Molecular Dynamics

Lipid-Peptide Interactions

Kevin Majewski

Outline

- Molecular Simulations
- Forces Behind it
- The System
- Results

Molecular Simulations

GROMACS – Simulation Program

University of Groningen

Groningen, Netherlands

Use Newton Based Mechanics

Forces/Energy

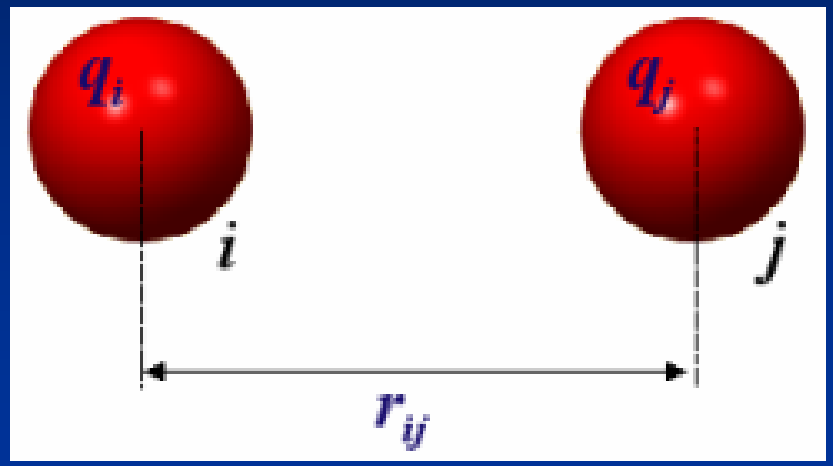
- Electro-Static (Non-Bonded Atoms)
- Van der Waals (Non-Bonded Atoms)
- Bond Stretching (Bonded Atoms)
- Bond Angles (Bonded Atoms)
- Proper Dihedrals (Bonded Atoms)
- Improper Dihedrals (Bonded Atoms)

Forces & Energy (Non-Bonded Atoms)

Electro Static (Coulomb) Interaction

$$\mathbf{F}_i = -\nabla_i V_B$$

$$U_{\mathrm{E}} = \frac{q_1 q_2}{4\pi\epsilon_0 r}$$



$$F = \frac{Q_1 Q_2}{4\pi\varepsilon_0 r^2},$$

Forces/Energy (Non-Bonded Atoms)

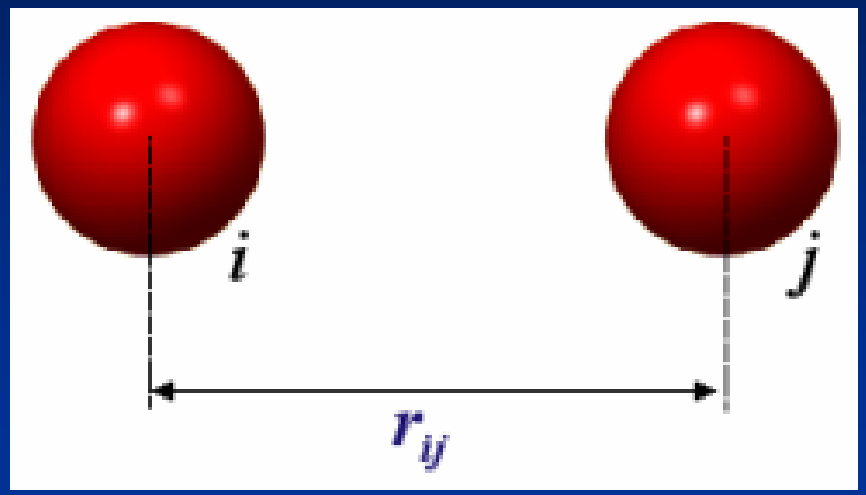
Van der Waals Interaction

Lennard-Jones Potential

$$V_{vdW} = 4\,\epsilon_{ij}\left(\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right)$$

$$\sigma_{ij} = \frac{1}{2}\left(\sigma_{ii} + \sigma_{jj}\right)$$

$$\epsilon_{ij} = \sqrt{\epsilon_{ii}\epsilon_{jj}}$$

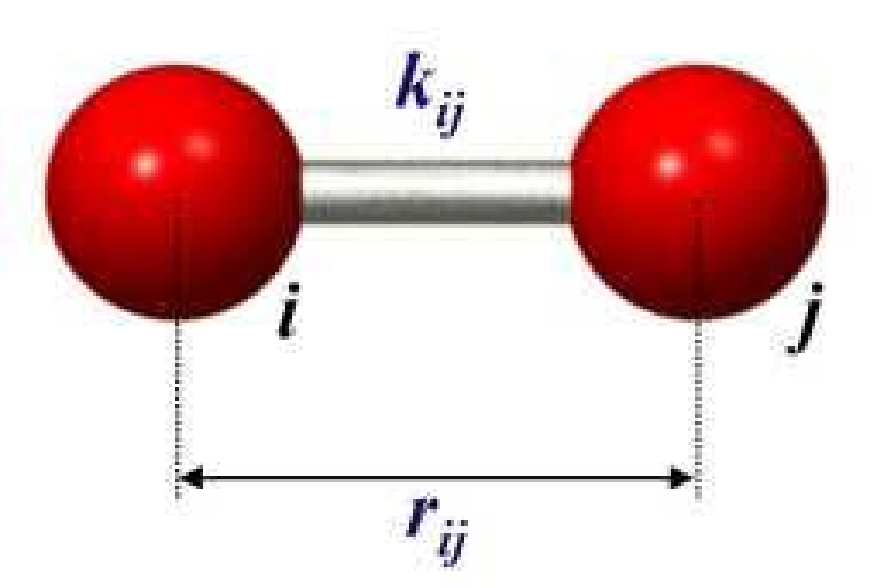


$$\mathbf{F}_i = \frac{48\,\epsilon_{ij}}{r_{ij}^2}\left(\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \frac{1}{2}\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right)\mathbf{r}_{ij}$$

Forces/Energy (Bonded Atoms)
Bond Stretching (Harmonic)

$$V_B = k_{ij}\left(r_{ij} - r_0\right)^2$$

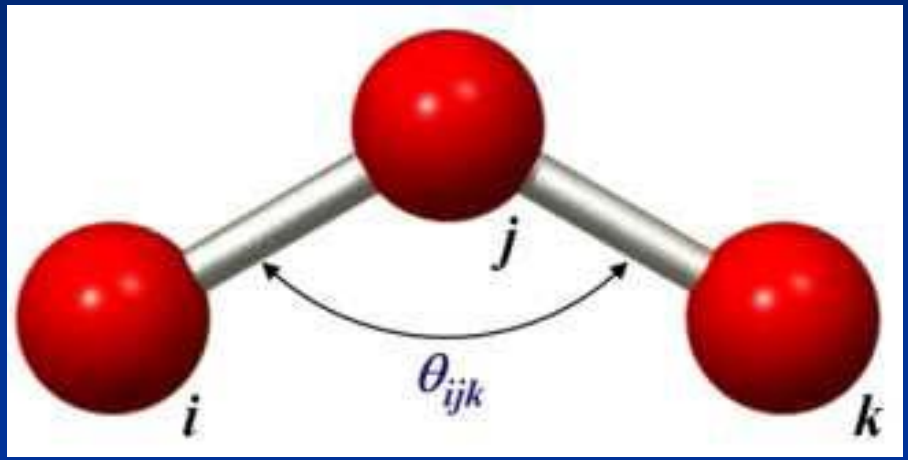
$$\mathbf{F}_i = -2k_{ij}\left(r_{ij} - r_0\right)\frac{\mathbf{r}_{ij}}{r_{ij}}$$



Forces/Energy (Bonded Atoms)
Bond Angles (Harmonic)

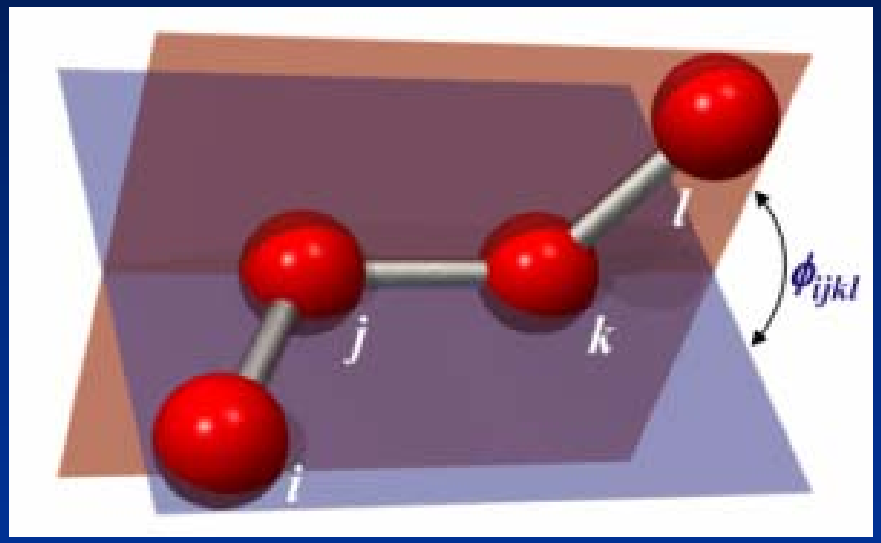
$$V_A = k_{ijk}^H \left(\theta_{ijk} - \theta_0\right)^2$$

$$\mathbf{F}_i = -\nabla_i V_A = -\frac{\partial V_A}{\partial \cos\theta_{ijk}} \frac{\partial \cos\theta_{ijk}}{\partial \mathbf{r}_i}$$



Forces/Energy (Bonded Atoms)
Proper Dihedrals (Staggered/Eclipsed)

$$V_D = k^C_{ijkl}\left(1 + \cos\left(n_{ijkl}\phi_{ijkl} - \phi_0\right)\right)$$

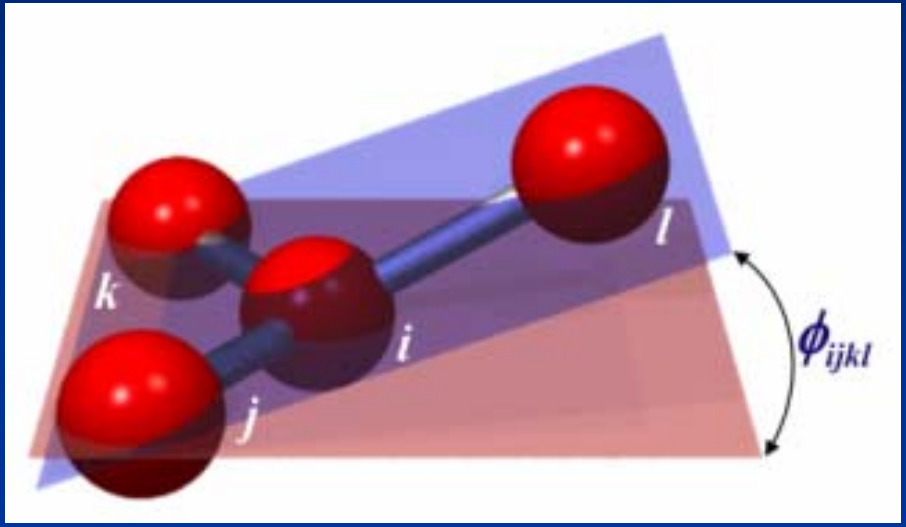


$$\mathbf{F}_i = -\nabla_i V_D = -\frac{\partial V_D}{\partial \phi_{ijkl}} \frac{\partial \phi_{ijkl}}{\partial \mathbf{r}_i}$$

Forces/Energy (Bonded Atoms)
Improper Dihedrals

$$V_I = k_{ijkl}\left(\phi_{ijkl} - \phi_0\right)^2$$

$$\mathbf{F}_i = -\nabla_i V_D = -\frac{\partial V_D}{\partial \phi_{ijkl}} \frac{\partial \phi_{ijkl}}{\partial \mathbf{r}_i}$$



The System

Lipid

1 Peptide ~120ns 2 Peptides ~200ns

Size ~ 28,000 Atoms
(far too large for QM~4)

Image of Lipid

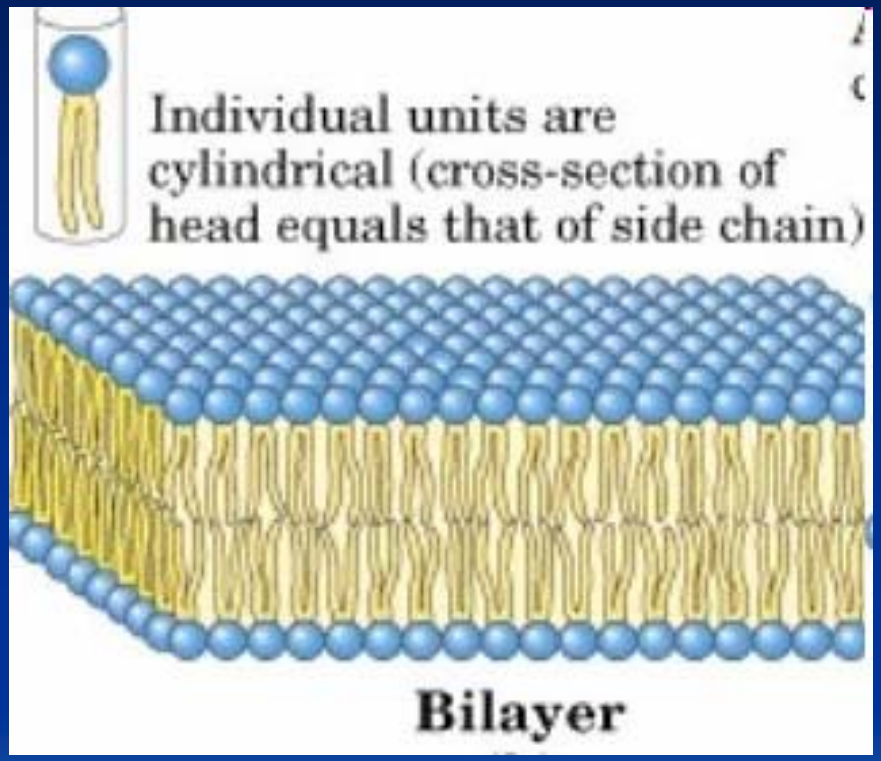
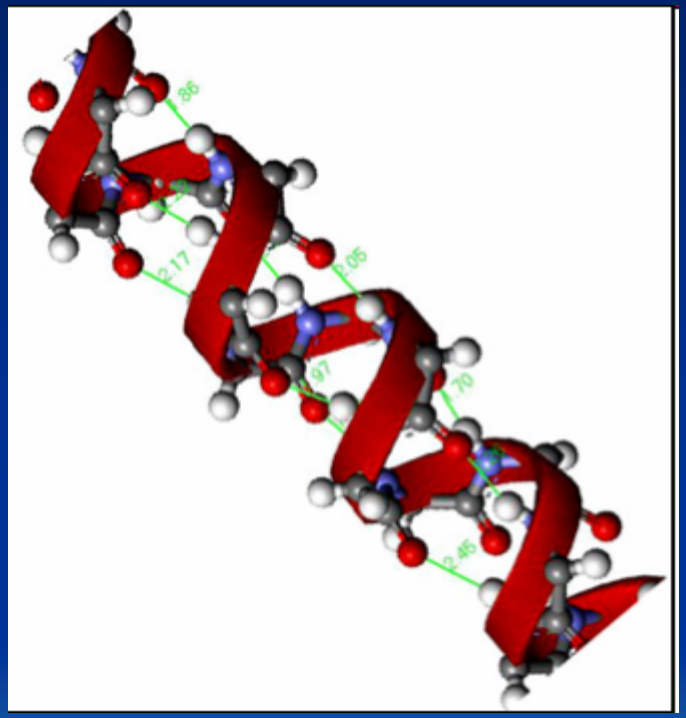
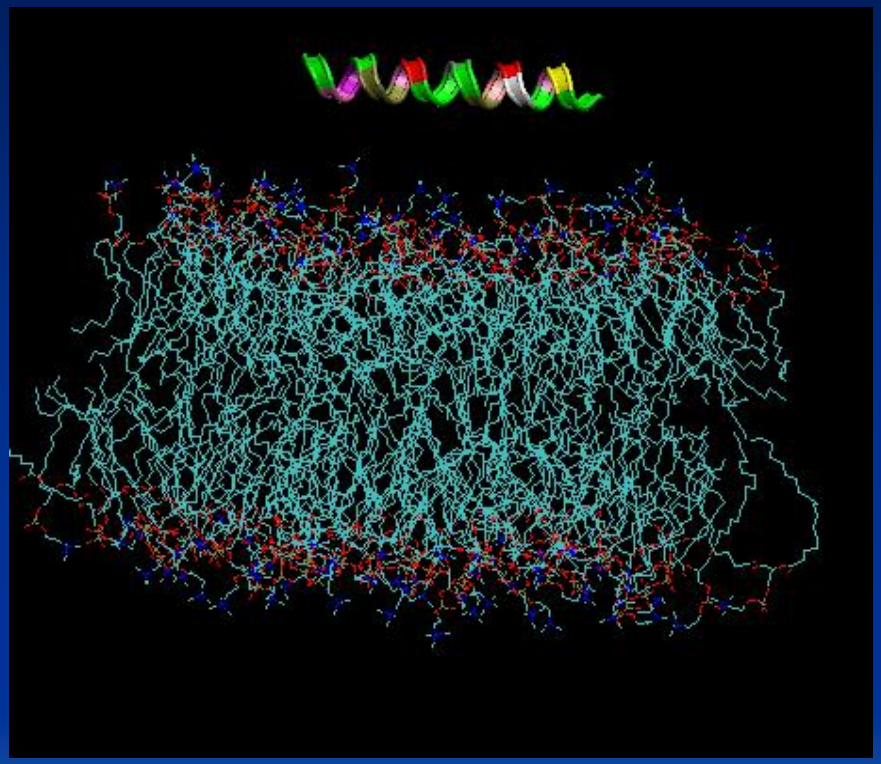


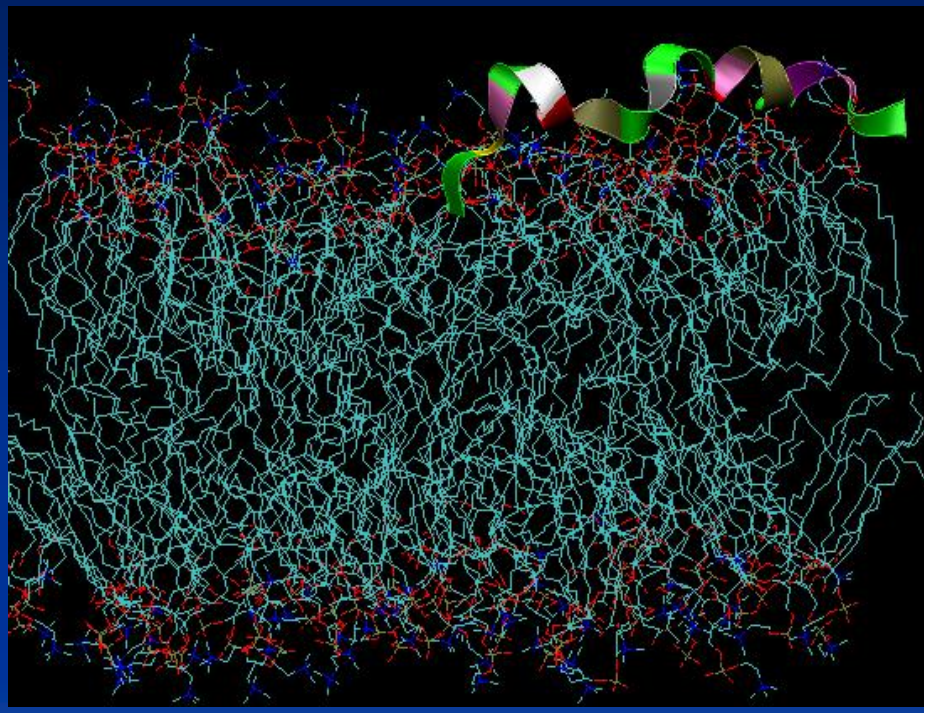
Image Peptide



System 1 Peptide (Time Scale)

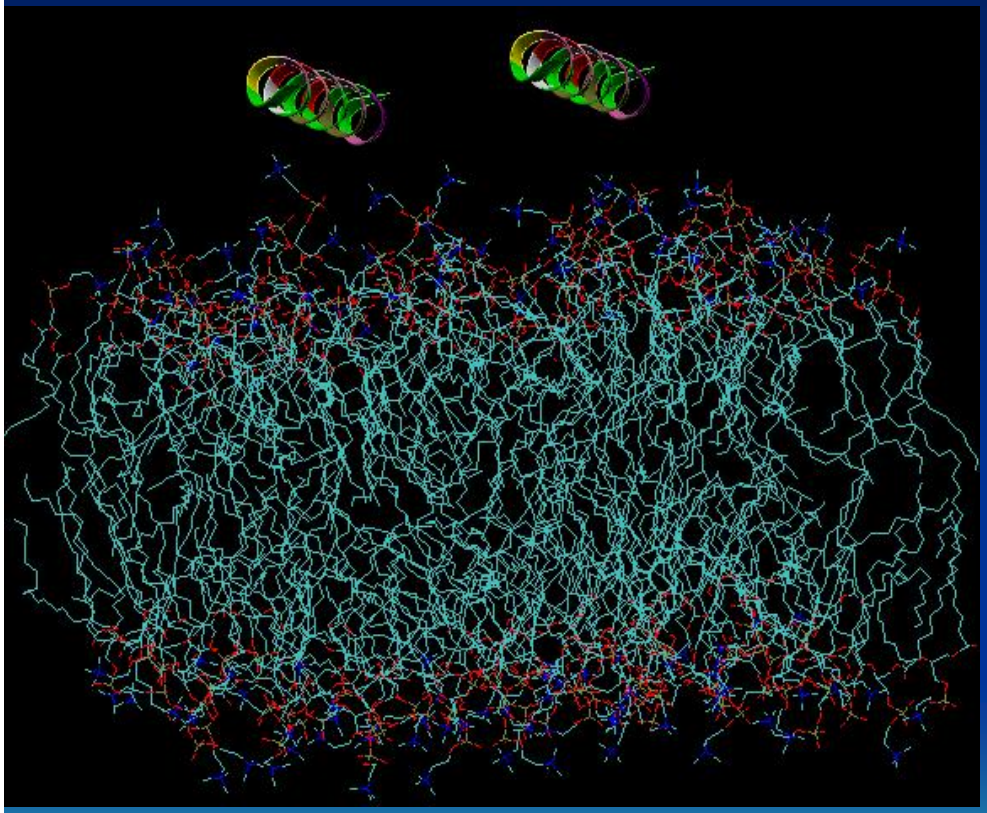


T=0ns

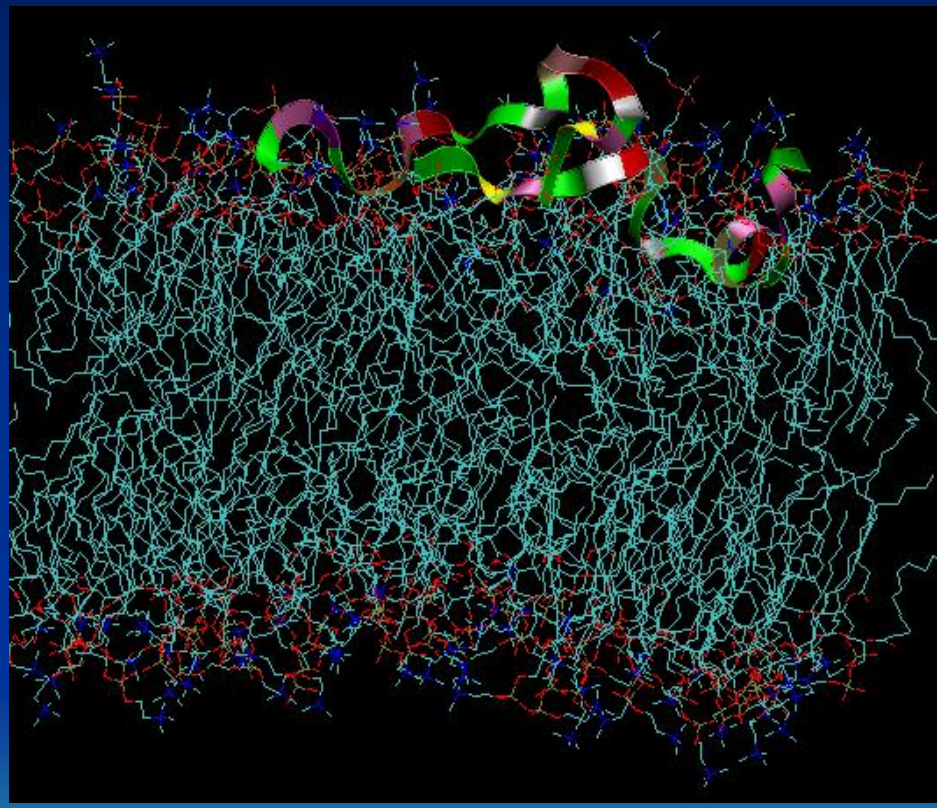


T=120ns

System 2 Peptides (Time Scale)



T=0ns



T=200ns

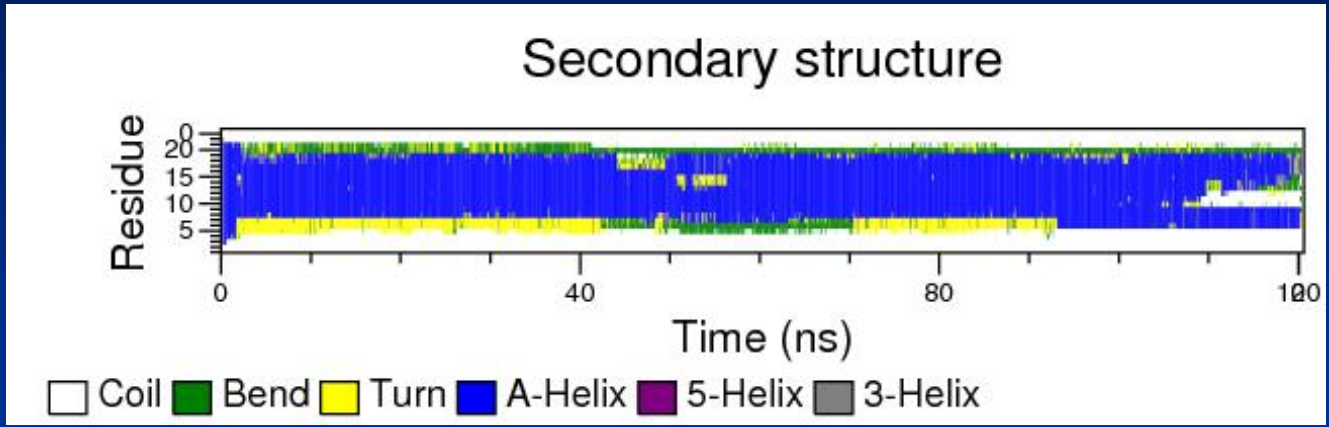
Antimicrobial Peptides

Antimicrobial peptides can carry drugs or antibiotics into a bacteria cell to kill the cell

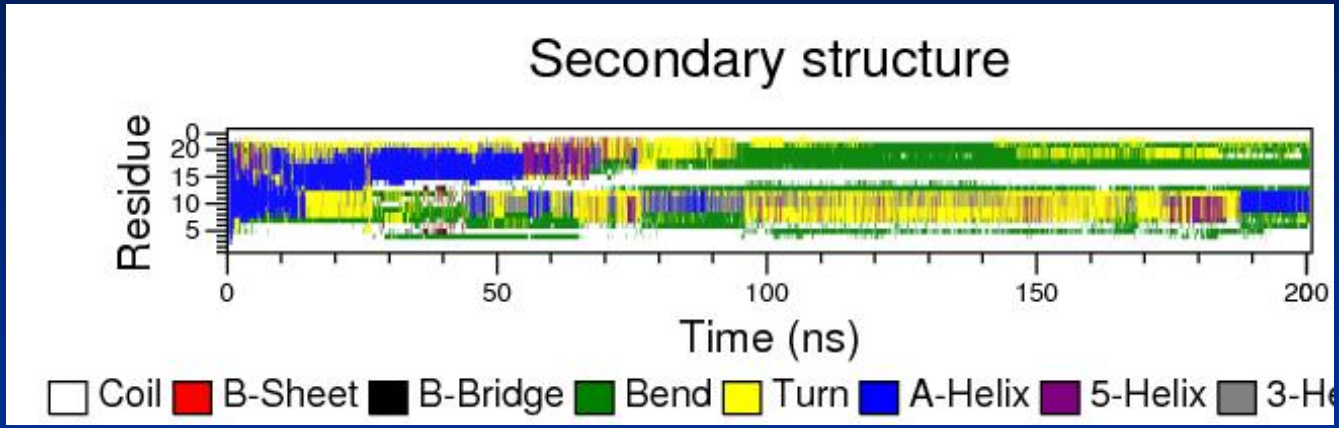
Upon entering cell, cause leakage of vital cell structures

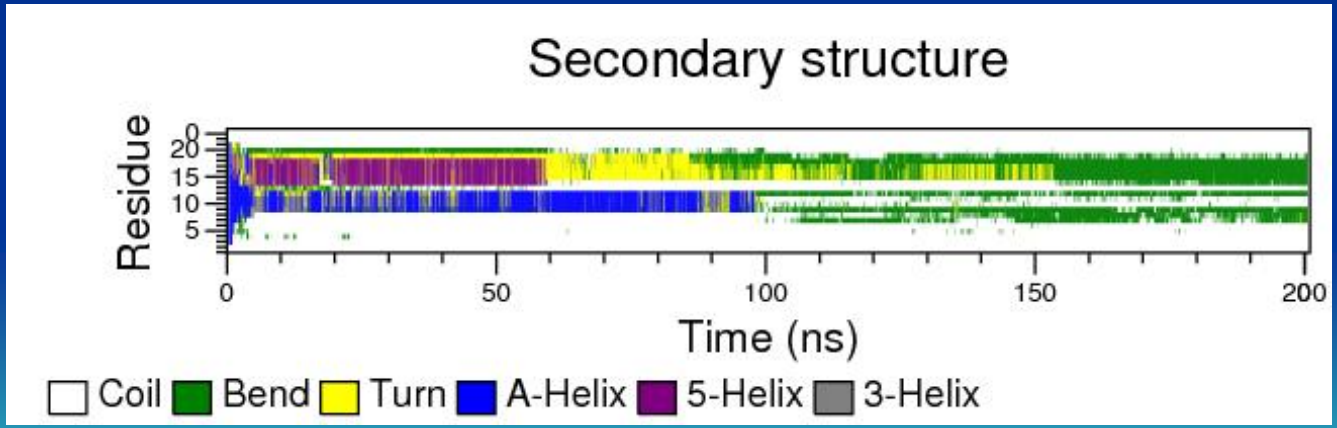
Synthetic peptide has Antimicrobial peptide type properties

DSSP P1


Secondary structure
Residue
0
20
15
10
5
0
40
80
120
Time (ns)
Coil
Bend
Turn
A-Helix
5-Helix
3-Helix

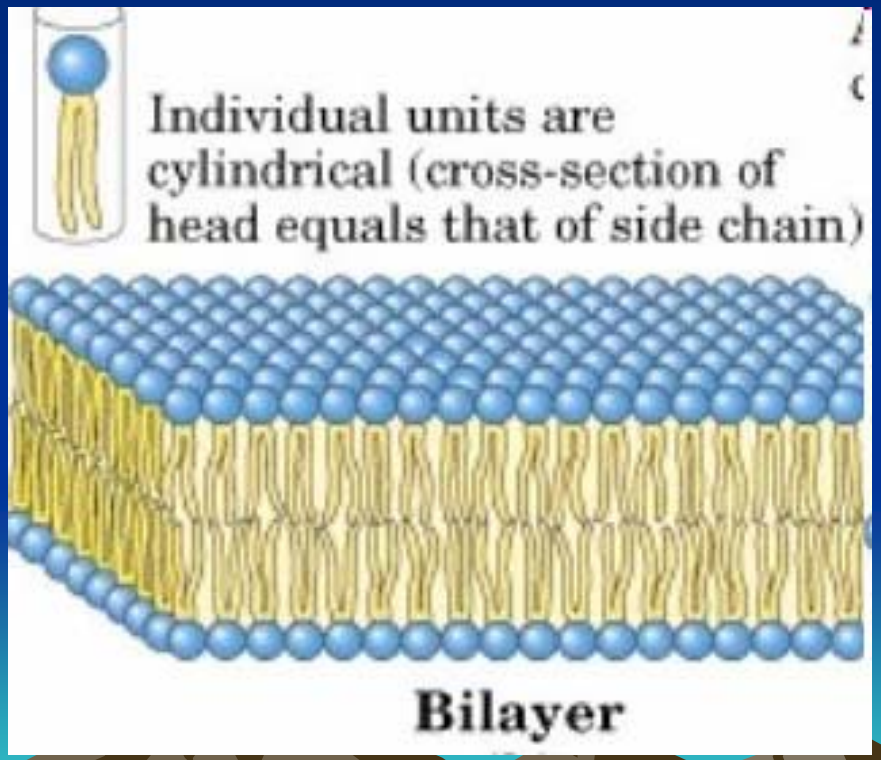
DSSP P2


Secondary structure
Residue
0
20
15
10
5
0
50
100
150
200
Time (ns)
Coil
B-Sheet
B-Bridge
Bend
Turn
A-Helix
5-Helix
3-He


Secondary structure
Residue
0
20
15
10
5
0
50
100
150
200
Time (ns)
Coil
Bend
Turn
A-Helix
5-Helix
3-Helix

Peptide

Ile-Ile-Ser-Thr-Ile-Gky-Asp-Leu-Val-Lys-Trp-Ile-Ile-Asp-Thr-Val-Asn-Lys-Phe-Thr-Lys-Lys



Lipid

Choline group (+)

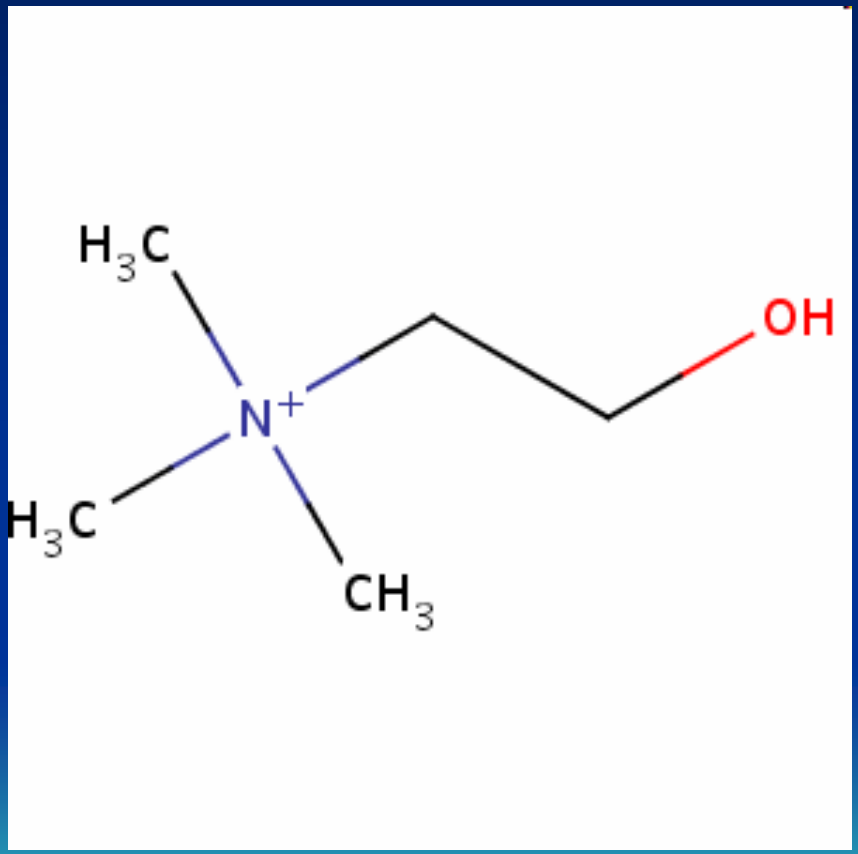
Phosphorous group (-)

Ester Group

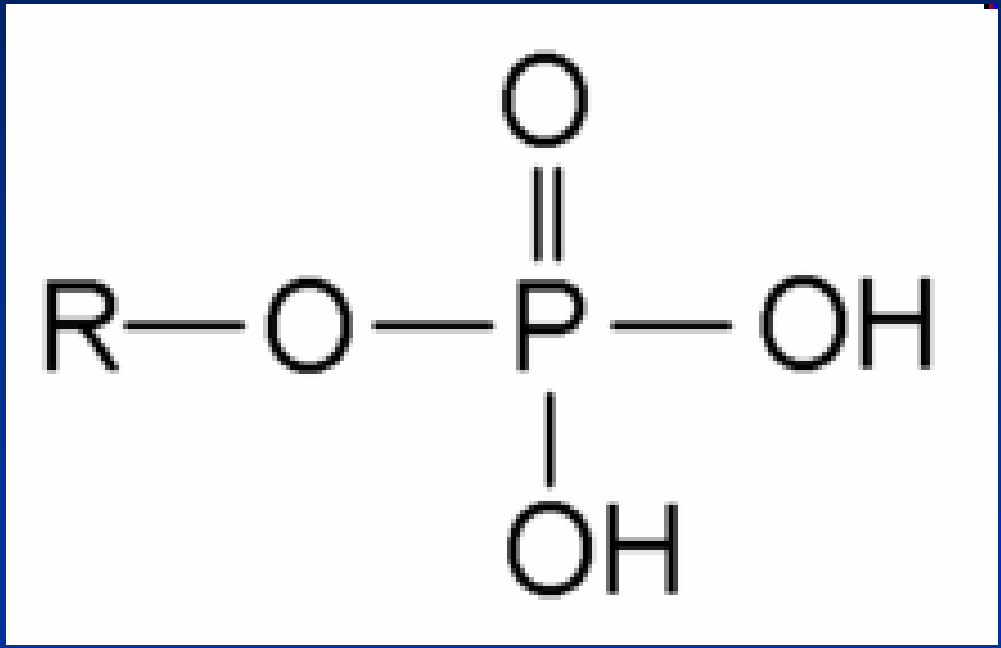
Tail Oxygen

Tail

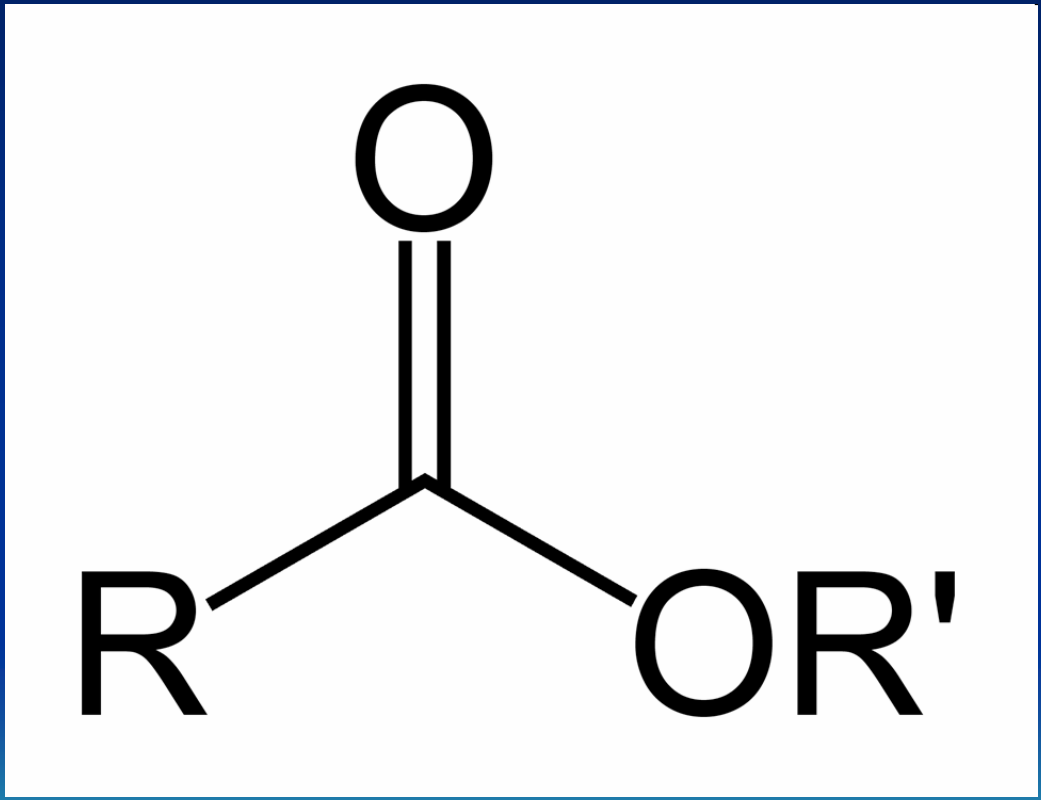
Choline Group (+)



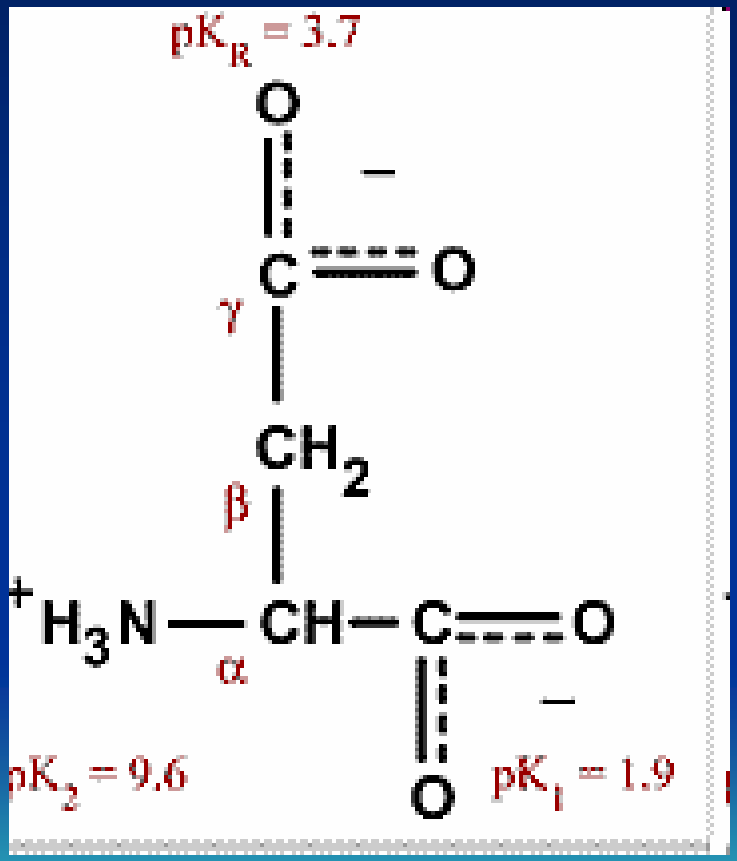
Phosphorus Group (-)

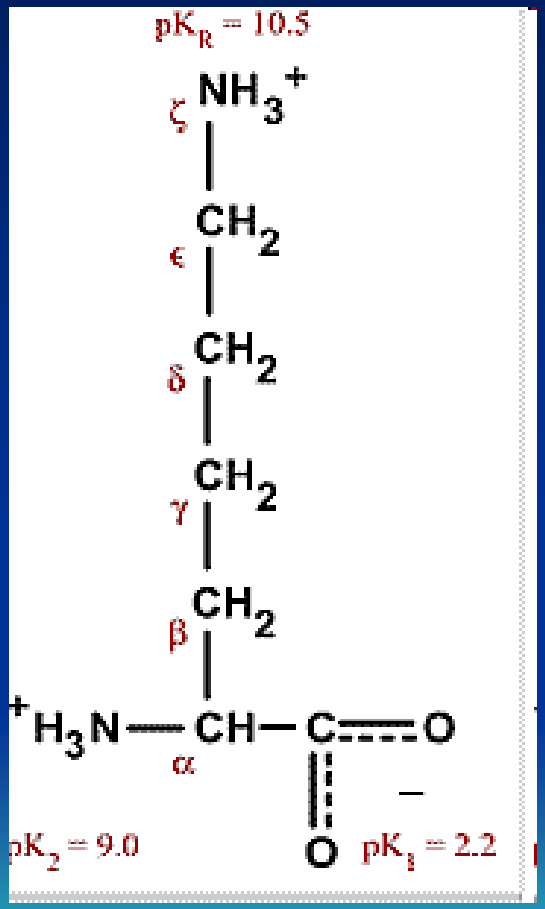


Ester Group

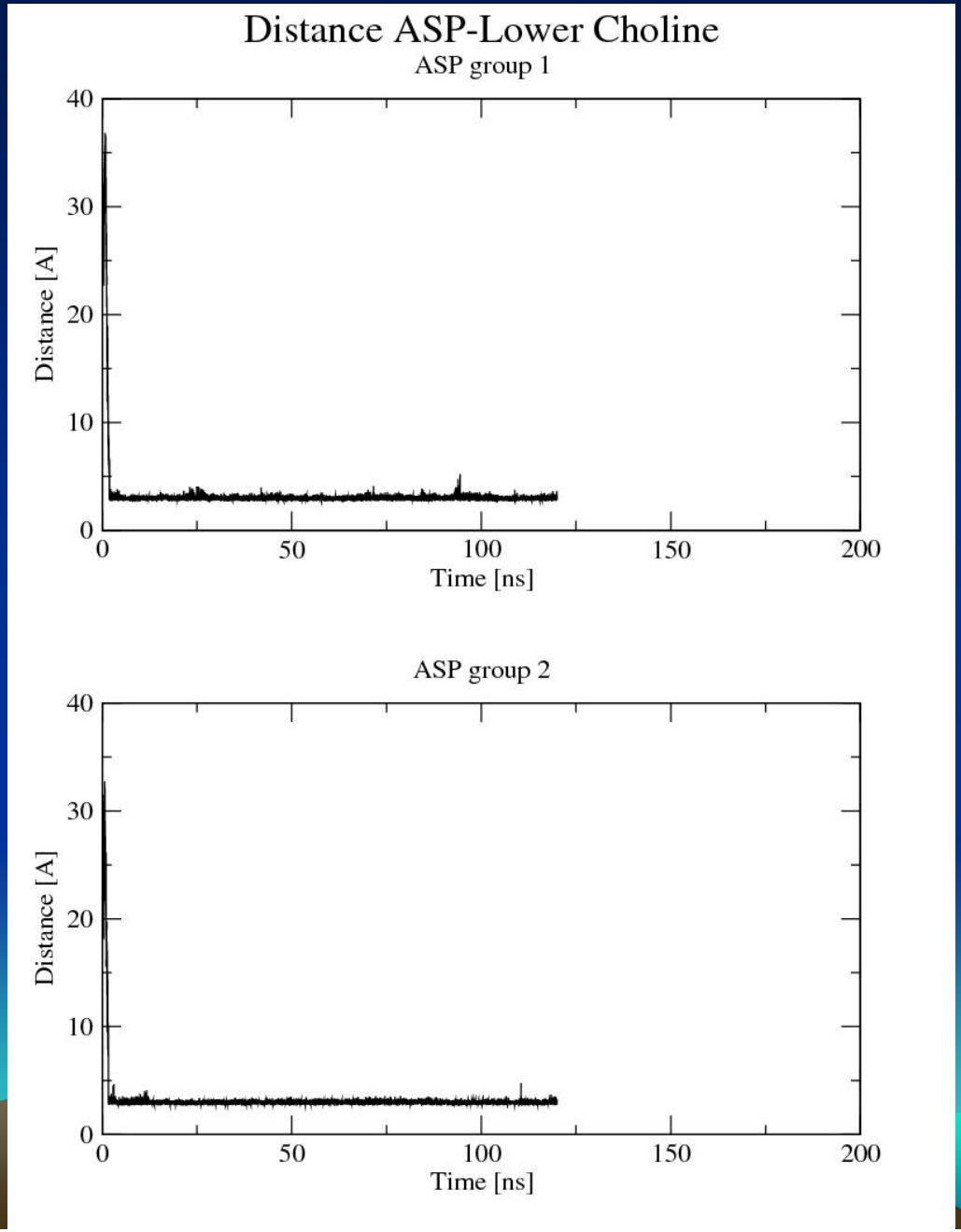


Aspartate (Asp) (-) & Lysine (Lys) (+)

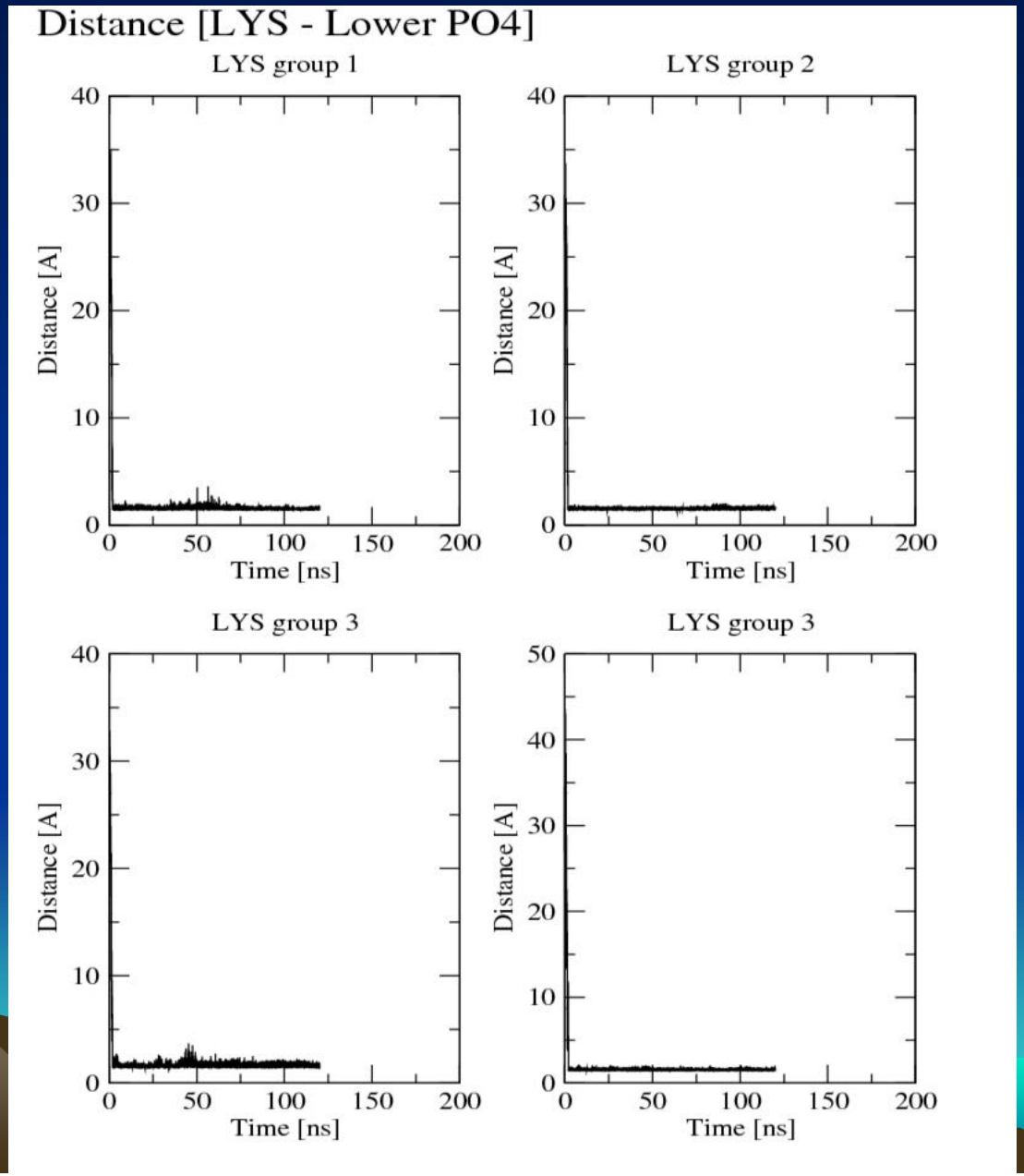




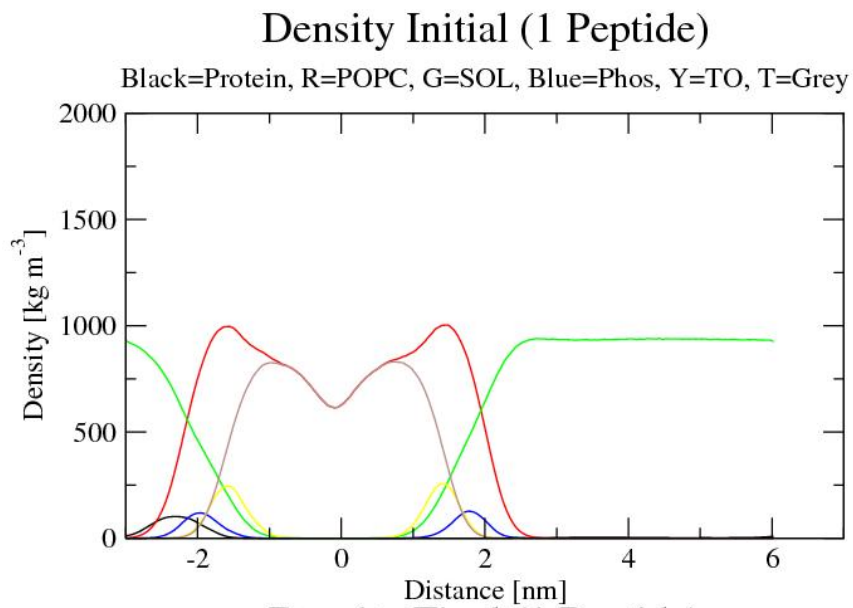
Minimum Distance P1

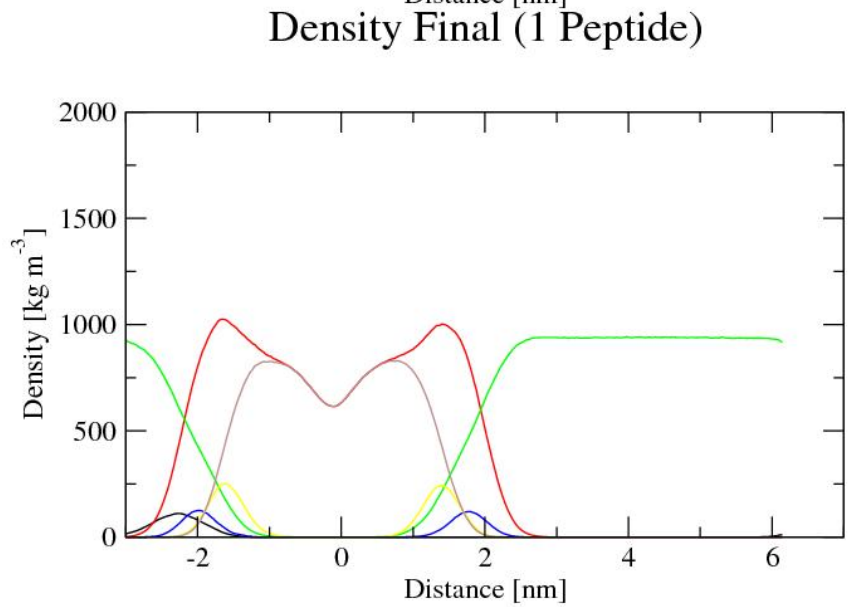


Minimum Distance P1

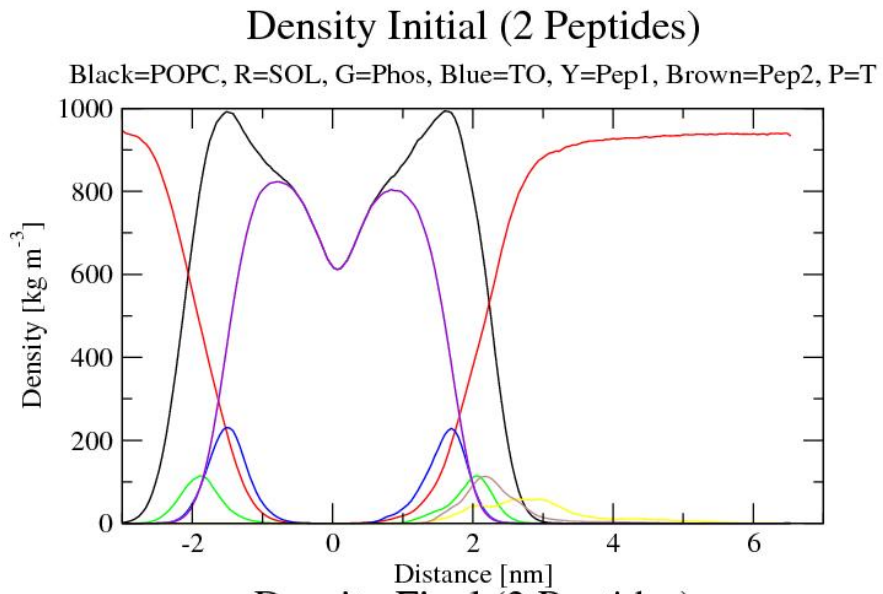


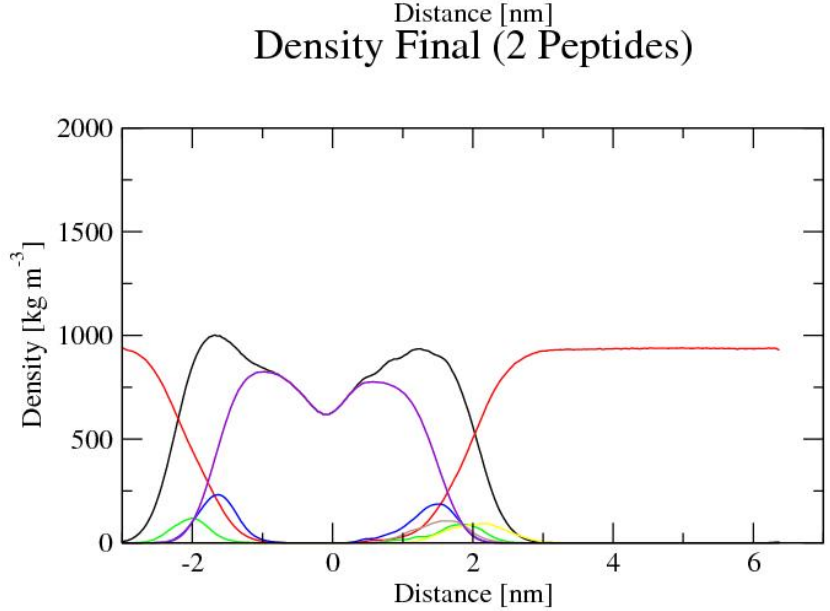
Density P1


Density Initial (1 Peptide)
Black=Protein, R=POPC, G=SOL, Blue=Phos, Y=TO, T=Grey
Density [kg m-3]
2000
1500
1000
500
0
-2
0
2
4
6
Distance [nm]

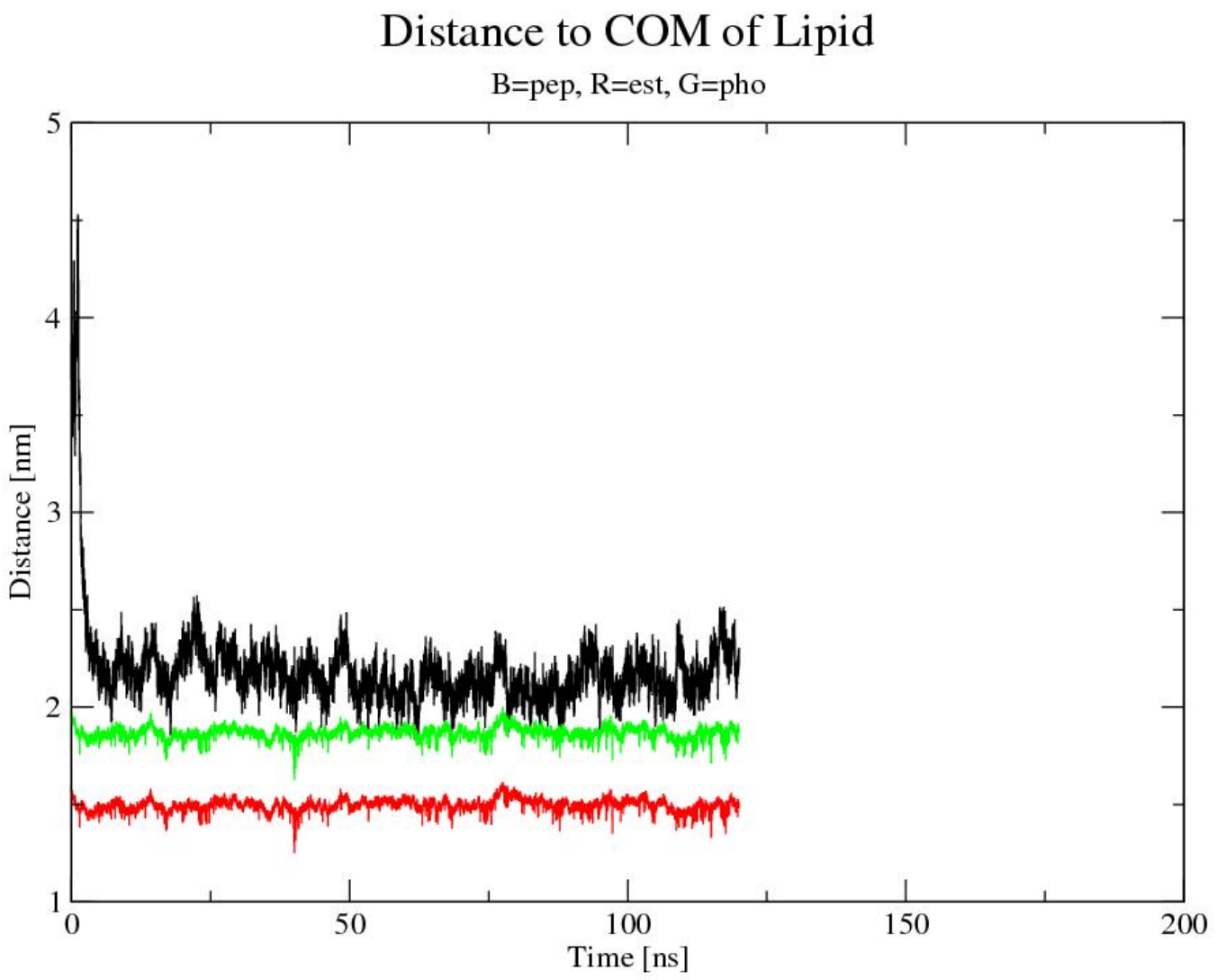

Density Final (1 Peptide)
Density [kg m-3]
2000
1500
1000
500
0
-2
0
2
4
6
Distance [nm]

Density P2

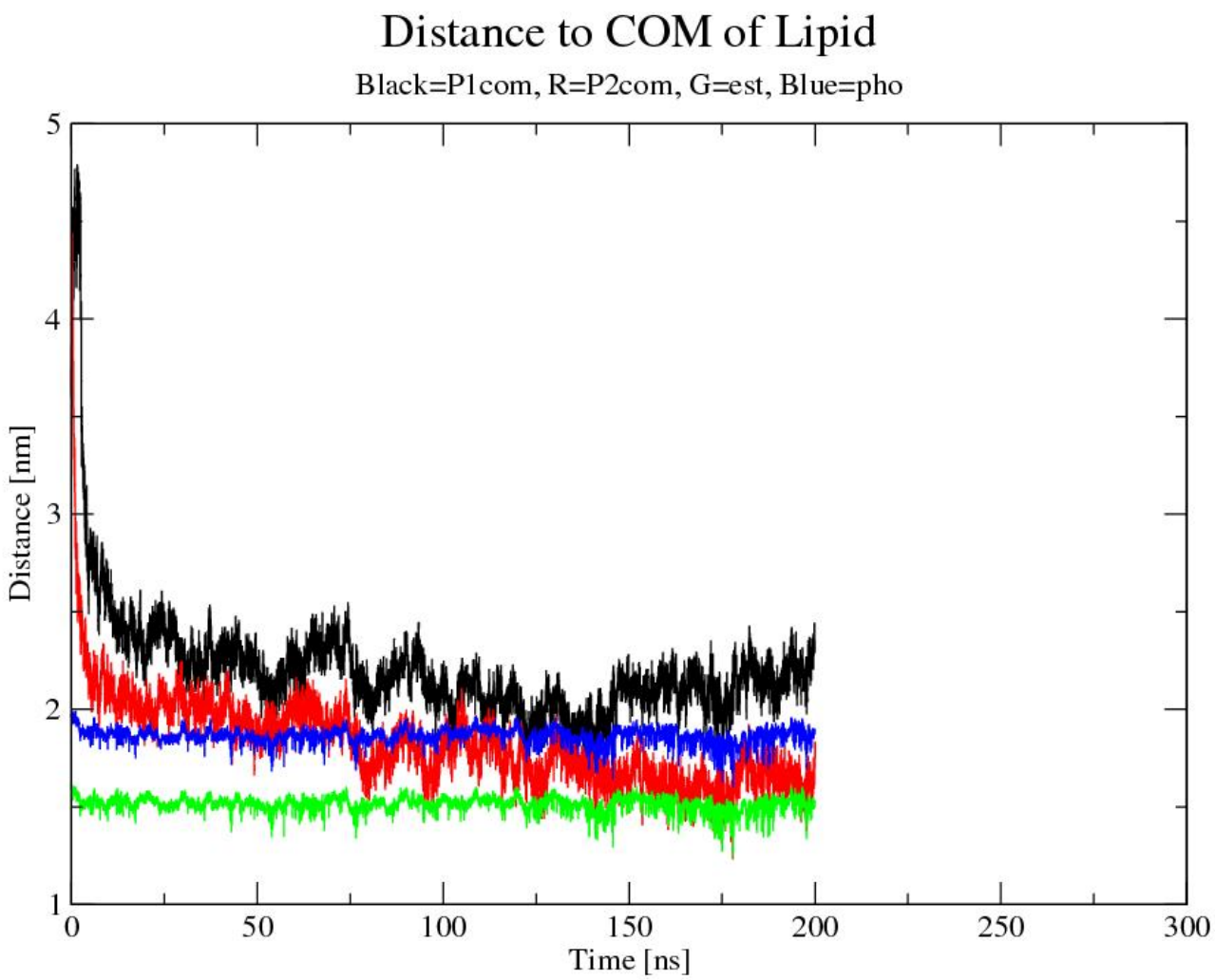

Density Initial (2 Peptides)
Black=POPC, R=SOL, G=Phos, Blue=TO, Y=Pep1, Brown=Pep2, P=T
Density [kg m-3]
1000
800
600
400
200
0
-2
0
2
4
6
Distance [nm]


Density Final (2 Peptides)
Density [kg m-3]
2000
1500
1000
500
0
-2
0
2
4
6
Distance [nm]

Distance Peptide (1)



Distance Peptide (2)

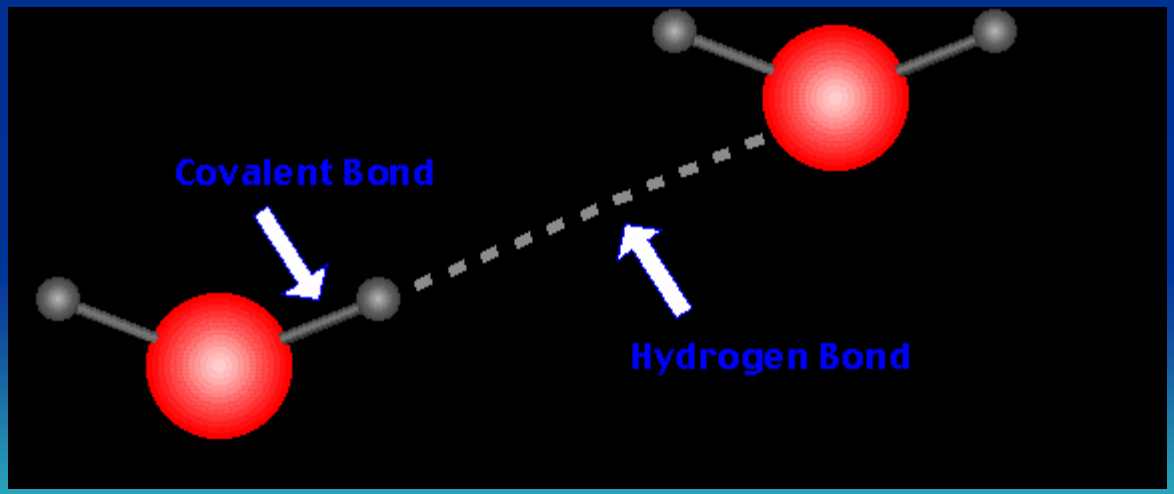


Hydrogen Bonding

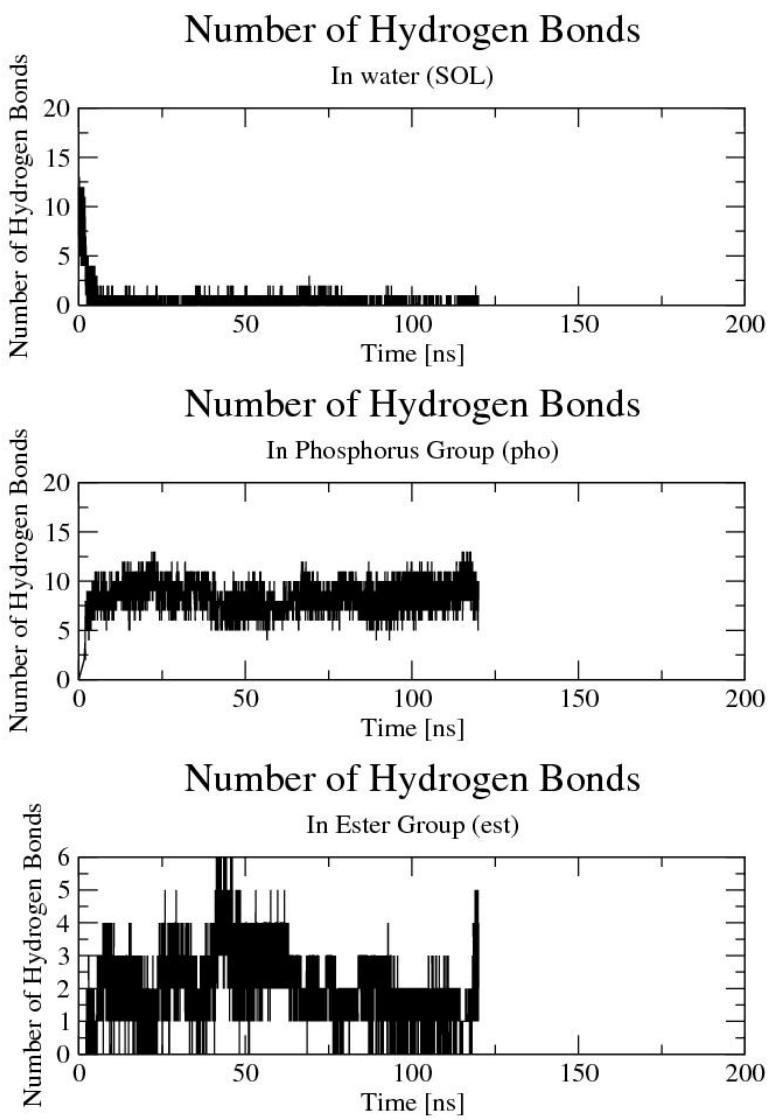
Electronegative differences (H & O,N,F)

Donate & Accept (O,N,F directly connected to H)

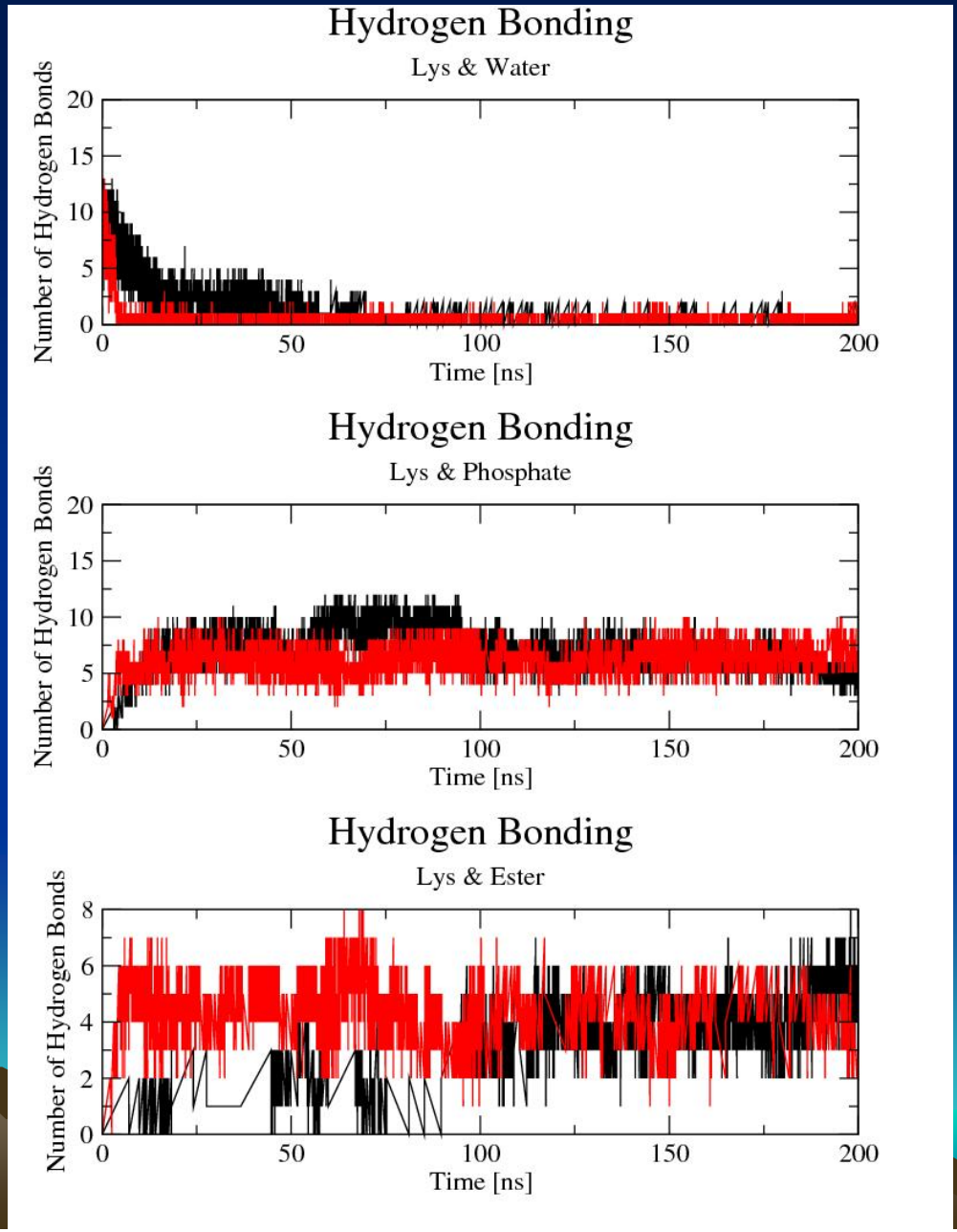
Accept (O,N,F exists in molecule)



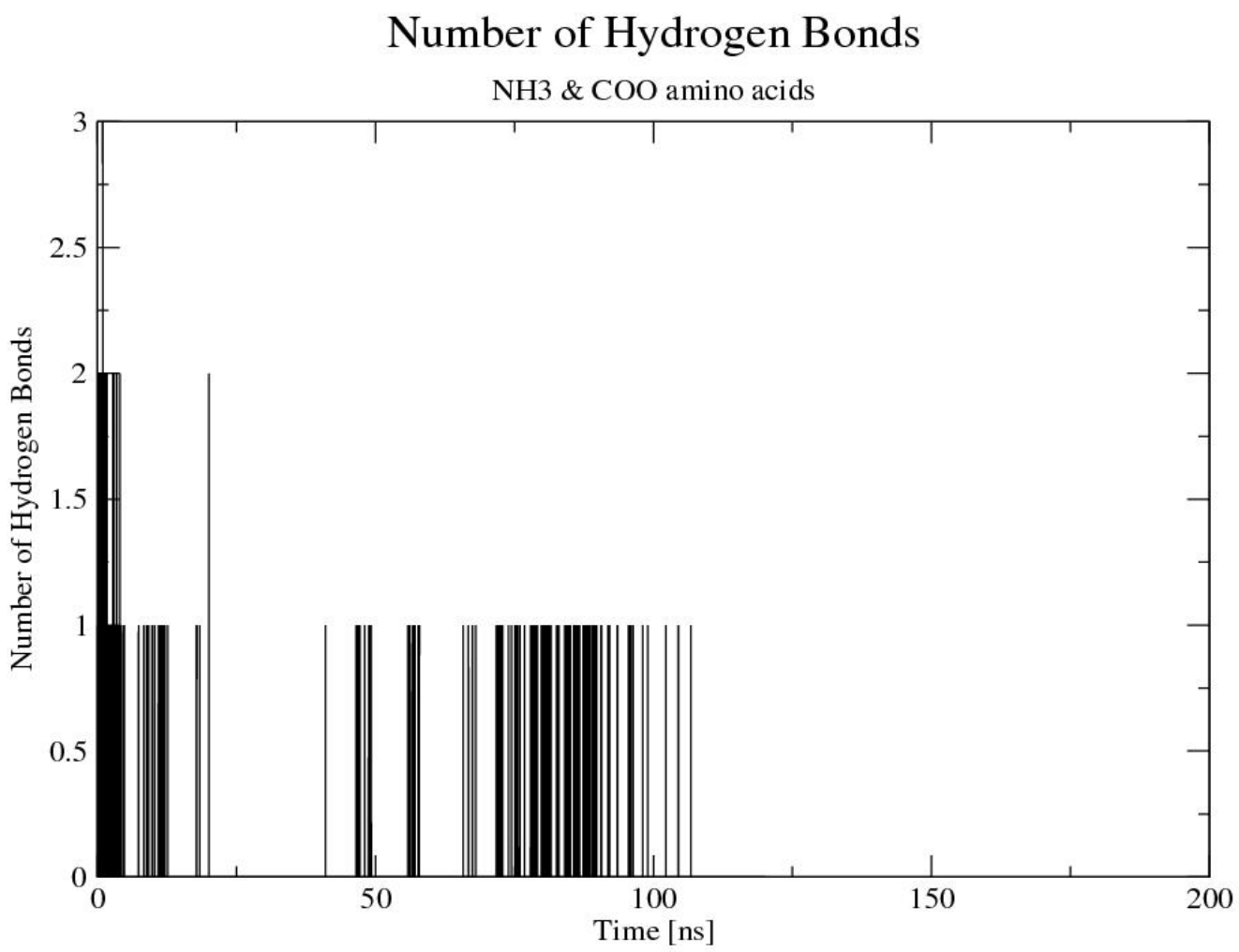
Hydrogen Bonding P1



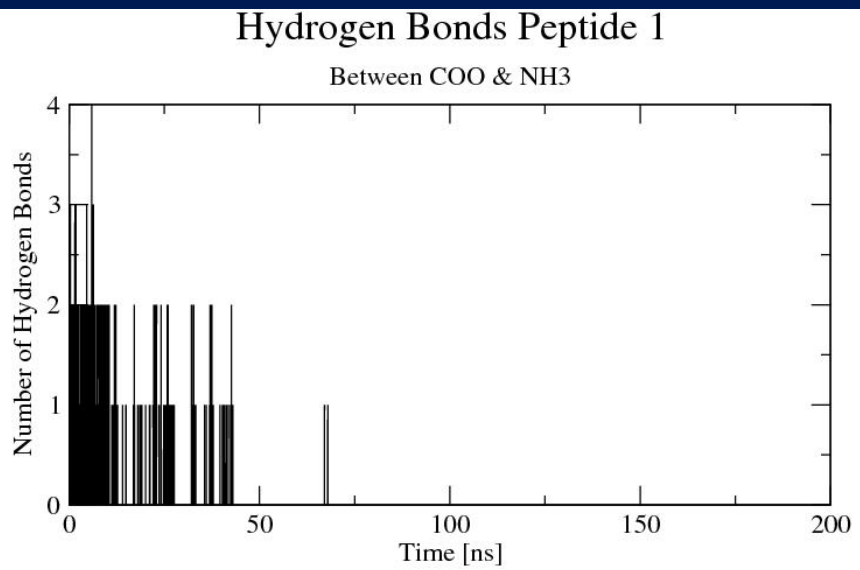
Hydrogen Bond (L-P2)

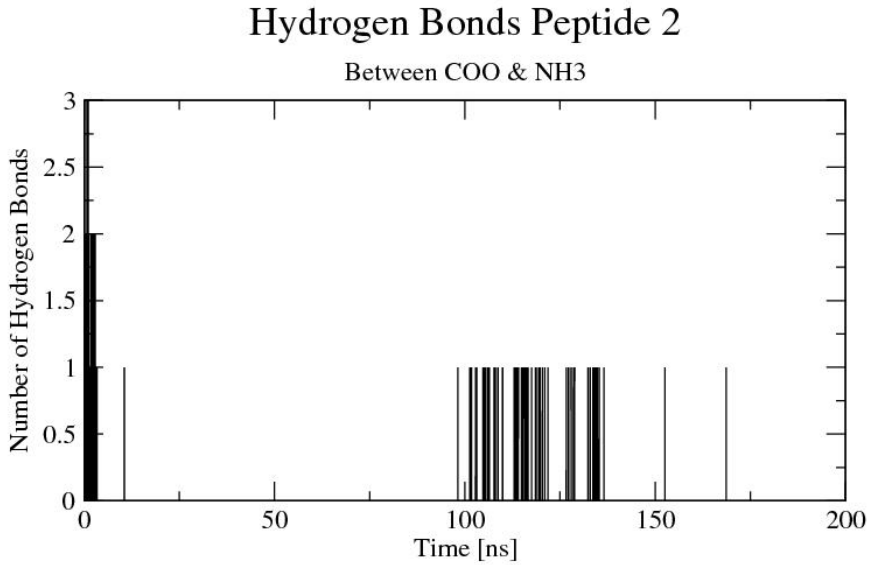


Hydrogen Bonds LYS-ASP P1



Hydrogen Bonds LYS-ASP P2





What's Next?

Increase number of peptides in system

Look at longer range of time

Work Cited Page

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Thank You

- Dr. Lee
- Dr. Davis