MI·DNA DISC

Modeliranje elektroporacije membrana simulacijama molekulske dinamike

Simulation of pore formation in Lipid Bilayer by Mechanical Stress and Electric Fields

D. Peter Tielman, H. Leontiadou, A. E. Marko, Siewert Jan Marrink, *J. AM. CHEM. SOC*. **125** (2003) 6328-6383.

Kemijski seminar I, 4.16 2025.

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SADRŽAJ

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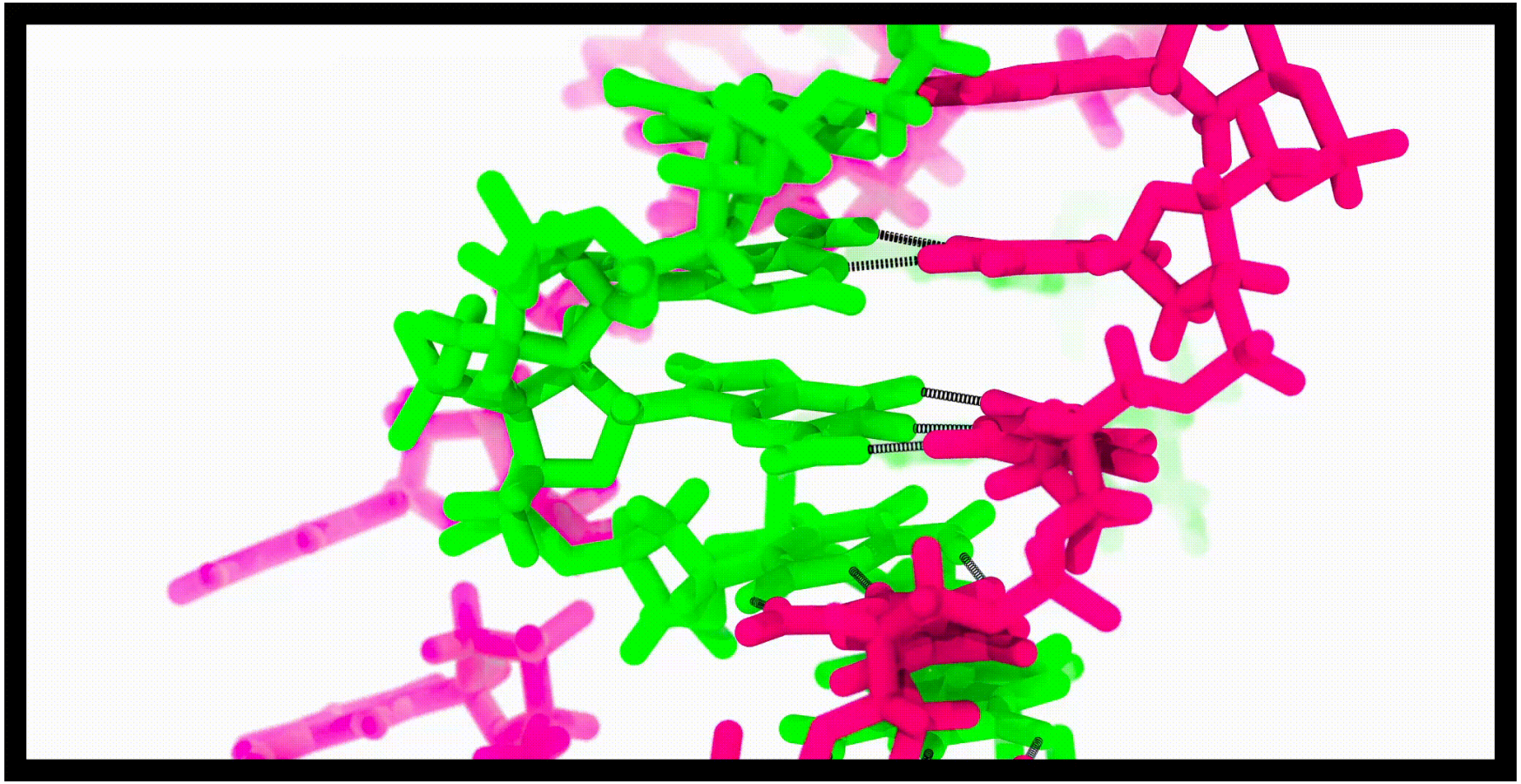
1.1 Simulacije molekulske dinamike

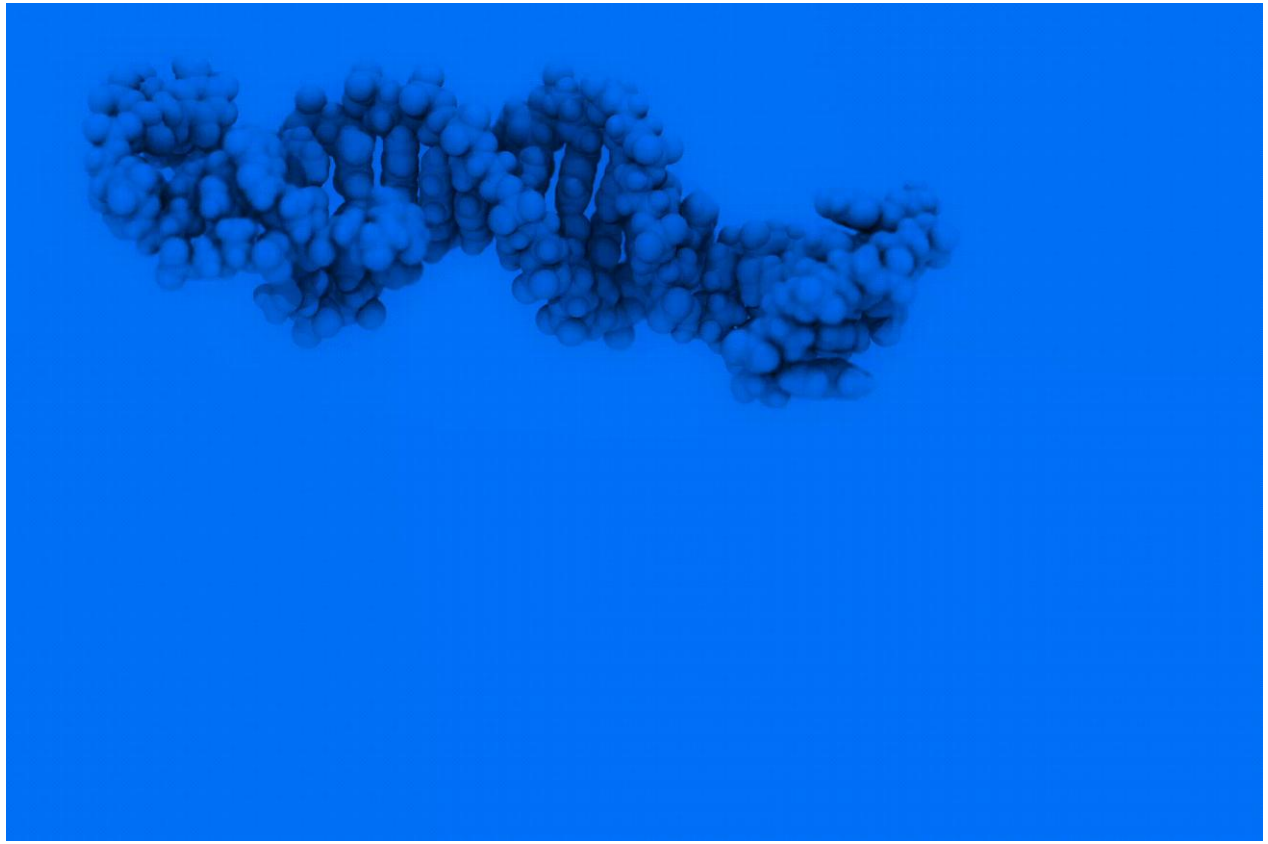


1.1 Simulacije molekulske dinamike

Tipovi simulacija

All atom (AA) – Simuliraju se svi atomi (slika). Svaki atom je svoja „kuglica”.

***Coarse Grained* (CG)** – Više atoma se aproksimira jednom kuglicom. Manje kuglica – manje stvari za računati.



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VALIDACIJA

Prije izvlačenja zaključaka, simulacije molekulske dinamike potrebno validirati usporedbom s eksperimentalnim rezultatima

2.0 PREGLED TEME

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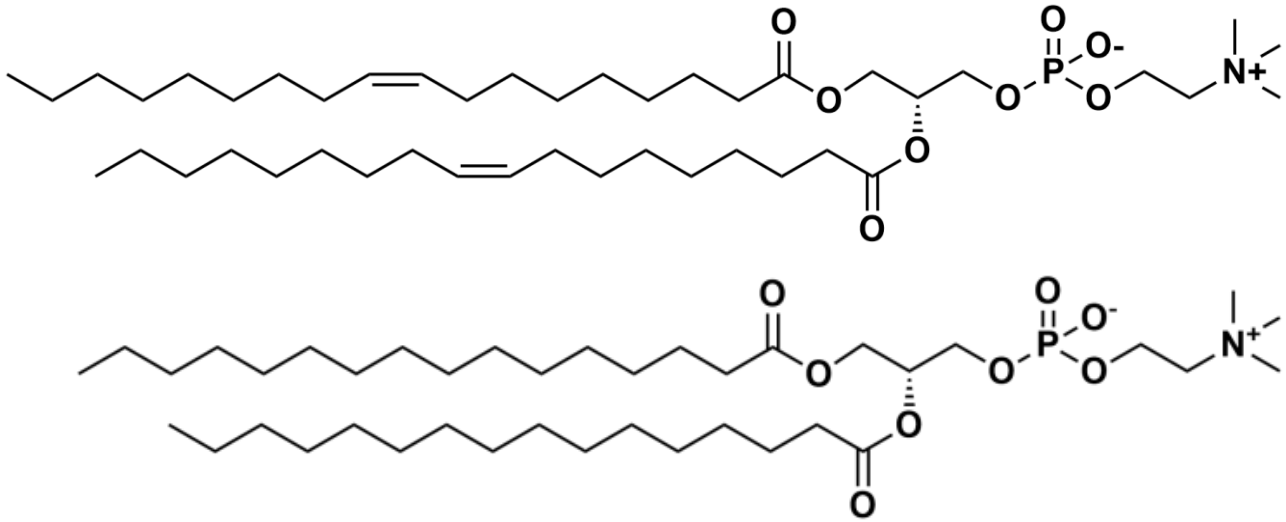
D. Peter Tielman, H. Leontiadou, A. E. Marko, Siewert Jan Marrink, J. *AM*. *CHEM*. *SOC*. **125** (2003) 6328-6383.

- Formacija pora uslijed djelovanja
  - Mehaničkog stresa
  - Vanjskog električnog polja

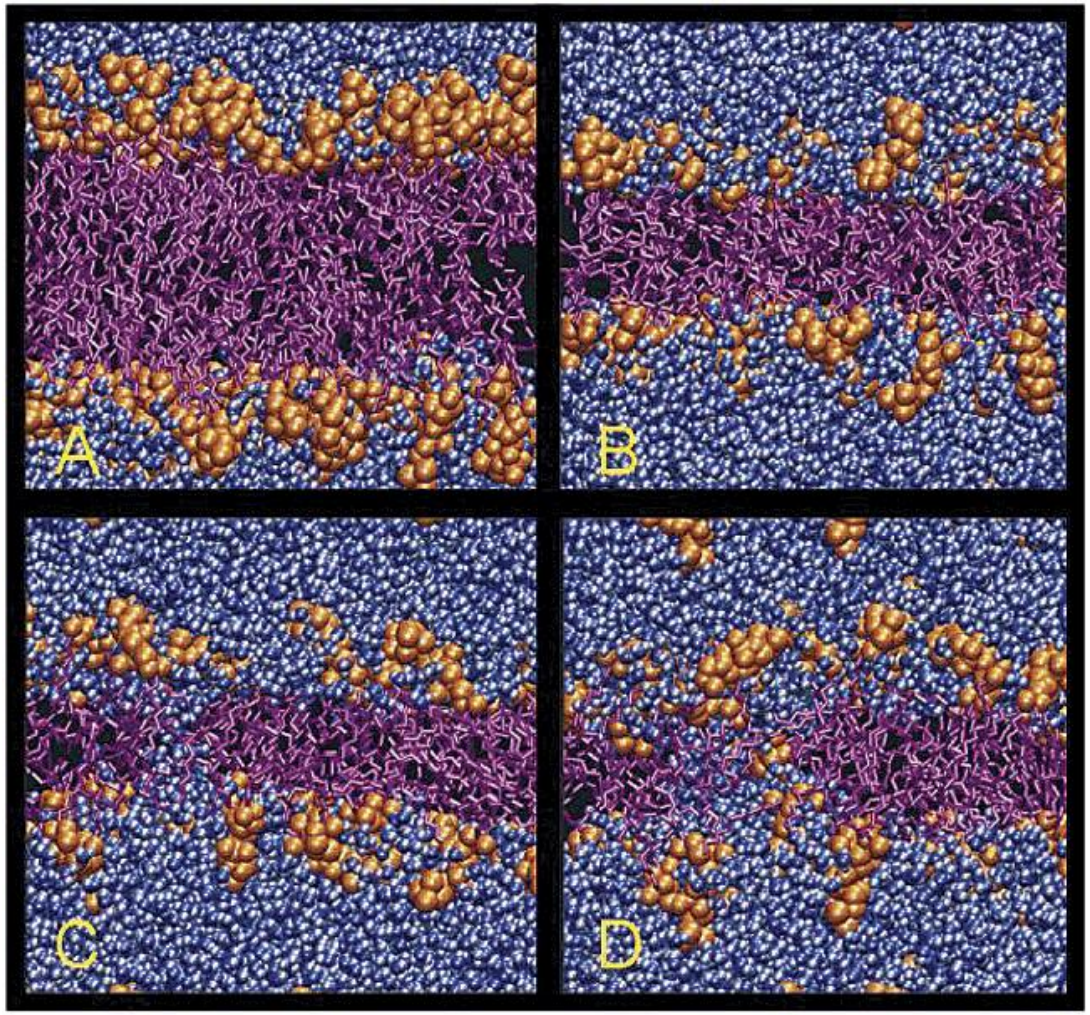
- DPPC i DOPC dvosloji



Fotografije preuzete s: https://www.polysciences.com/german/dppc (2025.3.31)

2.1 Mehanički stres

- Ukupno 128 DPPC lipida, 6029 molekula vode
- Temperatura od 323 K
- Anizotropan tlak, sistematski variran
- Simulacije do trajanja od 50 ns



REZULTATI:

Membrana se stanjuje
Formacija pore u prvih 4 do 12 ns
Raste površina po lipidu
Reorjentacija polarnih glava usred formacije predpore
Konačna destabilizacija membrane

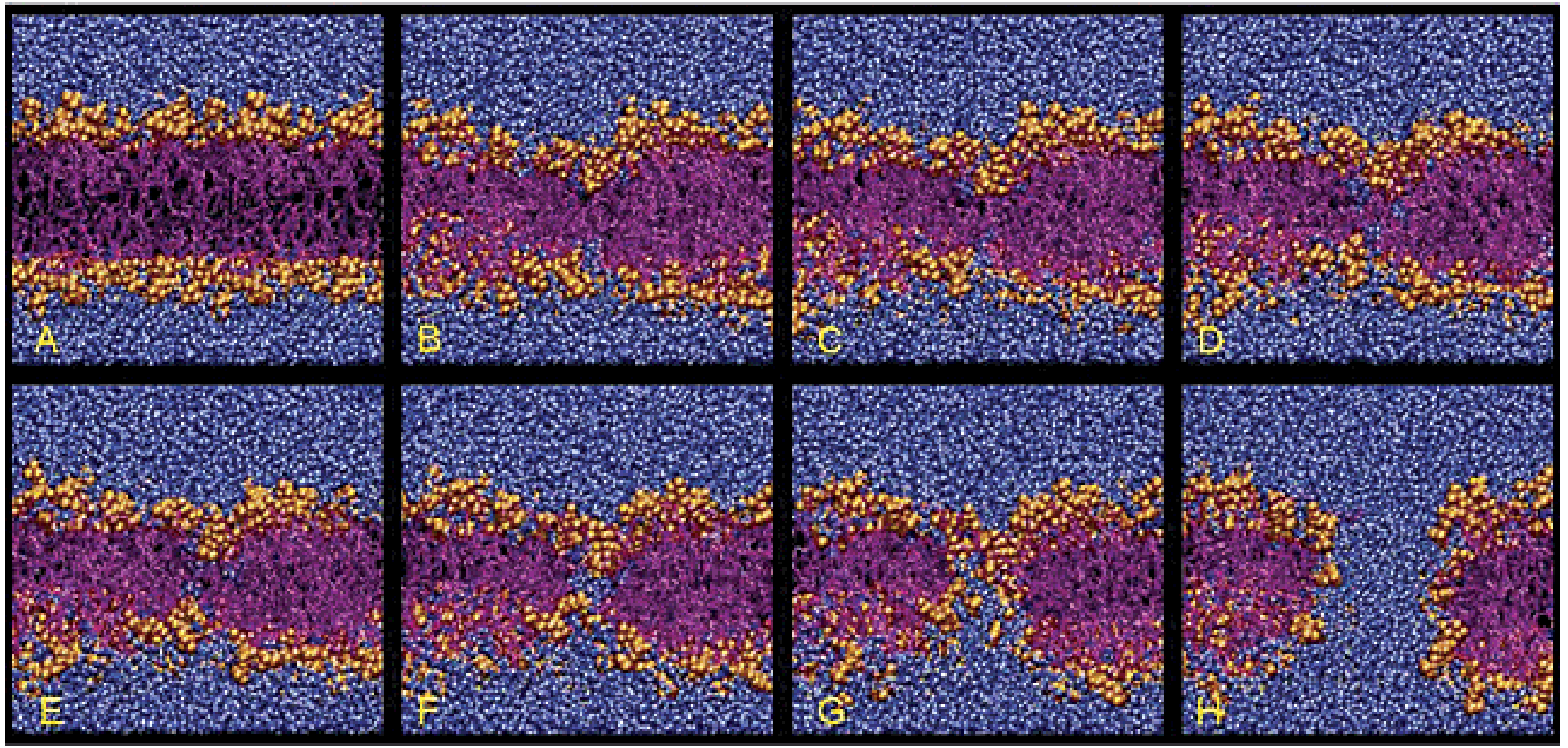
2.2 ELEKTRIČNO POLJE

- Ukupno 256 DOPC lipida
- 11 228 molekula voda
- Temperatura od 300 K
- Simulacije duljine 10 do 20 ns

- Električno polje od 0.33, 0.40, i 0.50 V / nm

2.2 ELEKTRIČNO POLJE

Kako unijeti nešto u DNA?



2.0 PREGLED TEME

U oba slučaja potrebno da se voda koja prodire u membranu spoji s obje strane
U oba slučaja dolazi do reorijentacije lipidnih glava

Mehanički stres:

Dolazi do stanjivanja membrane

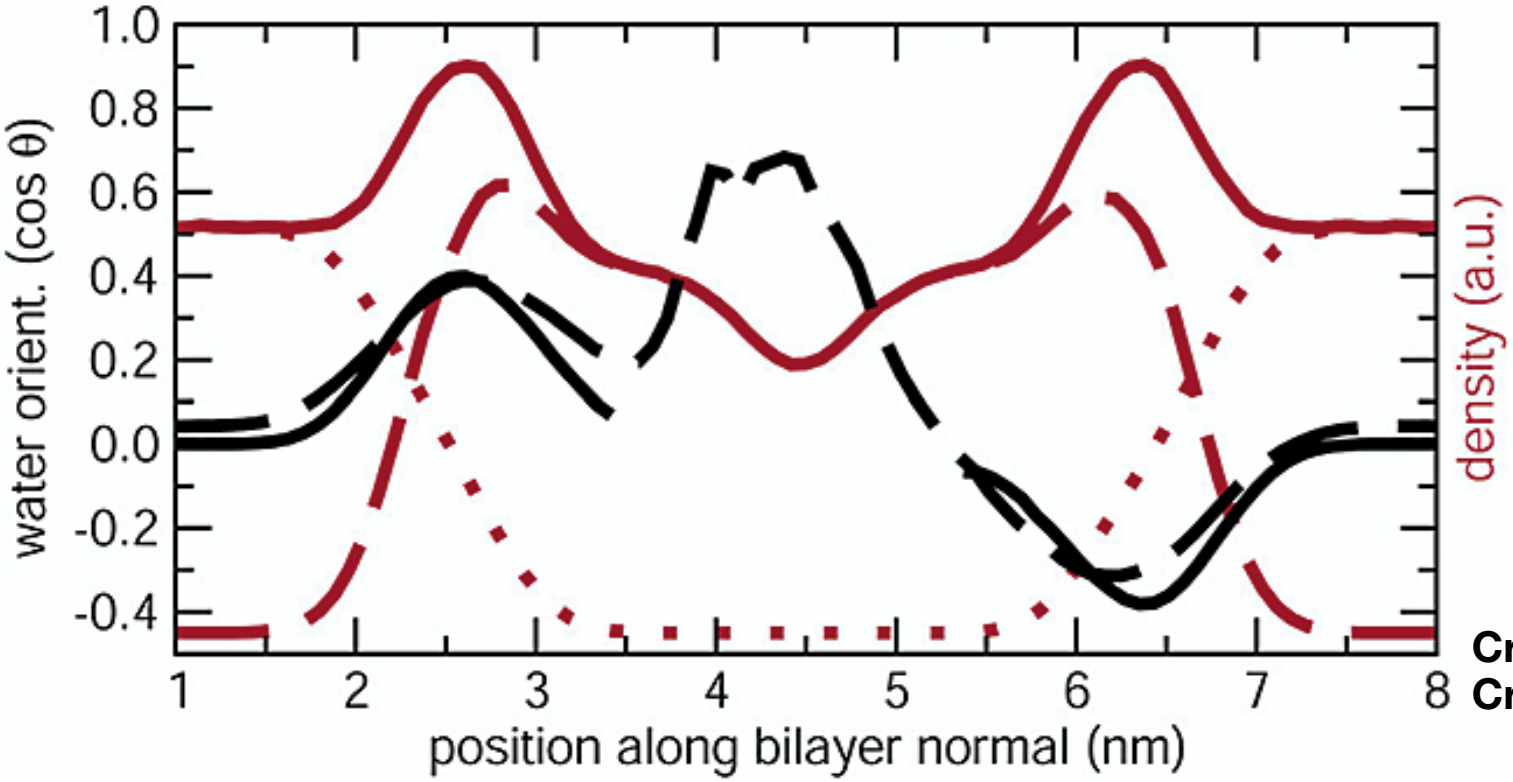
Električno polje:

Utječe na orijentaciju molekula vode

Molekule vode unutar predpore bivaju orjentirane

2.0 PREGLED TEME

Rezultati



Crno puno – Orijentacija voda prije el. Polja
Crno iscrtkano – Orijentacija voda nakon el. polja

Crveno puno – Distribucija svih specija
Crveno iscrtkao – Distribucija lipida
Crveno točkasto – Distribucija voda

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Prvi korak u formaciji pore je spajanje molekula vode koje prodiru u membranu s obje strane. Time se formira tzv. predpora. Slijedi brzo širenje predpore i reorijentacija fosfatnih glava, čime se formira zrela pora.

3.0 RETROSPEKTIVA RADA

Kako se polje razvija

„Obiteljsko stablo radova”

Simulation of pore formation in Lipid Bilayer by Mechanical Stress and Electric Fields
D. Peter Tielman, H. Leontiadou, A. E. Marko, Siewert Jan Marrink, *J. AM. CHEM. SOC.* **125** (2003) 6328-6383.

The molecular basis of electroporation
D. P. Tieleman, *BMC Biochemistry* **5** (2004) 12.

Membrane Electroporation: A molecular Dynamics Simulation
M. Tarek, *Biophysical Journal* **88** (2005) 4045 – 4053.

Molecular Dynamics Simulations of Lipid Membrane Electorporatino
L. Delmotte, M. Tarek, *J Membrane Biol* **245** (2012) 531-543.

Electroporation of archeal lipid membranes using MD simulations
A. Polak, M. Tarek, M. Tomšić, J. Valant, N. Polar Ulrih, A. Jamnik, P. Kramar, D. Miklavčić, *Biocelectrochemistry* **100** (2014) 18-26.

3.0 RETROSPEKTIVA RADA

Arhee (Arheje?)

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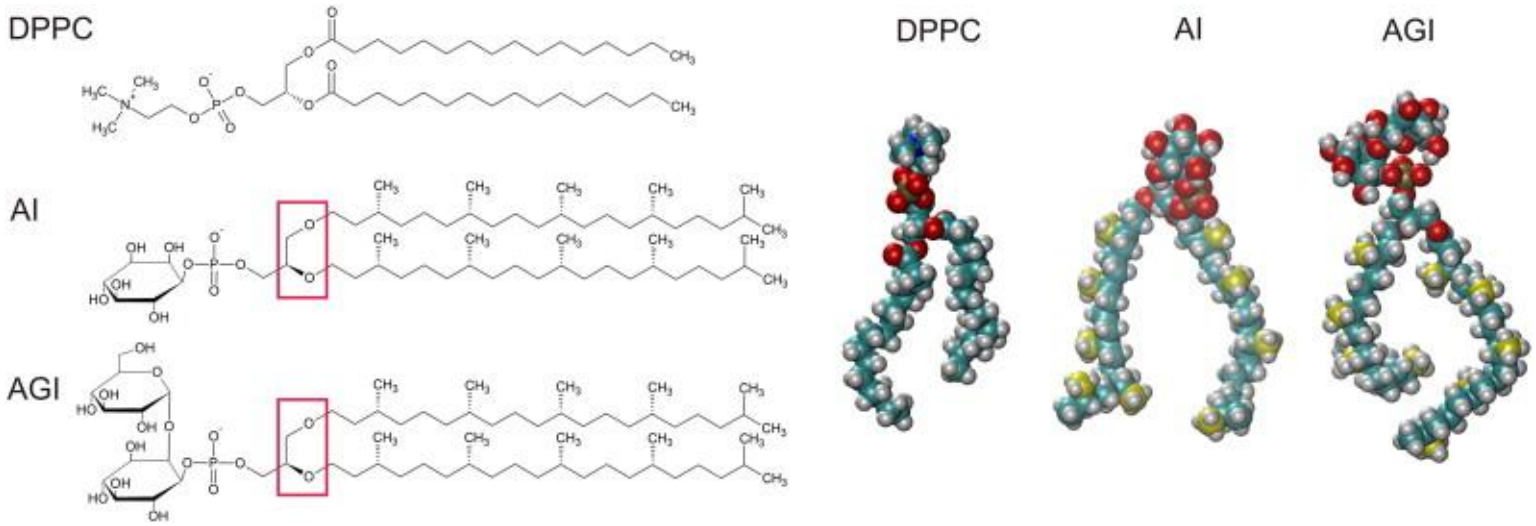
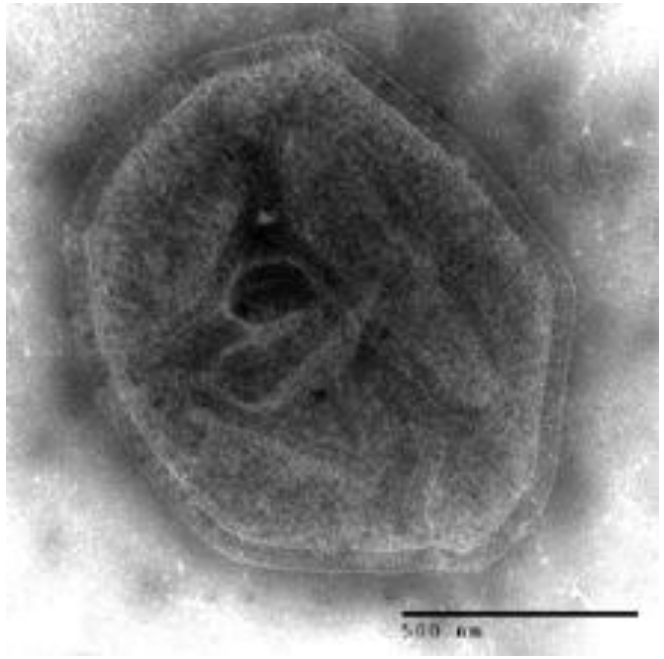


Aeropyrum pernix



Slike lijevo preuzeta iz rada navedenog u naslovu
Slika desno preuzeta s https://www.nite.go.jp/en/nbrc/genome/project/annotation/k1.html

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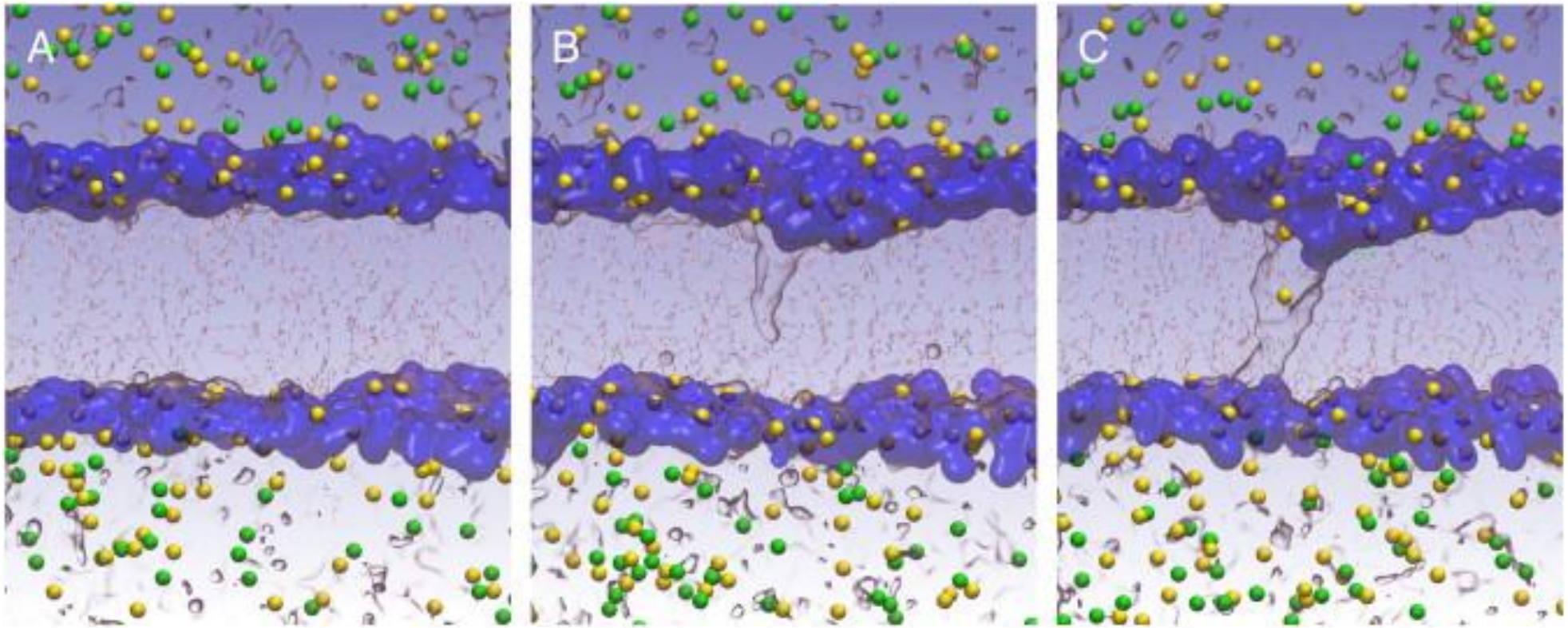

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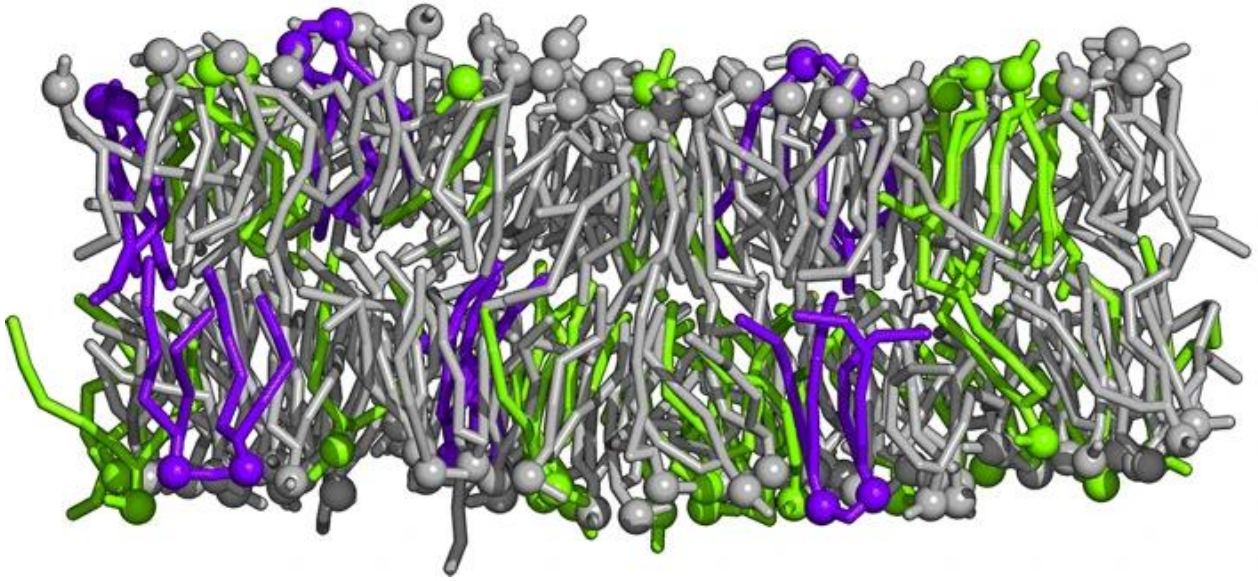
„We also showed that by mixing the archaeal lipids with phospholipids, one can lower their stability. Tuning in the electroporation threshold by lipid composition provides new routes for the design of liposomes composition that can be efficiently used as drug delivery carriers, and for which quantitatively monitored electroporation can serve for subsequent release of the drug when the carrier has reached proper location."

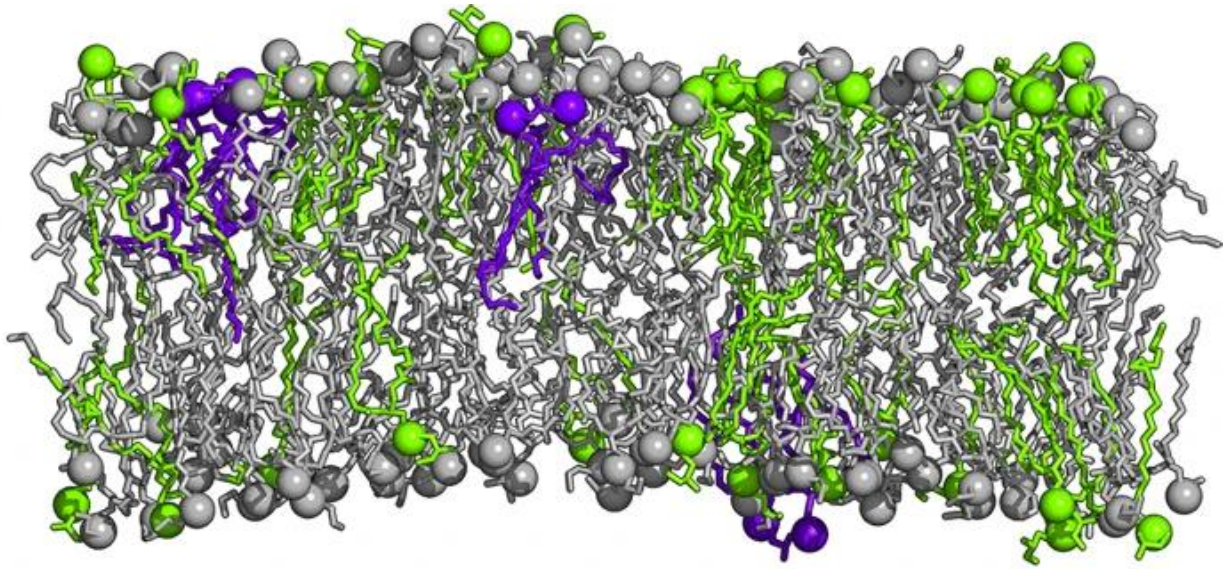
3.0 RETROSPEKTIVA RADA

A gdje idemo dalje?

Native-like membrane models of *E. coli* polar lipid extract shed light on the importance of lipid composition complexity

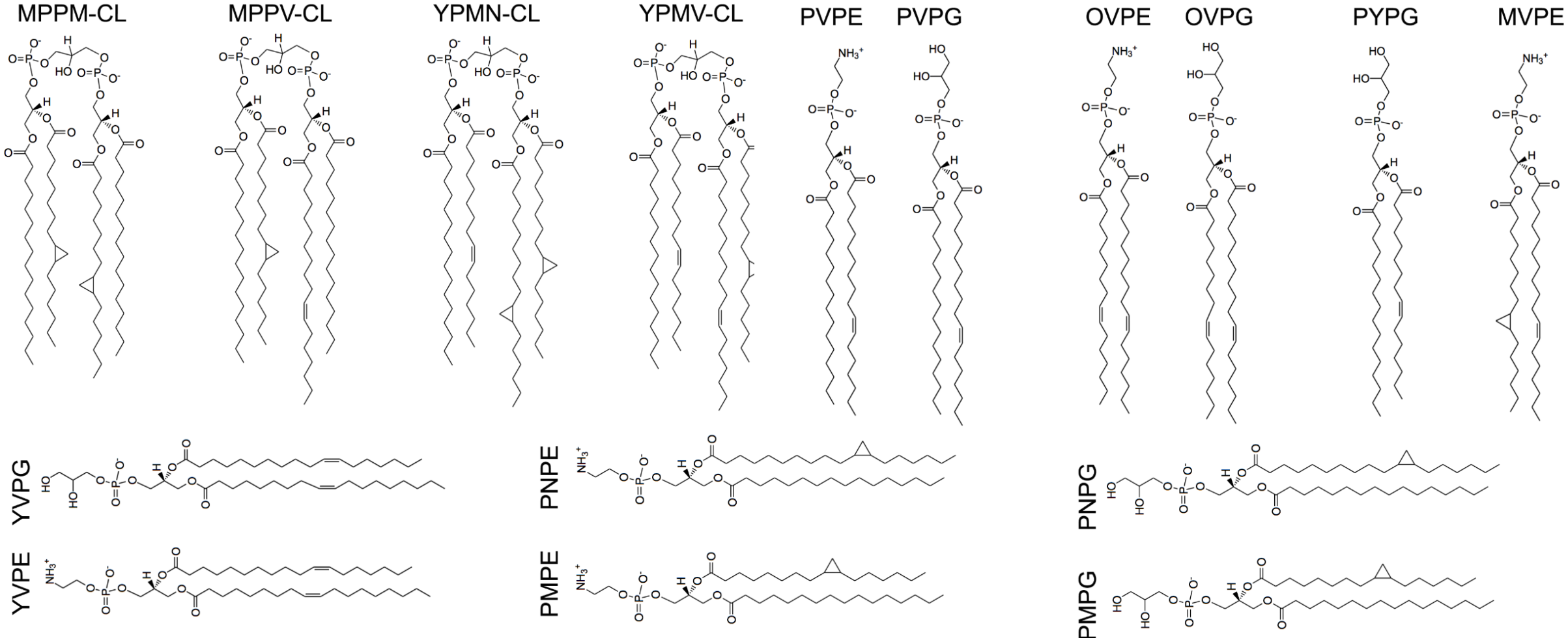
K. Pluhackova, A. Horner, *BMC Biology* (2021) **19:4**.

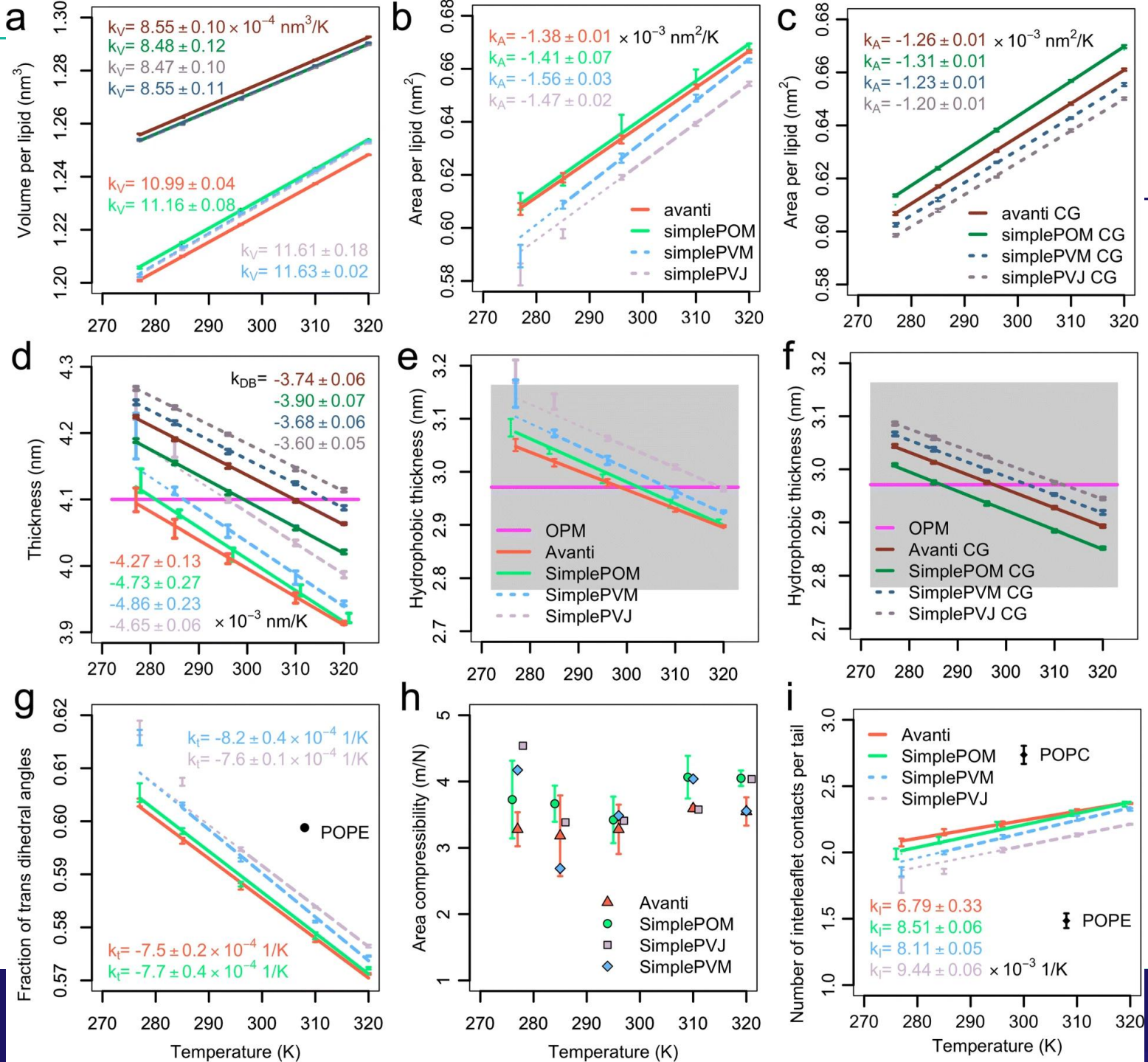




3.0 RETROSPEKTIVA RADA

Avanti membrane




a
Volume per lipid (nm³)
kV= 8.55 ± 0.10 × 10⁻⁴ nm³/K
kV= 8.48 ± 0.12
kV= 8.47 ± 0.10
kV= 8.55 ± 0.11
kV= 10.99 ± 0.04
kV= 11.16 ± 0.08
kV= 11.61 ± 0.18
kV= 11.63 ± 0.02
b
Area per lipid (nm²)
kA= -1.38 ± 0.01 × 10⁻³ nm²/K
kA= -1.41 ± 0.07
kA= -1.56 ± 0.03
kA= -1.47 ± 0.02
avanti
simplePOM
simplePVM
simplePVJ
c
Area per lipid (nm²)
kA= -1.26 ± 0.01 × 10⁻³ nm²/K
kA= -1.31 ± 0.01
kA= -1.23 ± 0.01
kA= -1.20 ± 0.01
avanti CG
simplePOM CG
simplePVM CG
simplePVJ CG
d
Thickness (nm)
kDB= -3.74 ± 0.06
-3.90 ± 0.07
-3.68 ± 0.06
-3.60 ± 0.05
-4.27 ± 0.13
-4.73 ± 0.27
-4.86 ± 0.23
-4.65 ± 0.06
× 10⁻³ nm/K
e
Hydrophobic thickness (nm)
OPM
Avanti
SimplePOM
SimplePVM
SimplePVJ
f
Hydrophobic thickness (nm)
OPM
Avanti CG
SimplePOM CG
SimplePVM CG
SimplePVJ CG
g
Fraction of trans dihedral angles
kt= -8.2 ± 0.4 × 10⁻⁴ 1/K
kt= -7.6 ± 0.1 × 10⁻⁴ 1/K
POPE
kt= -7.5 ± 0.2 × 10⁻⁴ 1/K
kt= -7.7 ± 0.4 × 10⁻⁴ 1/K
Temperature (K)
h
Area compressibility (m/N)
Avanti
SimplePOM
SimplePVJ
SimplePVM
Temperature (K)
i
Number of interleaflet contacts per tail
Avanti
SimplePOM
SimplePVM
SimplePVJ
POPC
kl= 6.79 ± 0.33
kl= 8.51 ± 0.06
kl= 8.11 ± 0.05
kl= 9.44 ± 0.06 × 10⁻³ 1/K
POPE
Temperature (K)

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Autori navode dobro slaganje rezultata njihovog modela s eksperimentalnim rezultatima, i u slučaju AA i u slučaju CG modela.

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Zaključno…

Polja sila – bolja nego ikada

Modeli membrana – bolji nego ikada

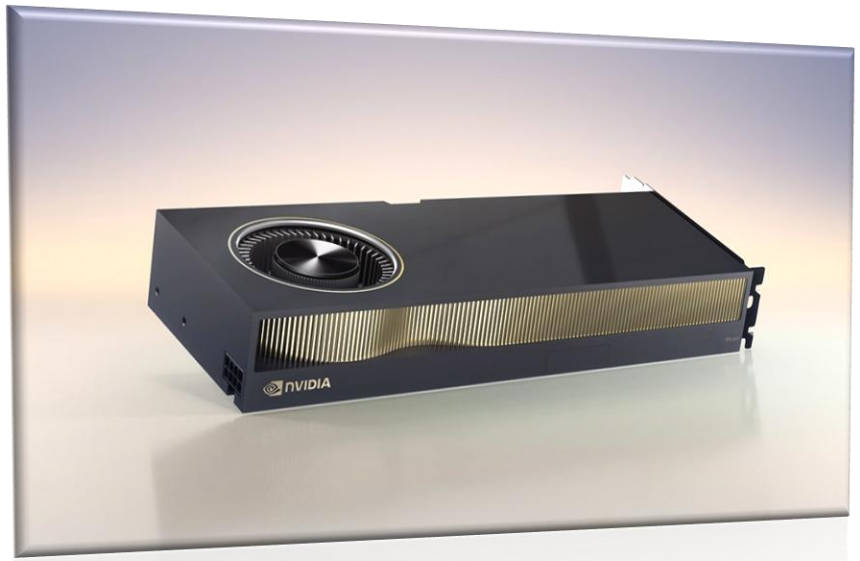
CG modeli – bolji nego ikada

Računalni resursi – bolji nego ikada

New MDS Workstation

Lenovo ThinkStation PX

3x NVIDIA RTX 6000 Ada



New MDS Workstation

~50 000 €

Lenovo ThinkStation PX

3x NVIDIA RTX 6000 Ada

~28 kg

SAGRAĐEN SPECIFIČNO ZA MD

FINANCIRANO SREDSTVIMA EUROPSKE UNIJE 🙏 🙏

Grant Agreement 101115215

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-- Hvala na poroznosti --

= Q & A =

www.midnadisc.eu

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