

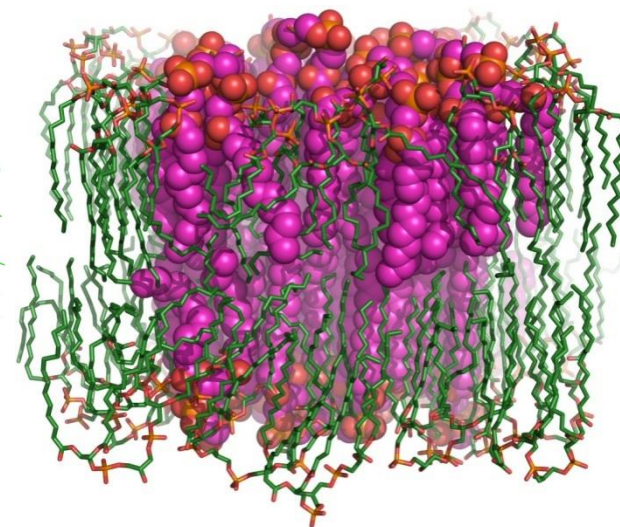
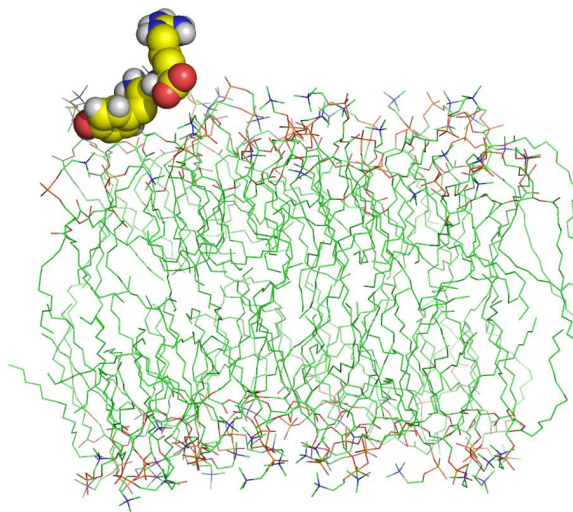
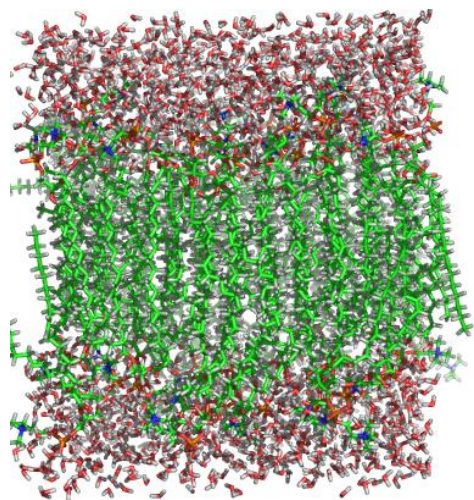


# Сучасні комп'ютерні методи дослідження нанорозмірних та біологічних систем



## Лекція № 8

### Повноатомні МД моделі ліпідного бішару та їх області використання. Середньозернисті моделі ліпиду та ліпідної мембрани

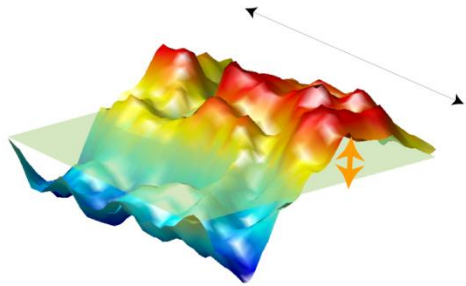


## **План Лекції № 8**

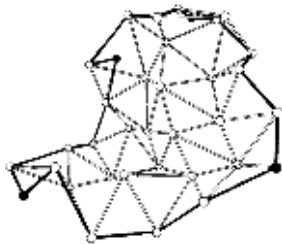
- Сучасні повноатомні МД моделі ліпідного бішару  
-та їх області використання**
- Зернисті моделі ліпиду та ліпідної мембрани**
- Поширені силові поля та програми для МД моделювання  
-ліпідних систем**
- Приклади МД моделювання ліпідних систем**

# Для разных задач необходимо разное атомное разрешение ...

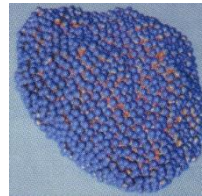
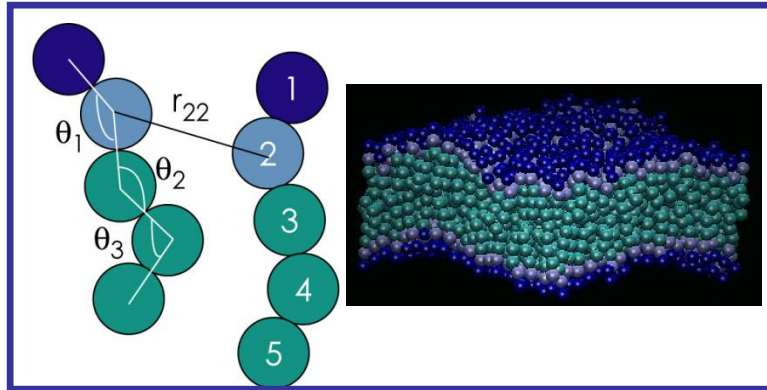
Более высокое разрешение (больше элементов) обычно обеспечивает более точные представления оригинала



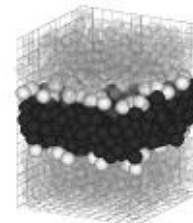
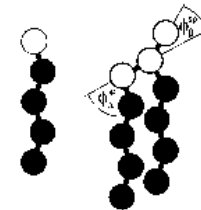
W. Helfrich, Z. Natuforsch, **28c**, 693 (1973)



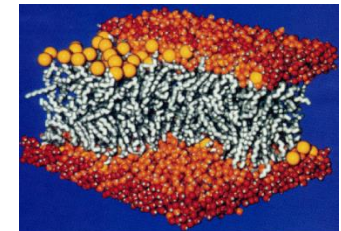
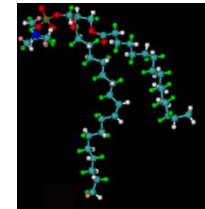
Y. Kantor, M. Kardar, and D.R. Nelson, Phys. Rev. A **35**, 3056 (1987)



J.M. Drouffe, A.C. Maggs, and S. Leibler, Science **254**, 1353 (1991)



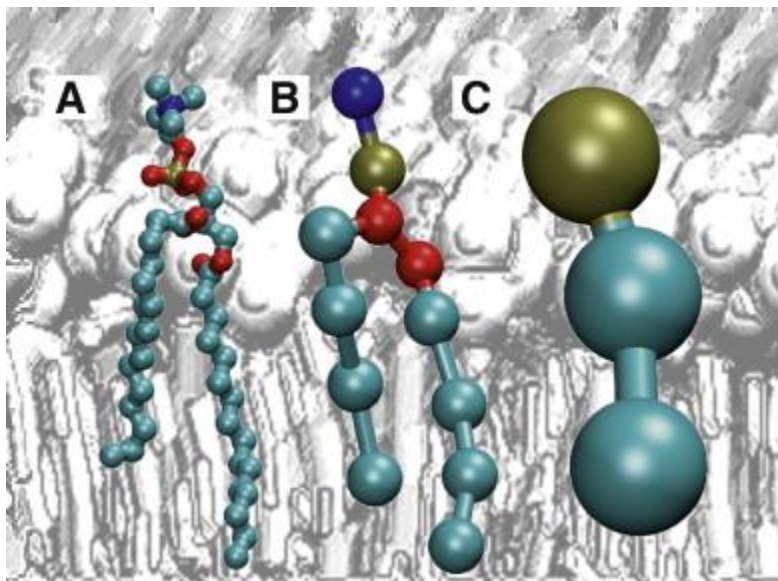
R. Goetz and R. Lipowsky, J. Chem. Phys. **108**, 7397 (1998)



Helmut Heller, Michael Schaefer, and Klaus Schulten, J. Phys. Chem **1993**, 8343 (1993)

## Что такое “зернистость” силового поля?

В зависимости от поставленной задачи, атомное разрешение и степень молекулярной детализации может быть различной



Полноатомная Модель  
“**мелкозернистая**”



Упрощенная Модель  
“**среднезернистая**”



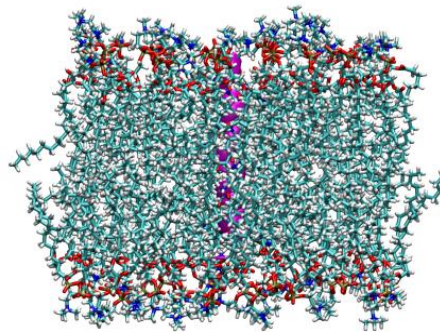
Фрагментированная Модель  
“**крупнозернистая**”

# Зачем нужна различная “зернистость” силового поля?

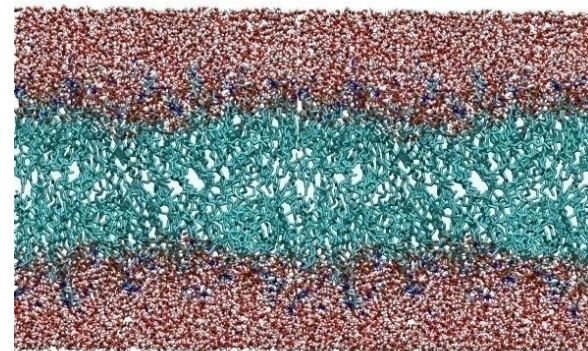
Полноатомная МД модель  
“**мелкозернистая**”

**AMBER, CHARMM, GROMACS, NAMD**

**фрагмент бислоя**



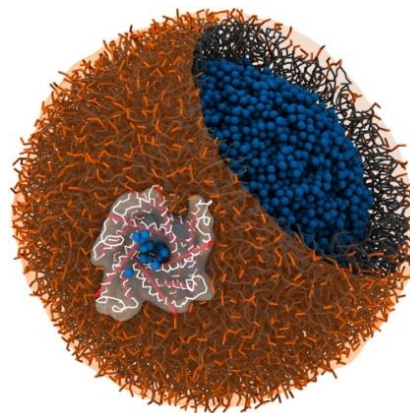
**гидротированный бислой**



Упрощенная МД модель  
“**среднезернистая**”

**GROMOS96, GROMACS**

**протеин внутри липосомы**

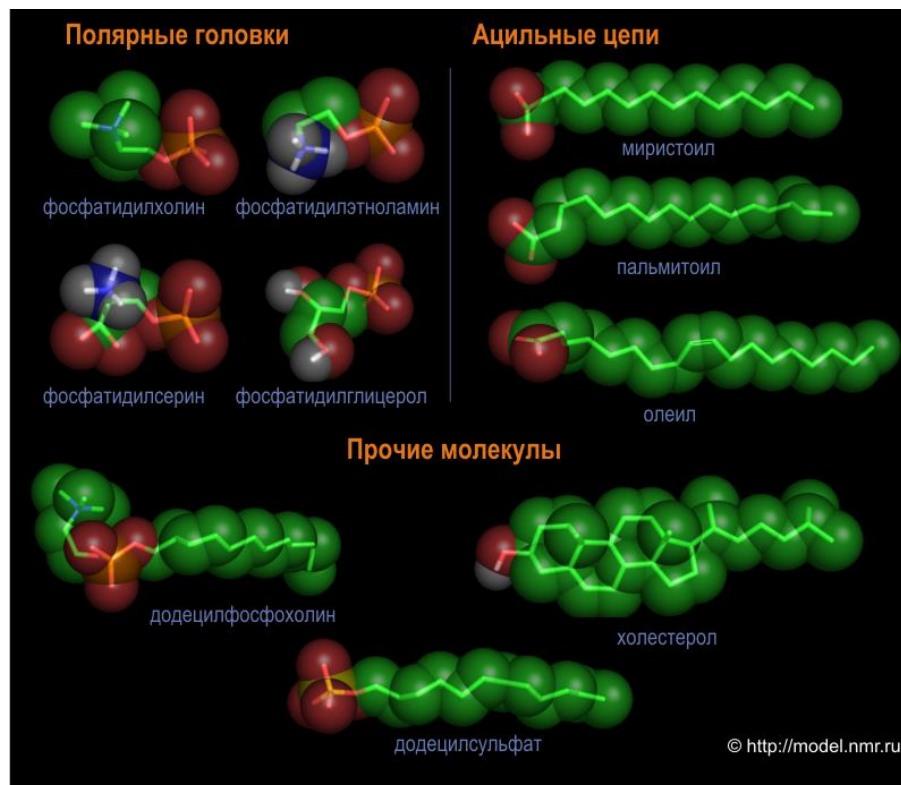
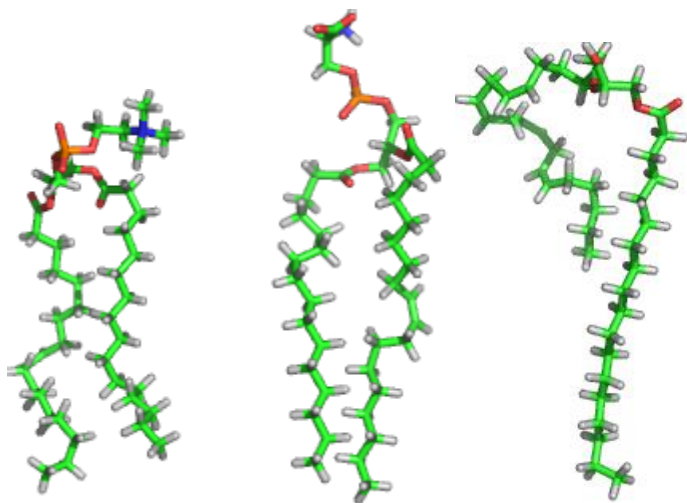


Фрагментированная МД модель  
“**крупнозернистая**”

**GROMACS, NAMD**

# Полноатомная (all-atom) модель липида

**Все атомы учитываются  
в явном виде,  
включая атомы водорода**



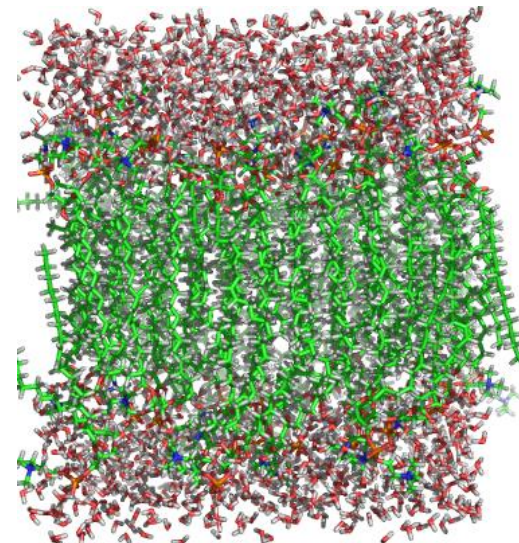
<http://proteomics.bioengr.uic.edu/metador/MD.html>

<http://model.nmr.ru/index.ru.phtml?page=work.projects.md-puremembr>

# Полноатомная модель мембраны

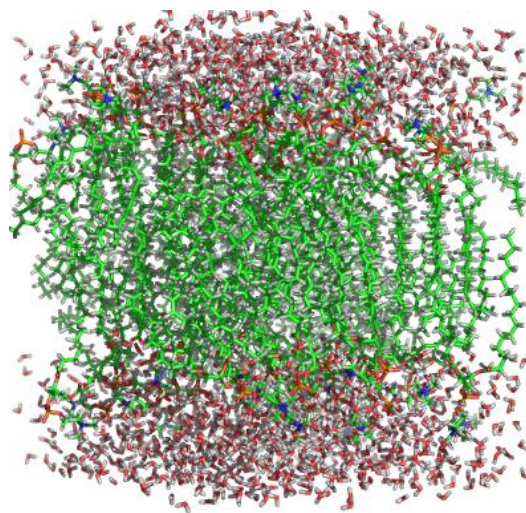
## Преимущества:

Наиболее полное описание изучаемой системы. Наиболее точное воспроизведение строения и конформации индивидуальных липидов и белков. Высокая степень детализации межмолекулярного взаимодействия



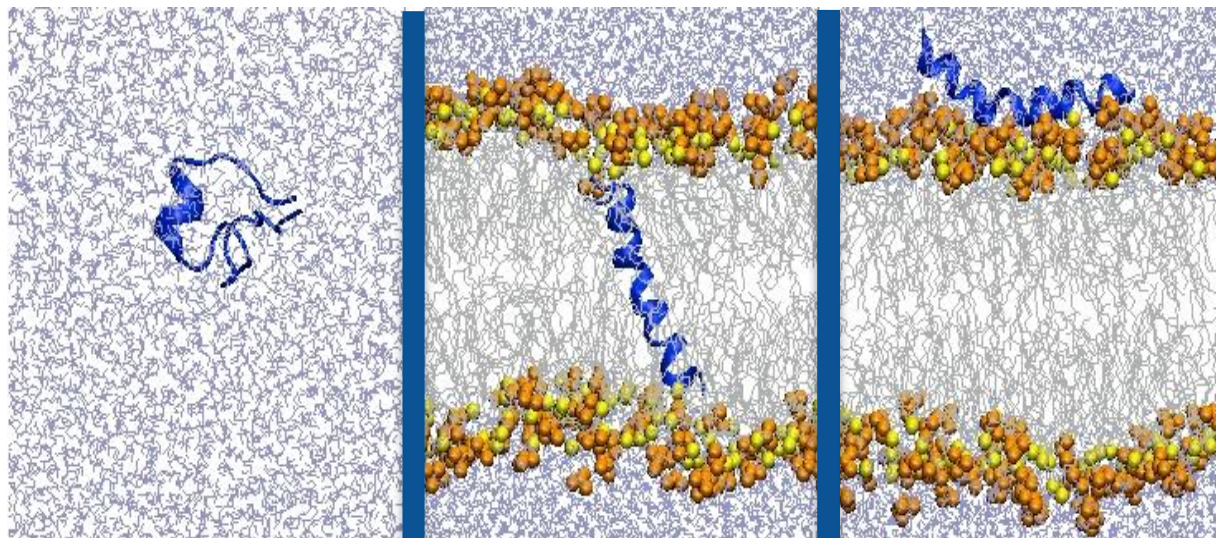
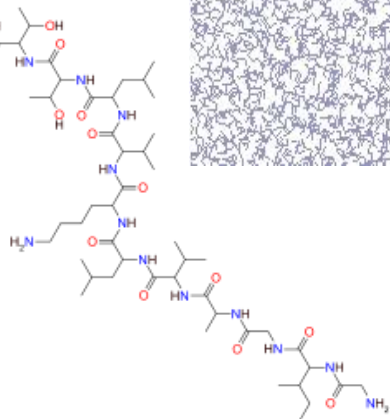
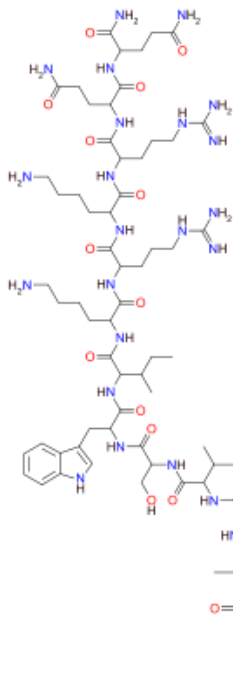
## Недостатки:

Наличие атомов водорода ограничивает максимальное время МД интегрирования до 2 фс. Увеличивается общее компьютерное время необходимое для проведения МД расчета. Ограничения по размеру мембраны (как правило всего до 256 липидов)



# Пример полноатомного МД моделирования взаимодействия пептида меллитина с липидной мембраной

**Меллитин**  
(пептид пчелиного яда) — обладающий свойствами поверхностно-активного вещества, выделенный из яда медоносной пчелы

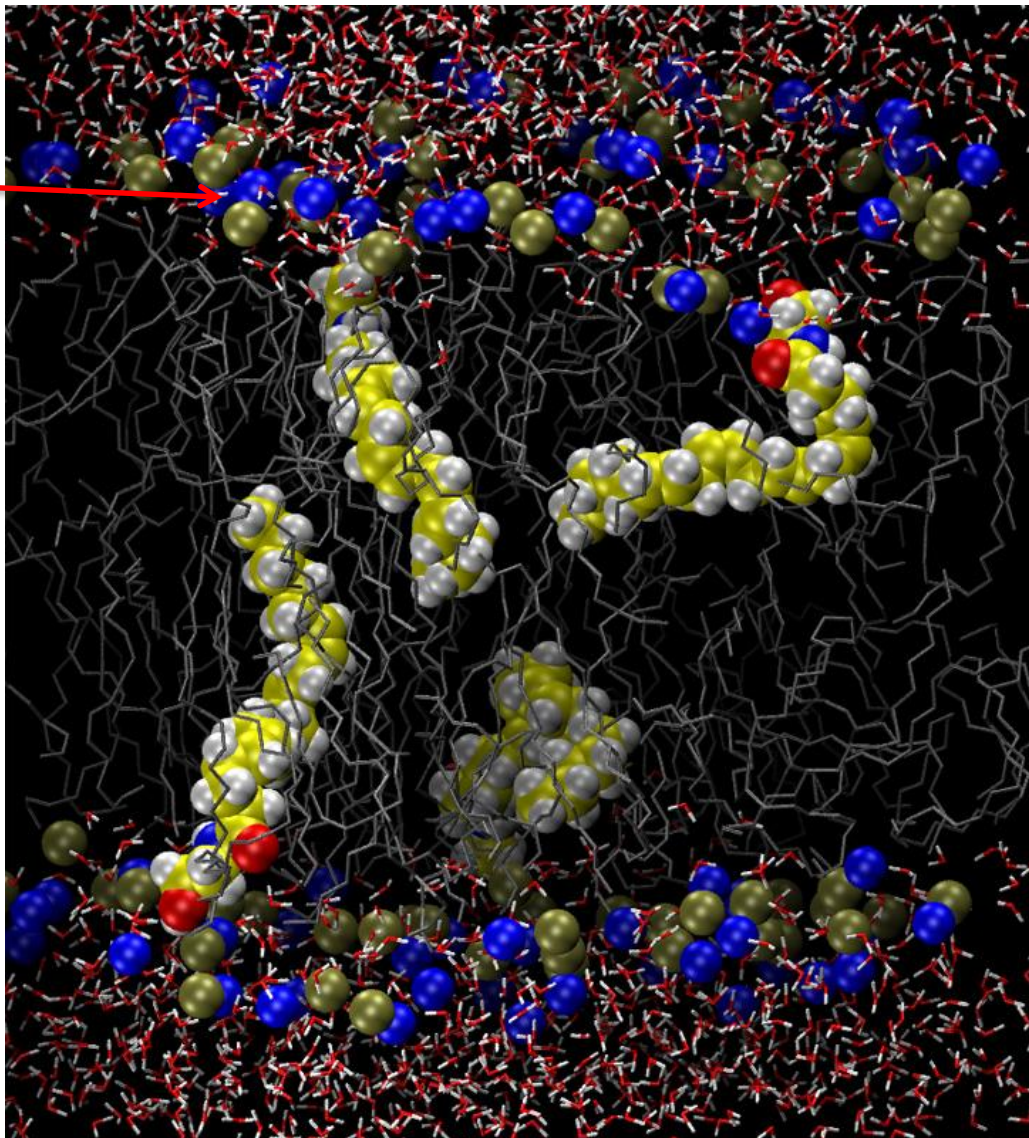


Сравнение устойчивости двух различных связанных форм меллитина с мембраной



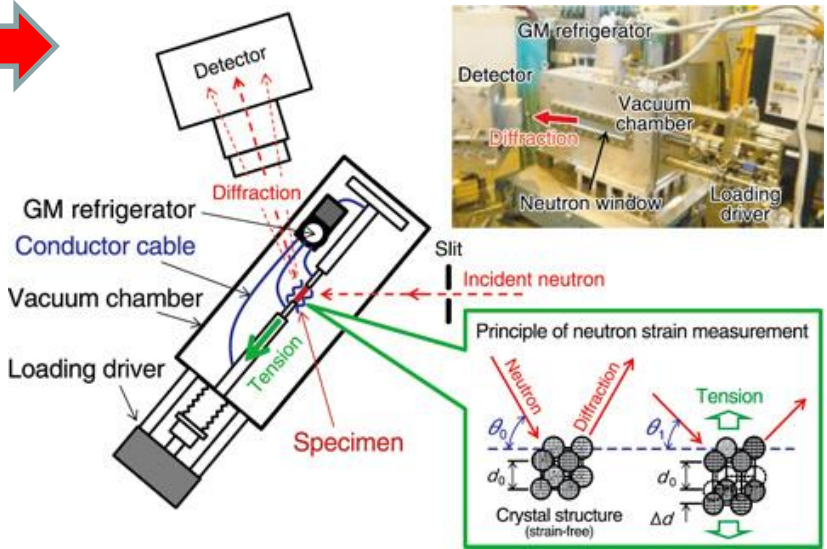
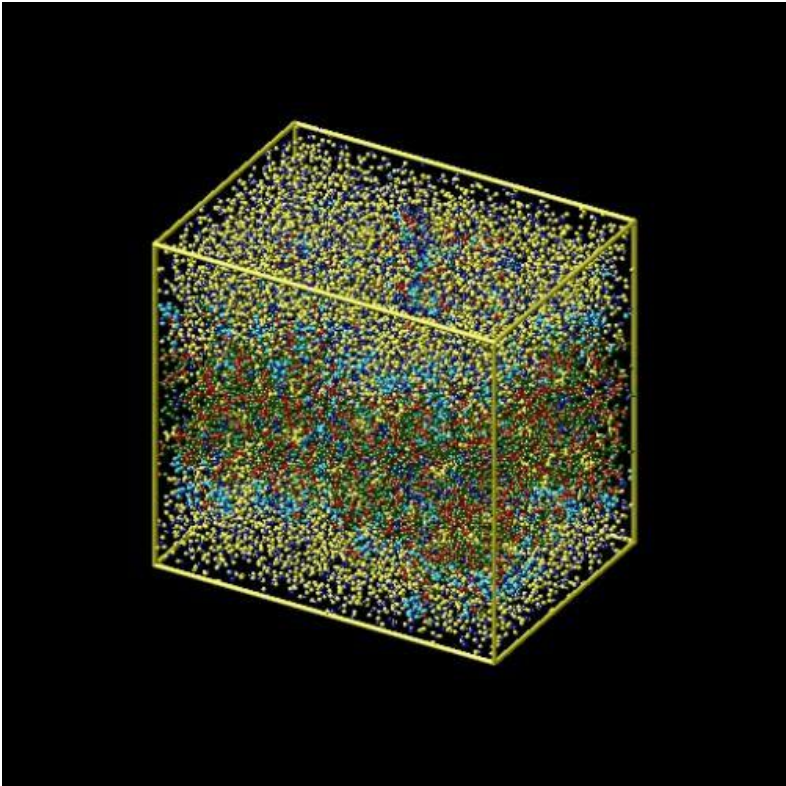
# Пример полноатомного МД моделирования липидной мембраны

**Ионы**



# Применение полноатомного МД моделирования для уточнения строения липидной мембраны

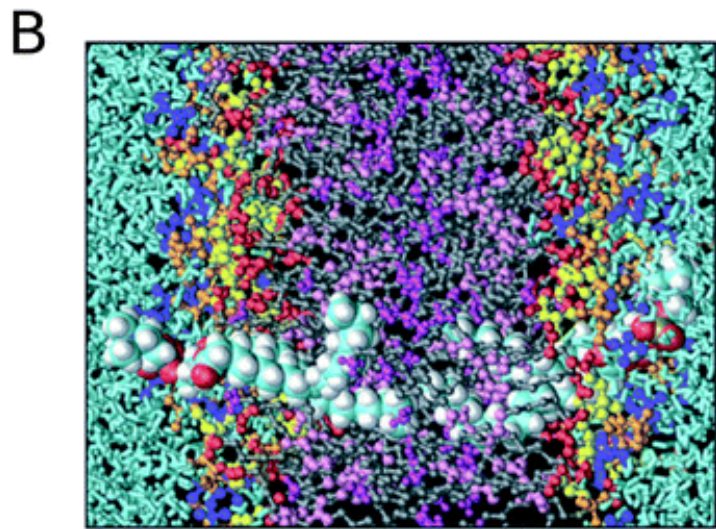
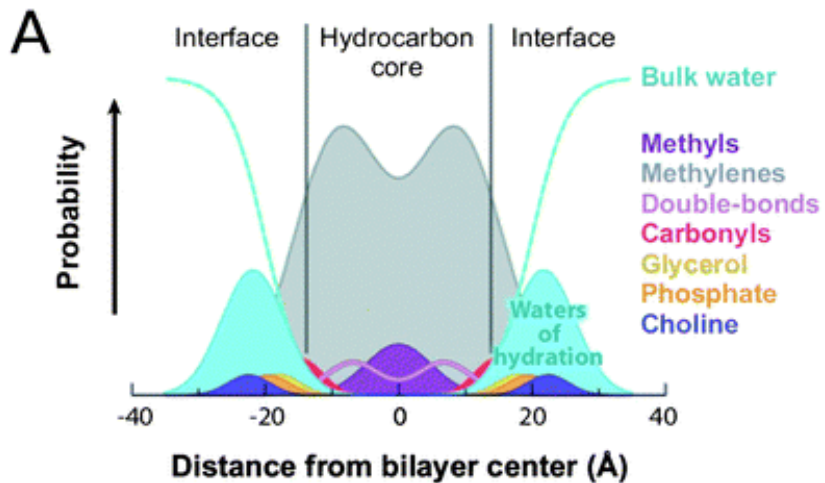
МД моделирование



Нейтронная дифракция

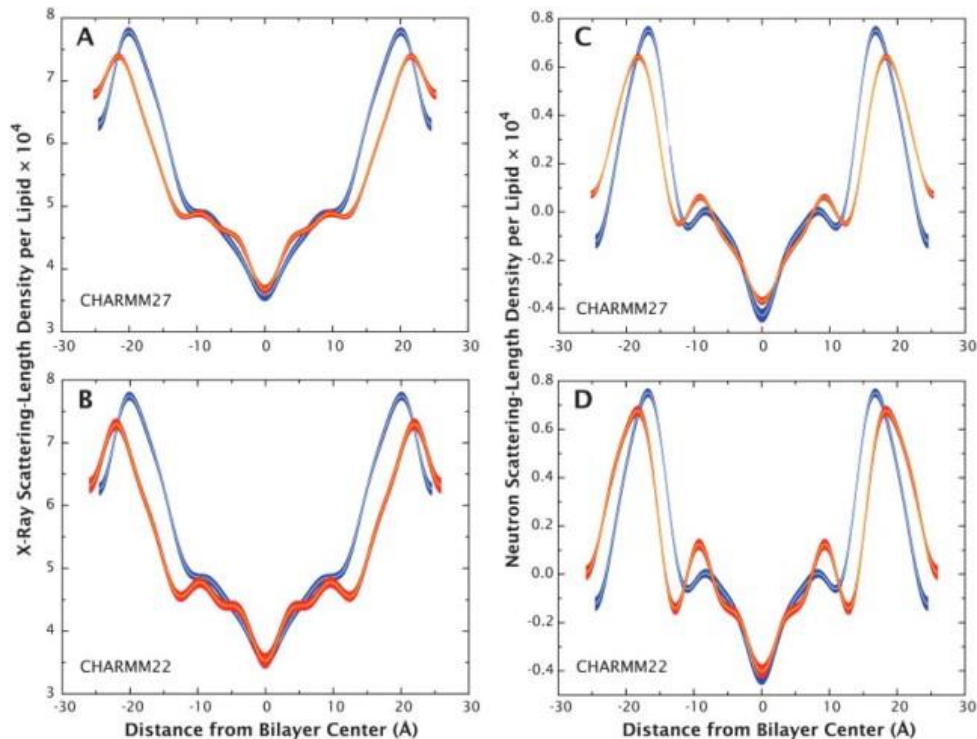


# Применение полноатомного МД моделирования для уточнения строения липидной мембраной

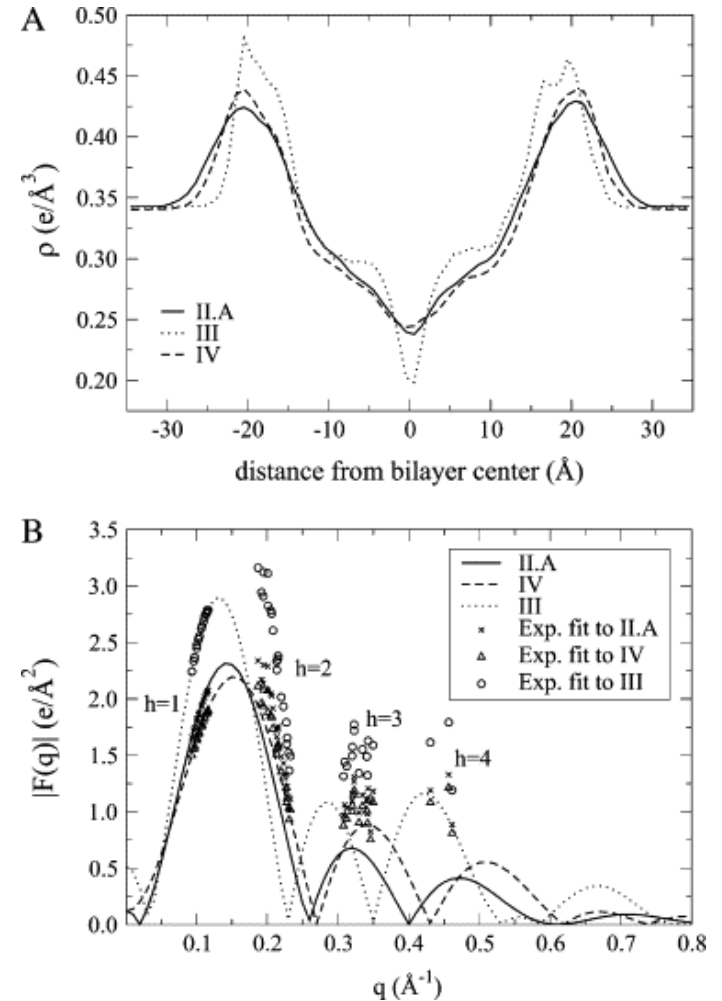


# Применение полноатомного МД моделирования для уточнения строения липидной мембраны

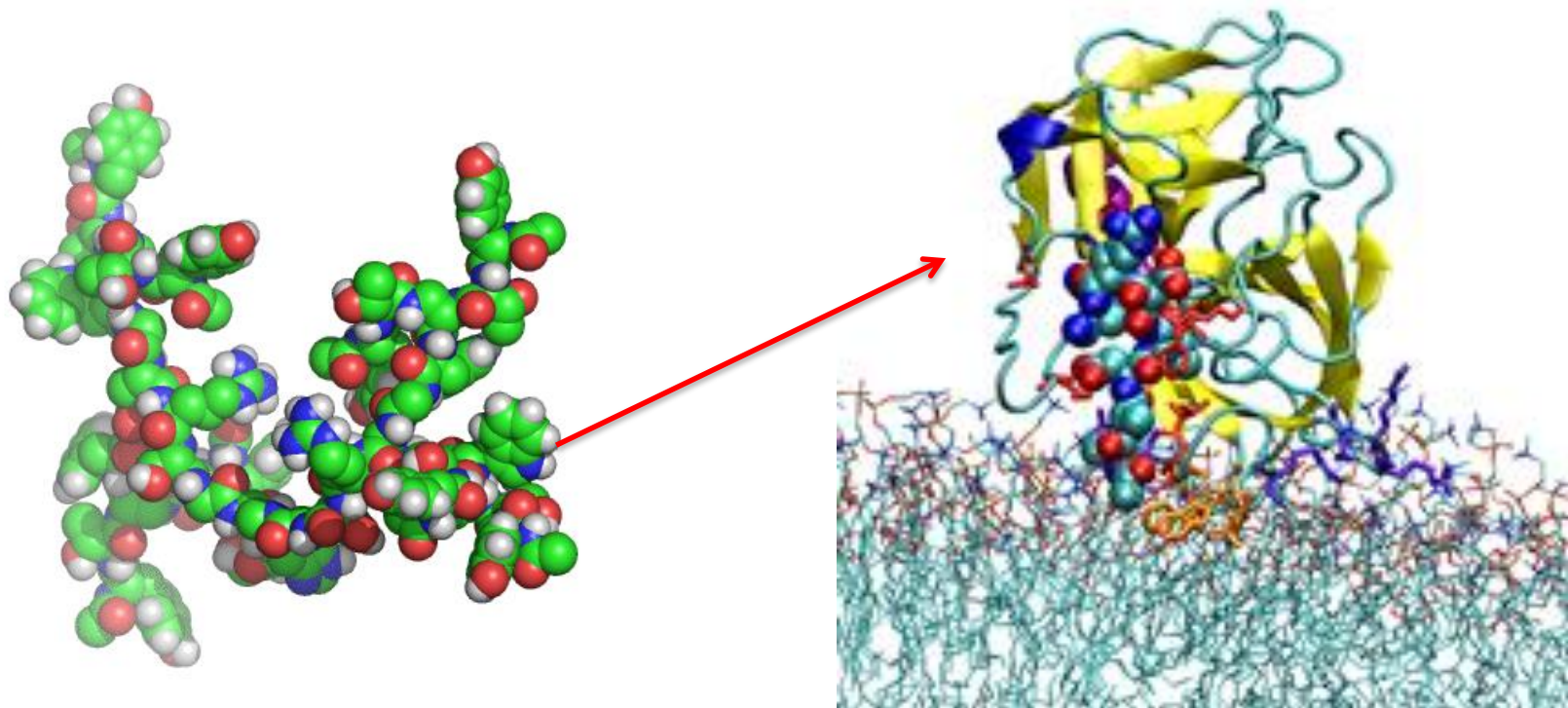
МД моделирование



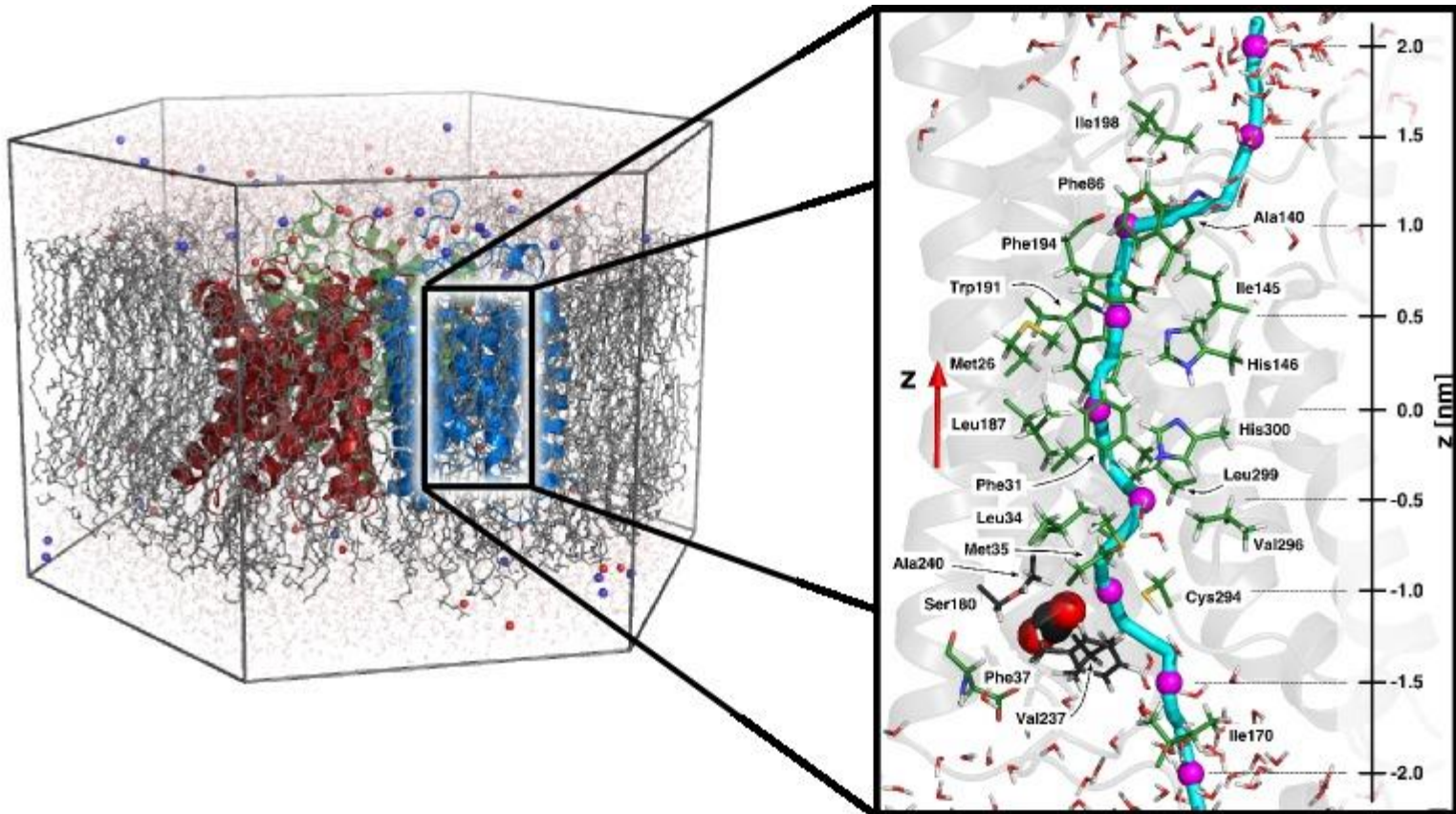
эксперимент



# Применение полноатомного МД моделирования для изучения протеин-липидного взаимодействия



# Применение полноатомного МД моделирования для изучения протеин-липидного взаимодействия



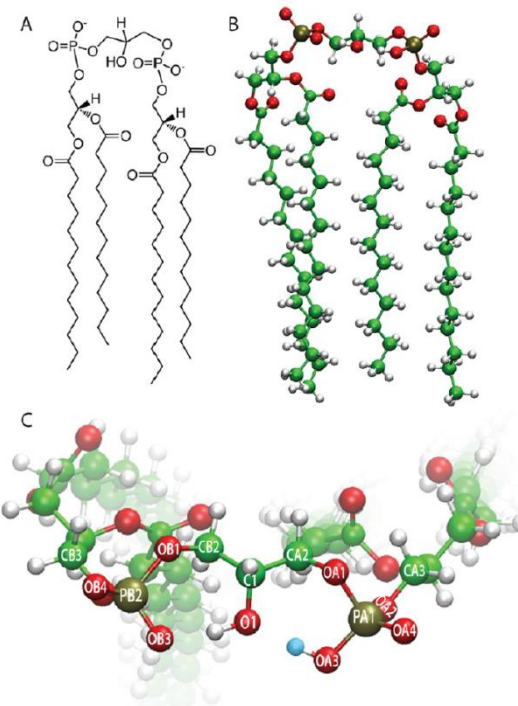
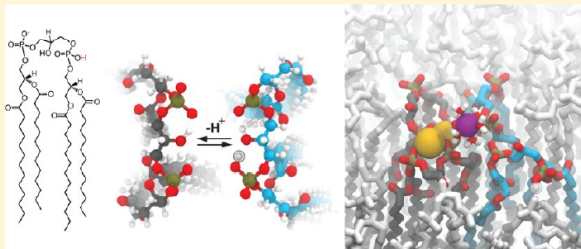
## Cardiolipin Models for Molecular Simulations of Bacterial and Mitochondrial Membranes

Thomas Lemmin,<sup>†</sup> Christophe Bovigny,<sup>†</sup> Diane Lançon, and Matteo Dal Peraro\*

Laboratory for Biomolecular Modeling, Institute of Bioengineering, School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Switzerland

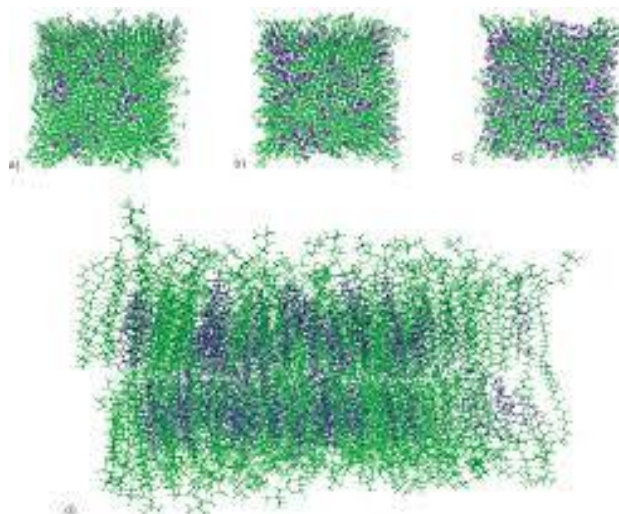
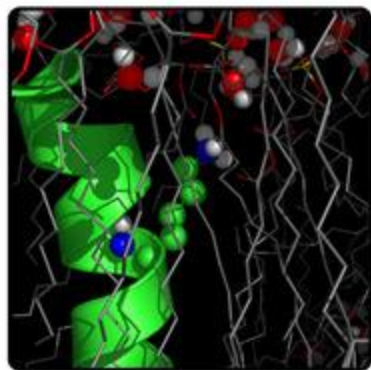
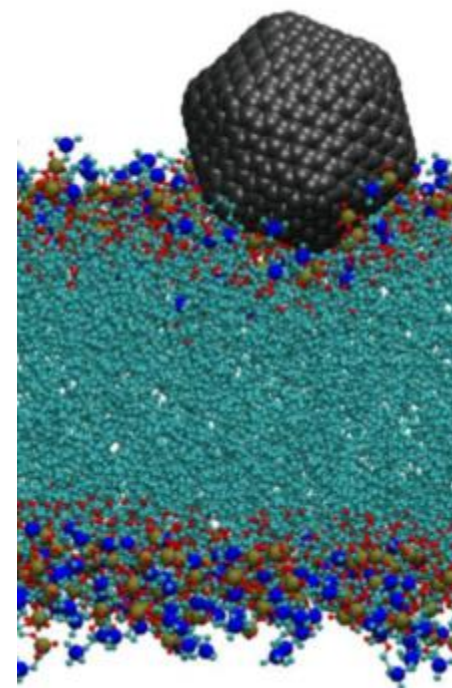
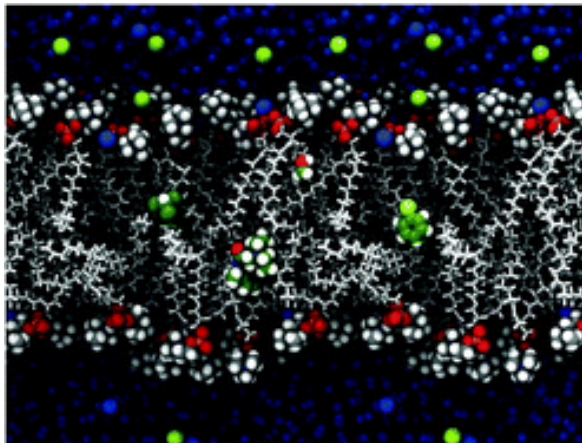
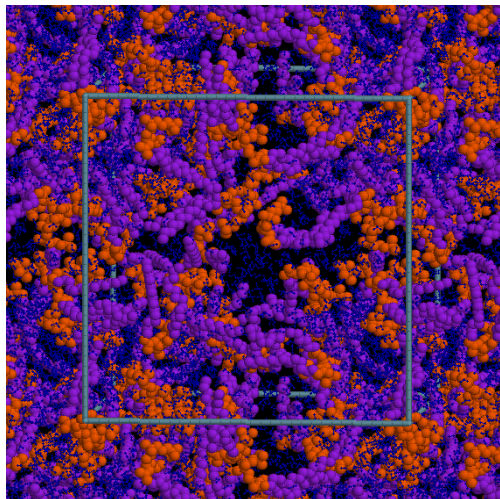
**S** Supporting Information

**ABSTRACT:** Present in bacterial and mitochondrial membranes, cardiolipins have a unique dimeric structure, which carries up to two charges (i.e., one per phosphate group) and, under physiological conditions, can be unprotonated or singly protonated. Exhaustive models and characterization of cardiolipins are to date scarce; therefore we propose an *ab initio* parametrization of cardiolipin species for molecular simulation consistent with commonly used force fields. Molecular dynamics simulations using these models indicate a protonation dependent lipid packing. A peculiar interaction with solvating mono- and divalent cations is also observed. The proposed models will contribute to the study of the assembly of more realistic bacterial and mitochondrial membranes and the investigation of the role of cardiolipins for the biophysical and biochemical properties of membranes and membrane-embedded proteins.



CHARMM36 или AMBER ff99SB

# Дополнительные примеры полноатомного МД моделирования липидных мембран



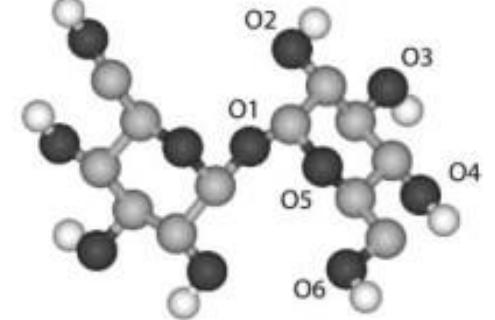
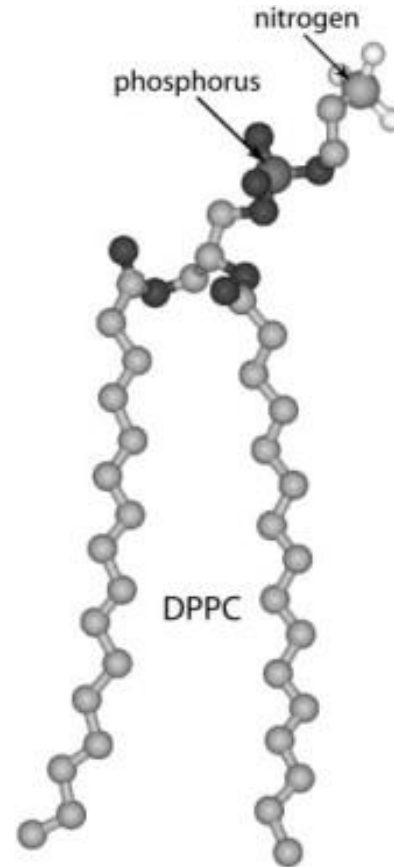
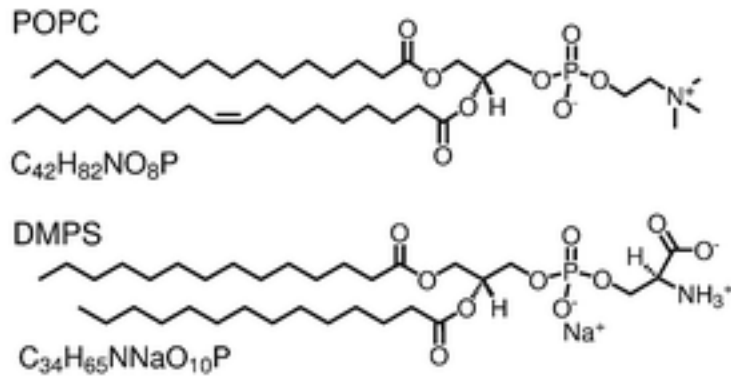


## Упрощенная (united) (“среднезернистая”) модель липида

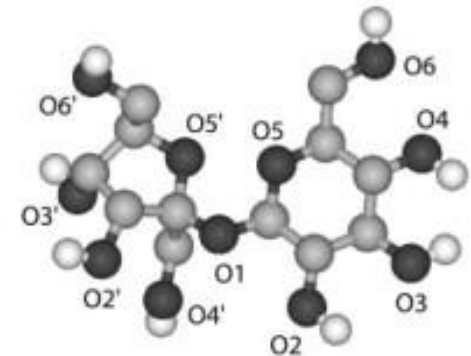
### Неполярные атомы водорода

отсутствуют, т.к.  
они “включены” в потенциал  
взаимодействия соответствующих  
тяжелых атомов

Полярные атомы водорода, которые  
могут образовывать водородную связь  
По прежнему представлены в  
явном виде



Trehalose



Sucrose

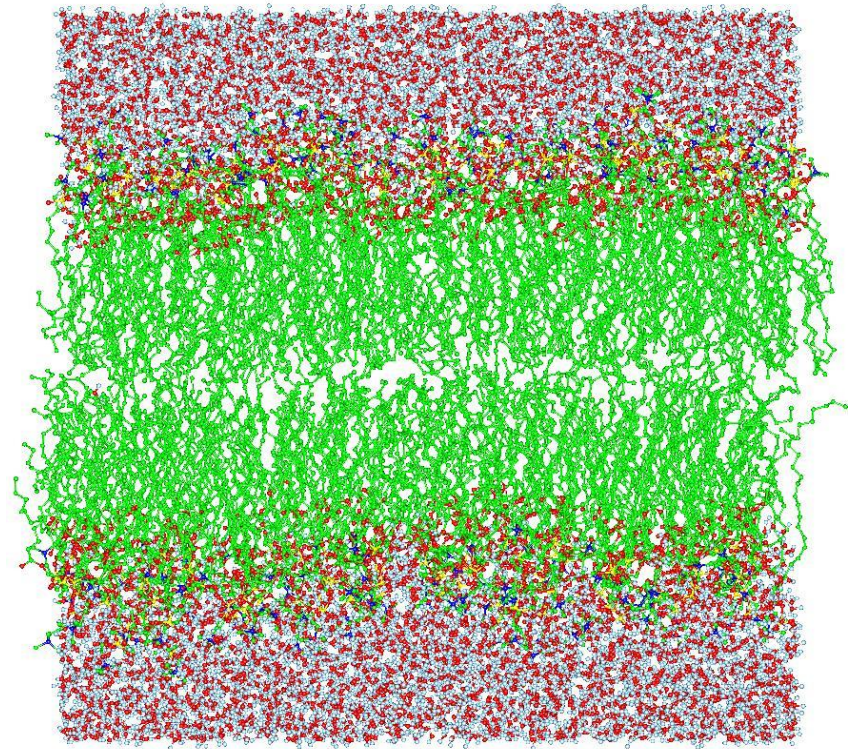
## Упрощенная модель мембраны

### Преимущества:

Точное описание макроскопических параметров изучаемой системы. Точное воспроизведение строения и конформаций индивидуальных липидов и белков. Адекватное определение энергии межмолекулярного взаимодействия. Позволяет проводить МД расчет в шкале до 500 нс

### Недостатки:

Не позволяет изучать мембранные процессы требующие длительной релаксации. Ограничения по размеру мембраны (как правило всего до 1000 липидов)



## CHARMM36 United Atom Chain Model for Lipids and Surfactants

Sarah Lee,<sup>†,||</sup> Alan Tran,<sup>†,||</sup> Matthew Allsopp,<sup>†,||</sup> Joseph B. Lim,<sup>†</sup> Jérôme Hénin,<sup>\*,‡</sup> and Jeffery B. Klauda<sup>\*,†</sup><sup>†</sup>Department of Chemical and Biomolecular Engineering, University of Maryland, College Park, Maryland 20742, United States<sup>‡</sup>Laboratoire de Biochimie Théorique, CNRS, Institut de Biologie Physico-Chimique, 13 rue Pierre et Marie Curie, 75005 Paris, France

## Supporting Information

**ABSTRACT:** Molecular simulations of lipids and surfactants require accurate parameters to reproduce and predict experimental properties. Previously, a united atom (UA) chain model was developed for the CHARMM27/27r lipids (Hénin, J., et al. *J. Phys. Chem. B.* 2008, 112, 7008–7015) but suffers from the flaw that bilayer simulations using the model require an imposed surface area ensemble, which limits its use to pure bilayer systems. A UA-chain model has been developed based on the CHARMM36 (C36) all-atom lipid parameters, termed C36-UA, and agreed well with bulk, lipid membrane, and micelle formation of a surfactant. Molecular dynamics (MD) simulations of alkanes (heptane and pentadecane) were used to test the validity of C36-UA on density, heat of vaporization, and liquid self-diffusion constants. Then, simulations using C36-UA resulted in accurate properties (surface area per lipid, X-ray and neutron form factors, and chain order parameters) of various saturated- and unsaturated-chain bilayers. When mixed with the all-atom cholesterol model and tested with a series of 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC)/cholesterol mixtures, the C36-UA model performed well. Simulations of self-assembly of a surfactant (dodecylphosphocholine, DPC) using C36-UA suggest an aggregation number of  $53 \pm 11$  DPC molecules at 0.45 M of DPC, which agrees well with experimental estimates. Therefore, the C36-UA force field offers a useful alternative to the all-atom C36 lipid force field by requiring less computational cost while still maintaining the same level of accuracy, which may prove useful for large systems with proteins.

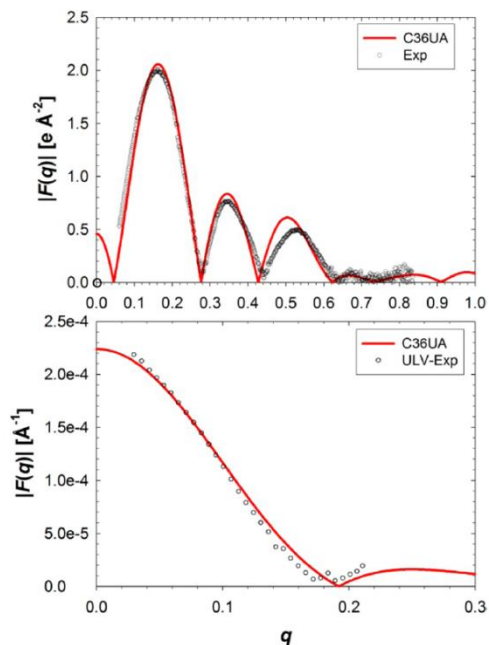
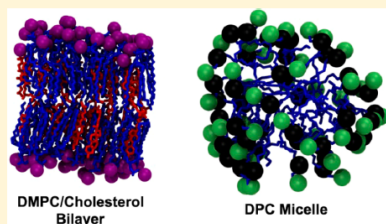


Figure 1. DOPC form factors from X-ray (top) and neutron (bottom) scattering.<sup>42,43</sup> ULV = unilamellar vesicles.  $F(q = 0) = 0$  for X-ray.

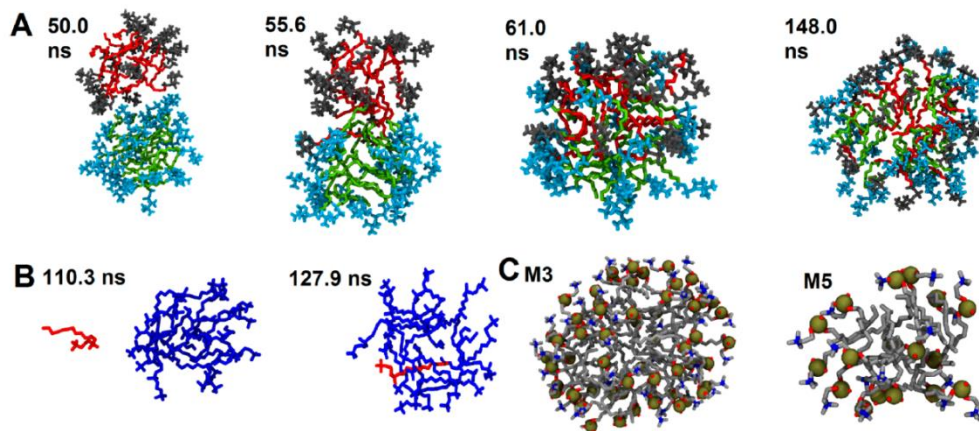


Figure 6. (A) Fusion of two micelles from M1. (B) Integration of a lone surfactant to a micelle in M4. (C) Micelles from M3 and M5 at 148.0 ns.

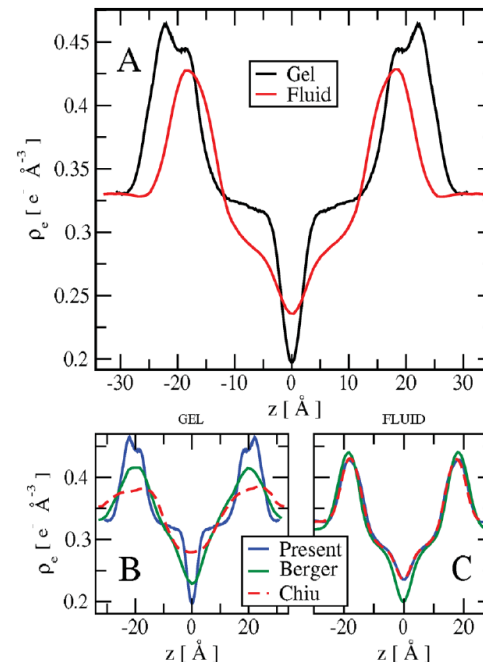
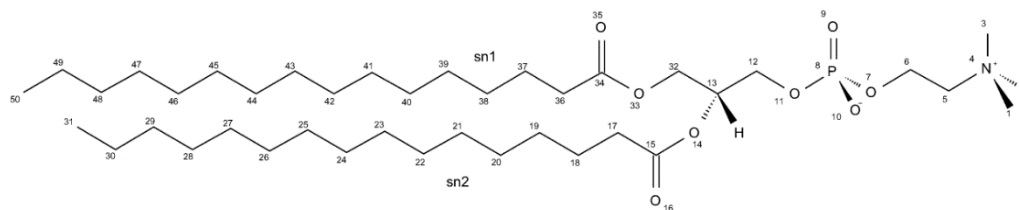
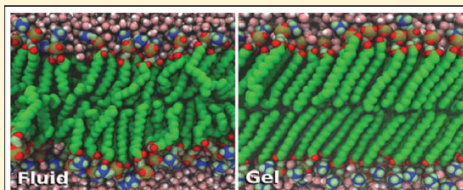
## Reparameterized United Atom Model for Molecular Dynamics Simulations of Gel and Fluid Phosphatidylcholine Bilayers

Richard Tjörnhammar and Olle Edholm\*

Theoretical Biological Physics, Department of Theoretical Physics, KTH Royal Institute of Technology, AlbaNova University Center, SE-106 91 Stockholm, Sweden

### Supporting Information

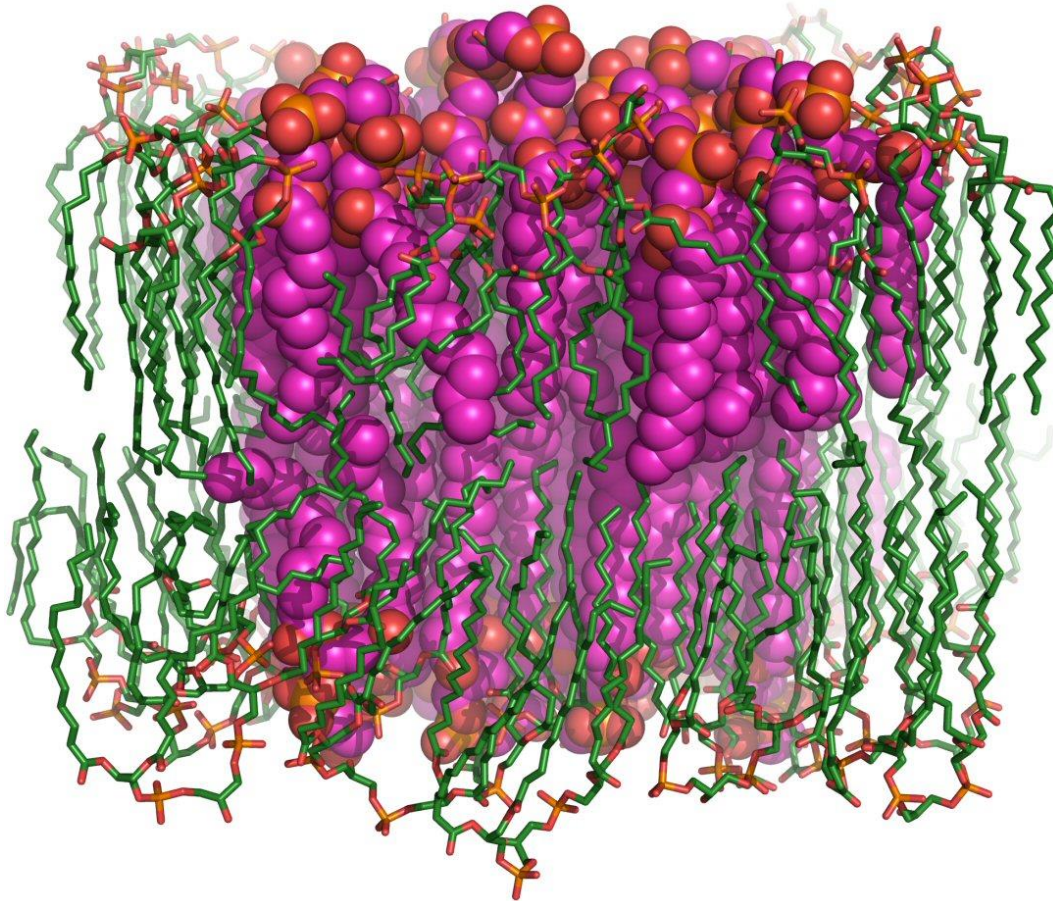
**ABSTRACT:** A new united atom parametrization of diacyl lipids like dipalmitoylphosphatidylcholine (DPPC) and the dimyristoylphosphatidylcholine (DMPC) has been constructed based on *ab initio* calculations to obtain fractional charges and the dihedral potential of the hydrocarbon chains, while the Lennard-Jones parameters of the acyl chains were fitted to reproduce the properties of liquid hydrocarbons. The results have been validated against published experimental X-ray and neutron scattering data for fluid and gel phase DPPC. The derived charges of the lipid phosphatidylcholine (PC) headgroup are shown to yield dipole components in the range suggested by experiments. The aim has been to construct a new force field that retains and improves the good agreement for the fluid phase and at the same time produces a gel phase at low temperatures, with properties coherent with experimental findings. The gel phase of diacyl-PC lipids forms a regular triangular lattice in the hydrocarbon region. The global bilayer tilt obtains an azimuthal value of  $31^\circ$  and is aligned between lattice vectors in the bilayer plane. We also show that the model yields a correct heat of melting as well as decent heat capacities in the fluid and gel phase of DPPC.



**Figure 8.** Calculated electron densities from the simulations. *A:* Comparison of the fluid and the gel for the present force field. *B:* Comparison of the Berger, Chiu, and present force field for the gel. *C:* Comparison of the Berger, Chiu, and present force field for the fluid.

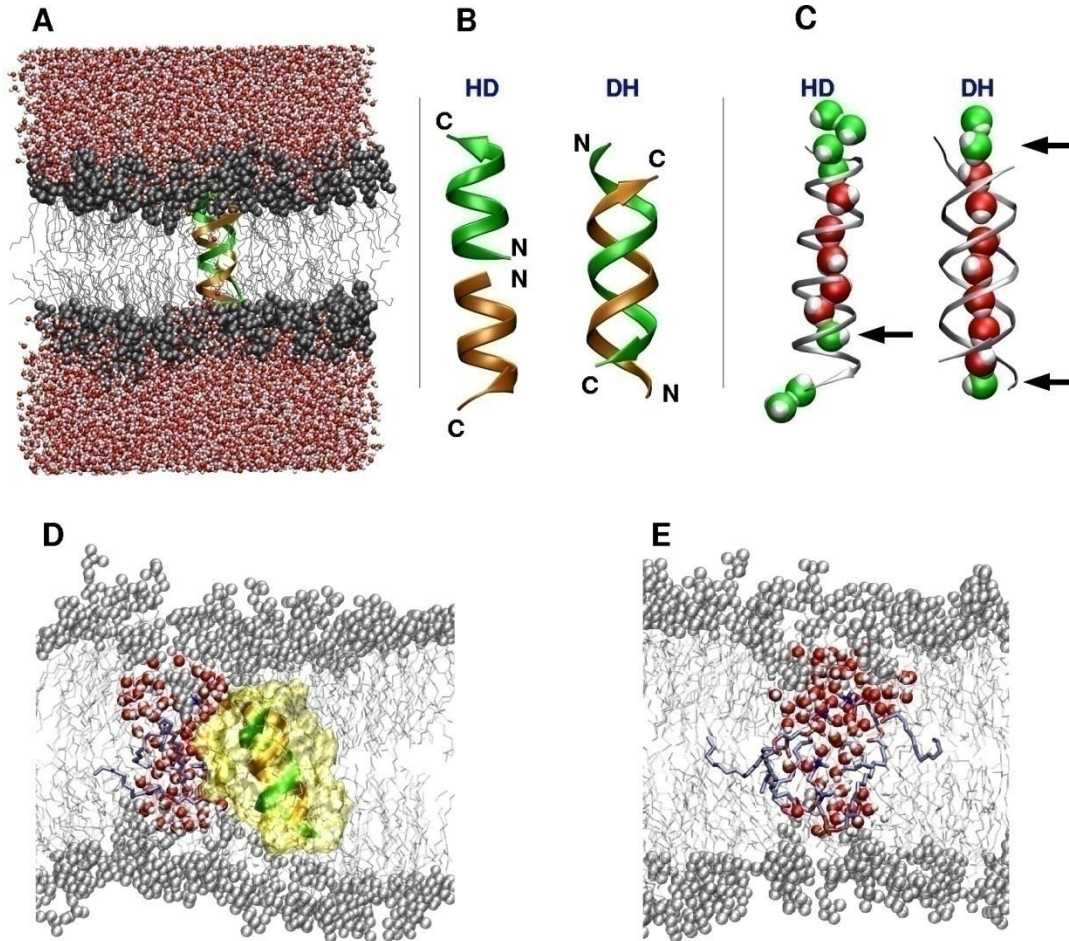
$$V(r) = 4\epsilon \left( \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^6 \right) = \frac{C_{12}}{r^{12}} - \frac{C_6}{r^6}$$

## Примеры упрощенного МД моделирования мембранных систем

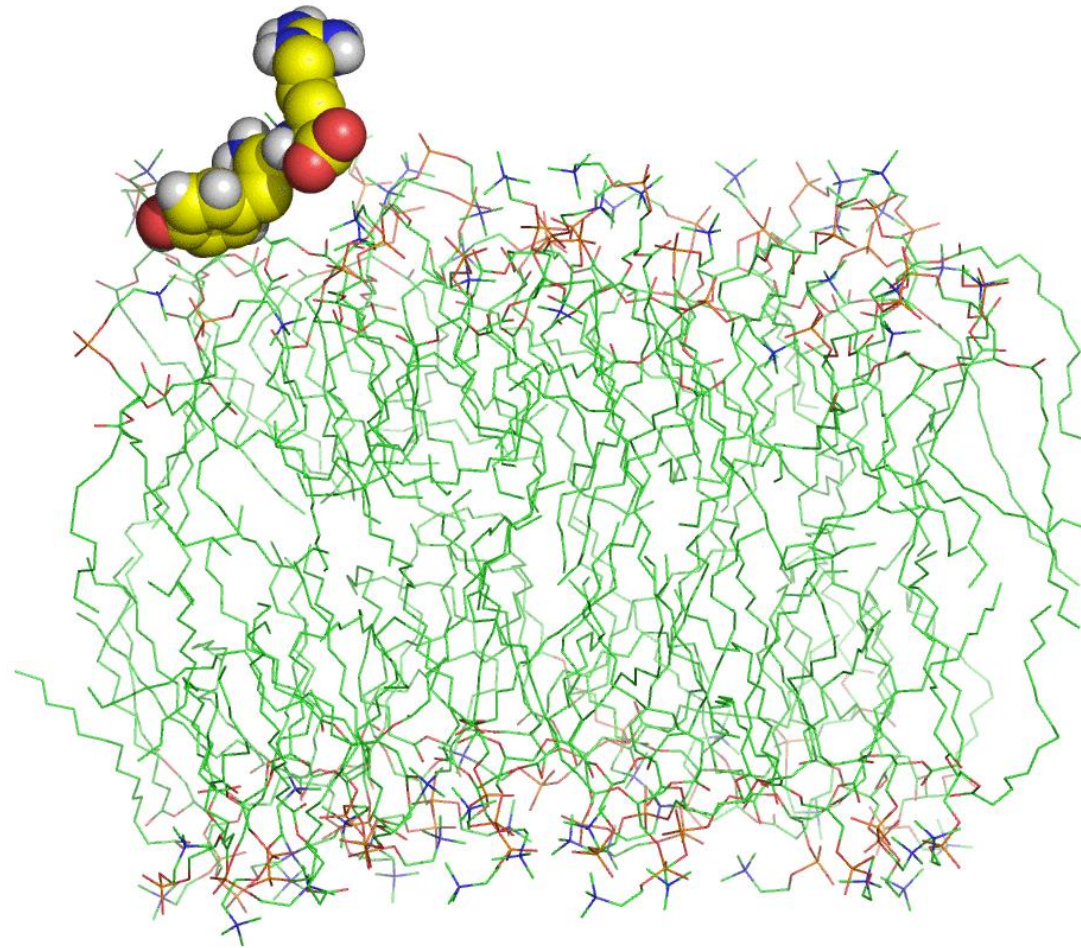


Кардиолипин в мембране

# Примеры упрощенного МД моделирования мембранных систем

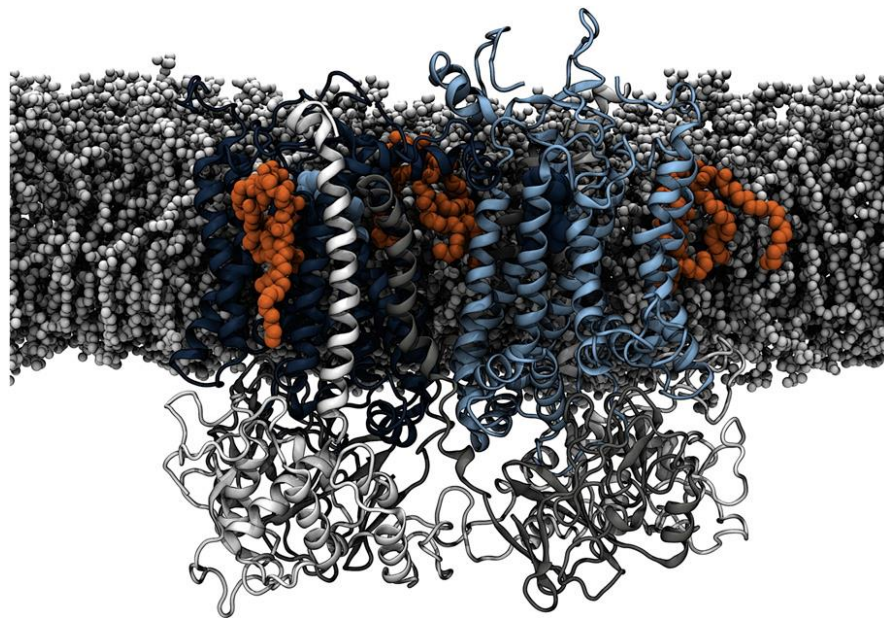
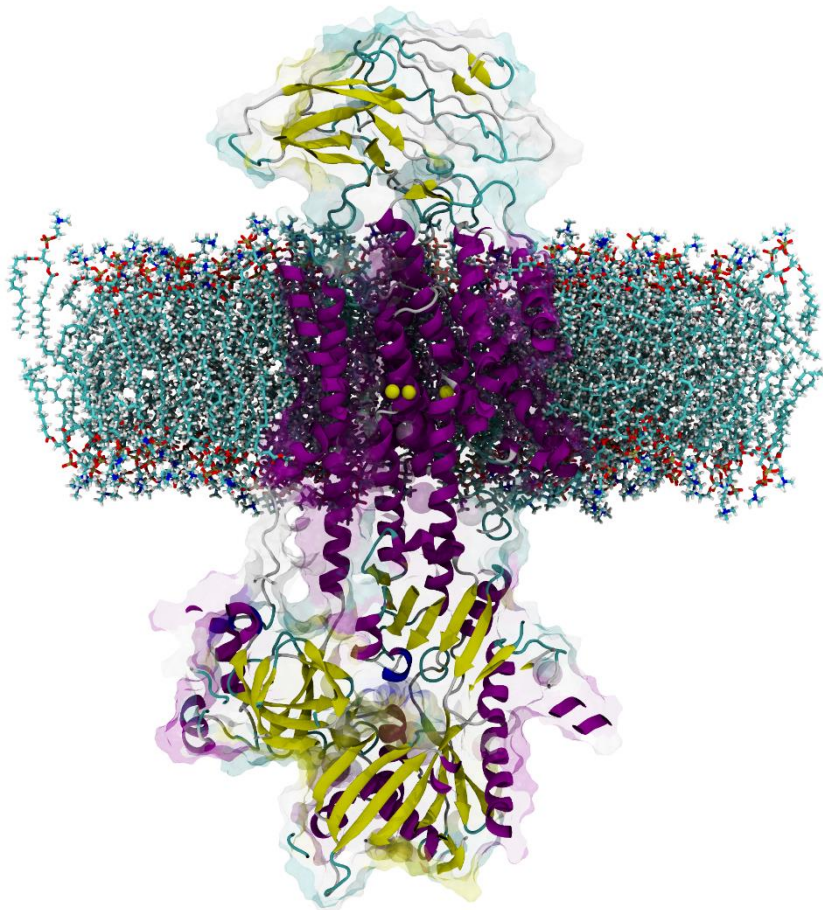


# Применение “среднезернистого” МД моделирования для изучения протеин-липидного взаимодействия



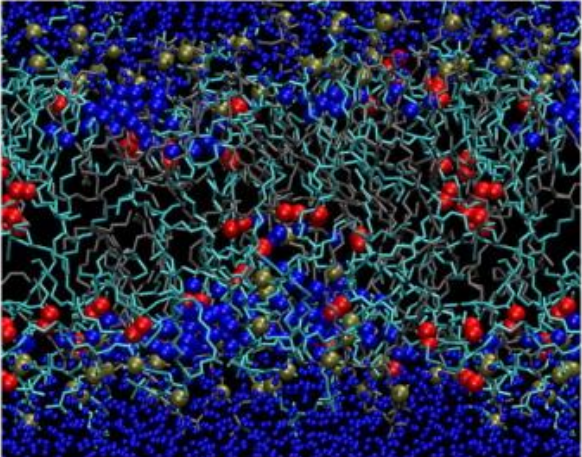
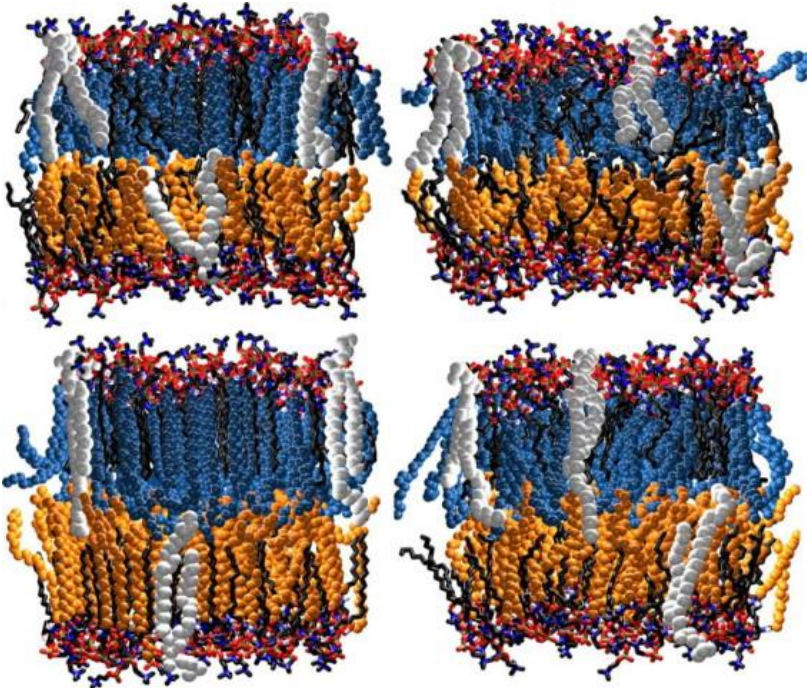
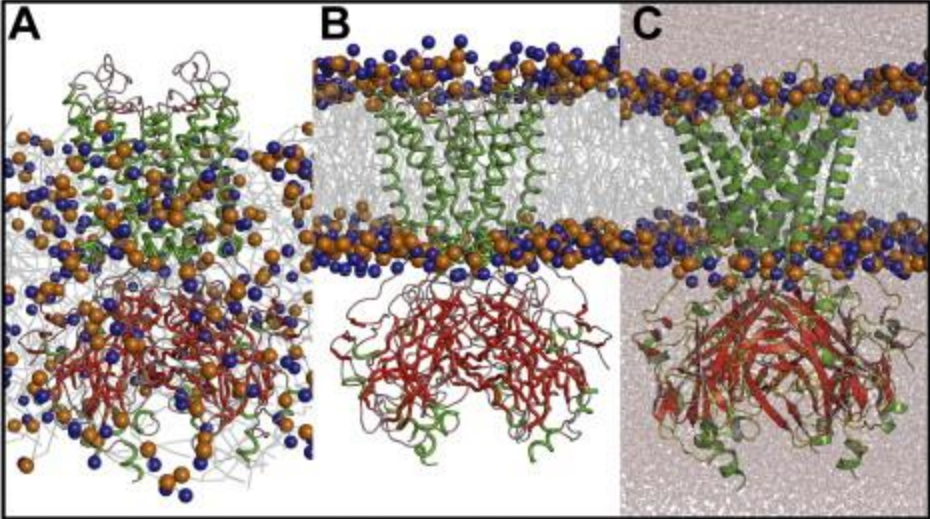
Пример анимация  
МД моделирования  
Взаимодействия  
пептида  
с бислоем

# Дополнительные примеры “среднезернистого” МД моделирования мембранных систем





# Дополнительные примеры “среднезернистого” МД моделирования мембранных систем



На сегодняшний день “среднезернистое” МД моделирование является самым популярным методом

## Как задать начальную геометрию мембраны?

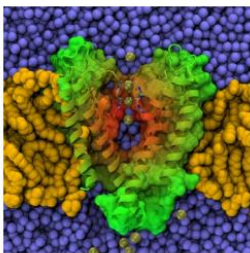
- **вручную**, располагая отдельные липиды на удаленном расстоянии, после этого необходима сольватация полученной системы и длительное МД моделирование “самоорганизации” мембраны
- **вручную**, используя операции симметрии можно создать мембрану в кристаллическом состоянии, после этого необходимо систему сольватировать и привести в термическое равновесие
- использовать **специальные программные пакеты (VMD)** способные конструировать мембрану определенного состава и нужного размера
- использовать **интернет-порталы** (серверы) способные в интерактивном режиме конструировать мембрану определенного состава и нужного размера
- позаимствовать **готовую геометрию** сольватированной равновесной мембраны из литературных источников, при этом не забывая цитировать этот источник

# Бесплатный программный пакет - [VMD Visual Molecular Dynamics](http://www.ks.uiuc.edu/Research/vmd/)

<http://www.ks.uiuc.edu/Research/vmd/>

University of Illinois at Urbana-Champaign  
Beckman Institute for Advanced Science and Technology  
Theoretical and Computational Biophysics Group  
Computational Biophysics Workshop

## Membrane Proteins Tutorial

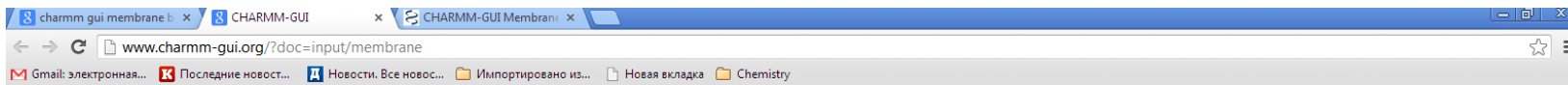


Alex Aksimentiev  
Marcos Sotomayor  
David Wells  
August 2009

A current version of this tutorial is available at  
<http://www.ks.uiuc.edu/Training/Tutorials/>  
Join the [tutorial-l@ks.uiuc.edu](mailto:tutorial-l@ks.uiuc.edu) mailing list for additional help.

The screenshot displays the VMD (Visual Molecular Dynamics) software interface. The main window shows a 3D visualization of a protein structure, likely a ribosome, rendered with red and blue spheres and yellow ribbons. The interface includes a menu bar (File, Molecule, Graphics, Display, Mouse, Extensions, Help), a molecule list, a graphical representations panel with various settings (Style, Color, Selection, Drawing Method, Spline Style, Aspect Ratio, Thickness, Resolution), and a console window at the bottom showing command execution and system output.

# CHARMM-GUI Web-Портал для построение мембраны



- Input Generator**
- PDB Reader
- Glycan Reader
- Solvator
- Quick MD Simulator
- Membrane Builder
- Boundary Potential Utilizer
- PBEQ Solver
- Implicit Solvent Modeller
- Normal Mode Analyzer
- Free Energy Calculator
- NMR Structure Calculator
- EMAP Utilizer
- GCMC/BD Ion Simulator

## Membrane Builder

Tutorial

The Membrane Builder helps the user generate a series of CHARMM inputs necessary to build a protein/membrane complex for molecular dynamics simulations. A brief description of each step is given below. Among various other building schemes, either the "insertion" or the "replacement" method can be chosen by the user in step 3. (user can choose one of them in step 3, see below).

- Insertion method  
*A protein is inserted into a pre-equilibrated lipid bilayer with a hole whose size is comparable to the protein size (the libraries of lipid bilayers are available in [archive](#))*
- Replacement method  
*A protein is first packed by lipid-like spheres whose positions are subsequently used to place randomly chosen lipid molecules from the library (the libraries of lipid molecules are available in [archive](#))*

Please note that

- **NAMD inputs (v2.7b3 or after) are now provided for equilibration and production (see [STEP6](#)). Input files can be found in "namd" directory when you download tar archive ("charmm-gui.tgz") after all the input file generation.**
- the protein must be oriented with respect to a membrane bilayer whose normal is parallel to the Z-axis and whose center is located at Z=0
- RCSB PDB structures are NOT pre-oriented, but can be oriented in step 2 (see below)
- OPM (<http://opm.phar.umich.edu>) provides pre-oriented protein coordinates with respect to the membrane normal
- a homogeneous lipid bilayer can be built with DMPC, DPPC, DOPC, POPC, DLPE, and POPE
- a heterogeneous lipid bilayer can be built with 32 different lipid molecules (see [lipid list](#))
- the heterogenous Membrane Builder can be used for a homogeneous lipid bilayer (only using the replacement method)
- the Membrane-ONLY Builder is now available
- rectangular and hexagonal geometries are available for a system shape in XY

References:

T. Woolf and B. Roux (1996) Structure, energetics, and dynamics of lipid-protein interactions: A molecular dynamics study of the gramicidin A channel in a DMPC bilayer [Proteins 24:92-114](#)

S. Jo, T. Kim, and W. Im (2007) Automated Builder and Database of Protein/Membrane Complexes for Molecular Dynamics Simulations. [PLoS ONE 2\(9\):e880](#)

S. Jo, J.B. Lim, J.B. Klauda, and W. Im (2009) CHARMM-GUI Membrane Builder for Mixed Bilayers and Its Application to Yeast Membranes. [Biophys. J. 97:50-58](#)

Protein/Membrane System

Download PDB File:  Download Source:

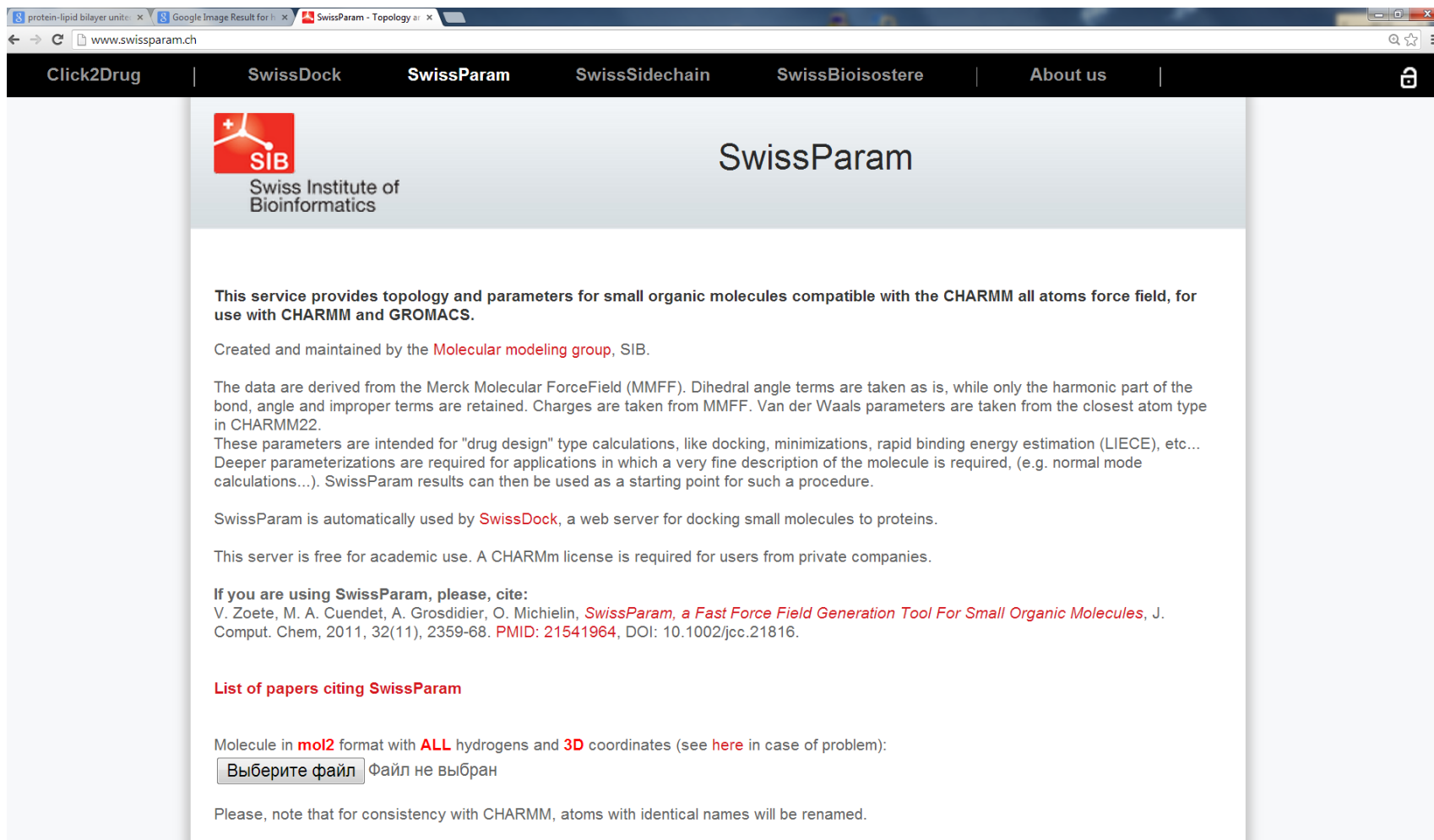
Upload PDB File:  Файл не выбран

PDB Format:  RCSB  CHARMM

Membrane Only System

Next Step: Select Model/Chain

# SwissParam Web-Портал для создания модели липида




The screenshot shows a web browser window with the URL [www.swissparam.ch](http://www.swissparam.ch). The browser's address bar and tabs are visible at the top. The website has a black navigation bar with the following links: Click2Drug, SwissDock, **SwissParam**, SwissSidechain, SwissBioisostere, and About us. The main content area features the SIB logo (Swiss Institute of Bioinformatics) and the title "SwissParam". The text on the page describes the service's purpose, its maintenance by the Molecular modeling group at SIB, and provides information on data sources (Merck Molecular ForceField), intended applications (drug design), and usage instructions. A file upload section is partially visible at the bottom.

protein-lipid bilayer unite x Google Image Result for : x SwissParam - Topology a x

www.swissparam.ch

Click2Drug | **SwissParam** | SwissSidechain | SwissBioisostere | About us

 **SwissParam**  
Swiss Institute of Bioinformatics

**This service provides topology and parameters for small organic molecules compatible with the CHARMM all atoms force field, for use with CHARMM and GROMACS.**

Created and maintained by the [Molecular modeling group](#), SIB.

The data are derived from the Merck Molecular ForceField (MMFF). Dihedral angle terms are taken as is, while only the harmonic part of the bond, angle and improper terms are retained. Charges are taken from MMFF. Van der Waals parameters are taken from the closest atom type in CHARMM22.

These parameters are intended for "drug design" type calculations, like docking, minimizations, rapid binding energy estimation (LIECE), etc... Deeper parameterizations are required for applications in which a very fine description of the molecule is required, (e.g. normal mode calculations...). SwissParam results can then be used as a starting point for such a procedure.

SwissParam is automatically used by [SwissDock](#), a web server for docking small molecules to proteins.

This server is free for academic use. A CHARMM license is required for users from private companies.

**If you are using SwissParam, please, cite:**  
V. Zoete, M. A. Cuendet, A. Grosdidier, O. Michielin, *SwissParam, a Fast Force Field Generation Tool For Small Organic Molecules*, J. Comput. Chem, 2011, 32(11), 2359-68. PMID: [21541964](#), DOI: [10.1002/jcc.21816](#).

**List of papers citing SwissParam**

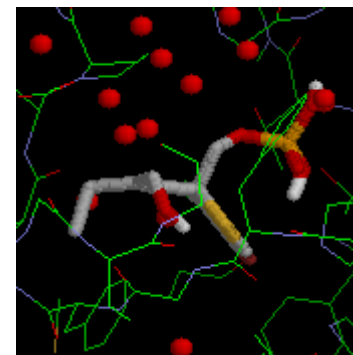
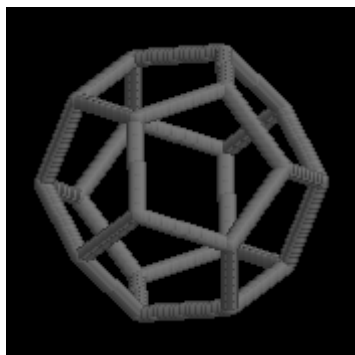
Molecule in **mol2** format with **ALL** hydrogens and **3D** coordinates (see [here](#) in case of problem):

Файл не выбран

Please, note that for consistency with CHARMM, atoms with identical names will be renamed.

# The GlycoBioChem PRODRG2 Server

## Web-Портал для создания модели липида



PRODRG Home [FAQ](#) [PRODRG Beta](#) [How to obtain](#) [Usage stats](#)

### The Dundee PRODRG2 Server

Finally, a FAQ is available [here](#), READ it before using this server

Molecular topologies for ... X-ray refinement/MD ... drug design/docking

Funded by:  
 The Wellcome Trust

... or ...

Paste your input here (PDB coordinates, MDL MOLfile, text drawing). See below for instructions.

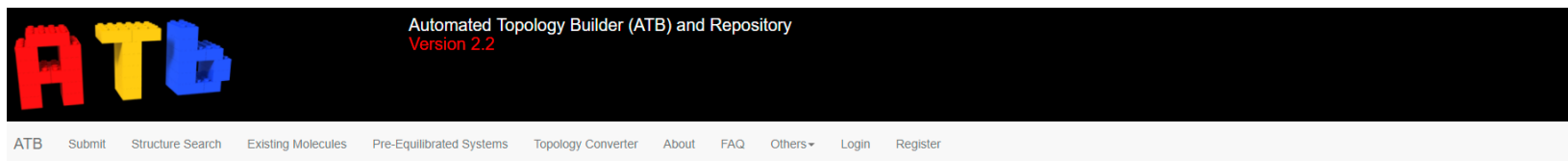
Chirality  Full charges  Energy minimization

Please be patient, this can take up to 2 minutes

<http://davapc1.bioch.dundee.ac.uk/cgi-bin/prodrpg/>

# Automated Topology Builder (ATB) and Repository

## Web-Портал для создания топологии молекулы



### Home

Welcome to the ATB version 2.2.

Version 2.2 includes improvements in the consistency of the pa

### Expanded range of formats

- GROMACS (gromos 53A6 and 54A7).
- GROMOS96 (gromos 53A6 and 54A7).
- GROMOS11 (gromos 53A6 and 54A7).
- LAMMPS (gromos 53A6 and 54A7).
- APBS (Adaptive Poisson-Boltzmann Solver) file format (.pqr).
- CNS (Crystallography & NMR System).
- CIF (compatible with the Phenix, CCP4 and Refmac5 X-ray refinement packages).
- An extended and generalized mmCIF format incorporating a complete description of all force field parameters including units.
- AMBER via a tool to convert GROMOS system topology files (.top) to the AMBER format (.prmtop).

### Existing Molecules

Selected Molecules (1-100 of 173,623) ←

Hide Search Options

IUPAC, common name, RNME or PDB hetid  Formula  Molid  Molecule Type

Curation  Has Experimental Free Energy  Show Processing Molecules

Molid	Formula	Iupac	Common Name	Chembl Id	Atoms	Charge	Date	Curation	Visibility	Details	Save
264187	C <sub>21</sub> H <sub>26</sub> N <sub>6</sub> S	-	-		56	0	2017-10-24	ATB	Public		<input type="button" value="🔗"/>
264159	C <sub>24</sub> H <sub>22</sub> N <sub>4</sub> O	-	4-Ethyl-N-(4-methyl-		51	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264155	C <sub>10</sub> H <sub>10</sub> N <sub>2</sub> O <sub>4</sub>	-	-		34	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264151	C <sub>24</sub> H <sub>18</sub> F <sub>3</sub> N <sub>6</sub> O <sub>2</sub>	-	-		52	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264150	C <sub>27</sub> H <sub>22</sub> FN <sub>7</sub> O	-	-		58	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264149	C <sub>27</sub> H <sub>23</sub> N <sub>7</sub> O	-	-		58	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264148	C <sub>29</sub> H <sub>31</sub> N <sub>5</sub> O	-	-		66	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264147	C <sub>28</sub> H <sub>23</sub> N <sub>7</sub> O	-	-		61	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264146	C <sub>30</sub> H <sub>30</sub> N <sub>6</sub> OS	-	-		68	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264145	C <sub>25</sub> H <sub>19</sub> F <sub>3</sub> N <sub>6</sub> O	-	-		54	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264144	C <sub>26</sub> H <sub>21</sub> F <sub>3</sub> N <sub>6</sub> O	-	-		57	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>
264143	C <sub>28</sub> H <sub>23</sub> F <sub>3</sub> N <sub>6</sub> O	-	-		61	0	2017-10-23	ATB	Public		<input type="button" value="🔗"/>

база данных  
из 173 тысяч  
готовых  
топологических  
моделей

<https://atb.uq.edu.au/index.py>

# Онлайн генератор топологии органических молекул в формате OPLS

← → 🔒 Не защищено | zarbi.chem.yale.edu/ligpargen/

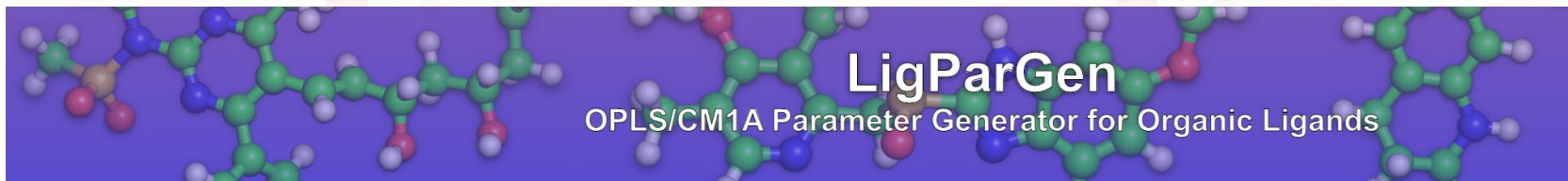
LigParGen

Draw Molecule

Alchemical Assistant

Tutorials -

Contact



LigParGen is a web-based service that provides force field (FF) parameters for organic molecules or ligands, offered by the Jorgensen group.

LigParGen provides bond, angle, dihedral, and Lennard-Jones OPLS-AA parameters with 1.14\*CM1A or 1.14\*CM1A-LBCC partial atomic charges.

Server provides parameter and topology files for commonly used molecular dynamics and Monte Carlo packages OpenMM, Gromacs, NAMD, CHARMM, LAMMPS, TINKER, CNS/X-PLOR, Q, DESMOND, BOSS and MCPRO. Also, the PQR file is generated.

Supported input formats: SMILES, MOL and PDB.

Maximum ligand size allowed is 200 atoms.

Check this link to use [LigParGen software from command-line](#) in your local computer.

Please, report any issue clicking in the following link: [LigParGen issues](#)



## References

If you use the LigParGen server, please cite the following references:

1. Potential energy functions for atomic-level simulations of water and organic and biomolecular systems. Jorgensen, W. L.; Tirado-Rives, J. *Proc. Nat. Acad. Sci. USA* 2005, 102, 6665-6670
2. 1.14\*CM1A-LBCC: Localized Bond-Charge Corrected CM1A Charges for Condensed-Phase Simulations. Dodda, L. S.; Vilseck, J. Z.; Tirado-Rives, J.; Jorgensen, W. L. *J. Phys. Chem. B*, 2017, 121 (15), pp 3864-3870
3. LigParGen web server: An automatic OPLS-AA parameter generator for organic ligands. Dodda, L. S.; Cabeza de Vaca, I.; Tirado-Rives, J.; Jorgensen, W. L. *Nucleic Acids Research*, Volume 45, Issue W1, 3 July 2017, Pages W331-W336

## Step 1: Input structure

SMILES

Enter SMILES Code

OR upload MOL / PDB file (Structures **MUST** include all hydrogens)

Выберите файл | Файл не выбран

## Step 2: Options

Molecule Optimization Iterations 0 ▾

Select charge model:

- 1.14\*CM1A-LBCC (Neutral molecules)
- 1.14\*CM1A<sup>1</sup> (Neutral or Charged molecules)

Molecule charge 0 ▾

Submit Molecule

Sample Benzene

<sup>1</sup> For charged molecules, CM1A charges are NOT scaled by a factor 1.14

<http://zarbi.chem.yale.edu/ligpargen/>



# Рекомендуемая литература

[1] A computer perspective of membranes: Molecular dynamics studies of lipid bilayer systems / Tieleman D. P., Marrink S. J. and Berendsen H. J. C. // *Biochim Biophys Acta Rev Biomembr.* — 1997. — V. 1331, № 3. — P. 235-270.

[2] Martinez-Seara H. and Róg T., Molecular dynamics simulations of lipid bilayers: Simple recipe of how to do it, *in Biomolecular simulations*, L. Monticelli and E. Salonen, Editors. 2013, *Springer Science+Business Media: New York*. p. 407-429.

[3]. Computer simulations of transport through membranes: Passive diffusion, pores, channels and transporters / Tieleman D. Peter // *Proc. Australian Physiol. Soc.* — 2006. — V. 37, — P. 15-27.

[4]. The importance of membrane defects—lessons from simulations / Bennett W. F. D. and Tieleman D. P. // *Acc. Chem. Res.* — 2014. — V. 47, № 8. — P. 2244-2251.

