

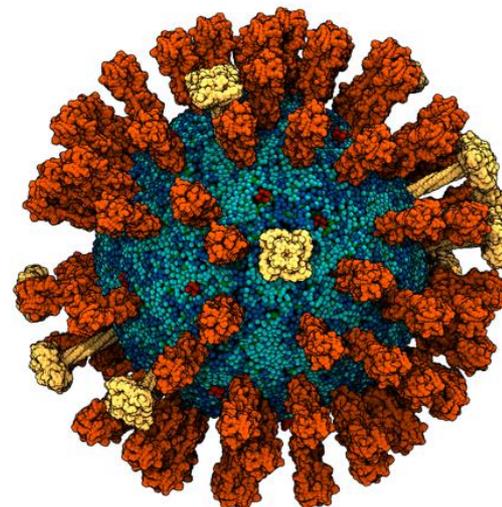
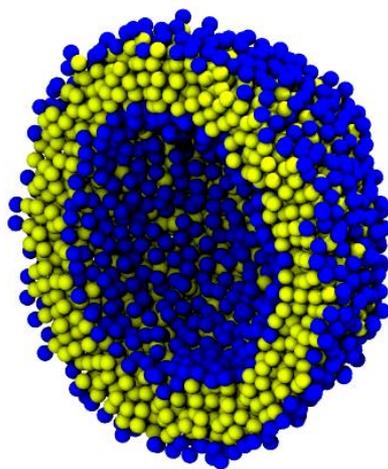
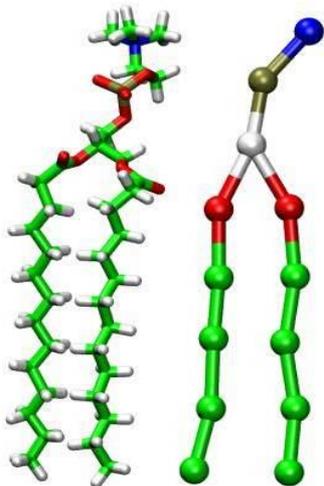


# Сучасні комп'ютерні методи дослідження нанорозмірних та біологічних систем



## Лекція № 9

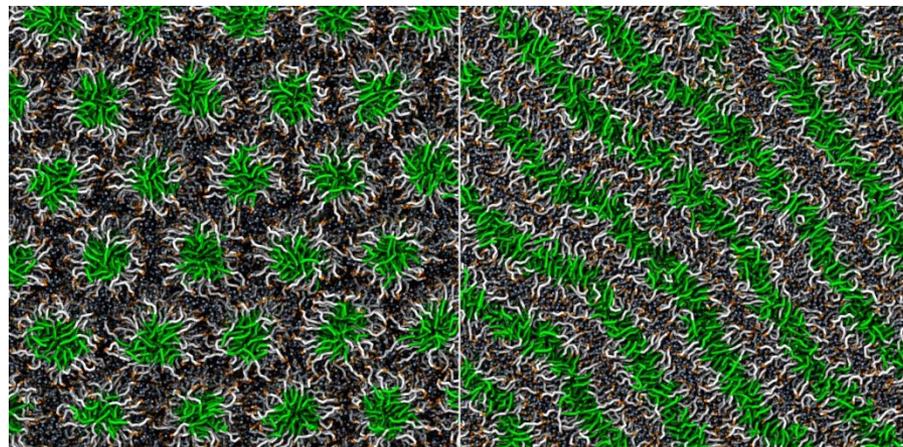
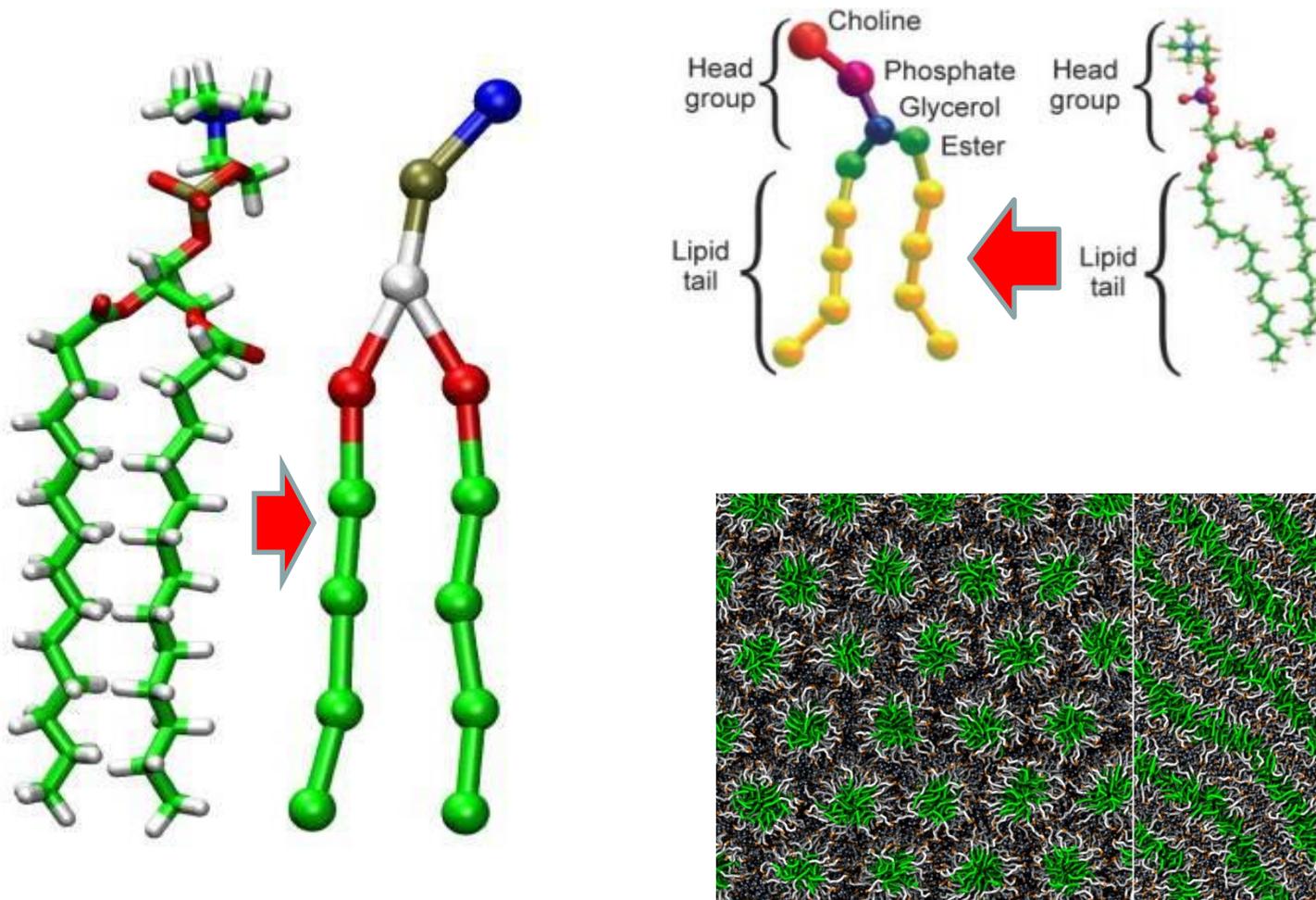
**Крупно-зерниста модель ліпиду та ліпідної мембрани.  
Порівняльна характеристика та області застосування різних МД моделей**



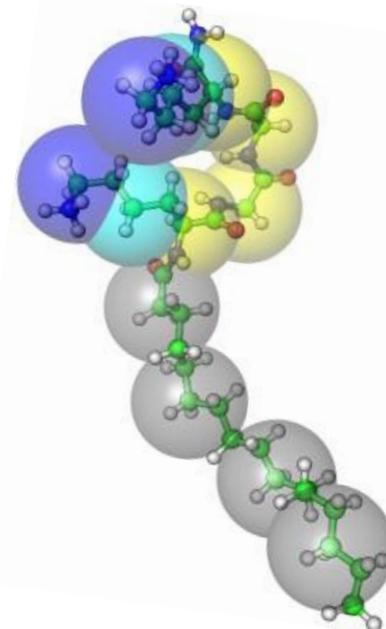
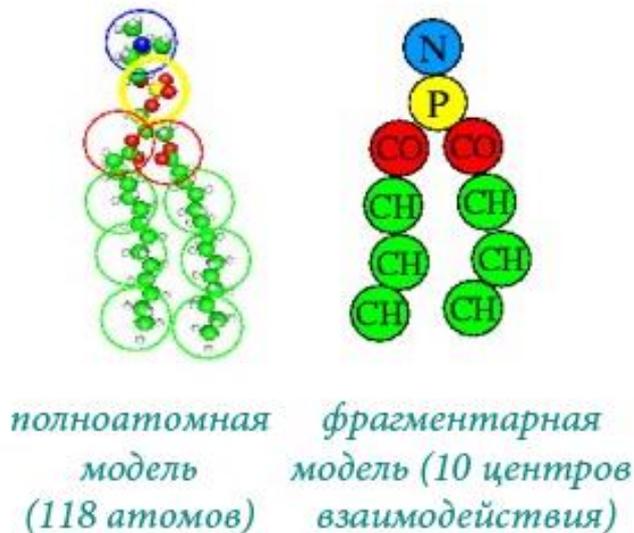
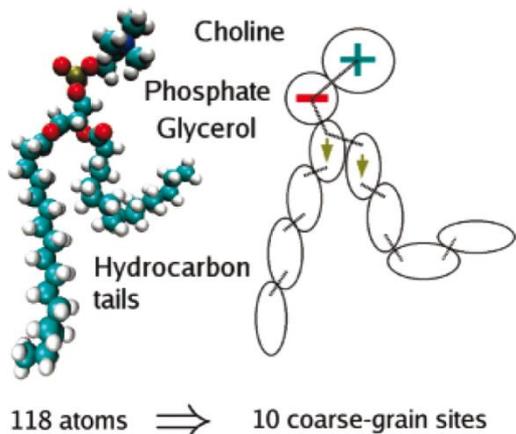
## **План Лекції № 9**

- Фрагментовані та “зернисті” моделі ліпиду та ліпідної мембрани**
- Поширені силові поля та програми для МД моделювання ліпідних систем**
- Порівняльна характеристика та області застосування різних МД моделей**
- Наявні програмні пакети для МД моделювання біологічних мембран**

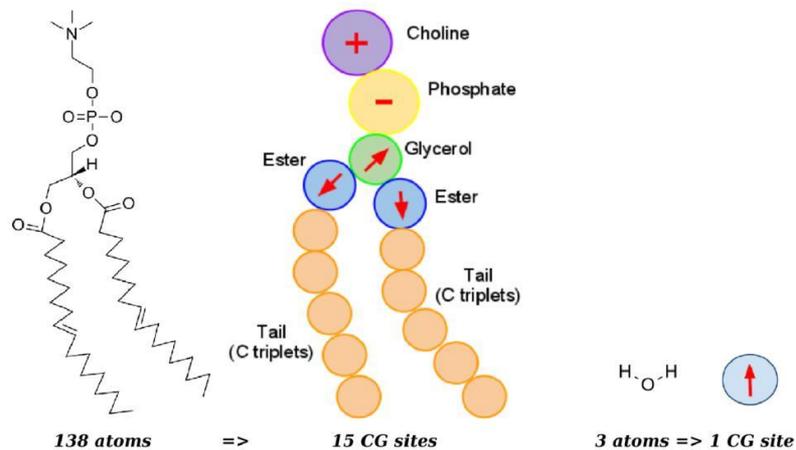
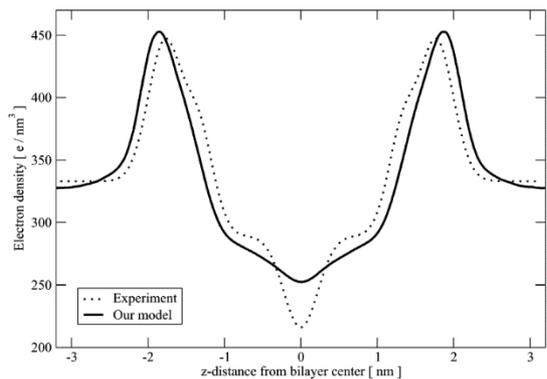
**“Фрагментарная”, “крупно-зернистая” или “грубо-зернистая”  
(coarse-grained) МД модель липида**



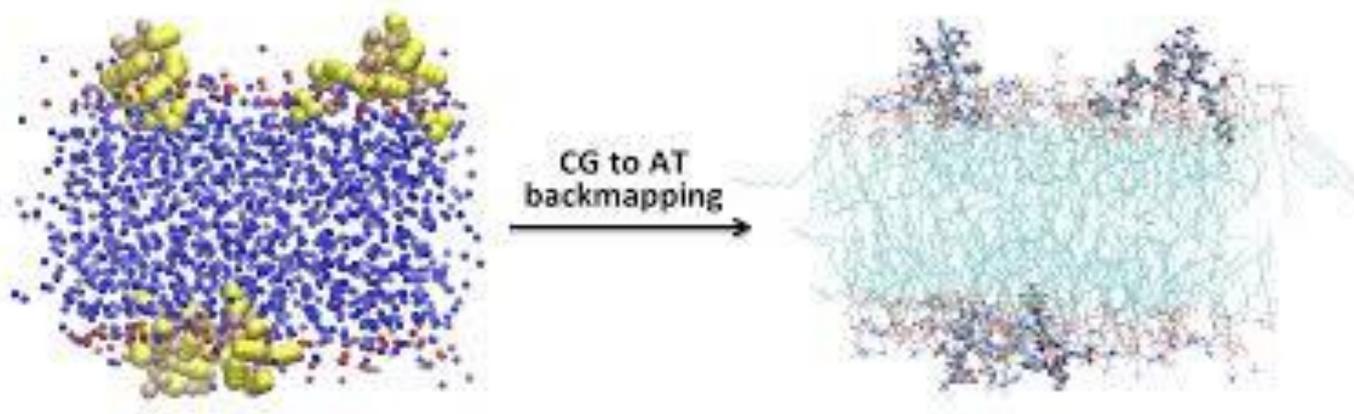
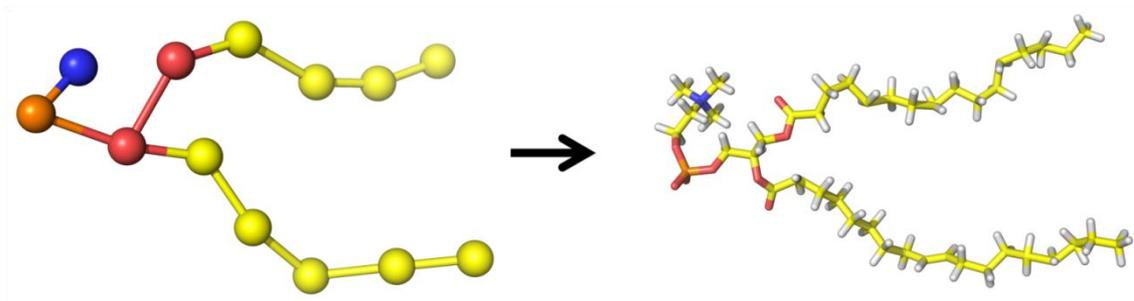
# “Фрагментарная” или “крупно-зернистая” МД модель липида



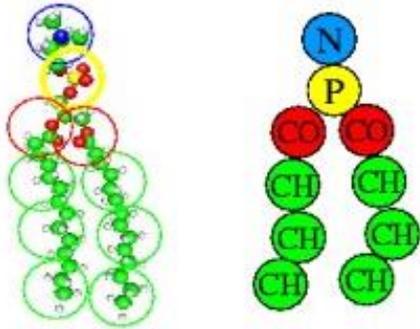
## критерий успешности модели



## Обратная трансформация “крупнозернистой” модели в полноатомную модель



# “Фрагментарная” МД модель липида



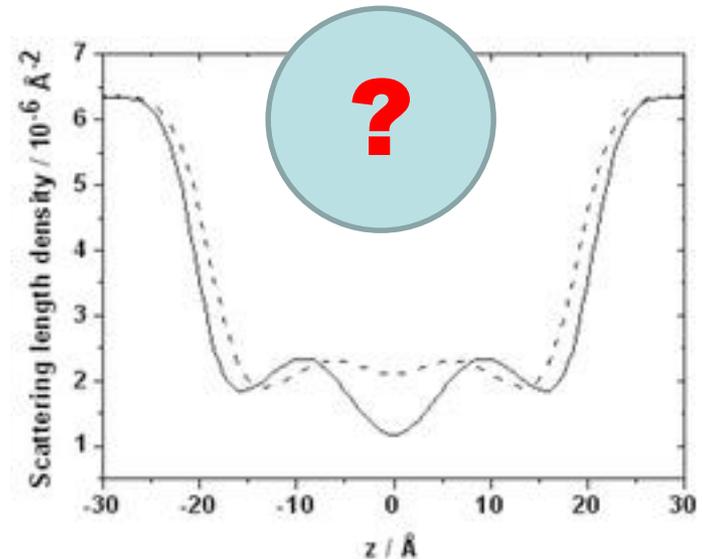
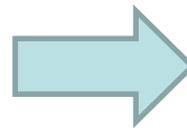
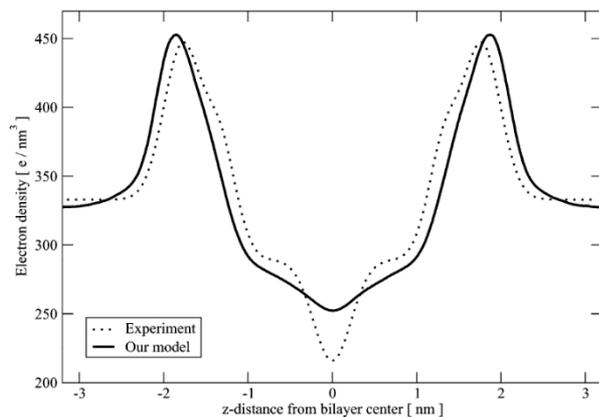
полноатомная модель (118 атомов)      фрагментарная модель (10 центров взаимодействия)

Уже предложено 8 различных моделей, с разной степенью фрагментации одной молекулы липида.

однако

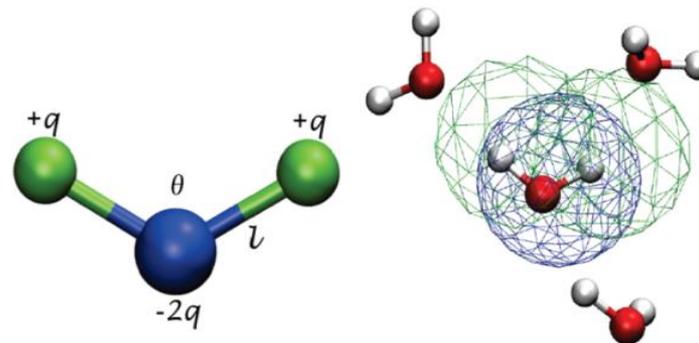
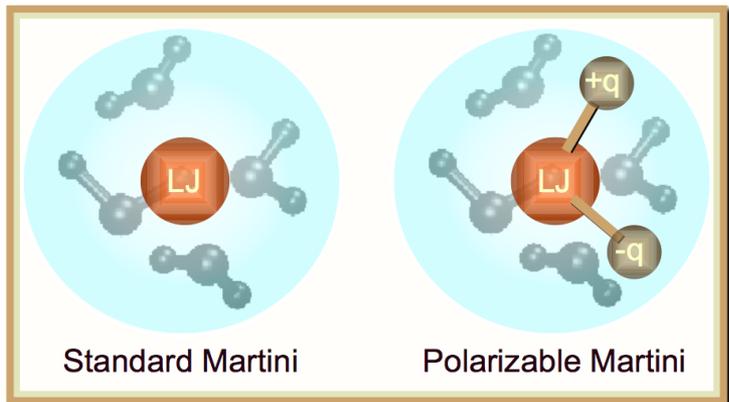
на определенном этапе происходит потеря разрешающей способности фрагментированной модели ...

критерий успешности модели = воспроизведение эксперимента

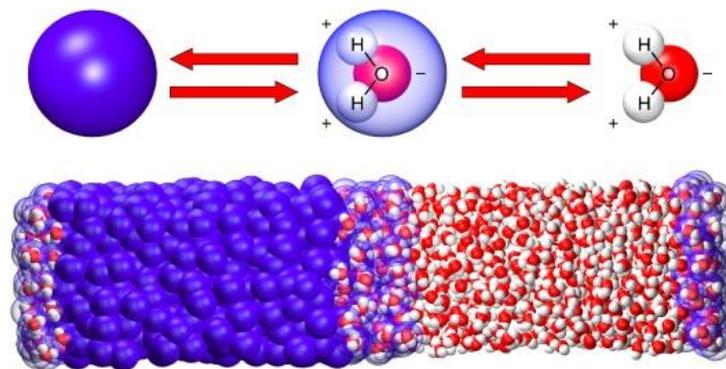
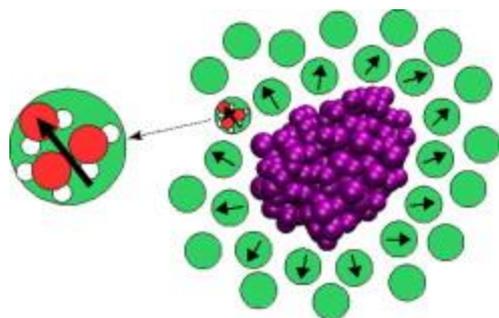


# “Фрагментарные” МД модели воды

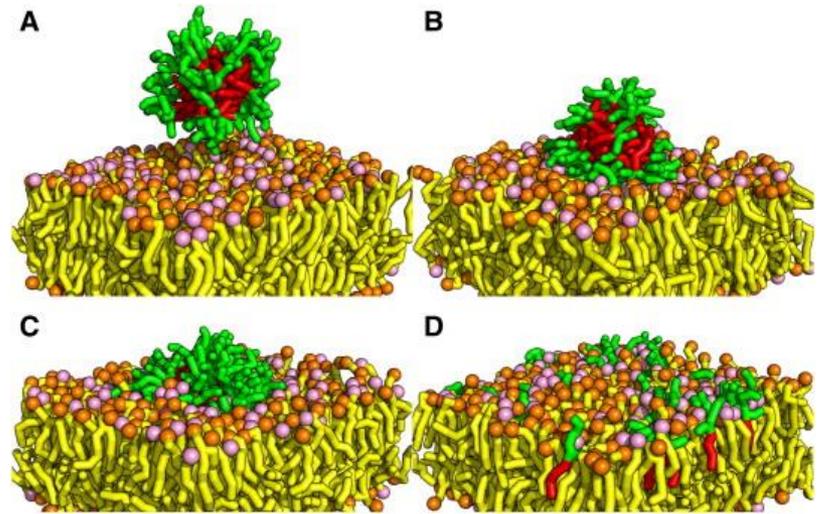
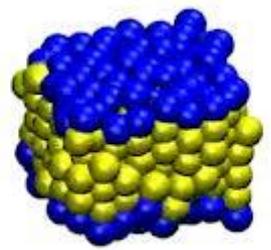
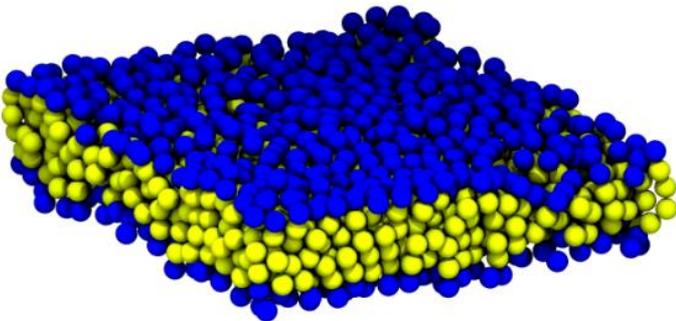
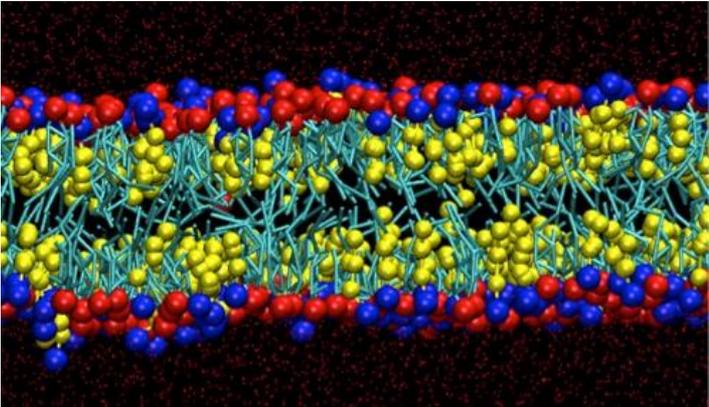
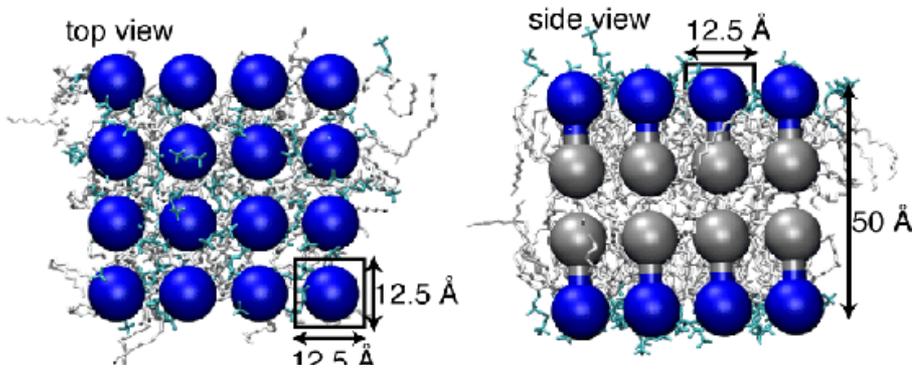
10526 *J. Phys. Chem. B, Vol. 114, No. 32, 2010*



**Figure 2.** A 4-water cluster is coarse grained into a three-site model with  $\theta = 120^\circ$ ,  $l = 1.2 \text{ \AA}$ ,  $q = 1e^-$ .



# “Фрагментарная” МД модель мембраны



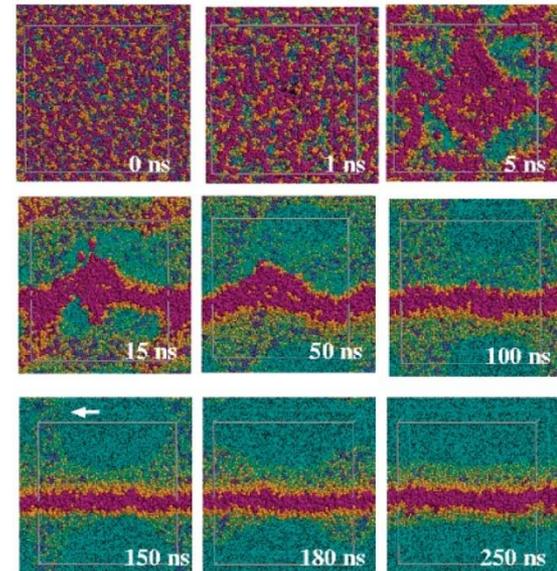
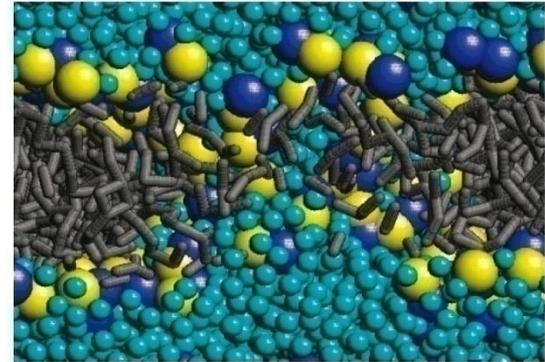
## “Фрагментарная” МД модель мембраны

### Преимущества:

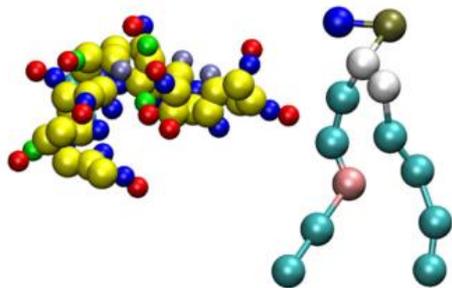
Адекватное описание макроскопических параметров мембран и везикул. Позволяет изучать процессы образования и слияния индивидуальных везикул. Позволяет проводить МД расчет в микросекундной шкале!

### Недостатки:

Утрачивается атомное разрешение в строение изучаемой системы. Невозможно различить детали межмолекулярного взаимодействия. Отсутствие адекватных моделей для водной фазы

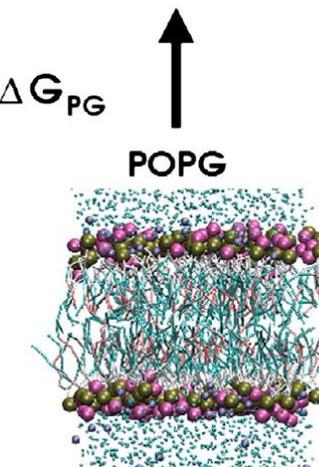
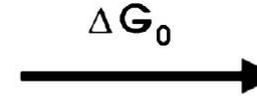
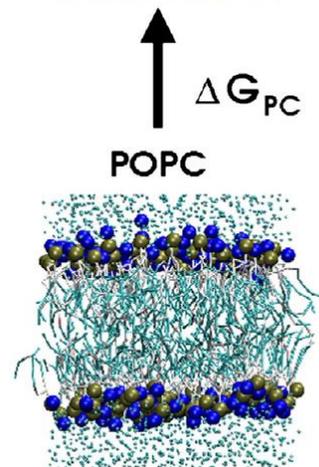
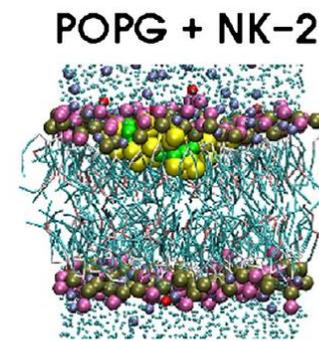
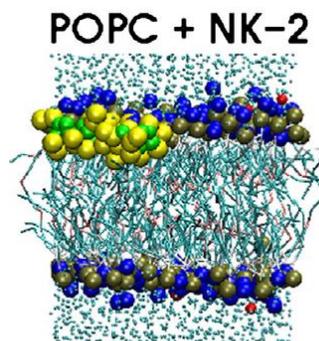
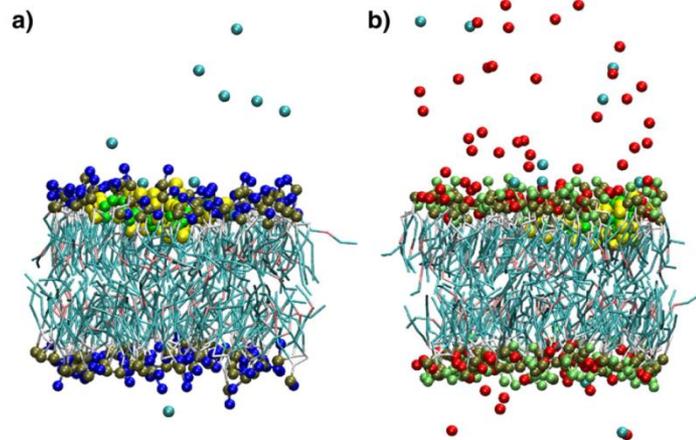


# Пример “крупнозернистой” МД модели

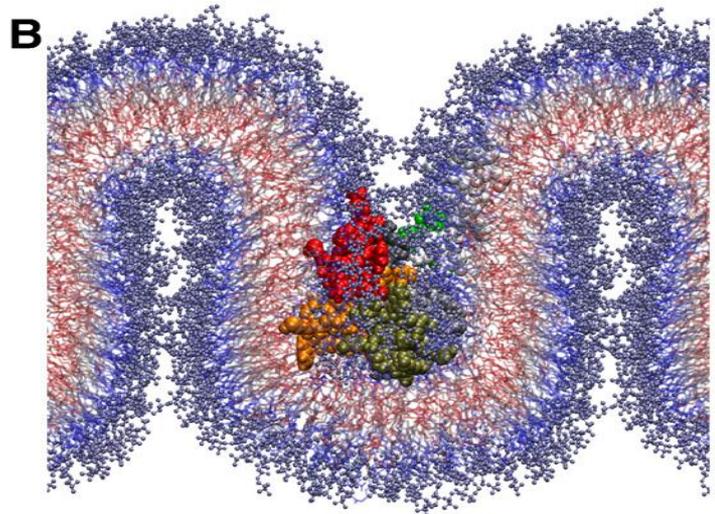
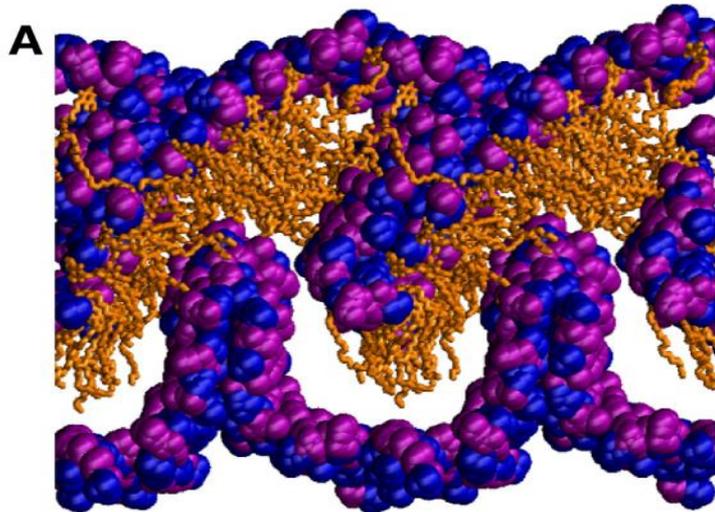


Пептид POPC липид

*C.I.E. von Deuster, V. Knecht / Biochimica et Biophysica Acta 1808 (2011) 2867–2876*



# Примеры “крупнозернистой” МД модели



Biochimica et Biophysica Acta 1788 (2009) 149–168



Contents lists available at ScienceDirect

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journal homepage: [www.elsevier.com/locate/bbamem](http://www.elsevier.com/locate/bbamem)



Review

## Lipids on the move: Simulations of membrane pores, domains, stalks and curves

Siewert J. Marrink <sup>a,\*</sup>, Alex H. de Vries <sup>a</sup>, D. Peter Tieleman <sup>b</sup>

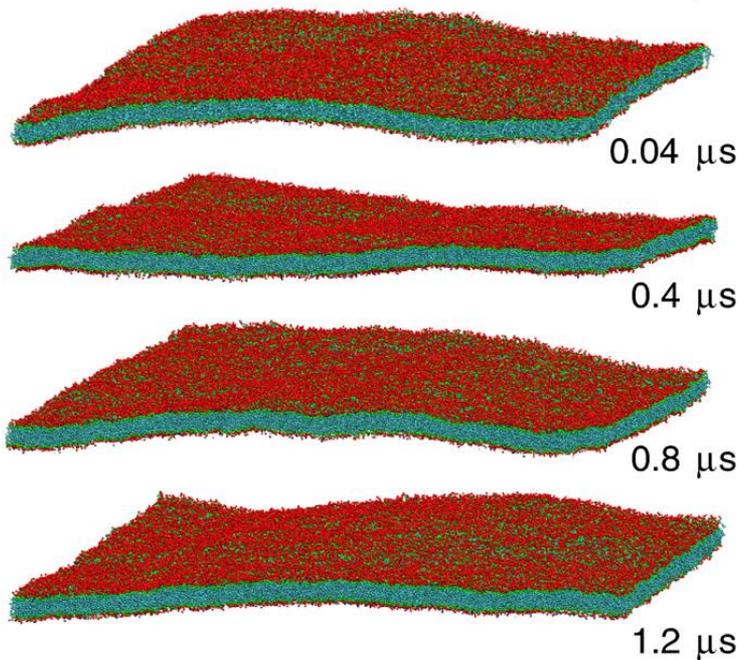
<sup>a</sup> Groningen Biomolecular Sciences and Biotechnology Institute and Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands  
<sup>b</sup> Department of Biological Sciences, University of Calgary, 2500 University Dr NW, Calgary, AB, Canada T2N 1N4

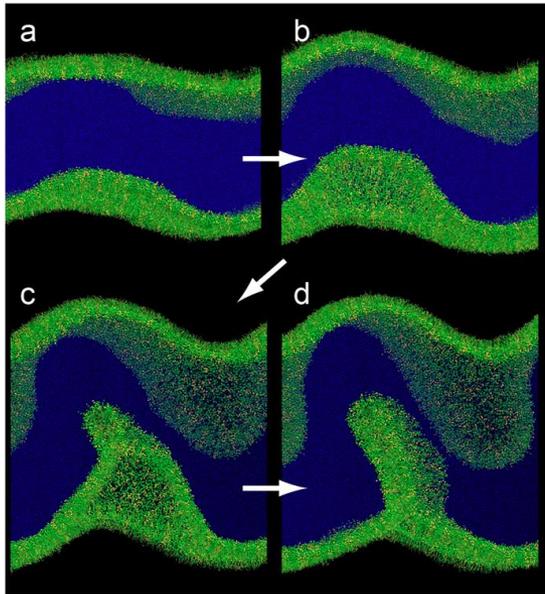
### ARTICLE INFO

*Article history:*  
Received 16 August 2008  
Received in revised form 13 October 2008  
Accepted 14 October 2008  
Available online 25 October 2008

### ABSTRACT

In this review we describe the state-of-the-art of computer simulation studies of lipid membranes. We focus on collective lipid–lipid and lipid–protein interactions that trigger deformations of the natural lamellar membrane state, showing that many important biological processes including self-aggregation of membrane components into domains, the formation of non-lamellar phases, and membrane poration and curving, are now amenable to detailed simulation studies.





## Computer simulations of lung surfactant☆



Svetlana Baoukina\*, D. Peter Tieleman

Department of Biological Sciences and Centre for Molecular Simulation, University of Calgary, 2500 University Dr. NW, Calgary, AB T2N 1N4, Canada

### ARTICLE INFO

**Article history:**

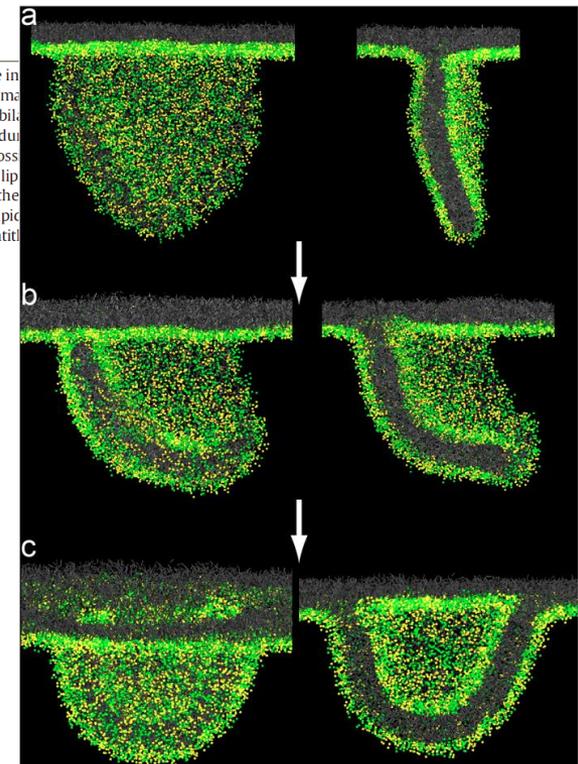
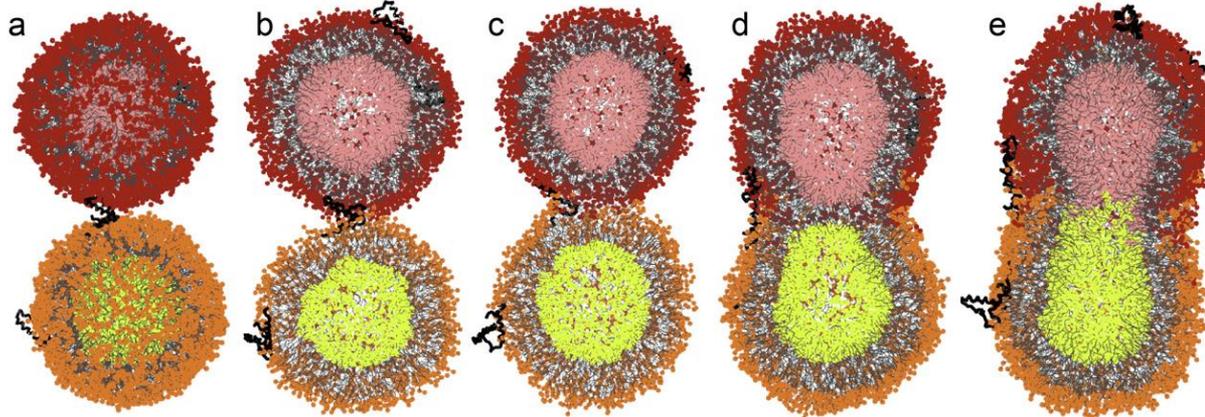
Received 31 December 2015  
 Received in revised form 21 February 2016  
 Accepted 23 February 2016  
 Available online 27 February 2016

**Keywords:**

Molecular dynamics  
 Pulmonary surfactant  
 Lipid monolayer  
 Monolayer collapse

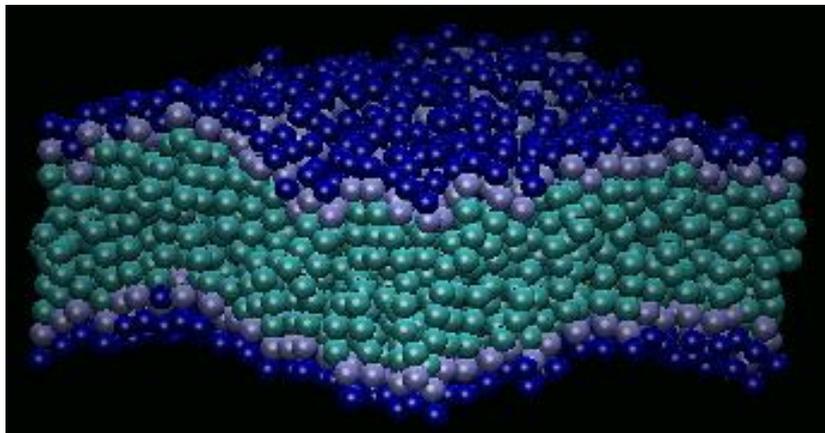
### ABSTRACT

Lung surfactant lines the gas-exchange in the air-water interface connected to the air-water interface by bilayers during breathing. Lung surfactant consists mainly of phospholipids and proteins. The monolayer and bilayers during breathing are connected to the air-water interface. Selected species are possible in the monolayer and bilayers during breathing. The exact roles of lipids in lung surfactant and the exact roles of lipids in lung surfactant are reviewed. This article is part of a Special Issue entitled “Recent simulation studies on the monolayer–bilayer transformations, lipid monolayer collapse and protein adsorption”.

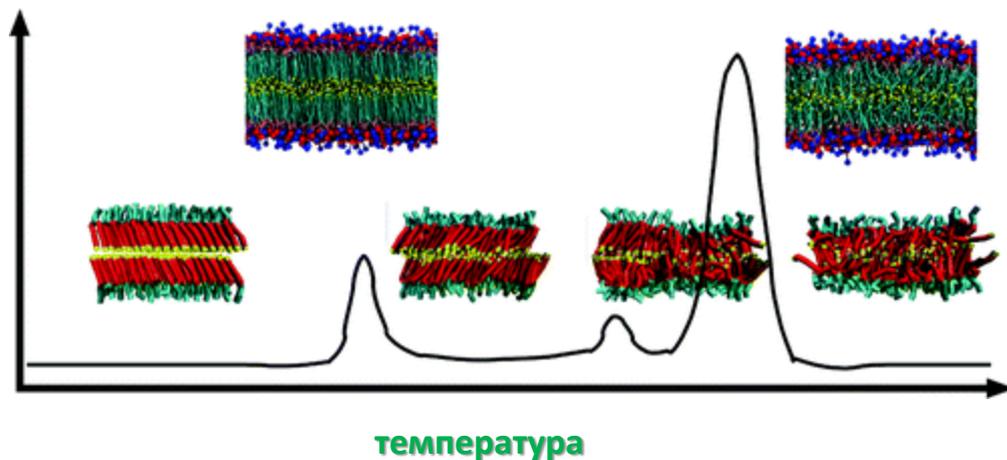


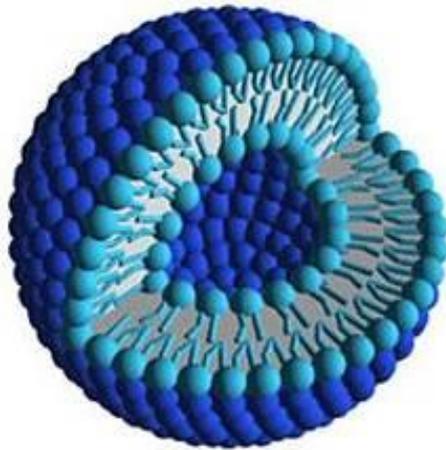
# МД моделирование фазового перехода с использованием крупнозернистой модели липида

“Жидкокристаллическое”

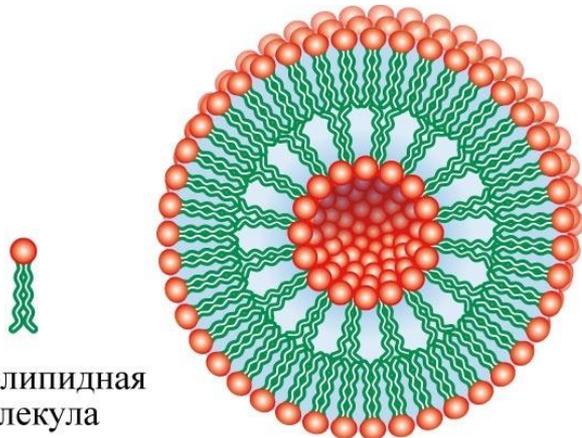


“Гелеобразное”

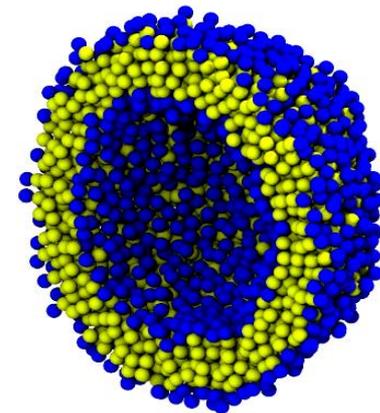
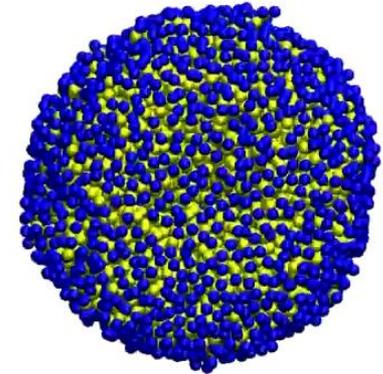
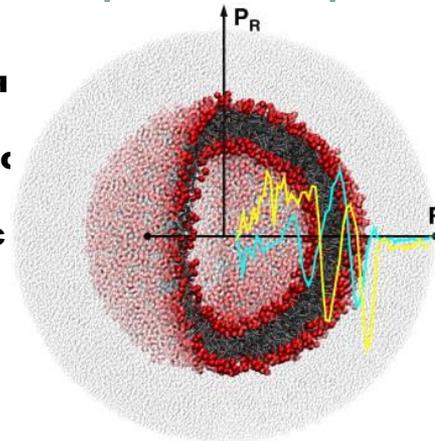




**Липосома**  
(липидная везикула) (от греч. липос – жир и сома – тельце или частица) – это замкнутая, сферическая система, которая образуется самопроизвольно в смесях фосфолипидов с водой.



фосфолипидная молекула



**биохимический микрореактор**

# Силовое поле “MARTINI”

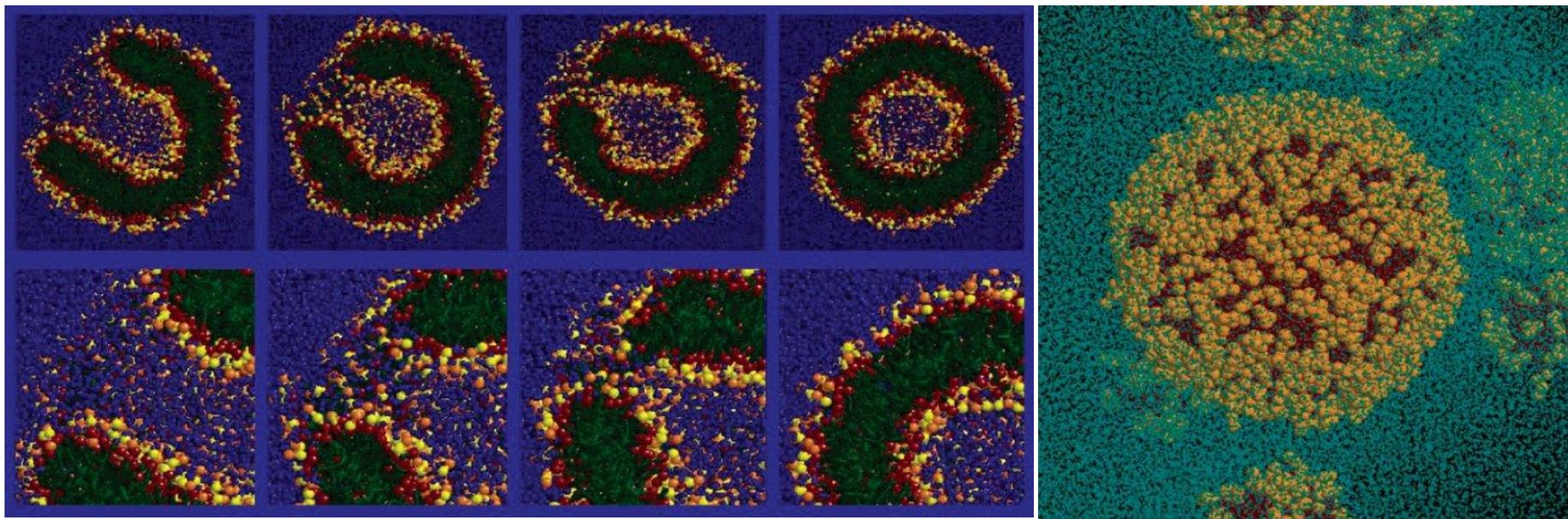
7812

*J. Phys. Chem. B* 2007, 111, 7812–7824

## The MARTINI Force Field: Coarse Grained Model for Biomolecular Simulations

Siewert J. Marrink,<sup>\*,†</sup> H. Jelger Risselada,<sup>†</sup> Serge Yefimov,<sup>‡</sup> D. Peter Tieleman,<sup>§</sup> and Alex H. de Vries<sup>†</sup>

*Groningen Biomolecular Sciences and Biotechnology Institute & Zernike Institute for Advanced Materials, Department of Biophysical Chemistry, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands, Zernike Institute for Advanced Materials, Department of Applied Physics, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands, and Department of Biological Sciences, University of Calgary, 2500 University Drive NW, Calgary AB T2N 1N4, Canada*



# МД моделирование липидных везикул

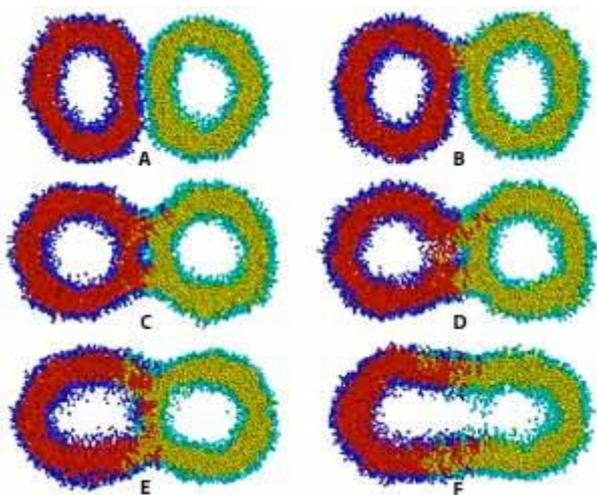
*J. Phys. Chem. B* 2009, 113, 4443–4455

## Solvent-Free Lipid Bilayer Model Using Multiscale Coarse-Graining

Sergei Izvekov and Gregory A. Voth\*

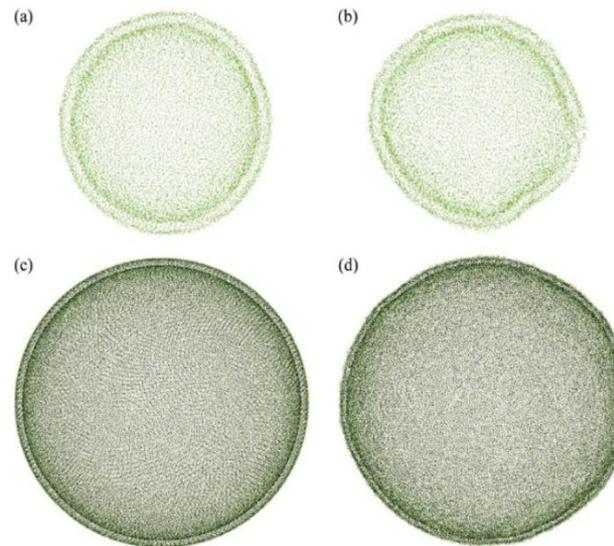
*Department of Chemistry and Center for Biophysical Modeling and Simulation, University of Utah, 315 S. 1400 E. Rm. 2020, Salt Lake City, Utah 84112-0850*

*Received: November 27, 2008; Revised Manuscript Received: January 17, 2009*

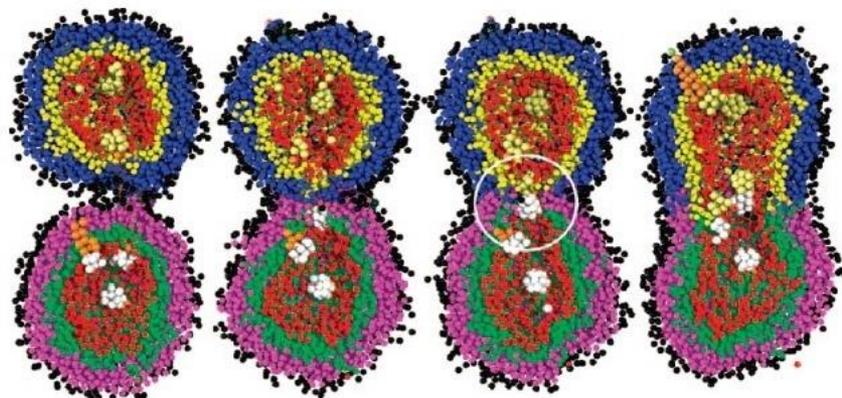


### слияние липидных везикул

**12000 липидов**

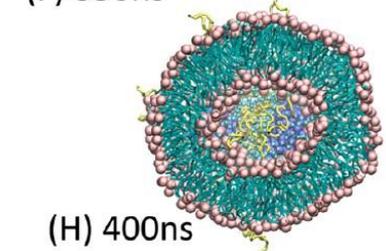
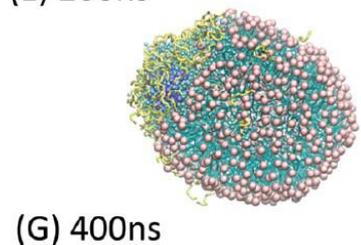
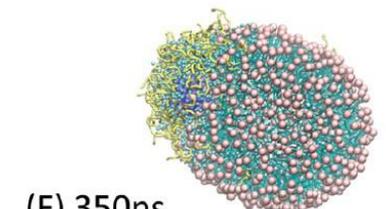
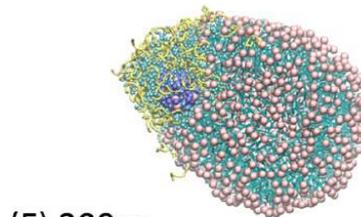
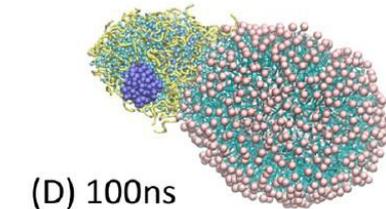
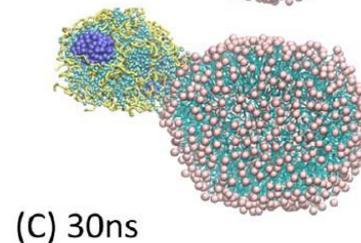
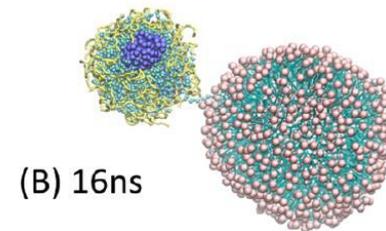
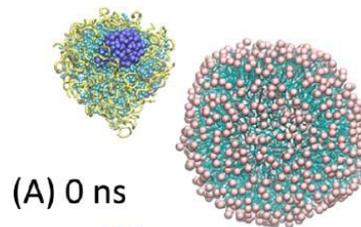
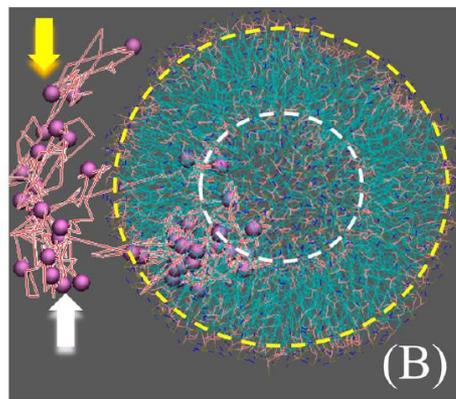
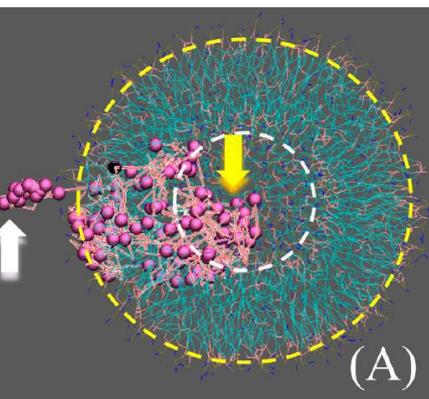
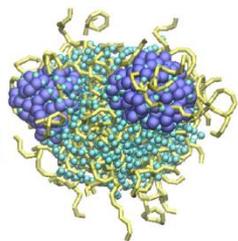
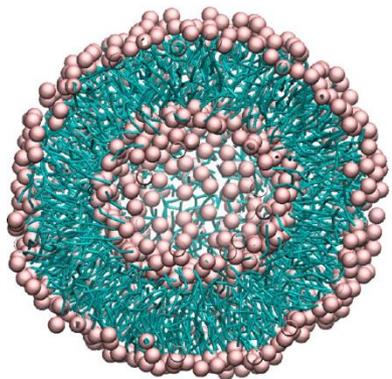
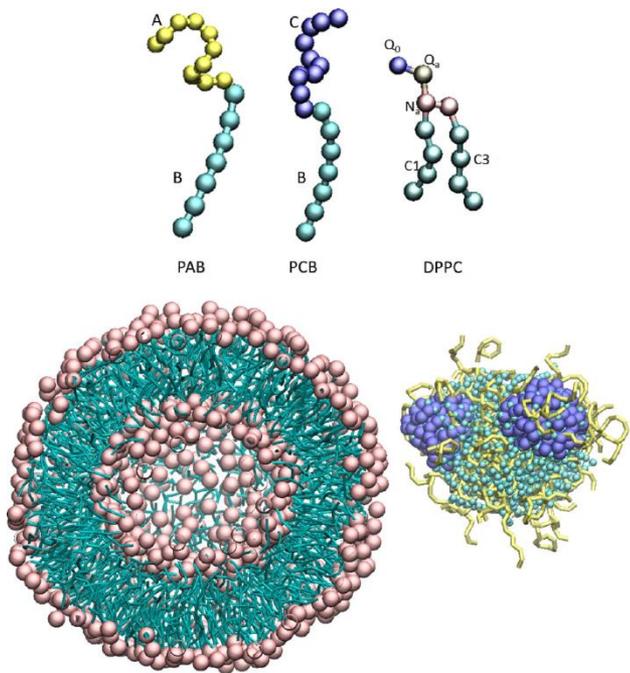


**79300 липидов**

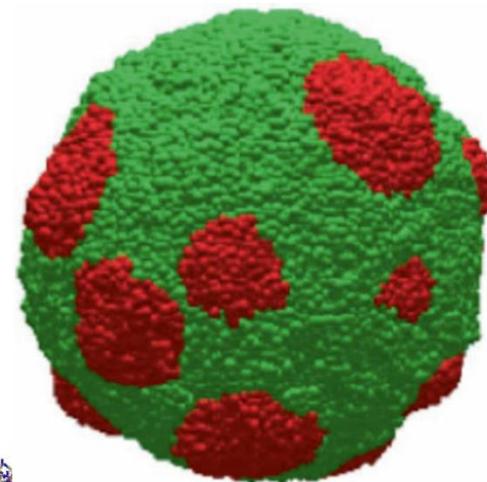
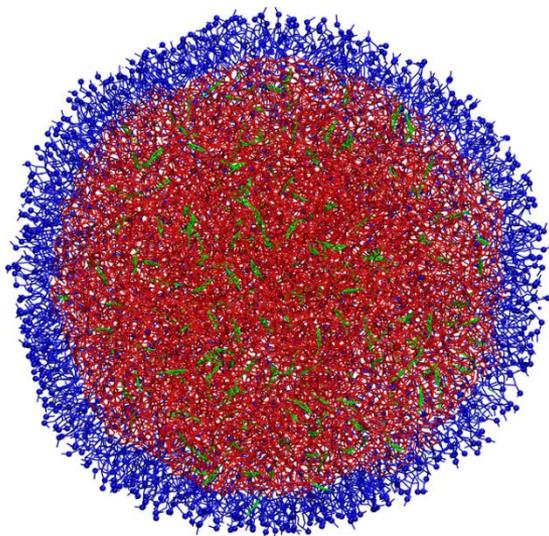
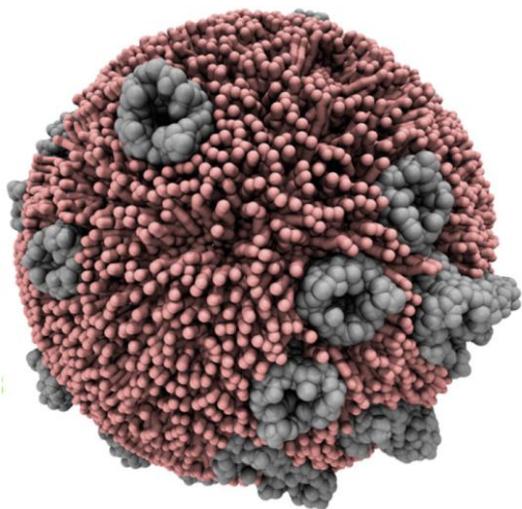


**256000 “фрагментов” (beads)**

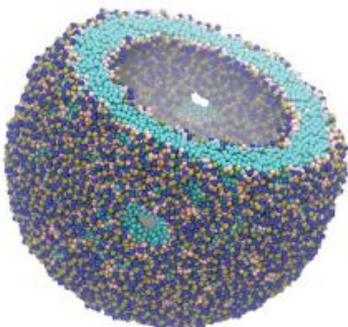
# Крупнозернистое МД моделирование липидных везикул и мицелл



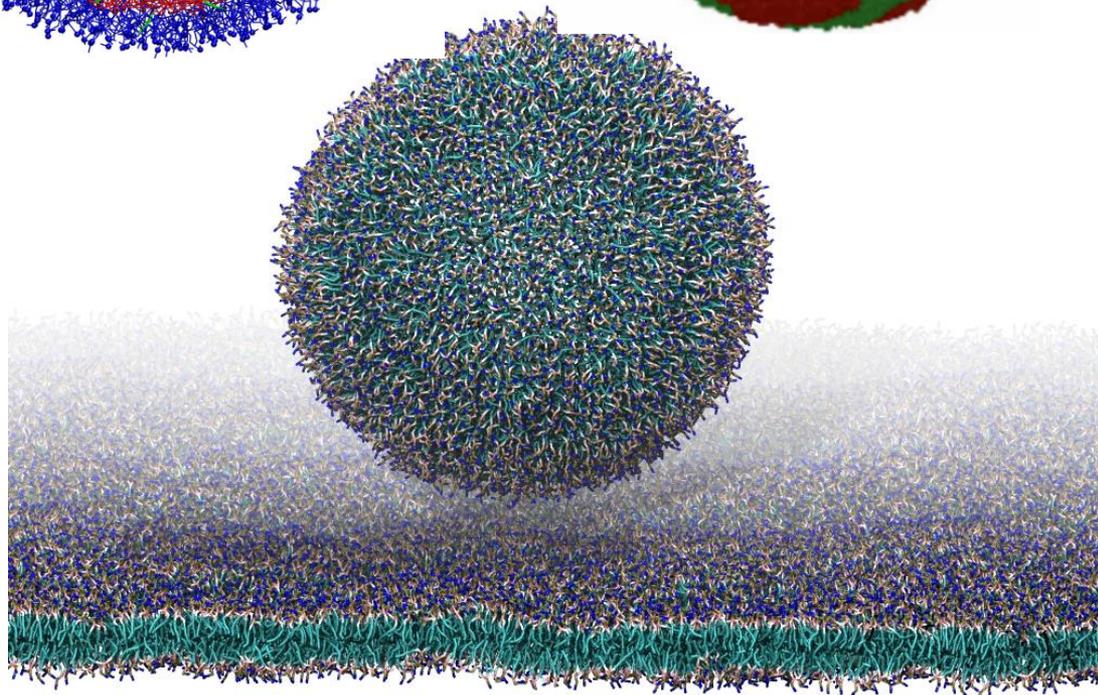
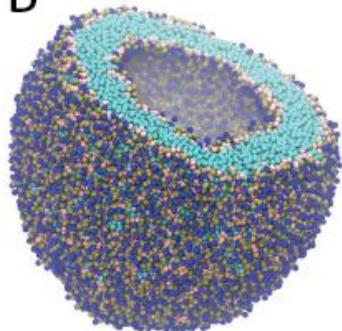
# Крупнозернистое МД моделирование липидных везикул и мембранных белков



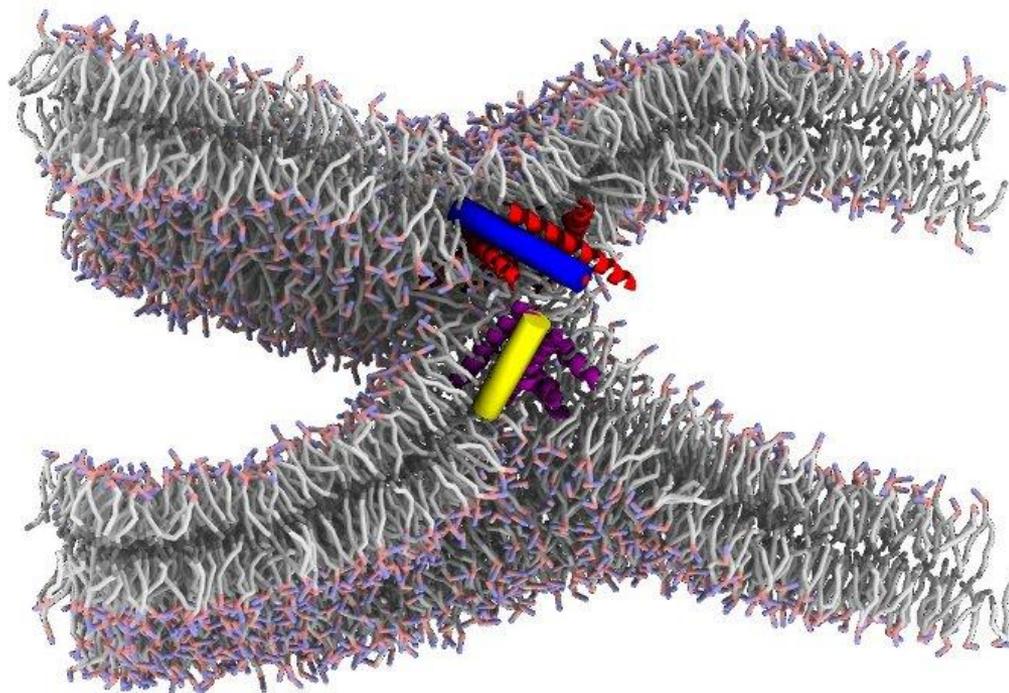
A



B



## Примеры “крупнозернистого” МД моделирования биомембран



**Изучение процессов слияния двух везикул,  
индуцированное определенными биомакромолекулами**



**Нобелевская премия по  
физиологии и медицине в 2013**



**Нобелевскую премию по физиологии и  
медицине в 2013 году получили три  
американских ученых**

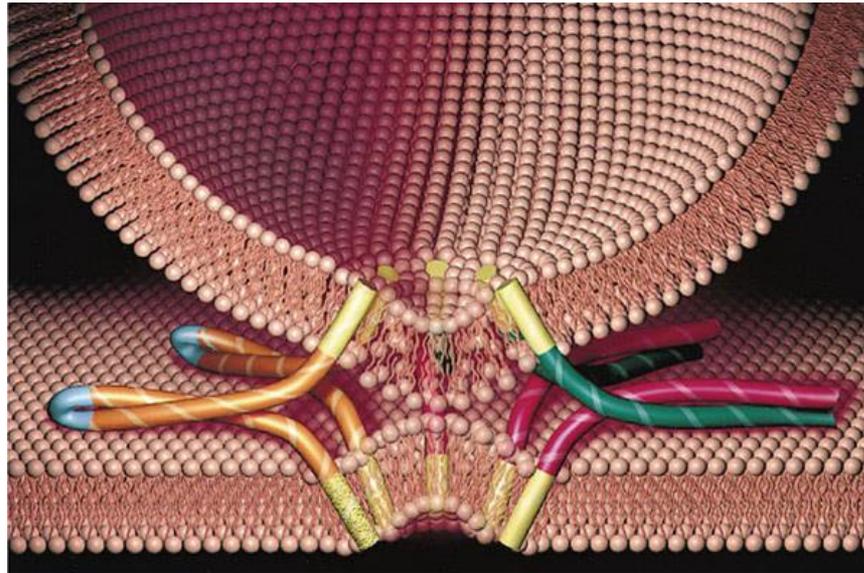
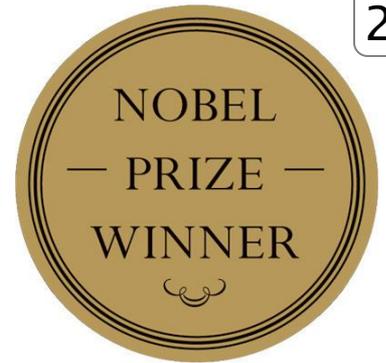
**Ренди Шекман, Джеймс Ротман и Томас Зюдоф**

**за**

**«Исследование механизмов, регулирующих  
везикулярный транспорт»**



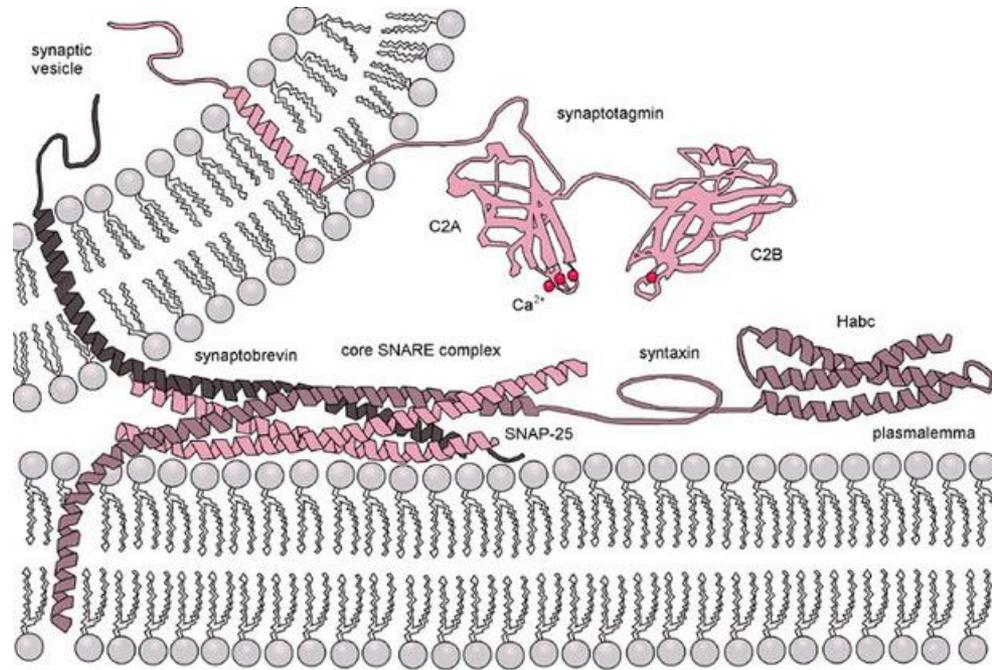
**Нобелевская премия по  
физиологии и медицине в 2013**



Слияние везикулы с клеточной мембраной: цилиндрами показаны белки-рецепторы SNARE (справа) и вирусные белки, имитирующие их работу (слева).



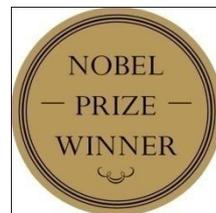
## Нобелевская премия по физиологии и медицине в 2013



SNARE комплекс формируется в результате сплетения четырех альфа-спиралей белков синаптобревина (v-SNARE), синтаксина (t-SNARE) и SNAP-25. Синаптотагмин служит кальциевым сенсором.



## Нобелевская премия по химии в 2013



23

Nobelpriset 2013 The Nobel



# The Nobel Prize in Chemistry 2013



**Martin Karplus**  
Université de Strasbourg,  
France and Harvard  
University, Cambridge,  
MA, USA

**Michael Levitt**  
Stanford University School of  
Medicine, CA, USA

**Arieh Warshel**  
University of Southern  
California, Los Angeles, CA,  
USA

*"För utvecklandet av flerskalemodeller för komplexa kemiska system."*

*"For the development of multiscale models for complex chemical systems."*

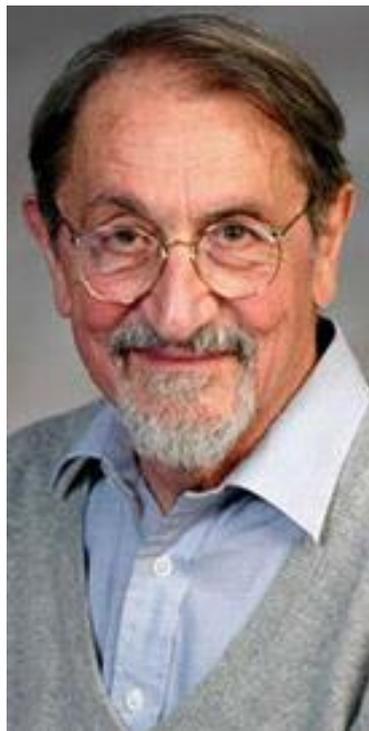
© Kungl. Ve



# Нобелевская премия по химии в 2013

NOBEL  
— PRIZE —  
WINNER

24



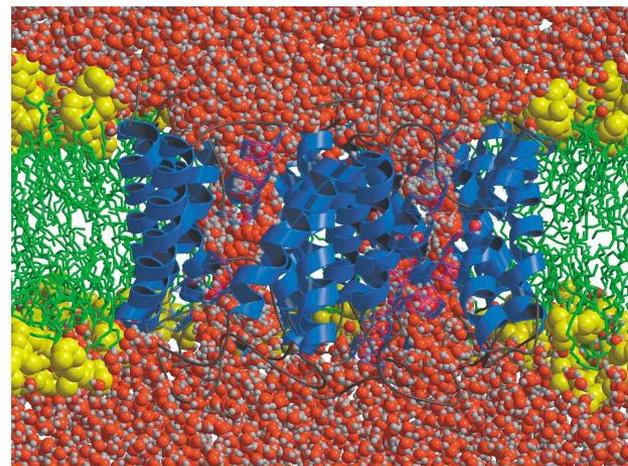
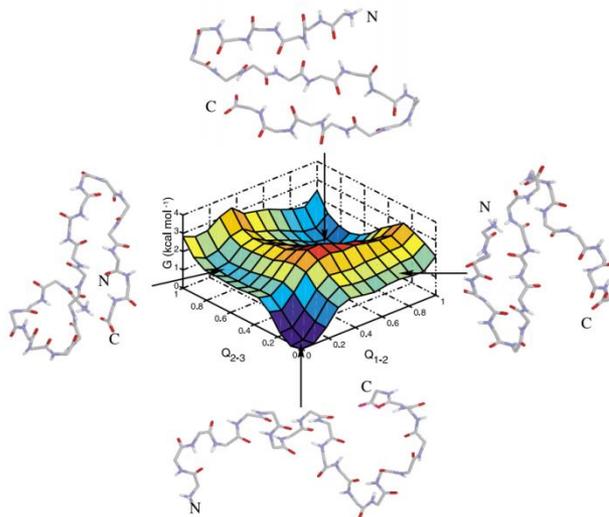
Мартин Карплус

## review

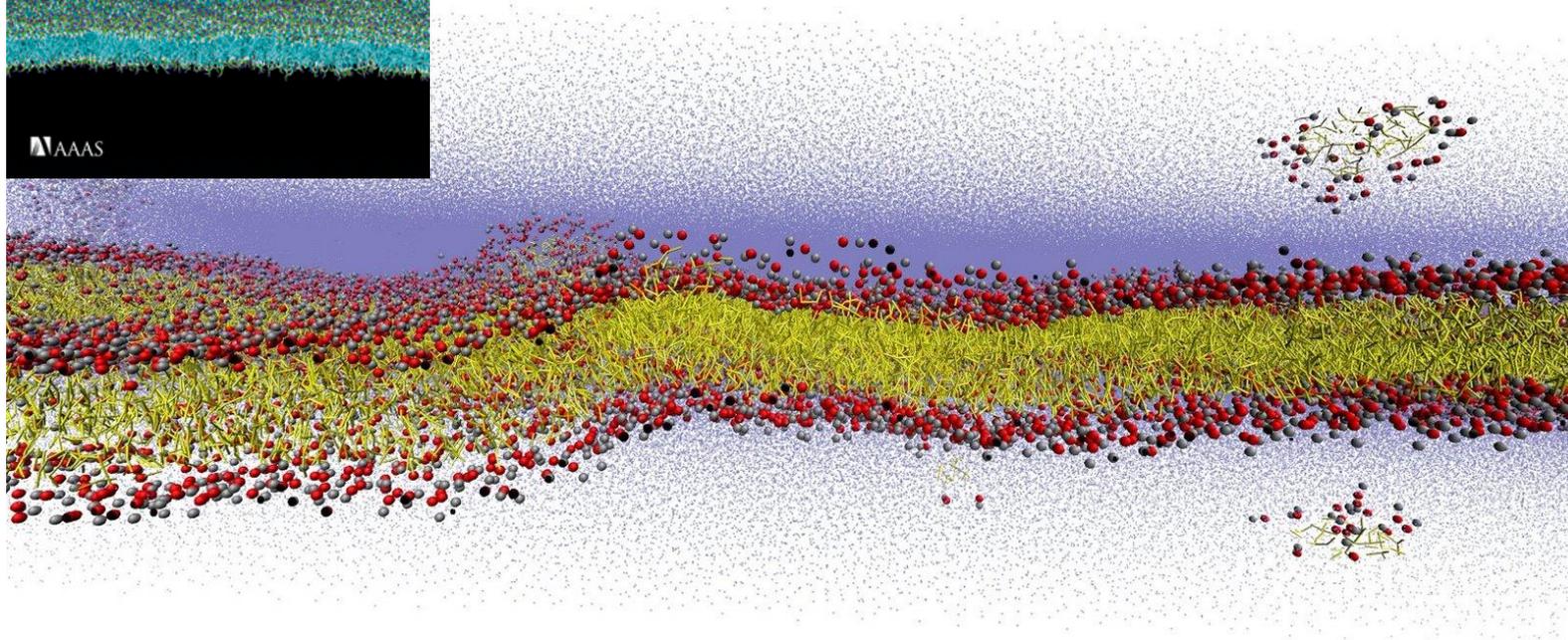
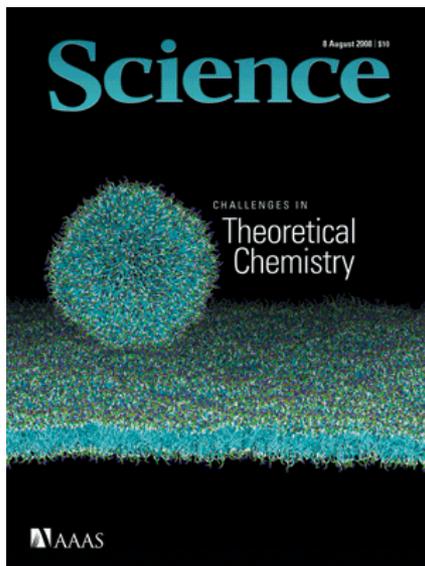
# Molecular dynamics simulations of biomolecules

Martin Karplus<sup>1,2</sup> and J. Andrew McCammon<sup>3</sup>

**Molecular dynamics simulations are important tools for understanding the physical basis of the structure and function of biological macromolecules. The early view of proteins as relatively rigid structures has been replaced by a dynamic model in which the internal motions and resulting conformational changes play an essential role in their function. This review presents a brief description of the origin and early uses of biomolecular simulations. It then outlines some recent studies that illustrate the utility of such simulations and closes with a discussion of their ever-increasing potential for contributing to biology.**

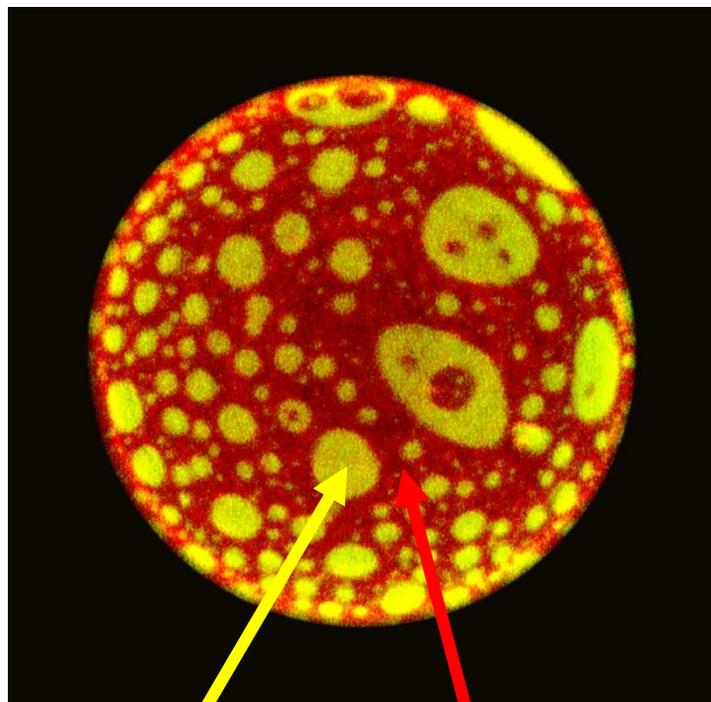


# Примеры “крупнозернистого” МД моделирования биомембран

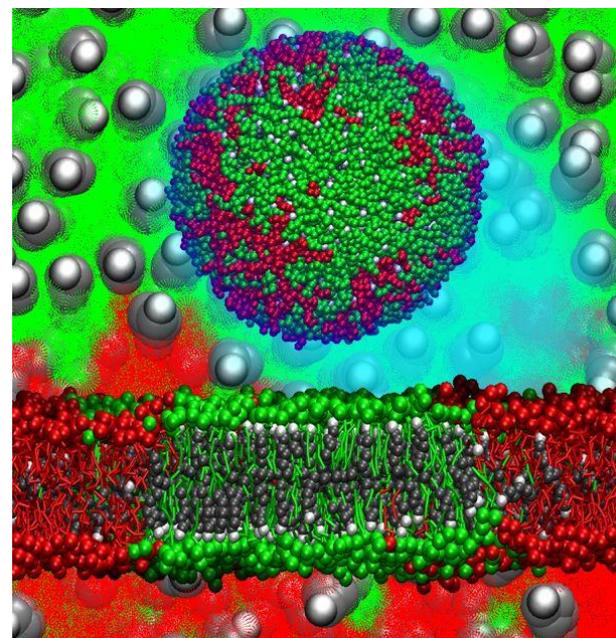


**“крупнозернистая” модель биомембраны состоящая из 2 000 000 частиц ...**

# Образование труднорастворимых холестериновых доменов в мембране



**эксперимент**



<http://md.chem.rug.nl/cgmartini/index.php/about/martini-projects/rafts>

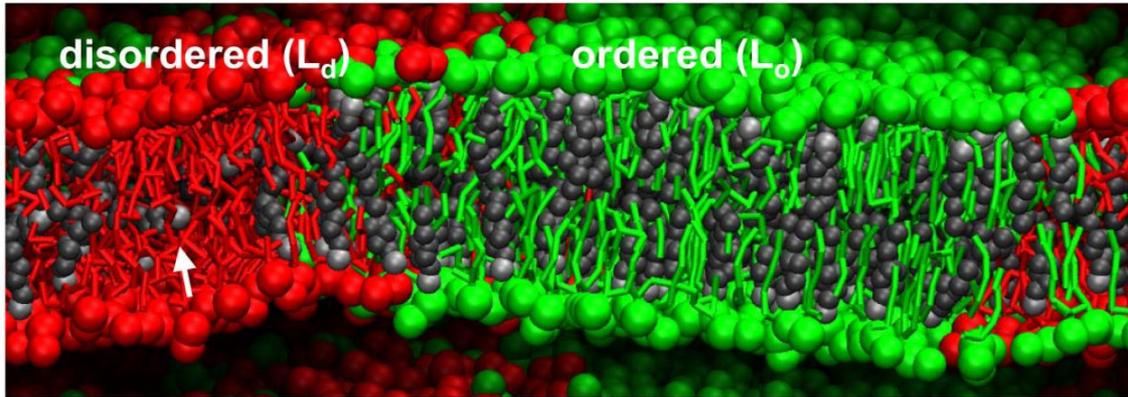


**МД модель**

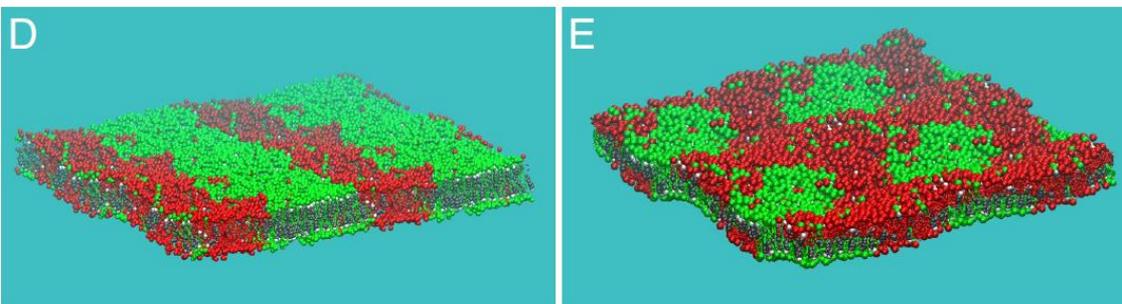
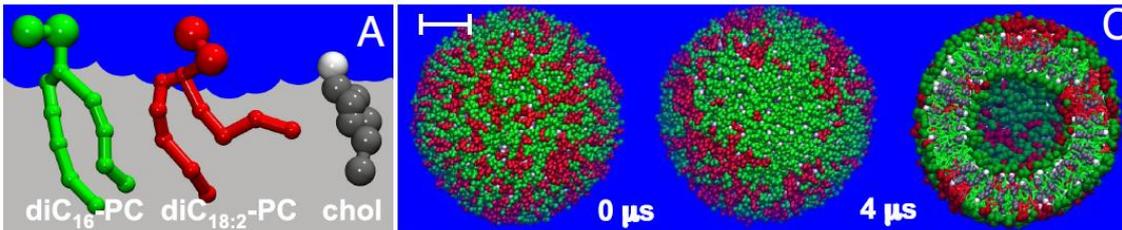
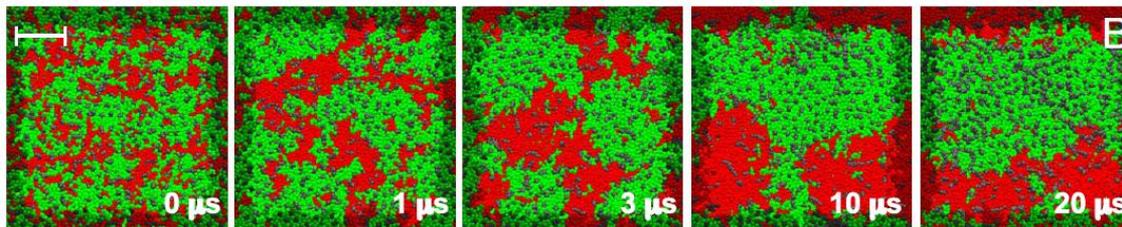
**Холестерин**

**POPC липид**

# Формирование фосфолипидных доменов в мембране



Силовое Поле MARTINI  
Вычисления выполнены в  
GROMACS 3.3



The Molecular Face of Lipid Rafts in Model Membranes.  
H. J. Risselada and S. J. Marrink,  
Proceedings of the National  
Academy of Science of USA, 2008,  
v104, 17367-17372

# Моделирование процессов экстракции холестерина молекулами циклодекстрина из липидных доменов в мембране

SCIENTIFIC REPORTS



OPEN

## Computational microscopy of cyclodextrin mediated cholesterol extraction from lipid model membranes

SUBJECT AREAS:  
COMPUTATIONAL BIOPHYSICS  
COMPUTATIONAL CHEMISTRY  
MEMBRANE BIOPHYSICS  
THERMODYNAMICS

Cesar A. López, Alex H. de Vries & Siewert J. Marrink

Groningen Biomolecular Sciences and Biotechnology Institute and Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 7, 9747 AG Groningen, The Netherlands.

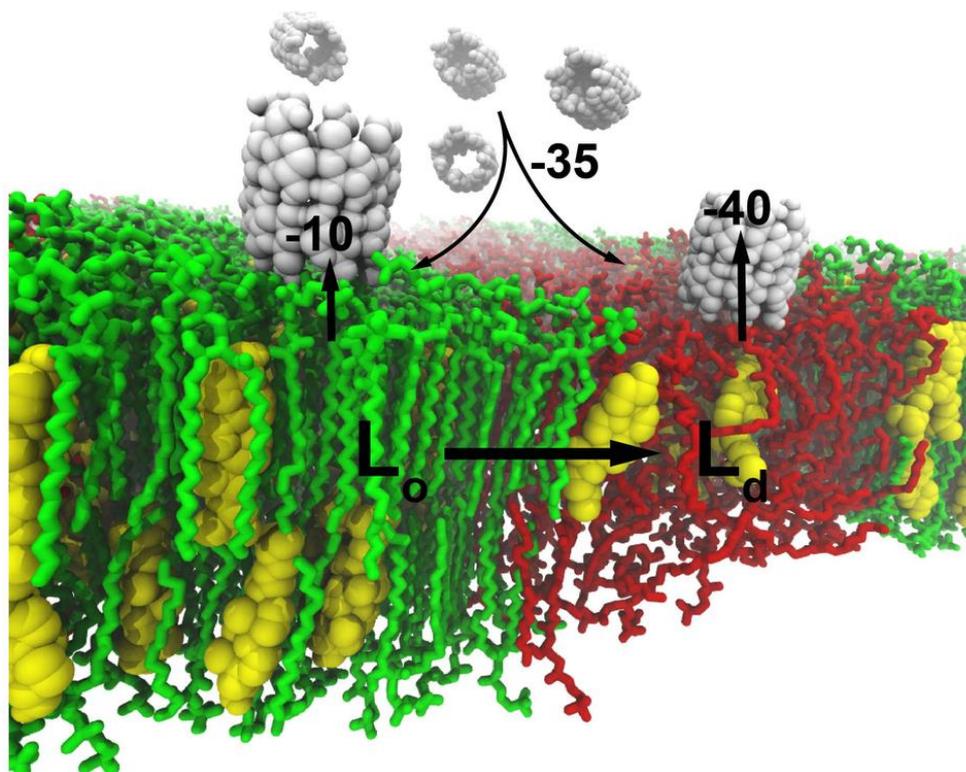
Received 21 March 2013

Accepted 6 June 2013

Published 25 June 2013

Correspondence and requests for materials

Beta-cyclodextrins ( $\beta$ -CDs) can form inclusion complexes with cholesterol, and are commonly used to manipulate cholesterol levels of biomembranes. In this work, we have used multiscale molecular dynamics simulations to provide a detailed view on the interaction between  $\beta$ -CDs and lipid model membranes. We show that cholesterol can be extracted efficiently upon adsorption of  $\beta$ -CD dimers at the membrane/water interface. However, extraction is only observed to occur spontaneously in membranes with high cholesterol levels. Free energy calculations reveal the presence of a kinetic barrier for cholesterol extraction in the case of low cholesterol content. Cholesterol uptake is facilitated in case of (poly)unsaturated lipid membranes, which increases the free energy of the membrane bound state of cholesterol. Comparing lipid/cholesterol compositions typical of liquid-disordered ( $L_d$ ) and liquid-order ( $L_o$ ) domains, we furthermore show that cholesterol is preferentially extracted from the disordered regions, in line with recent experimental data.



# “Очень крупнозернистая” МД модель мембраны и везикулы

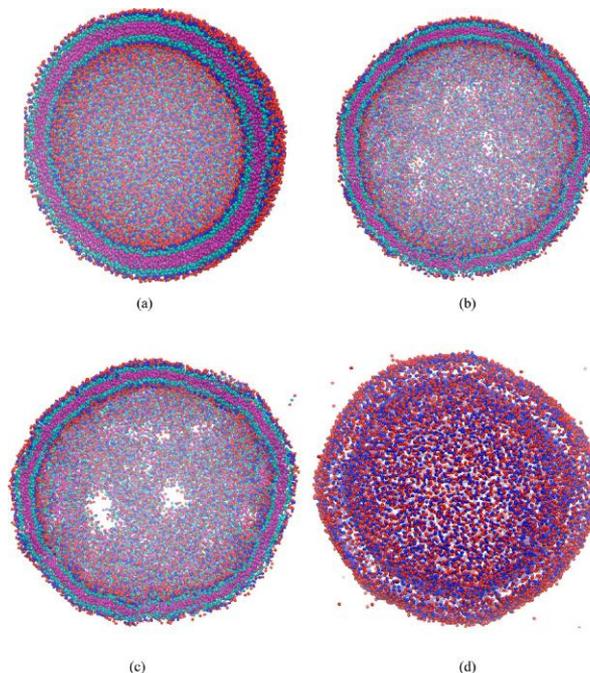
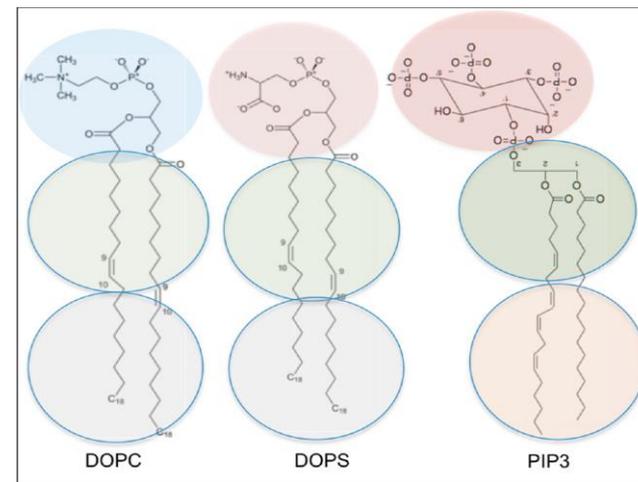
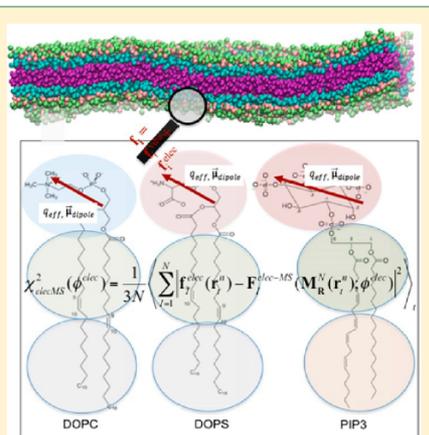
## Solvent-Free, Highly Coarse-Grained Models for Charged Lipid Systems

Anand Srivastava and Gregory A. Voth\*

Department of Chemistry, Institute for Biophysical Dynamics, James Franck Institute, and Computation Institute, The University of Chicago, 5735 S. Ellis Ave., Chicago, Illinois 60637, United States

Supporting Information

**ABSTRACT:** We present a methodology to develop coarse-grained lipid models such that electrostatic interactions between the coarse-grained sites can be derived accurately from an all-atom molecular dynamics trajectory and expressed as an effective pairwise electrostatic potential with appropriate screening functions. The reference non-bonded forces from the all-atom trajectory are decomposed into separate electrostatic and van der Waals (vdW) forces, based on the multiscale coarse-graining method. The coarse-grained electrostatic potential is assumed to be a general function of unknown variables and the final site–site interactions are obtained variationally, where the residual of the electrostatic forces from the assumed field is minimized. The resulting electrostatic interactions are fitted to screened electrostatics functions, with a special treatment for distance-dependent dielectrics and screened dipole–dipole interactions. The vdW interactions are derived separately. The resulting charged hybrid coarse-graining method is applied to various solvent-free three-site models of anionic lipid systems.

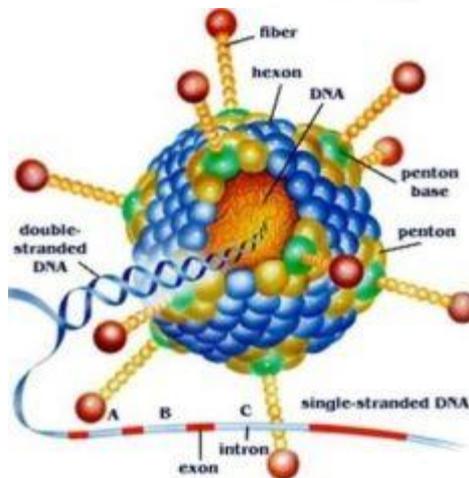
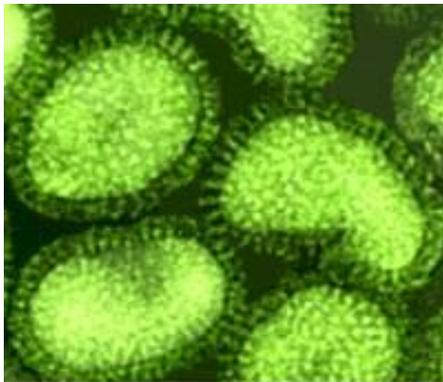
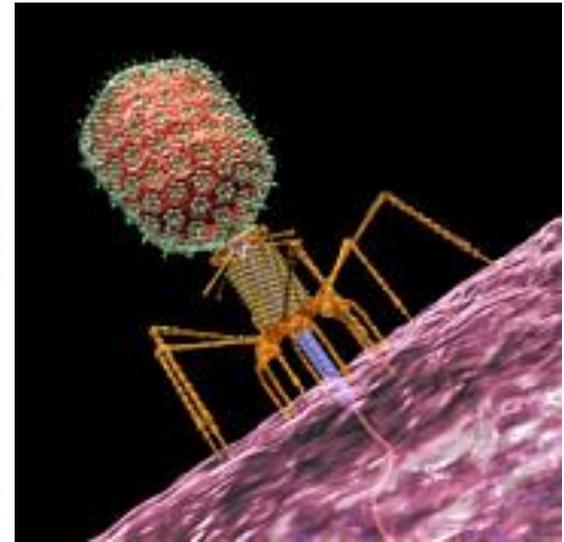
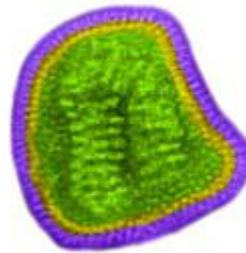
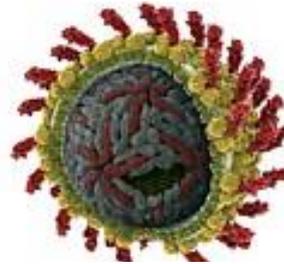
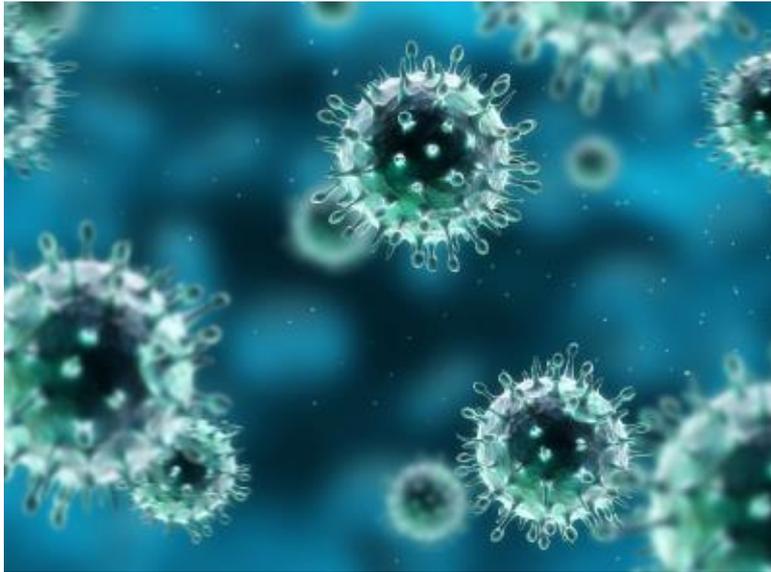


$$U_{SR}(R_{IJ}) = 4\epsilon \left[ \left( \frac{\sigma}{R_{IJ}} \right)^m - \left( \frac{\sigma}{R_{IJ}} \right)^n \right] \quad R_{IJ} \leq R_{SR}$$

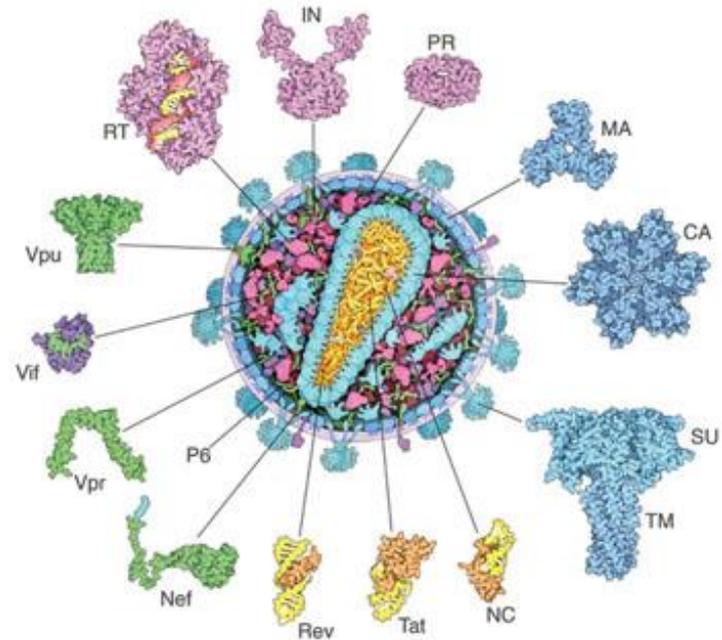
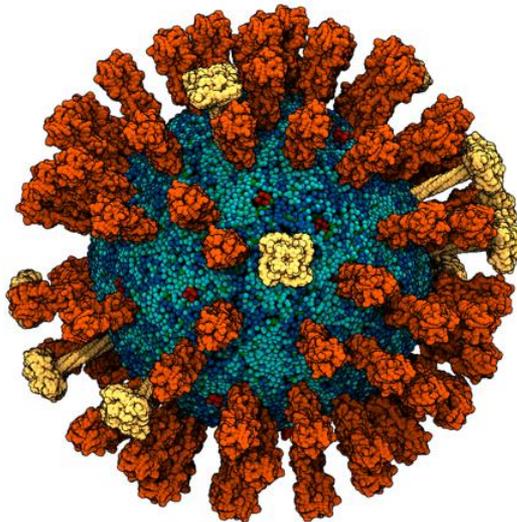
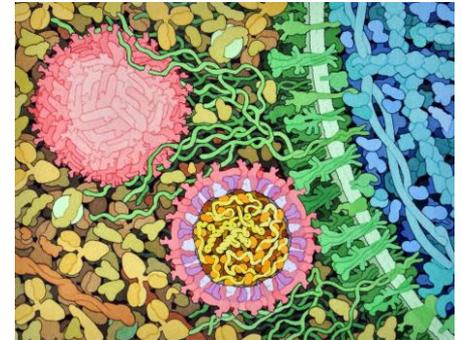
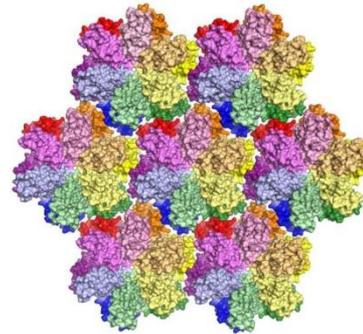
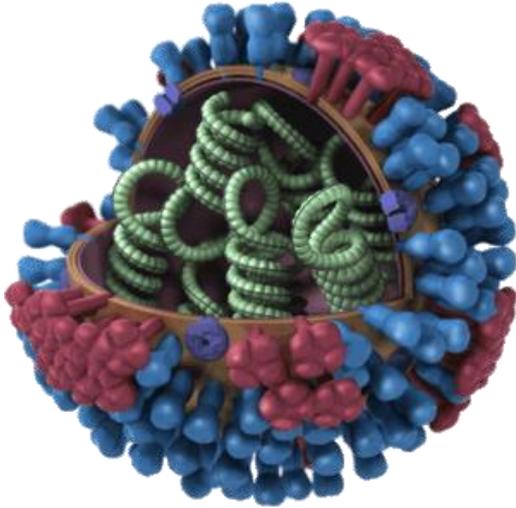
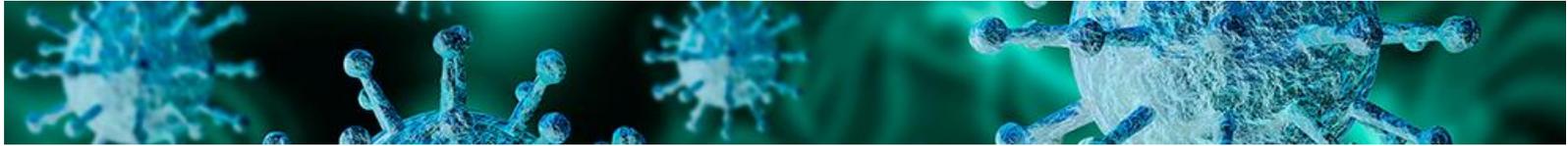
## Современные тенденции и перспективы в “крупнозернистом” МД моделировании мембран и везикул

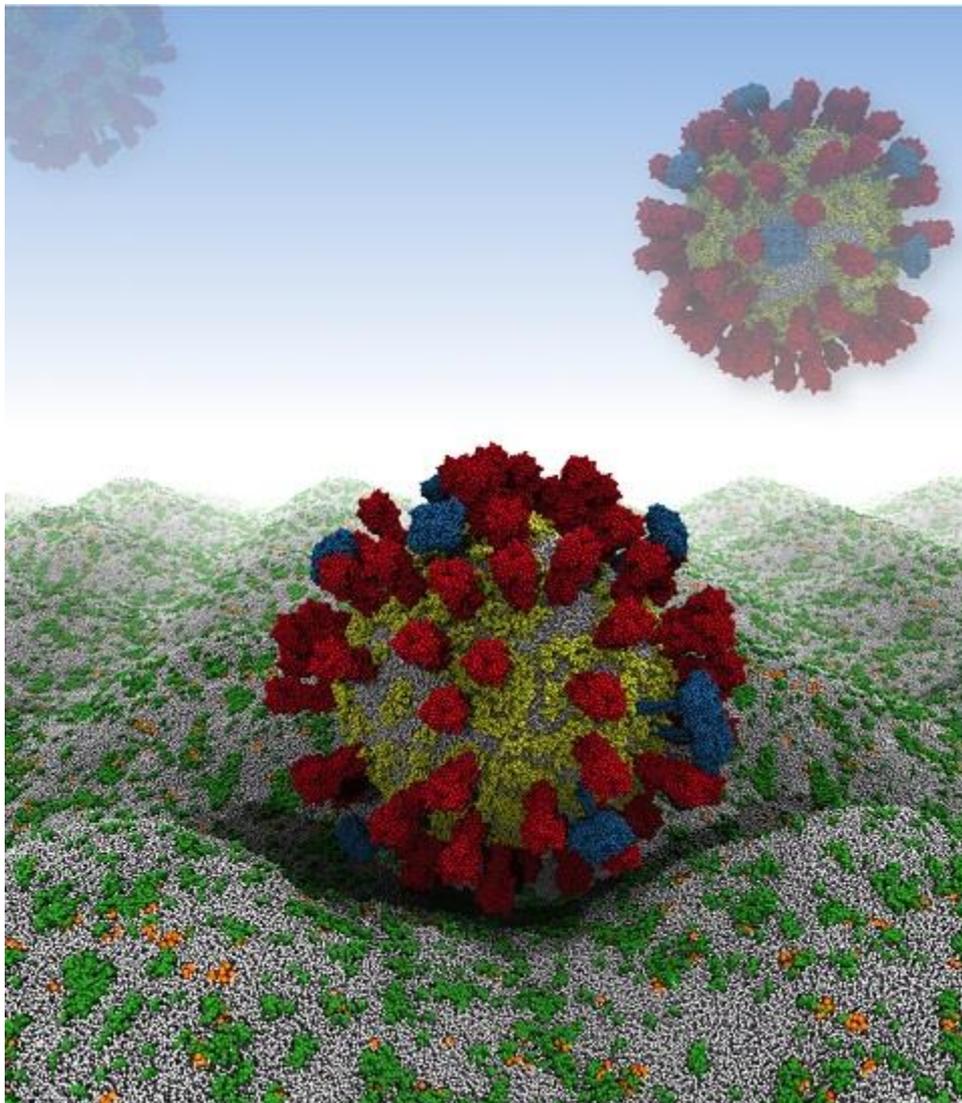
- Разработка новых **“супер-крупнозернистых”** (ultra coarse graining) МД моделей
- Разработка МД моделей в **неявных (implicit) растворителях**
- Обязательная проверка МД модели на воспроизведение **“самосборки”**
- Обязательная возможность **обратной трансформации** к полноатомной модели

# Есть ли возможность МД моделирование вирусов?



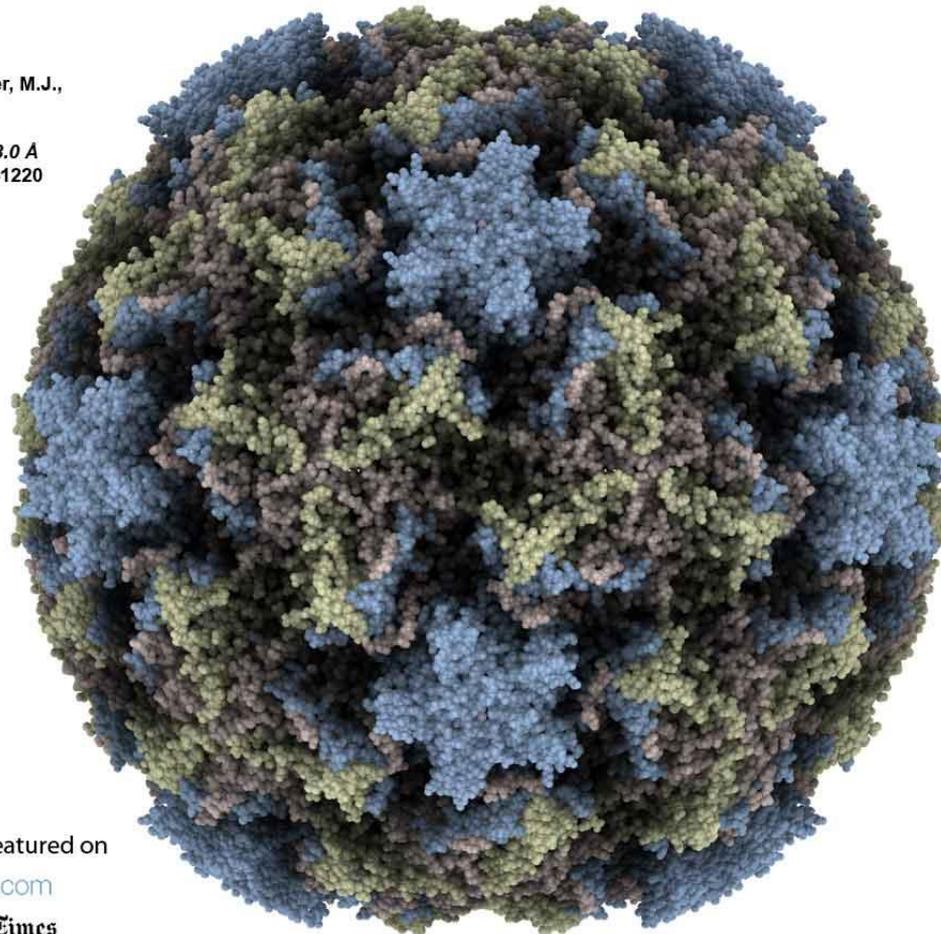
# “Крупнозернистое” МД моделирование вирусов





## Human rhinovirus 3 PDB ID: 1rhi

Zhao, R., Pevear, D.C., Kremer, M.J.,  
Giranda, V.L., Kofron, J.A.,  
Kuhn, R.J., Rossmann, M.G.  
(1996) *Human rhinovirus 3 at 3.0 Å  
resolution*. Structure 4: 1205-1220



20Å

Quetmol image by Jean-Yves Sgro ©2009  
images at [virology.wisc.edu/virusworld](http://virology.wisc.edu/virusworld)

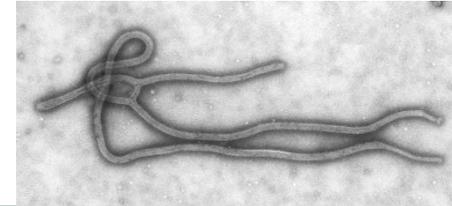
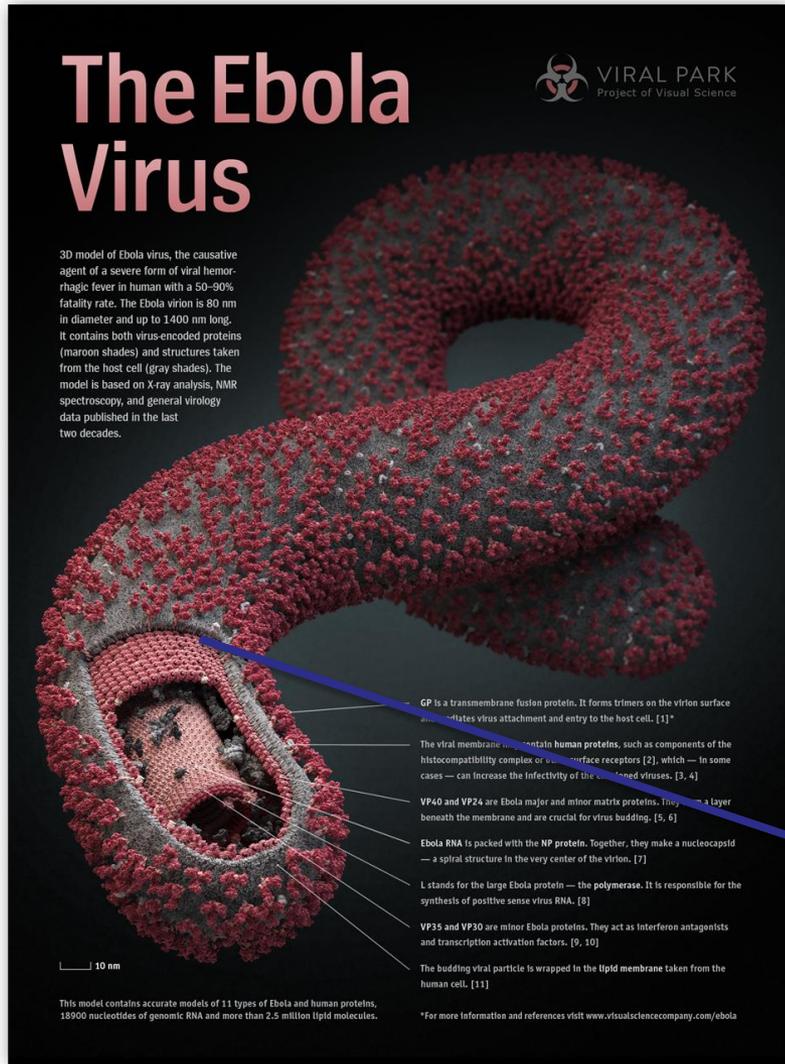


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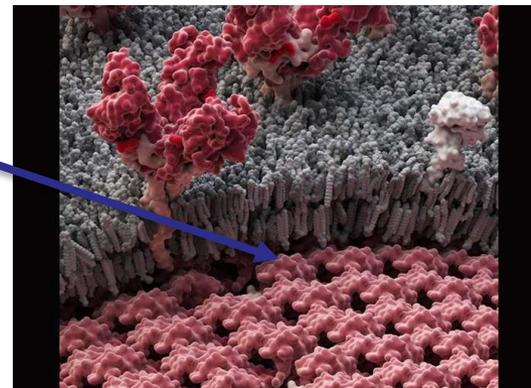
**CNN**health.com

The New York Times

Риновирусы (лат. *Rhinovirus*, от др.-греч. ῥίς / ῥίνος — нос) — группа мелких РНК-содержащих видов вирусов рода энтеровирусов, вирионы которых не имеют наружной оболочки, а геном представлен одноцепочечной линейной нефрагментированной молекулой РНК, связанной с белком VPg; включает возбудителей острых респираторных заболеваний (ОРЗ).



**Ebolavirus** (эболавирус, вирус Эбола или вирус Эбола) — род вирусов из семейства филовировусов (*Filoviridae*), вызывающих геморрагическую лихорадку Эбола у высших приматов. Морфологические признаки эболавирусов схожи с вирусом Марбург, также принадлежащим семейству филовировусов и вызывающим подобное заболевание. Кроме рода, вирусом Эбола могут называть конкретного представителя рода — чаще всего *Zaire ebolavirus*, который был выделен первым из рода в 1976 году в бассейне реки Эбола в Заире, от чего и образовалось название. Эболавирусы, особенно вид *Zaire ebolavirus*, стали причиной нескольких широко освещённых серьёзных эпидемий



# Моделирование биологической активности вируса Эбола

## Вирус Эбола

Страх распространения лихорадки Эбола в Африке затронул почти весь мир, многие страны вне Африки уже приняли экстренные меры по профилактике заболевания. Эксперты считают, что России пока ничего не угрожает

Лихорадка Эбола в Западной Африке «вышла из-под контроля» по заявлению неправительственной международной организации «Врачи без границ». Эпидемия угрожает распространиться дальше.

### Симптомы

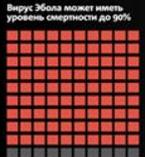
Мышечная слабость, интенсивные головные боли и боль в горле

В мире не существует единого метода лечения лихорадки Эбола. Вместо этого врачи устраняют различные симптомы, укрепляя иммунную систему пациента.

Когда инфицированный человек умирает, вирус в организме не погибает сразу. Он может жить в биологических жидкостях мертвых организмов в течение определенного периода. Труп необходимо сжигать.

Внутреннее и внешнее кровотечение

Почечная и печеночная дисфункция



**Болезнь**  
Вирус Эбола встречается в природе у некоторых видов летучих мышей, обитающих в лесах районов Африки. С момента своего появления в 1976 году было 18 вспышек этой лихорадки в таких странах, как Демократическая Республика Конго, Габон, Уганда и Судан.

**Виды Эбола**  
Этот вирус назван в честь реки, которая находится вблизи первой вспышки эпидемии в Демократической Республике Конго.

Виды лихорадки названы по месту их открытия	
Судан и Заир	(1976)
Рестон	(1989)
Ката-Ивуар	(1994)
Бундибуто	(2007)



### Диагностика

Сначала необходимо исключить другие заболевания, такие как малярия, брюшной тиф, дифтерия, холера, лептоспироз, чума, возвратный тиф, менингит, гепатит и другие вирусные геморрагические лихорадки.

Вирус Эбола может быть диагностирован различными лабораторными тестами

- Иммуно-ферментный анализ (EISA)
- Тест на обнаружение антигенов
- Реакция сывороточной нейтрализации

Изоляция вируса в культуре клеток  
Образцы вируса, полученные от пациентов, представляют собой огромную опасность, и работы должны выполняться в условиях максимальной биологической изоляции.

### Развитие



**Дни 7-9**  
Головная боль, усталость, лихорадка и боль в мышцах

**День 10**  
Внезапная высокая температура и рвота с кровью

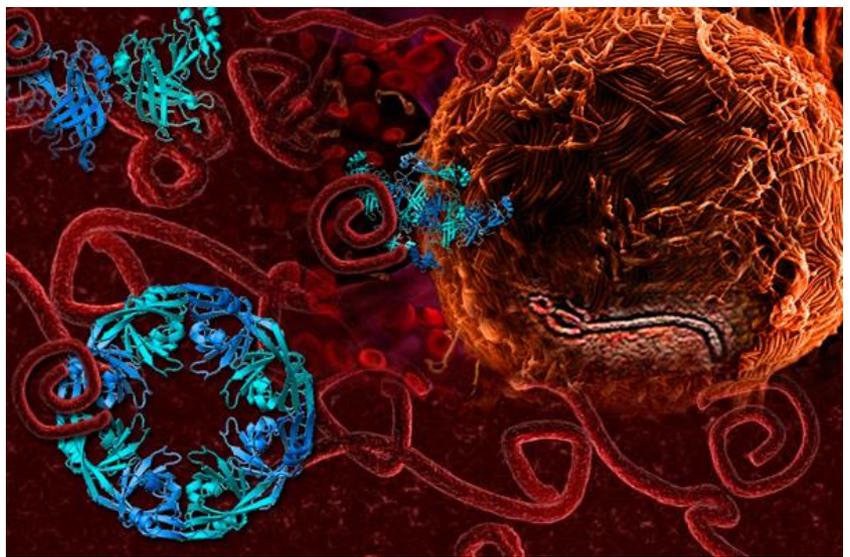
**День 11**  
Геморагия, повреждение головного мозга, кровотечение из носа, глаз, рта и ануса

**День 12**  
Судороги, потеря сознания, сильное кровотечение и смерть



Вирус

ИСТОЧНИКИ: OMS / AGENCES



## Перспективные направления в области МД моделирования мембранных систем

- **Гибридные МД модели**, в которых различные компоненты системы, такие как мембрана, сольватная среда и изучаемое соединение могут рассматриваться на разном уровне молекулярной детализации, включая полноатомные, упрощенные и фрагментированные модели.
- **Смешанные молекулярно-динамические\квантово-химические модели (ММ/QM)**, в которых изучаемое соединение рассматривается на уровне *ab-initio*, в то время мембрана и водная фаза описываются силовым полем МД.
- ***Ab-initio* молекулярная динамика всей системы мембрана\вода.**

# Программные пакеты для МД моделирования

Практически все популярные МД программы имеют готовые полноатомные и упрощенные силовые поля и геометрии липидных мембран для простых однокомпонентных липидных систем!

Программы:

**GROMOS**

<http://www.gromos.net/>

**GROMACS**

<http://www.gromacs.org/>

**NAMD**

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

**CHARMM**

<http://www.charmm.org/>

**AMBER**

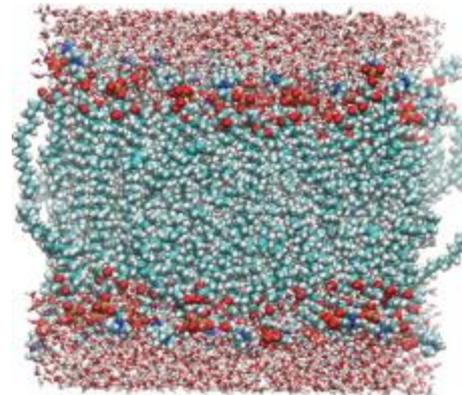
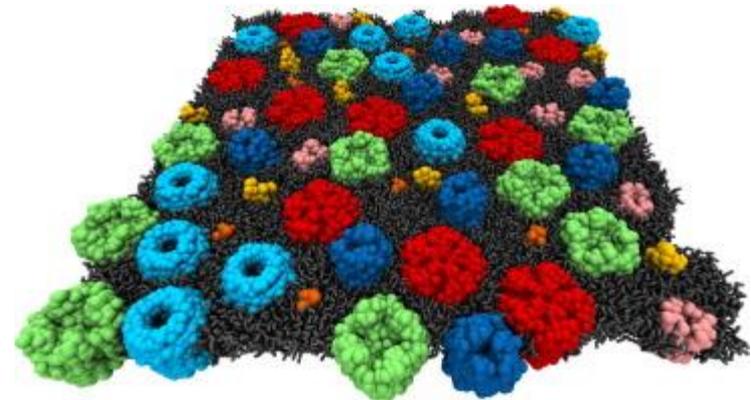
<http://ambermd.org/>

**LAMMPS**

<http://lammps.sandia.gov/>

**DL\_POLY**

<http://www.stfc.ac.uk>



$$m \vec{a} = \vec{F} = \left\{ \begin{array}{l} \text{CHARMM ?} \\ \text{AMBER ?} \\ \text{GROMOS ?} \\ \text{Slipids ?} \\ \dots ? \end{array} \right.$$

**Ваша собственная программа ...**

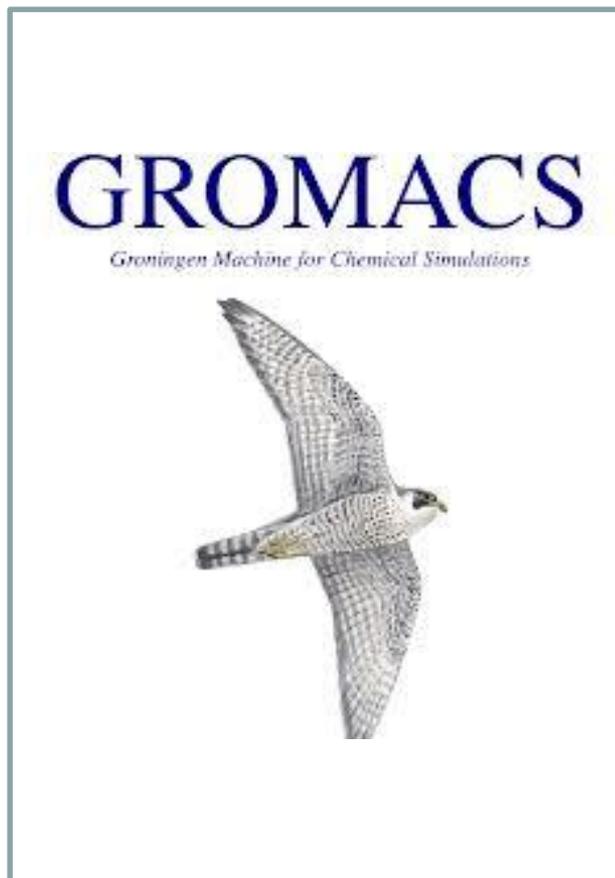
# Популярные программные пакеты для МД моделирования

## GROMACS

<http://www.gromacs.org/>

## GROMACS

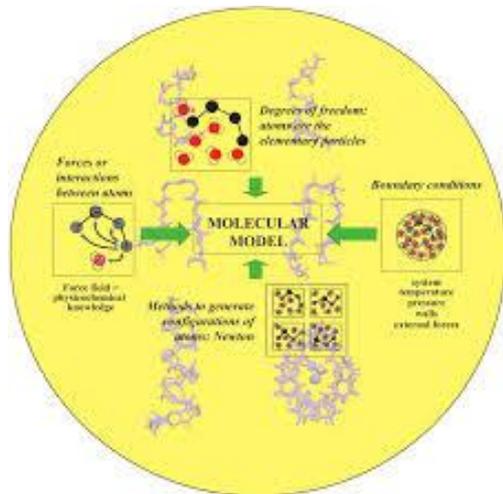
FAST.  
FLEXIBLE.  
FREE.



# Популярные программные пакеты

## GROMOS

<http://www.gromos.net/>



- About GROMOS
- How to get GROMOS
- Downloads
- GROMOS updates
- BIOMOS
- FAQ
- Contact

### About the GROMOS software for biomolecular simulation

#### 1. What is GROMOS

GROMOS™ is an acronym of the GRONingen MOlecular Simulation computer program package, which has been developed since 1978 for the dynamic modelling of (bio)molecules, until 1990 at the University of Groningen, The Netherlands, and since then at the ETH, the Swiss Federal Institute of Technology, in Zürich, Switzerland. Its development is driven by the research group of Wilfred van Gunsteren.

Since the last official release of the GROMOS software and manual in 1996, called GROMOS96, no comprehensive release occurred. Yet the GROMOS software has seen a steady development since 1996, see e.g. Christen *et al.* J. Comput. Chem. **26** (2005) 1719. The programming language has been changed from FORTRAN to C++, the documentation has been put into electronic form, and many new features have been included in the software.

To the development of the new code and manuals many current and former members of the research group for Informatikgestützte Chemie (igc) have contributed: Jane Allison, Dirk Bakowies, Ulf Börjesson, Roland Bürgi, Alexandra Choutko, Clara Christ, Markus Christen, Jozica Dolenc, Andreas Eichenberger, Daan Geerke, Alice Glättli, Halvor Hansen, Bruno Horta, Philippe Hünenberger, Mika Kastenholz, Anna-Pitschna Kunz, Katharina Meier, Chris Oostenbrink, Christine Peter, Maria Reif, Sereina Riniker, Heiko Schäfer, Nathan Schmid, Denise Steiner, Dongqi Wang, Haibo Yu, to mention a few.

The GROMOS *software* is to be distinguished from the GROMOS *force fields* for biomolecular systems, of which the latest versions are coded as:

45A3/4	J. Comput. Chem. <b>22</b> (2001) 1205-1218
	Eur. Biophys. J. <b>32</b> (2003) 67-77
	J. Comput. Chem. <b>26</b> (2005) 725-737
	J. Comput. Chem. <b>26</b> (2005) 1400-1412
53A5/6	J. Comput. Chem. <b>25</b> (2004) 1656-1676
54A7	J. Comput. Chem. <b>31</b> (2010) 1117-1125
	Eur. Biophys. J. <b>40</b> (2011) 843-856

#### 2. GROMOS documentation

The GROMOS software manuals that accompanied the major releases of 1987 and 1996 are:

W. F. van Gunsteren and H. J. C. Berendsen, *Groningen Molecular Simulation (GROMOS) Library Manual*, Biomos, Groningen, The Netherlands, 1987, pp. 1-221.



# Популярные программные пакеты

## NAMD

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



NIH CENTER FOR MACROMOLECULAR MODELING & BIOINFORMATICS | UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

Type Keywords

THEORETICAL *and* COMPUTATIONAL BIOPHYSICS GROUP

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- Software**
  - ▶ NAMD
  - ▶ VMD
  - ▶ GPU Computing
  - ▶ BioCoRE
  - ▶ MDFF
  - ▶ Other
- Outreach
- Download NAMD
- Download VMD
- Parallel Programming Laboratory



NAMD, recipient of a 2002 Gordon Bell Award and a 2012 Sidney Fernbach Award, is a parallel molecular dynamics code designed for high-performance simulation of large biomolecular systems. Based on Charm++ parallel objects, NAMD scales to hundreds of cores for typical simulations and beyond 200,000 cores for the largest simulations. NAMD uses the popular molecular graphics program VMD for simulation setup and trajectory analysis, but is also file-compatible with AMBER, CHARMM, and X-PLOR. NAMD is distributed free of charge with source code. You can build NAMD yourself or download binaries for a wide variety of platforms. Our tutorials show you how to use NAMD and VMD for biomolecular modeling.

- NEW** The 2005 reference paper Scalable molecular dynamics with NAMD has over 3000 citations as of July 2013.
- NEW** Wit, grit and a supercomputer yield chemical structure of HIV capsid (article referring to NAMD simulations on Blue Waters reported in Zhao *et al.*, *Nature*, 497:643-646, 2013.)
- NEW** Rapid parameterization of small molecules using the force field toolkit. JCC, 2013.

Search all NAMD resources:

Spotlight: Probing Parkinson's (Apr 2007)

Other Spotlights

**SDSC News Release:** SDSC and UC San Diego researchers are using NAMD to zero in on the causes of **Parkinson's disease, Alzheimer's disease, rheumatoid arthritis and other diseases.** The April 2007 **FEBS Journal cover story** offers—for the first time—a model for the complex process of aggregation of a protein known as alpha-synuclein, which in turn leads to harmful ring-like or pore-like structures in human membranes, the kind of damage found in Parkinson's and Alzheimer's patients. The researchers also found that the destructive properties of alpha-synuclein can be blocked by beta-synuclein—a **finding that could lead to treatments for many debilitating diseases.**

Lead author Igor Tsigelny, SDSC researcher and project scientist in chemistry and biochemistry at UCSD, said that the team's research helped confirm what researchers had suspected. "The present study—using molecular modeling and molecular dynamics simulations in combination with biochemical and ultrastructural analysis—shows that alpha-synuclein can lead to the formation of pore-like structures on membranes." In contrast, he said, "beta-synuclein appears to block the propagation of alpha-synucleins into harmful structures."

"This is one of the first studies to use supercomputers to model how alpha-synuclein complexes damage the cells, and how that could be blocked," said Eliezer Masliah, professor of neurosciences and pathology at UC San Diego. "We believe that these ring- or pore-like structures might be deleterious to the cells, and we have a unique opportunity to better understand how alpha-synuclein is involved in the pathogenesis of Parkinson's disease, and how to reverse this process."



### Overview

- Having Problems with NAMD?
- Why NAMD? (in pictures)
- Molecular Dynamics Flexible Fitting
- Steered Molecular Dynamics
- Interactive Molecular Dynamics
- Features and Capabilities
- Performance Benchmarks
- Publications and Citations
- Credits and Development Team

Availability



### Announcements

- NAMD 2.10 New Features **NEW**
- NAMD 2.9 New Features
- NAMD 2.9 (April 2012)
- 2011 User Survey Report
- NAMD 2.8 New Features
- NAMD 2.8 (May 2011)
- NAMD 2.7 New Features
- NAMD 2.7 (Oct 2010)
- How to Cite NAMD
- Previous Announcements

Documentation



# Популярные программные пакеты

## CHARMM

<http://www.charmm.org/>



- ▶ CHARMM
- ▶ Package
- ▶ Development
- ▶ Documentation

## CHARMM

### CHARMM News (Oct. 22, 2012):

The most recent release of CHARMM makes available to users significant performance enhancements for conventional molecular dynamics calculations, e.g., MD with explicit solvent and periodic boundary conditions using PME. This enhanced performance comes from the development and introduction of the DOMDEC module, by Antti-Pekka Hynninen and Michael Crowley, for simulations on parallel architectures, and for GPU accelerated molecular dynamics from the CHARMM/OpenMM interface, developed by Michael Garrahan and Charles Brooks, which leverages the relatively mature OpenMM API developed by Vijay Pande and coworkers at Stanford. For more information, please see this page.

### CHARMM News (Apr. 30, 2012):

An advanced CHARMM tutorial will be held from May 7-10, 2012, at the National Institutes of Health main campus in Bethesda, MD. A full schedule may be found on the CHARMM forums.

CHARMM (Chemistry at HARvard Macromolecular Mechanics):

- is a versatile and widely used molecular simulation program with broad application to many-particle systems
- has been developed with a primary focus on the study of molecules of biological interest, including peptides, proteins, prosthetic groups, small molecule ligands, nucleic acids, lipids, and carbohydrates, as they occur in solution, crystals, and membrane environments
- provides a large suite of computational tools that encompass numerous conformational and path sampling methods, free energy estimates, molecular minimization, dynamics, and analysis techniques, and model-building capabilities
- is useful for a much broader class of many-particle systems
- can be utilized with various energy functions and models, from mixed quantum mechanical-molecular mechanical force fields, to all-atom classical potentials with explicit solvent and various boundary conditions, to implicit solvent and membrane

# Популярные программные пакеты

## AMBER

<http://ambermd.org/>

### Amber Home Page



"AMBER is better, it goes up to 12".  
(Learn more about real Amber)

[AmberTools13](#) [Amber12](#) [GPU info](#) [Reference Manuals](#) [Tutorials](#) [Updates](#) [Mail lists](#) [Force Fields](#) [Contacts](#) [Developers](#)

News

Aug 2013, GTX-780 and Titan GPUs now officially supported. Updated benchmarks and recommended hardware available.

AmberTools13 released on April 22, 2013

Jan 2013, Kepler K20/K20X GPU Benchmarks and Updated Recommended GPU Hardware

Nov 2012, AMBER MD Workstations Announced - Recommended Hardware for GPU Acceleration

Sep 2012, Major GPU Update Patch Released

Quick links

[Amber force fields](#)

[Amber-related links](#)  
[Benchmarks](#)  
[GPU Summary](#)

**The AMBER community congratulates Martin Karplus, Michael Levitt and Arieh Warshel on winning the 2013 Nobel Prize in chemistry for their work in computational biology**

Assisted Model Building with Energy Refinement

"Amber" refers to two things: a set of molecular mechanical *force fields* for the simulation of biomolecules (which are in the public domain, and are used in a variety of simulation programs); and a *package of molecular simulation programs* which includes source code and demos.

Amber is distributed in two parts: *AmberTools13* and *Amber12*. You can use AmberTools13 without Amber12, but not *vice versa*. See [below](#) for information on how to obtain Amber12.

**A good general overview of the Amber codes can be found in:**

R. Salomon-Ferrer, D.A. Case, R.C.Walker. An overview of the Amber biomolecular simulation package. *WTREs Comput. Mol. Sci.* **3**, 198-210 (2013). ([PDF](#))

D.A. Case, T.E. Cheatham, III, T. Darden, H. Gohlke, R. Luo, K.M. Merz, Jr., A. Onufriev, C. Simmerling, B. Wang and R. Woods. The Amber biomolecular simulation programs. *J. Computat. Chem.* **26**, 1668-1688 (2005).

An overview of the Amber protein force fields, and how they were developed, can be found in: J.W. Ponder and D.A. Case. Force fields for protein simulations. *Adv. Prot. Chem.* **66**, 27-85 (2003). Similar information for nucleic acids is given by T.E. Cheatham, III and M.A. Young. Molecular dynamics simulation of nucleic acids: Successes, limitations and promise. *Biopolymers* **56**, 232-256 (2001).

**Please cite the use of AMBER 12 and AmberTools 13 as:**  
D.A. Case, T.A. Darden, T.E. Cheatham, III, C.L. Simmerling, J. Wang, R.E. Duke, R. Luo, R.C. Walker, W. Zhang, K.M. Merz, B. Roberts, S. Havik, A. Roitberg, G. Seabra, J. Swails, A.W. Goetz, I. Kolossvary, K.F. Wong, F. Paesani, J. Vanicek, R.M. Wolf, J. Liu, X. Wu, S.R. Brozell, T. Steinbrecher, H. Gohlke, Q. Cai, X. Ye, J. Wang, M.-J. Hsieh, G. Cui, D.R. Roe, D.H. Mathews, M.G. Seetin, R. Salomon-Ferrer, C. Sagui, V. Babin, T. Luchko, S. Gusarov, A. Kovalenko, and P.A. Kollman (2012). *AMBER 12*, University of California, San Francisco.

**For use of the GPU accelerated code please also cite the following:**  
*PME:* Romelia Salomon-Ferrer; Andreas W. Goetz; Duncan Poole; Scott Le Grand; & Ross C. Walker\* "Routine microsecond molecular dynamics simulations with AMBER - Part II: Particle Mesh Ewald", *J. Chem. Theory Comput.*, 2013, in press. DOI: [10.1021/ct400314y](https://doi.org/10.1021/ct400314y)  
*GB:* Andreas W. Goetz; Mark J. Williamson; Dong Xu; Duncan Poole; Scott Le Grand; & Ross C. Walker\* "Routine microsecond molecular dynamics simulations with AMBER - Part I: Generalized Born", *J. Chem. Theory Comput.*, (2012), **8** (5), pp 1542-1555, DOI: [10.1021/ct200909j](https://doi.org/10.1021/ct200909j)



# Популярные программные пакеты

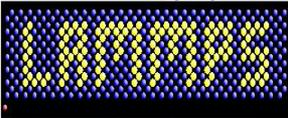
## LAMMPS

<http://lammps.sandia.gov/>

LAMMPS Molecular Dynamics Simulator

*lamp: a device that generates light, heat, or therapeutic radiation; something that illumines the mind or soul -- www.dictionary.com*

hover to animate -- [input script](#)



[physical analog \(start at 3:25\) & explanation](#)

Big Picture	Code	Documentation	Results	Related Tools	Context	User Support
<a href="#">Features</a>	<a href="#">Download</a>	<a href="#">Manual</a>	<a href="#">Publications</a>	<a href="#">Pre-Post processing</a>	<a href="#">Authors</a>	<a href="#">Mail list</a>
<a href="#">Non-features</a>	<a href="#">SourceForge</a>	<a href="#">Developer guide</a>	<a href="#">Pictures</a>	<a href="#">Pizza.py Toolkit</a>	<a href="#">History</a>	<a href="#">Workshops</a>
<a href="#">FAQ</a>	<a href="#">Latest features &amp; bug fixes</a>	<a href="#">Tutorials</a>	<a href="#">Movies</a>	<a href="#">Offsite LAMMPS packages &amp; tools</a>	<a href="#">Funding</a>	<a href="#">User scripts and HowTos</a>
<a href="#">Wish list</a>	<a href="#">Unfixed bugs</a>	<a href="#">MD to LAMMPS glossary</a>	<a href="#">Benchmarks</a>	<a href="#">Visualization</a>	<a href="#">Open source</a>	<a href="#">Contribute to LAMMPS</a>
	<a href="#">Pull requests</a>	<a href="#">Commands</a>	<a href="#">Citing LAMMPS</a>	<a href="#">Related modeling codes</a>		



LAMMPS is a classical molecular dynamics code, and an acronym for Large-scale Atomic-Molecular Massively Parallel Simulator.

LAMMPS has potentials for solid-state materials (metals, semiconductors) and soft matter (biomolecules, polymers) and coarse-grained or mesoscopic systems. It can be used to model atoms or, more generically, as a parallel particle simulator at the atomic, meso, or continuum scale.

LAMMPS runs on single processors or in parallel using message-passing techniques and a spatial-decomposition of the simulation domain. Many of its models have versions that provide accelerated performance on CPUs, GPUs, and Intel Xeon Phi. The code is designed to be easy to modify or extend with new functionality.

LAMMPS is distributed as an [open source code](#) under the terms of the [GPL](#). The current version can be downloaded [here](#). Links are also included to older F90/F77 versions. Periodic releases are also available on [SourceForge](#).

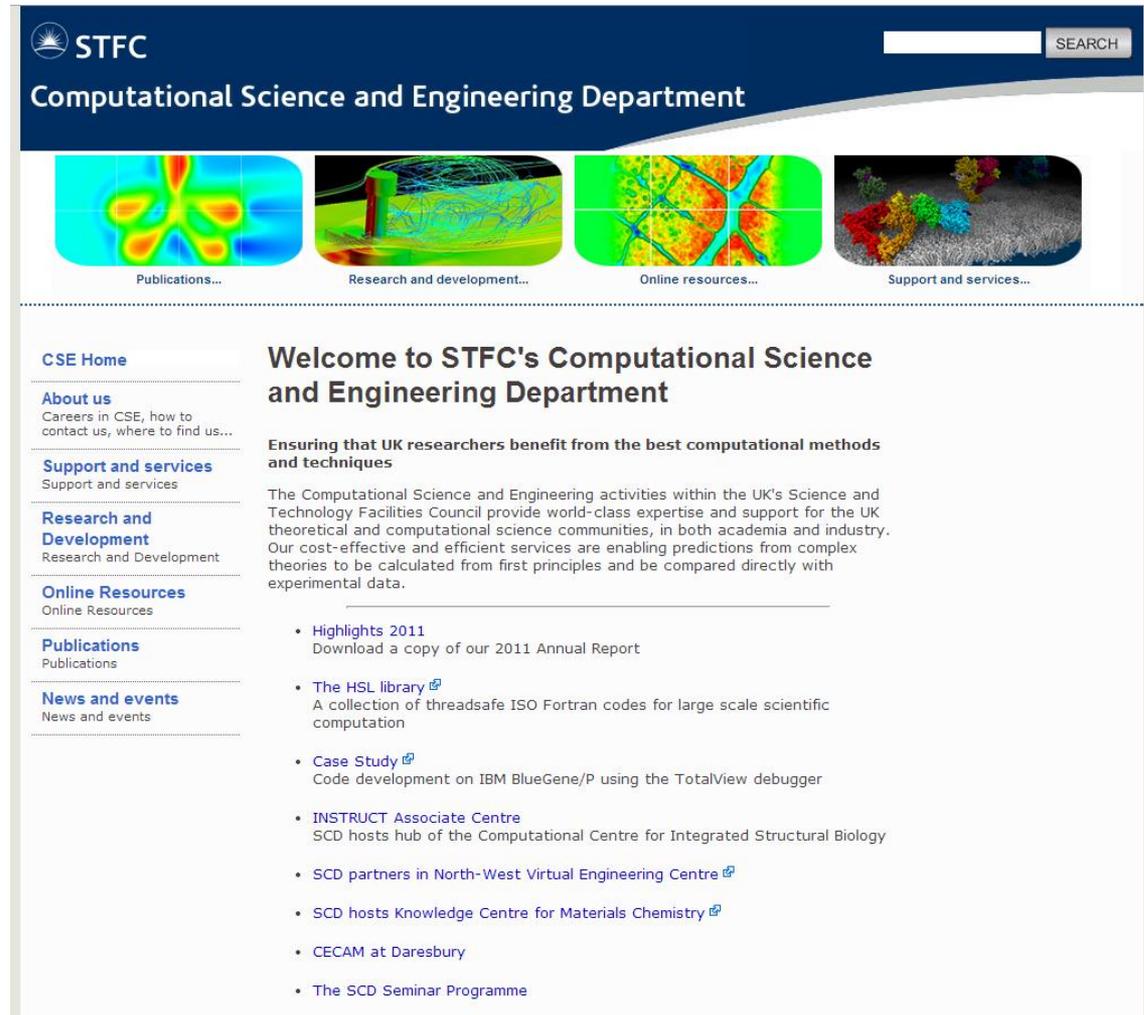
LAMMPS is distributed by [Sandia National Laboratories](#), a US [Department of Energy](#) laboratory. The main authors of LAMMPS are listed on [this page](#) along with contact info and other contributors. Funding for LAMMPS development has come primarily from DOE (OASCR, OBER, ASCI, LDRD, Genomes-to-Life) and is [acknowledged here](#).

The LAMMPS web site is hosted by Sandia, which has this [Privacy and Security statement](#).

Search the LAMMPS web pages

# Популярные программные пакеты

**DL\_POLY**  
<http://www.stfc.ac.uk>



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## Выводы

**В зависимости от поставленной задачи необходимо выбрать адекватную по молекулярной детализации и сложности МД модель мембраны и программный пакет**

## 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, Humana Press. 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.

