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Molecular and supramolecular modeling – A primer

olivier.vitrac@agroparistech.fr

(Senior scientist INRAE | Directeur de Recherche INRAE)

UMR 0782 SayFood Food & Bioproduct Engineering | UMT ACTIA 22.07 UMT SAFEMAT SAFETY OF PACKAGING

UMR0782 SayFood Paris-Saclay Food and Bioproduct Engineering Research Unit

Group MODIC MODeling and Computational Engineering

Office E207, Palaiseau

ICE STRUCTURE

Medium-density amorphous ice

Alexander Rosu-Finsen[1], Michael B. Davies[2,3], Alfred Amon[1], Han Wu,[4] Andrea Sella[1], Angelos Michaelides[2,3]*, Christoph G. Salzmann[1]*

Amorphous ices govern a range of cosmological processes and are potentially key materials for explaining the anomalies of liquid water. A substantial density gap between low-density and high-density amorphous ice with liquid water in the middle is a cornerstone of our current understanding of water. However, we show that ball milling "ordinary" ice *Ih* at low temperature gives a structurally distinct medium-density amorphous ice (MDA) within this density gap. These results raise the possibility that MDA is the true glassy state of liquid water or alternatively a heavily sheared crystalline state. Notably, the compression of MDA at low temperature leads to a sharp increase of its recrystallization enthalpy, highlighting that H_2O can be a high-energy geophysical material.

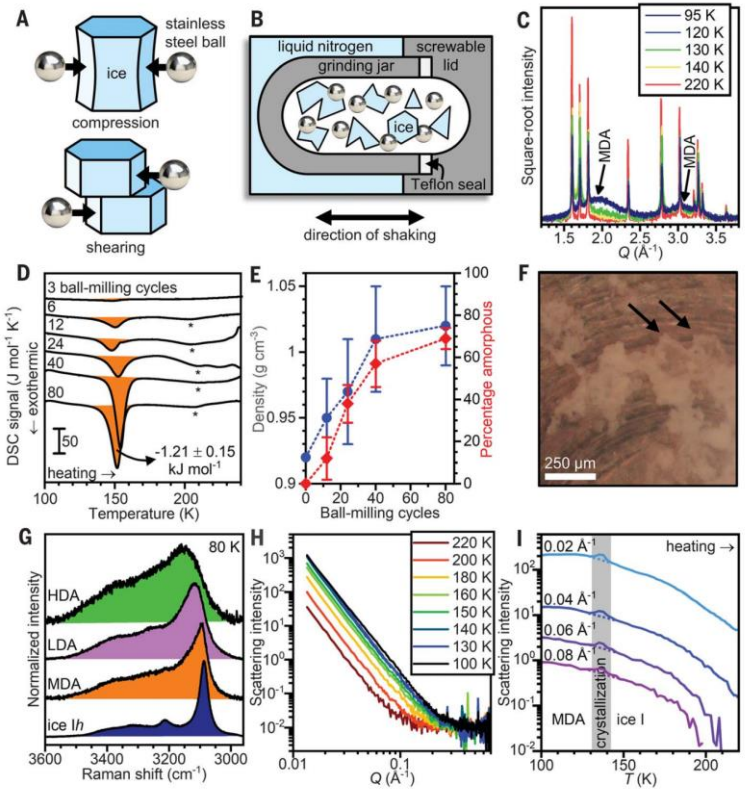


Fig. 1. Preparation and physical properties of MDA. (**A**) Illustration of the ball-crystal-ball impact events

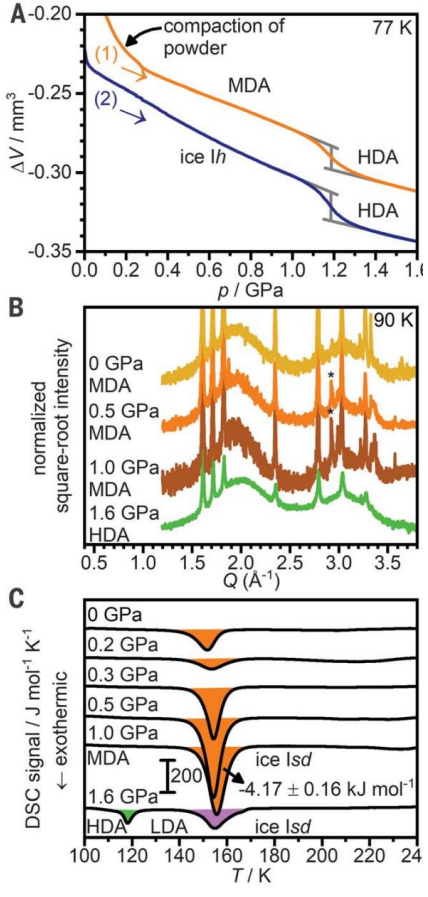


Fig. 3. Effect of pressure on MDA. (**A**) In situ

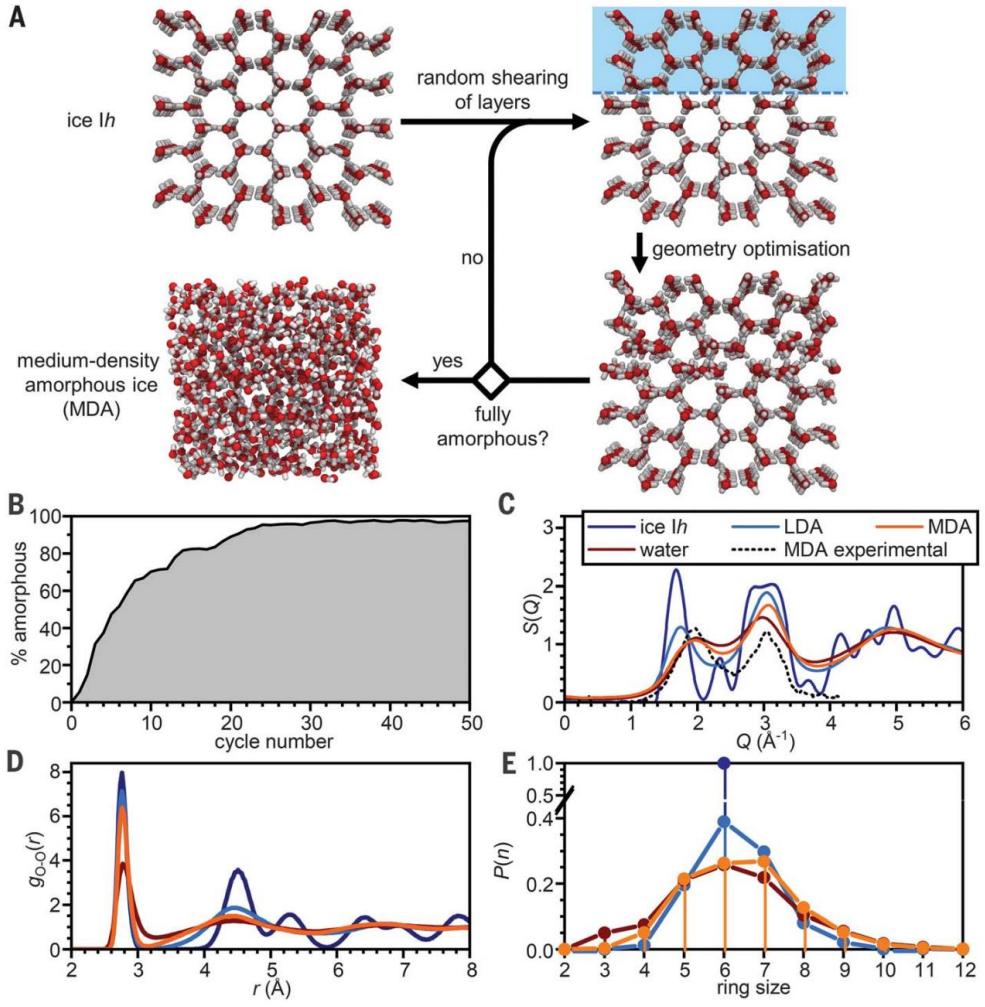
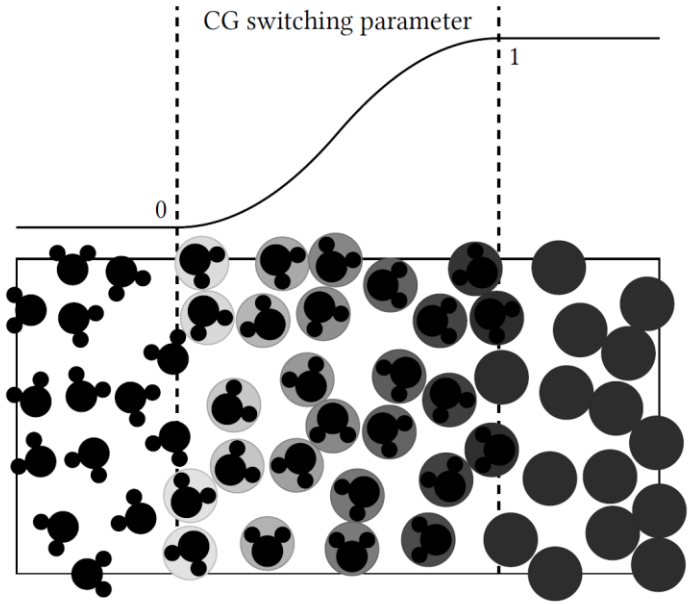


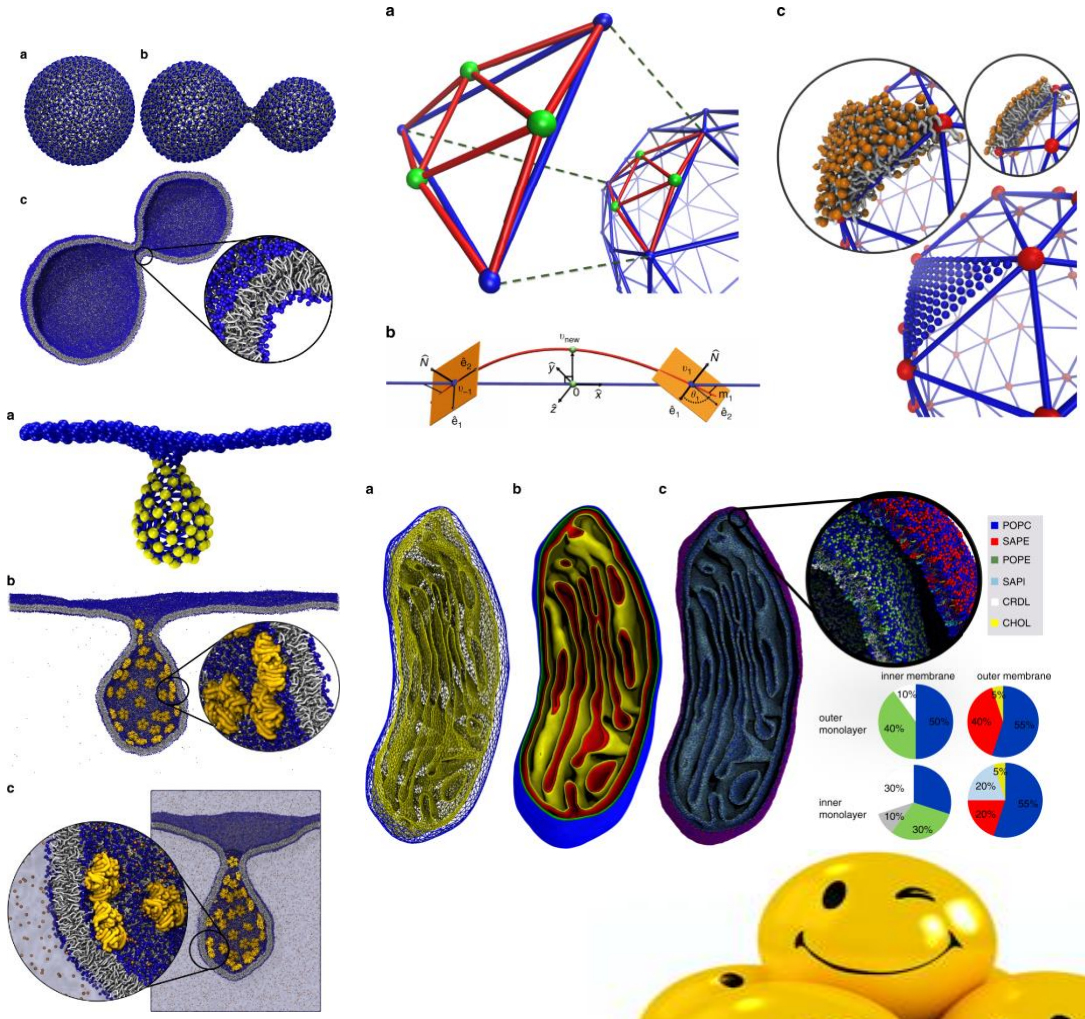
Fig. 2. Computational investigation into the mechanism of formation of MDA. (**A**) Schematic of the computational protocol that yields MDA upon repeated shearing and geometry-optimization steps. (**B**) Percentage amorphous with increasing computational cycles using the local structural analysis shown in fig. S18. (**C**) Experimental and computational x-ray structure factors of MDA, water, LDA, and ice *Ih*. (**D**) Corresponding oxygen-oxygen pair distribution functions and (**E**) primitive ring-size distributions. All simulations were carried out using periodic boxes with approximate dimensions of 4.5 nm in *x*, *y*, and *z*.

University College London, London
Dpts of Chemistry, Physics and Astronomy

Science 379, 474–478 (2023)

Multiscale modeling



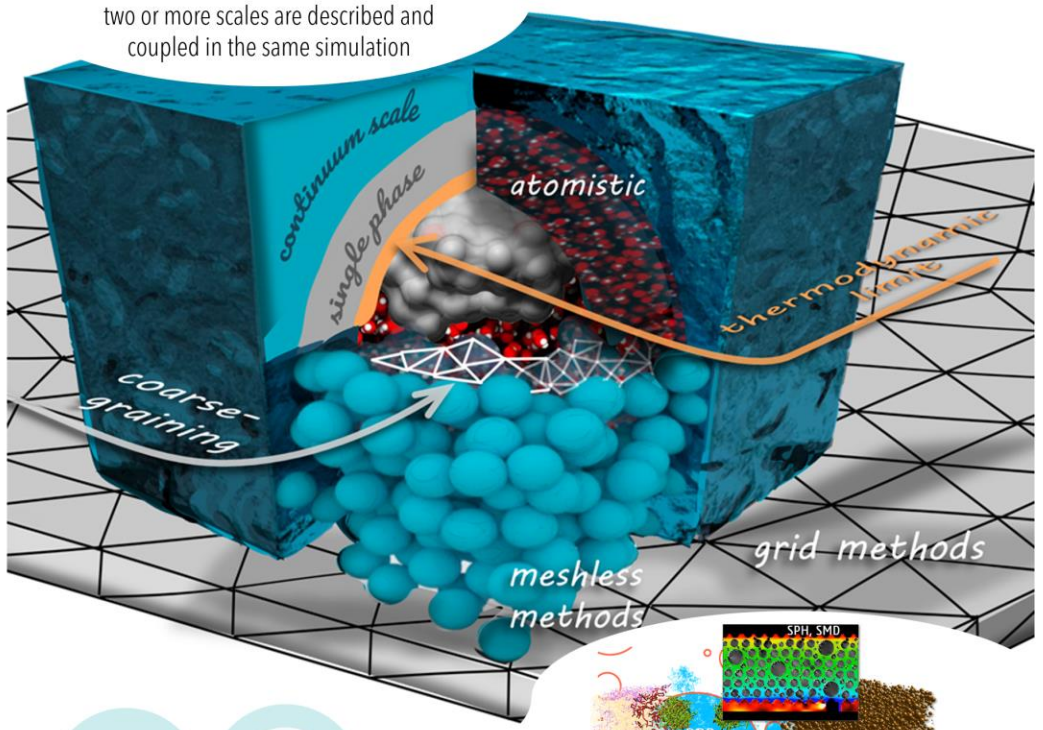


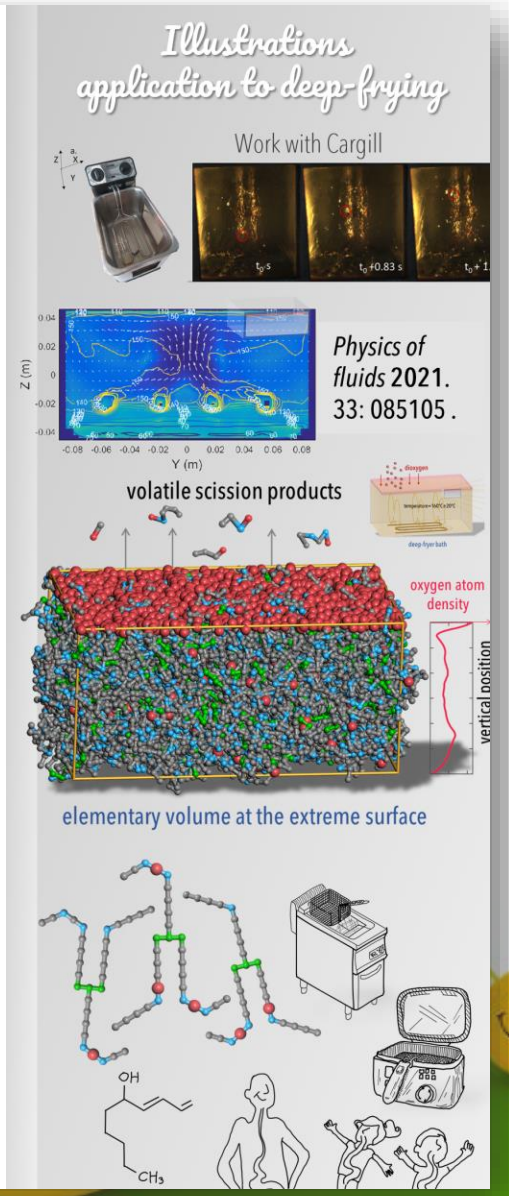
Computer Simulation of Liquids, 2nd Ed., 2017, p404.
Nature Communications 2020, 11, 2296

Who we are

SayFood group modeling and computational engineering research axis: Concurrent multiscale modeling

- **Zoom in on details down to molecules within the same simulation** (food, packaging)
- **Breakthrough approaches**: integration of chemical and structural information, image-based modeling, chemical reactions.
- **Public-private partnership**





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HPC

open source

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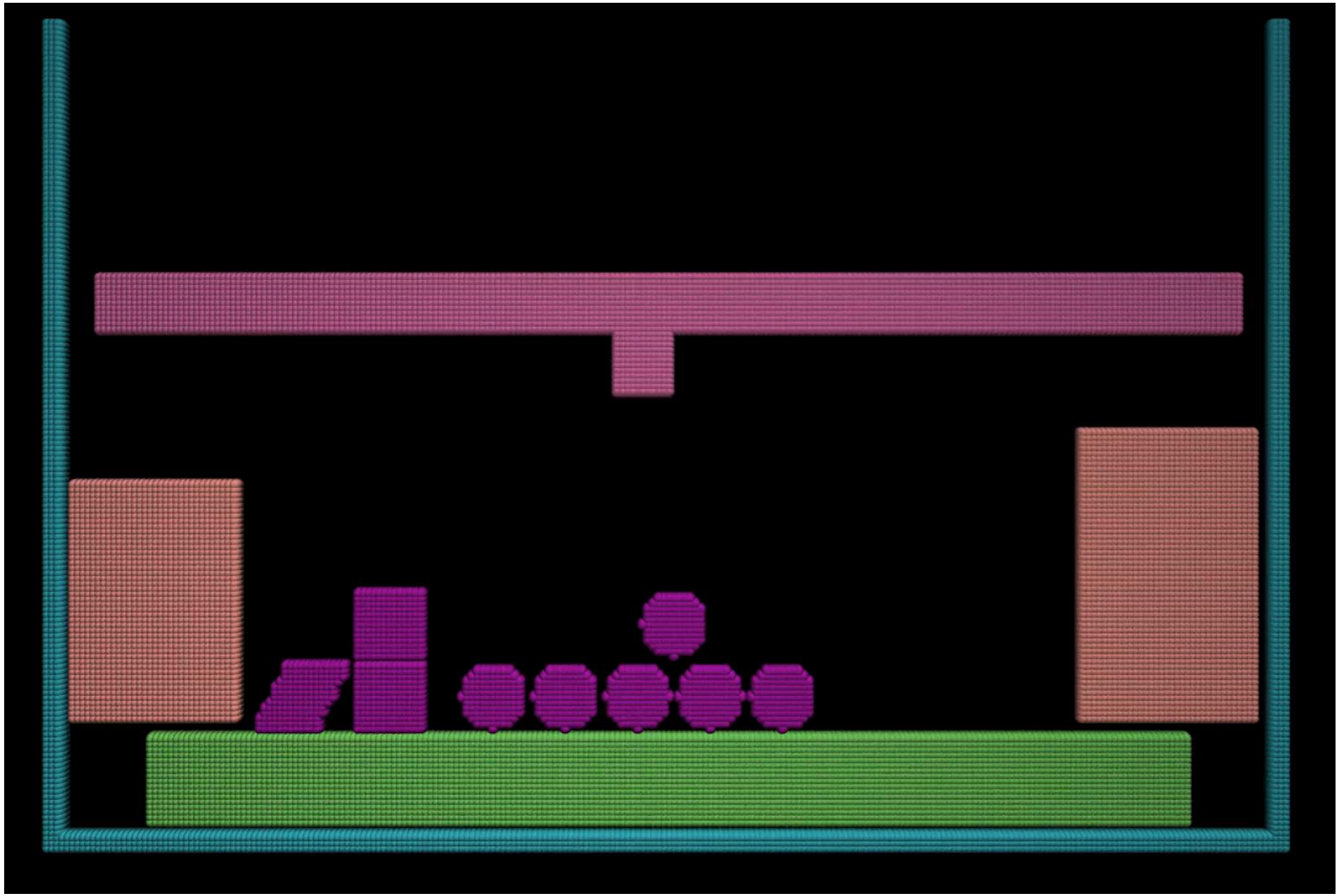
https://link.springer.com/article/10.1007/s42452-020-03272-2



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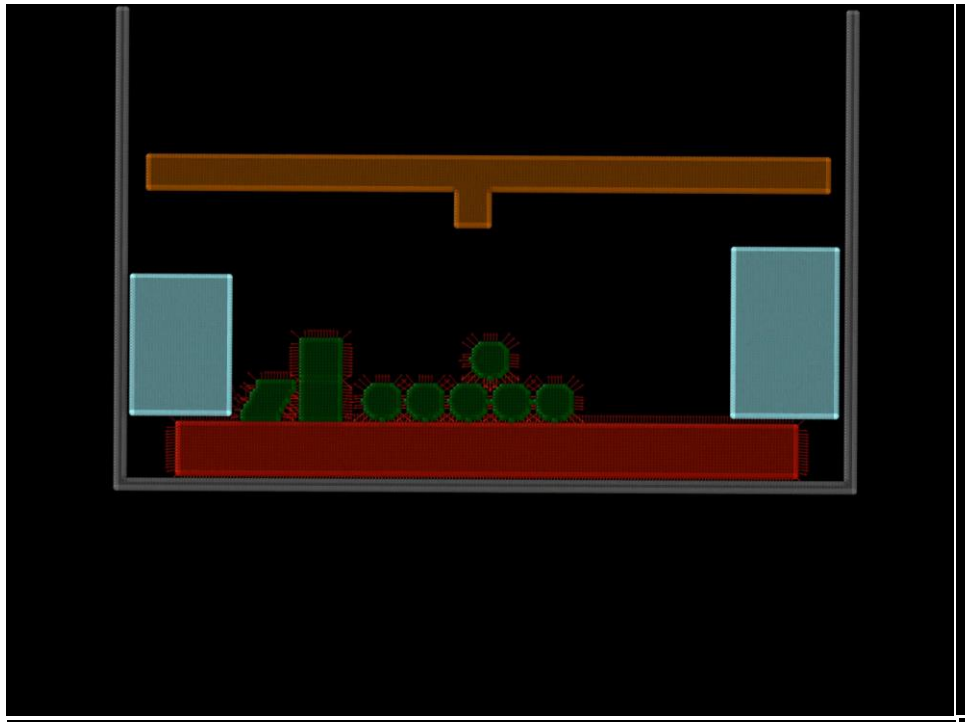


Force along y (reaction)
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c_s[2]
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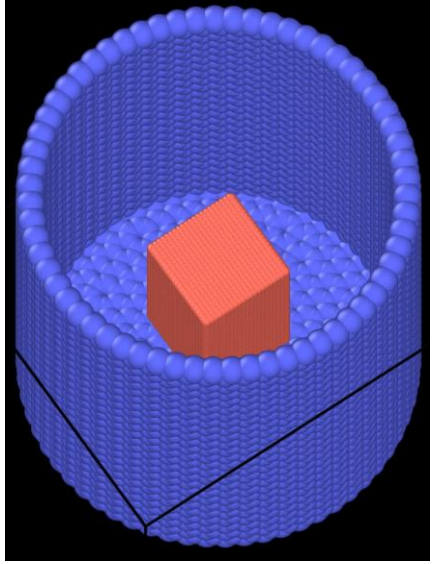

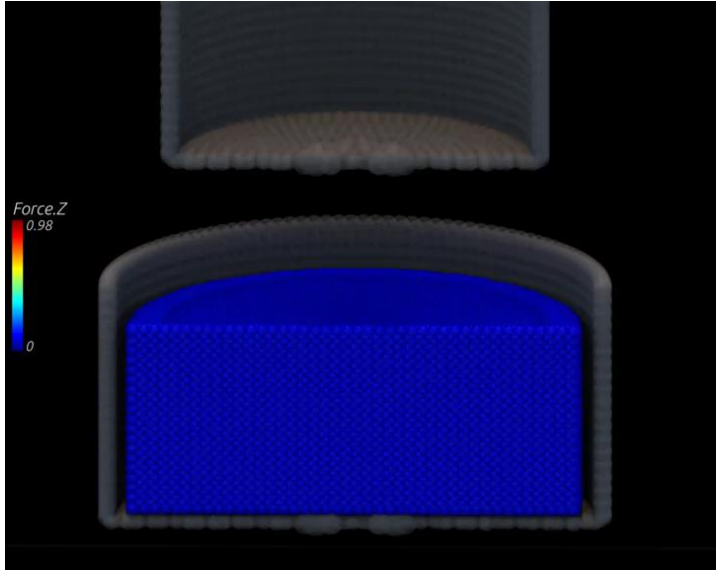
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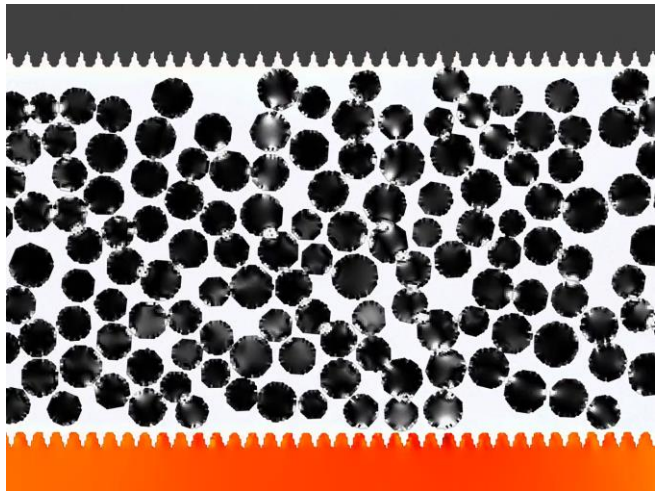

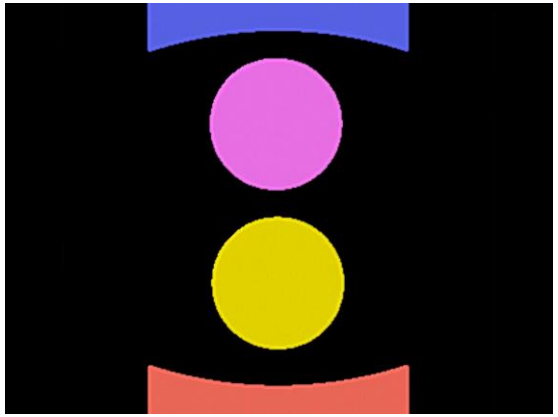

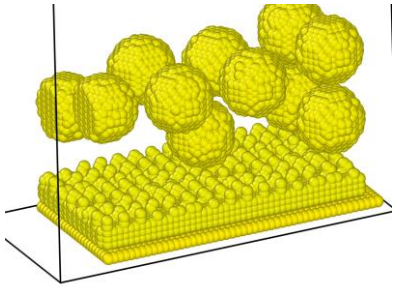

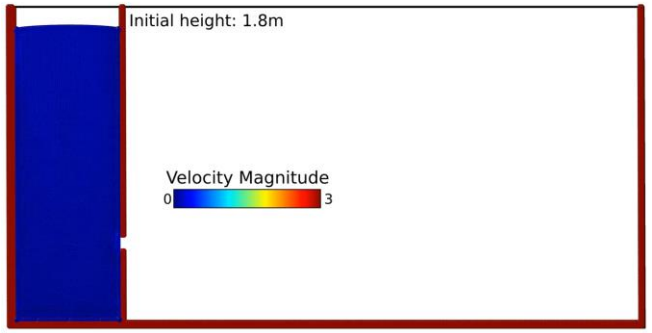
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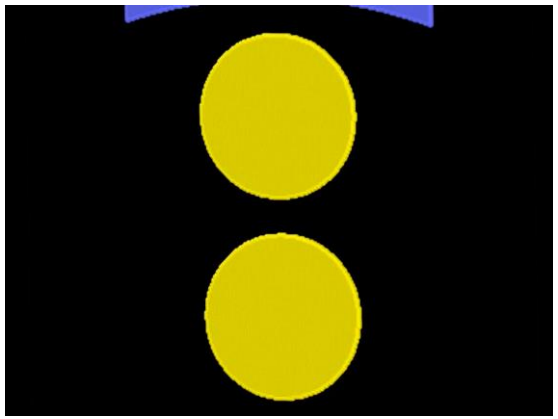

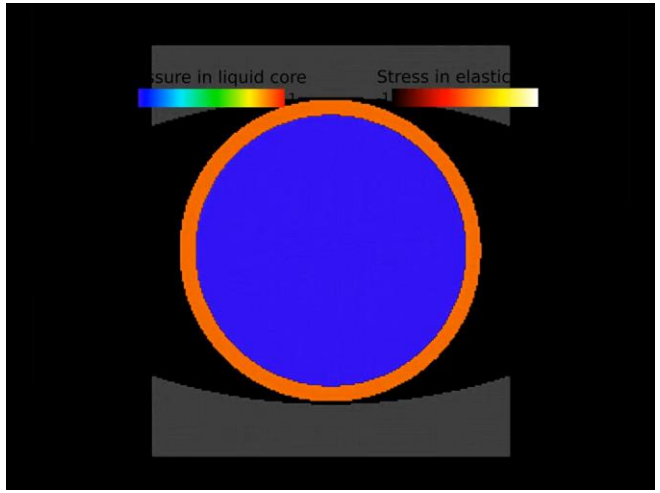
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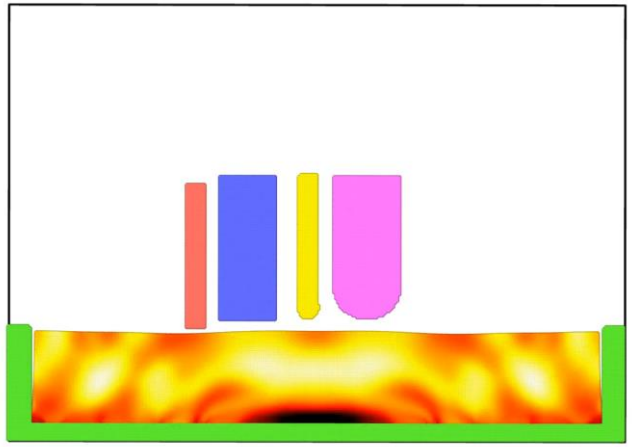

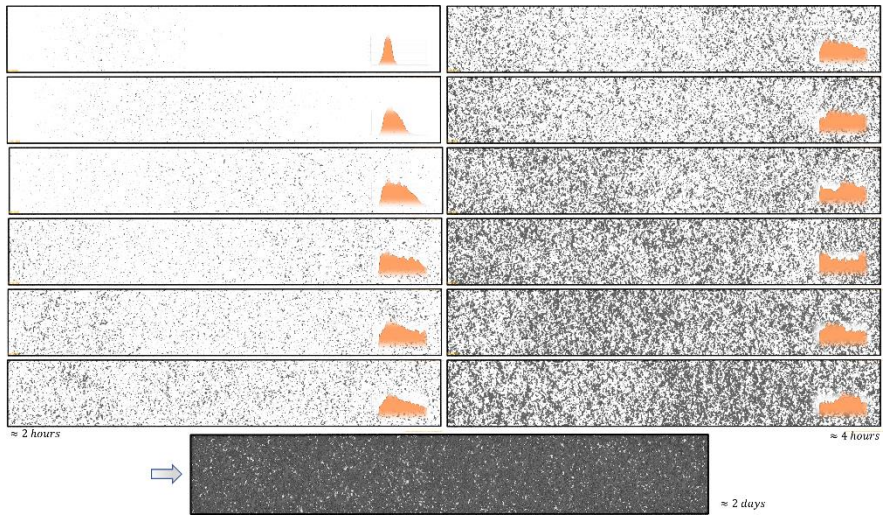
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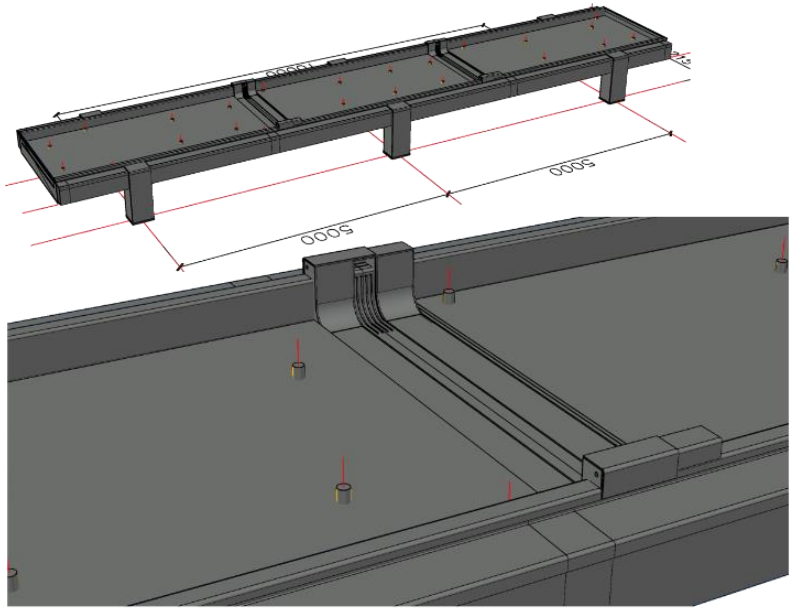
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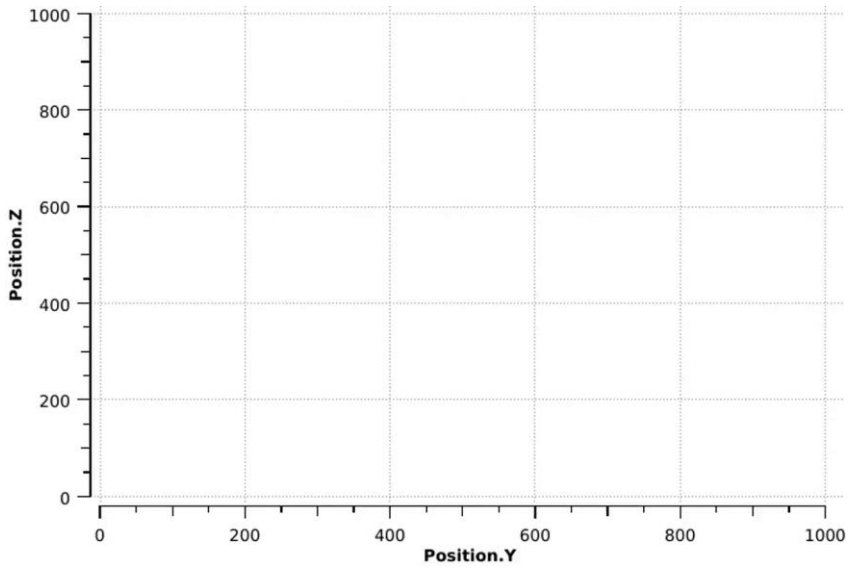
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iter=0
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Is molecular modeling a hot topic?

nature International weekly journal of science

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Published online 7 May 2010 | Nature | doi:10.1038/news.2010.223

Column

Molecular modelling's $10-million comeback?

Is Bill Gates's decision to invest in software company Schrödinger an early sign of a new computer-aided era for drug design, asks Derek Lowe. Or is it just another small step on what's been a rather lengthy journey?

Derek Lowe

Computational drug design has always seemed like a good idea. Compared to traditional drug discovery, it seems to offer a way to soar over what can be a trackless swamp. Finding a lead structure from millions of possible drug molecules is no small undertaking in itself. And once found, turning such a lead into a plausible drug candidate is notoriously difficult. That level of success, though, merely buys you the chance to spend your real money in the clinic, where 90% of the compounds that go in never come out.

Derek Lowe. *T. Hashemi*

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- Investment
- Software
- Bill Gates

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Far better to sit at a keyboard in some quiet room, hit the 'run' button, and come back later for the answers. The greatest period of enthusiasm for this vision was probably during the late 1980s, when advances in both hardware and software put molecular-modelling technology into more hands than ever before. But the new converts soon found themselves up against a whole suite of challenging problems. The shapes of drug molecules, how they change in both the presence of water molecules and their protein targets, and the shapes of the proteins themselves all had to be dealt with.

The act of 'docking' a drug candidate computationally into its target protein has to take all these factors into account, and fundamental problems remain. Even so basic (and crucial) a thing as the weak hydrogen bonds between atoms can be very difficult to model realistically. Then there's the dynamics-versus-statics problem: drug molecules and their binding targets never stop moving, folding and flexing. Modelling this realistically is hard, and increases the computational burden substantially.

Billionaire investors

Schrödinger, headquartered in New York and a respected company in the field, occupies an unusual niche. A number of other companies, such as their biggest competitor, Accelrys, based in San Diego, California, exist in the computational chemistry area. Unlike Schrödinger, however, very few have attempted to produce a broad range of computational products that attempt to address exactly the sort of problems listed above. Many other modelling-software vendors have left the field over the years, apparently because they could find no good way to make money at it.

> **"The Gates investment fits in well, making Schrödinger one of the few companies independently funded by two billionaires."**

Schrödinger, however, remains a private company, and in some ways is the most academic of the drug-discovery software vendors. It has had the benefit of a long relationship with David Shaw, a Wall Street investment manager with a scientific modelling background who has kept a hand in the area. In that sense, the Gates investment fits in well, making Schrödinger one of the few companies independently funded by two billionaires. The company does not release financial data, but has said that its revenues are somewhere above US$20 million per year. In that environment, a $10-million investment is substantial.

The company is likely to use its extra dollars for long-term projects:

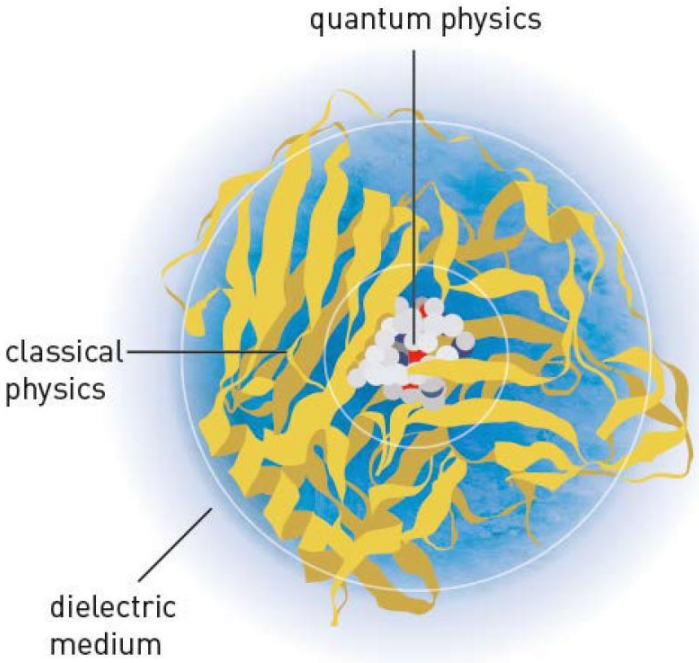
Scientific Background on the Nobel Prize in Chemistry 2013

DEVELOPMENT OF MULTISCALE MODELS FOR COMPLEX CHEMICAL SYSTEMS

Martin Karplus
Université de Strasbourg, France
and Harvard University, Cambridge, MA, USA
Michael Levitt
Stanford University School of Medicine, Stanford, CA, USA
Arieh Warshel
University of Southern California, Los Angeles, CA, USA

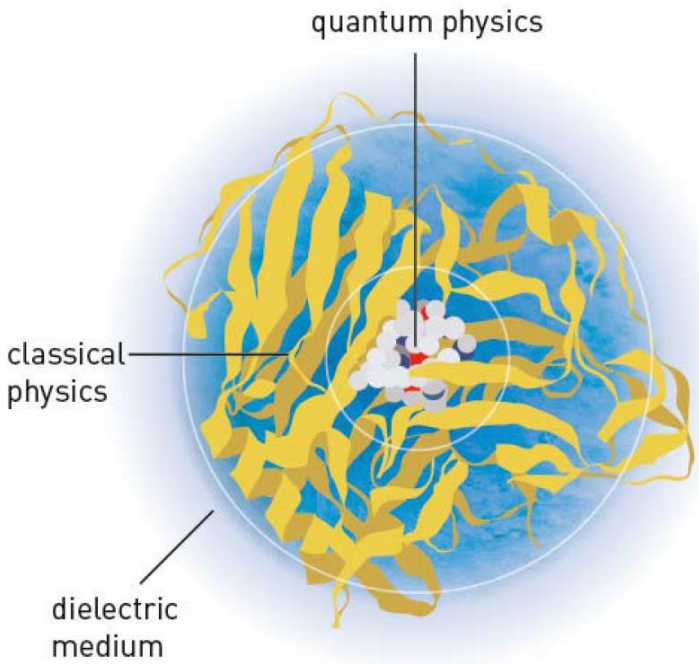
Previously, classical physics and quantum chemistry belonged to rivalling worlds.

Multi-copper-oxidase embedded in water

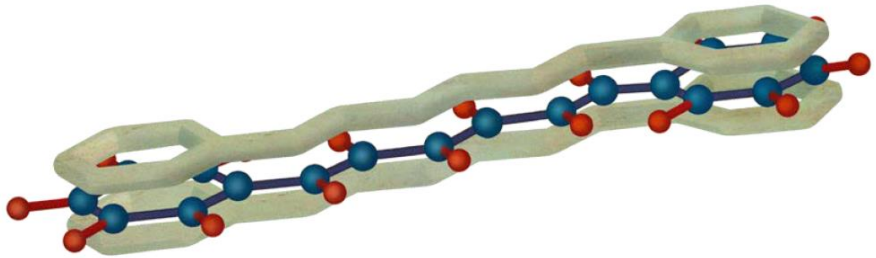


The Nobel Laureates in Chemistry 2013 have opened a gate between those worlds and have brought about a flourishing collaboration.

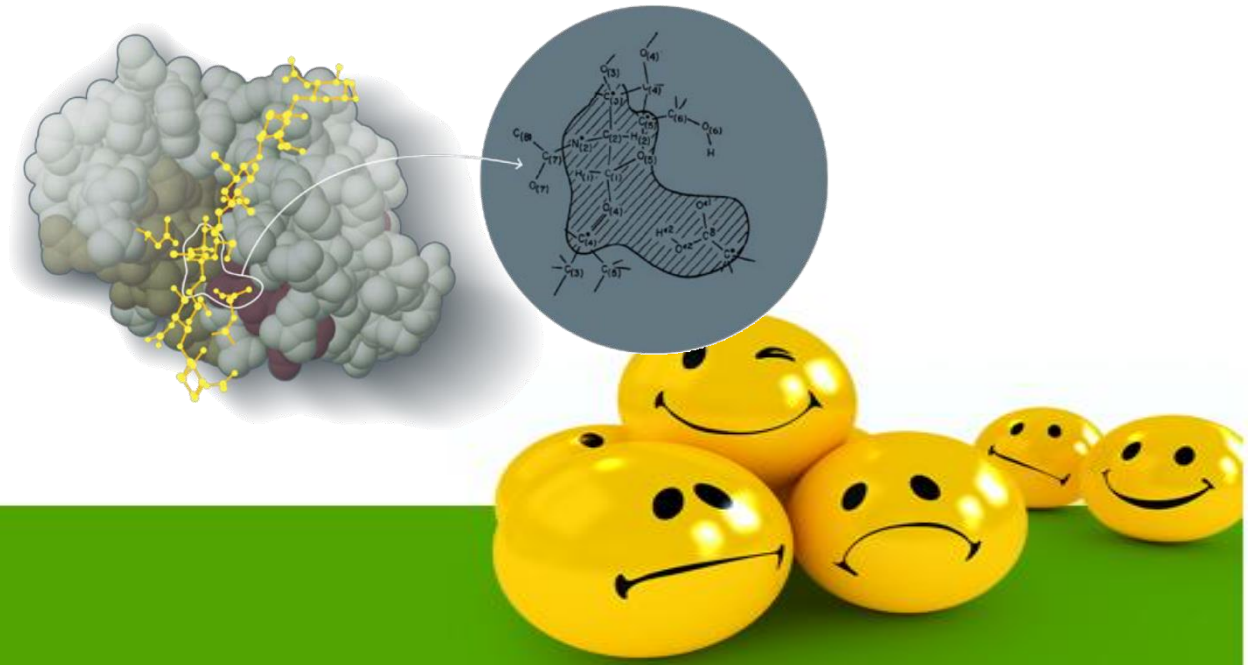
Today, when scientists model molecular processes, they apply the computer power where it is needed. At the heart of the system, calculations are based on quantum physics. Further away from the action, they are based on classical physics, and at the outermost layers, atoms and molecules are even lumped together to a homogenous mass. These simplifications make it possible to perform calculations on really large chemical systems.



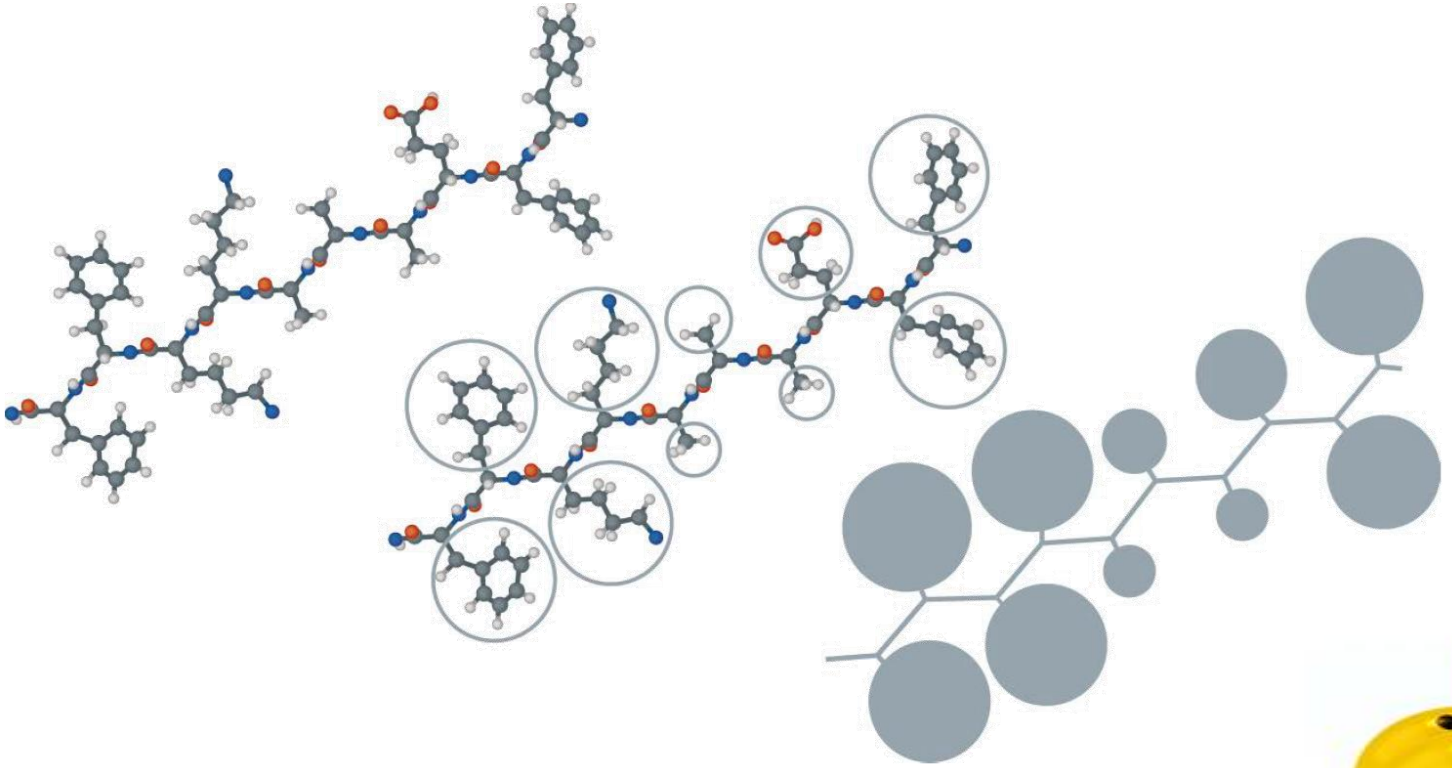
The mirror symmetric molecule 1,6-Diphenyl-1,3,5-hexatriene studied by Martin Karplus and Arieh Warshel



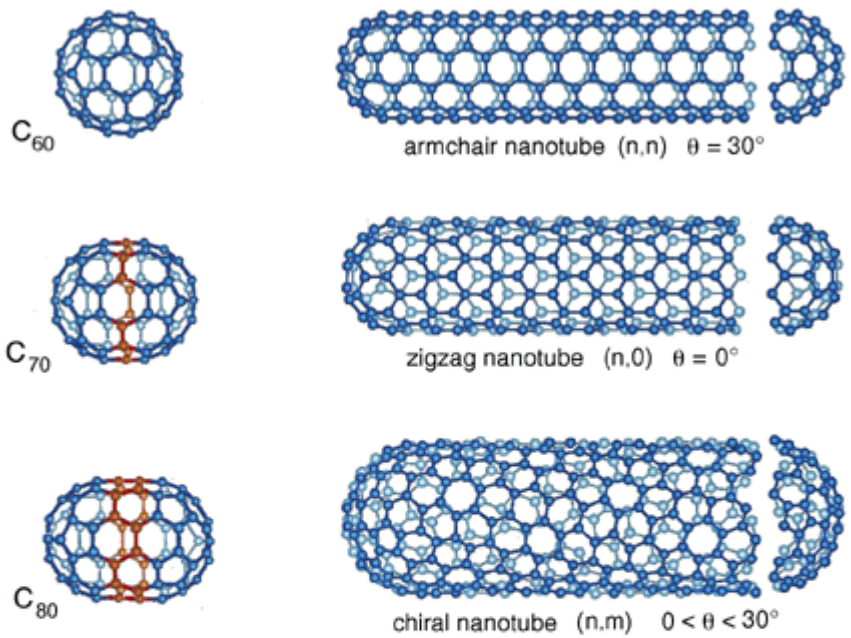
To understand how lysozyme cleaves a glycoside chain, it is necessary to model only the relevant parts of the system using quantum chemistry, while most of the surrounding may be treated using molecular mechanics or a continuum model.

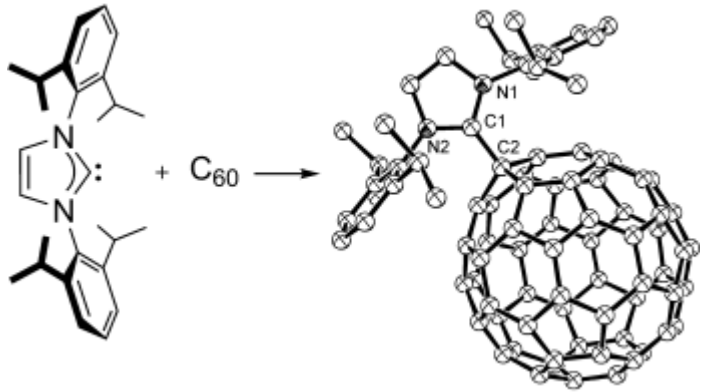


The detailed structure of a polypeptide chain (top) is simplified by assigning each amino acid residue with an interaction volume (middle) and the resulting string-of-pearls like structure (bottom) is used for the simulation.



Other examples





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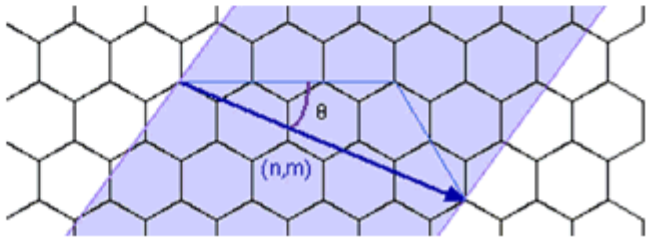
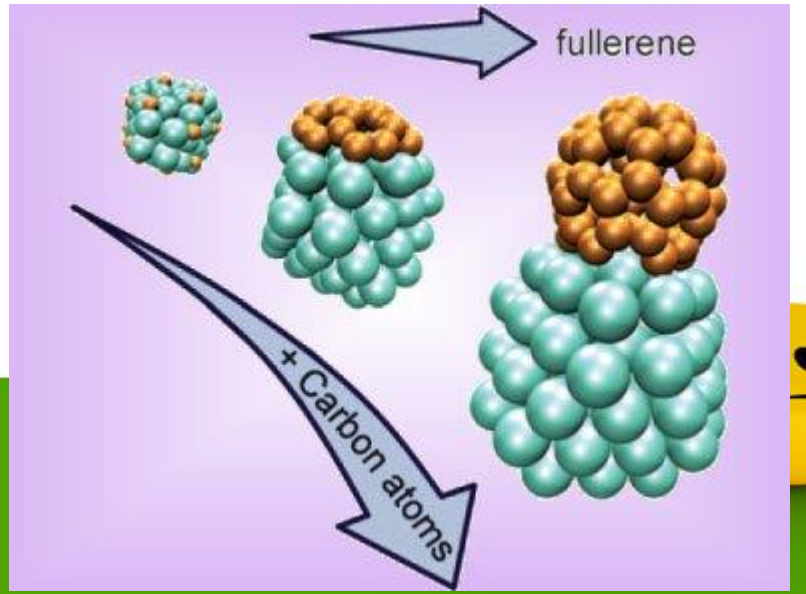
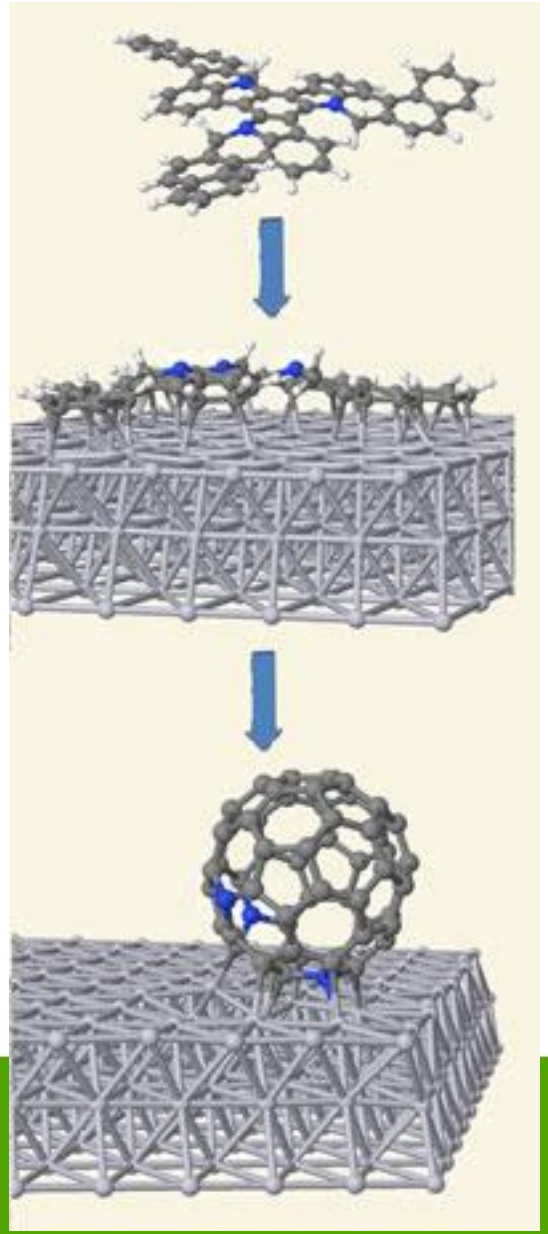
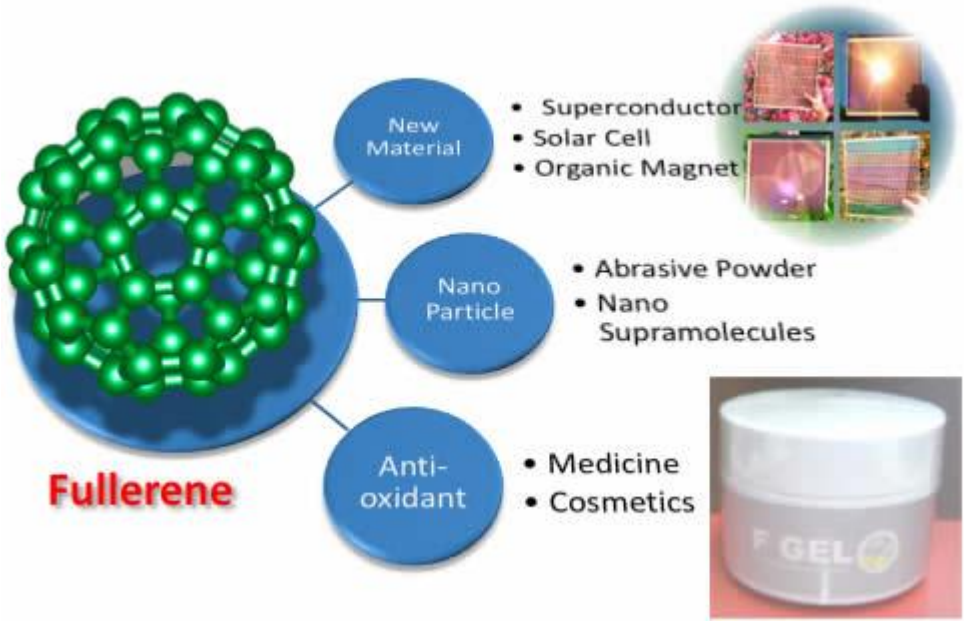
$$\theta = \tan^{-1}\left(\frac{m\sqrt{3}}{m+2n}\right)$$





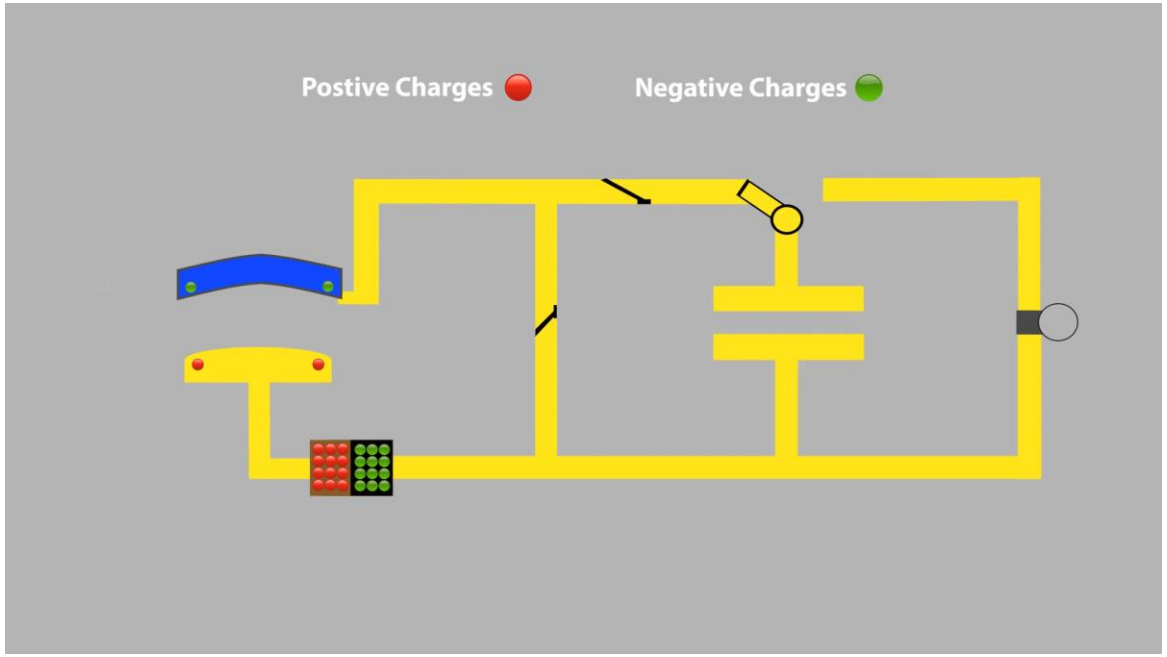
Beyond

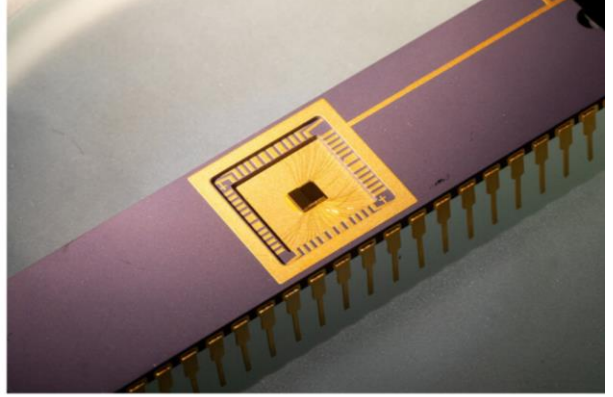



Fullerene
New Material
• Superconductor
• Solar Cell
• Organic Magnet
Nano Particle
• Abrasive Powder
• Nano Supramolecules
Anti-oxidant
• Medicine
• Cosmetics

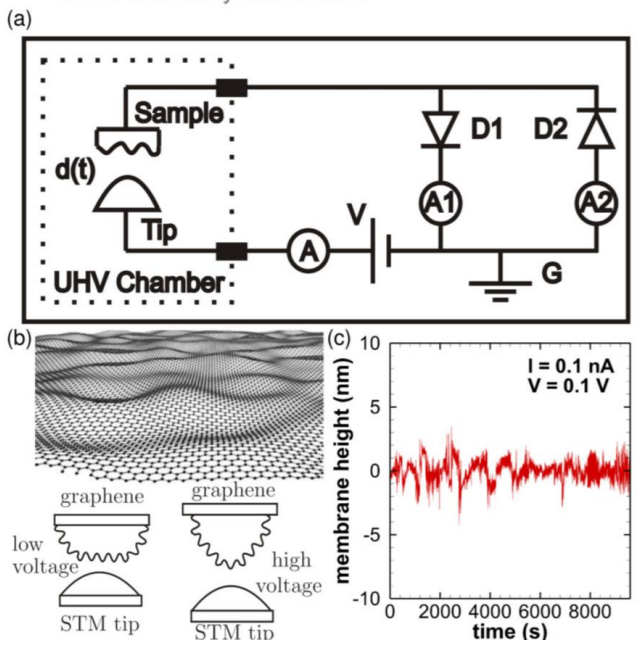
Physicists build circuit that generates clean, limitless power from graphene

2 October 2020





Credit: University of Arkansas



Fluctuation-induced current from freestanding graphene
Phys. Rev. E **102**, 042101

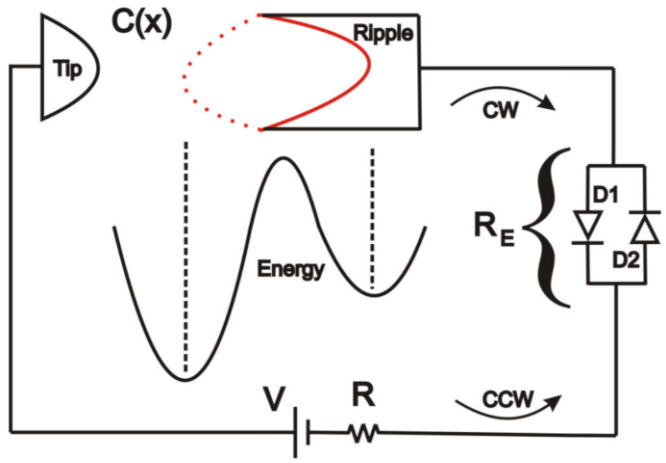


FIG. 3. Sketch of circuit model with energy barrier diagram.

Science. 1983 Dec 23;222(4630):1325-1327.

Van der Waals Surfaces in Molecular Modeling: Implementation with Real-Time Computer Graphics

Abstract. *A method is described for generating van der Waals molecular surfaces with a real-time interactive calligraphic color display system. These surfaces maintain their proper representation during bond rotation and global transformations, and an interior atom removal method yields a comprehensible picture of the molecular surface for large molecules. Both algorithms are faster than previous methods. This combination provides a powerful tool for real-time interactive molecular modeling.*

Molecular modeling with interactive color computer graphics in real time is a powerful method for studying the structures of molecules and their interactions (*1–3*). Computer-generated skeletal models maintain a consistent representation during manipulations such as bond rotations and global transformations but have the disadvantage that they give no indication of the physical space occupied by the atoms. We describe here a method for representing molecular surfaces that, unlike previous methods, is suitable for real-time interaction and manipulation.

With raster graphics atomic surfaces may be represented by shaded colored spheres. The displayed molecular surface is constructed by removing hidden surfaces of intersecting and overlapping spheres (*4, 5*) and shows a molecule in a given orientation and conformation. To view the molecule from another angle or in another conformation, one must generate an entirely new surface. Because hidden surface elimination may take several minutes on present equipment, this representation is of limited use in real-time molecular modeling. Several methods based on line drawing displays are available for similar static hidden-line representations (*6*). Other methods are based on an original idea by Richards (*7*) in which a "solvent-accessible surface" is traced out by the inward-facing surface of a "solvent sphere" making contact with the van der Waals surface of atoms in the molecule. This was first developed for studies of molecular interactions by using an interactive monochrome display (*8*), and later extended (*9*) for an interactive color display by using dots to represent the exterior solvent-accessible surface and internal cavities. A similar molecular surface may be generated more rapidly by using a "bit" lattice (*10*). Although these surfaces (*8–10*) may be globally manipulated in real time, bond rotation still requires recalculation of the area affected by the change. Therefore, modeling with molecular surfaces of this variety and frequent changes in torsion angles is laborious.

We have developed a method that generates a molecular surface faster than the above method and which has the significant advantage that the space-filling representation is retained during interactive real-time bond rotation. The ability to change the conformation of the molecular surface in real time cannot be overemphasized (*11, 12*).

For each atom surfaced, we generate a set of points distributed uniformly over a sphere whose radius is the van der Waals radius of the atom. Each point is com-

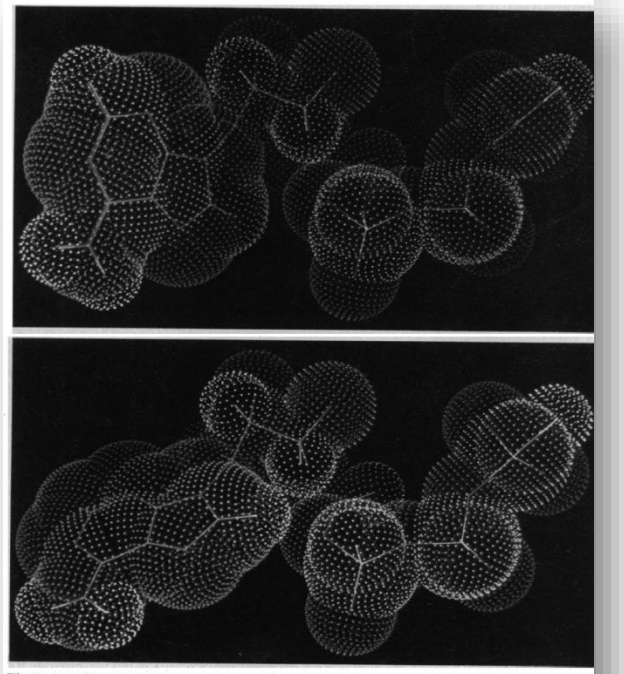


Fig. 1. (top) Van der Waals molecular surface of ATP, shown at a density of 25 dots per square angstrom. The surface is color-coded by atom type: carbon (green), nitrogen (blue), oxygen (red), and hydrogen (white). (bottom) The same surface after real-time rotation about the glycosyl bond.

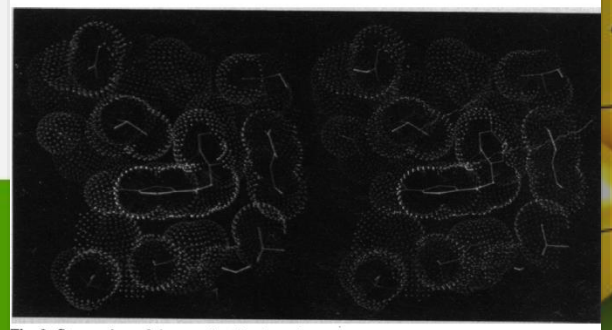


Fig. 2. Stereo view of the van der Waals surface of the noninterior atoms in a section of the active site of dihydrofolate reductase (blue dots), the skeletal model of the residues in the active site (red lines), and the methotrexate molecule and its van der Waals molecular surface (green lines and red dots).

Systems Analysis at the Molecular Scale

HERSCHEL RABITZ

Problems involving physiochemical phenomena on both the microscopic and macroscopic scales often raise similar sets of generic issues and questions. The complexity of these problems is beginning to make inoperative the traditional intuition-based approaches to their analysis and solution. The common characteristics of large, multivariable, complex molecular systems call for a new, more systematic approach to guide theoretical and experimental efforts. With mathematical modeling becoming an essential ingredient in the studies, it is argued that molecular systems analysis and especially the systematic tools of sensitivity analyis can play an increasingly important role in understanding and finding solutions to complex, chemically based problems.

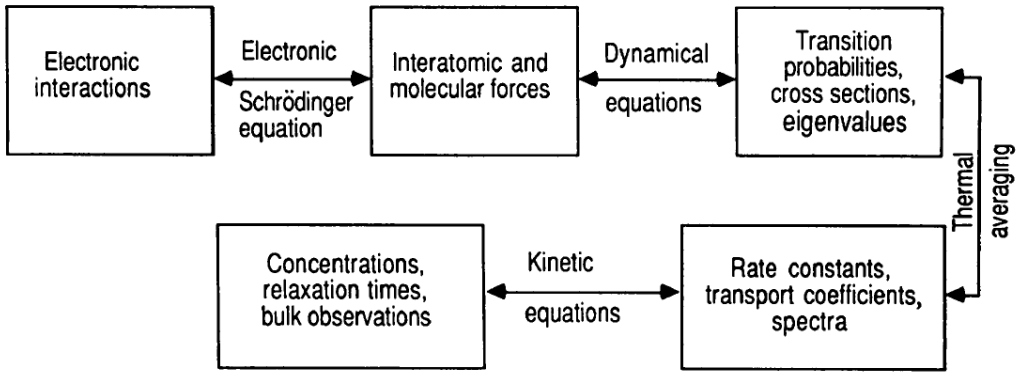
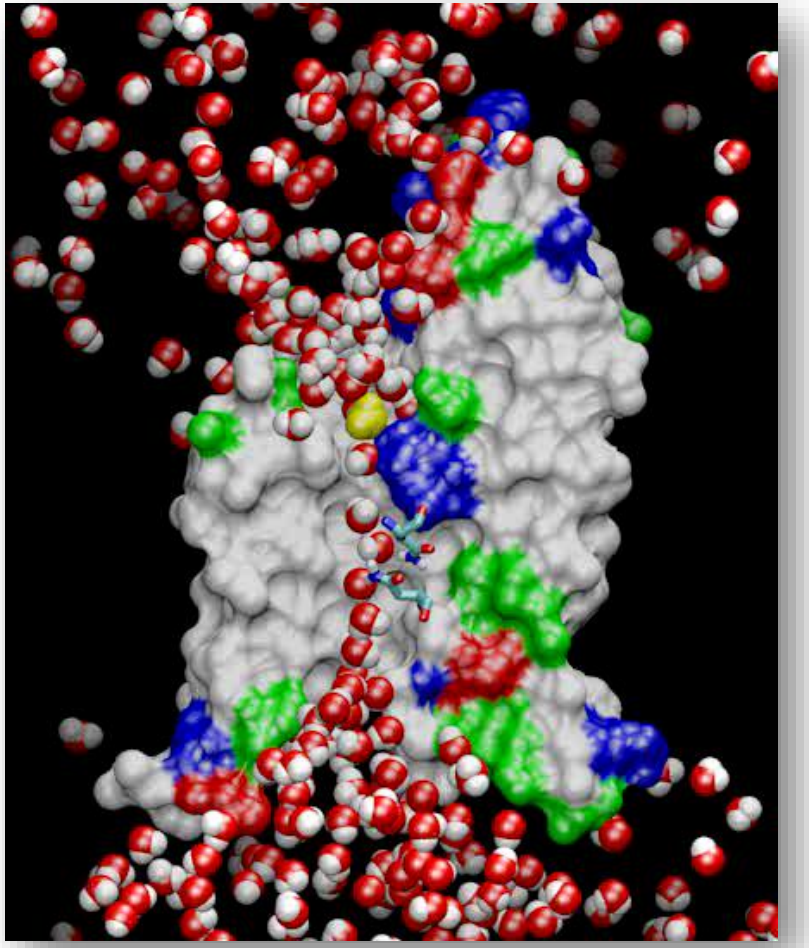
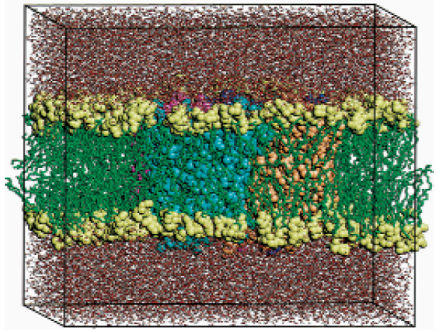


Fig. 1. Flow chart illustrating the hierarchical connection between microscopic and macroscopic variables in chemical dynamics and kinetics. Sensitivity analysis techniques may be developed to specifically probe the parametric and functional interconnections between the levels of the flow chart. The double-headed arrows connecting elements in the flow chart imply that both forward and inverse questions may be explored.

Science 13 October 1989:
Vol. 246 no. 4927 pp. 221-226





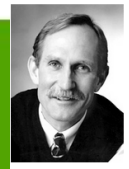
Modeling Molecular Filtration

Proteins in the aquaglyceroporin family passively conduct small, non-ionic molecules (water and glycerol) across biological membranes. How they do this at high rates (10^9 molecules per second) with high specificity (water instead of protons and glycerol instead of water) is a mystery. Now, de Groot and Grubmüller (p. 2353; see the Perspective by Berendsen) present real-time molecular dynamics analysis of permeation events through the water transporter AQP1 and the glycerol transporter GlpF. These simulations support the proposal that the conserved asparagine-proline-alanine motif functions primarily as a size filter and suggest that a newly identified region, called ar/R for its aromatic and arginine elements, serves as a barrier to proton transport.

Tajkhorshid, E., Nollert, P., Jensen, M.O., Miercke, L.J., O'Connell, J., Stroud, R.M., and Schulten, K. (2002). Science 296, 525-530
B.L. de Groot and H. Grubmüller (2001), Science, 294, 2353-2357

The Nobel Prize in Chemistry 2003
Peter Agre, Roderick MacKinnon

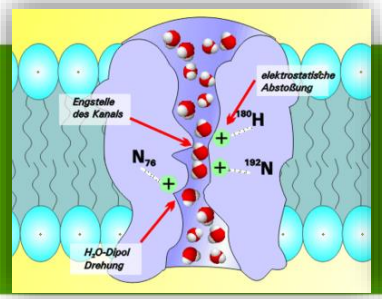
The Nobel Prize in Chemistry 2003

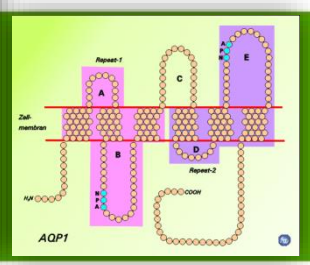


Peter Agre

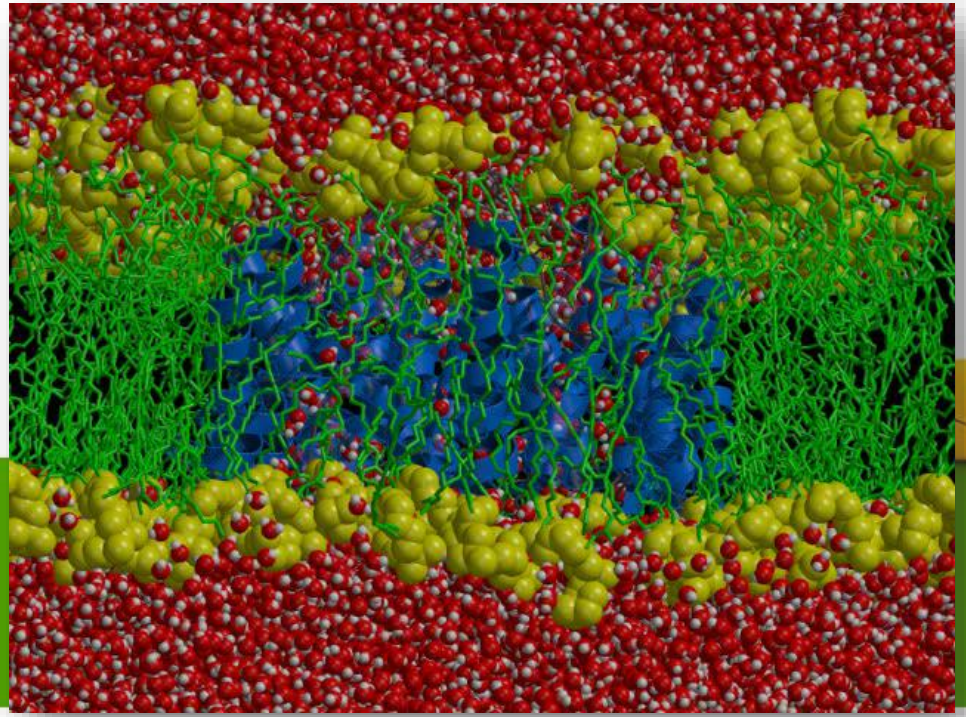
Roderick MacKinnon

The Nobel Prize in Chemistry 2003 was awarded *"for discoveries concerning channels in cell membranes"* jointly with one half to Peter Agre *"for the discovery of water channels"* and with one half to Roderick MacKinnon *"for structural and mechanistic studies of ion channels"*.





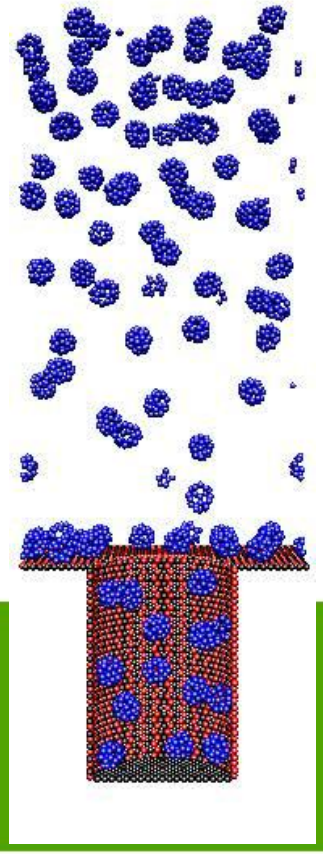
Water channels In cell membranes

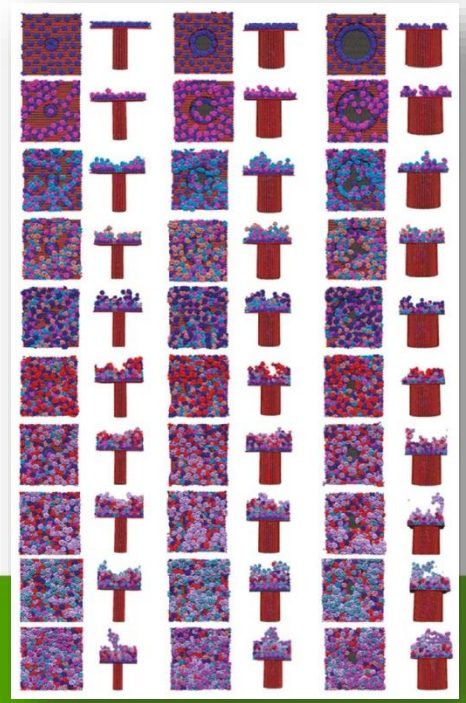


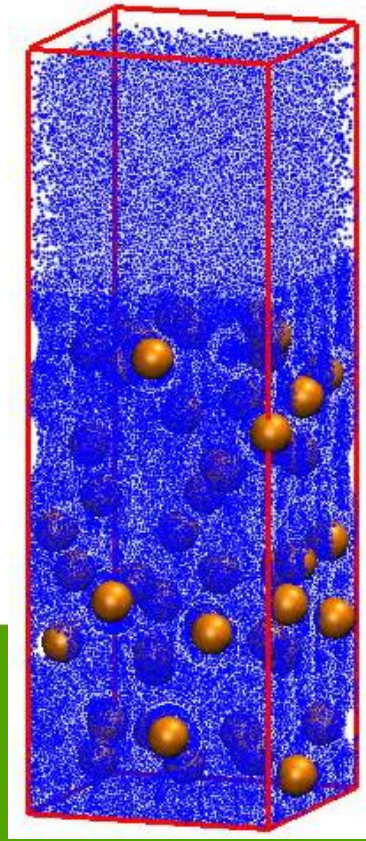
Beyond the sole biology

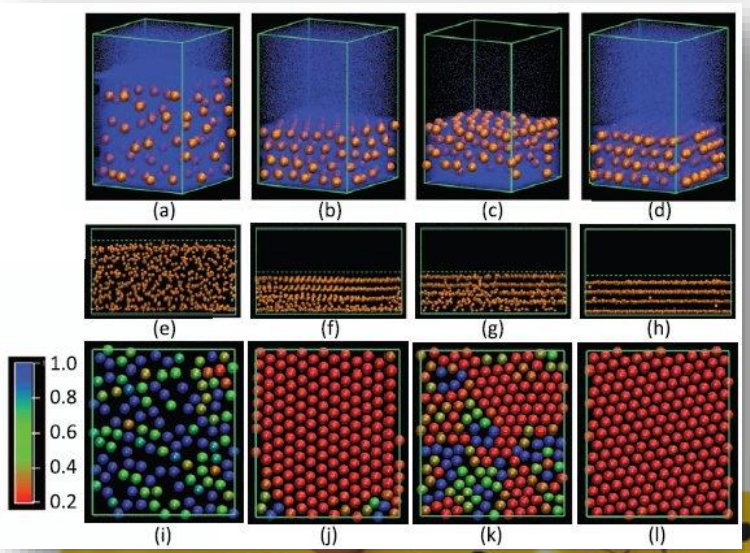
Layer-by-Layer Assembly of Charged Nanoparticles on Porous Substrates: Molecular Dynamics Simulations, J.-M. Carrillo and A. V. Dobrynin, ACS Nano, 5, 3010-3019 (2011).

Molecular dynamics simulations of evaporation-induced nanoparticle assembly, S. Cheng and G. S. Grest, J Chem Phys, 138, 064701 (2013).



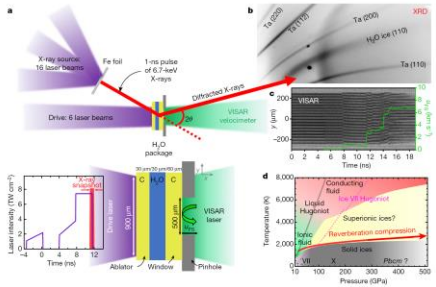


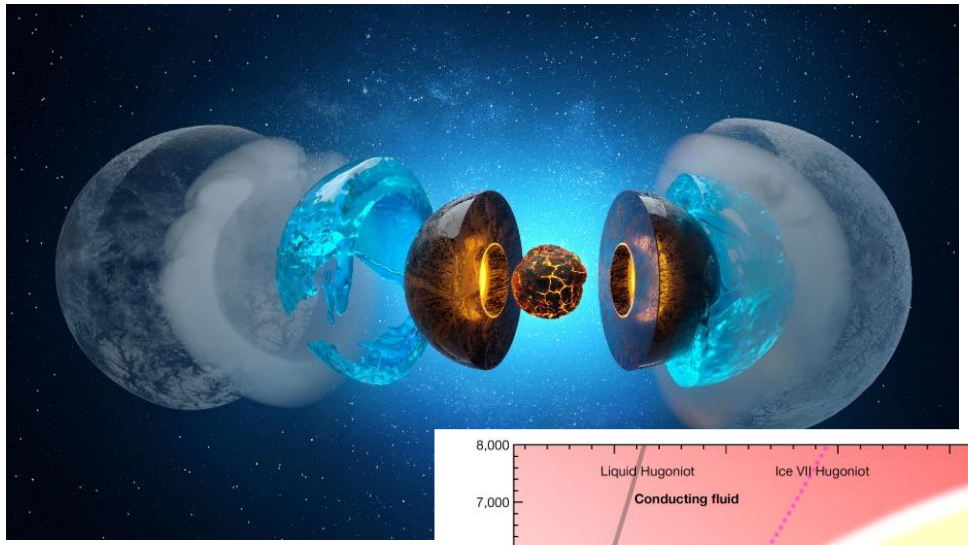


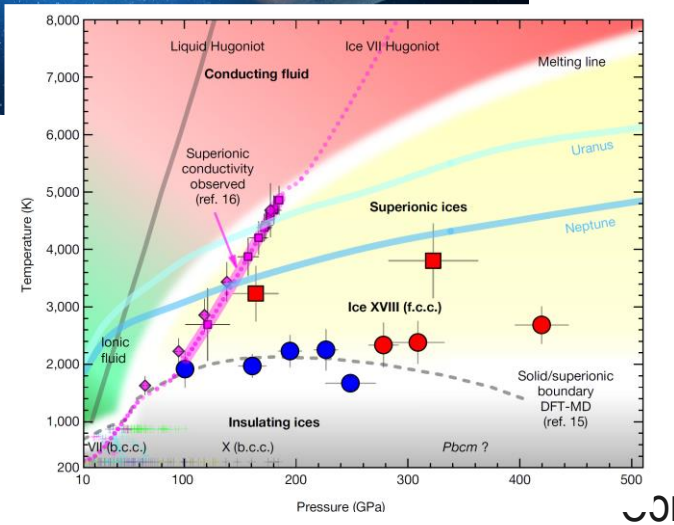


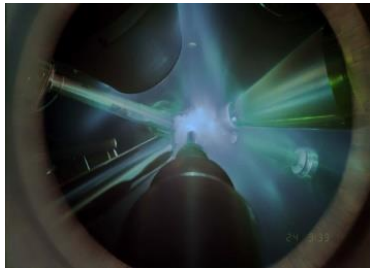
9 MAY 2019 | VOL 569 | N A T U RE | 251-255

Nanosecond X-ray diffraction of shock-compressed superionic water ice

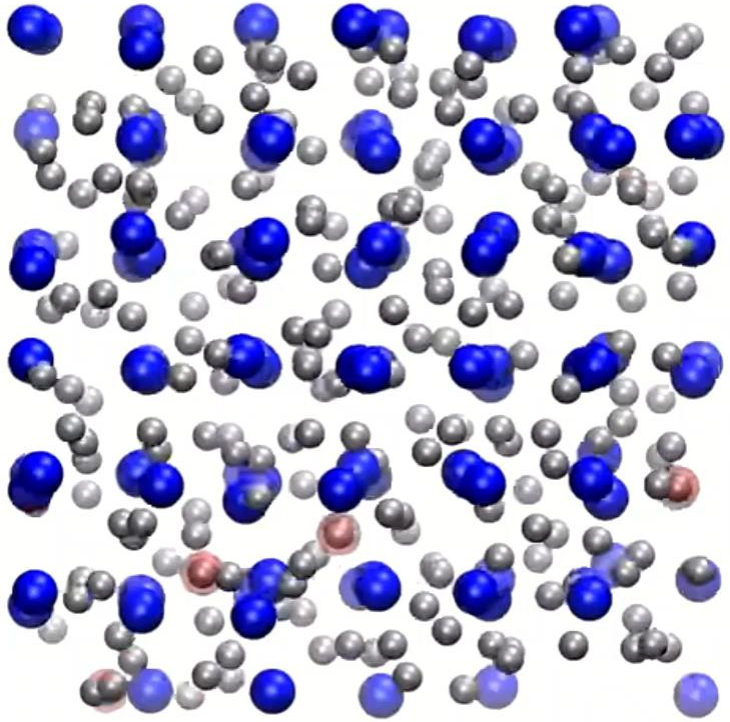








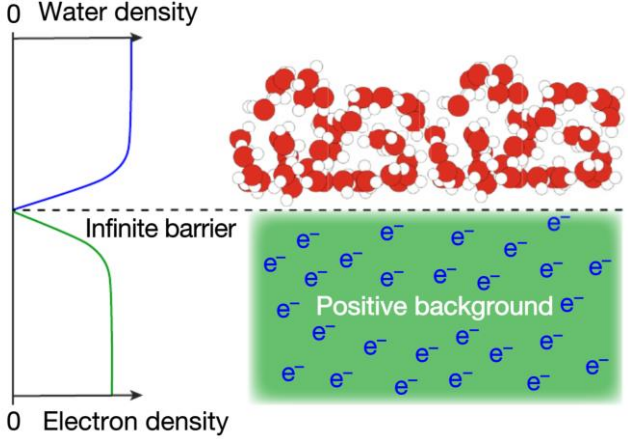
The discovery of superionic ice potentially solves the puzzle of what giant icy planets like Uranus and Neptune are made of. They're now thought to have gaseous, mixed-chemical outer shells, a liquid layer of ionized water below that, a solid layer of superionic ice comprising the bulk of their interiors, and rocky centers.



Computer simulation of the new superionic water ice phase, illustrating the random, liquid-like motion of the hydrogen ions (gray, with a few highlighted in red) within a face-centered cubic lattice of oxygen ions (blue).

Nature | Vol 602 | 3 February 2022 | 84-91

Fluctuation-induced quantum friction in nanoscale water flows



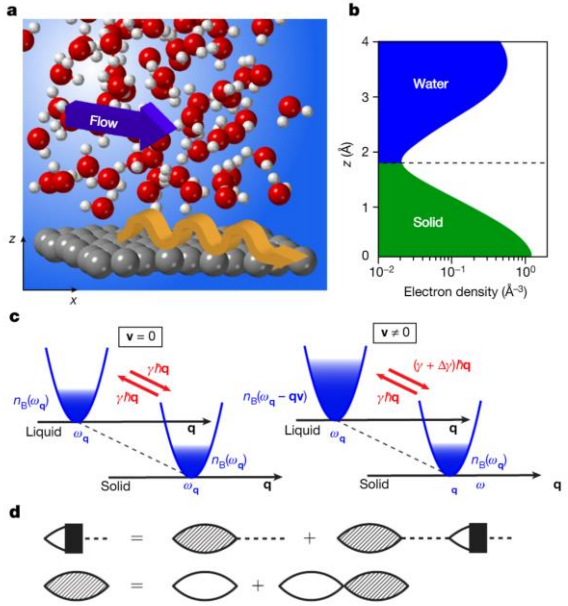


Fig. 1 | Theory of solid–liquid quantum friction. a, Artist's view of the quantum friction phenomenon: water charge fluctuations couple to electronic excitations within the solid surface, represented by the orange arrow. **b**, Average electronic density, as obtained from density functional calculations (Supplementary Section 7), at the water–graphene interface. **c**, Schematic of the quantum friction mechanism, showing quasiparticle tunnelling between two surface modes at wavevector **q** and frequency $\omega_{\mathbf{q}}$. The filling of the blue parabolas represents the occupation of each mode, according to the Bose–Einstein distribution n_B. The back and forth tunnelling rates γ are different in the presence of flow, resulting in a net momentum transfer from the liquid to the solid. Further details are given in Supplementary Section 2.8. **d**, Feynman diagram representation of the Dyson equation for the electron–water density correlation function. Full lines represent electron propagators and dashed lines represent water propagators. The equation expresses the fact that electron–water correlations are mediated by all possible coupled fluctuations of the water and electron densities.

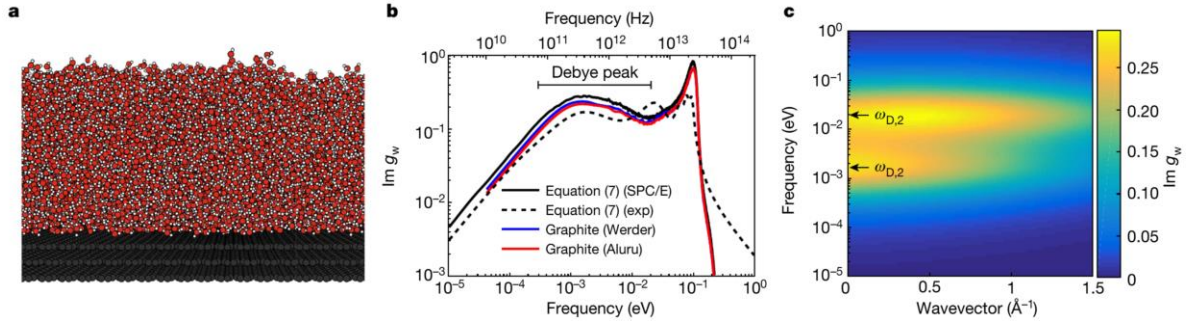
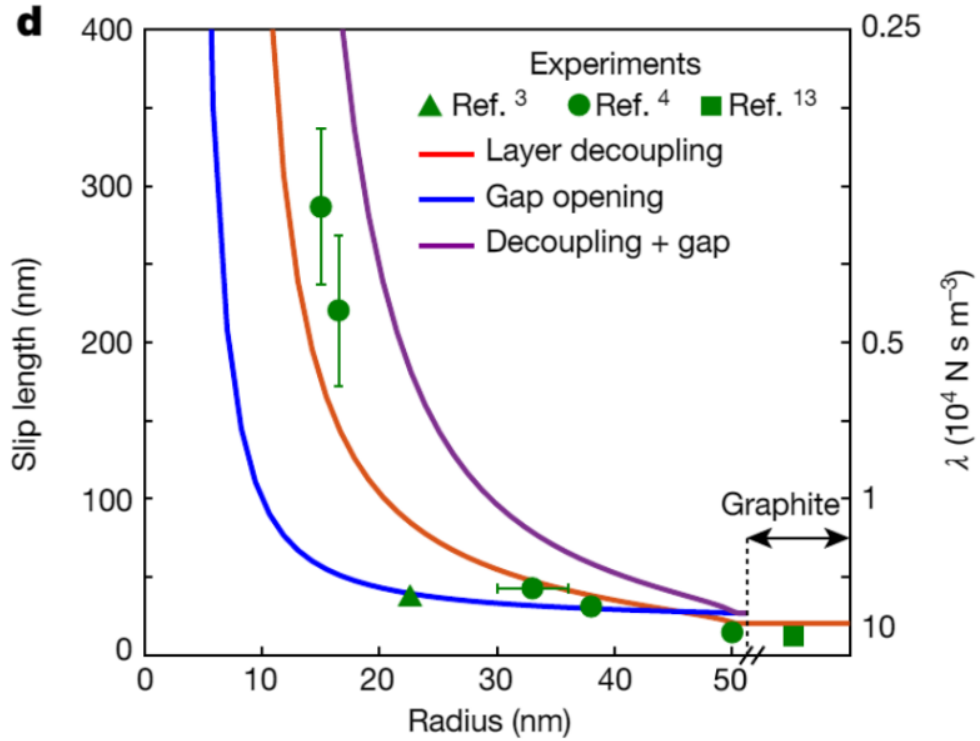
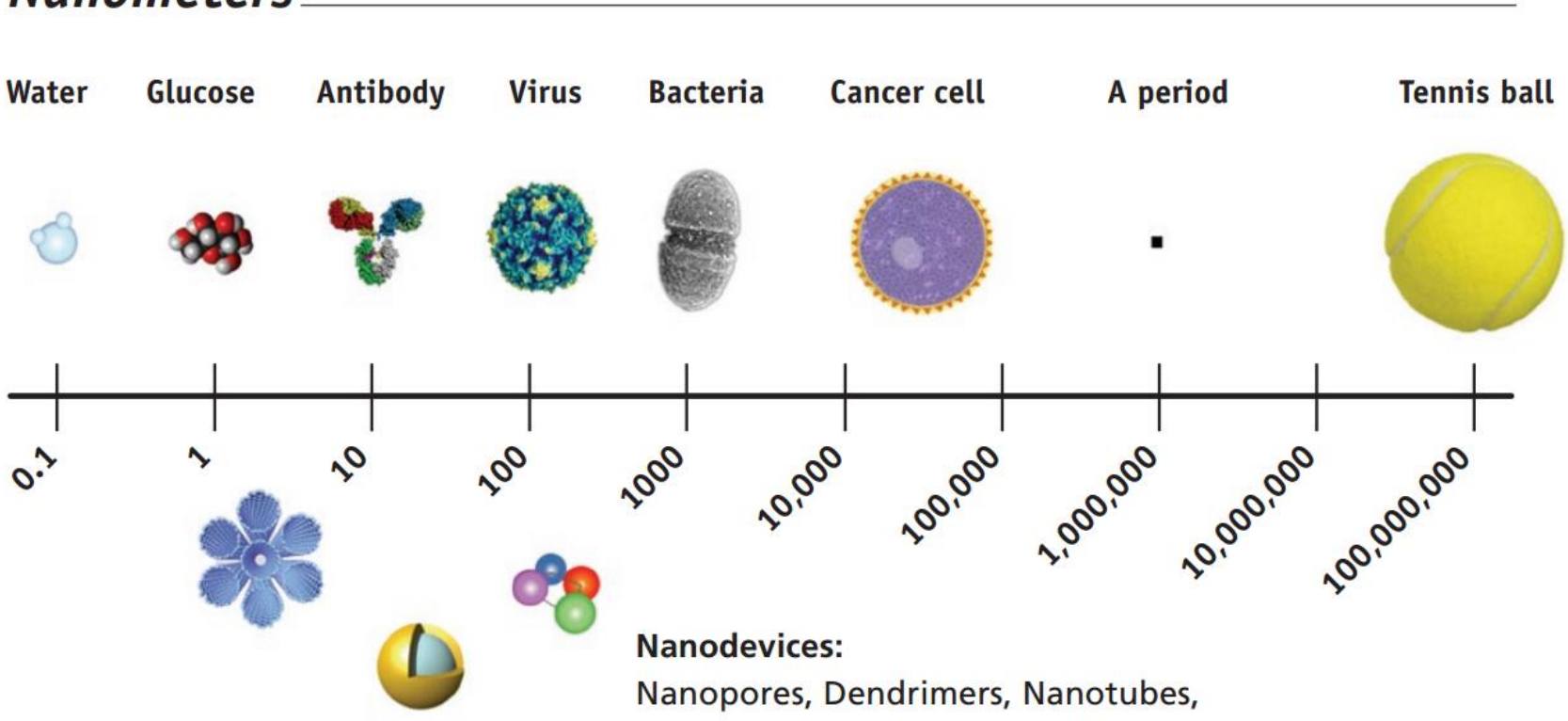


Fig. 2 | Surface dielectric response of water. a, Snapshot of the MD simulation used for determining the water surface response function. The graphene supercell size is 128 × 123 Å^2. **b**, Surface response function g_w of water versus frequency, in the long wavelength limit ($q \to 0$). The various curves correspond to results obtained from MD simulations of the water–graphite interface with two different sets of molecular parameters (named 'Aluru' and 'Werder', see Supplementary Section 4), and to the $q = 0$ prediction of equation (7), obtained from the experimental (exp) and simulated with the extended simple point charge model (SPC/E) bulk dielectric constant. All the determinations of the surface response function agree well in the long wavelength limit. **c**, Surface response function of water in energy–momentum space, as obtained by fitting the simulation data with two Debye peaks (equation (8)).





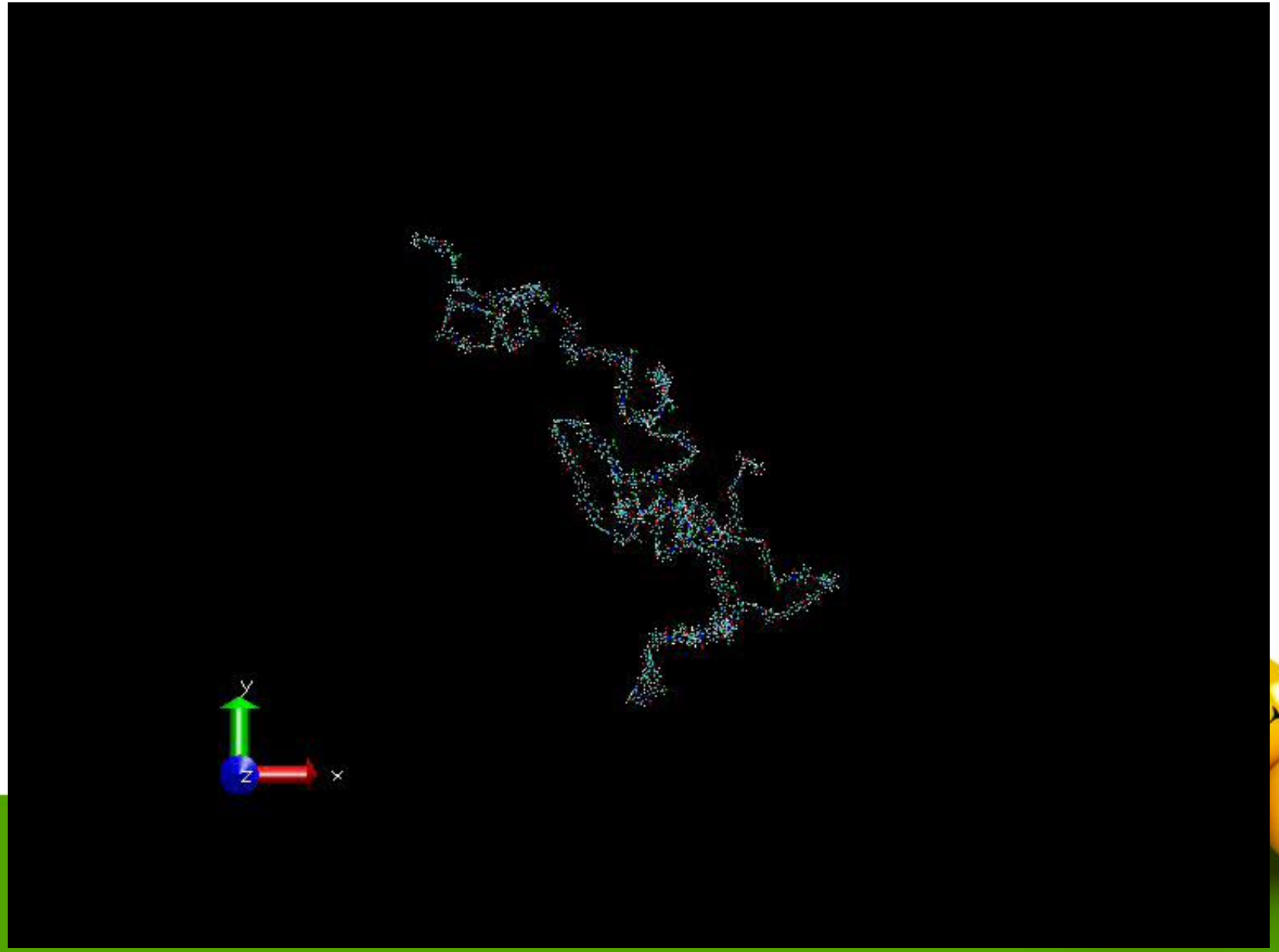
Quantum modelin

Molecular modeling

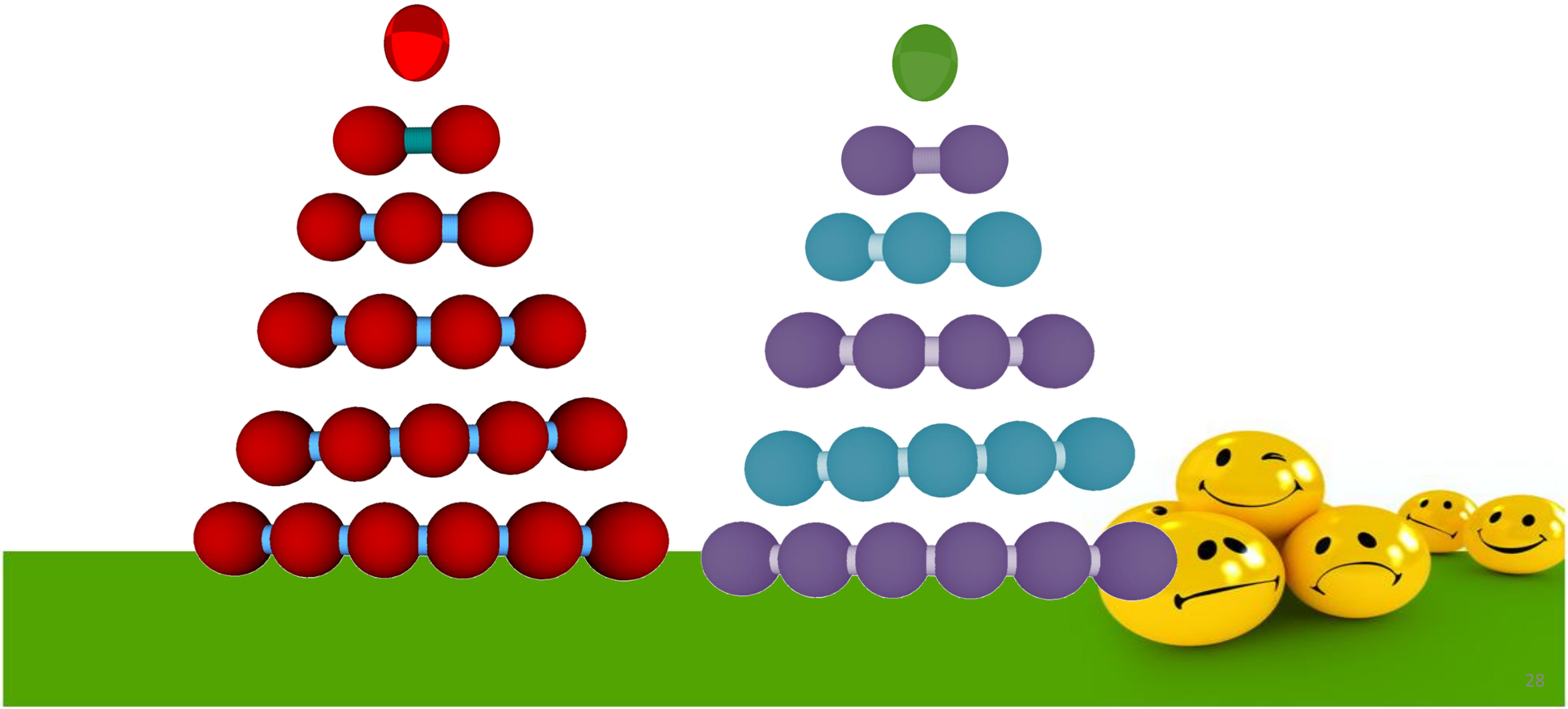
Supramolecular modeling

Stochastic methods

What is molecular modeling?



What is molecular modeling?



Why Molecular Modeling?

Moore's law

- Computing speeds double every 18 months = order of magnitude every 5 years
- Add 2-3 orders of magnitude from parallelization (cheap today)
- Costs driven by consumer market

Costs for experiment?

- Labor-intensive, high capital costs

Costs for theory?

Do graduate students and/or lab personnel/equipment improve by an order of magnitude every five years?

Our cluster (AgroParisTech Massy, C200)
20 nodes
~500 cores

Main contributions of molecular modeling

- Three main roles:
  - **Predicting fundamental properties used in engineering correlations**
    - E.g., critical constants, molecular structure, dipole moment
  - **Predicting required properties directly**
    - E.g., phase equilibrium of mixture, transport properties, mechanical properties
  - **Providing conceptual molecular-level understanding of properties**
    - E.g., developing correlations, evaluate theory, guide/supplement/replace experiment
- **Other roles**: chemometrics (extracting information from chemical systems by data-driven means)

Applications in our group:
Safety of food contact materials, new barrier materials
reverse osmosis, pervaporation, thermodynamics of liquid mixtures

...no experimental but simulated data...

Extreme Point of View

Self-assembling nanofibers from Thiophene-peptide oligomers

A. K. Shaytan, E.-K. Schillinger, P. G. Khalatur, E. Mena-Osteritz, J. Hentschel, H.G. Börner, P. Bäuerle, A. R. Khokhlov, ACS Nano, 5, 6894-6909 (2011),

Self-assembling nanofibers from Thiophene-peptide oligomers

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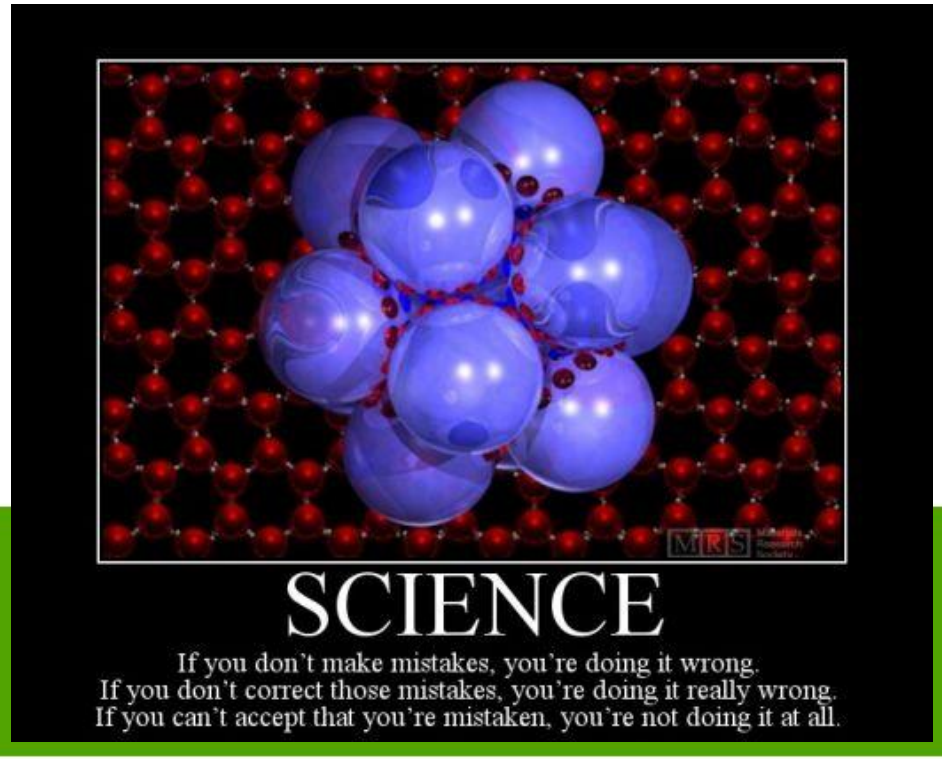
Molecular modeling is quantively-oriented

- performance characterization,
- model selection,
- verification & validation,
- figures of merit

Think **before** you model

Think **while** you model

Think **after** you model



My perspective

Sept 2001

- Description of migration of packaging constituents with Fick Equations and appropriate boundary condition
- Stochastic solution of transport equations (all parameters are replaced by statistical distributions)
- Optimized identification of transport coefficients (D,K) from concentration profiles/desorption experiments
- Relating molecular descriptors to D and K
- **Molecular modeling of excess chemical potentials (from scratch)**
- **Molecular simulation of scaling laws $D(M,T,\tau) \propto M^{-\alpha(T)}$**
- Experimental determinations of D from fluctuations methods
- Design of new barriers materials with optimized properties.
- New D models including T-Tg

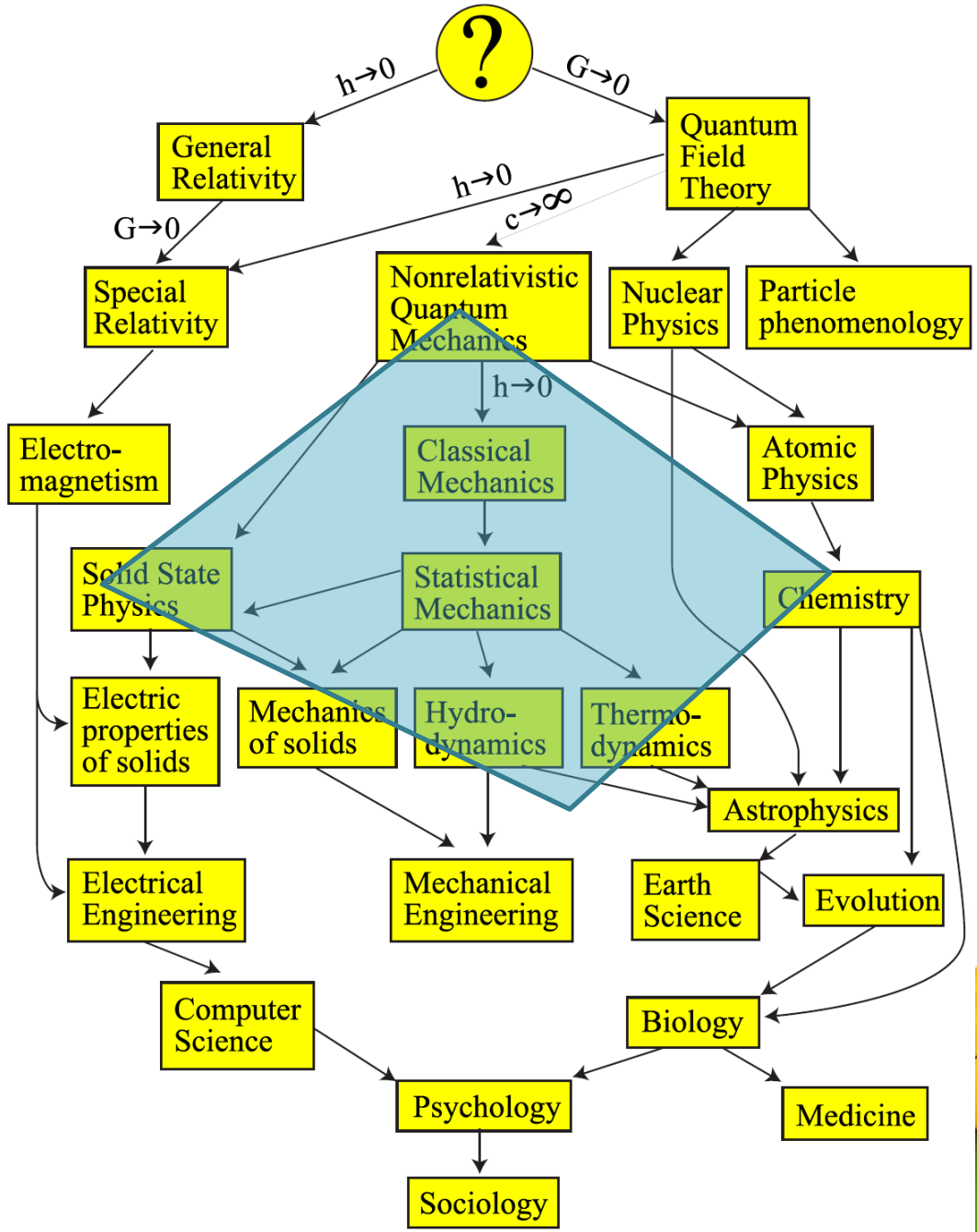
2014

Industrial Contracts using these approaches:
SOLVAY, Arkema, AMCOR, Safran, EDF, Cargill, McCain, etc.
Expertises: UE, ANSES, FDA

My perspective

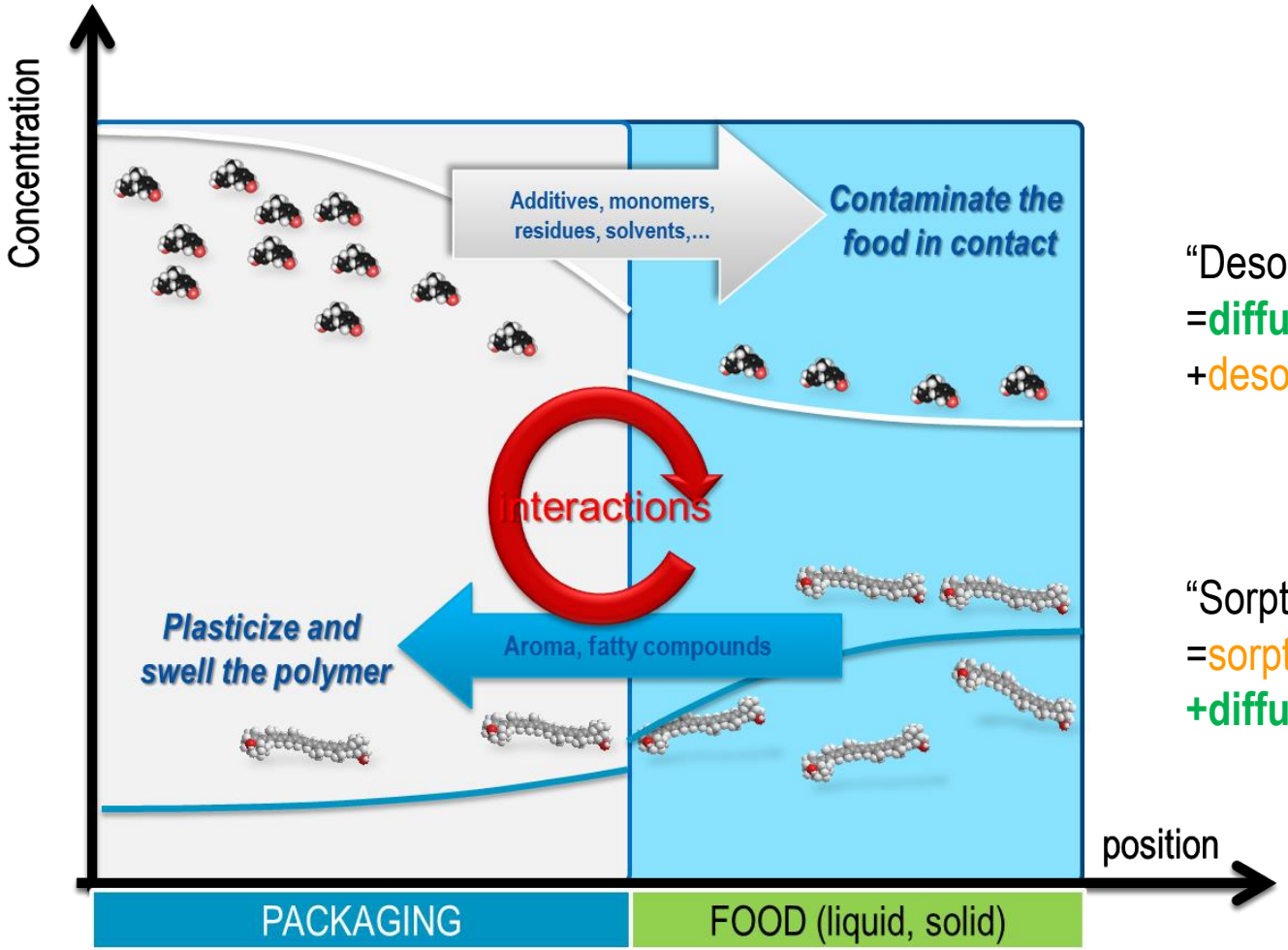
EFFECTIVE LAWS

FUNDAMENTAL LAWS



From “the Mathematical Universe”
Tegmark, M. *Found.Phys.* 38:101-150 (**2008**)

Goujot and Vitrac, 2013; Vitrac & Hayert, 2006; Sagiv 2001-2002



"Desorption"
=diffusion (diffusion coefficient)
+desorption (partition coefficient)

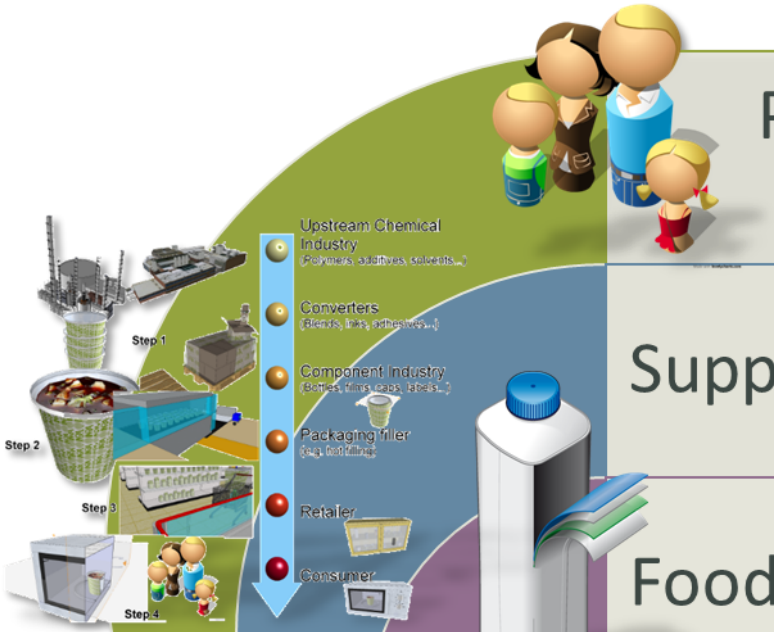
"Sorption"
=sorption (partition coefficient)
+diffusion (diffusion coefficient)

OUR RESEARCH AREA

Joint Research Unit 1145 between INRA and AgroParisTech

Group "Interactions between Materials and Media in Contact"

MODELING HIERARCHY

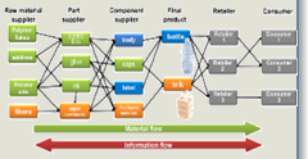


Population exposure

- Probabilistic modeling

Supply chain

- Chained simulations
- Bayesian modeling

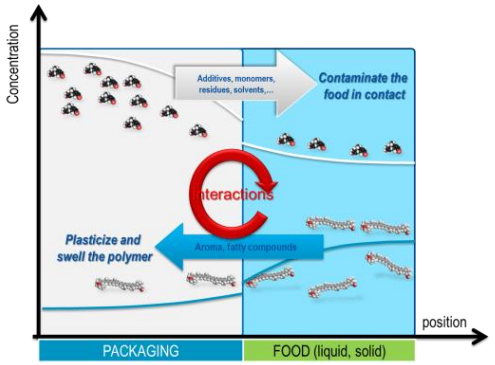


Food packaging

- Continuum mechanics simulation

Molecular modeling

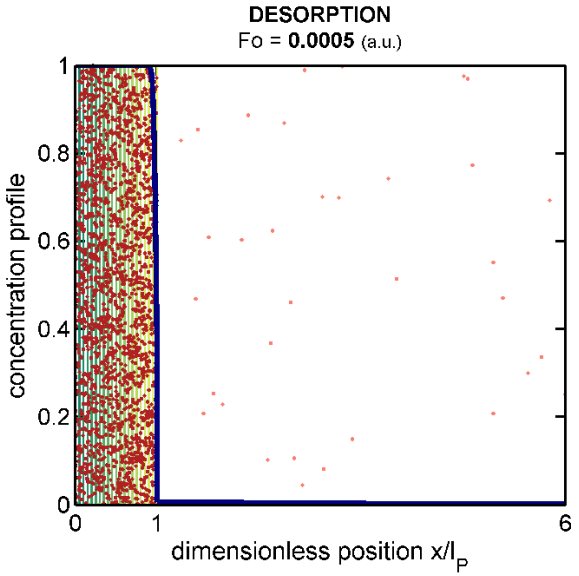
- Monte-Carlo sampling
- Molecular Dynamics simulation
- Molecular theories



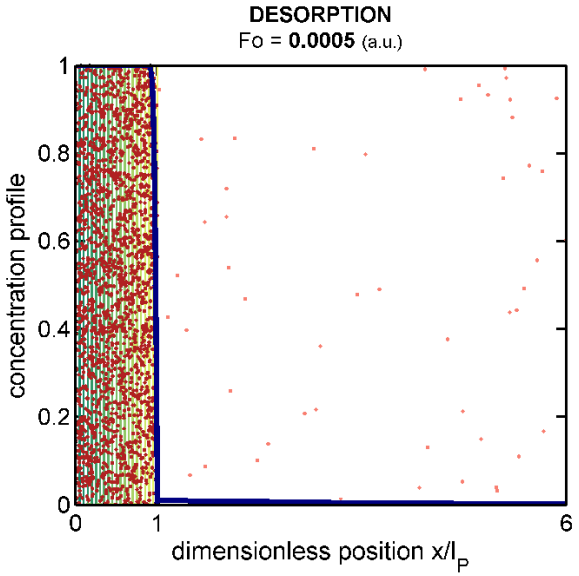
Scope of molecular modeling

supplying diffusion coefficients (D) and activity/partition coefficients (K) from molecular structures in sorption/desorption models

Higher chemical affinity for the packaging

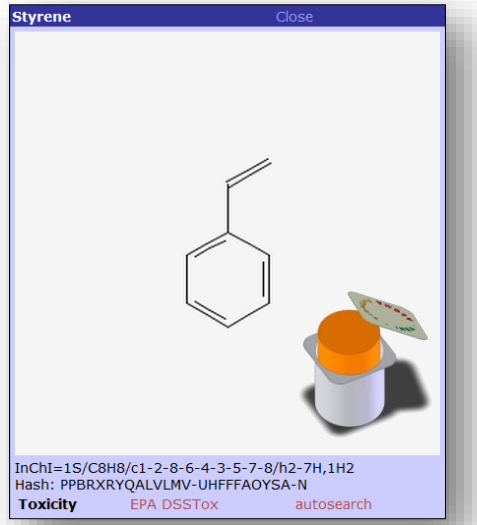


Higher chemical affinity for the food



Consumer Exposure to styrene from yogurt pots in France

6122 Households –1,930,257 Purchased units in one year

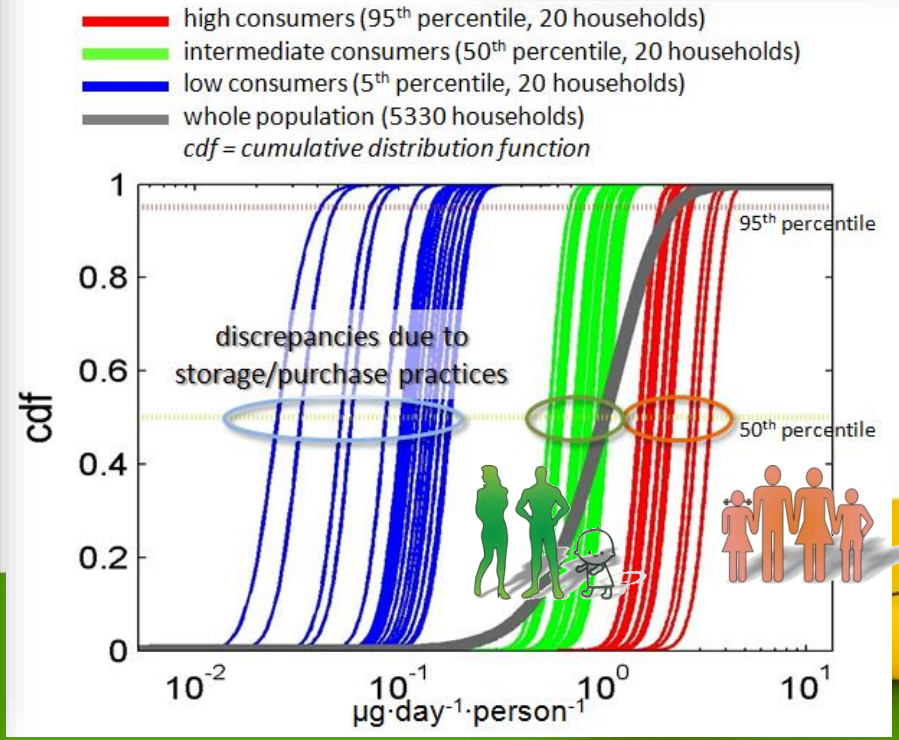


Help

Styrene

Name: Styrene (*Benzene, ethenyl-;Bulstren K-525-19;Cinnamene;Phenethylene;Phenylethene;Phenylethylene;S (Germa...)*
CAS: 100-42-5
REF: 24610
InChIKey: PPBRXRYQALVLMV-UHFFFAOYSA-N
Formula: C8H8
M: 104.15 g/mol

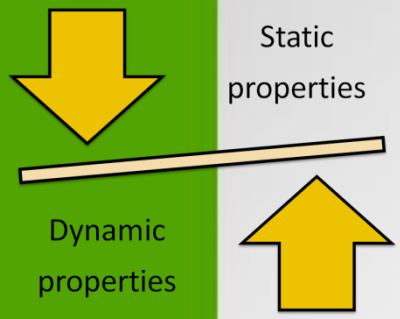
SML: 60 ppm
EFSA: Several oral studies performed: 6-month rat, 19-month dog, carcinogenicity in mice (3) and in rats (4), 3-generation reproduction and teratogenicity in rats. Mutagenicity studies positive only with activation. (RIVMdoc. 1990-05-03 (CS/PM/428), BGAdoc. 1990-07-17 (CS/PM/475), CS/PM/915). NOTA BENE: the wg wishes to establish a limit for styrene in food and asked the Commission to provide migration data. The wg of the SCF has the intention to recommend to the Commission a ban for styrene in oven ware due to unacceptably high migration.
EU Regulation: *+Positive List*
SCF opinion=undefined



Vitrac and Leblanc, 2007

cdf = cumulative density function

CONTENT

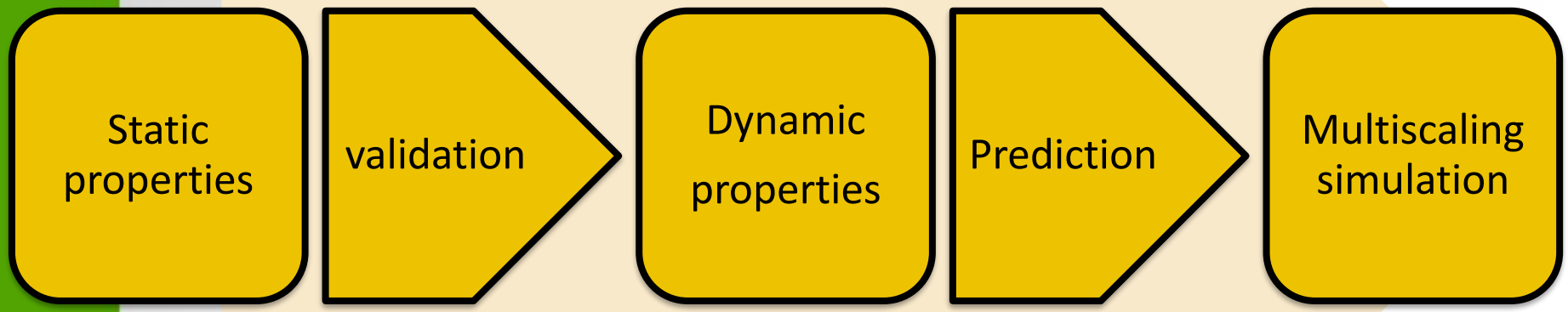


Some concepts and questions: computational-force microscope, multi-scale modeling

Case study: molecular diffusion

Case study: Chemical potentials

Extensions to non-thermal noise

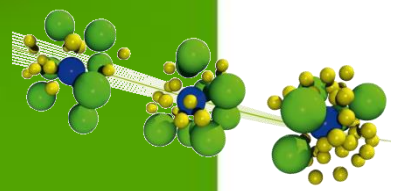


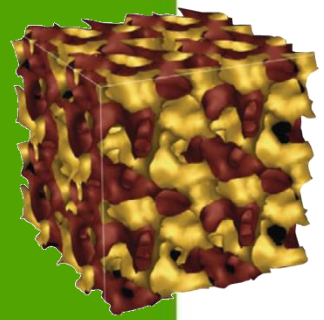
MODELISATION MOLECULAIRE ET SUPRAMOLECULAIRE

SOME CONCEPTS AND SOME QUESTIONS

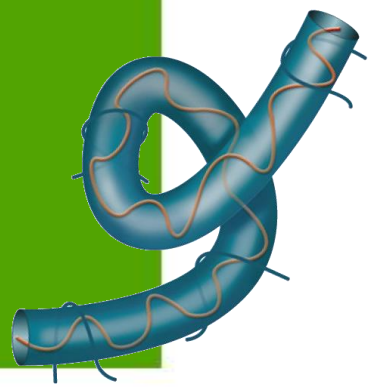
INRA SCIENCE & IMPACT

A short story



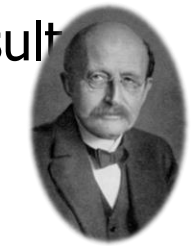


A computer simulation of a microemulsion showing a continuous fine network of oil and water phases



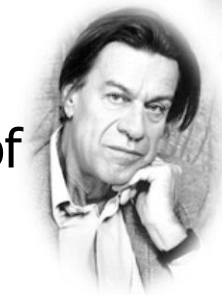
Isaac Newton's Principia (1687): physical modeling of the world (calculus: differential equation with time and space)

Ludvig Boltzmann (<1900): entropy as a result of stochastic collisions



Max Planck's Quantum theory (1900)

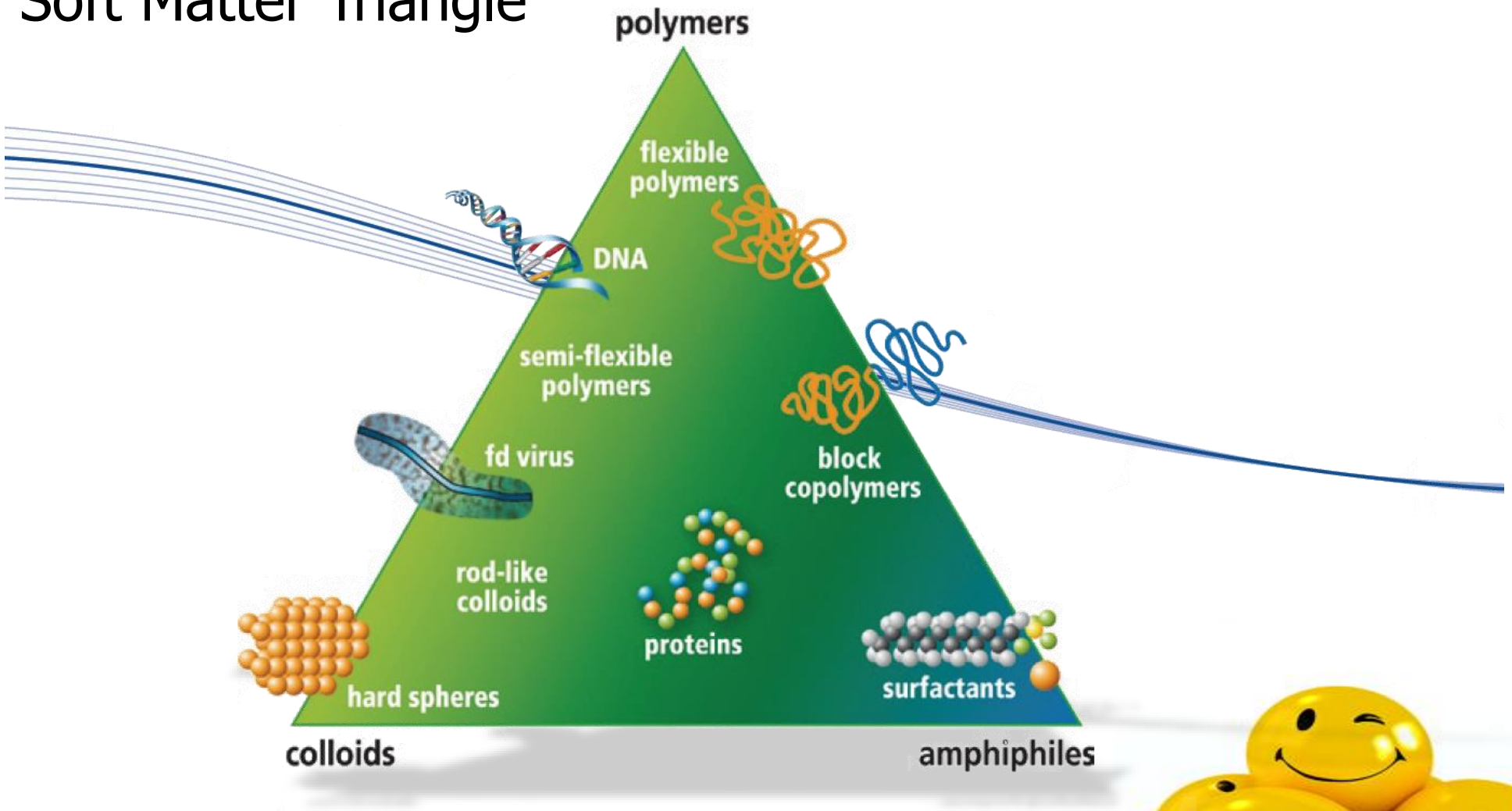
Paul Flory (Nobel Prize in chemistry, 1974): excluded volume, theta point, solution theory



Pierre-Gilles de Gennes founded the concept of "soft matter" (Nobel Prize in physics, 1991)

Soft matter self-organizes into mesoscopic physical structures that are much larger than the microscopic scale (the arrangement of atoms and molecules), and that are much smaller than the macroscopic (overall) scale of the material.

Soft Matter Triangle



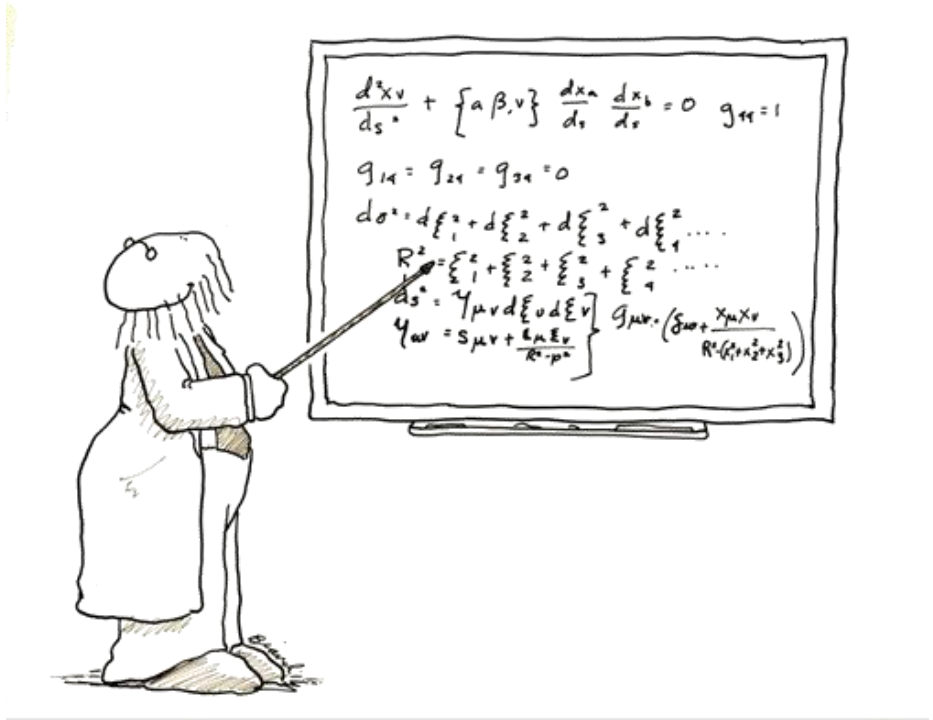
The "soft-matter triangle" encompasses a broad, continuous range of materials, from colloidal suspensions of particles to flexible long-chain polymer molecules and amphiphilic, or soap-like, systems. Many biological systems such as proteins, DNA and viruses have the characteristics of all these soft-matter types

Molecular modeling?

Statistical Mechanics?

Statistical Physics?

Statistical Thermodynamics?



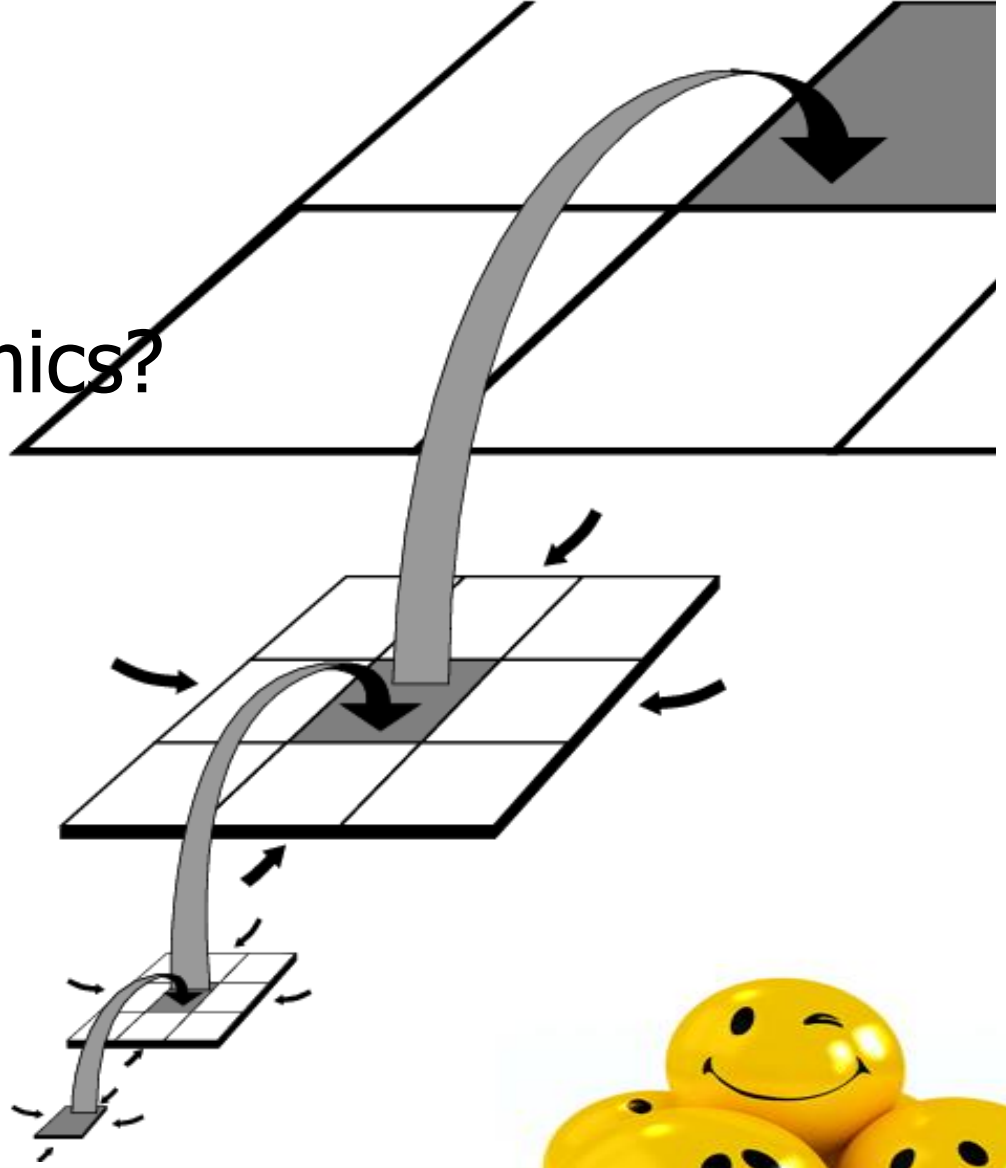
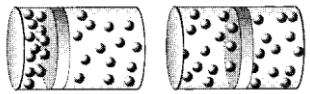
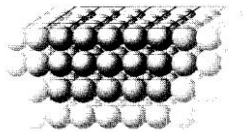
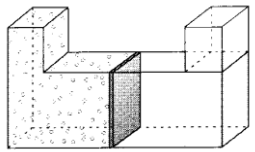
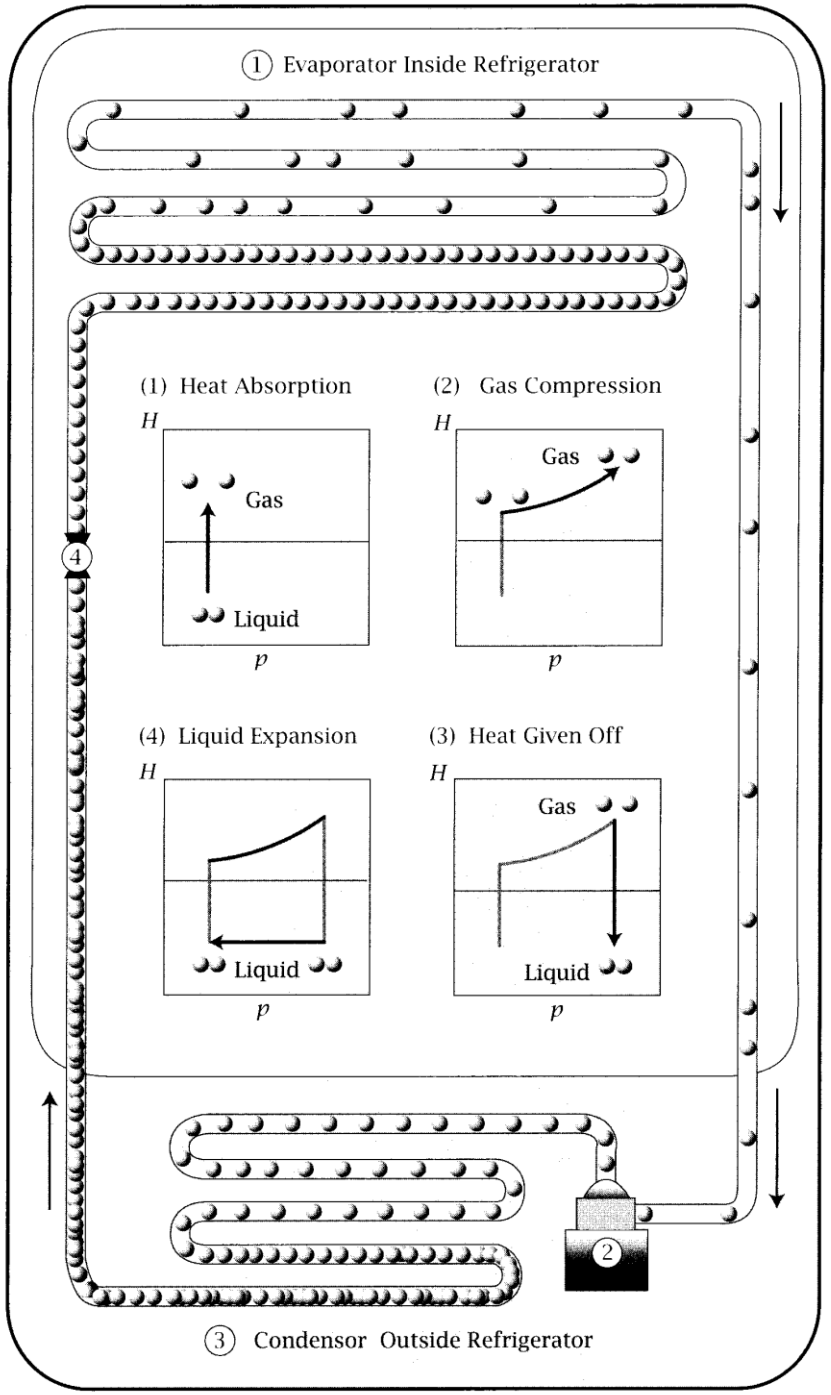


Figure 14.9 The thermodynamic cycle of a refrigerator. The spheres indicate the relative densities of the refrigerant molecules as they move through the system. There are four steps in the cycle. (1) Heat is absorbed from inside the refrigerator compartment to boil the working fluid. (2) The fluid is compressed and pumped. (3) Heat is dumped outside. The gas refrigerant re-condenses into a liquid. (4) The fluid is expanded until it is ready to boil.

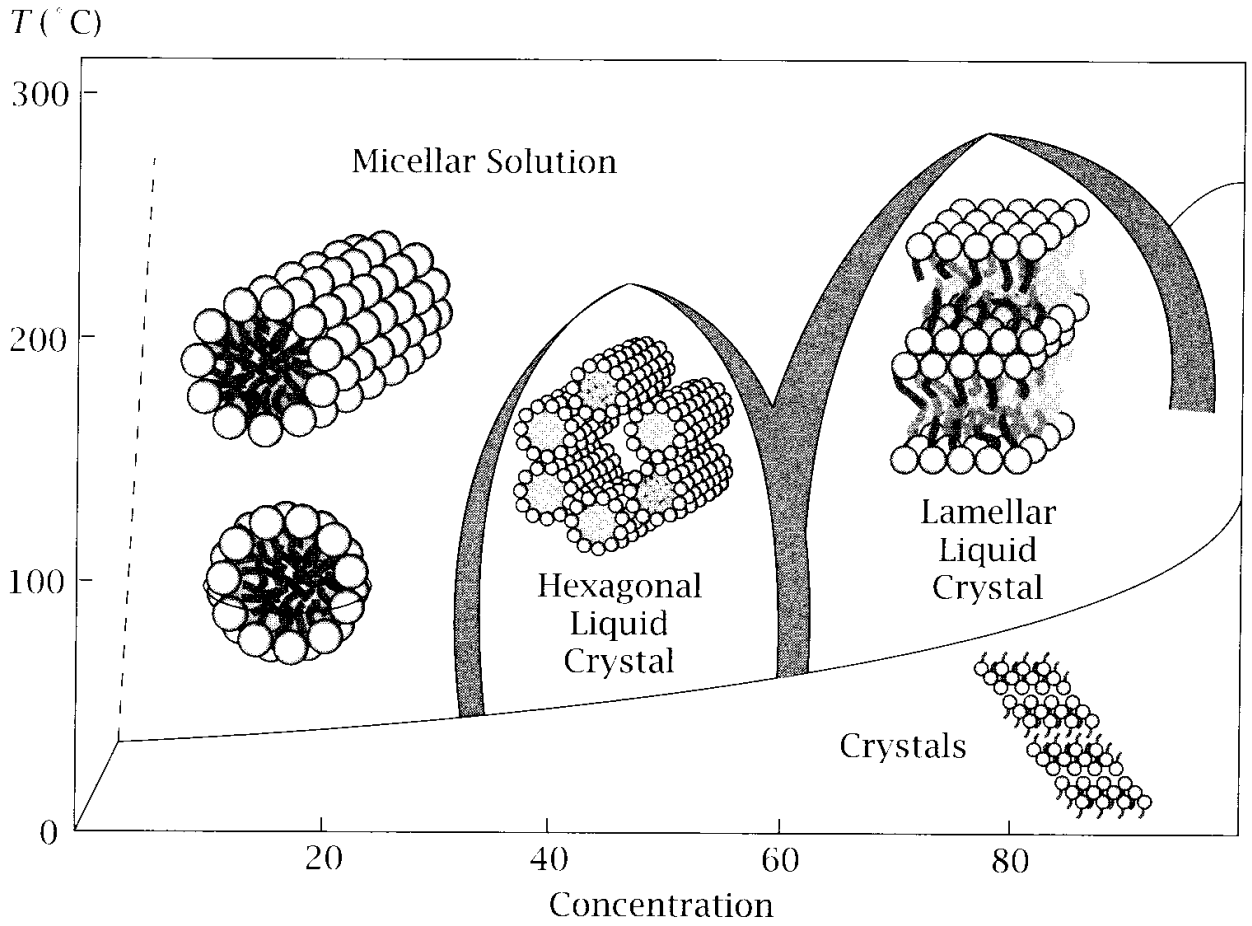








A molecular fridge



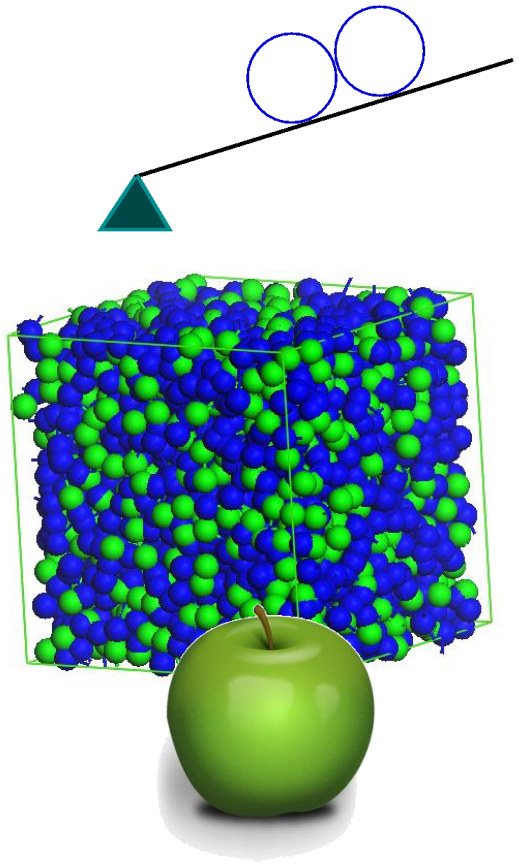
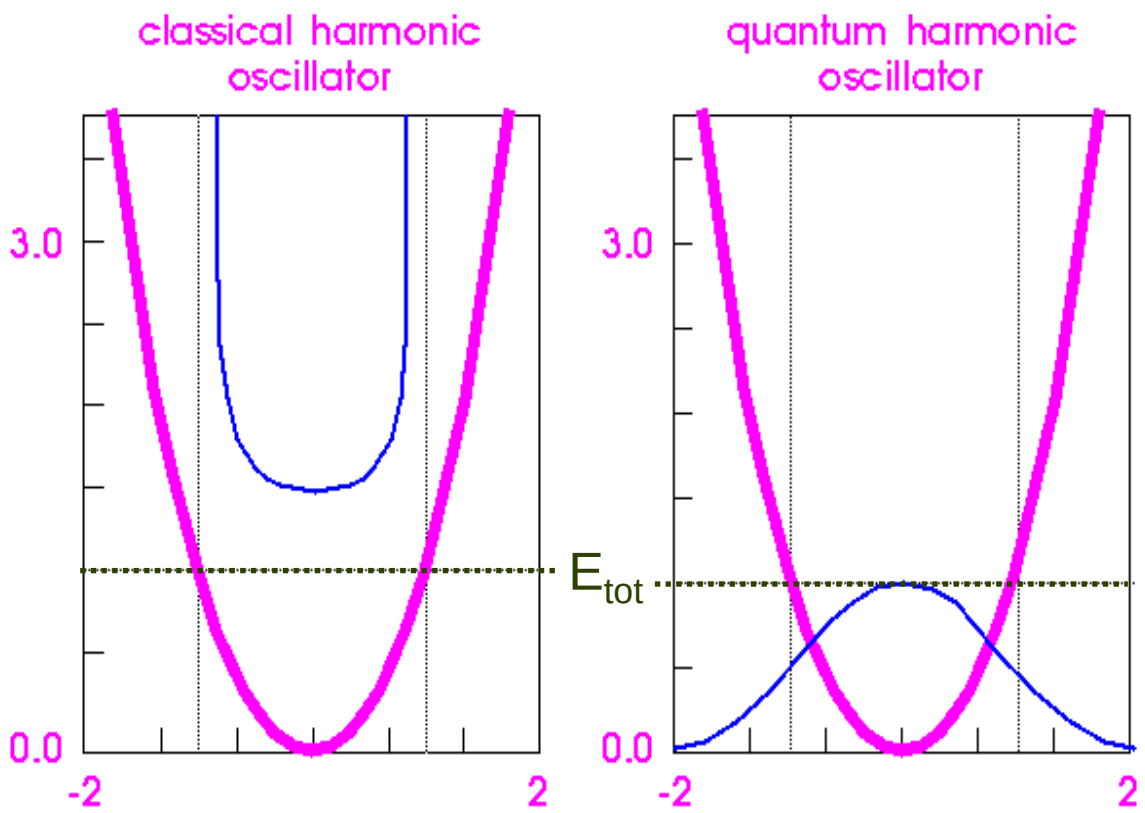
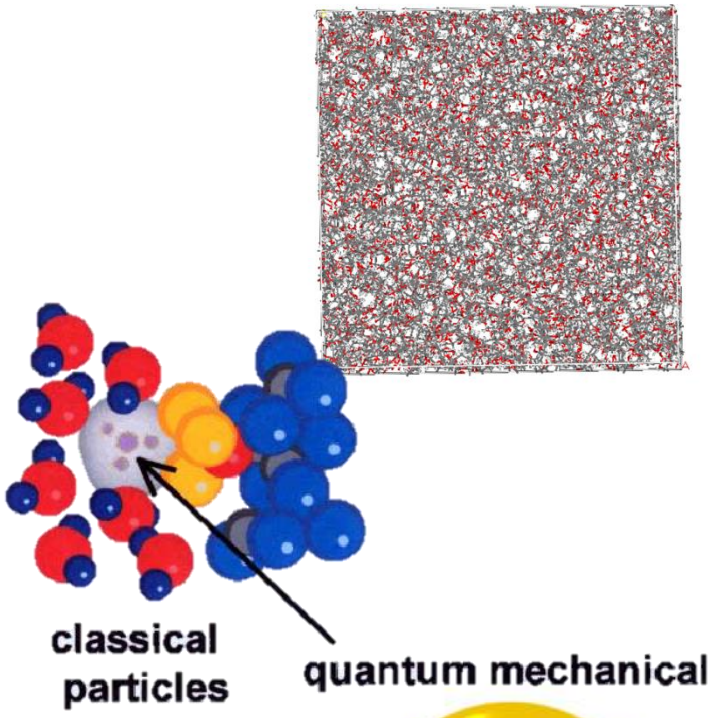


Figure 25.21 Phase diagram for surfactant molecules. Surfactants can form micelles that are spheres, cylinders, or planar bilayers, with increasing surfactant concentration. Critical micelle concentration (– – –). Source: HT Davis, *Statistical Mechanics of Phases, Interfaces, and Thin Films*, VCH, New York, 1996.

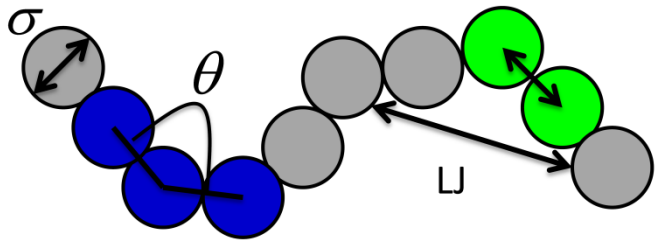
Q: what is the force?
A: potential

Classical or quantum potential?





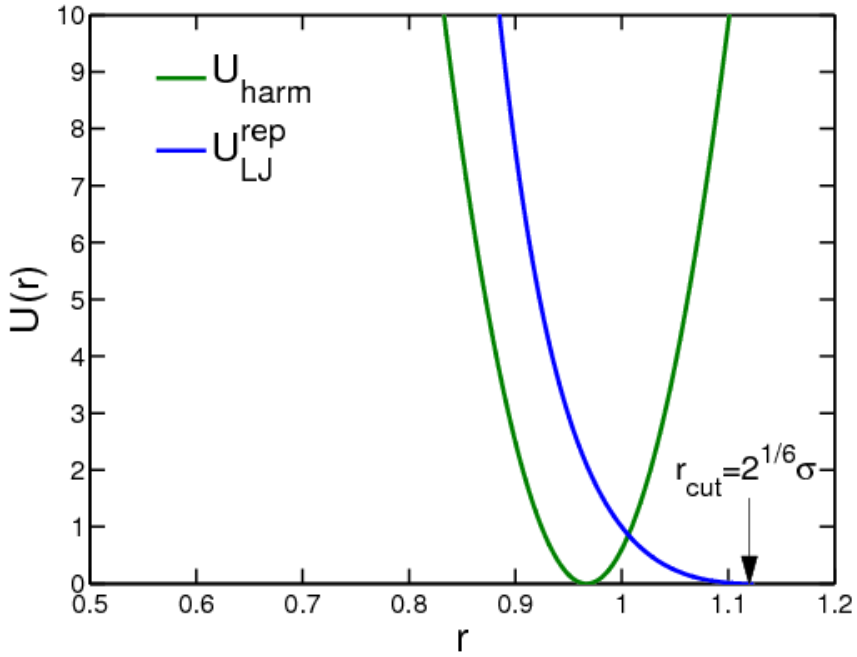
Example of simple potentials



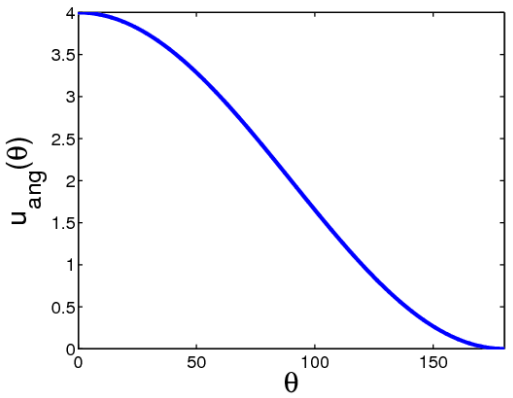
$$U_{\mathrm{LJ}} = 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right]$$

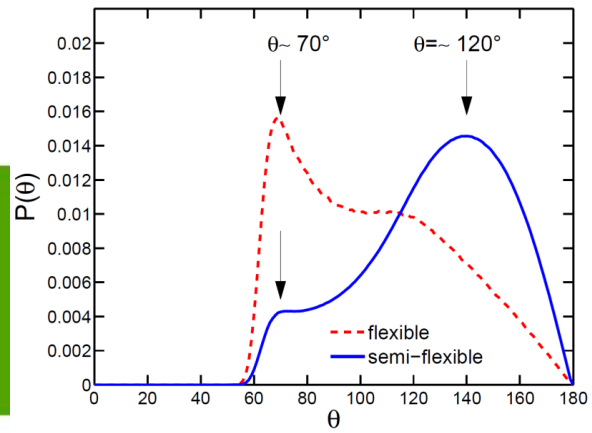
$$U_{\mathrm{harm}} = \frac{k}{2}(l - l_0)^2$$

l_0	0.967
γ	0.1
ρ	0.85

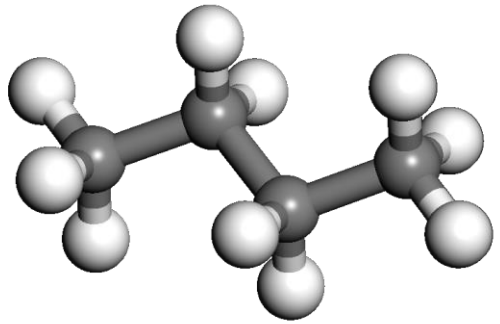


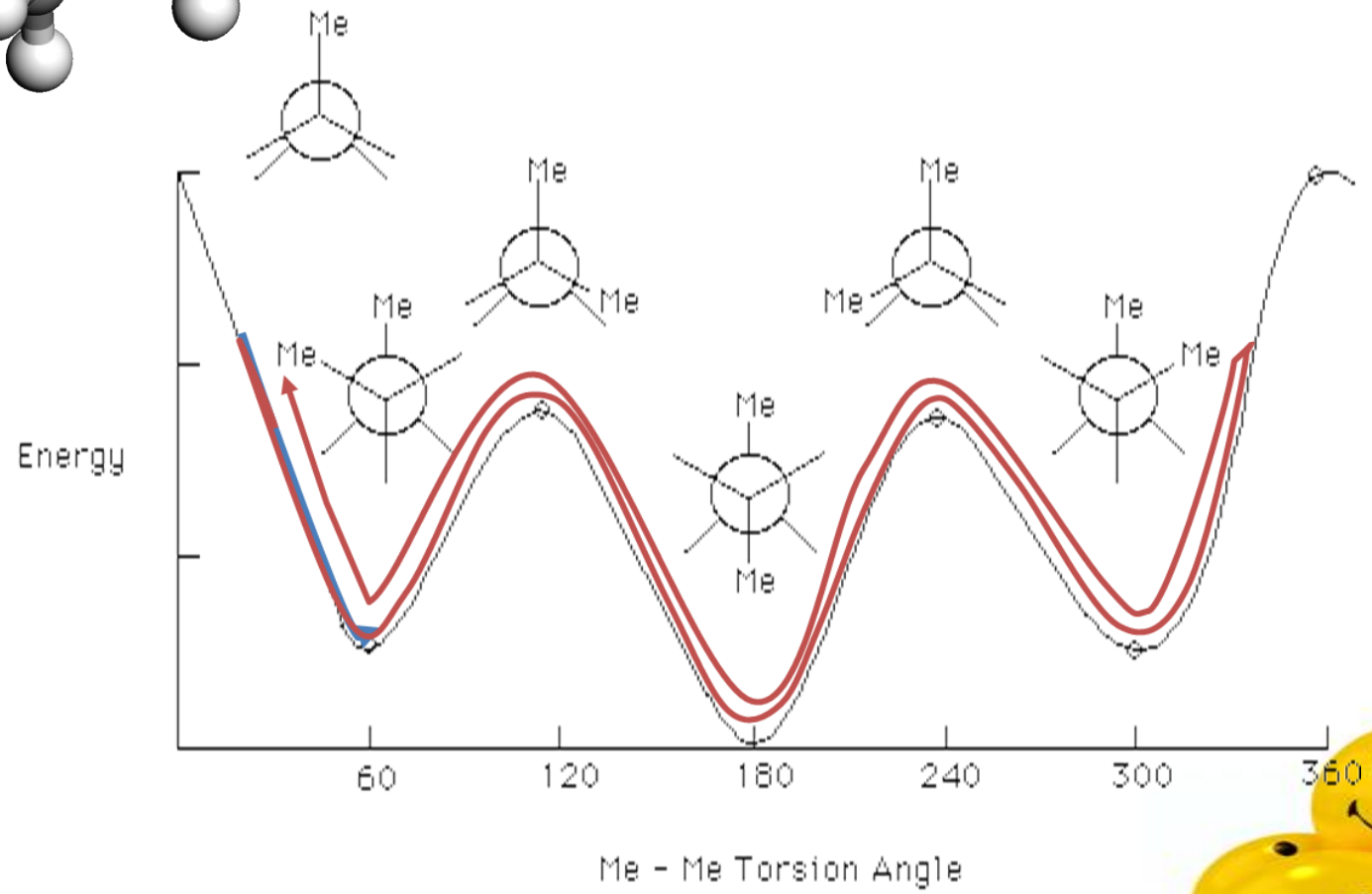
$$U_{ang} = B(1+\cos(\theta)), B = 2$$





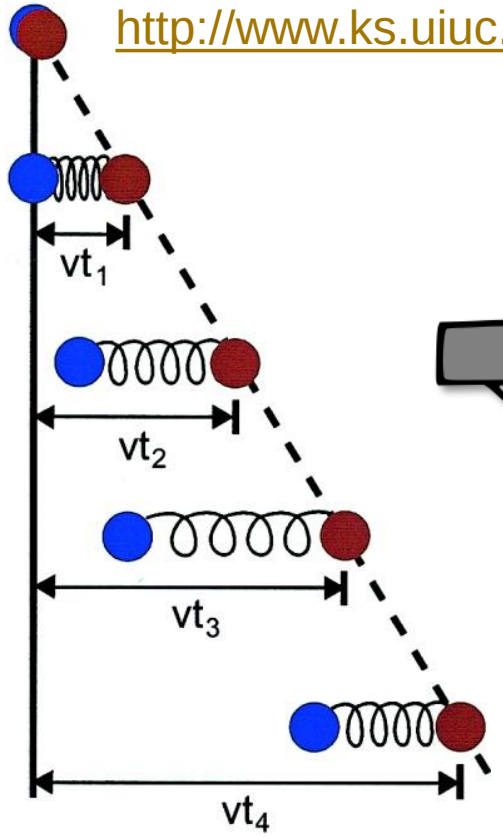
POTENTIALS

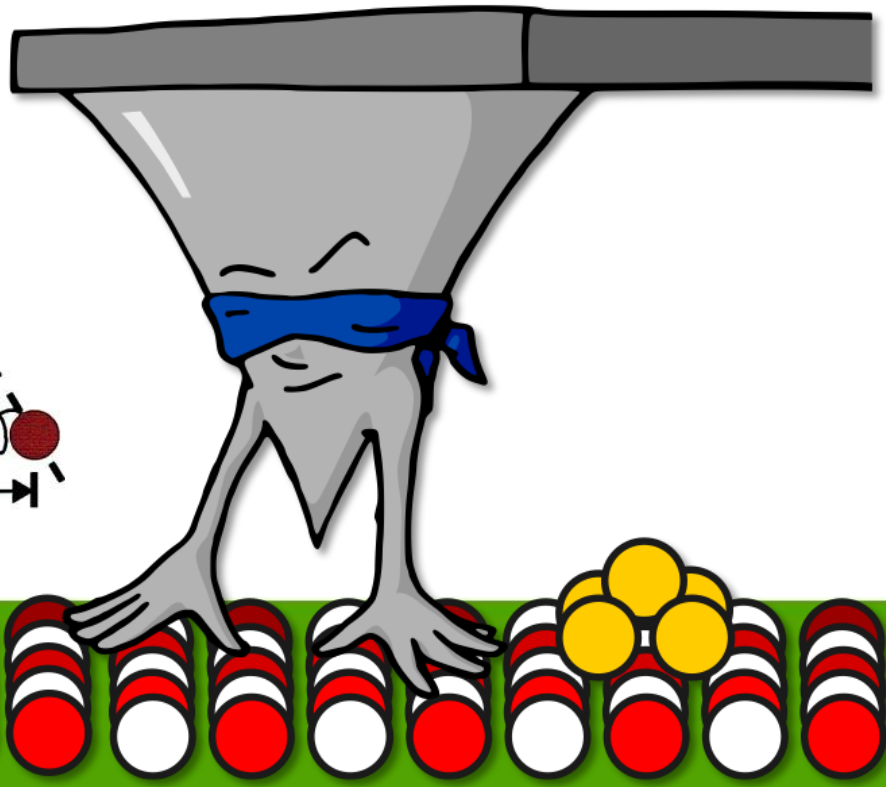


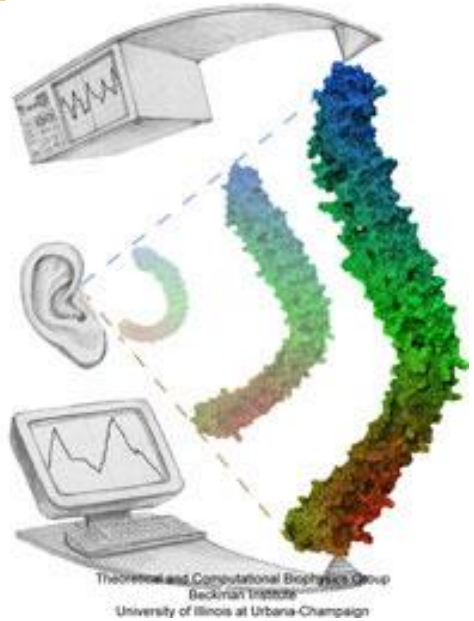

Me
Me
Me
Me
Me
Me
Me
Me
Me
Me
Me
Energy
60
120
180
240
300
360
Me - Me Torsion Angle

Molecular modeling = computational force microscope?

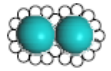
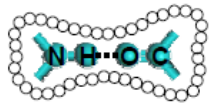
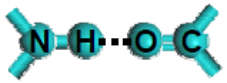
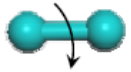
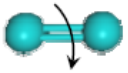
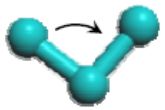
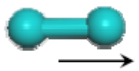
http://www.ks.uiuc.edu/Research/smd_imd/cfm/cfmreview.html







ENERGY RANGE

Interaction	Energy (kcal/mol)	
van der Waals in water	- 0.1	
van der Waals in vacuum	- 0.3	
Hydrogen bond in water	- 1.0	
Hydrogen bond in vacuum	- 5.0	
Torsion barrier about single bond C–C	+3.0	
Torsion barrier about double bond C=C	+20	
Barrier to breaking a bond	+100	
Energy to change a bond angle by 10°	+2.0	
Energy to stretch a bond length by 0.1A	+2.5	
Thermal energy at 300K	+0.6	*k*T

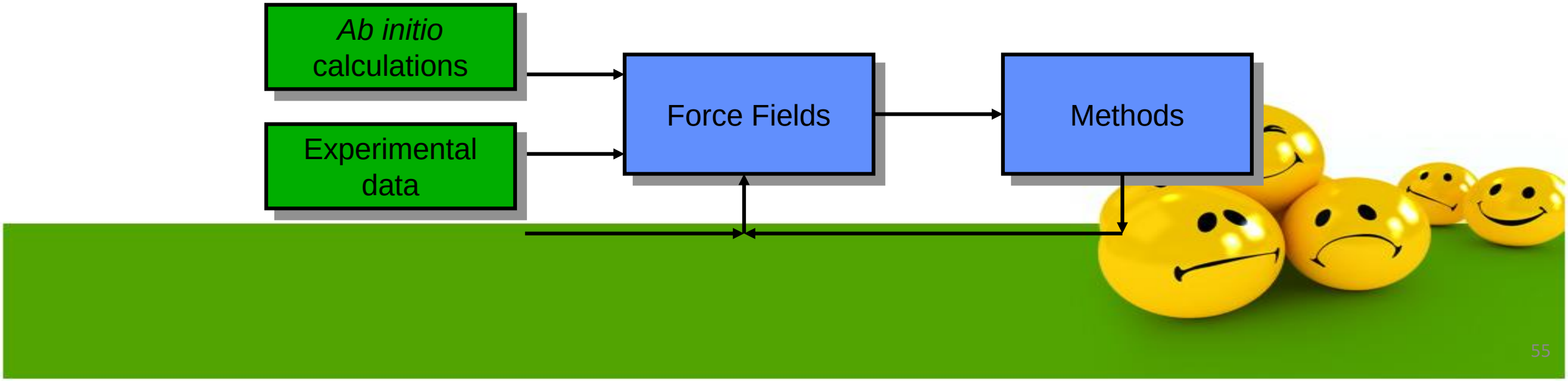
$$U = \underbrace{U_b + U_\theta}_{U_{bonded}} + \underbrace{U_{vdW} + U_{elec}}_{U_{non-bonded}}$$

$$-\frac{dU}{dR} = m\frac{d^2R}{dt^2}$$

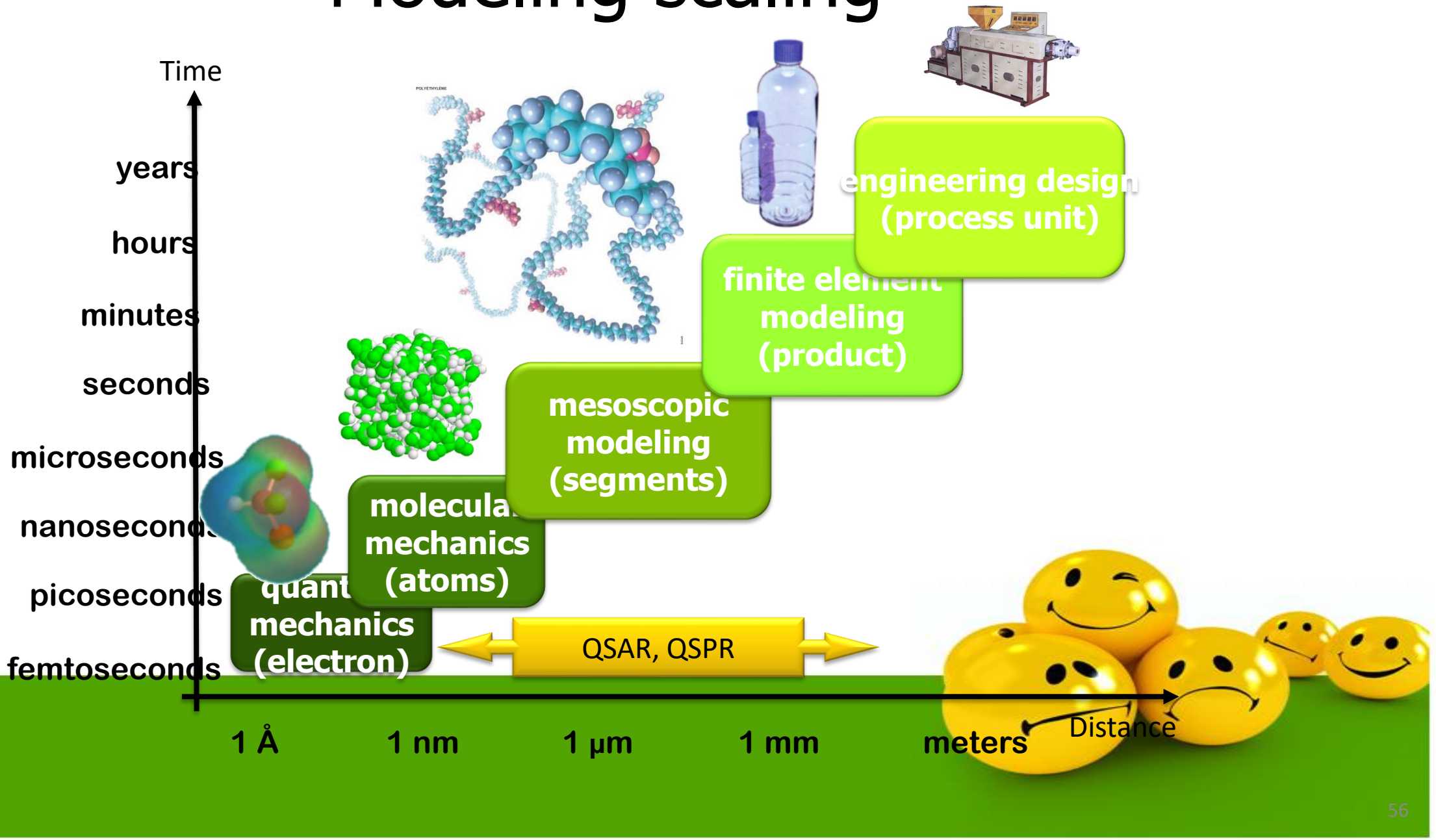
Newton's equation of motion

How to derive forcefields?

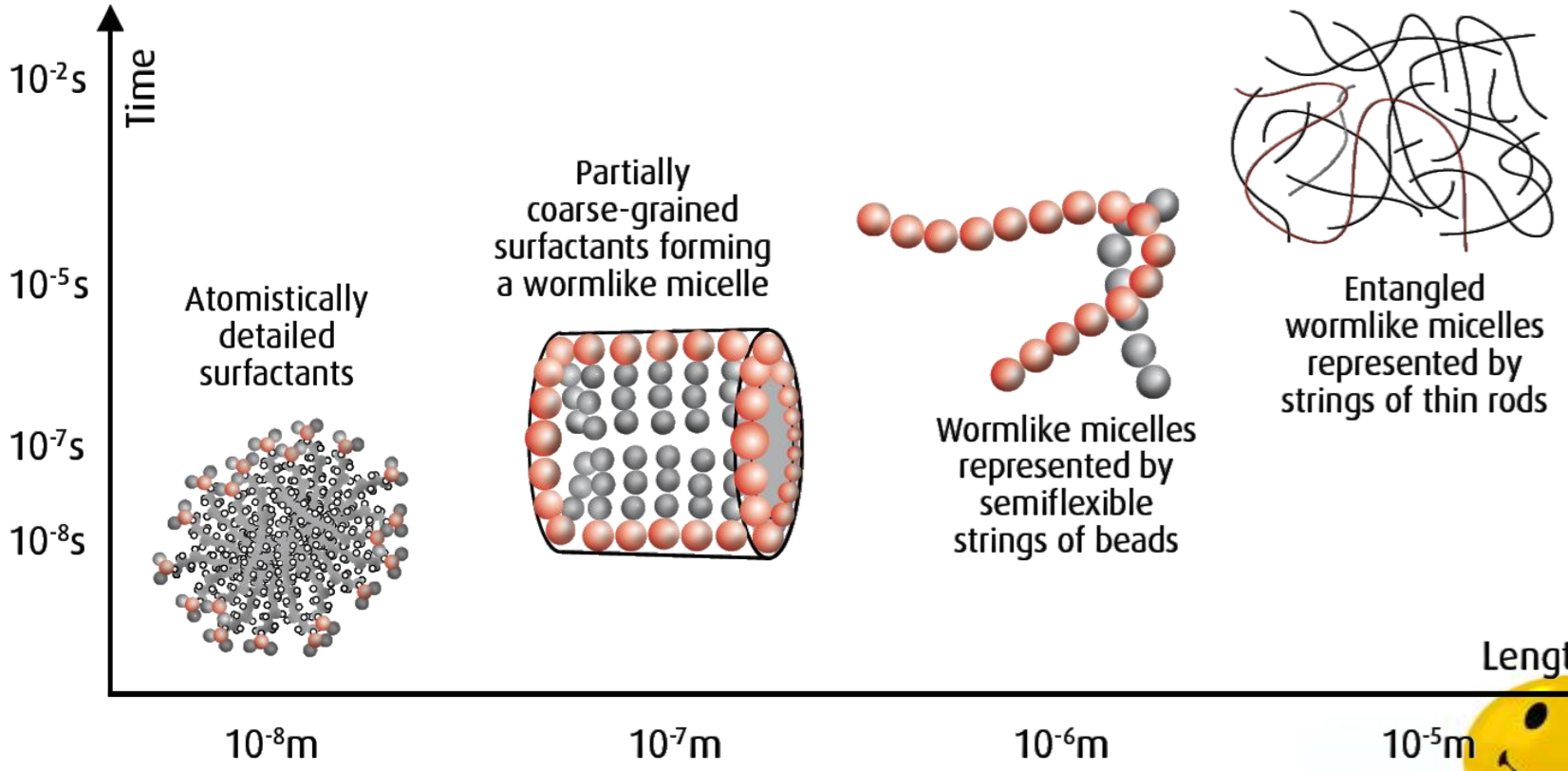
- Force field development dominated by requirements for drug design (25-35°C, <5 bar)
- Industrial processing requires force fields valid over wide ranges of temperature and density/pressure: vapor-liquid equilibrium, supercritical fluids,….
- Development of such force fields is rapidly growing in wake of new methods developments: GEMC, Gibbs-Duhem, ...



Modeling scaling



Worm-like micelles



LMOPS
Laboratoire Matériaux Organiques à Propriétés Spécifiques

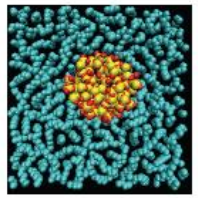
Molecular Dynamics Example of Limitations

Low volume fraction systems

Target volume fraction of Silica ~ 4.5%

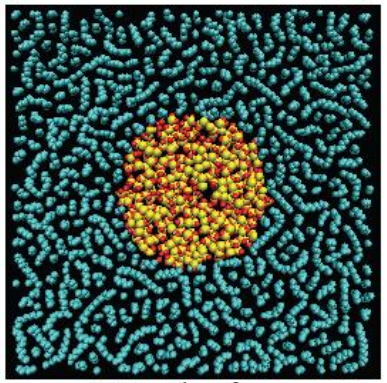
Radii of inclusions, R_n, of 15, 30 & 60 Å

~68 Å



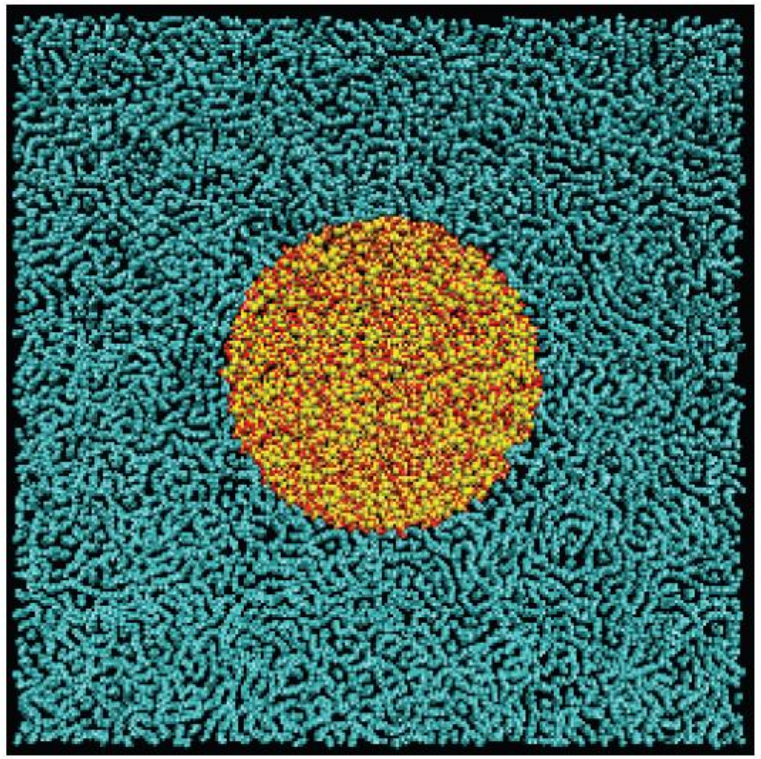
10 chains
R_n=15 Å
10926 atoms

~136 Å



80 chains
R_n=30 Å
87856 atoms

~272 Å



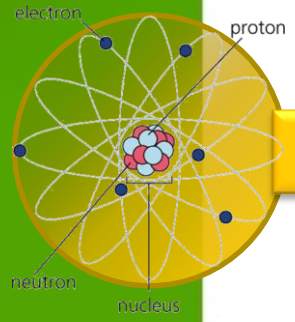
640 chains, R_n=60 Å
705181 atoms!

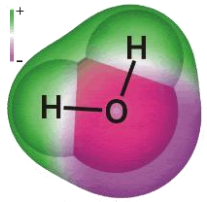
Preparation and relaxation at 100 K (< T_g)

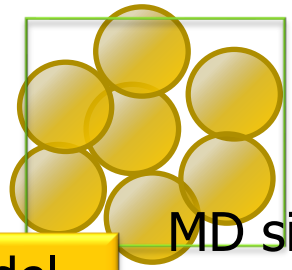
Pressure of 5000 bars applied to compensate

neglect of attractive interactions.

COARSE-GRAINING PROCESS





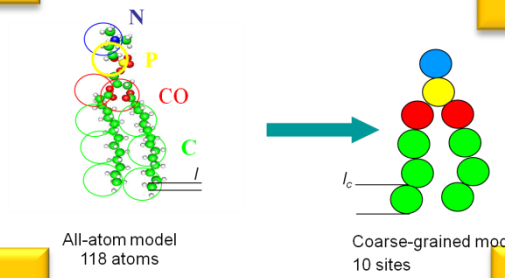


All-atomic model

MD simulation

Full information
(but limited scale)

Coarse-graining –
simplified model

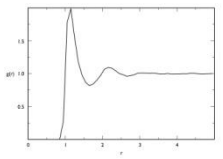


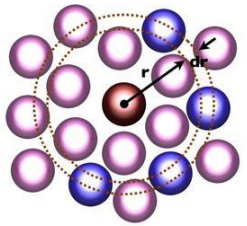
RDFs for selected
degrees of freedom

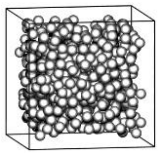
Reconstruct potentials
(inverse Monte Carlo)

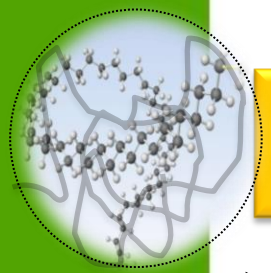
Effective potentials
for selected sites

Increase
scale



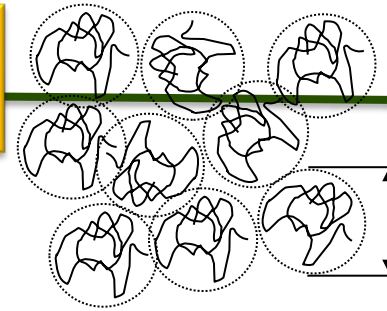






100 nm

Effective
potentials

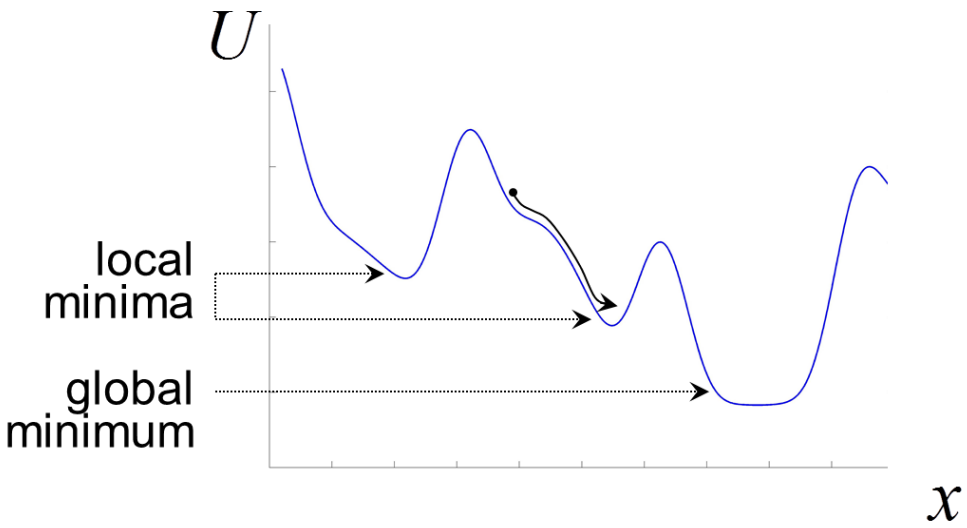


Properties on a larger
length/time scale

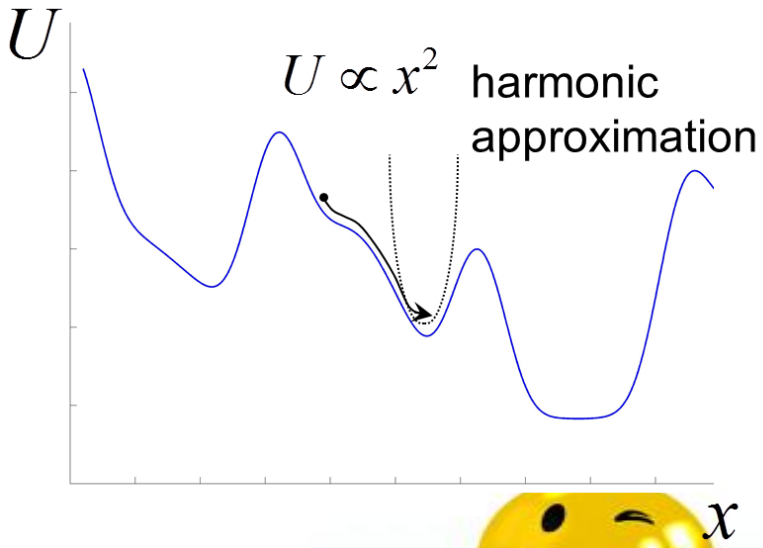
$L \sim N^{1/2} b$

How to move on energy surfaces?

MINIMIZATION

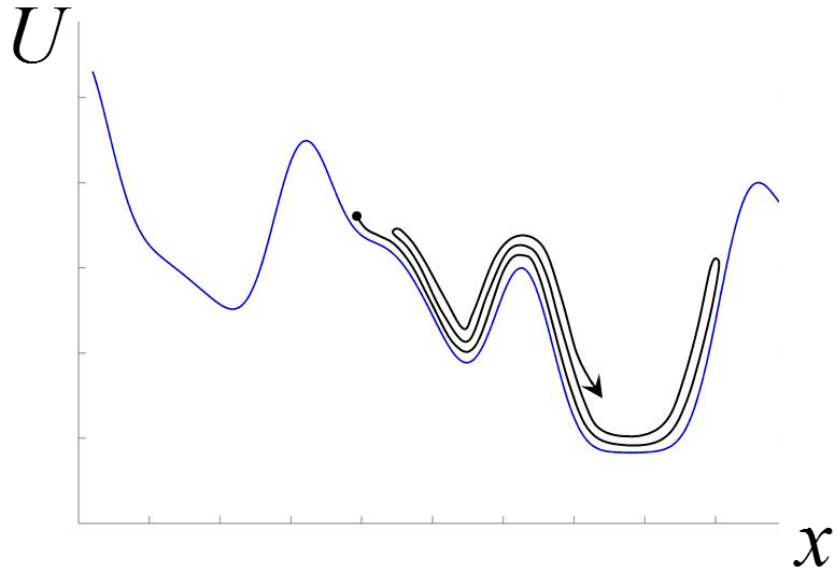


NORMAL MODE ANALYSIS

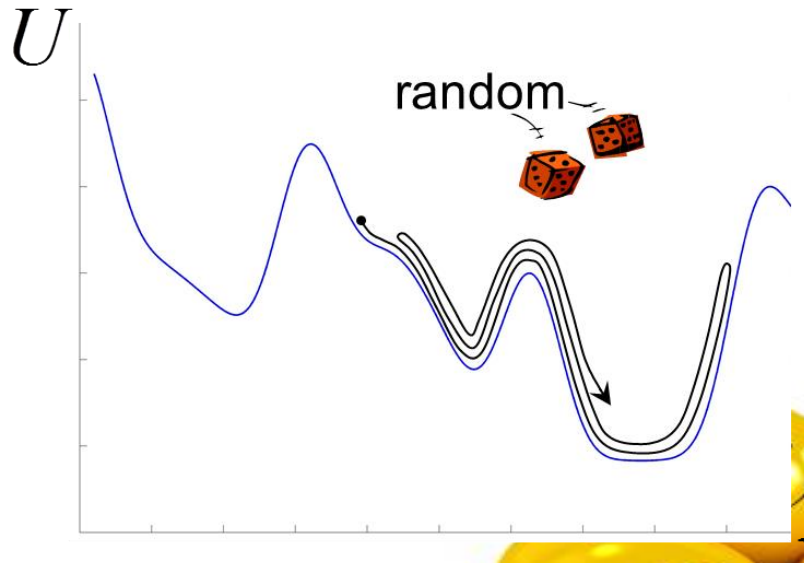


How to move on energy surfaces?

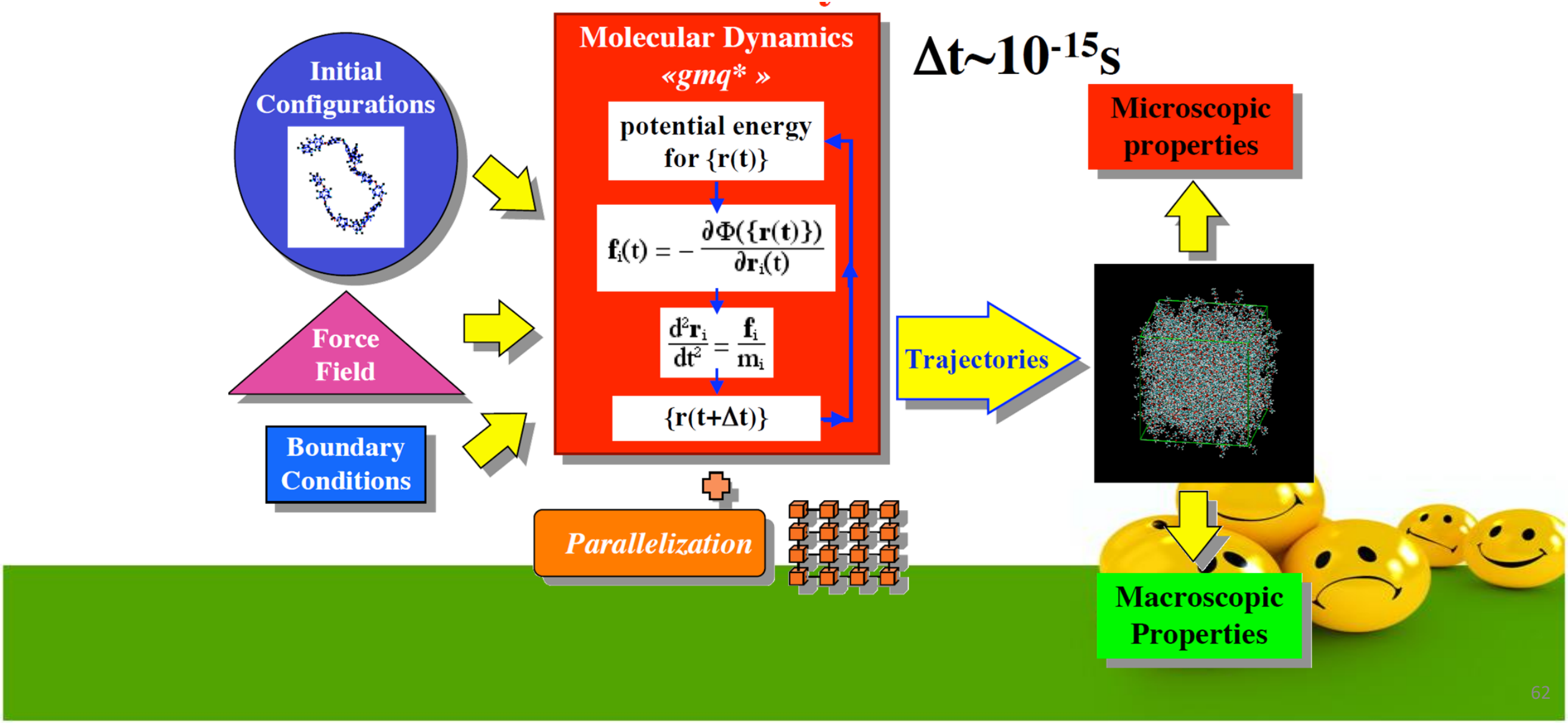
MOLECULAR DYNAMICS



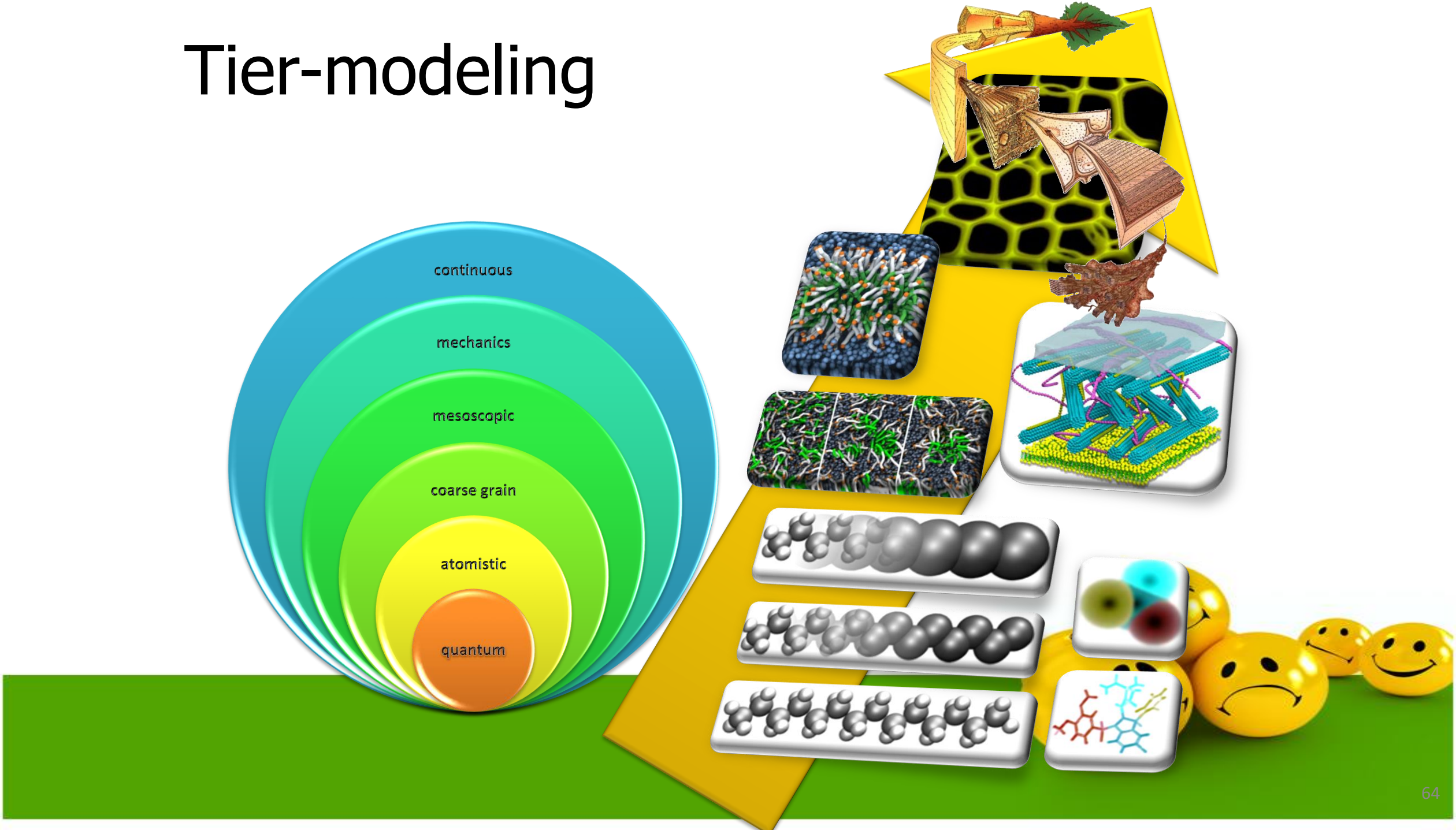
MONTE-CARLO (MC)



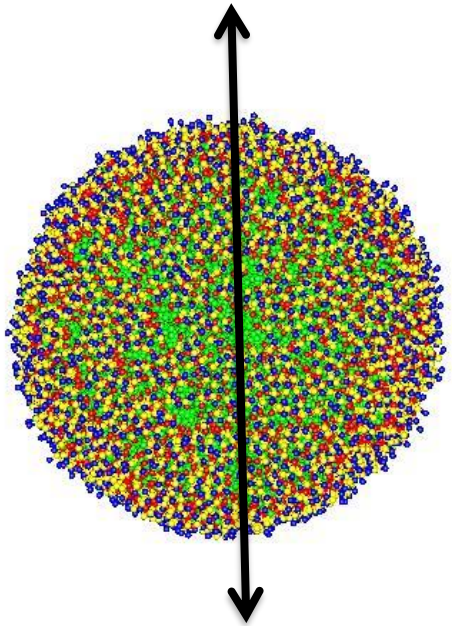
Molecular dynamics



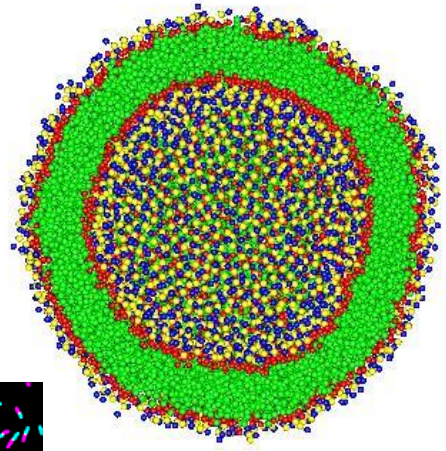
Tier-modeling

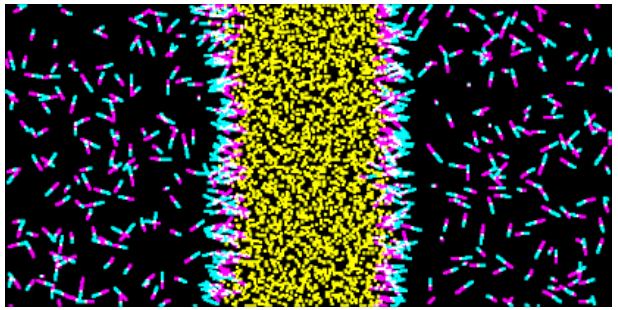


Vesicle formation



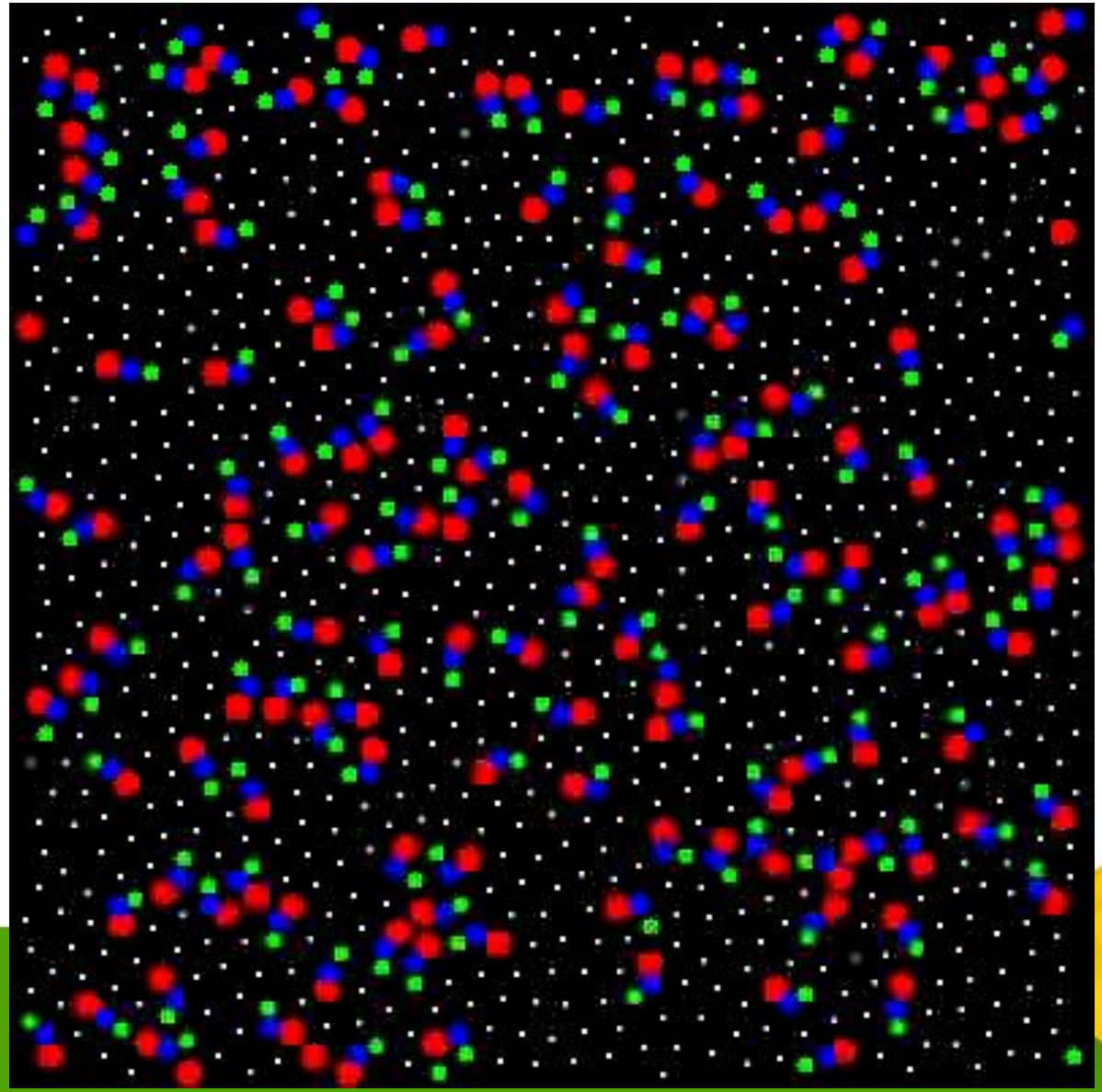
325x325 Å, 3592 lipids





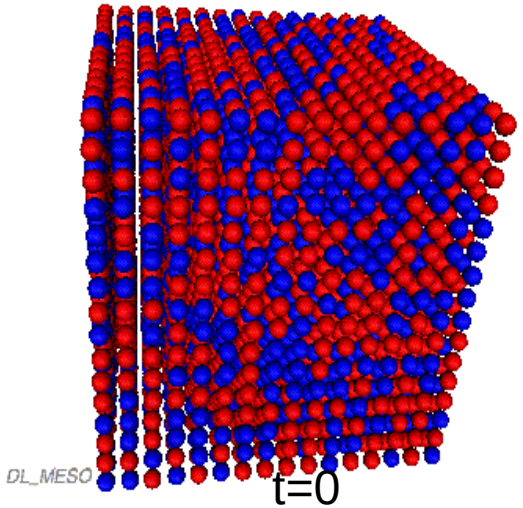
Credits: Alexander Lyubartsev (Univ. Amsterdam)

Micelle formation (2D)

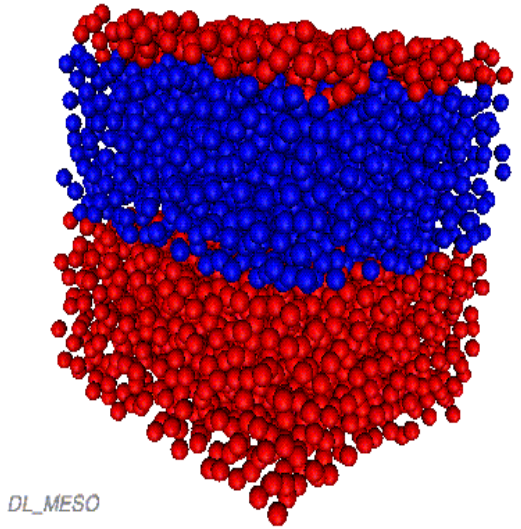


Phase separation

number percent of blue balls is larger than 27



t=0



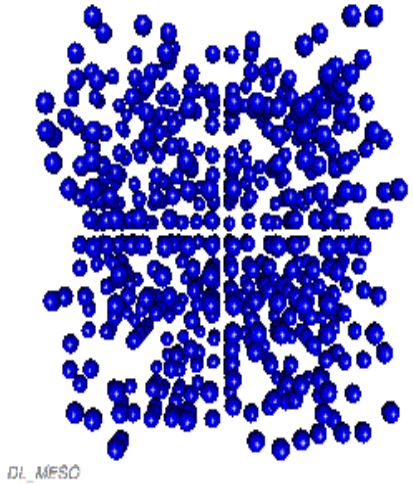
t=0

t=9500

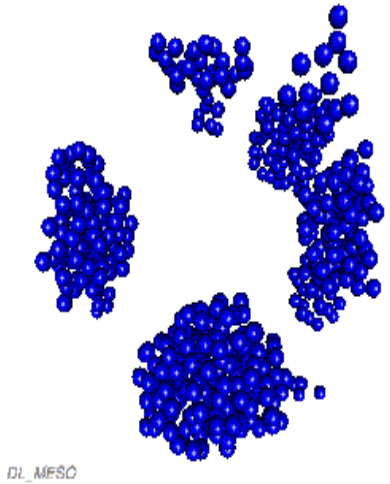
blue beads 45%

4000 balls at 10×10×10 volume

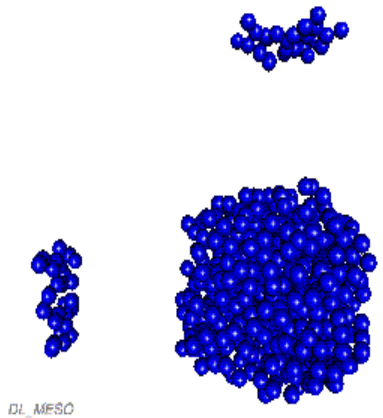
Phase separation: morphology



t=0



t=9500



t=19500

blue balls 15%

4000 balls at 10×10×10 volume

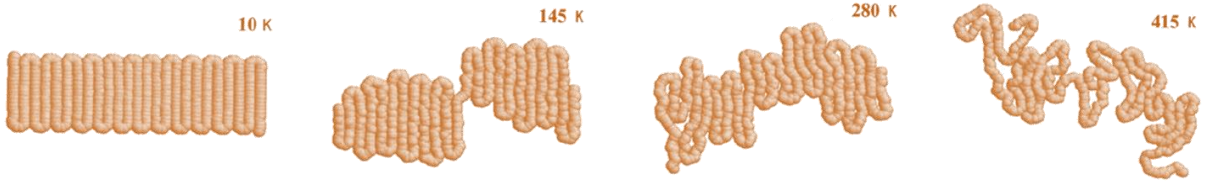
Melting / Crystalization

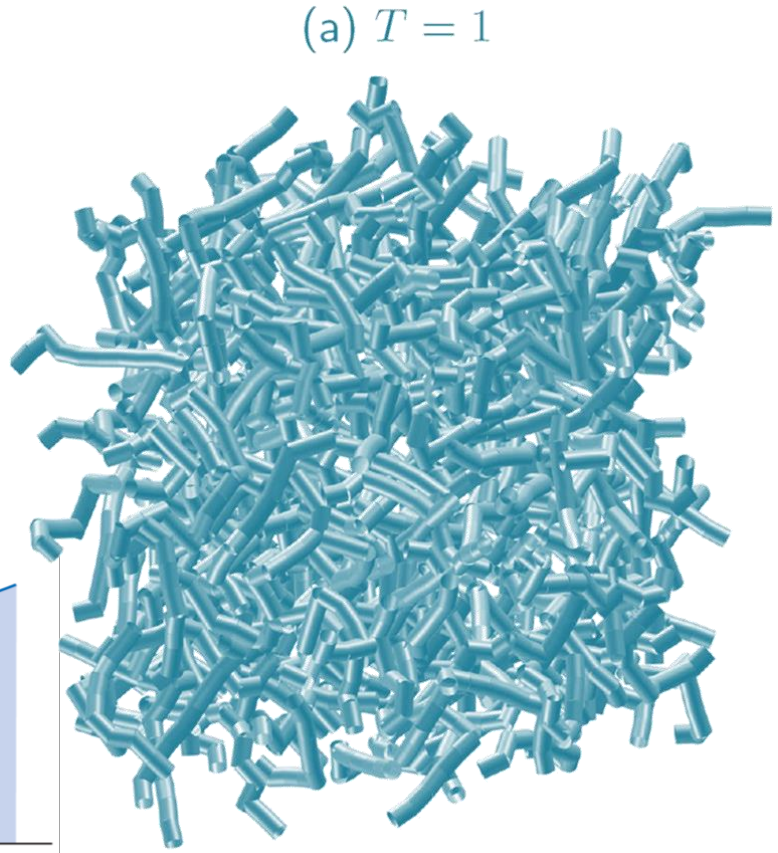
Effect of

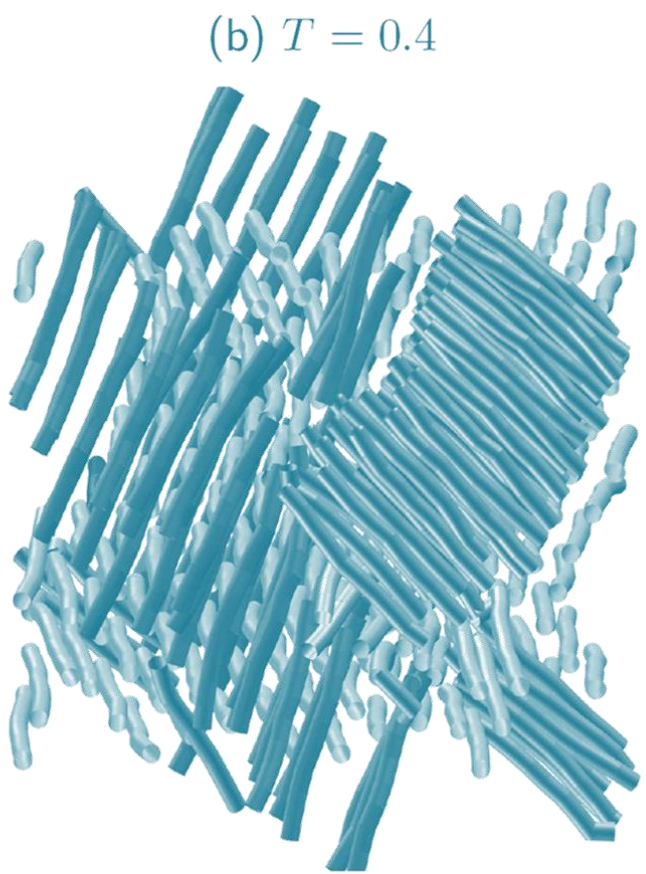
Yamamoto

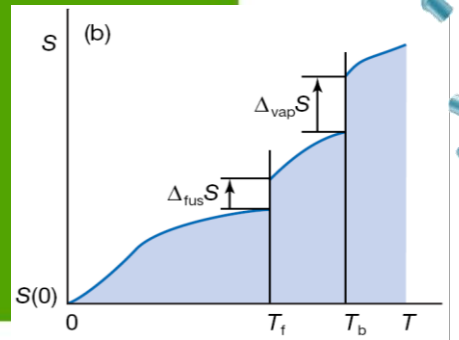
Effect co

Vettorel et

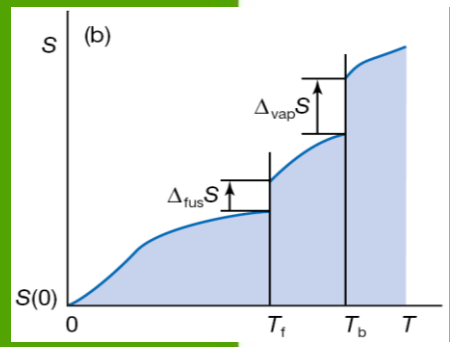


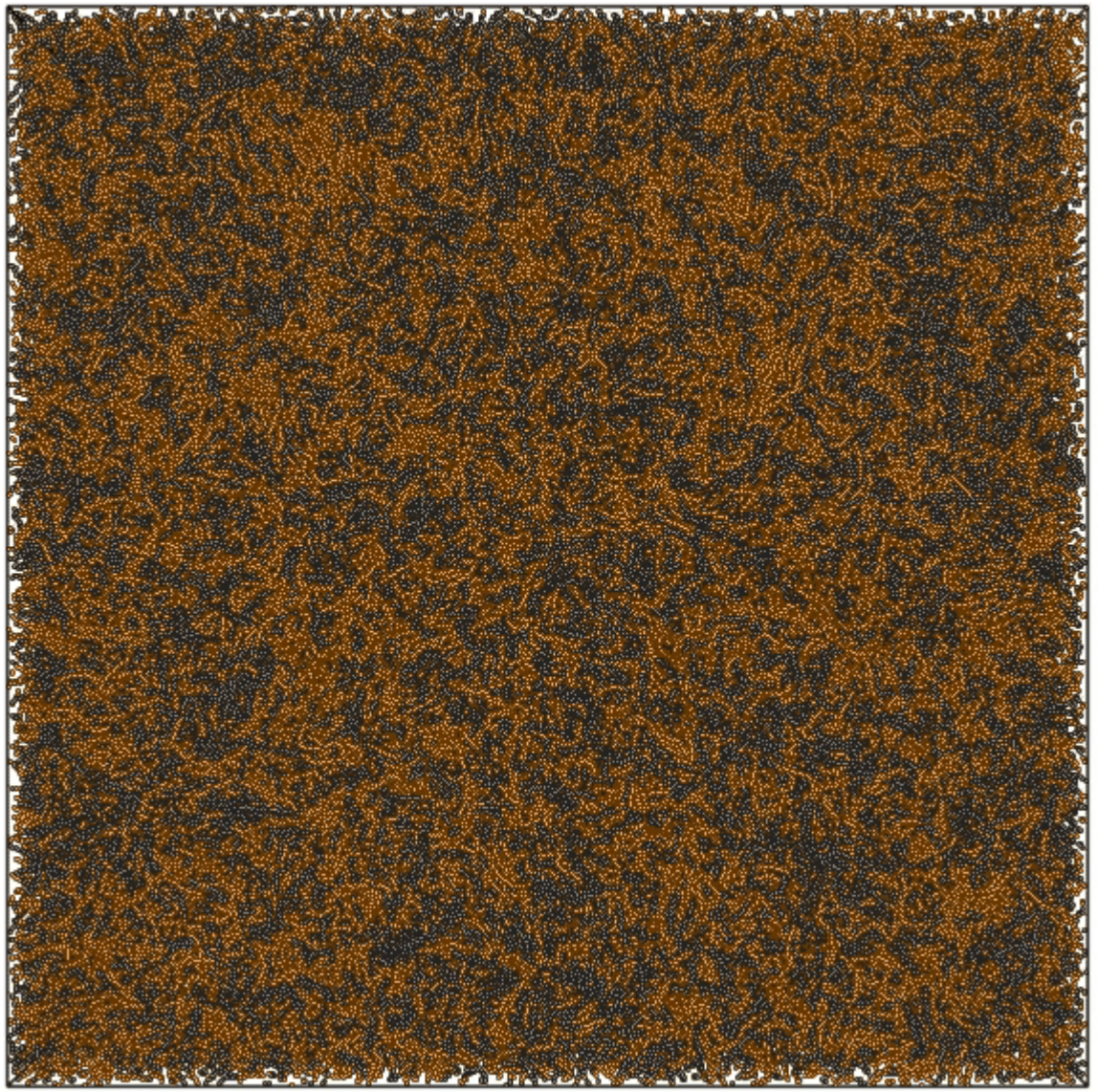




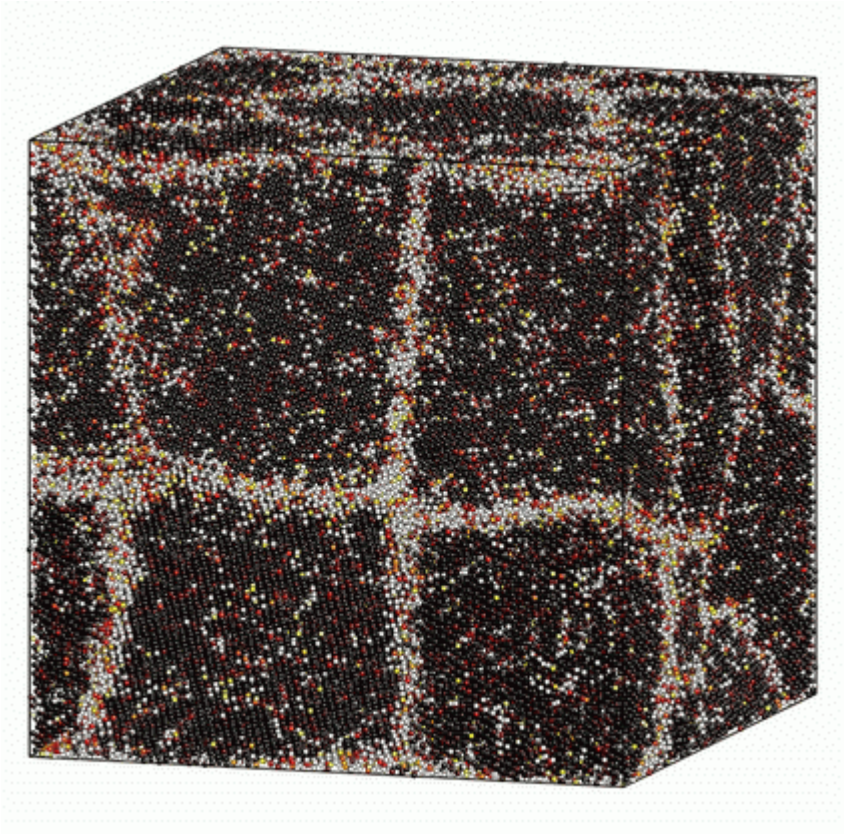


Crystallization PE (45 ns)



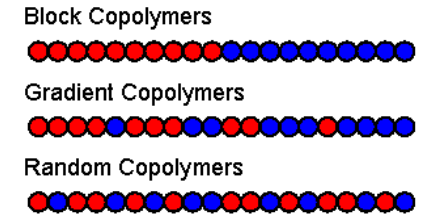


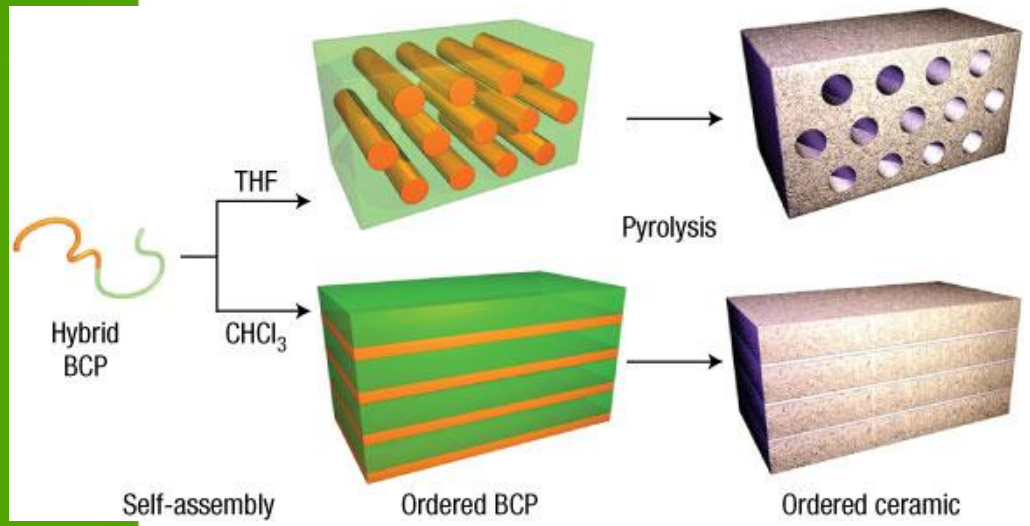
Metling Metals

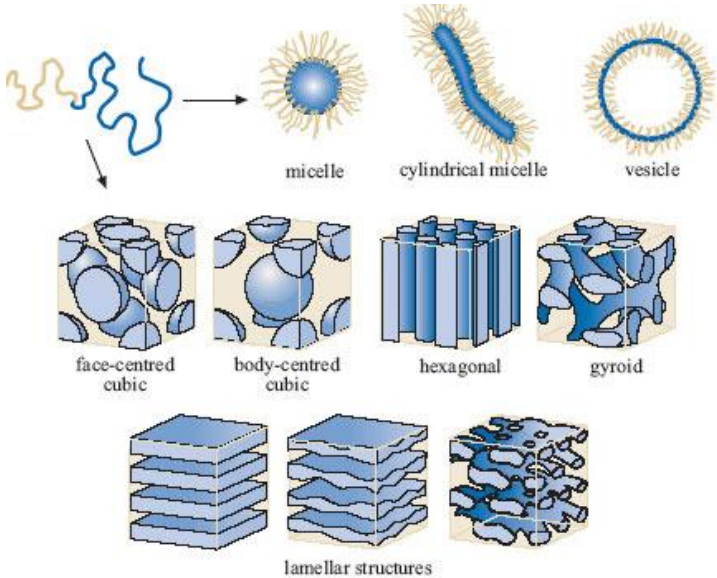


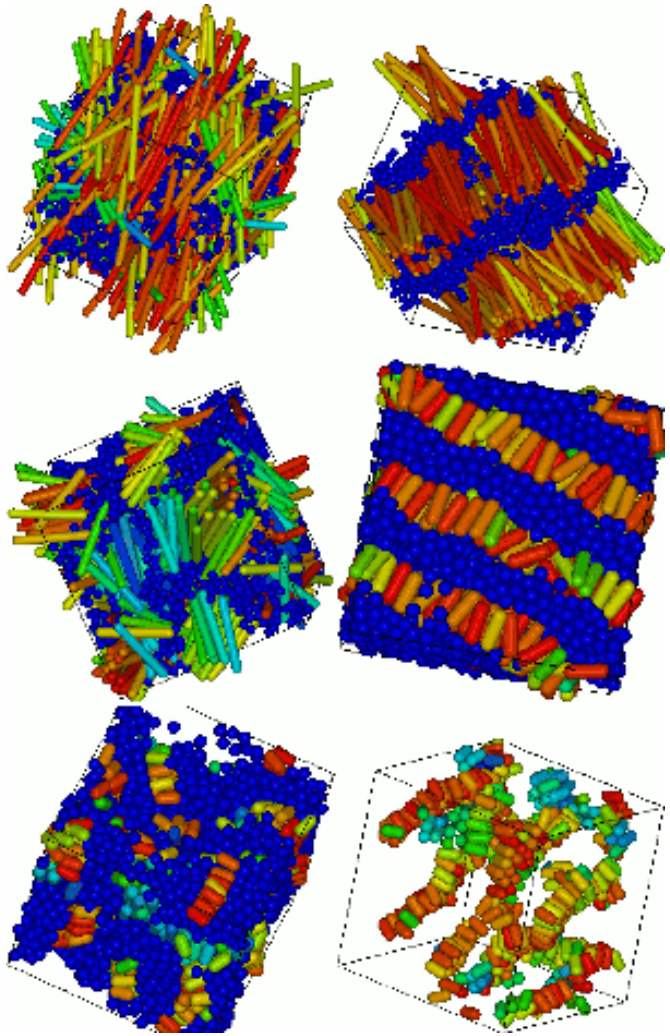
A. Y. Kuksin, G. E. Norman, V. V. Stegailov, and A. V. Yanilkin, Comp Phys Comm, 177, 34-37 (2007)

Block polymer
micro-phase separation

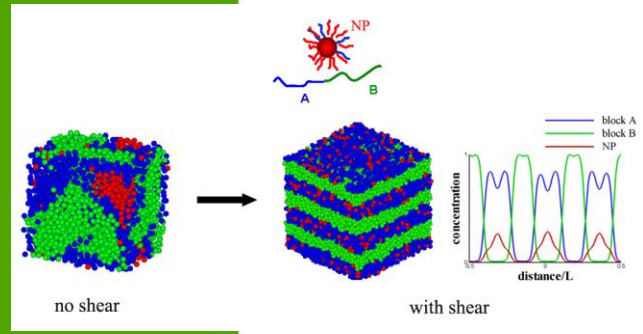




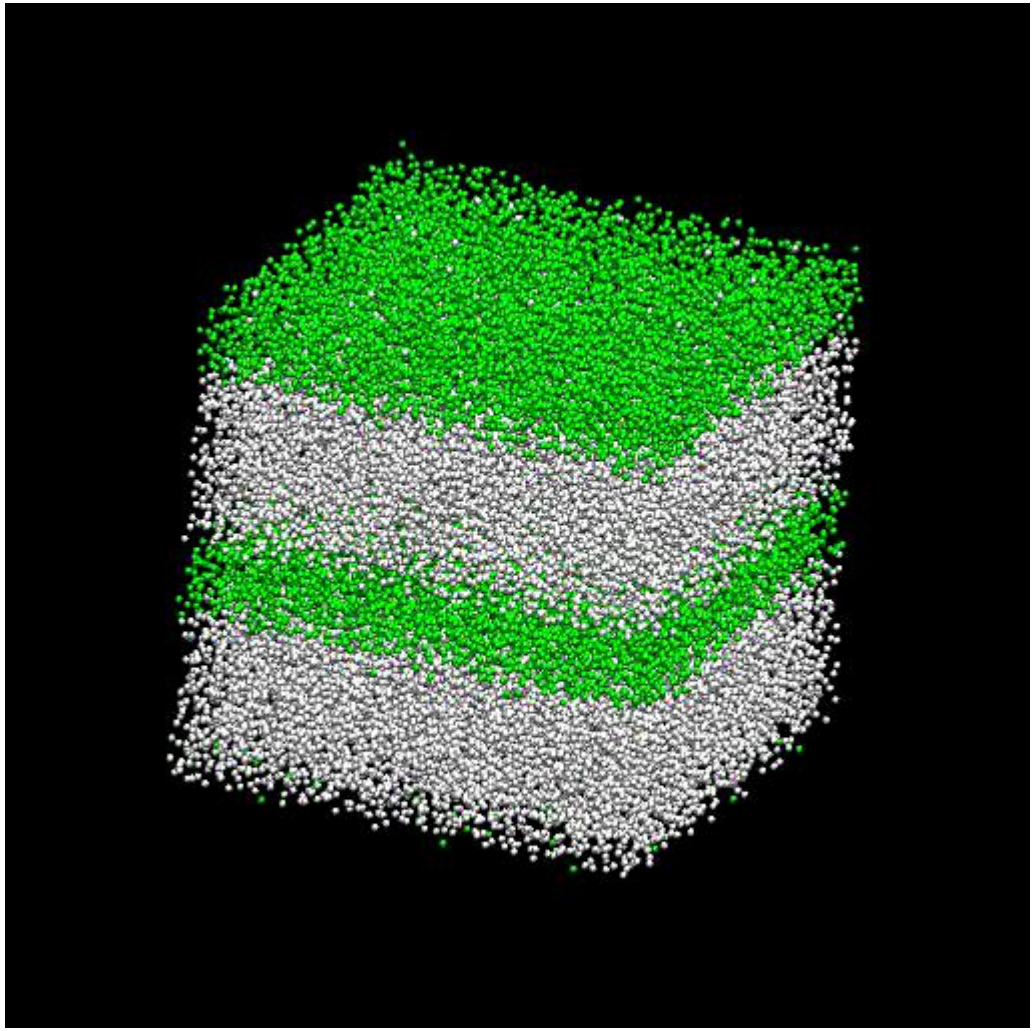




Block polymer



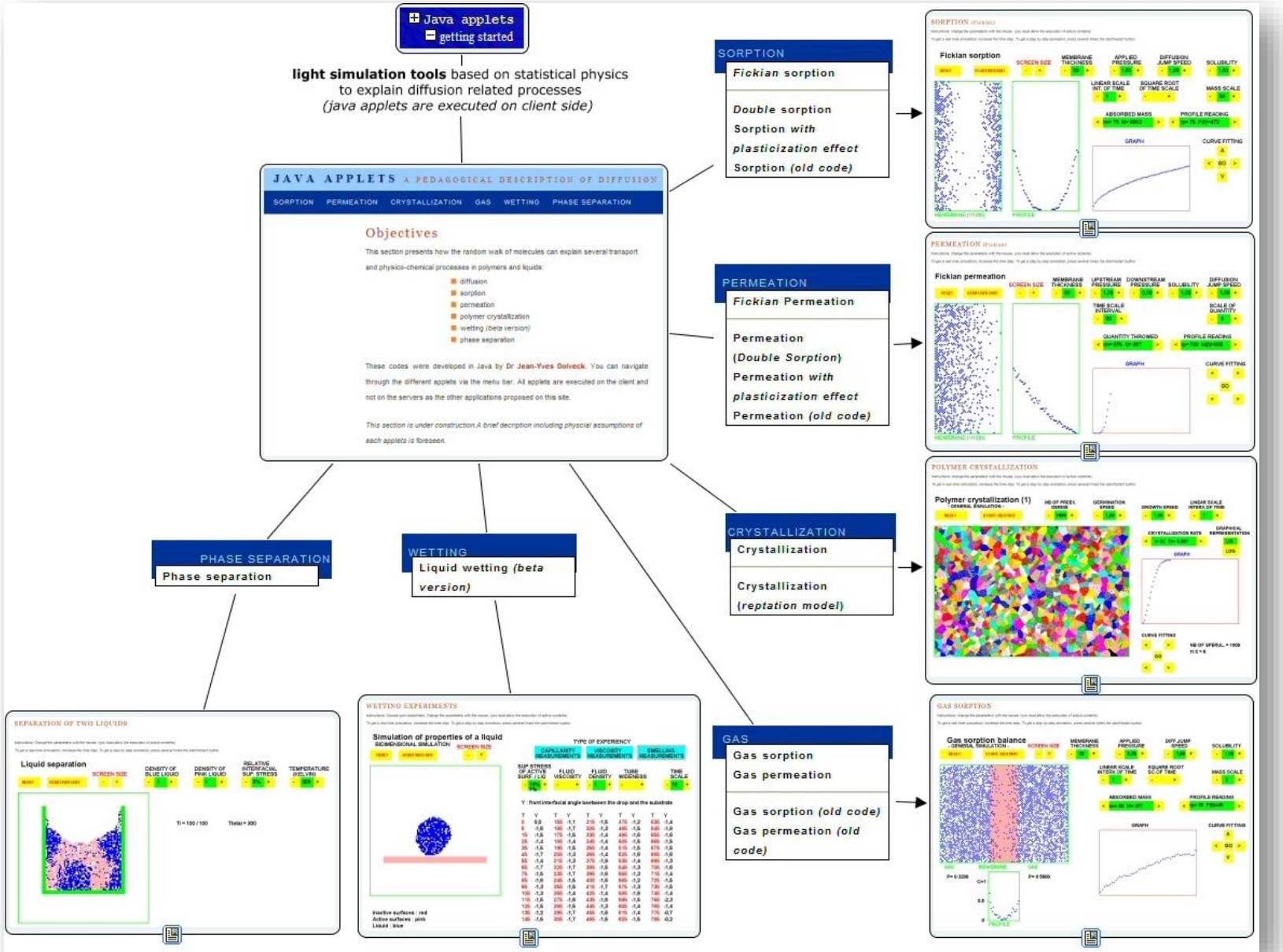
Credit: softsimu



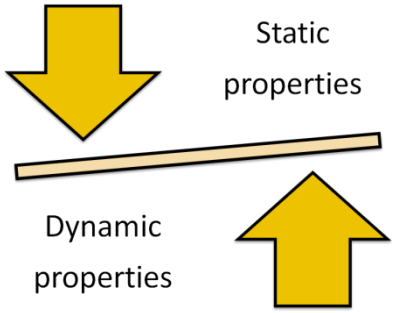
Petri Nikuner
Karttunen, ar
Vattulainen C
Comm. 153, -
(2003)

STAT. PHYS. Pedagogical tools

http://modmol.agroparistech.fr/java/



CONTENT



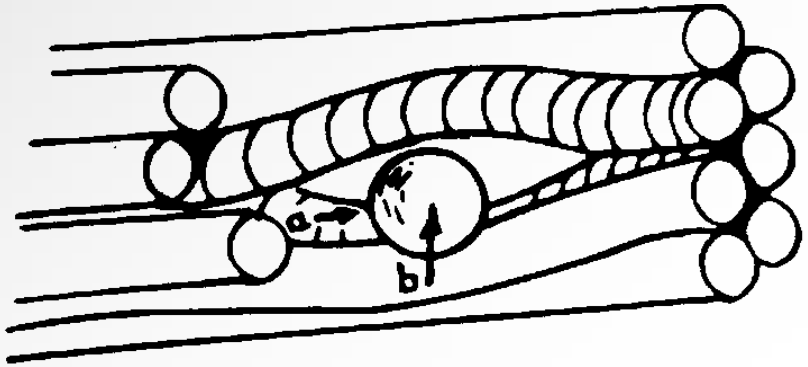
Some concepts and questions: computational-force microscope, multi-scale modeling

Case study: molecular diffusion

Case study: Chemical potentials

Extensions to non-thermal noise

Brandt, 1959



CASE-STUDY

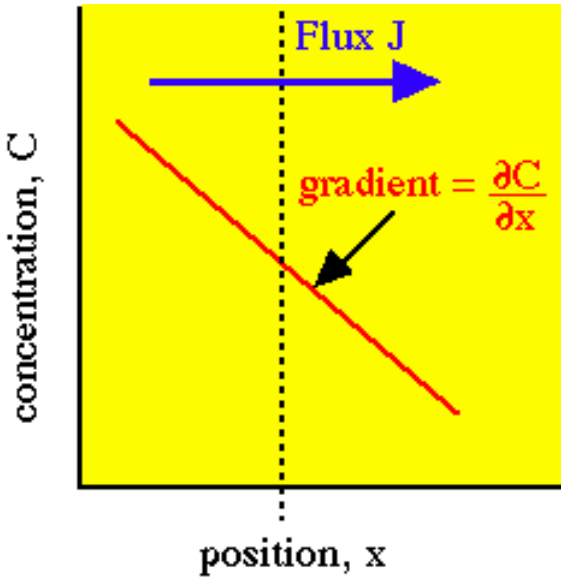
DIFFUSION WITH NO EXTERNAL POTENTIAL IN POLYMERS

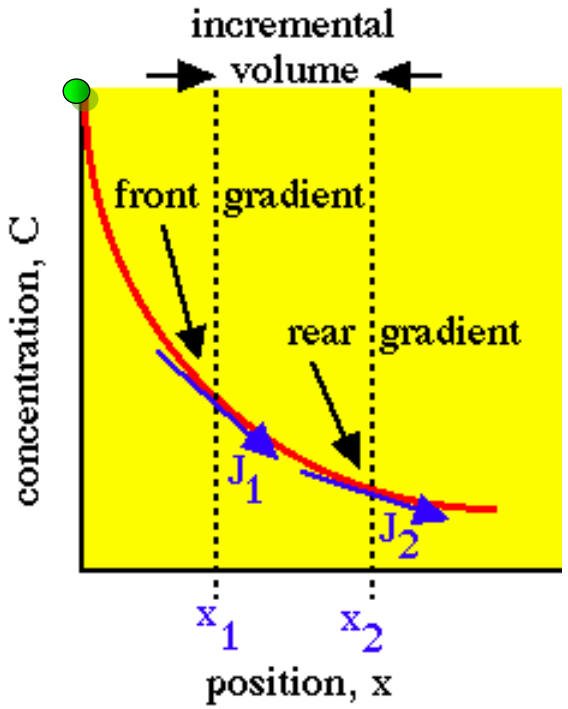
INRA SCIENCE & IMPACT

PHENOMENOLOGICAL DESCRIPTION

concentration gradient is the driving force of mass transfer

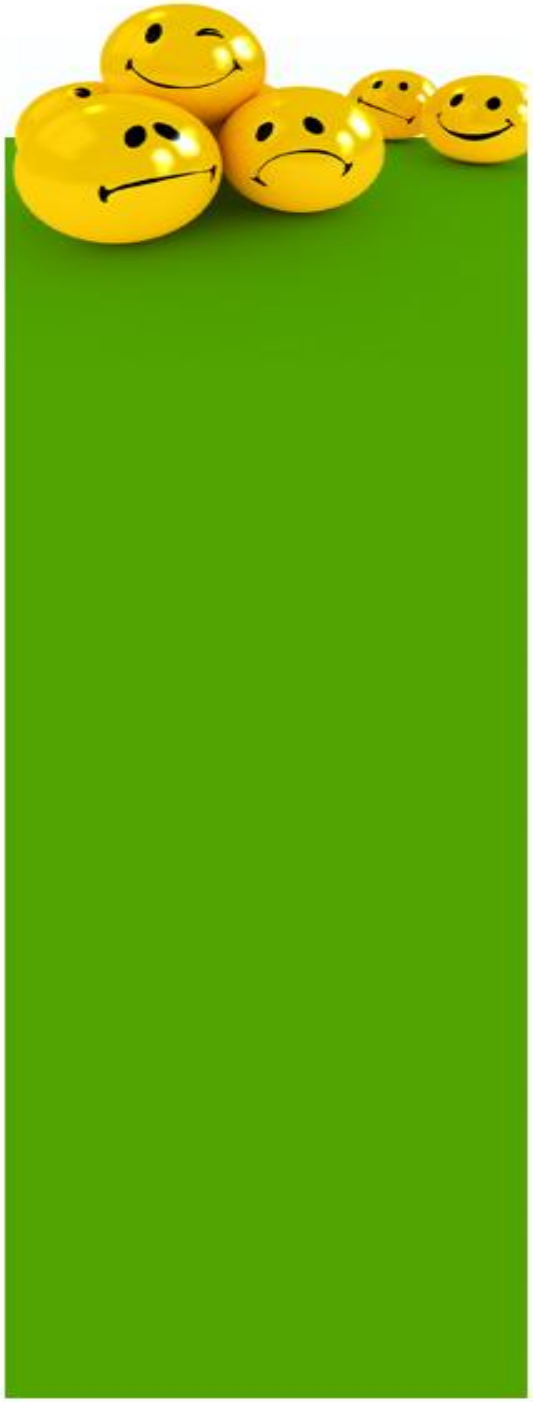
$$J = -D\frac{\partial C}{\partial x}$$



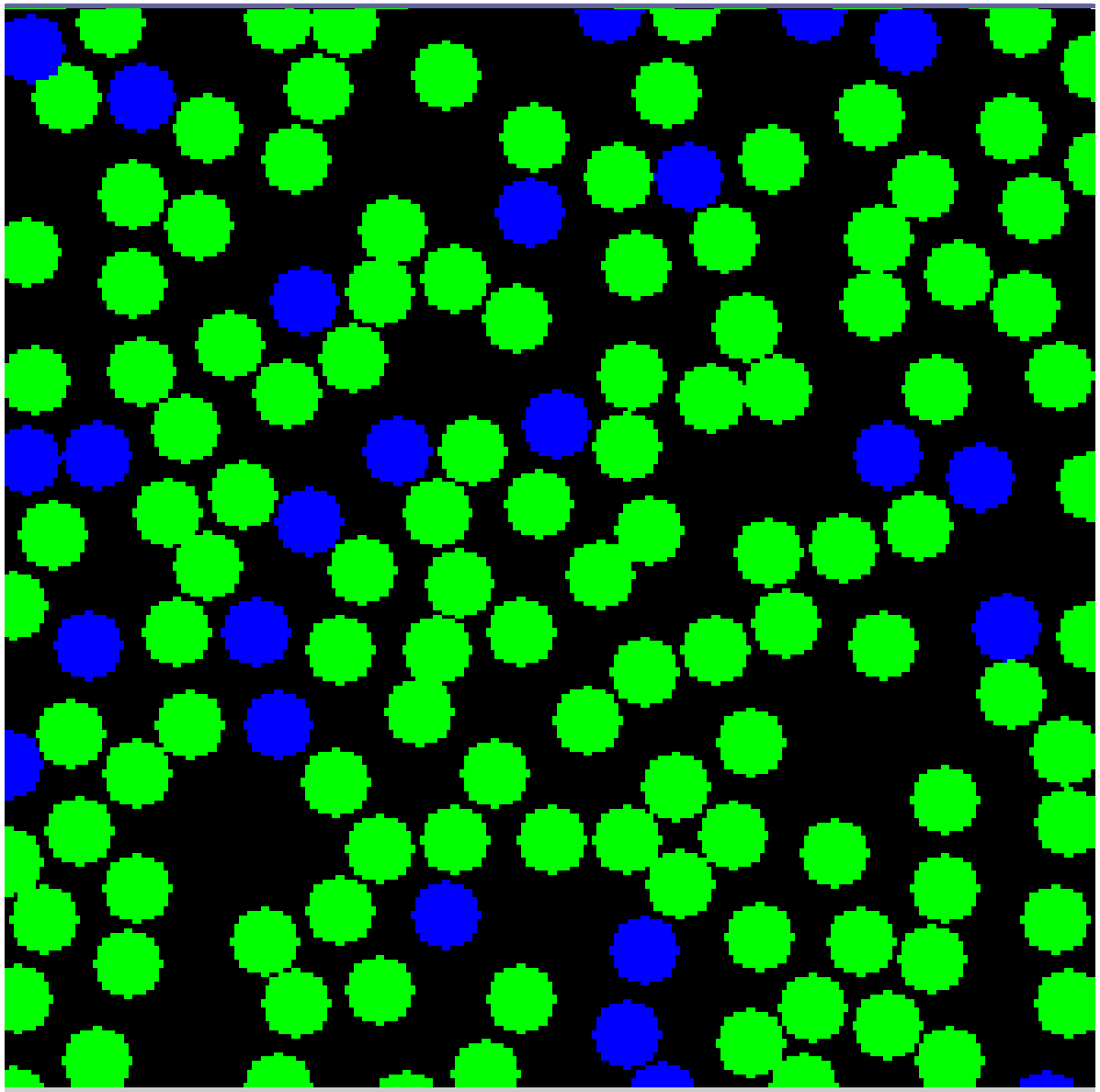


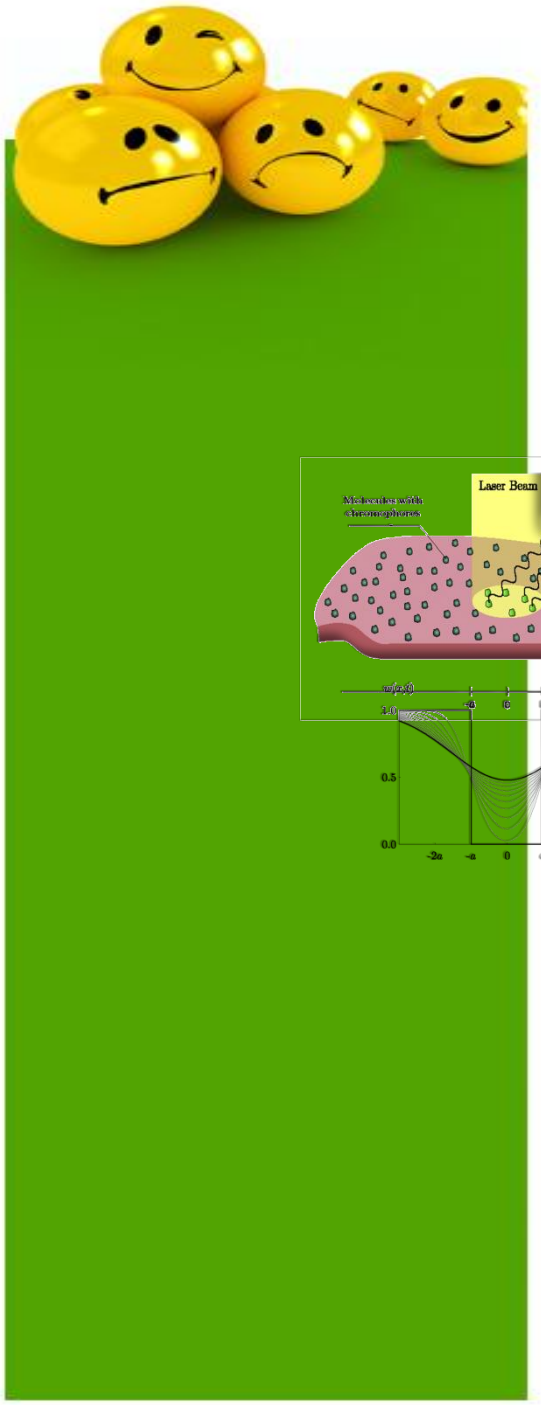
local mass balance

$$\frac{\partial C}{\partial t} \approx \lim_{x_1 \to x_2} \frac{J_1 - J_2}{x_2 - x_1} = \frac{\partial}{\partial x}\left(D\frac{\partial C}{\partial x}\right)$$

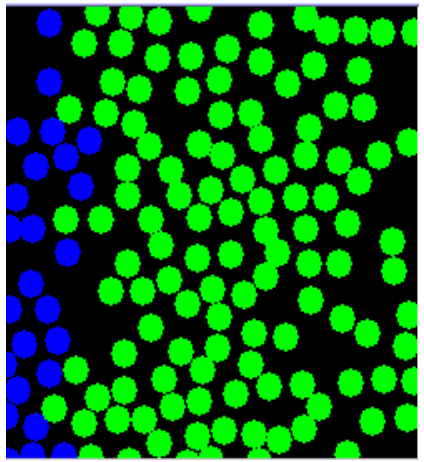


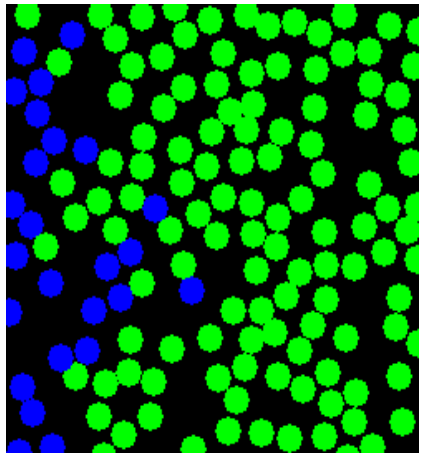
Mutual diffusion

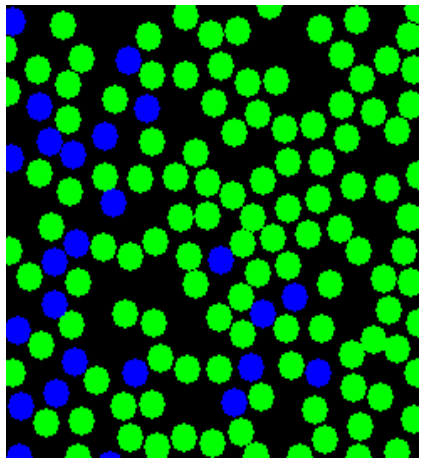


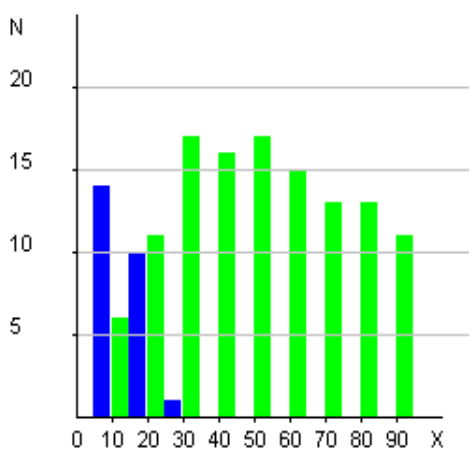


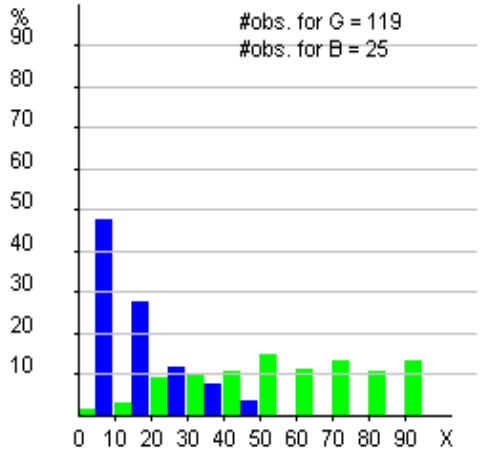
Interpretation 1/2

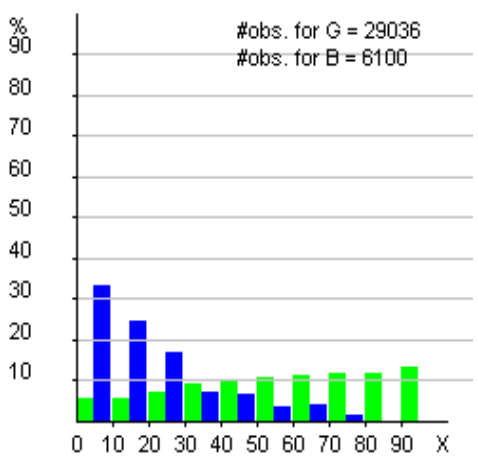




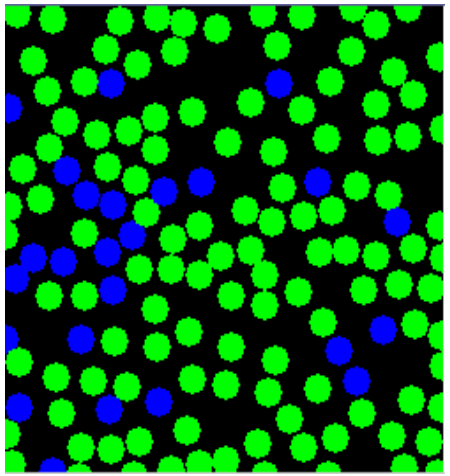


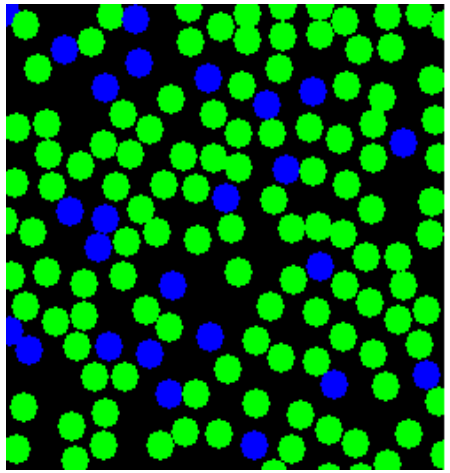


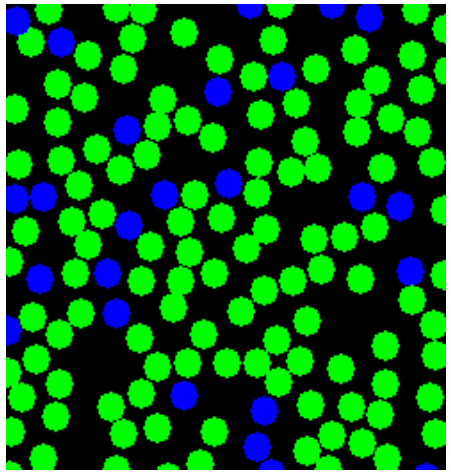


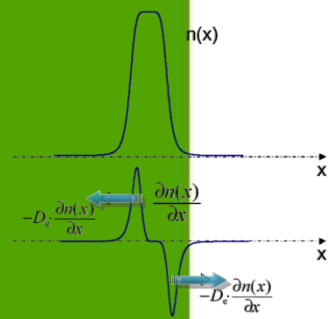


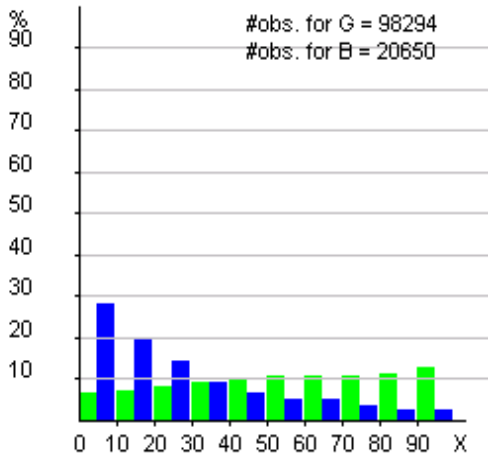
Interpretation 2/2

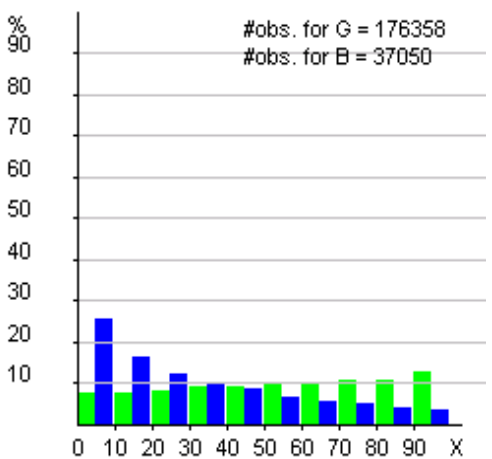


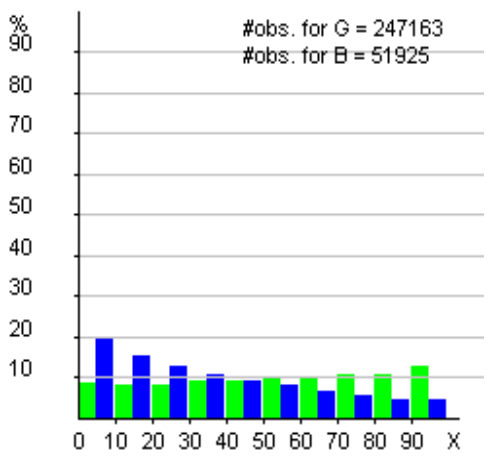








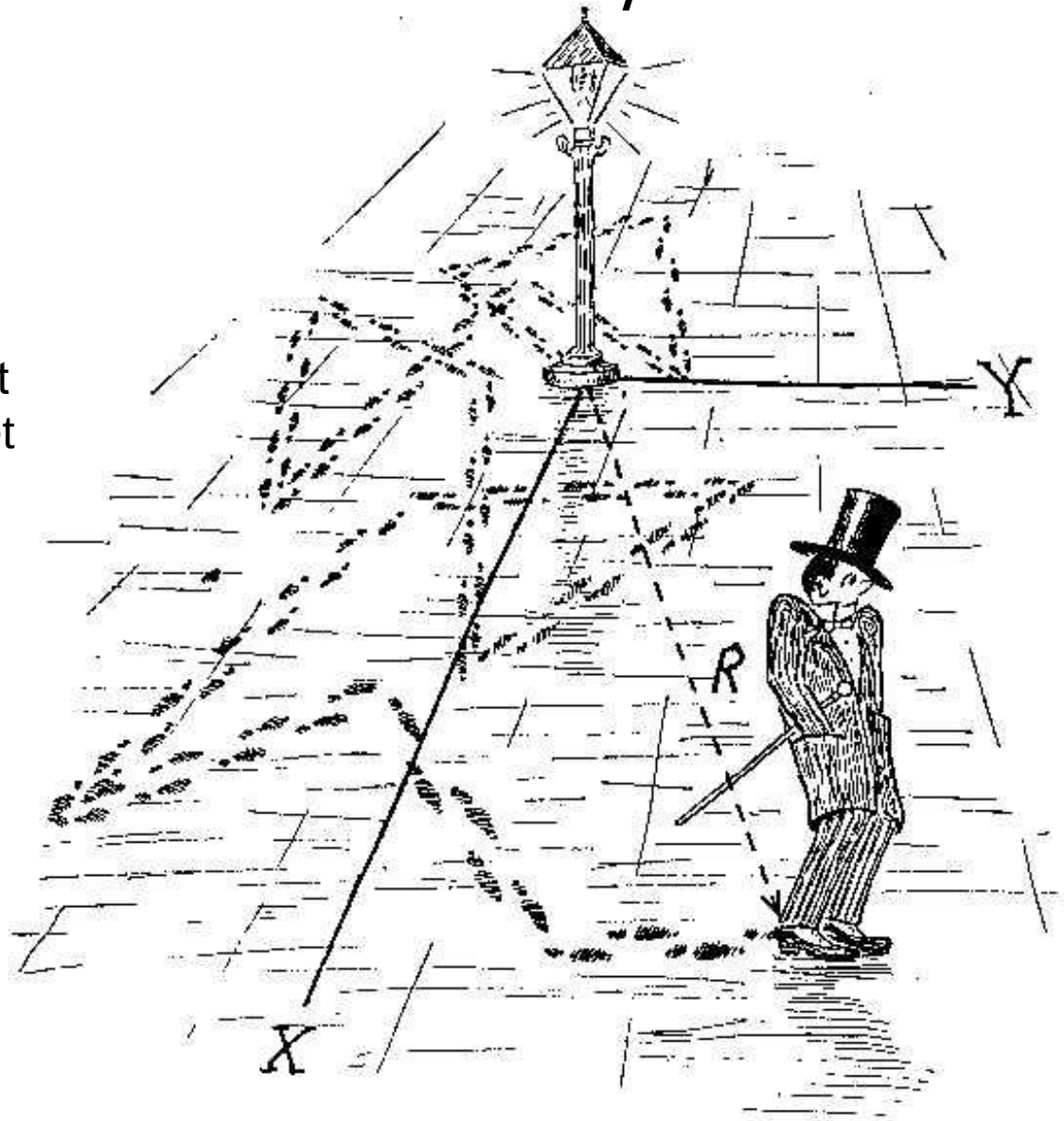




WHAT IS SELF/TRACER DIFFUSION?

« l'irrégularité du mouvement est quantitativement établie et c'est là sans doute une des plus belles applications des lois du hasard ».

J. Perrin



drunk Walker from G. Gamow, *One, two, three....Infinity*

MOLECULAR DIFFUSION

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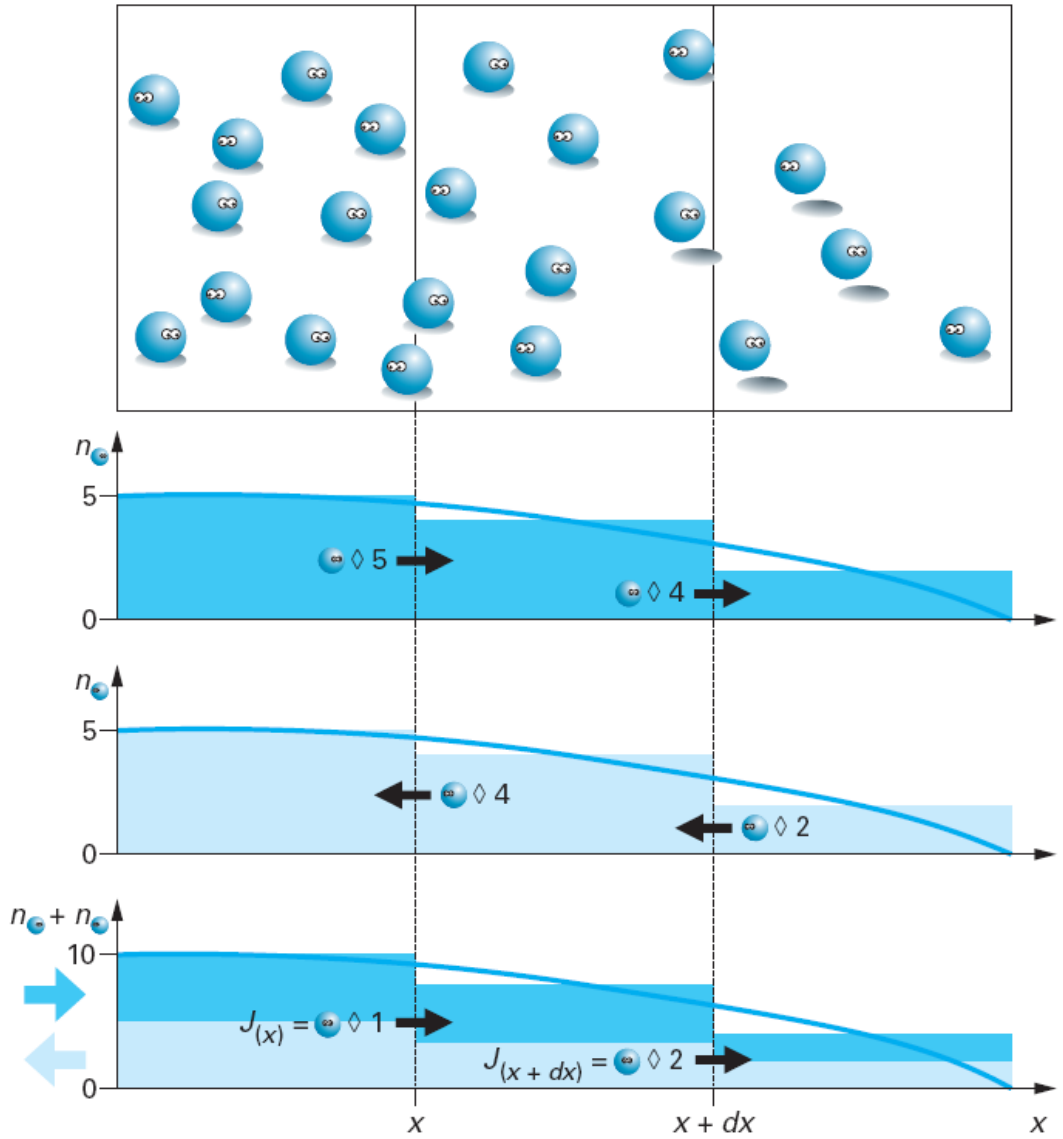
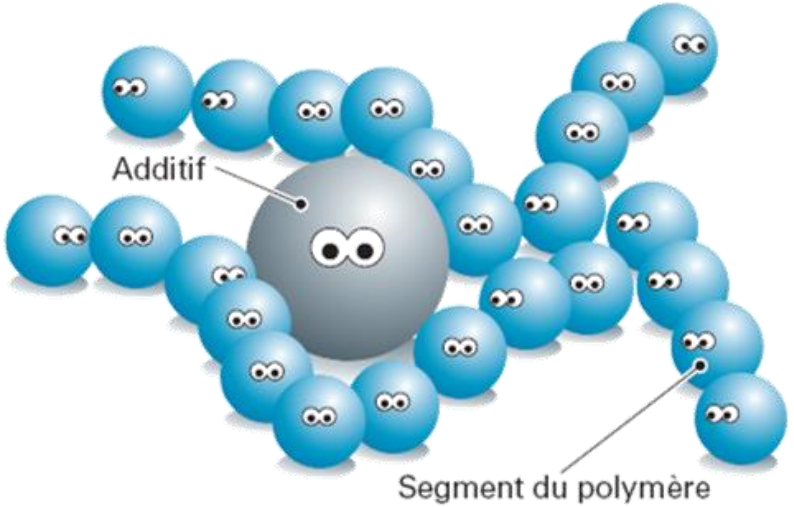
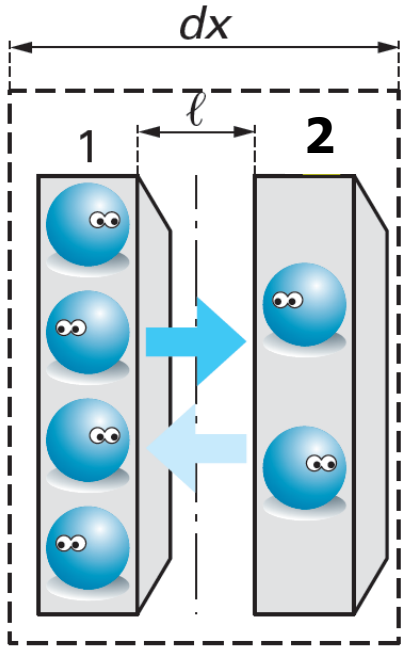
$$\frac{d}{dt}\left(\frac{n}{V}\right)=\frac{J_{(x)}-J_{(x+dx)}}{dx}$$



MOLECULAR DIFFUSION

Mutual diffusion of additive
Among polymer segments





$$j_{\rightarrow} = \nu \cdot n^1_{\bullet} = \frac{1}{2} \cdot \nu \cdot n^1_{\bullet}$$

$$j_{\leftarrow} = \nu \cdot n^2_{\bullet} = \frac{1}{2} \cdot \nu \cdot n^2_{\bullet}$$

$$\frac{\mathrm{d}}{\mathrm{d}x} C_{\bullet} = \frac{n^2_{\bullet}/\ell - n^1_{\bullet}/\ell}{\ell}$$

$$J = j_{\rightarrow} - j_{\leftarrow} = -\underbrace{\frac{1}{2} \cdot \nu \cdot \ell^2}_{D} \cdot \frac{\mathrm{d}}{\mathrm{d}x} C_{\bullet}$$

$n_{\bullet}$ nombre de billes

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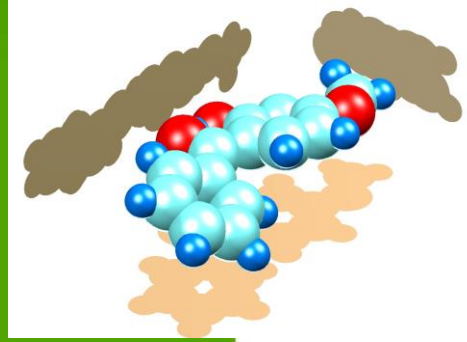


Chimassorb 90

QSPR-MS version 1.0

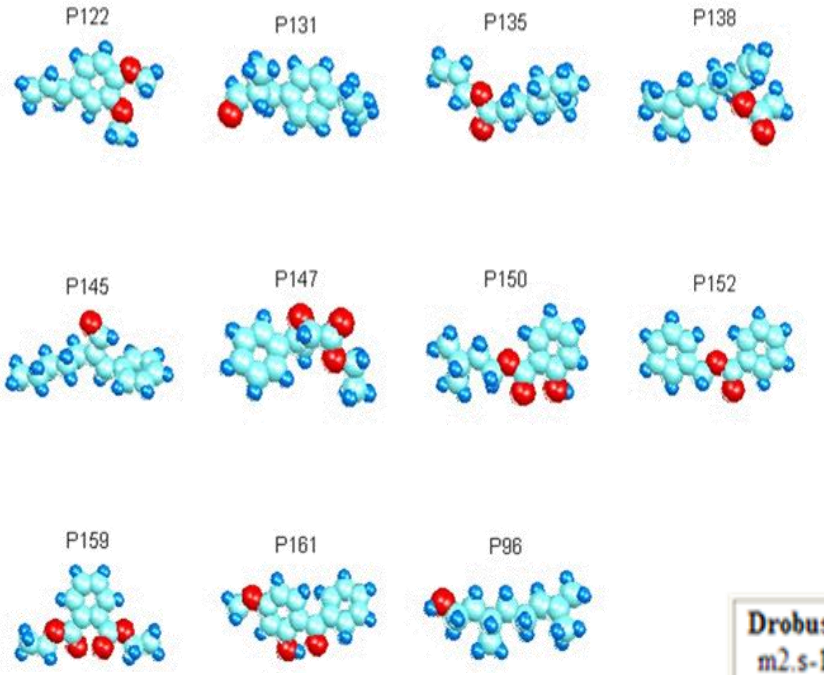
Molecule: **P161**
"2-Hydroxy-4-methoxybenzophenone (Chimassorb 90)"
CAS# **131-57-7**

Polymer: **LDPE 23°C**

class size: **11**

Similar 3D structures for *D* prediction

(pruning level: **20**)



List of molecules in the current class

code	formula	M g.mol-1	CAS #	chemical name
P122	C11 H14 O2	178	93-16-3	2-Methoxy-4-propenylanisol (Methylisoeugenol)
P131	C13 H18 O1	190	103-95-7	2-Methyl-3-(4-isopropyl)phenylpropanal (Cyclamen aldehyde)
P135	C12 H20 O2	196	2705-87-5	Allyl-3-cyclohexylpropionate
P138	C12 H20 O2	196	115-95-7	3,7-Dimethyl-1,6-octadien-3-ylacetate (Linalylacetate)
P145	C14 H18 O1	202	122-40-7	Amylcinnamicaldehyde or 2-Phenylmethylene-heptanal
P147	C12 H14 O3	206	77-83-8	3-Methyl-3-phenylglycidate (Aldehyde C16)
P150	C12 H16 O3	208	NaN	Iso-amylsalicilate
P152	C14 H12 O2	212	120-51-4	Benzylbenzoate
P159	C12 H14 O4	222	84-66-2	Diethylphthalate (DEP)
P161	C14 H12 O3	228	131-57-7	2-Hydroxy-4-methoxybenzophenone (Chimassorb 90)
P96	C10 H20 O1	156	106-22-9	3,7-Dimethyl-6-octen-1-ol (Citronellol)

summarized 3D molecular information

prop 3D	min value	median value	max value
M	156	202	228
VdW volume	180	206	217
Gyration radius	3.54	3.9	4.11
Inertial along z	261	383	449
Inertial along x	28.2	61.9	103
Section xy	48.4	65.1	76.8
Section yz	23.1	30.9	75.4
Dipolar moment	1.23	2.99	4.2
Flexion	2.59	4.46	6.24

***D* robust statistics**

Drobust m2.s-1	stand. dev. m2.s-1	*n class size*	Dmin m2.s-1	Dmed m2.s-1	Dmax m2.s-1
2.24e-013	**1.54e-013**	12	1.2e-013	**2.3e-013**	7e-013

***D* robust statistics**

Drobust m2.s-1	stand. dev. m2.s-1	*n class size*	Dmin m2.s-1	Dmed m2.s-1	Dmax m2.s-1
2.24e-013	**1.54e-013**	12	1.2e-013	**2.3e-013**	7e-013

Vitrac *et al.* J. Appl. Polym. Sci. 2006

Einstein's derivation (1902)

$$u(x,t=0)=\delta(x)$$

$$\frac{\partial u}{\partial t}=D\frac{\partial^2 u}{\partial x^2}\Rightarrow\int_{-\infty}^{+\infty}\left(\frac{\partial u}{\partial t}x^2\right)dx=\int_{-\infty}^{+\infty}\left(x^2D\frac{\partial^2 u}{\partial x^2}\right)dx$$

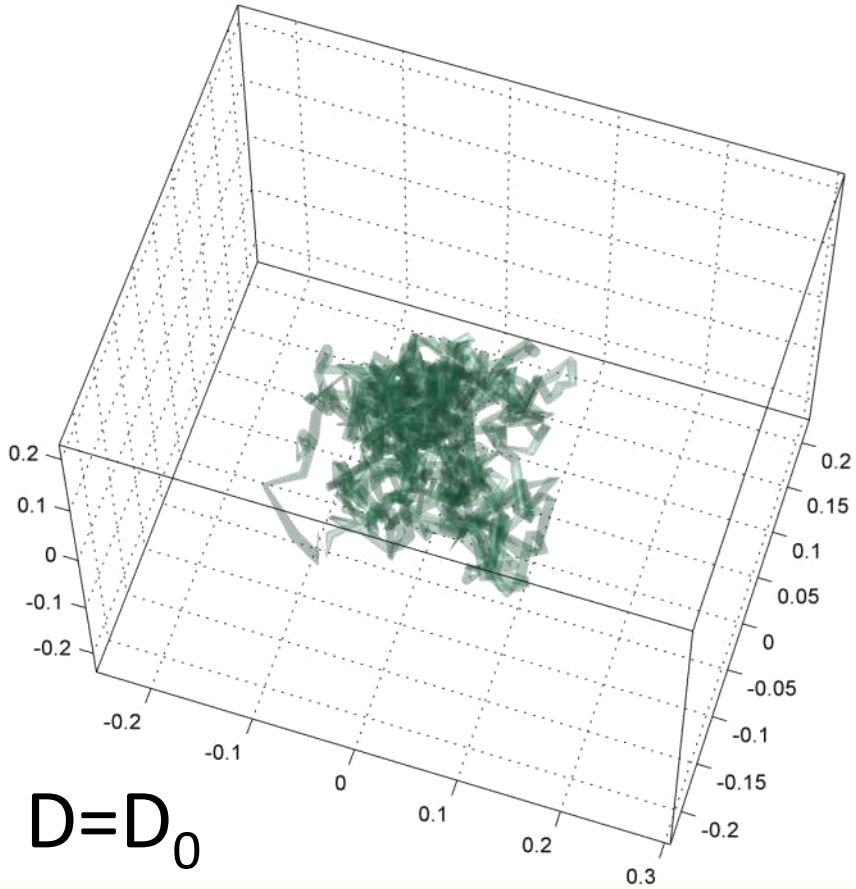
$$\Rightarrow\frac{\partial}{\partial t}\int_{-\infty}^{+\infty}ux^2dx=D\cdot\int_{-\infty}^{+\infty}\frac{\partial}{\partial x}\left(x^2\frac{\partial u}{\partial x}\right)dx-D\int_{-\infty}^{+\infty}\left(\frac{\partial x^2}{\partial x}\frac{\partial u}{\partial x}\right)dx$$

$$\Rightarrow\frac{\partial}{\partial t}\left\langle x^2\right\rangle=0-2D\int_{-\infty}^{+\infty}\left(x\frac{\partial u}{\partial x}\right)dx=-2D\left[\int_{-\infty}^{+\infty}\frac{\partial}{\partial x}(xu)dx-\int_{-\infty}^{+\infty}\left(\frac{\partial x}{\partial x}u\right)dx\right]$$

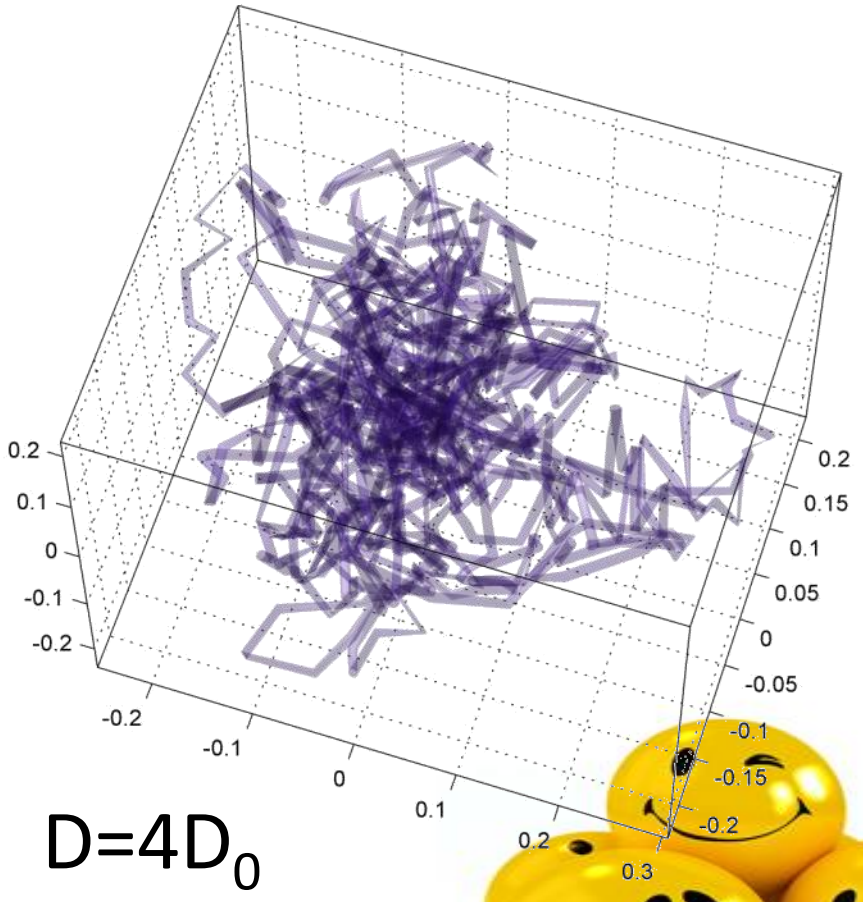
$$\Rightarrow\frac{\partial}{\partial t}\left\langle x^2\right\rangle=-2D\left\{\underbrace{[xu]_{-\infty}^{+\infty}}_{0}-\underbrace{\int_{-\infty}^{+\infty}udx}_{1}\right\}$$

$$\left\langle x^2\right\rangle=2Dt+Cste$$

Einstein equation



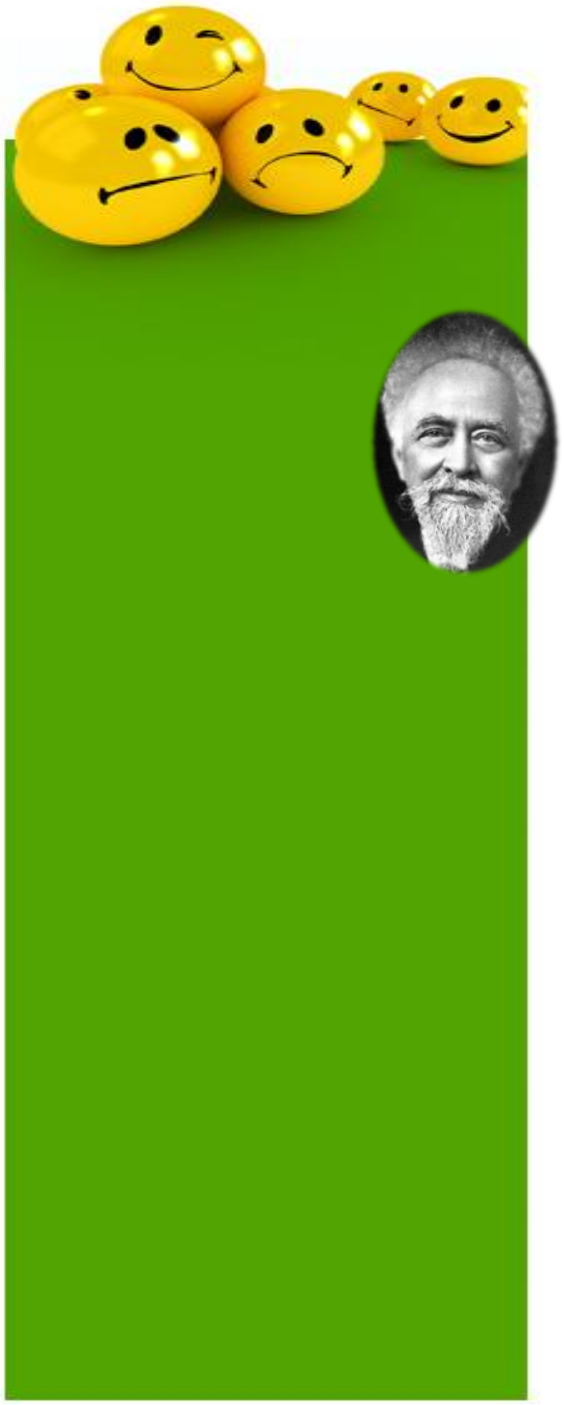
$D=D_0$



$D=4D_0$

mean square displacement:msd

$$D = \lim_{t\to\infty} \frac{1}{2d}\frac{\partial}{\partial t}\left\langle \left\| \vec{\mathbf{r}}_t - \vec{\mathbf{r}}_{t_0} \right\|^2 \right\rangle_{all\ t_0}$$



Perrin experiment (1908)

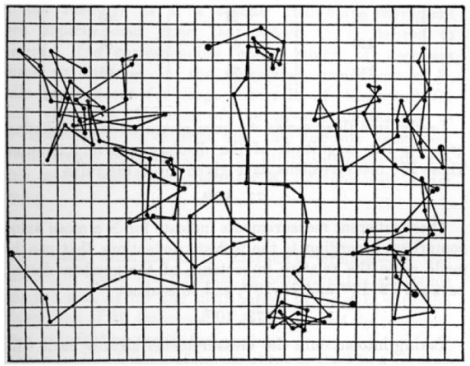
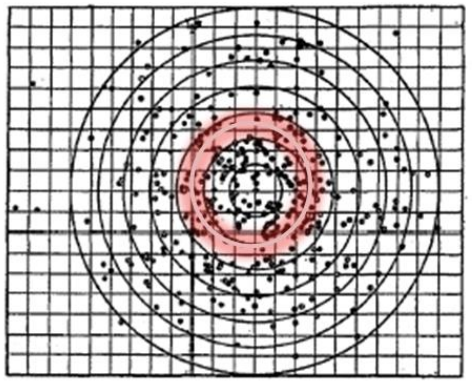


Fig. 1. These tracks of three particles are by J. Perrin.[6] The dots show the particle positions at 30-second intervals, with lines joining successive points. The scale is 1 division equals 0.0003125 cm. The particle radius is 0.52 μm.

$$D = \frac{k_B T}{f} = \frac{k_B T}{6\pi\eta a} = \frac{1}{N_A}\frac{RT}{6\pi\eta a}$$

$$G_s(\mathbf{r}, t) = \frac{1}{N}\left\langle \sum_{j=1}^{N} \delta(\mathbf{r} + \mathbf{r}_j(0) - \mathbf{r}_j(t)) \right\rangle$$

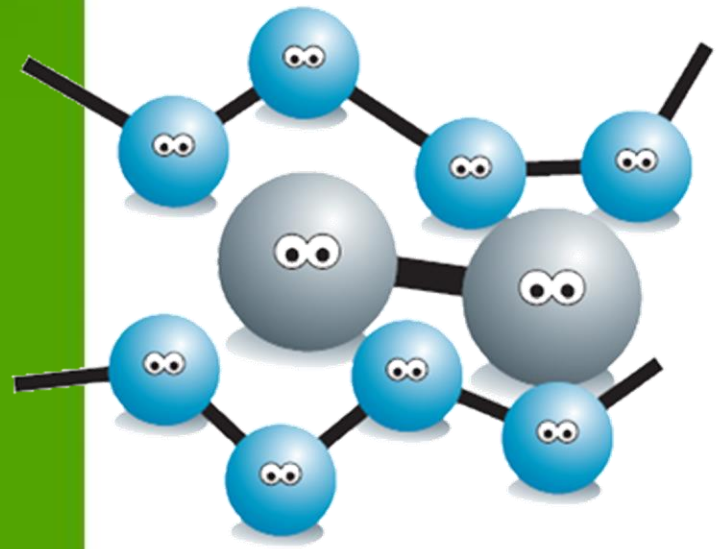


Déplacements (en μ) compris entre :	n observé.	n calculé.
0 et 2	24	27
2 et 4	76	71
4 et 6	90	84
6 et 8	67	76
8 et 10	45	54
10 et 12	34	30
12 et 14	20	14
14 et 16	4	5
16 et ∞	5	4

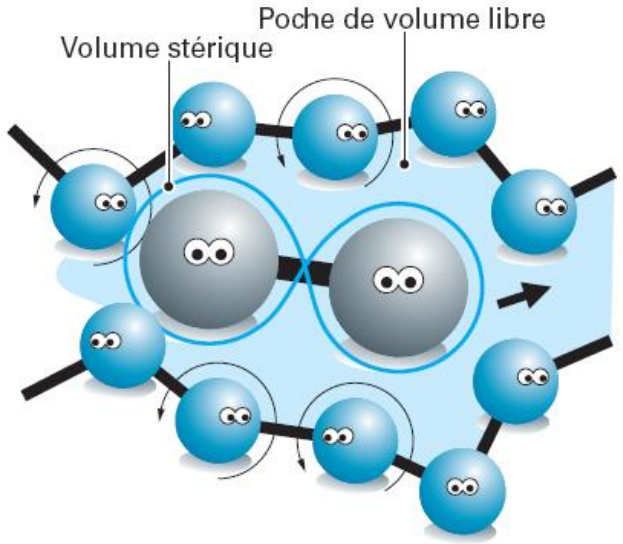
$$n(r,t) = 4\pi r^2 G_S \quad r \quad = N_0 \frac{4\pi r^2}{4\pi D t}^{3/2} \exp\left(-\frac{r^2}{4Dt}\right)$$

G_S: self part of the van Hove self-correlation function

D scaling with M

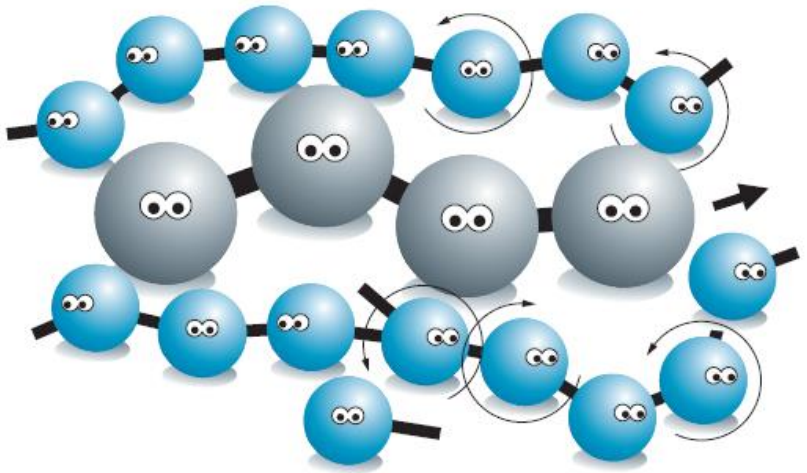


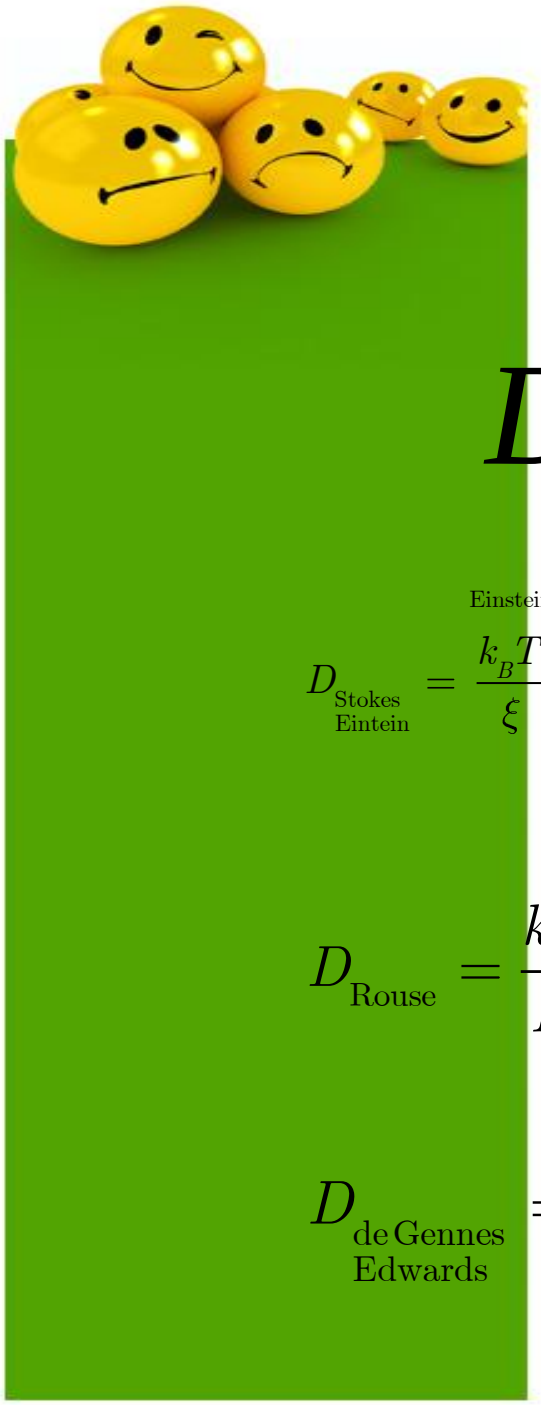
Local and temporary trapping of additive between polymer segments



Additive translation controlled by the relaxation of polymer itself and by the rate of creation of free volumes.

The relative free volume required for the translation of large additives is smaller as displacements of atoms/patterns are more likely not to be correlated together.





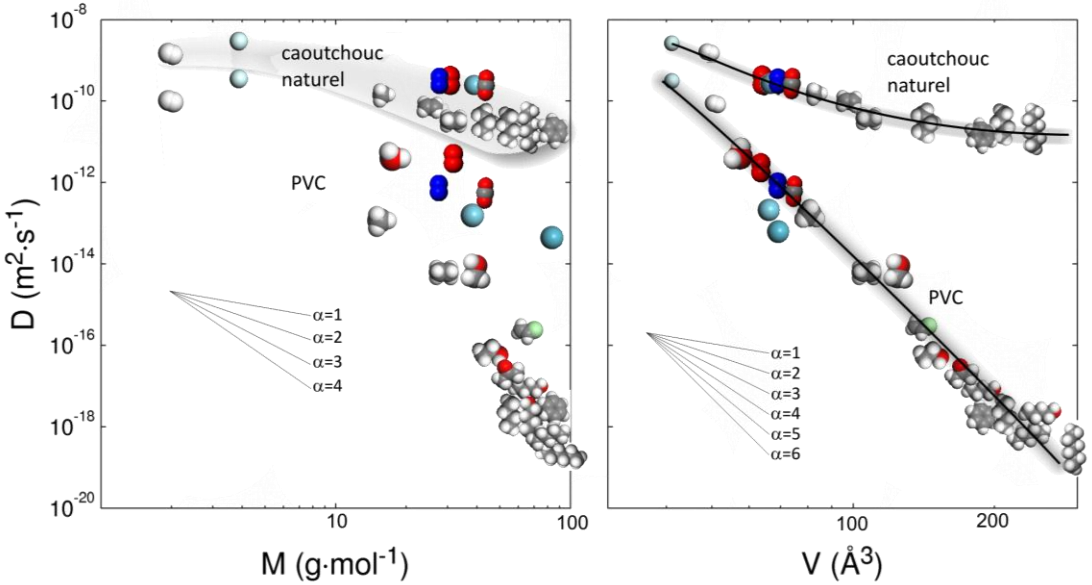
COMMON ? values for D ∝ M-?

(for simplicity M∝N with N=#atoms)

$$D \propto M^{-\alpha}$$

$$D_{\substack{\text{Stokes}\\\text{Eintein}}} = \frac{k_B T}{\xi} = \frac{k_B T}{\underbrace{6\pi\eta R_g}_{\text{Stokes}}} \propto N^{-\frac{1}{2}}$$

Einstein



$$D_{\text{Rouse}} = \frac{k_B T}{N\xi} \propto N^{-1}$$

$$\text{msd}_{\text{G}}(t) = 6\frac{k_{\text{B}}T}{N\xi_0}t + 4\sum_{p=1}^{N-1}\langle \mathbf{X}_p^2(0)\rangle \left[1-\exp(-t/\tau_p)\right]$$

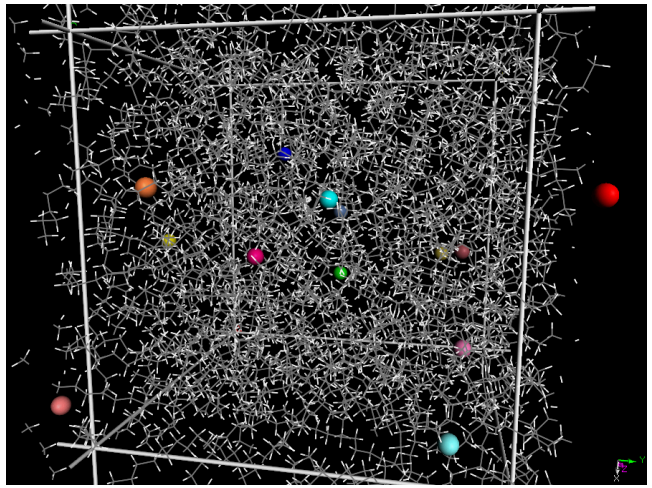
$$D_{\substack{\text{de Gennes}\\\text{Edwards}}} = \frac{k_B T}{N\xi \qquad \chi} \propto N^{-2}$$

$\propto\tau$=residence time in the tube $\propto d_{ee}^2 \propto N$

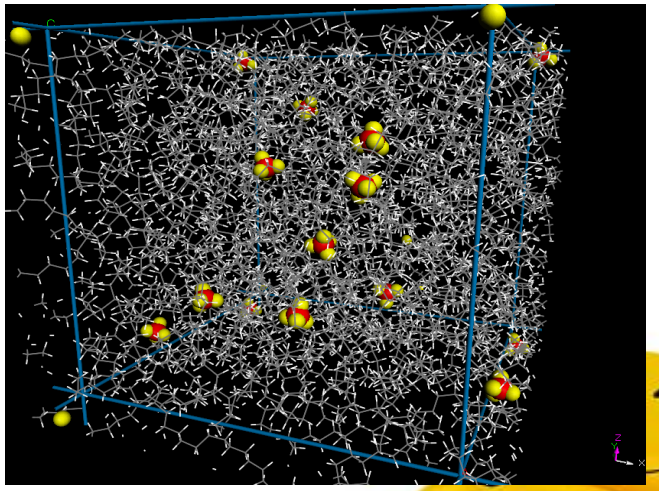
$$\text{msd}_{\text{G}}(t) = \begin{cases} \dfrac{k_B T}{N\xi} t & t \ll \dfrac{\tau}{B} \\ \dfrac{k_B T}{N\xi B} & \dfrac{\tau}{B} \ll t \ll \tau \\ \dfrac{k_B T}{N\xi B} t & t \gg \tau \end{cases}$$

Diffusion in polymers for different solute sizes

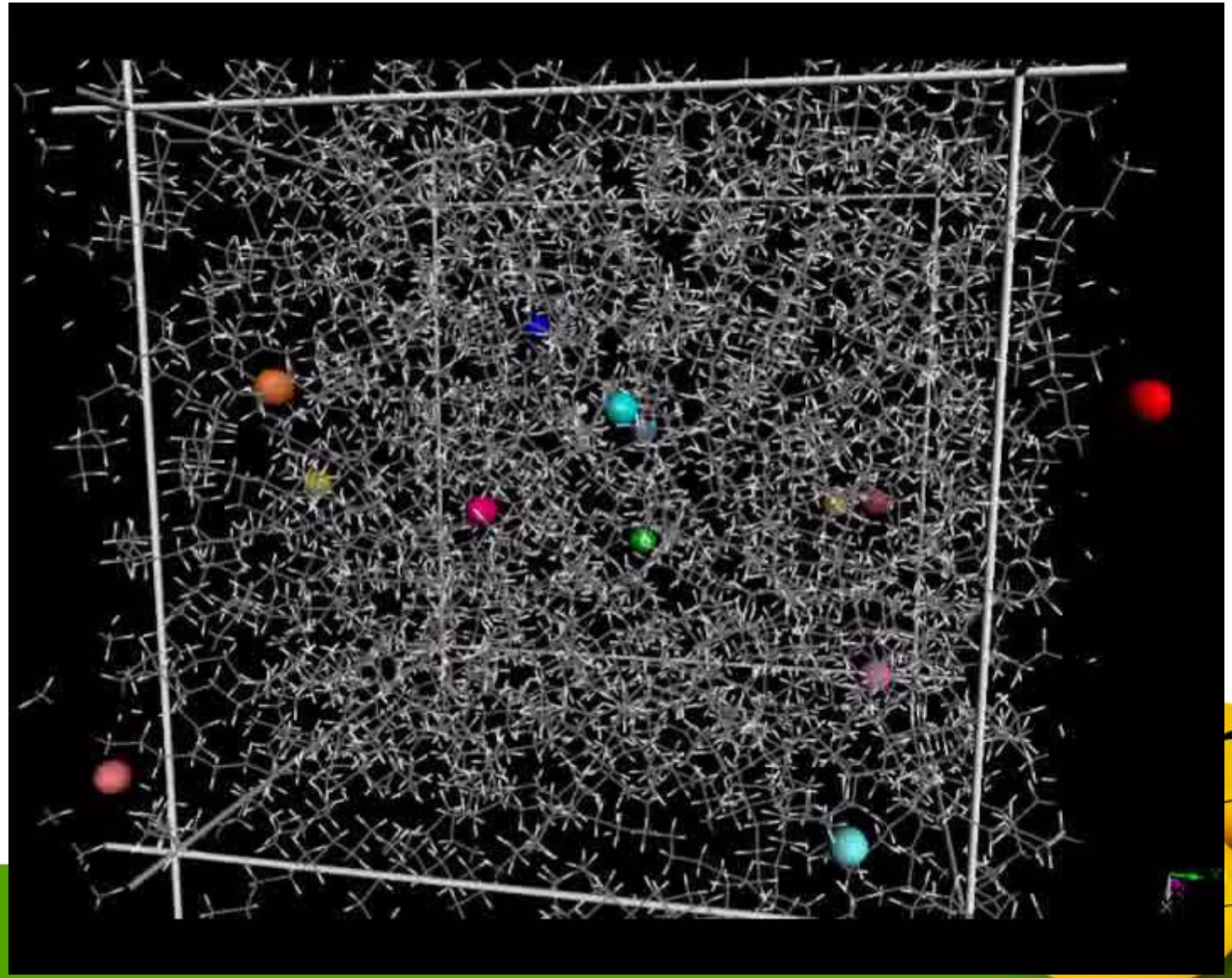
10 He in HDPE



10 CH_4 in HDEP

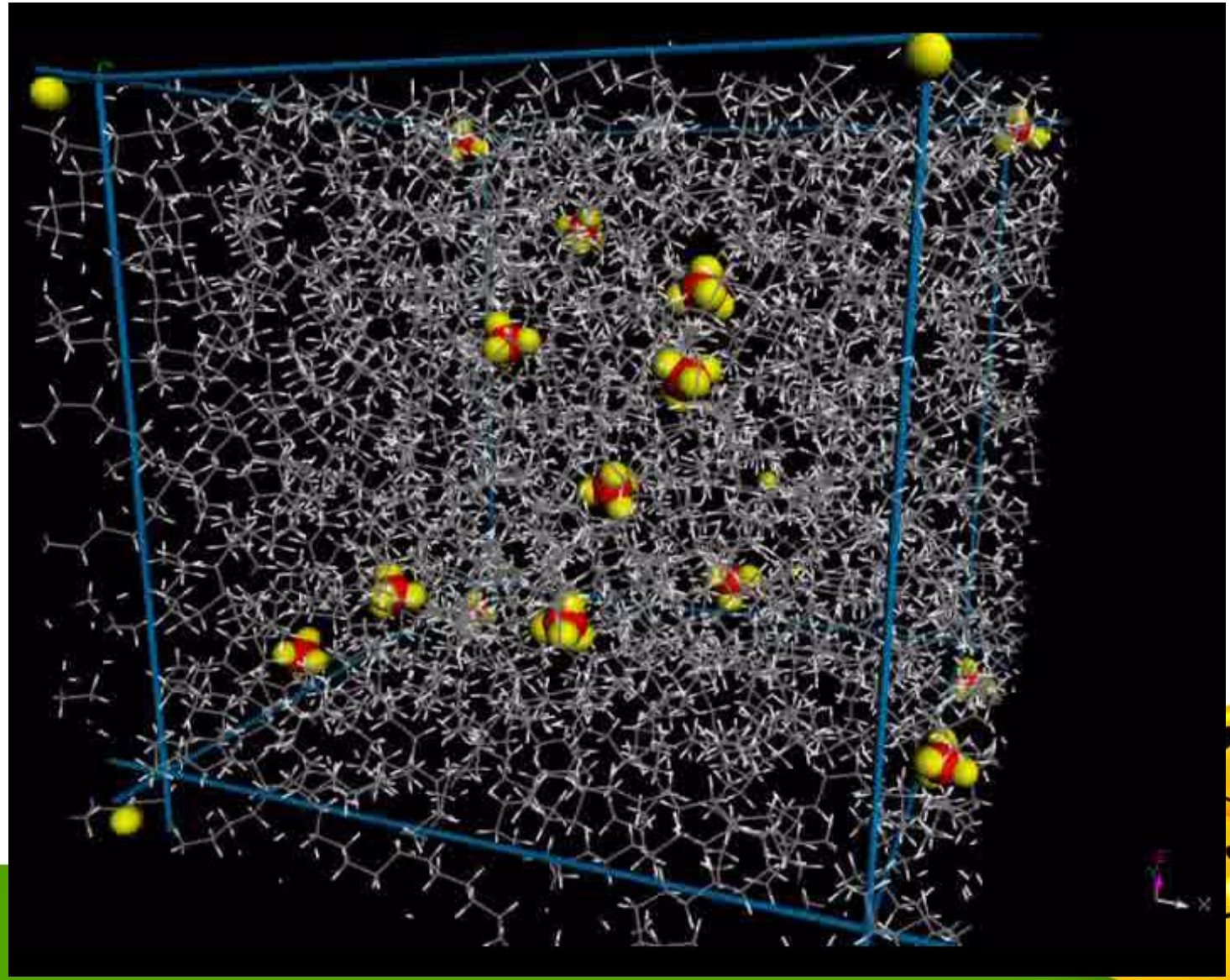


HE in HDPE



10 He in HDPE (500 ps NVT simulation, T=298K, PBC)

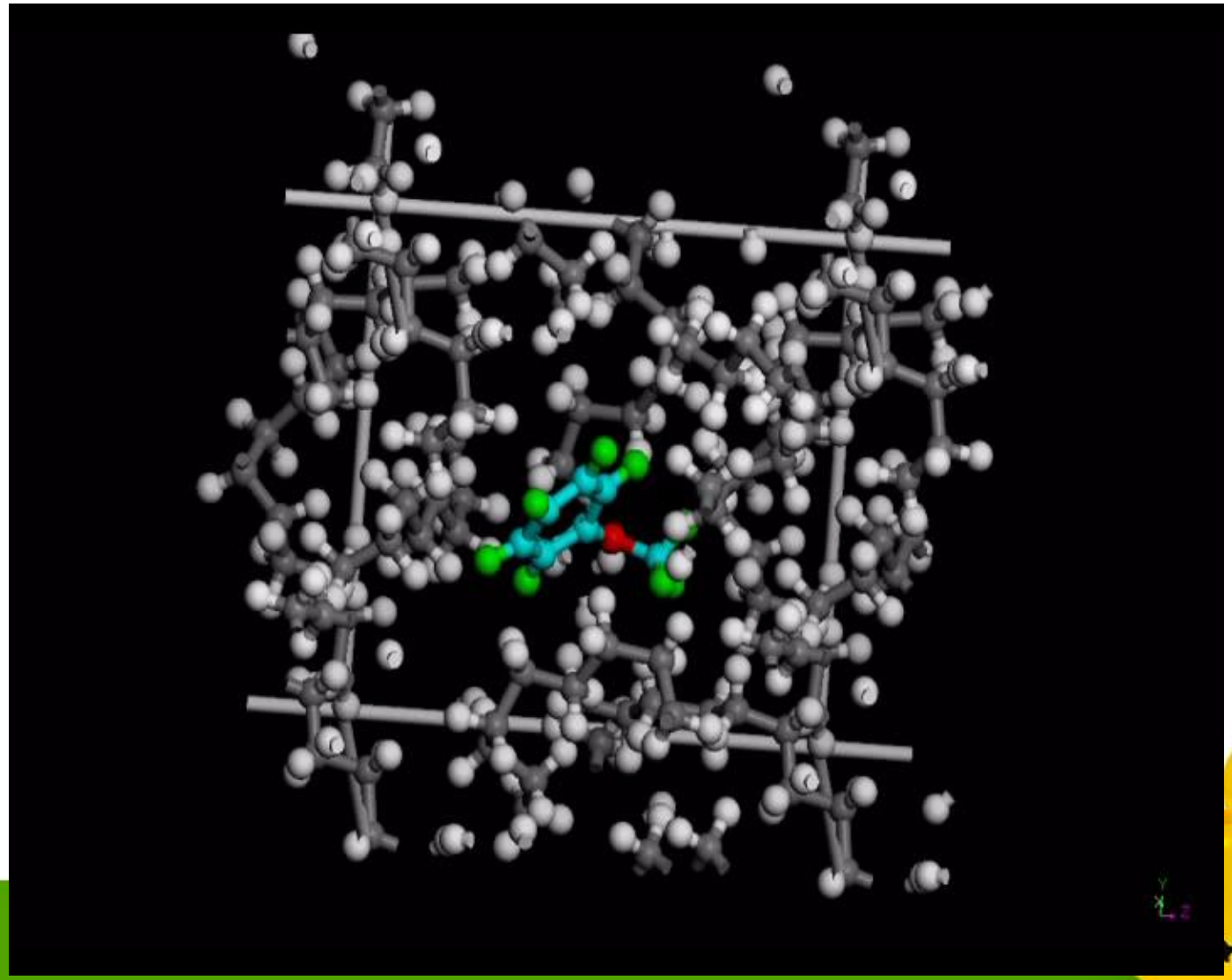
CH_4 in HDPE



10 CH_4 in PE (500 ps simulation, T=298K, PBC)

DIFFUSION IN ENTANGLED POLYMERS

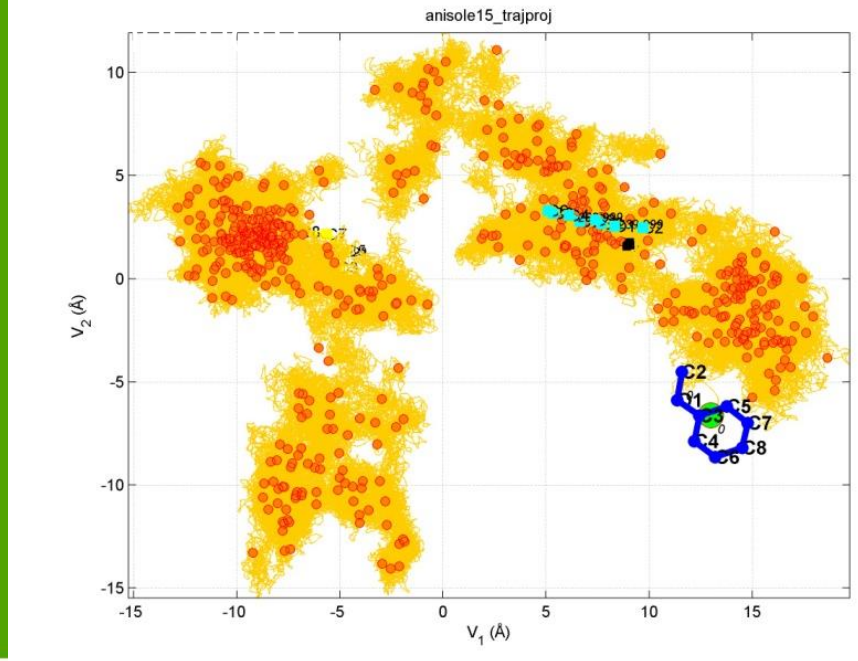
ANISOLE in HDPE

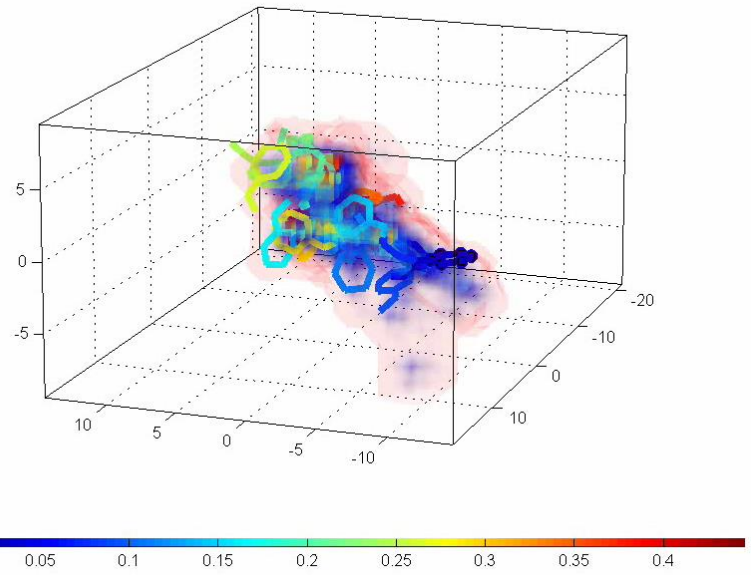


Anisole in PE (500 ps simulation, T=298K, PBC)

25 ns movies

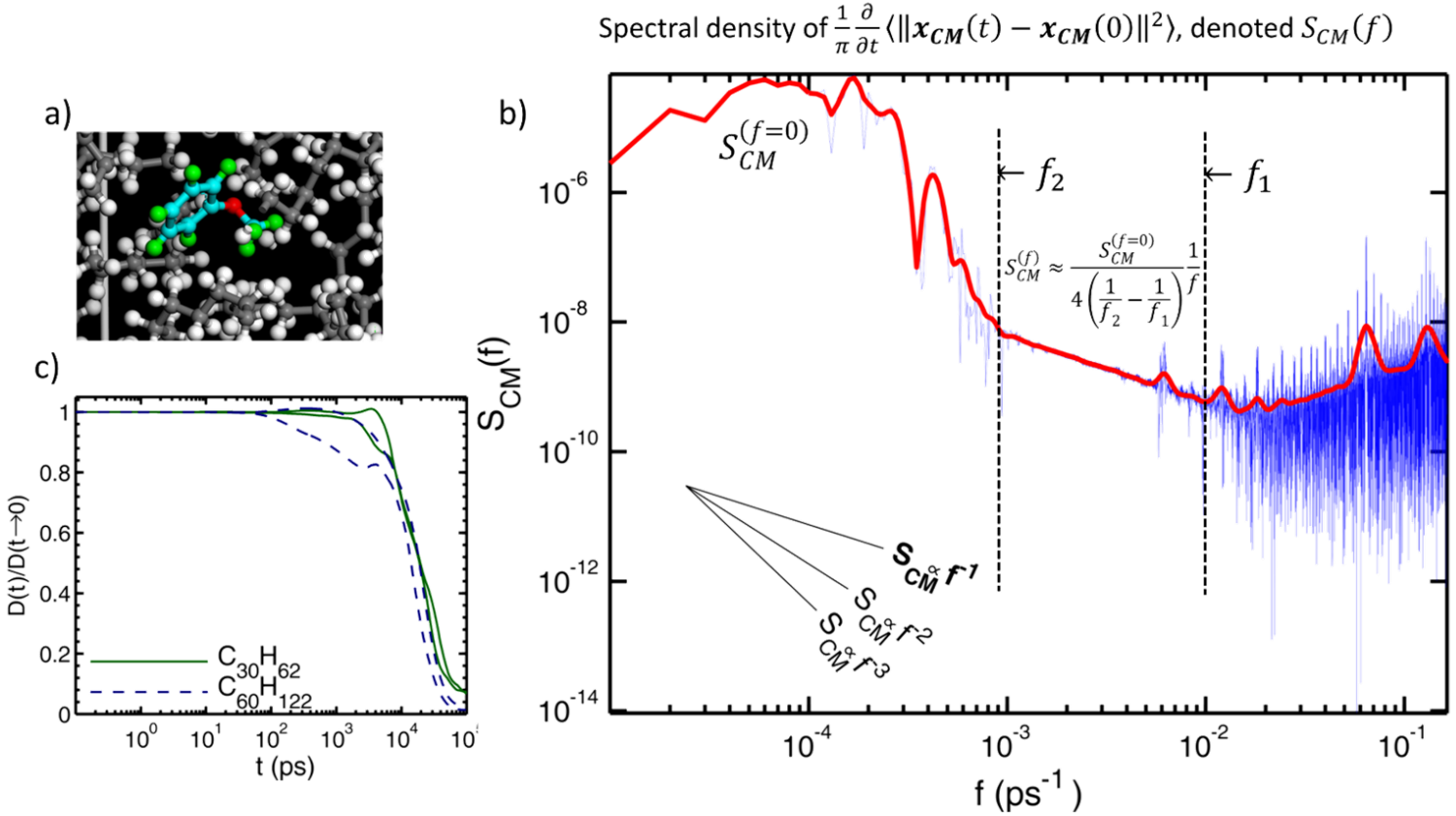
1 frame =
(25 frame
1 plot ea
— 1 s (m
— 0.25 n



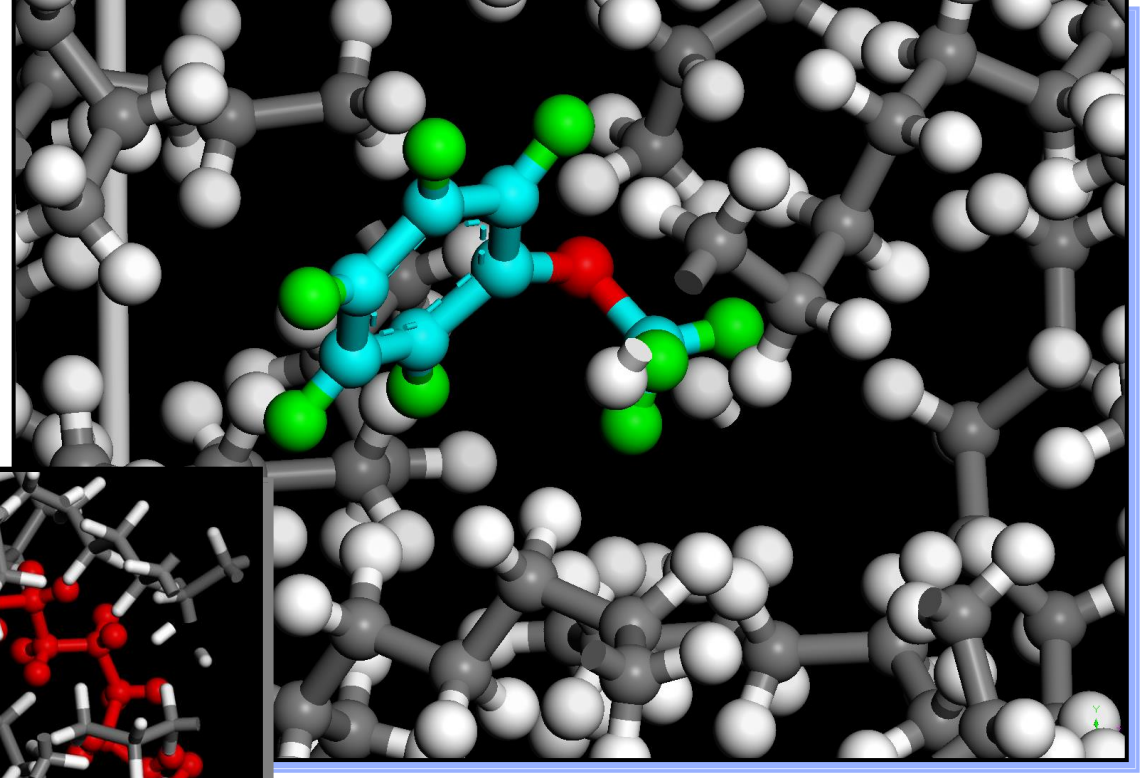


STICKING EVENTS CONTROL THE SCALING OF DIFFUSION

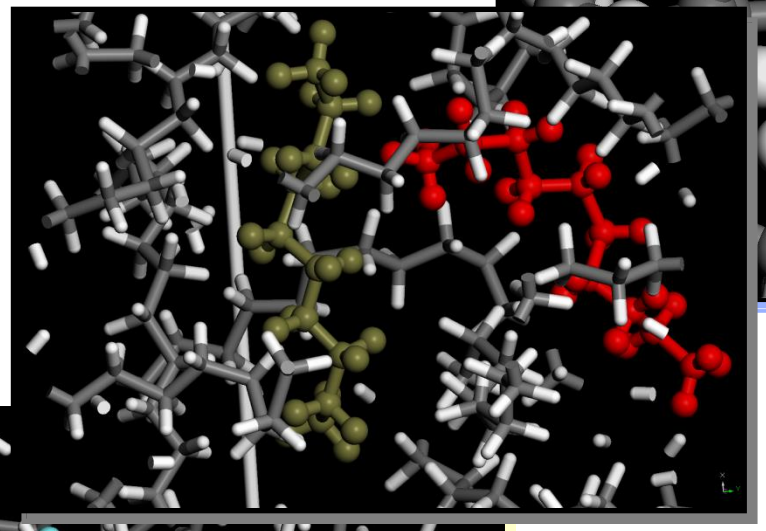
Example:
Molecular
Dynamics
simulation
methoxy
benzene i
amorphou
polyethyle
298 K

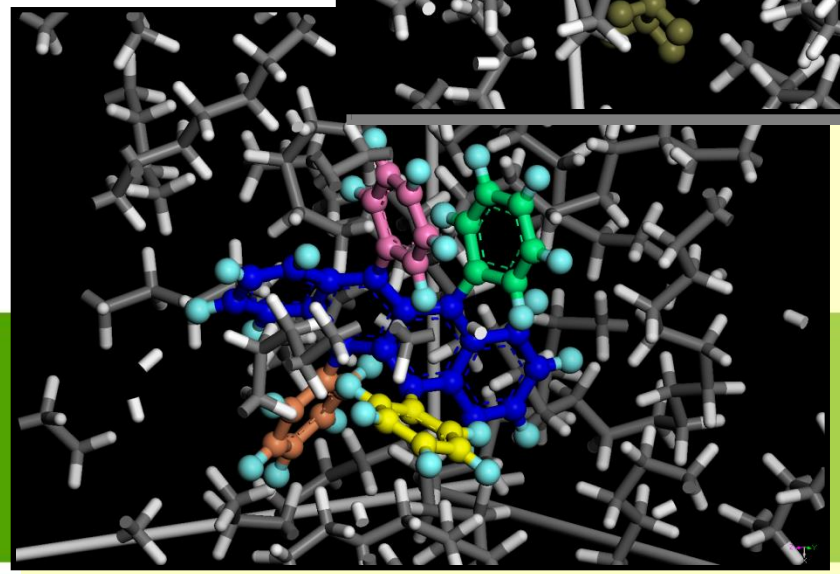


ANISOLE
108 g·mol^{-1}



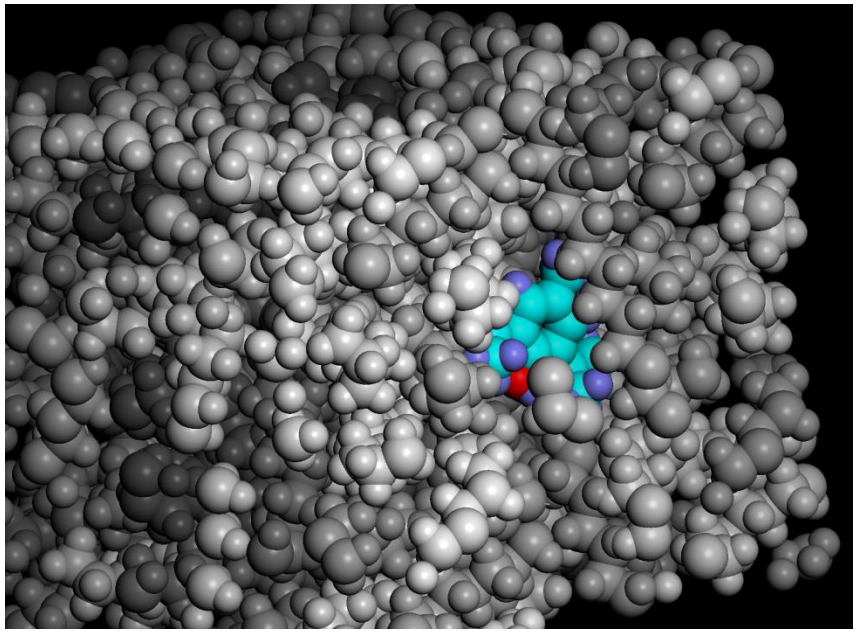
DECANE
142 g·mol^{-1}

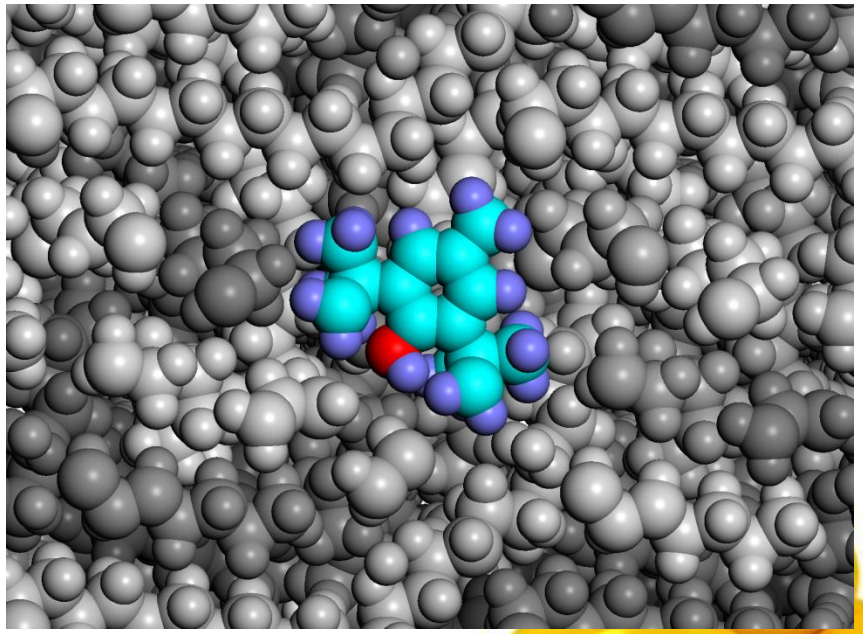




RUBRENE
532 g·mol^{-1}

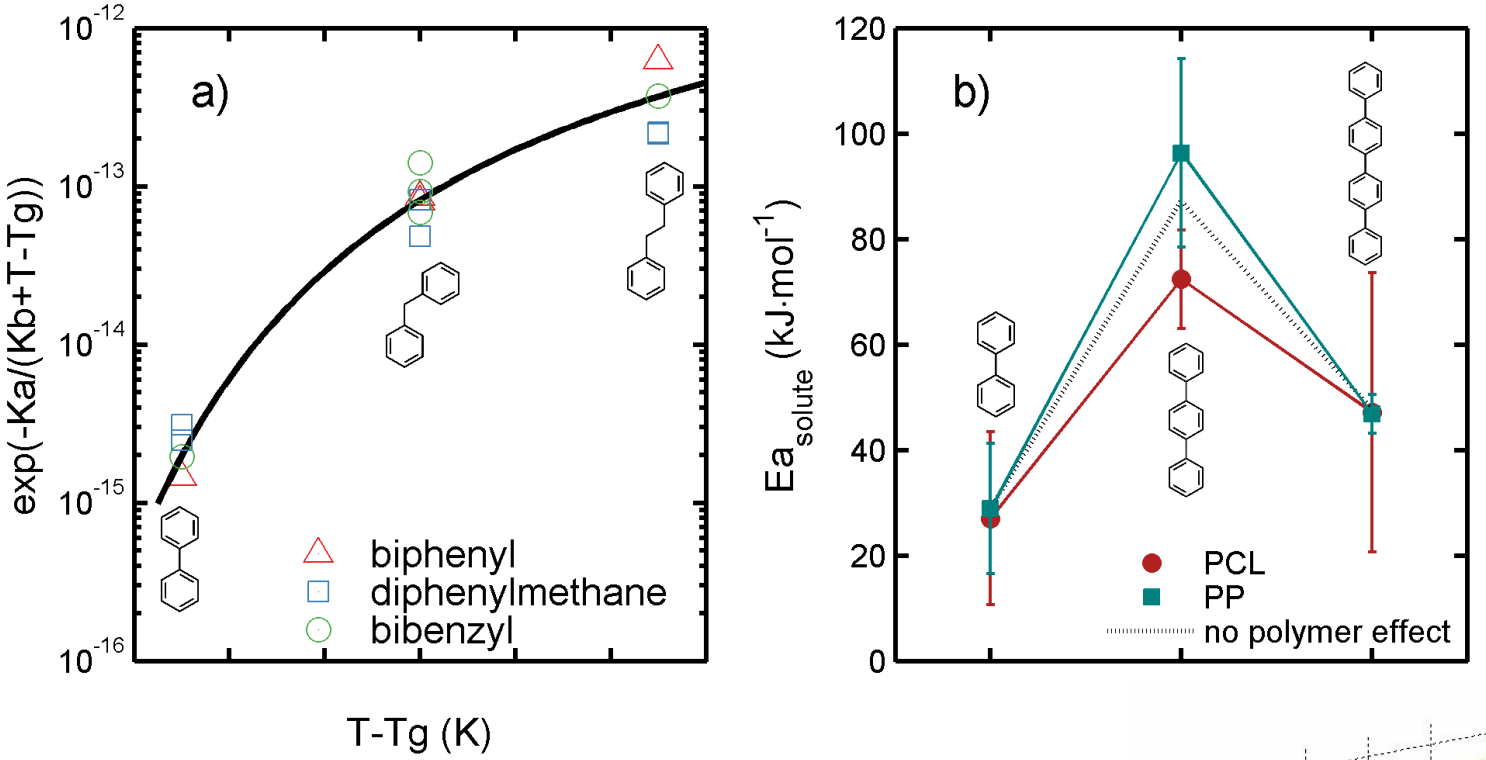
TRANSLATION MECHANISMS

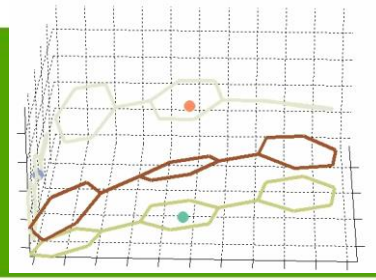


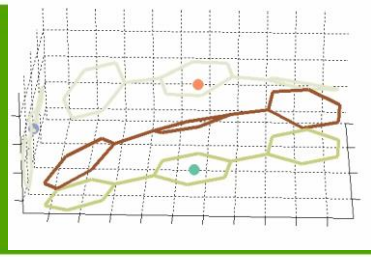


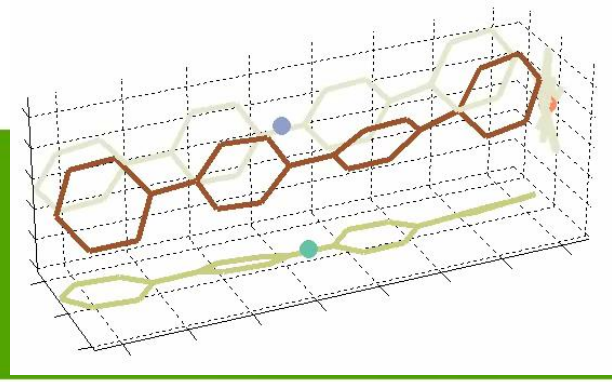
Scaling D with polymer

$$D = \bar{D}_0 \exp\left(-\frac{E_{solute}}{RT}\right)\exp\left(-\frac{K_a}{K_b + T - Tg_2}\right)$$









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Macromolecules
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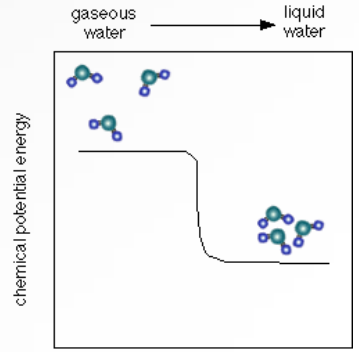
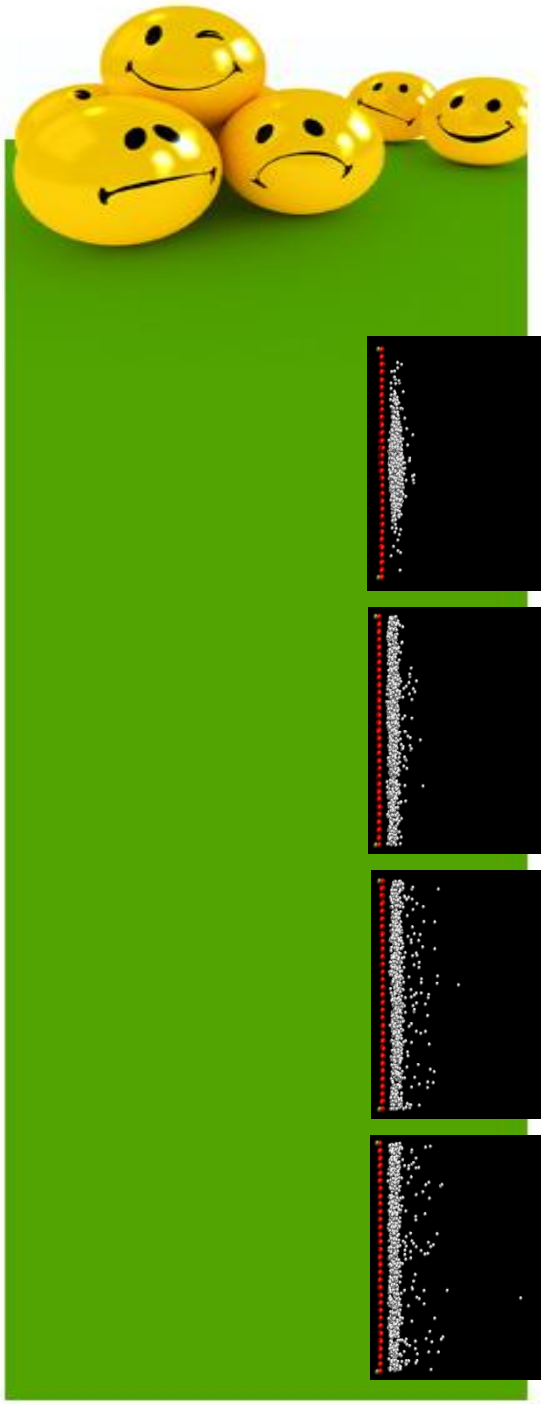
$$\mu_i = \left(\frac{\partial A}{\partial n_i}\right)_{T,V,n_i}$$

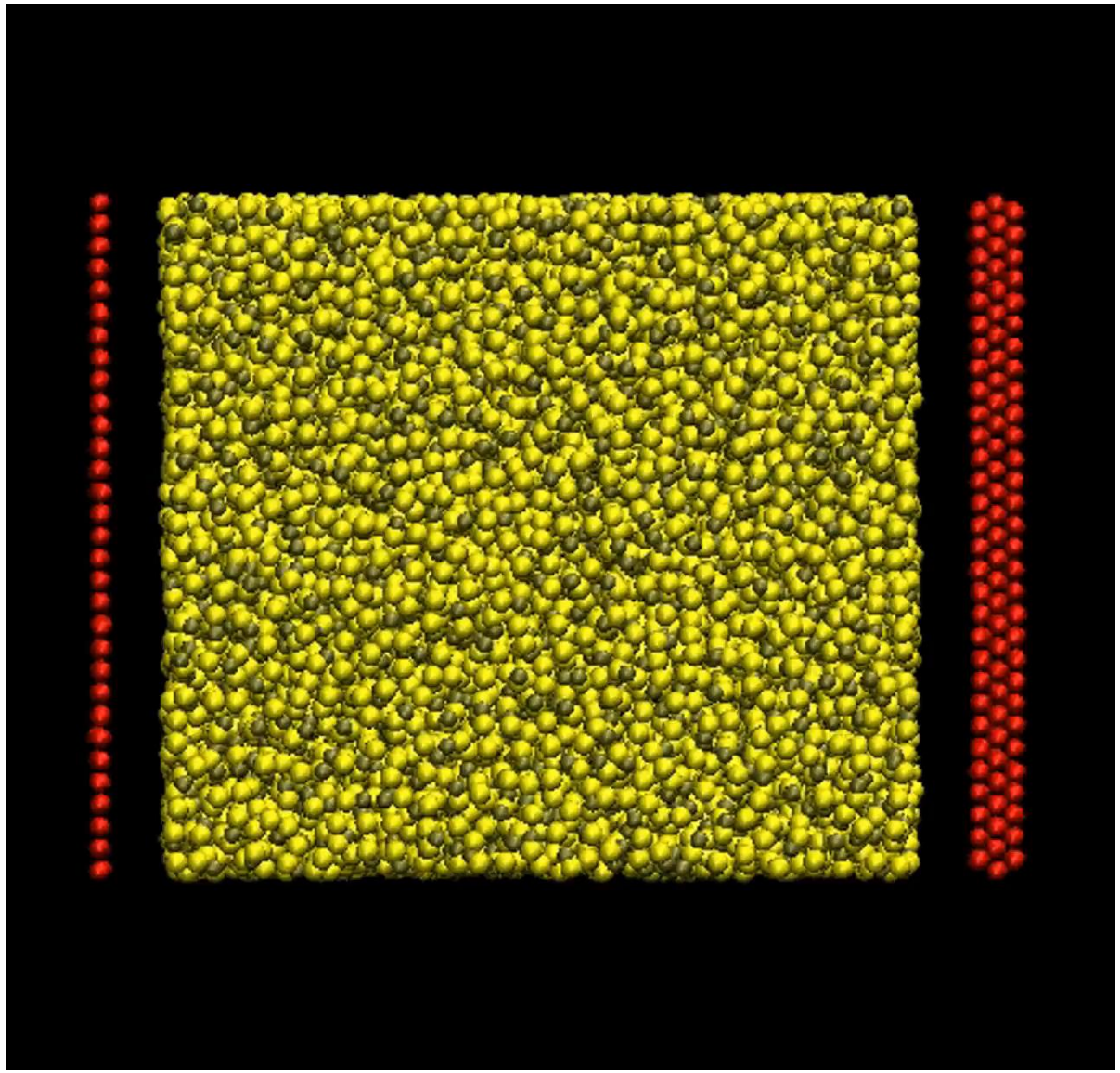


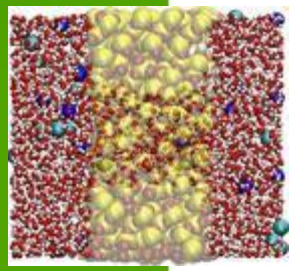
FOOD AND PACKAGING SYSTEMS

CHEMICAL POTENTIALS



Permeation





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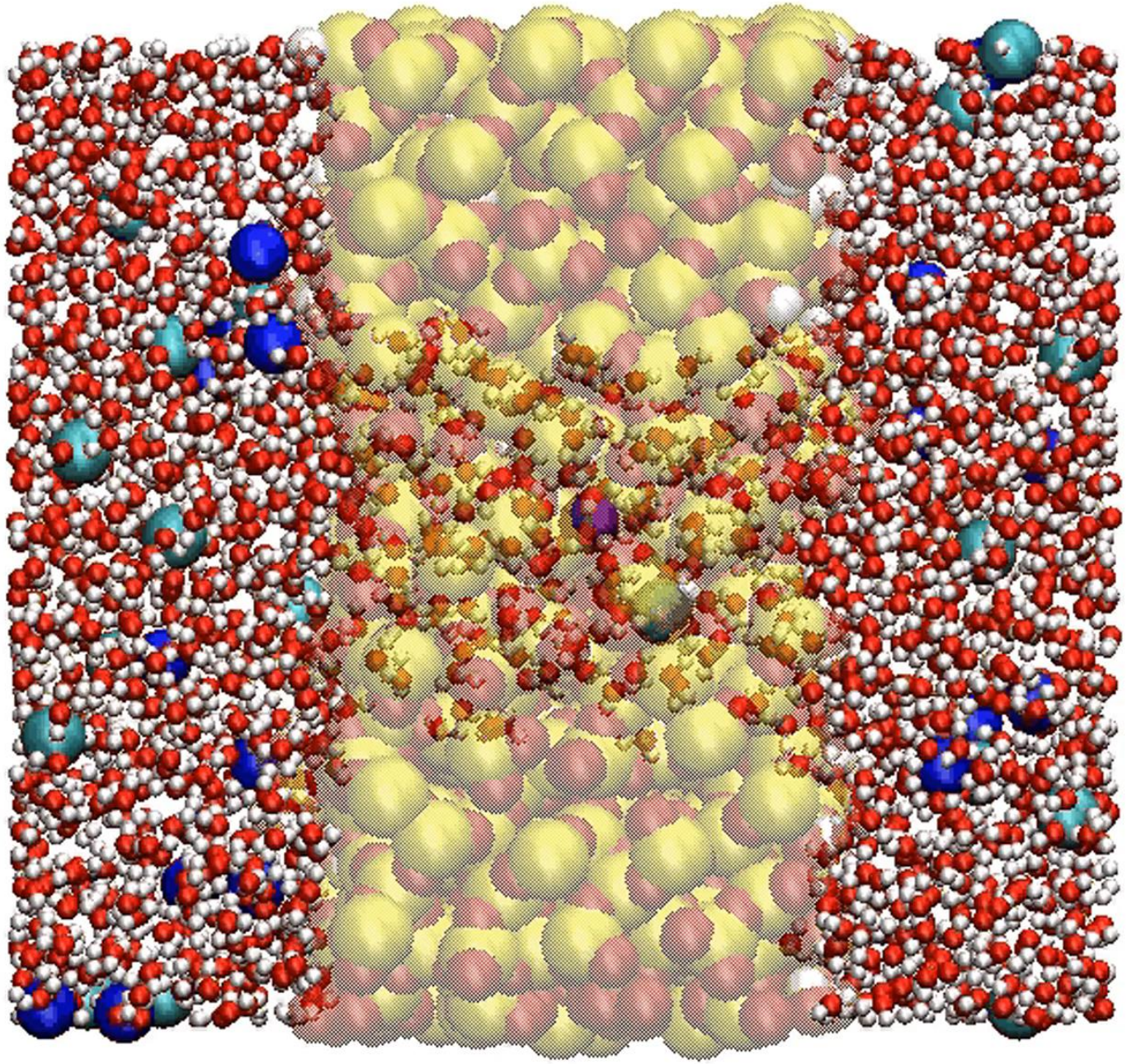
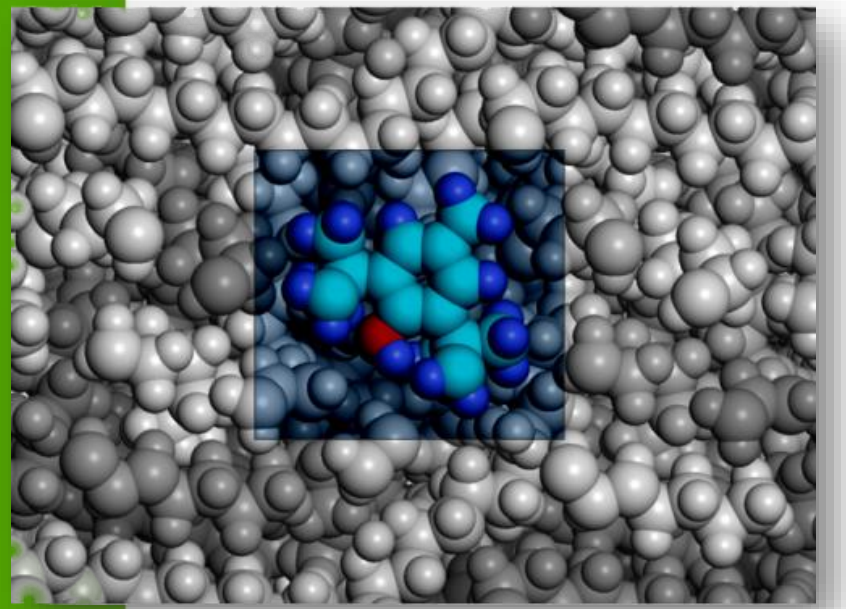


METHODS TO CALCULATE EXCESS CHEMICAL POTENTIAL IN POLYMERS FOR **MOLECULES DIFFERING IN SIZE AND SHAPE**

0: system state without solute
1: system state with one solute



$\langle \rangle_0$ =ensemble average for a given state 0

(averaging over 0 may be required)

- **Free energy perturbation**

$$\exp\left(-\frac{F_1-F_0}{k_BT}\right)=\left\langle \exp\left(-\frac{U_1-U_0}{k_BT}\right)\right\rangle_0$$

- **based on Jarsynski's equality** (1997)

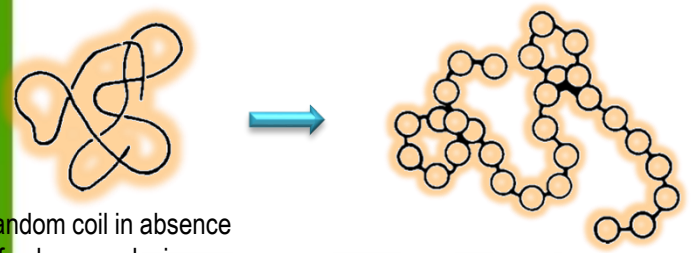
$$\exp\left(-\frac{F_1-F_0}{k_BT}\right)==\left\langle \exp\left(-\frac{W^{fast}}{k_BT}\right)\right\rangle_0$$

- **Thermodynamic integration** to extended ensembles

$$\frac{\partial}{\partial\lambda}F=\left\langle\frac{\partial}{\partial\lambda}U\right\rangle_\lambda$$

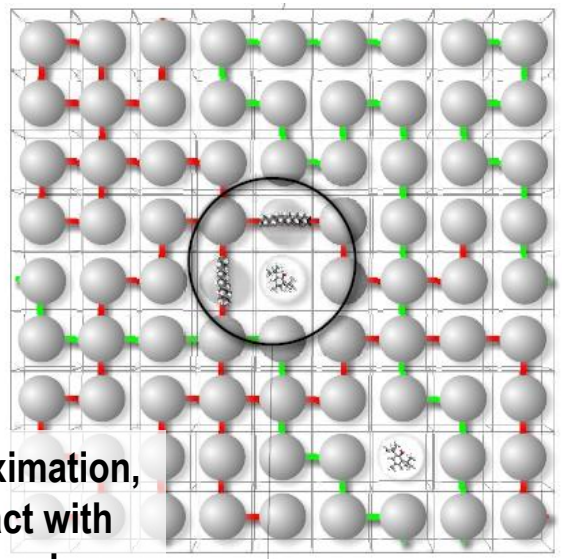
- **Replica exchange methods** = variant of above but without reaction coordinates (Metropolis algorithm to select likely configurations)
- **Possible biases**: only thermally accessible configurations contribute to exponential averaging

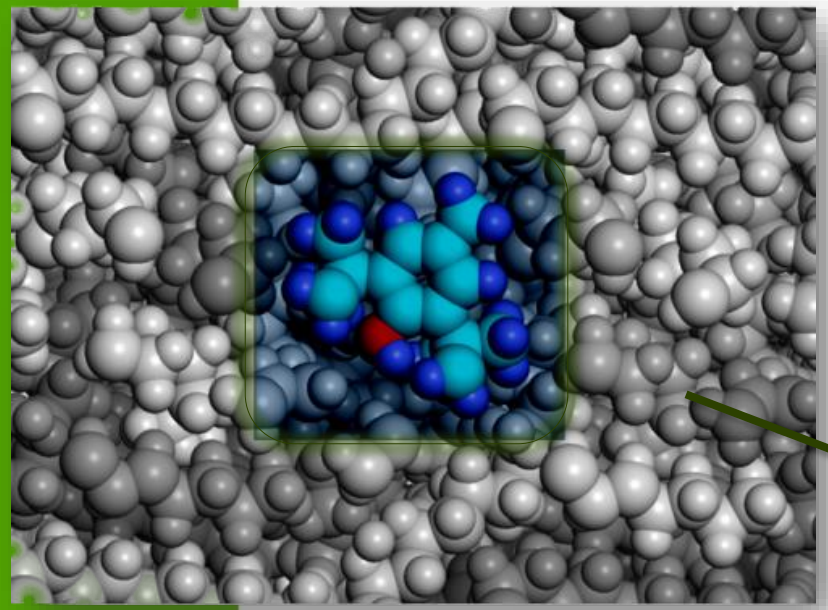
METHODS TO CALCULATE EXCESS CHEMICAL POTENTIAL IN POLYMERS FOR **MOLECULES DIFFERING IN SIZE AND SHAPE**



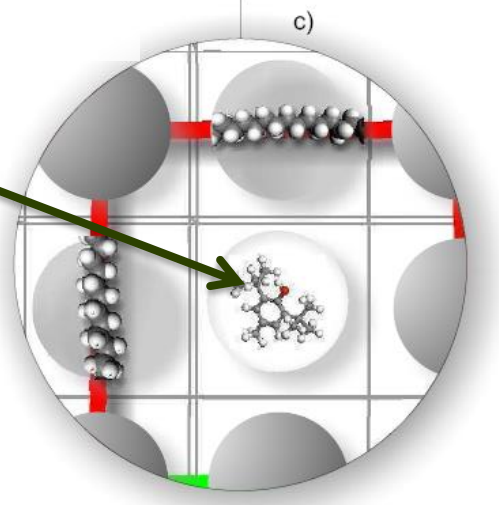
random coil in absence of volume exclusion

same configuration with excluding volumes



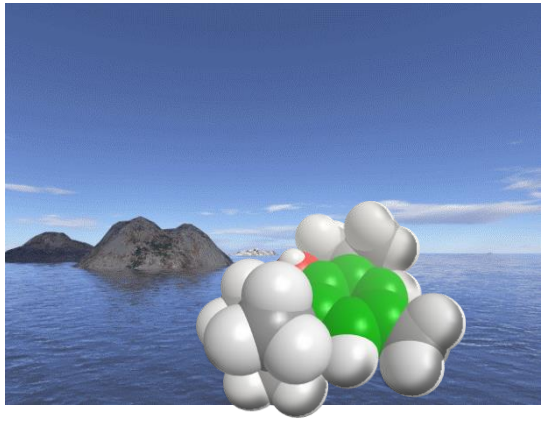


Flory approximation, solute interact with neighboring polymer blobs.



2,6-di-*tert*-butyl-4-methylphenol in 30 chains of HDPE ($C_{60}H_{120}$) = 5440 atoms

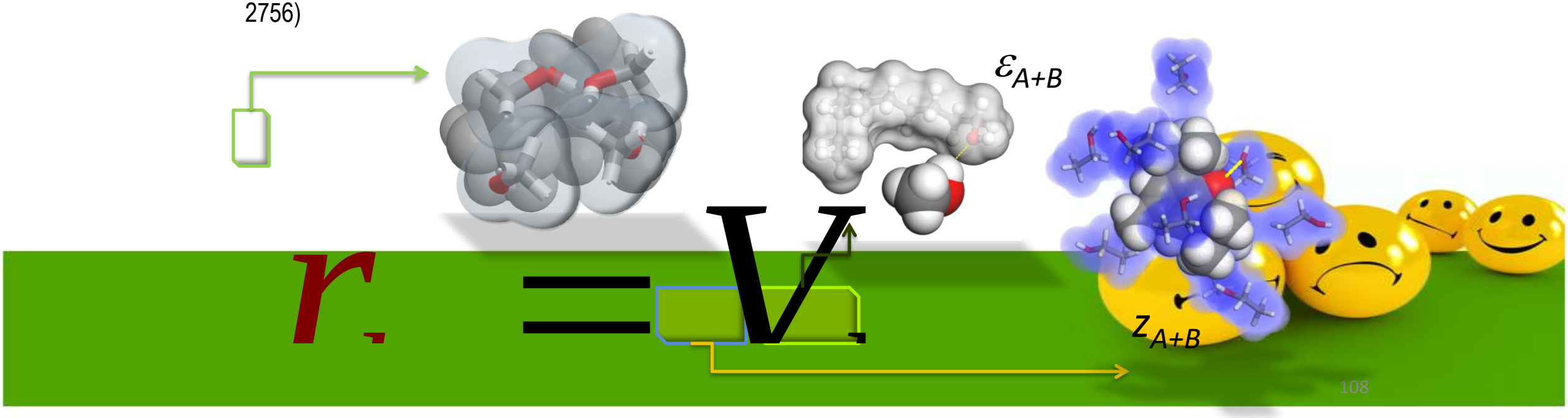
Off-Lattice Flory-Huggins Formulation of Excess Chemical Potentials in **Binary Blend-void Systems**



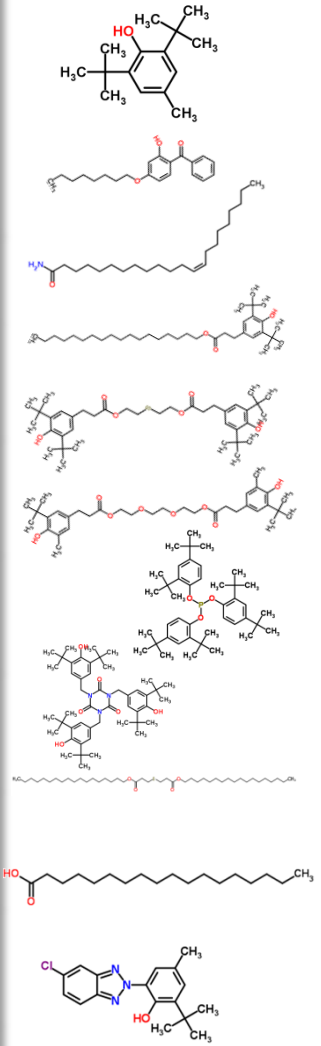
Flory expression at infinite dilution in *k*=P or in *k*=F

$$\int ,, ^{exc}$$

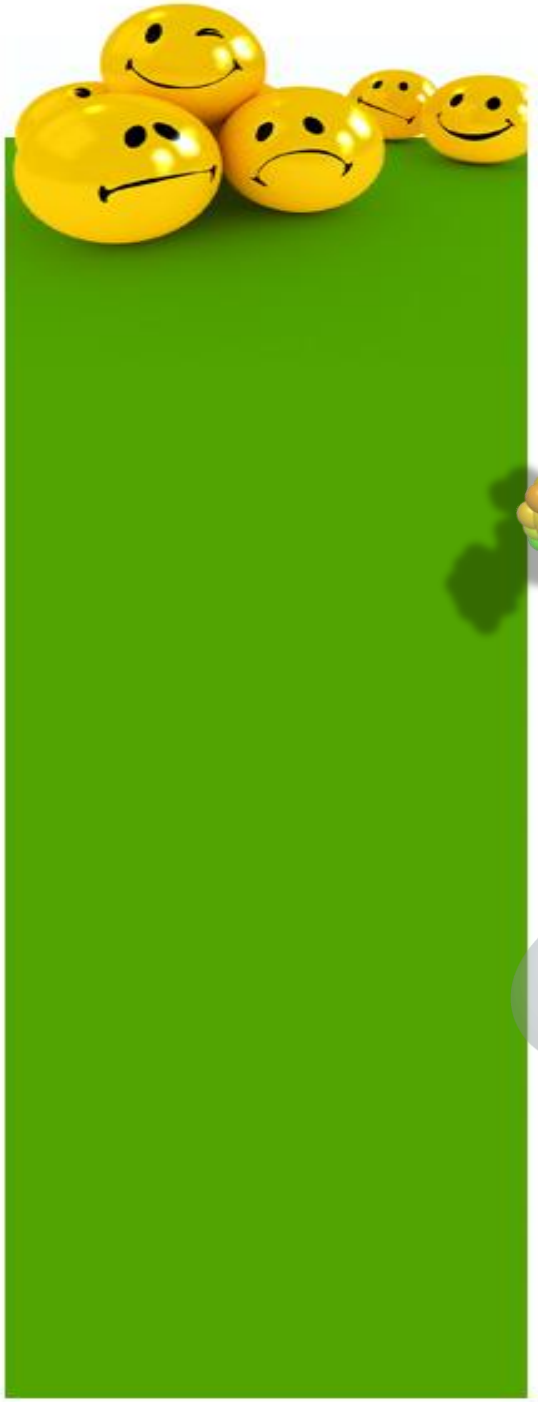
Off-lattice extension (Bawendi M. G., Freed K. F., *J. Chem. Phys*. 1988, 88, 2741-2756)

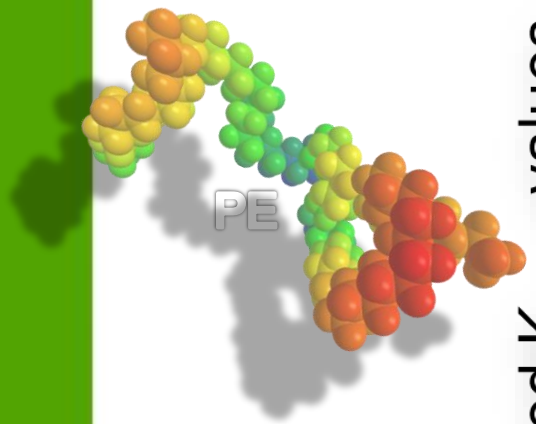


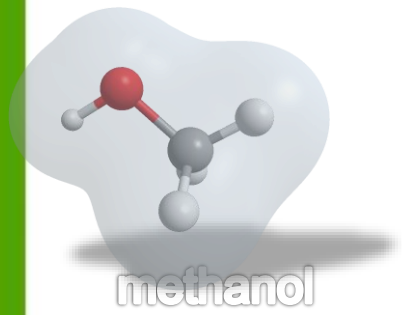
Alkanes	Alcohols	Volatiles	Plastics additives
decane	decanol	camphor	BHT
undecane	undecanol	diphenyl oxide	chimassorb 81
dodecane	dodecanol	diphenylmethane	Erucamide
tridecane	tridecanol	d-limonene	Irganox 1076
tetradecane	tetradecanol	dl-menthol	Irganox 1035
pentadecane	pentadecanol	eugenol	Irganox 245
hexadecane	hexadecanol	isoamyl acetate	Irgafos 168
heptadecane	heptadecanol	linalyl acetate	Irganox 3114
octadecane	octadecanol	phenylethyl alcohol	Irganox ps802
nonadecane	nonadecanol		stearic acid

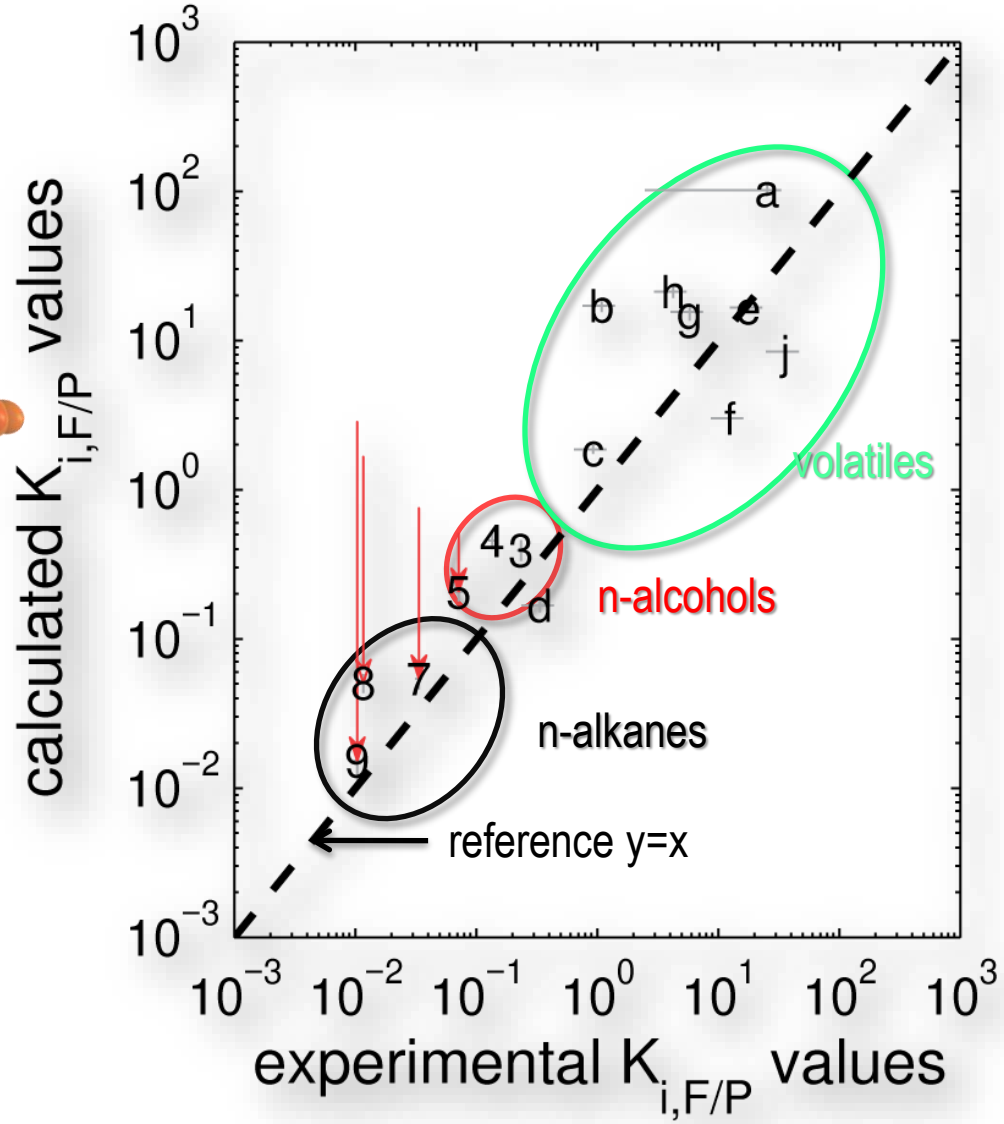


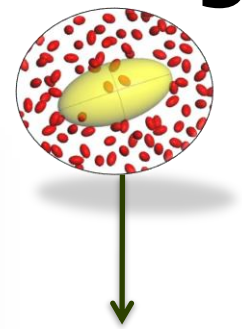
Liquid-polymer partitioning





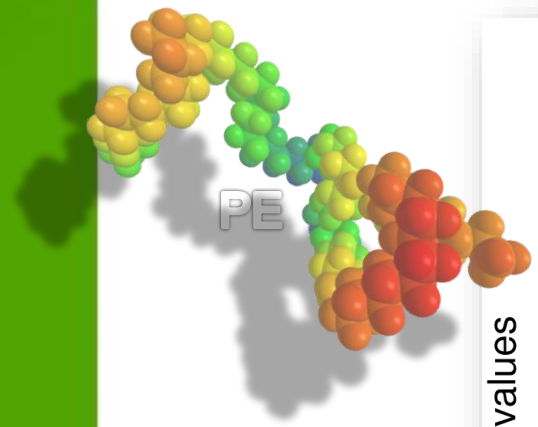


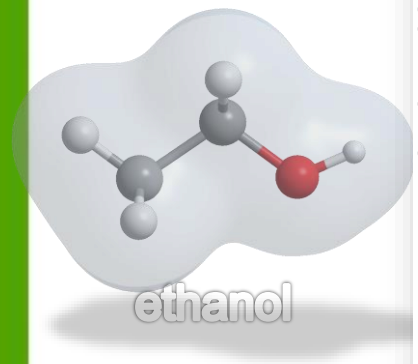


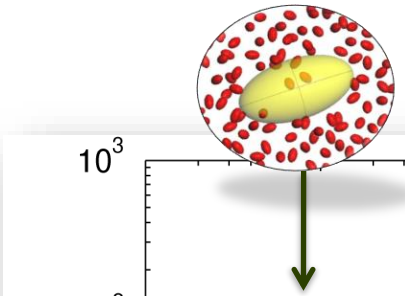


Effect of overlapping F molecules

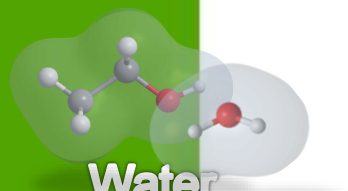
Liquid-polymer partitioning

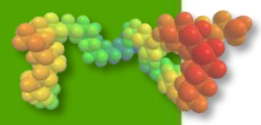






Partitioning with ternary mixtures

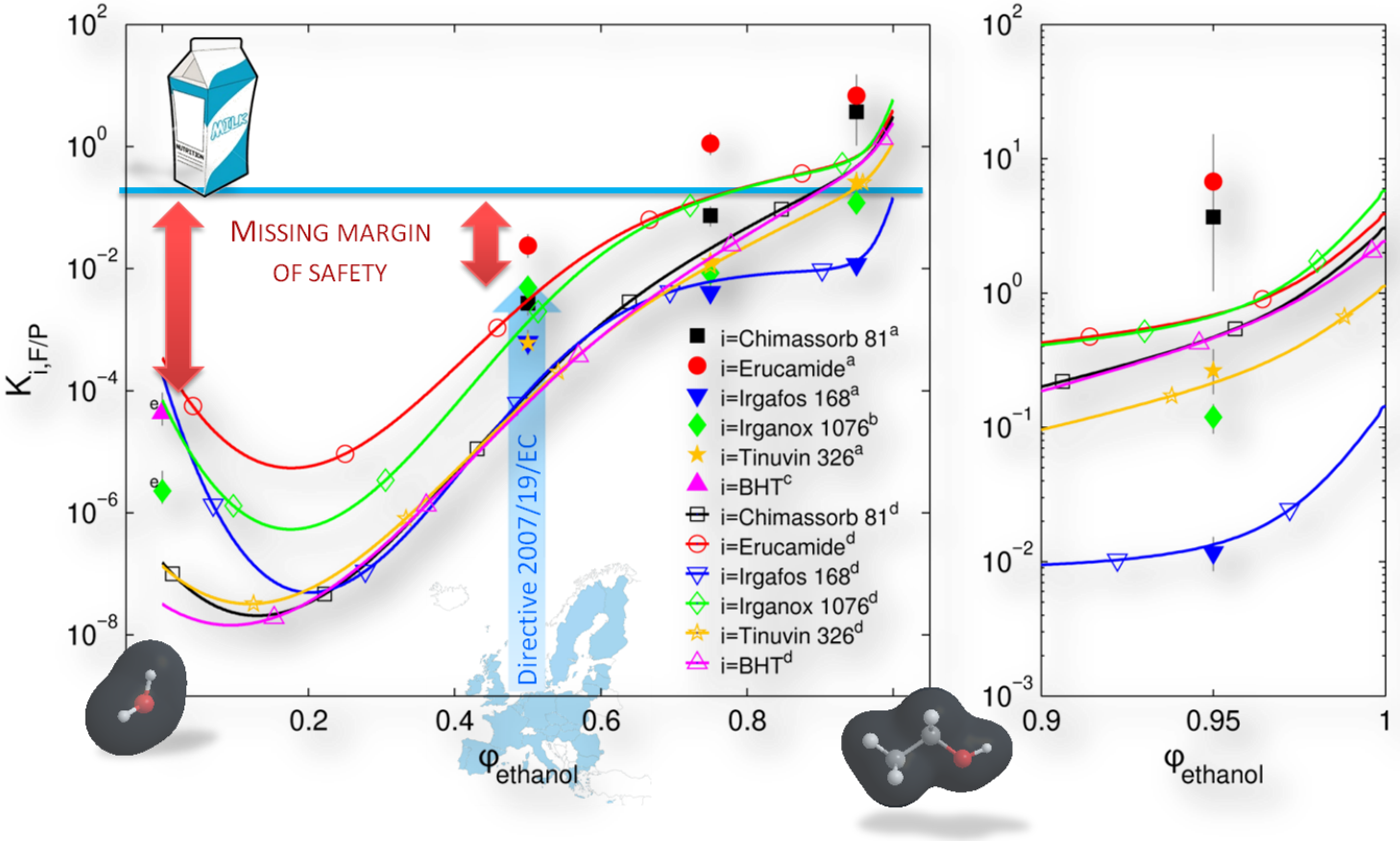




$$\ln K_{i,(F_1+F_2)/P} = 1 + \chi_{i,P} - \ln \gamma^{v}_{i,F_1+F_2} \approx -2\frac{V_i^{vdw}}{V_{F_2}^{P}}\frac{\partial \chi_{F_1,F_2}}{\partial \phi_{F_2}}\phi_{F_2}^3 + \frac{V_i^{vdw}}{V_{F_2}^{P}}\left(\chi_{F_1,F_2} + 3\frac{\partial \chi_{F_1,F_2}}{\partial \phi_{F_2}}\right)\phi_{F_2}^2$$

$$+\left(r_{i,F_2}^{-1} - r_{i,F_2}^{-1} + \chi_{i,F_1} - \frac{V_i^{vdw}}{V_{F_2}^{P}}\chi_{i,F_2} + \frac{V_i^{vdw}}{V_{F_2}^{P}}\chi_{F_1,F_2} - \frac{V_i^{vdw}}{V_{F_2}^{P}}\frac{\partial \chi_{F_1,F_2}}{\partial \phi_{F_2}}\right)\phi_{F_2}$$

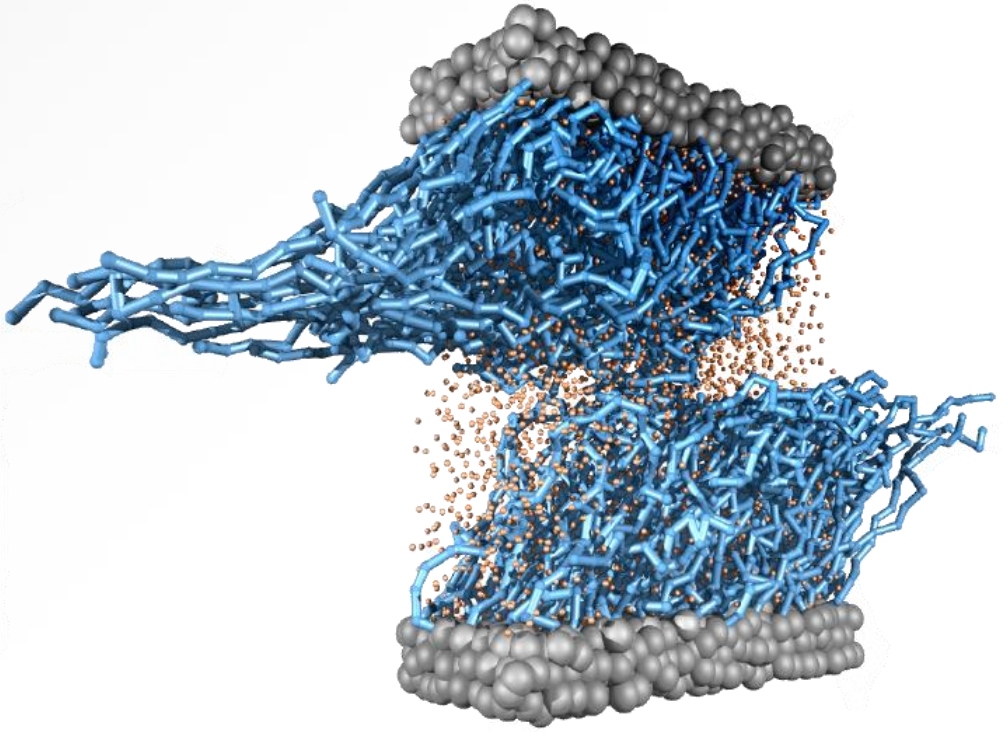
$$+r_{i,F_1}^{-1} + \chi_{i,P} - \chi_{i,F_1} + o(\text{ternary interaction term})$$



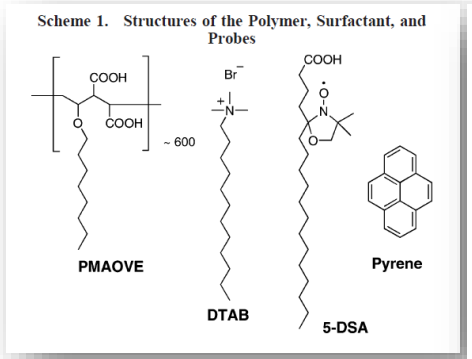
Gillet G., Vitra
Desobry S. (20
Prediction of P
Coefficients of
Additives betw
Packaging Mat
Food Simulant
& Engineering
Research, 49(1

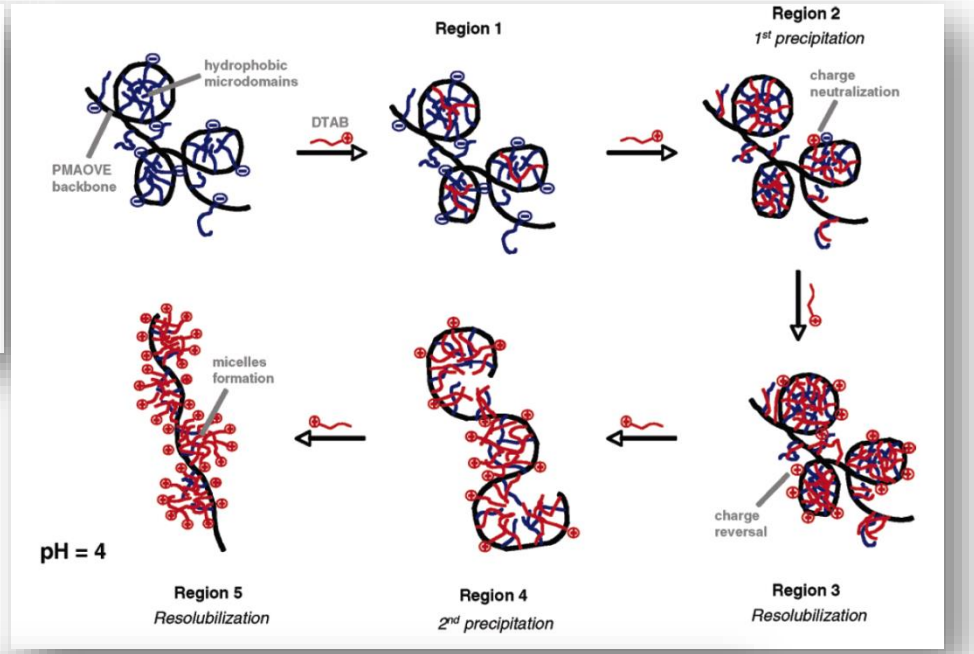
Examples of works (unofficial review)

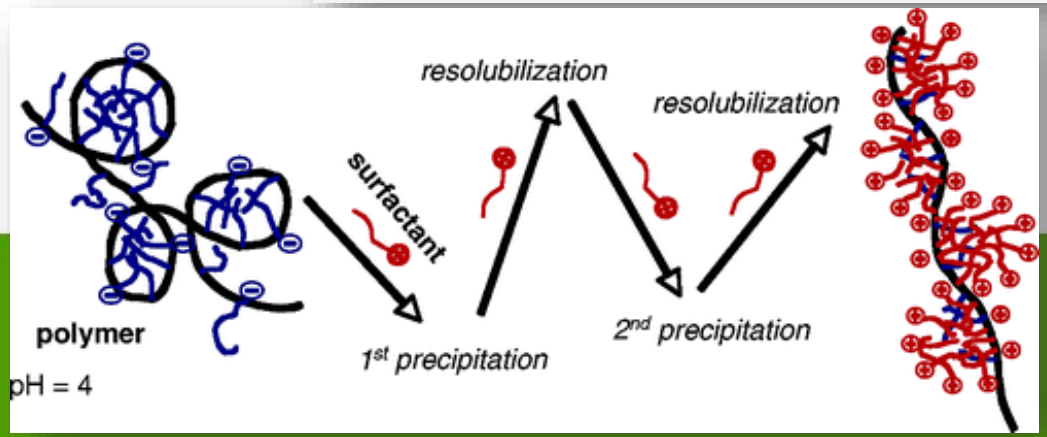
UNILEVER



Interactions of a Hydrophobically Modified Polymer with Oppositely Charged Surfactants







Industrial collaborator Dr. K. P. Ananthapadmanabhan, Unilever Research, Trumbull, CT.

Hydrophobically modified polelectrolytes are important in a range of applications due to their ability to associate with materials that are important in cosmetics, paints and foods.

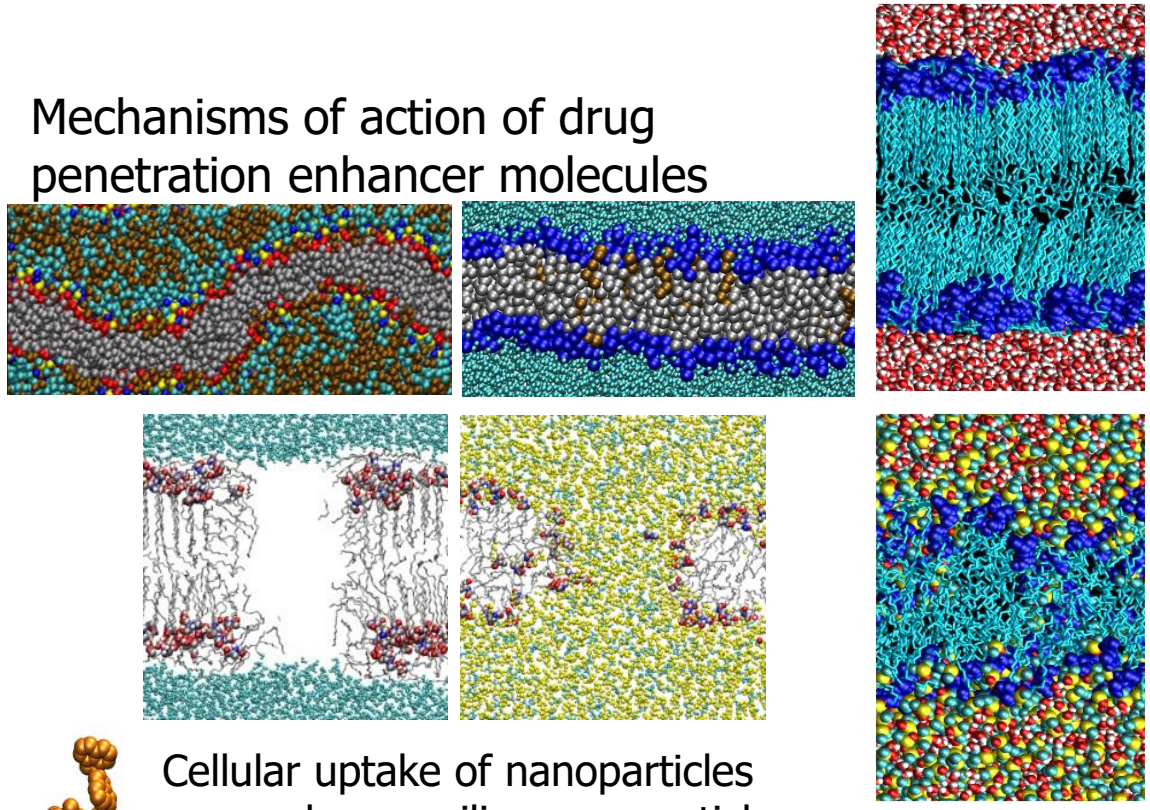
The mechanism of association/dissociation of a hydrophobically modified anionic polymer with a cationic surfactant was elucidated by a multi-pronged battery of techniques.

Reference: Langmuir, *23*, 5906-5913 (2007).

Modeling transdermal permeation.

Predicting the dermatopharmacokinetics of percutaneous solutes

Mechanisms of action of drug penetration enhancer molecules



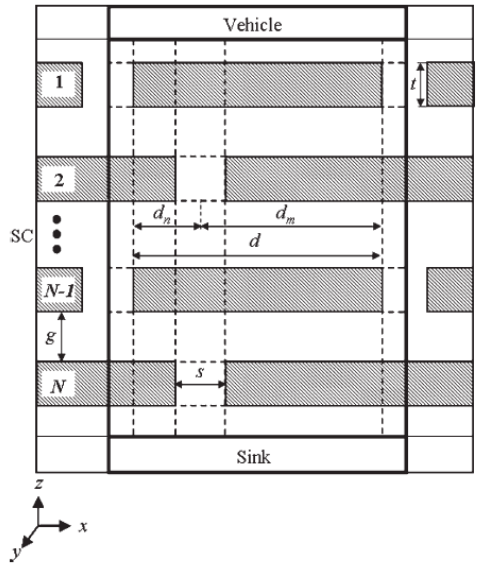
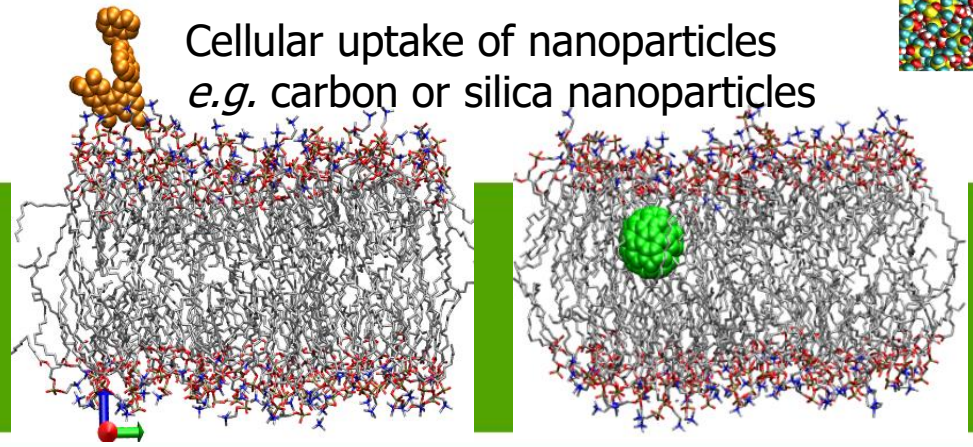


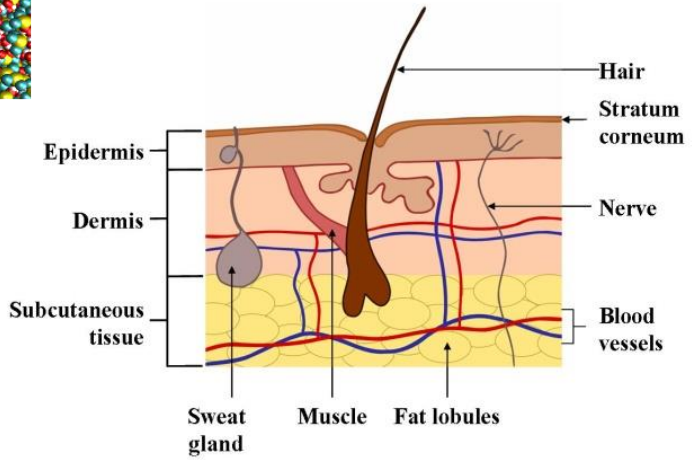
Figure 2. Schematic diagram of the "bricks-and-mortar" model of human stratum corneum (SC).

Corneocyte width (d), corneocyte thickness (t), number of corneocyte layers (N), the vertical gap between corneocytes (g), the lateral spacing between corneocytes (s), and the offset ratio ($w = d_m/d_n$).

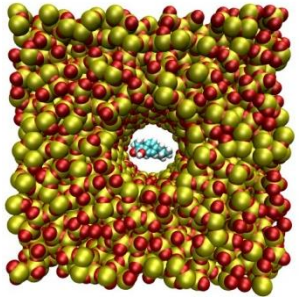
AIChE J., 2010, 56(10), 2551-2560
Biophys. J., 2007, 93:2056.
Biophys. J., 2008, 95:4763

Cellular uptake of nanoparticles
e.g. carbon or silica nanoparticles

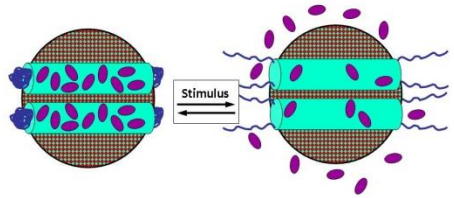




Multifunctional nanoparticles

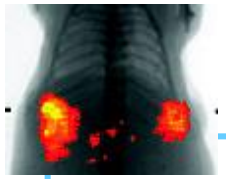


Encapsulation

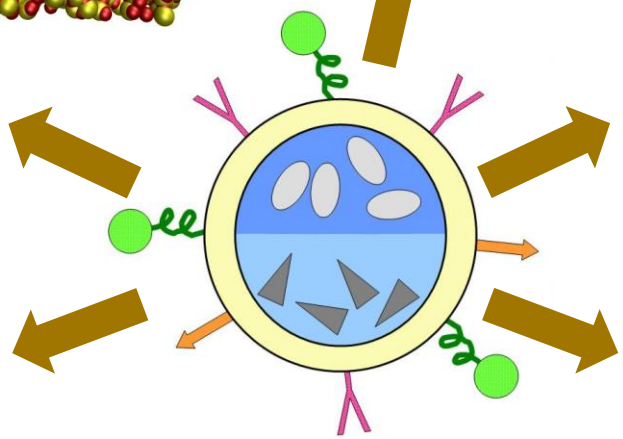


Site-targeted delivery *e.g.* tumours

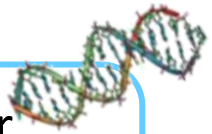
Controlled release



Imaging: combined diagnostics and therapeutics



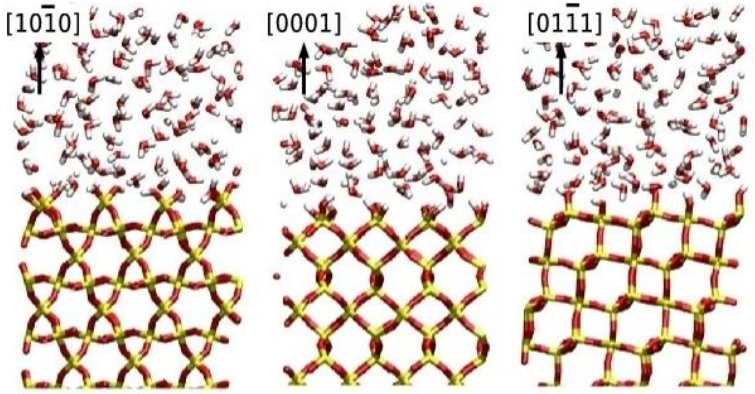
Multifunctional inorganic nanoparticles



Technology for **challenging molecules** (gene therapy)

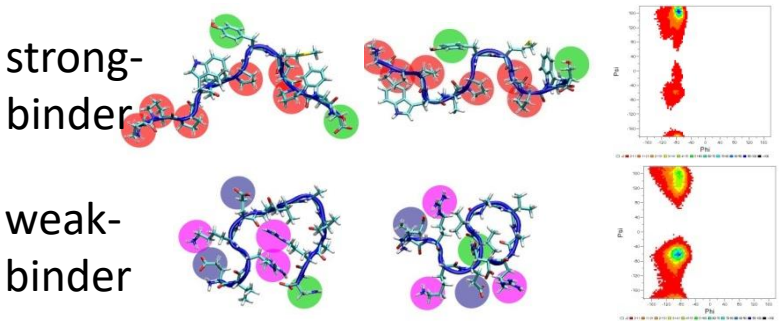
Interactions with inorganic surfaces

Structure and dynamics of water on quartz surfaces



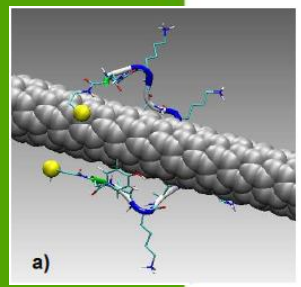
Notman, R. and Walsh, T. R., *Molecular dynamics studies of the interactions of water and amino acid analogues with quartz surfaces*, Langmuir, **2009**, 3:1638.

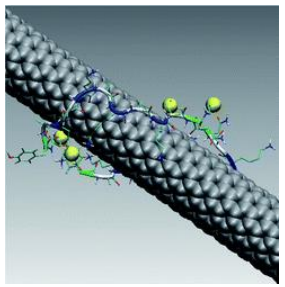
Conformation and energetics of peptides in solution

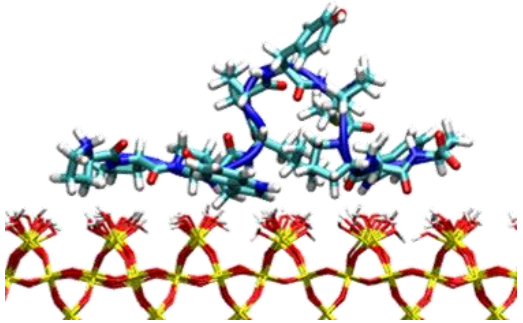


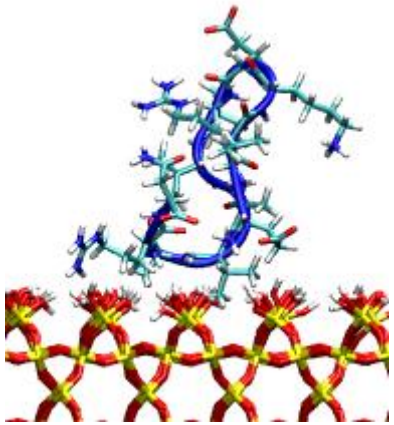
Friling, S. R., Notman, R. and Walsh, T. R., *Probing diameter-selective solubilisation of carbon nanotubes by reversible cyclic peptides using molecular dynamics simulations*, Nanoscale, **2010**, in press.

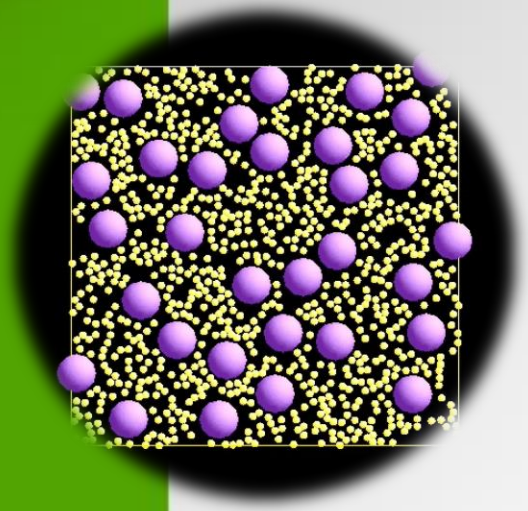
Peptides binding

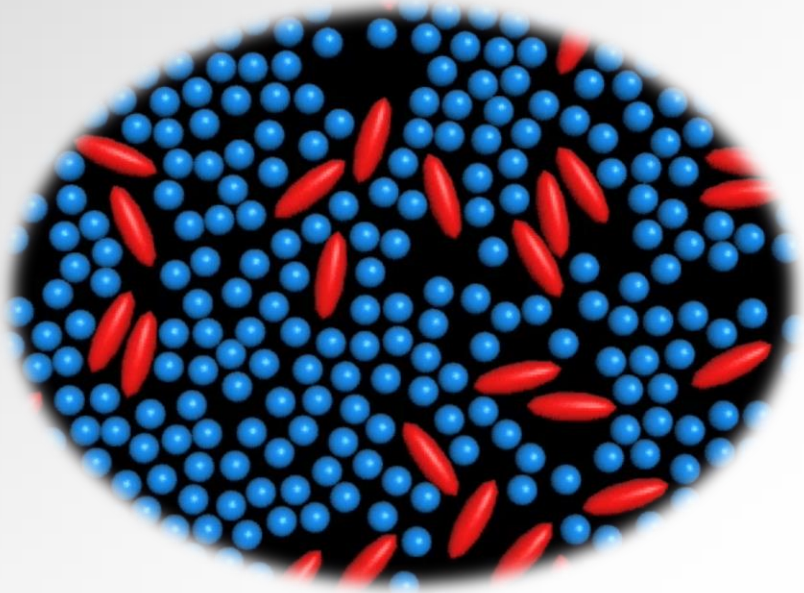










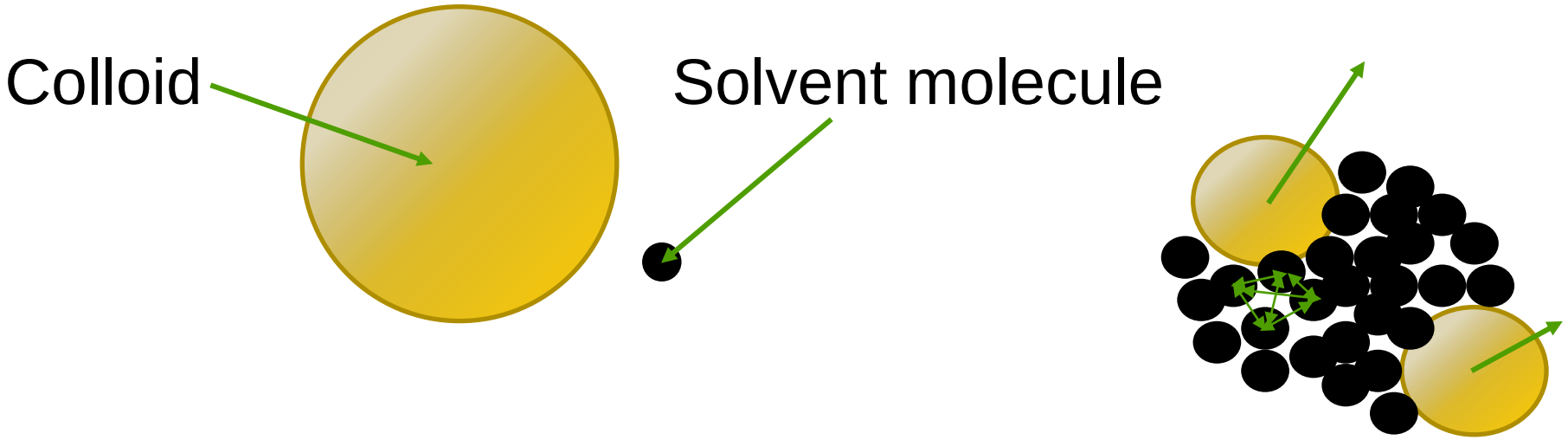


Brownian – Hydrodynamic interactions

EXTENSION TO NON-THERMAL NOISE

INRA SCIENCE & IMPACT

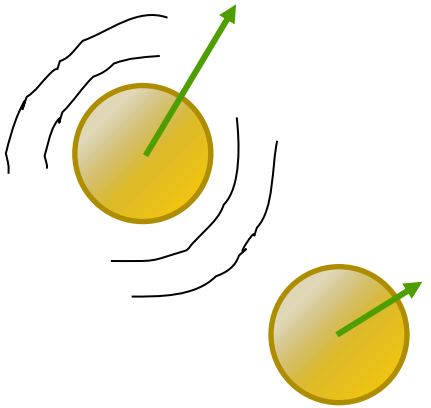
The problem



- Colloids >> solvent molecules
  - Stupendous amount of solvent molecules; E.g 10^{11} water molecules per R=1 μm colloid.
  - Coarse-graining is necessary

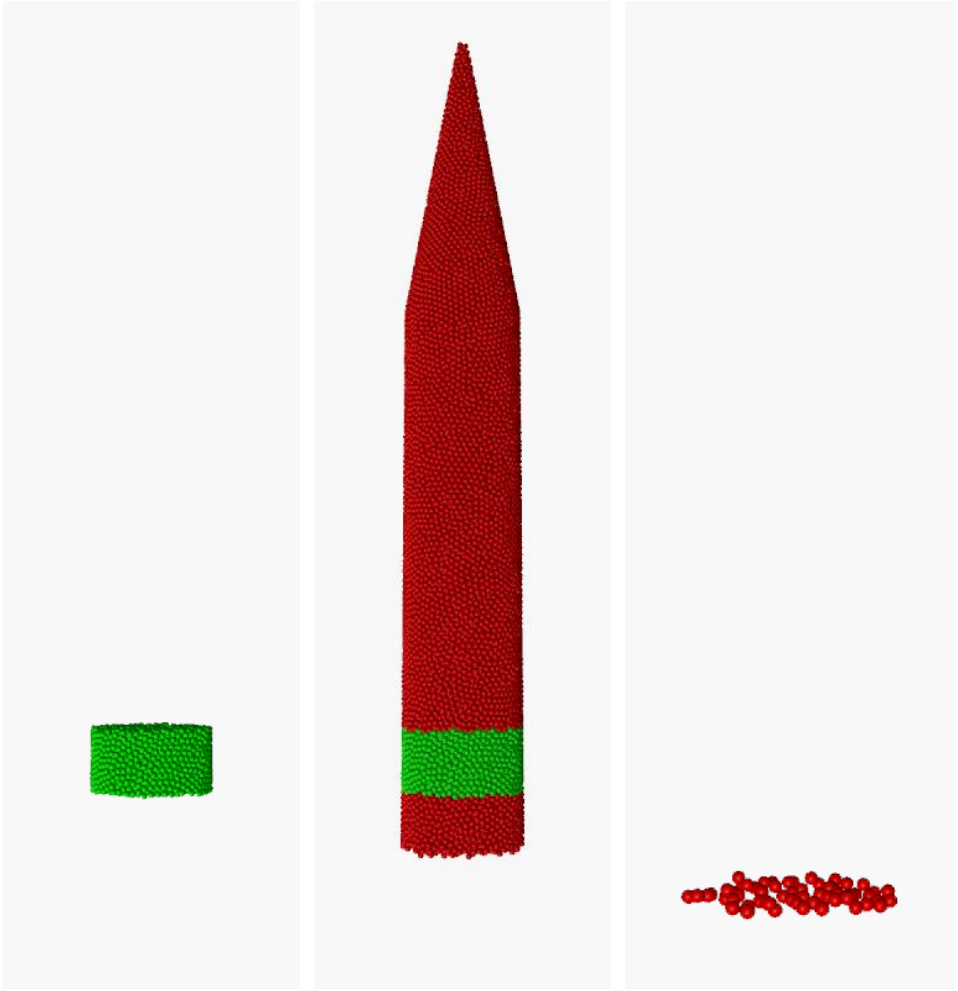
Stokesian Dynamics

- Approximate solution of Stokes' equation for many spheres in a solvent ("Oseen tensor")
- No explicit solvent
- Only correct at low densities of spheres
- Only correct in the bulk
- Non-spherical particles extremely difficult
- Relatively expensive



J.F. Brady and G. Bossis, Ann. Rev. Fluid Mech. **20**, 111 (1988)

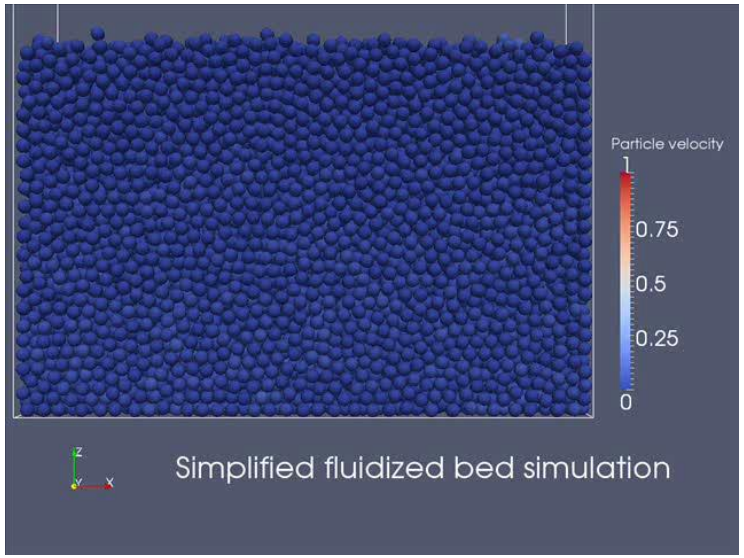
Hopper flow

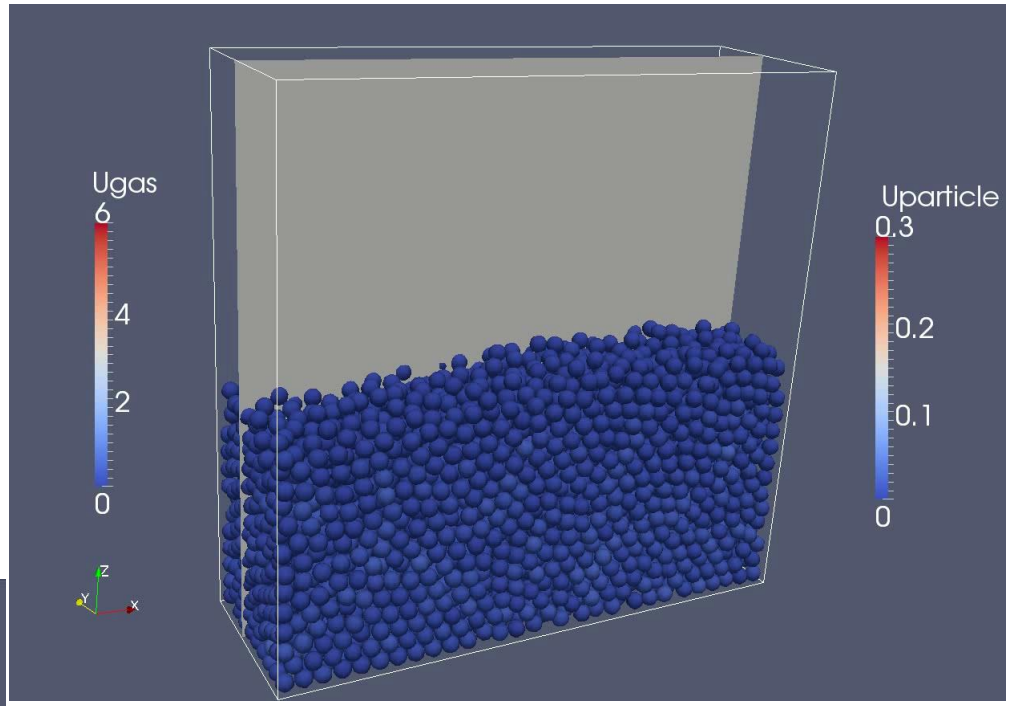


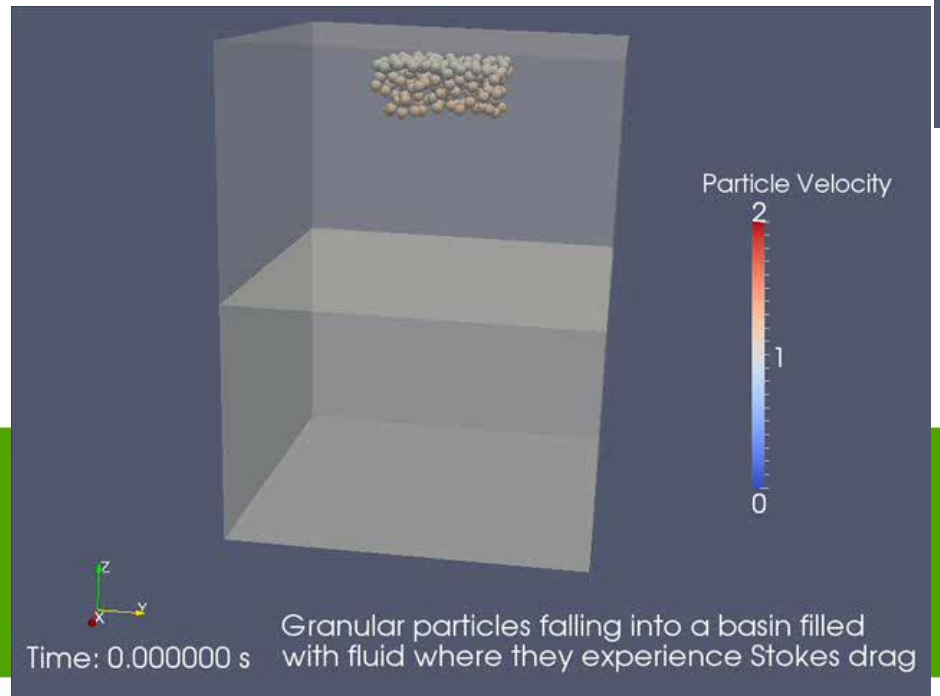
This is work by James Landry (jwlandry at gmail.com), formerly at Sandia, now at MIT Lincoln Labs, modeling flow of granular material from a hopper. Such models can be used to study flow rates and mixing as a function of geometry, or jamming that can occur near the mouth of the hopper.

J. W. Landry, G. S. Grest, L. E. Silbert, S. J. Plimpton, Phys Rev E, 67, 041303 (2003)

Stokesian Dynamics

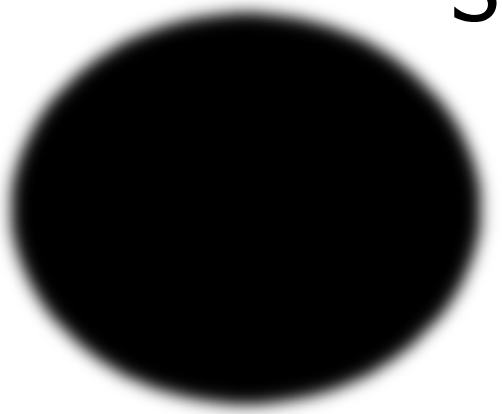


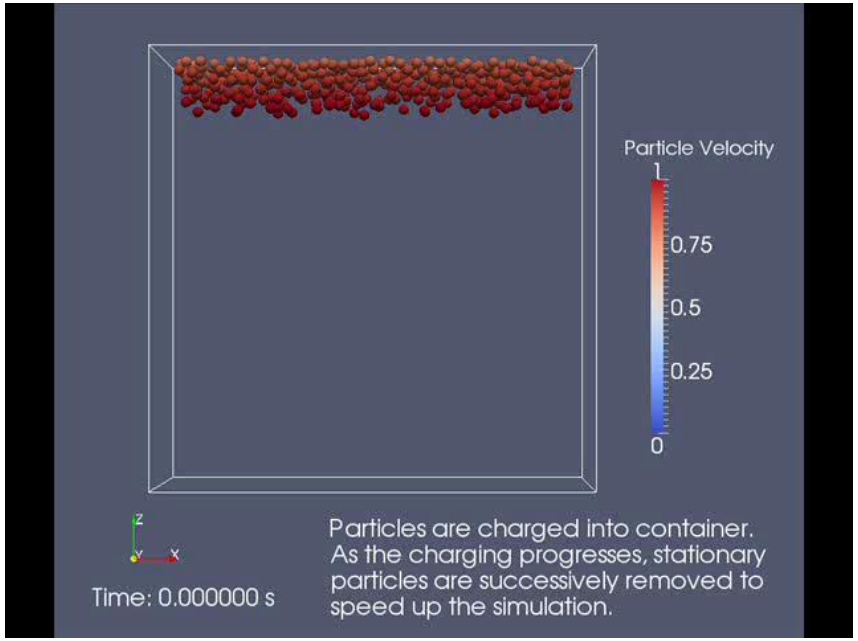


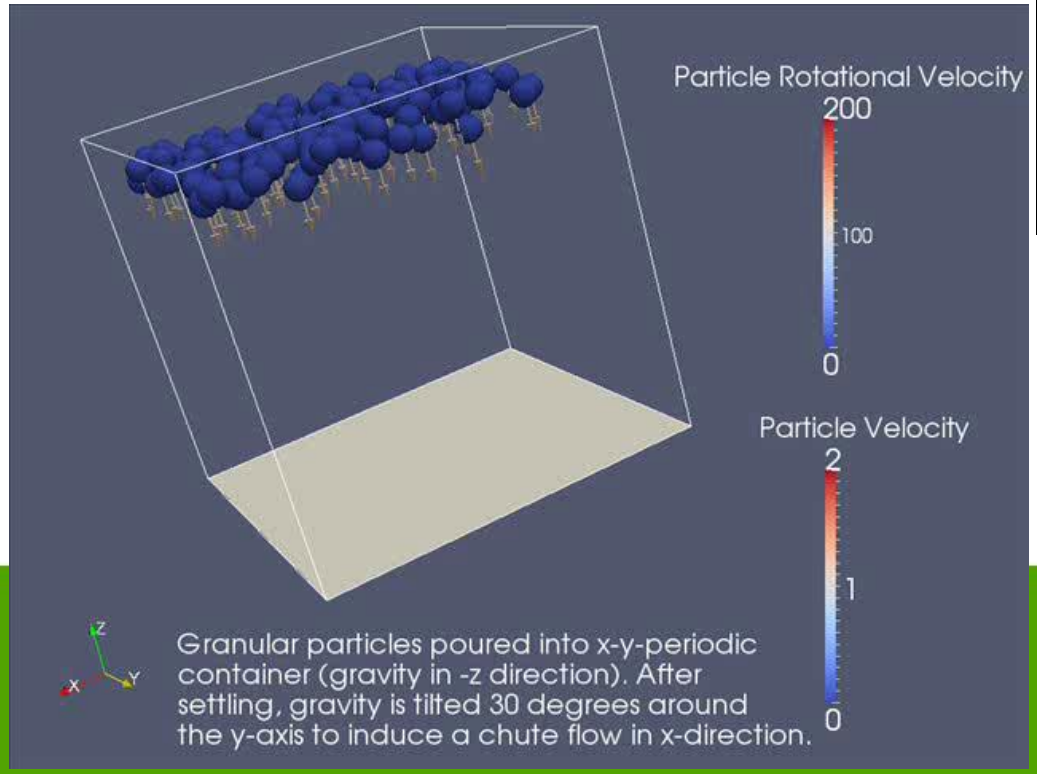


by Christoph Kloss (christoph.kloss at jku.at) and Christoph Goniva at the Johannes Kepler University (JKU) in Austria,

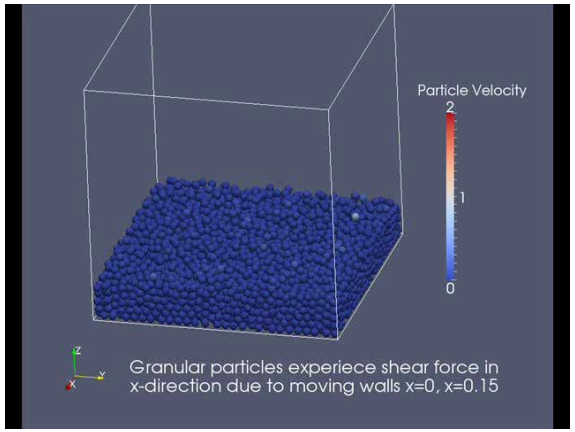
Stokesian Dynamics

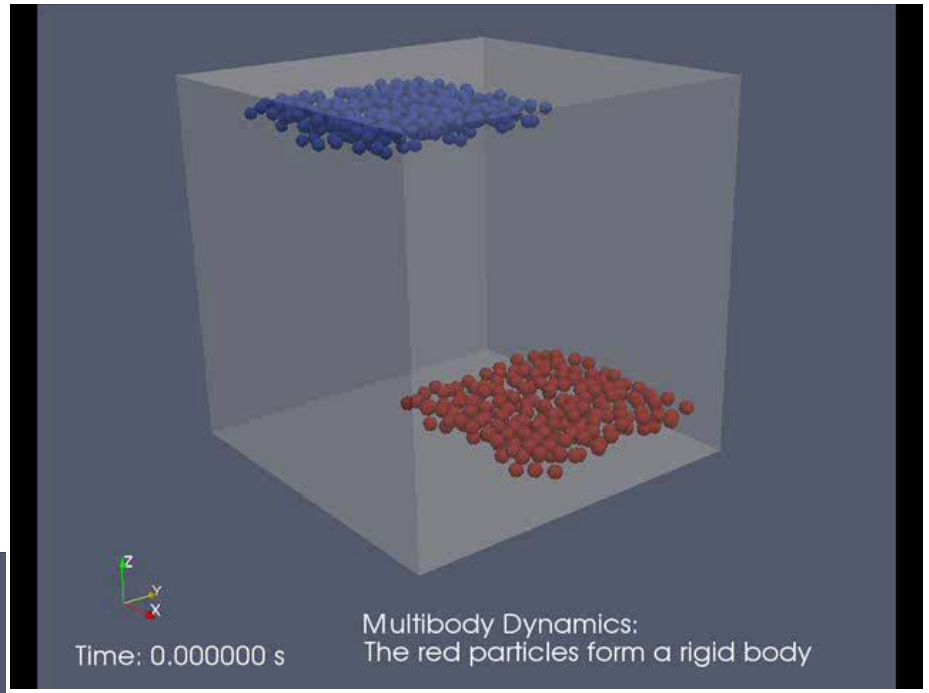


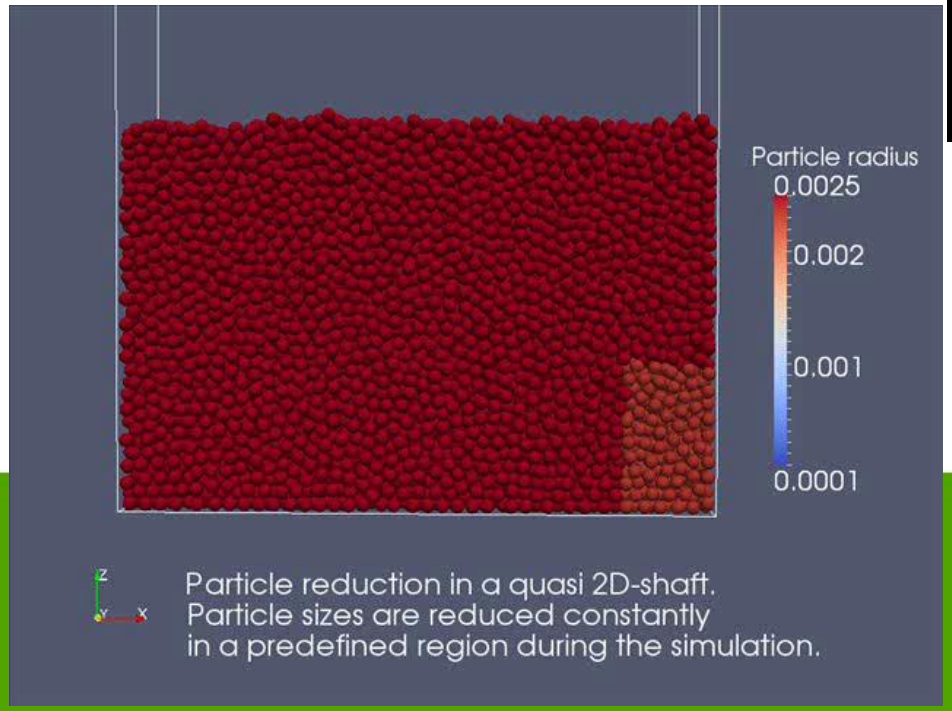




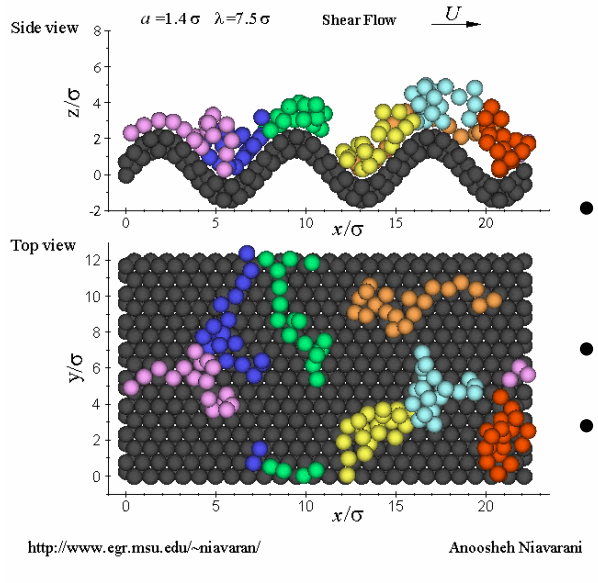
Stokesian Dynamics



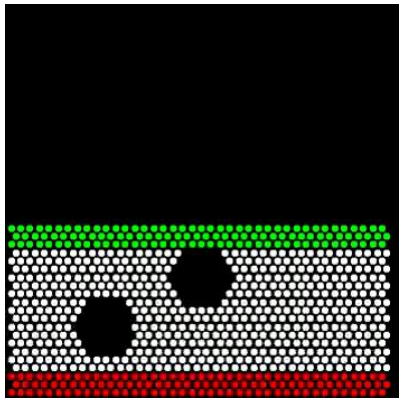




Dissipative Particle Dynamics (DP)

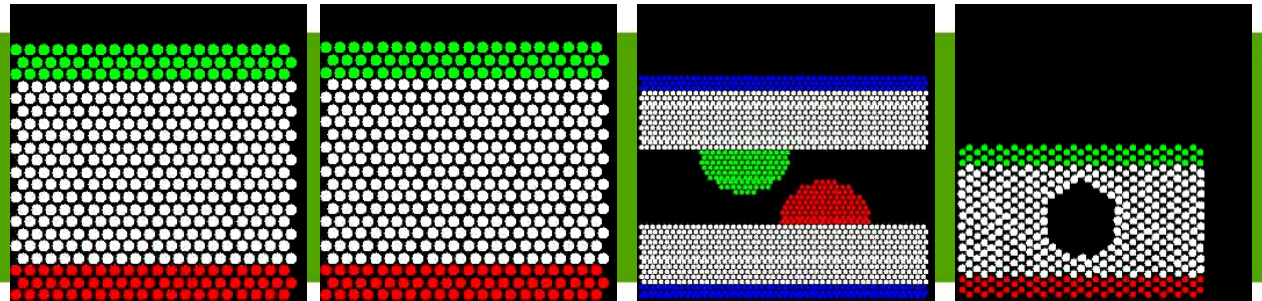


- Each DPD particle represents a group of solvent molecules
- Pairwise conservative forces
- Pairwise friction & random forces
  - Conservation of momentum (unlike traditional Brownian Dynamics)

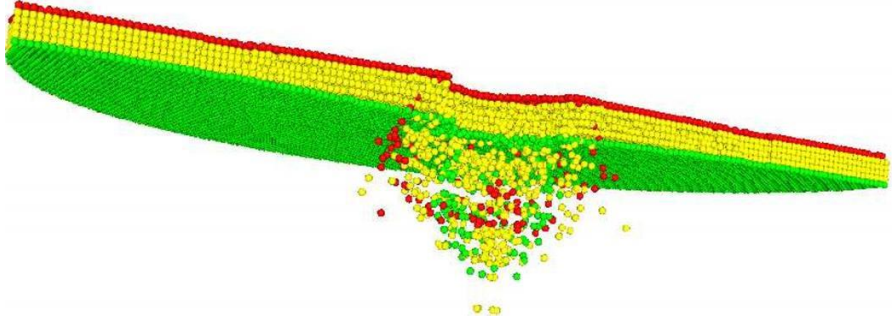


R.D. Groot and P.B. Warren, J. Chem. Phys. **107**, 4423 (1997)

See also Sodderman, Dünweg and Kremer, PRE **69,** 046702 (2003)

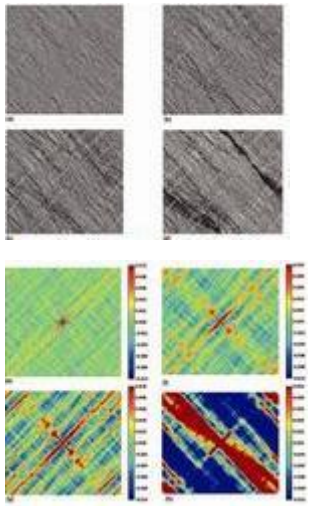


Rupture



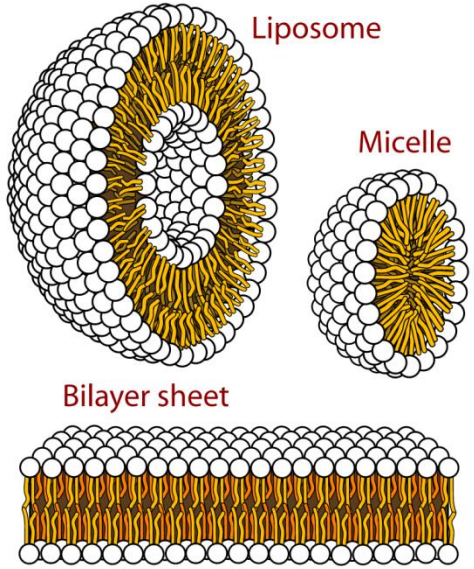
Implementing peridynamics within a molecular dynamics code, M. L. Parks, R. B. Lehoucq, S. J. Plimpton, S. A. Silling, Comp Phys Comm, 179, 777-783

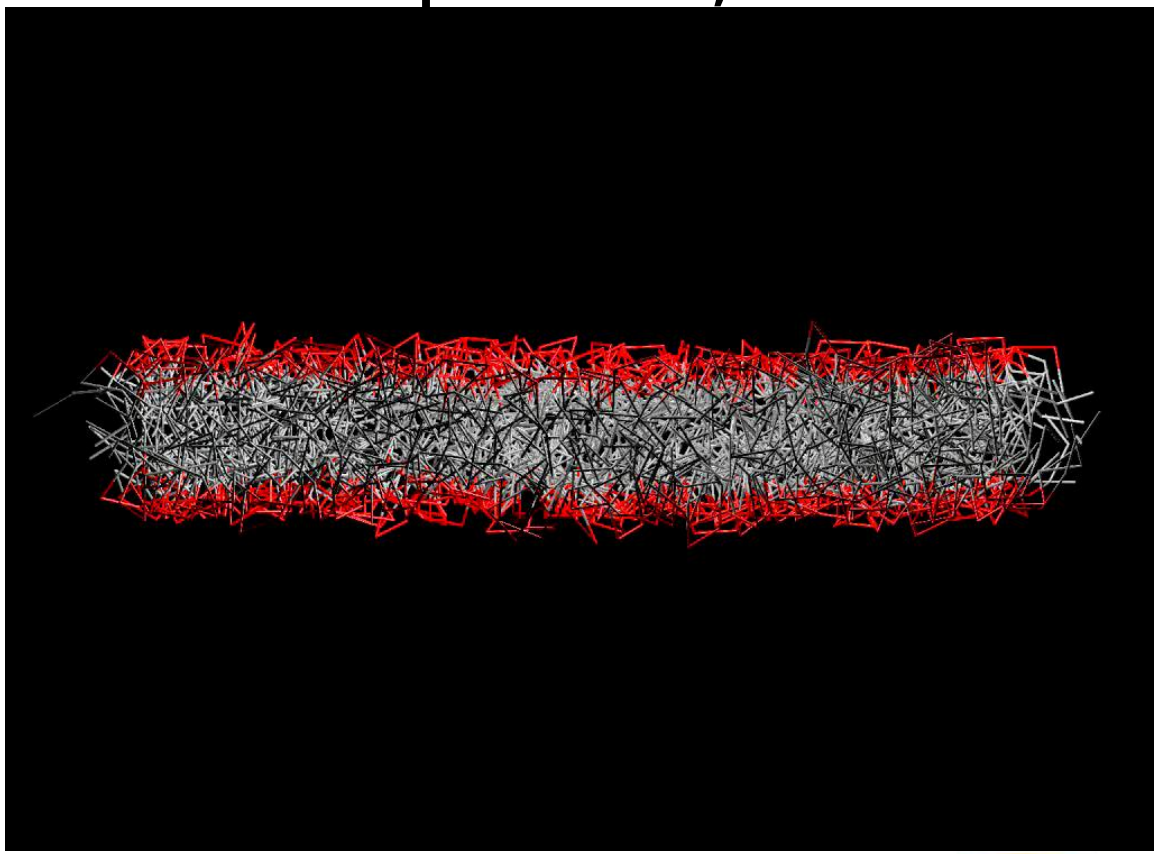
Shear faults in a model brittle solid

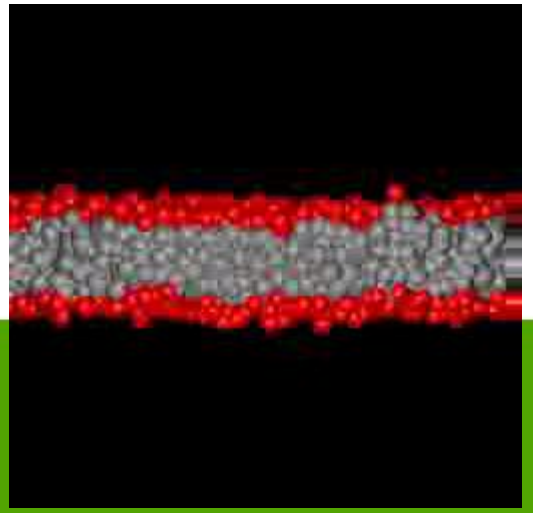


C. E. Maloney and M. O. Robbins, Chaos, 17, 041105 (2007).

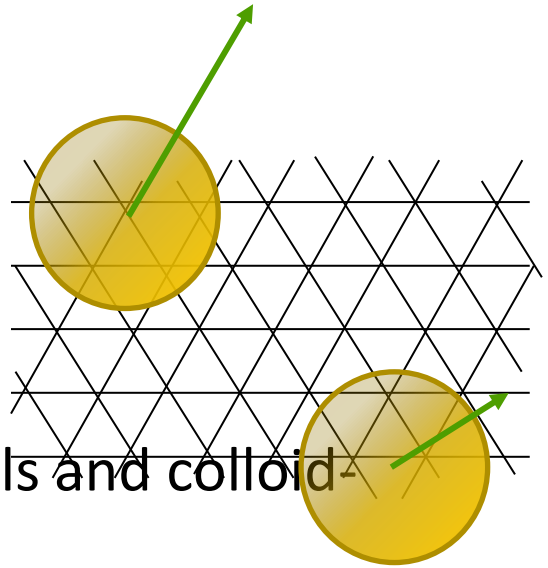
Liposome, micelle formation





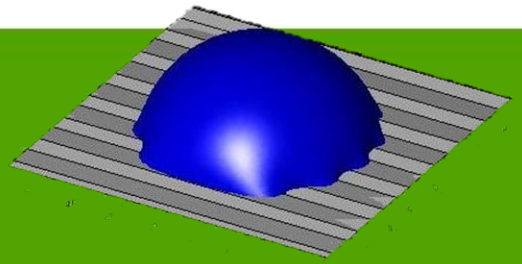


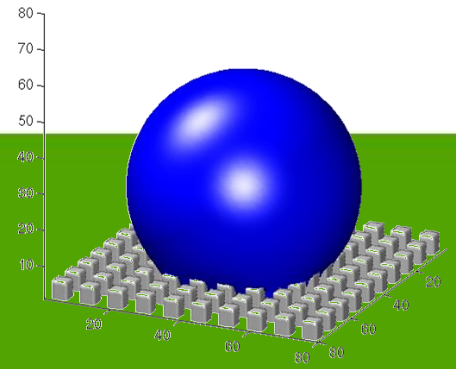
Lattice Boltzmann

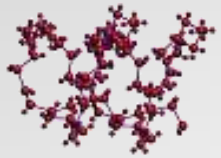


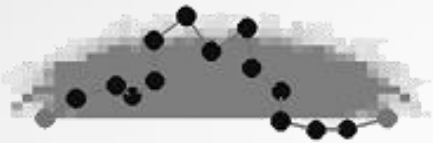
- Solvent hydrodynamics emerges from collisions on a lattice
- Computationally cheap (order *N*)
- Discretisation problems with boundaries (walls and colloid-solvent interactions)
- Brownian motion does not emerge naturally, but must be added “by hand”

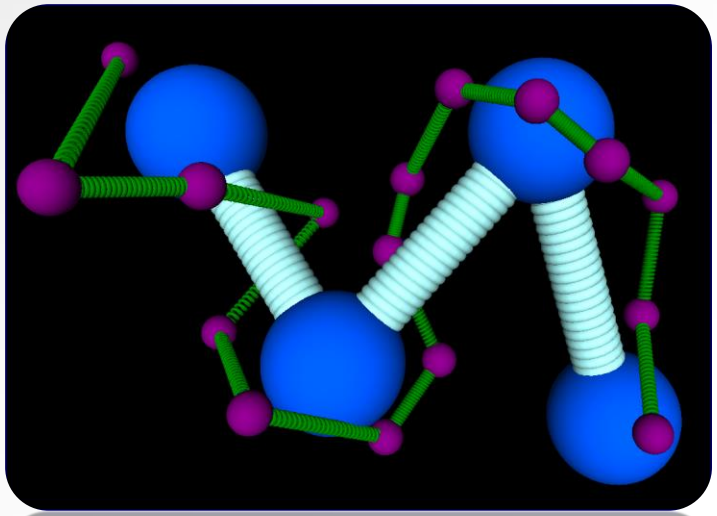
  A.J.C. Ladd and R. Verberg, J. Stat. Phys. **104**, 1191 (2001)
- See also Lobaskin & Dünweg NJP, **6**, 54 (2004) and Cates et al. JPCM (2004) for ways to include Brownian forces





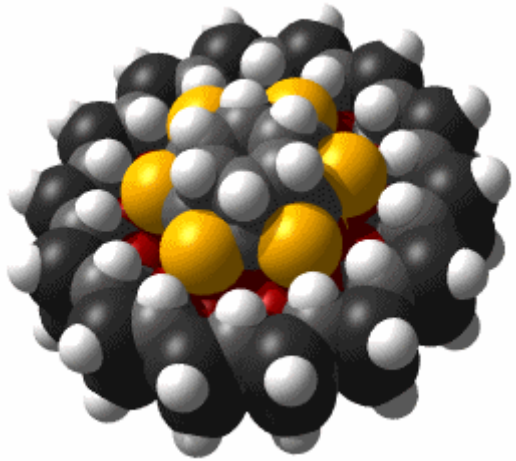


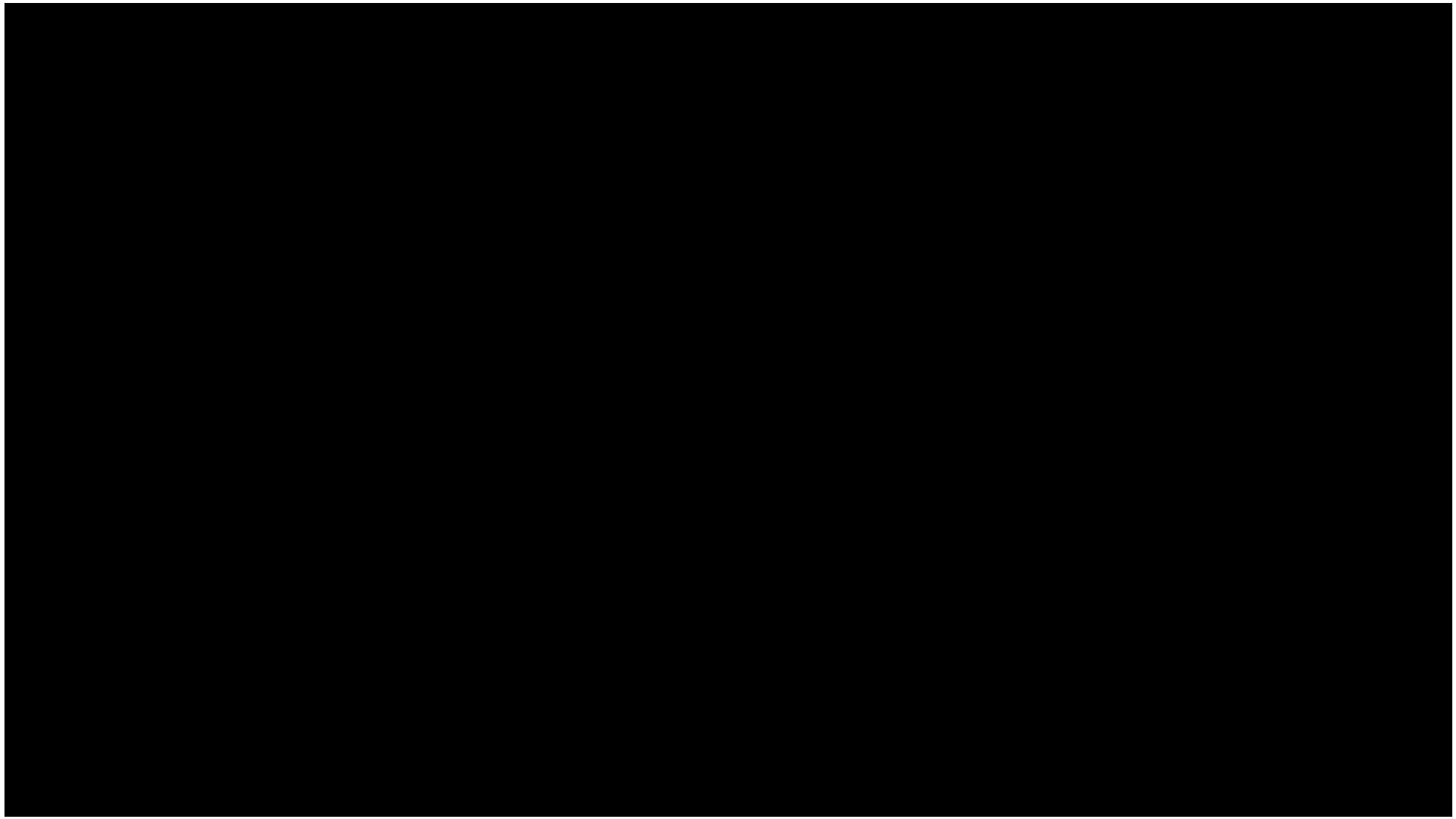




MOLECULAR AND SUPRAMOLECULAR MODELING

CONCLUSIONS

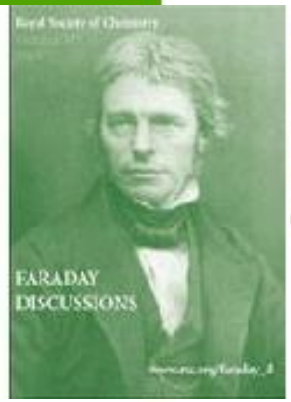




NOT LIMITED TO CLASSICAL PHYSICS: double slit simulation

TRENDS

- Atomistic modeling of liquids, polymers (in solution, melts, semi-crystalline)
- Many properties are accessible: mechanical, rheological
- Transport of small solutes is well studied
- Larger and longer simulations are now possible
- System size and simulation time limit resolution
- Coarse-graining (+back mapping) extends possibilities but still requires validation
- Polarizable forcefields are now available
- Reactivities are tractable with reactive forcefields or QM-MM



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