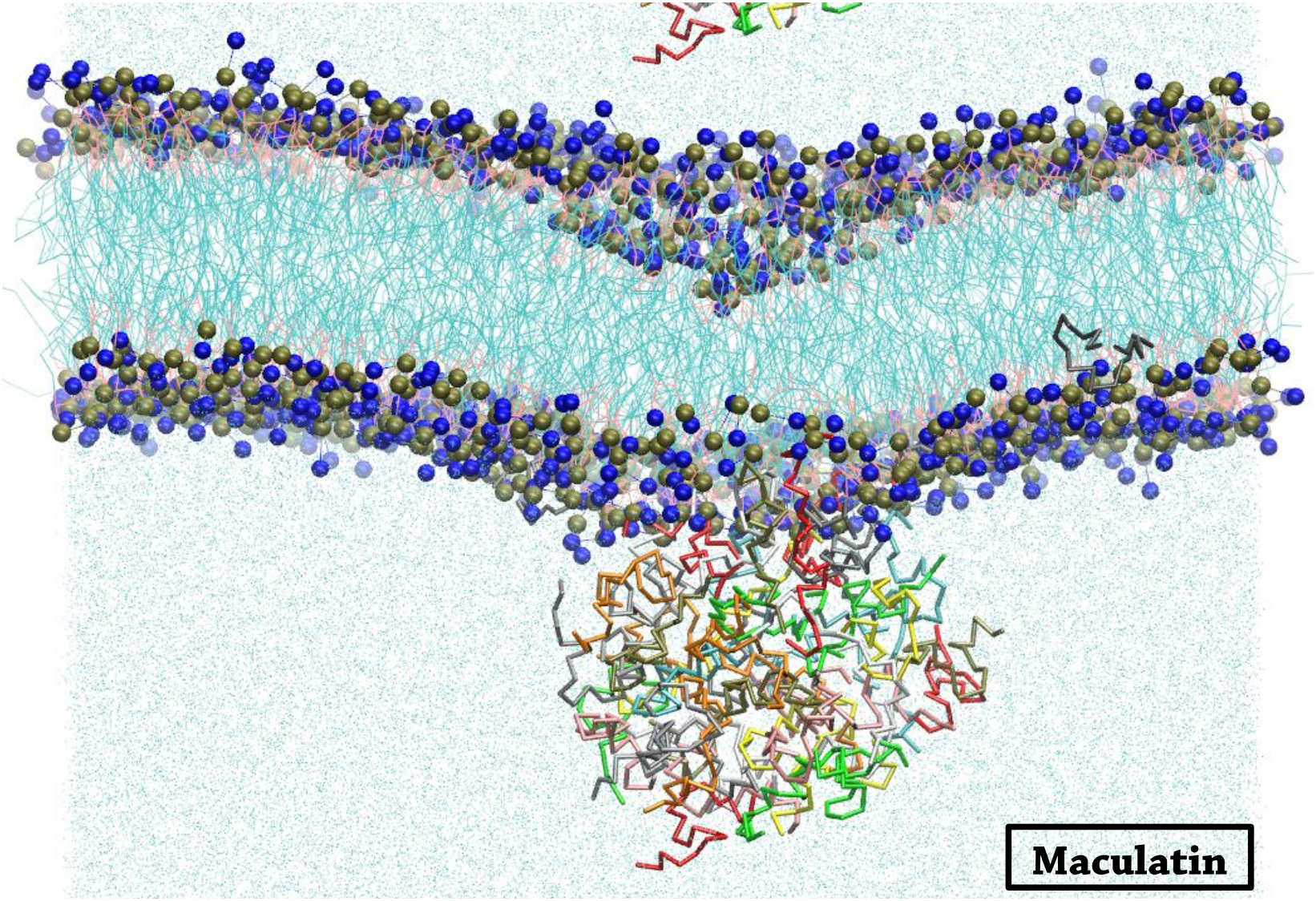
50 MACULATINS
1000 POPC



20 MACULATINS
1000 POPC

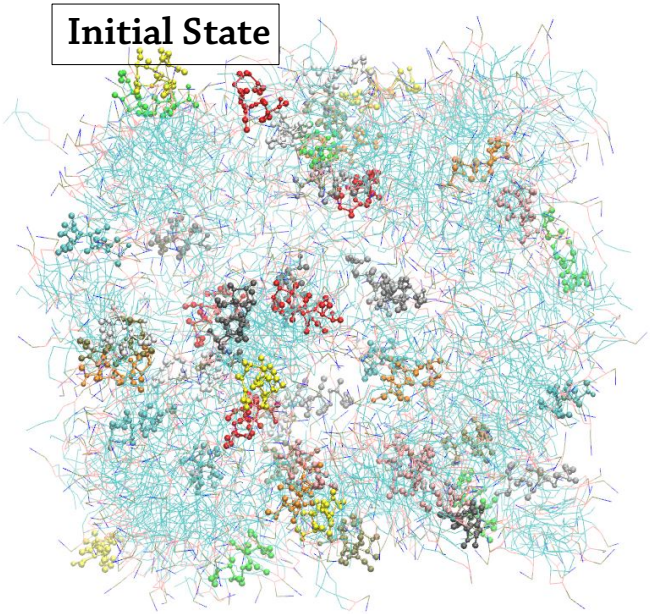
CI: 50PP/1000LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar .

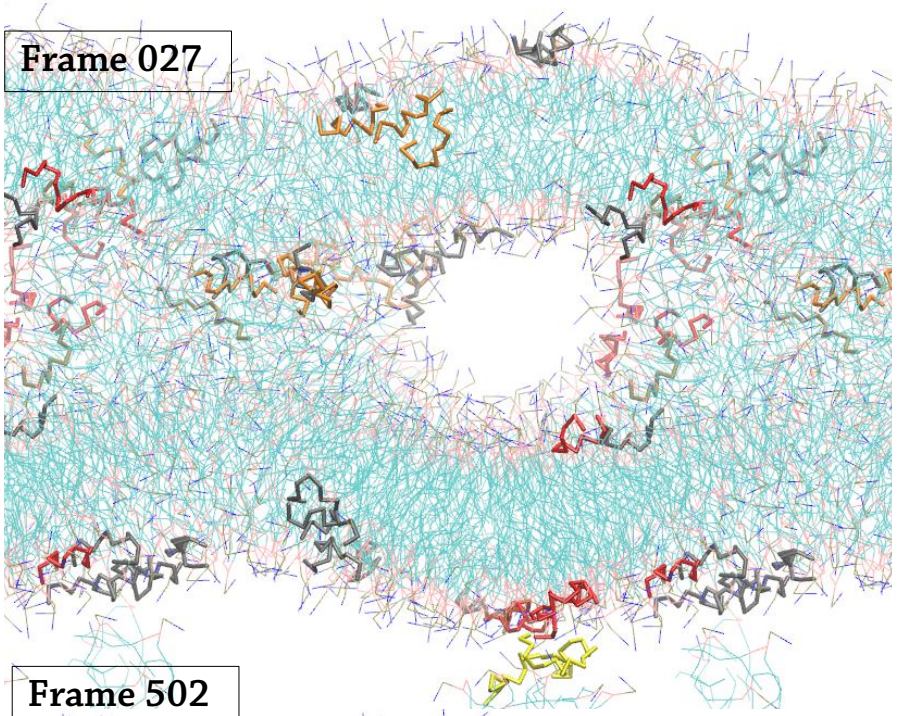
Maculatin: a curvature inducer?

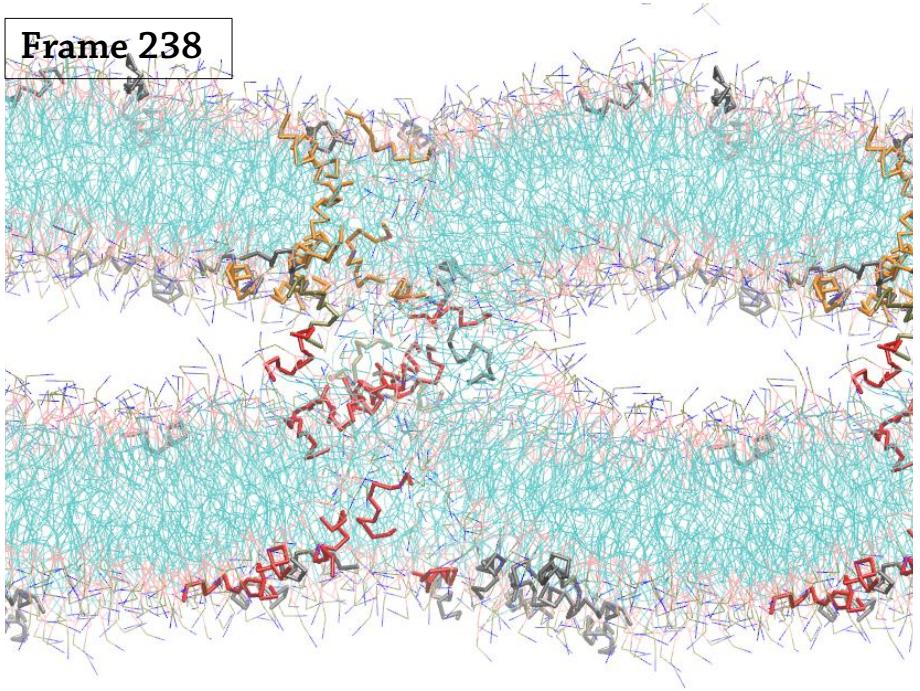


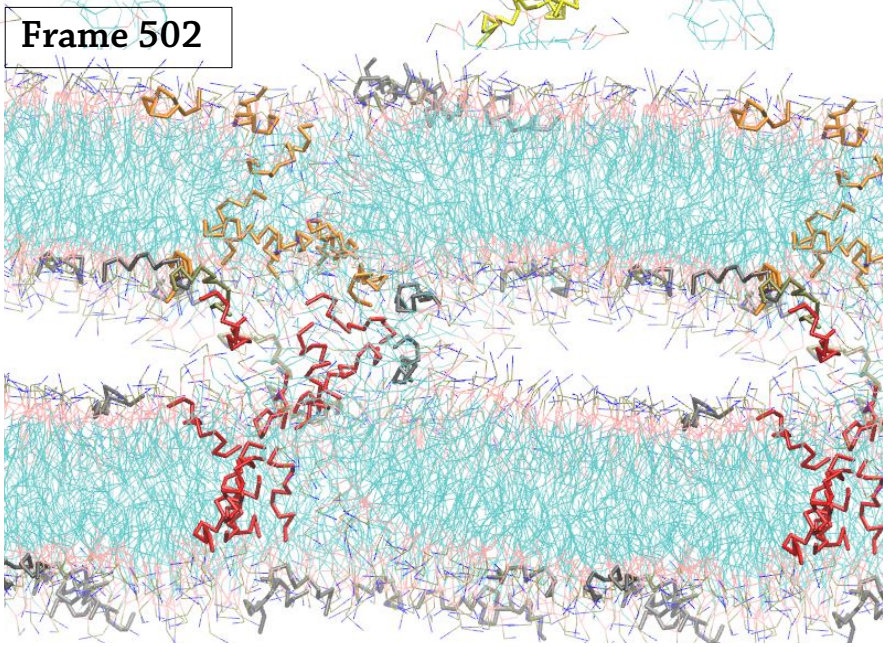
CI: 50PP/1000LL/PW/NaCl 0,15M. 1200 ns. NPT ensamble, 323 K, 1 bar . Martini FF

Self assembly essay with Aurein

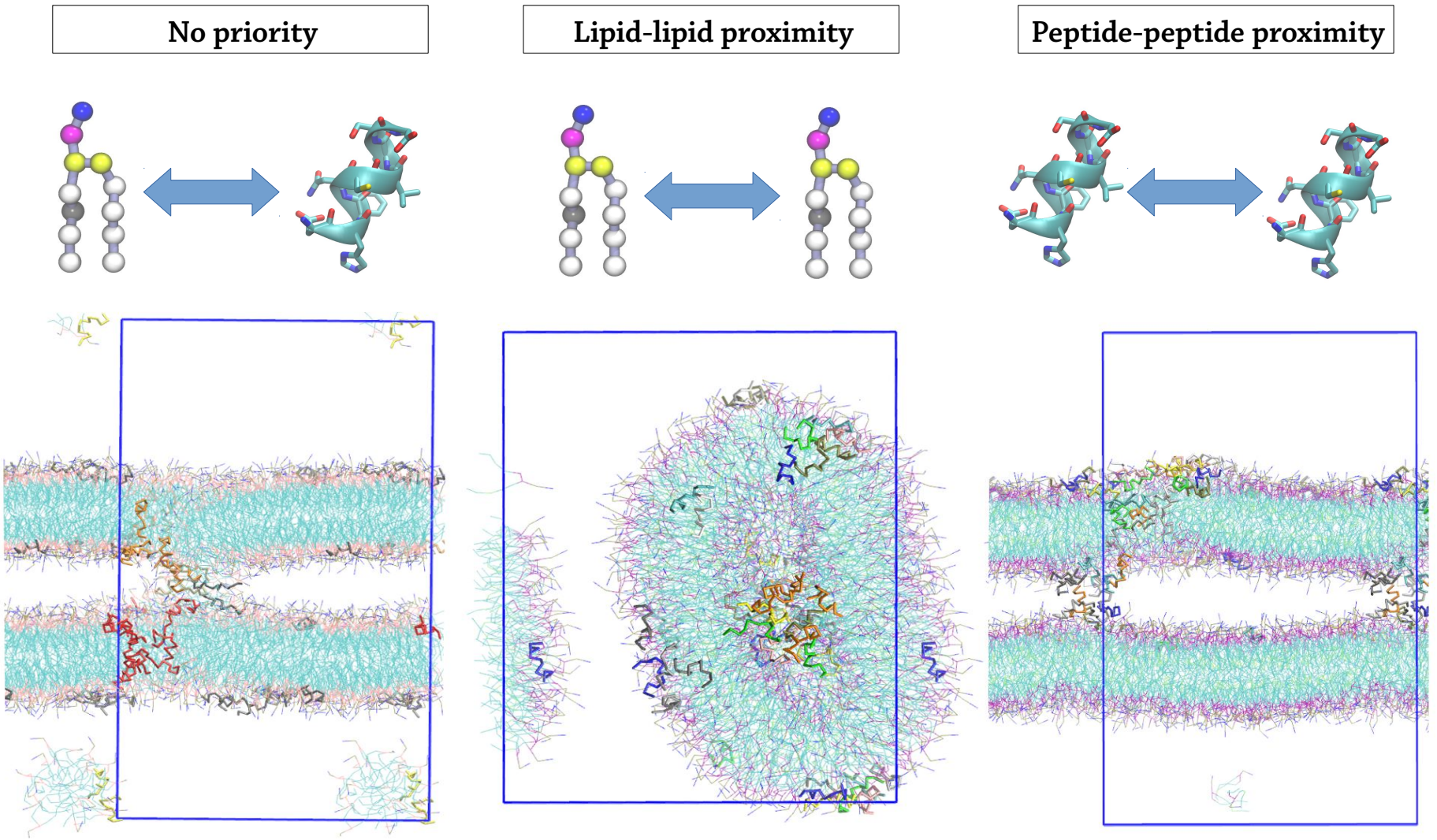




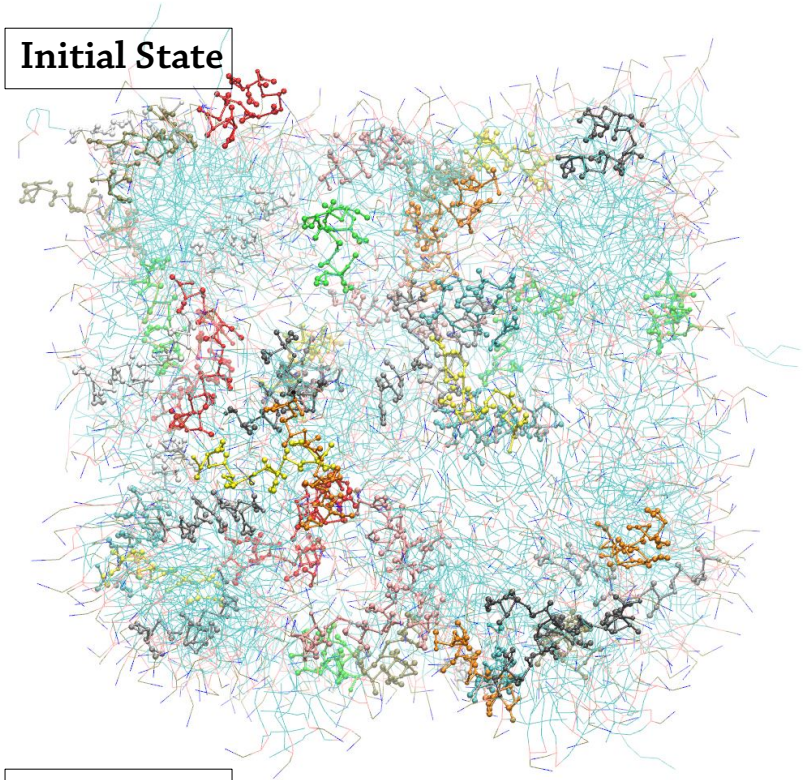


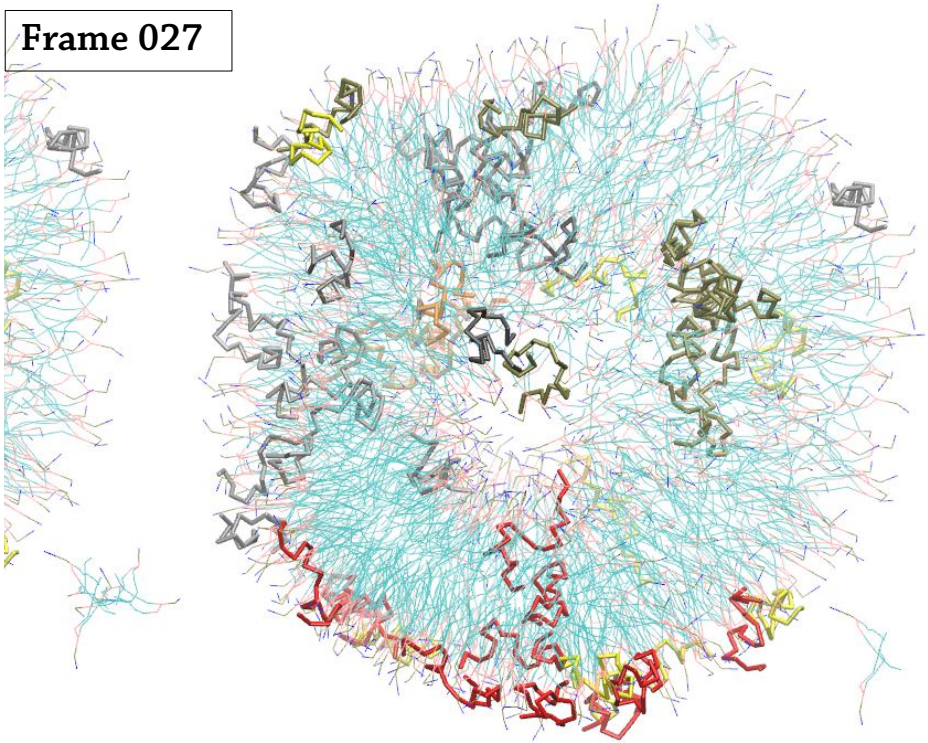


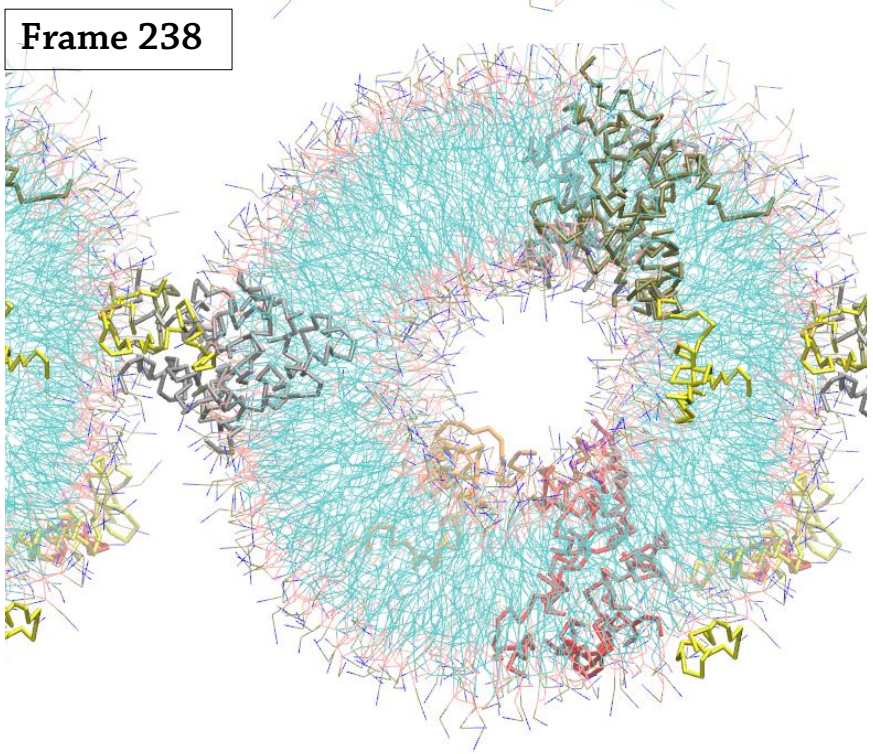
Self assembly from != initial conditions

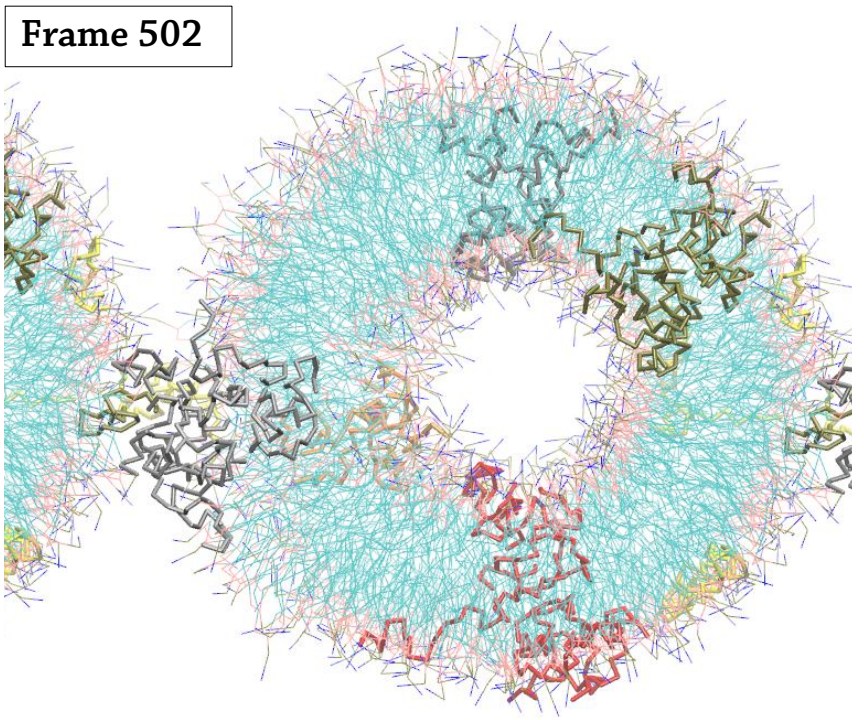


CI: 50PP/1000LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar .


Initial State

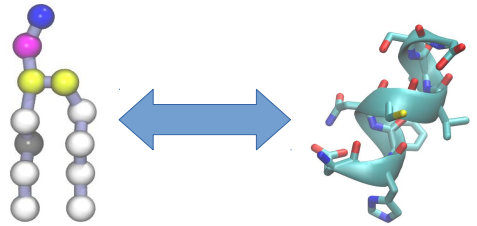

Frame 027


Frame 238

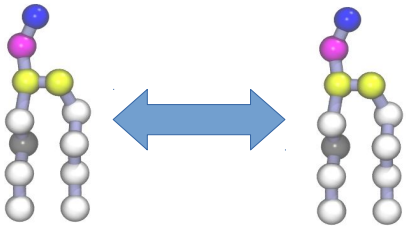

Frame 502

Self assembly from != initial conditions

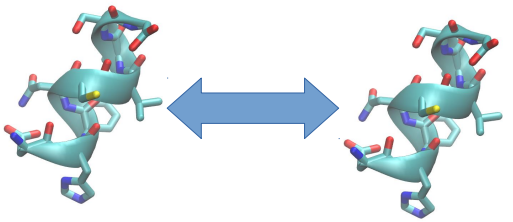
No priority

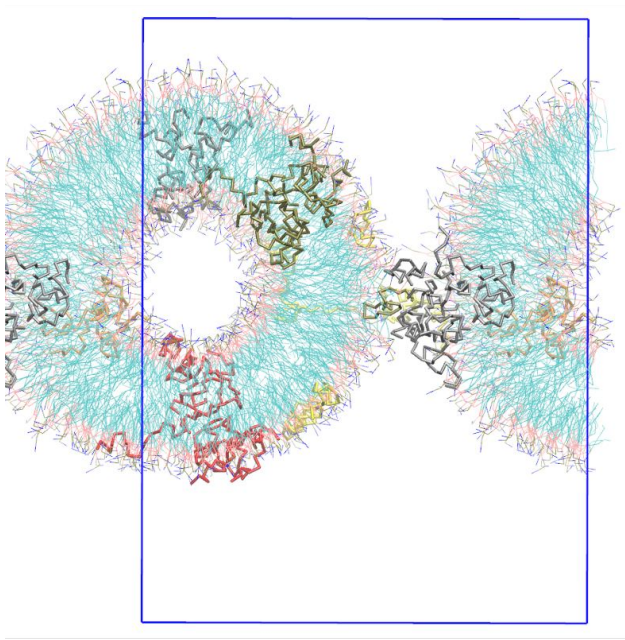


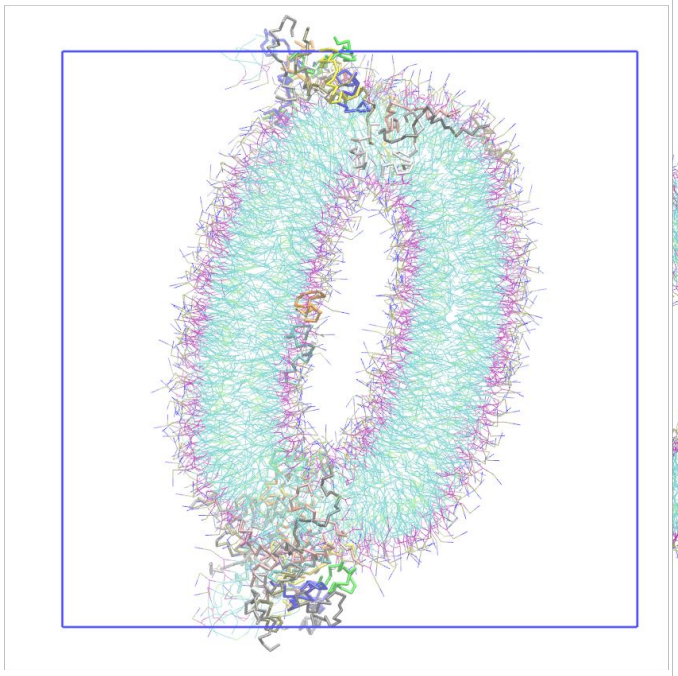
Lipid-lipid proximity

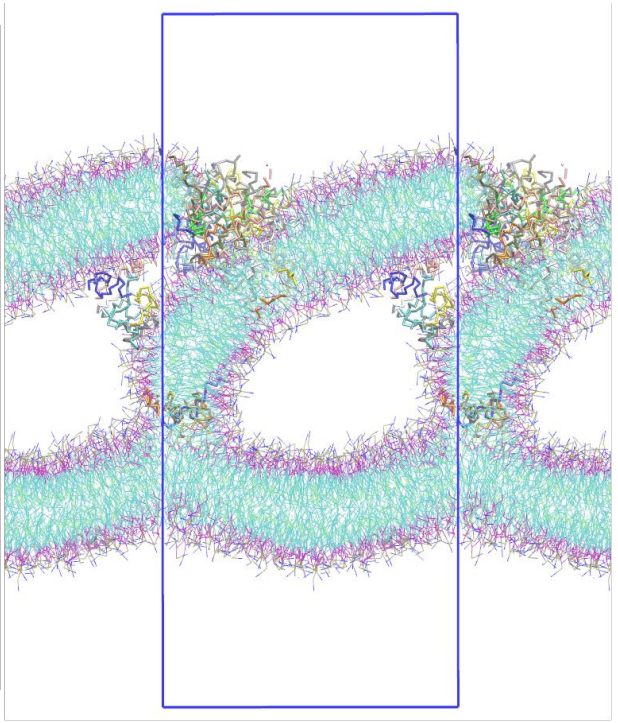


Peptide-peptide proximity





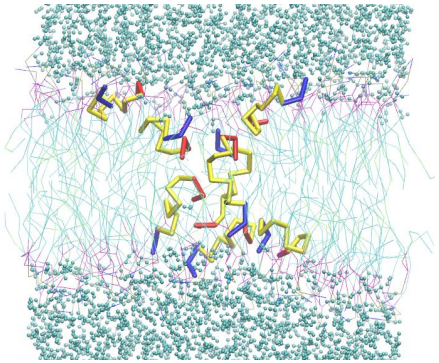




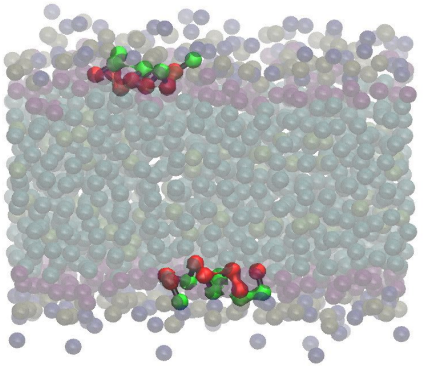
CI: 50PP/1000LL/PW/NaCl 0,15M. 1000 ns. NPT ensamble, 323 K, 1 bar .

Aurein remarks

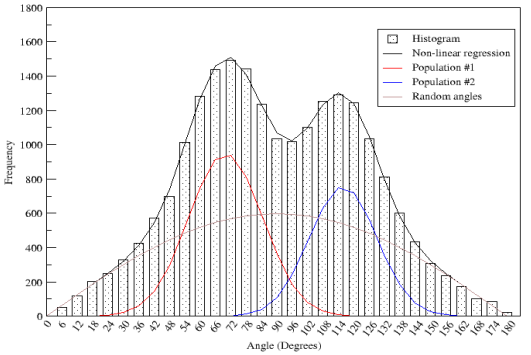
Aurein acts with a well defined orientation, with an **amphiphilic** behavior



NT/CT orientation

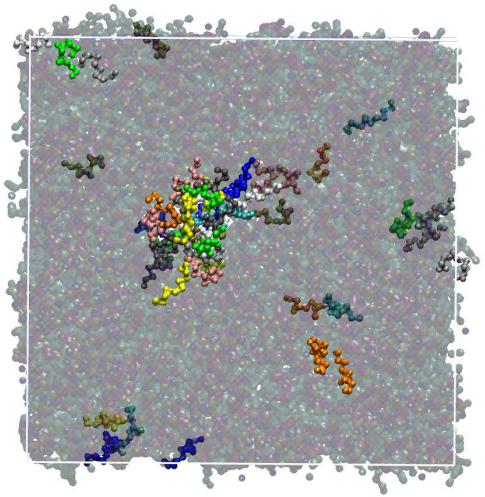


Facial orientation

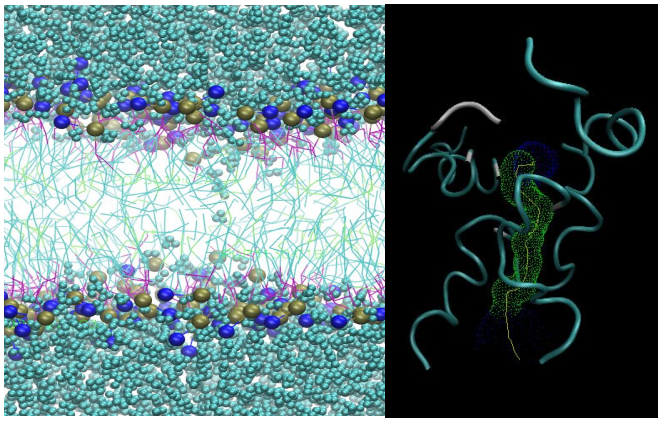


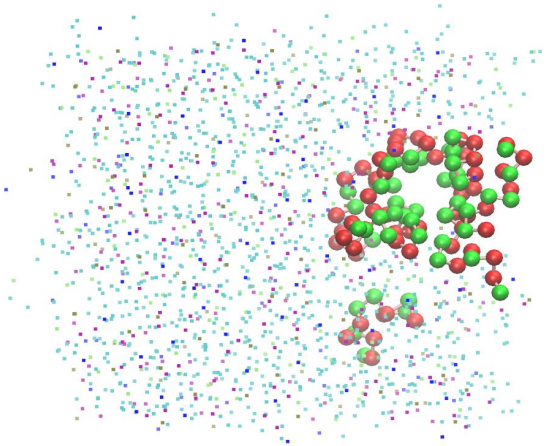
Tilt angle

Isolated molecules population



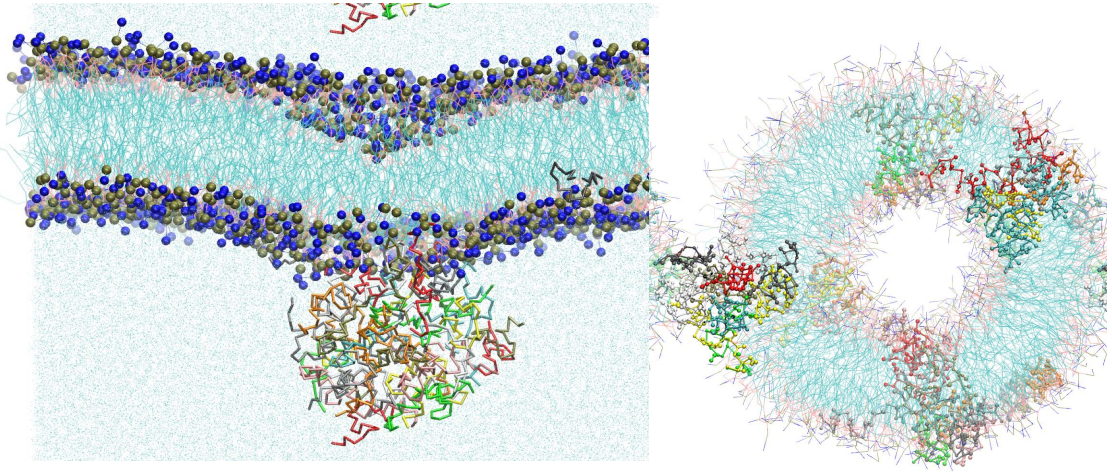
Pore structures conform a **hydrophilic channel**



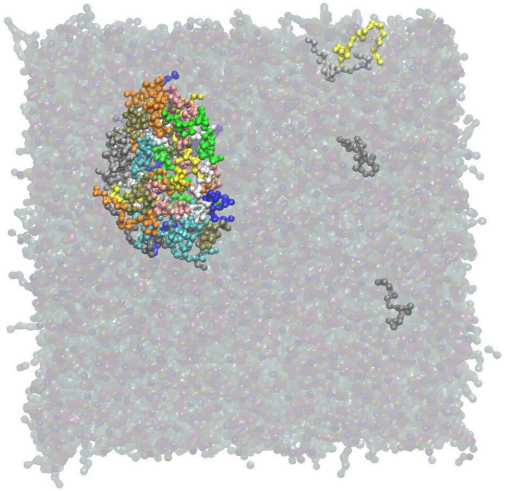


Maculatin remarks

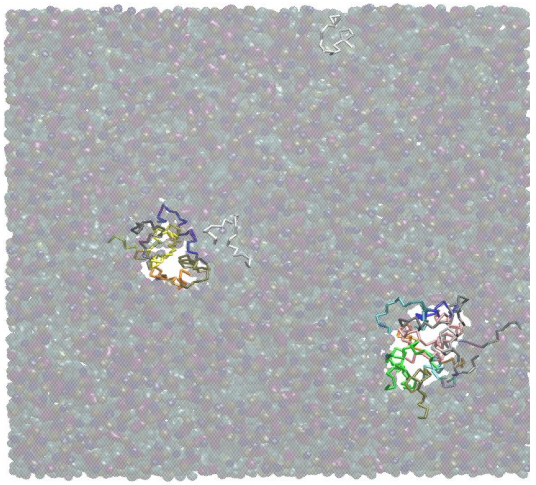
Maculatin **induces curvature** strongly

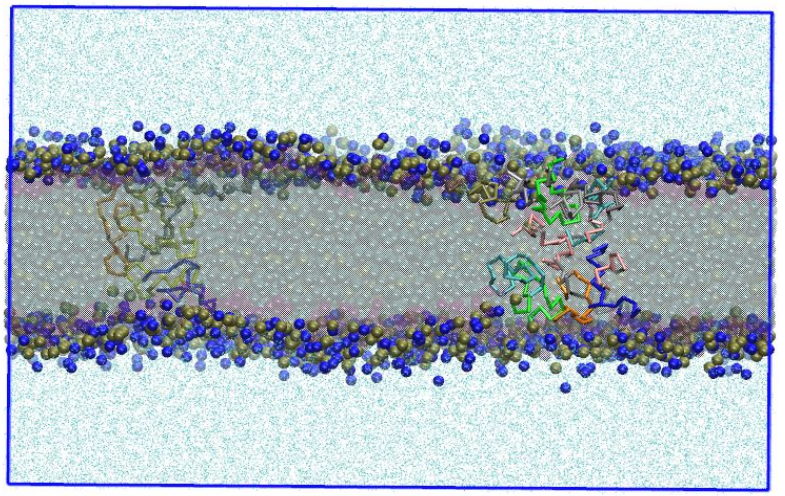


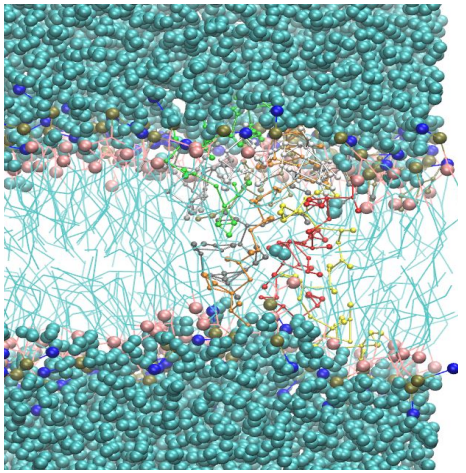
High tendency to **aggregation**



High **efficiency** in pore formation with lower water permeability







Prof. Mónica Pickholz
IFIBA INSTITUTE
University of Buenos Aires

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Dr. M. Florencia Martini
IQUIMEFA INSTITUTE
University of Buenos Aires
CONICET

Prof. Gerardo Fidelio
CIQUIBIC INSTITUTE
University of Córdoba

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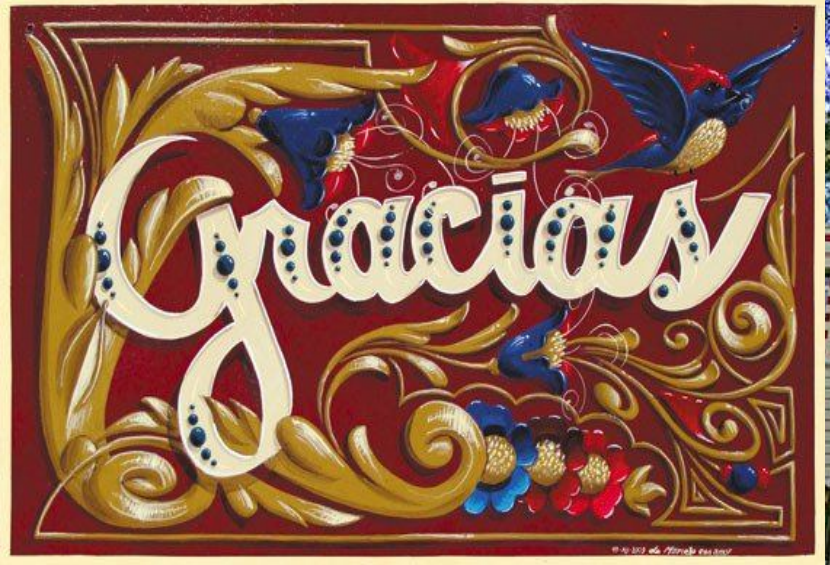
Gracias

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