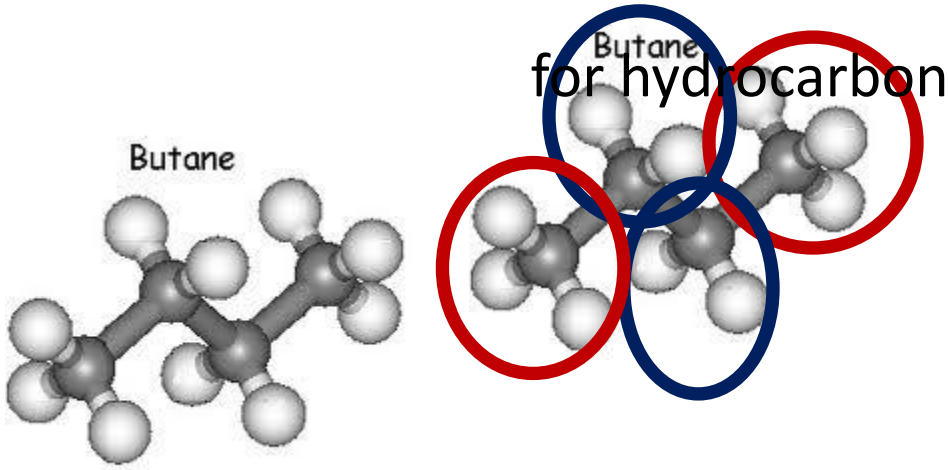
CHEM-E4115
Computational Chemistry I (5op)
2nd part: molecular modelling

Some other modelling methods for molecular systems

- Very briefly
  - Coarse-grained molecular modelling
  - Non-equilibrium MD (NEMD)
  - Dissipative particle dynamics
  - Brownian dynamics & Langevin dynamics
- non-particle based molecular modelling methods even more briefly
  - FEM (finite element method)

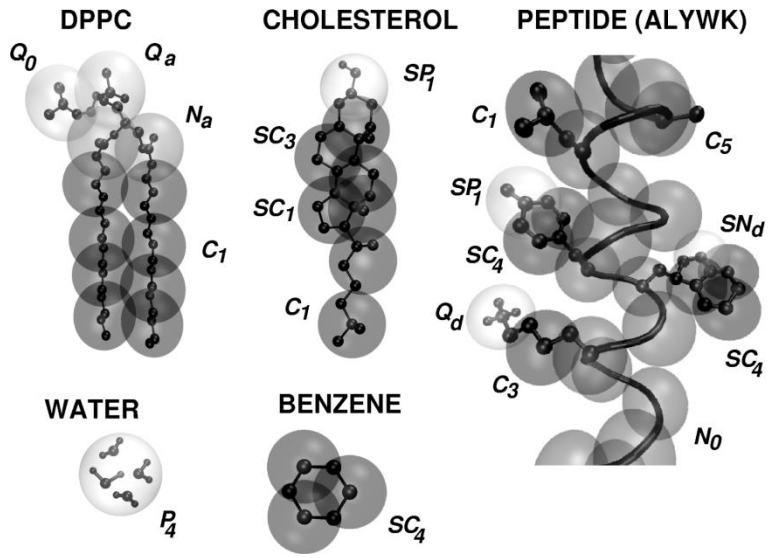
Coarse-grained molecular modelling: All-atom vs united atom force-fields

- Number of non-bonded interactions scales as ~N^2 (N is number of interaction sites)
- Clearly advantageous to reduce interaction sites
  - Done by making atom compounds (instead of several interaction sites, one)
  - Most simple: non-polar hydrogens with neighboring atom
  - Methyl group: a single pseudoatom
  - Typically ~2x faster than all-atom, for hydrocarbons even more



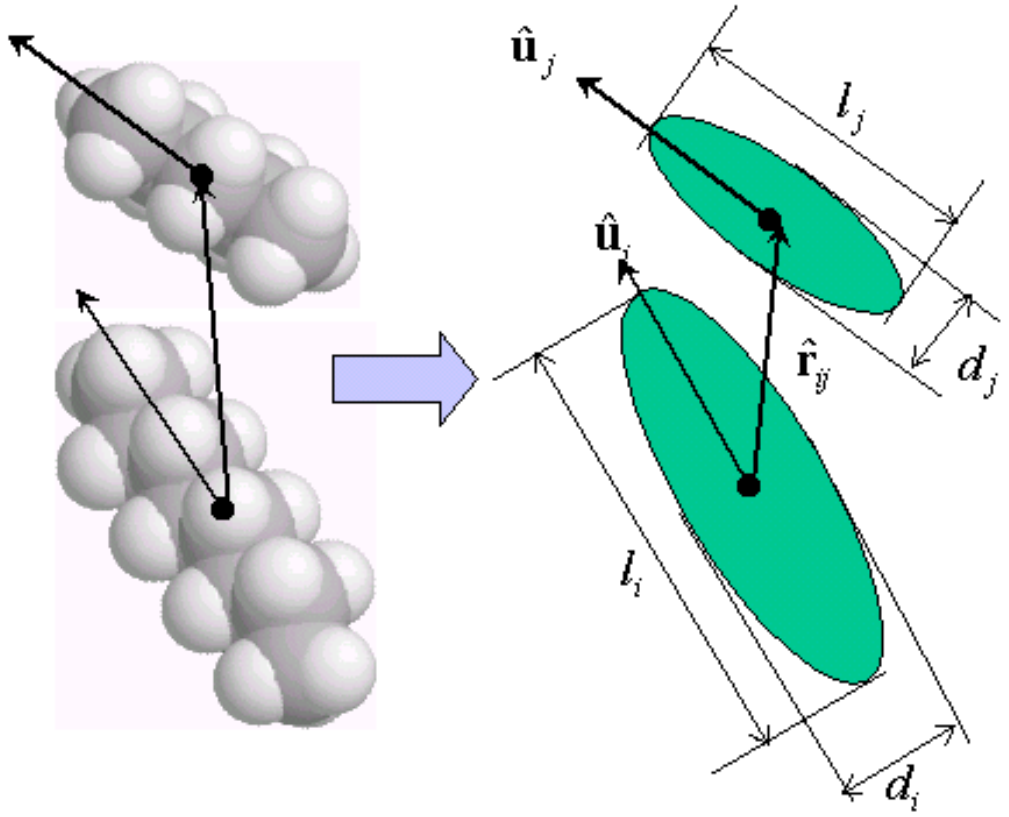
Example: Martini coarse-grained molecular model

- four-to-one mapping (on average four heavy atoms are by a single interaction center
- four main types of interaction sites are defined: polar (P), non-polar (N), apolar (C), and charged (Q)
  - Subtypes to account for more detailed chemistry
- Parametrization: reproduction of partitioning free energies between polar and apolar phases
- Fast
- Drawbacks: localized charge description, water properties, ion interactions, hydrogen bonding



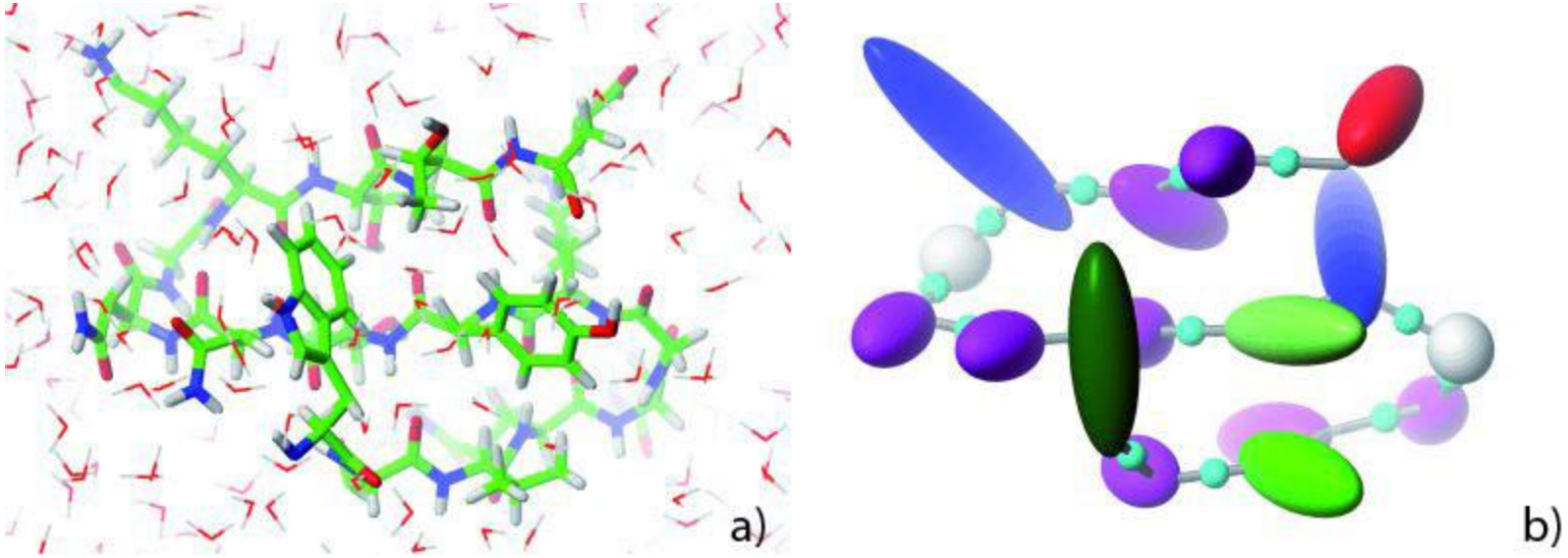
http://md.chem.rug.nl/cgmartini/index.php/about

Coarse-graining further: Hydrocarbon



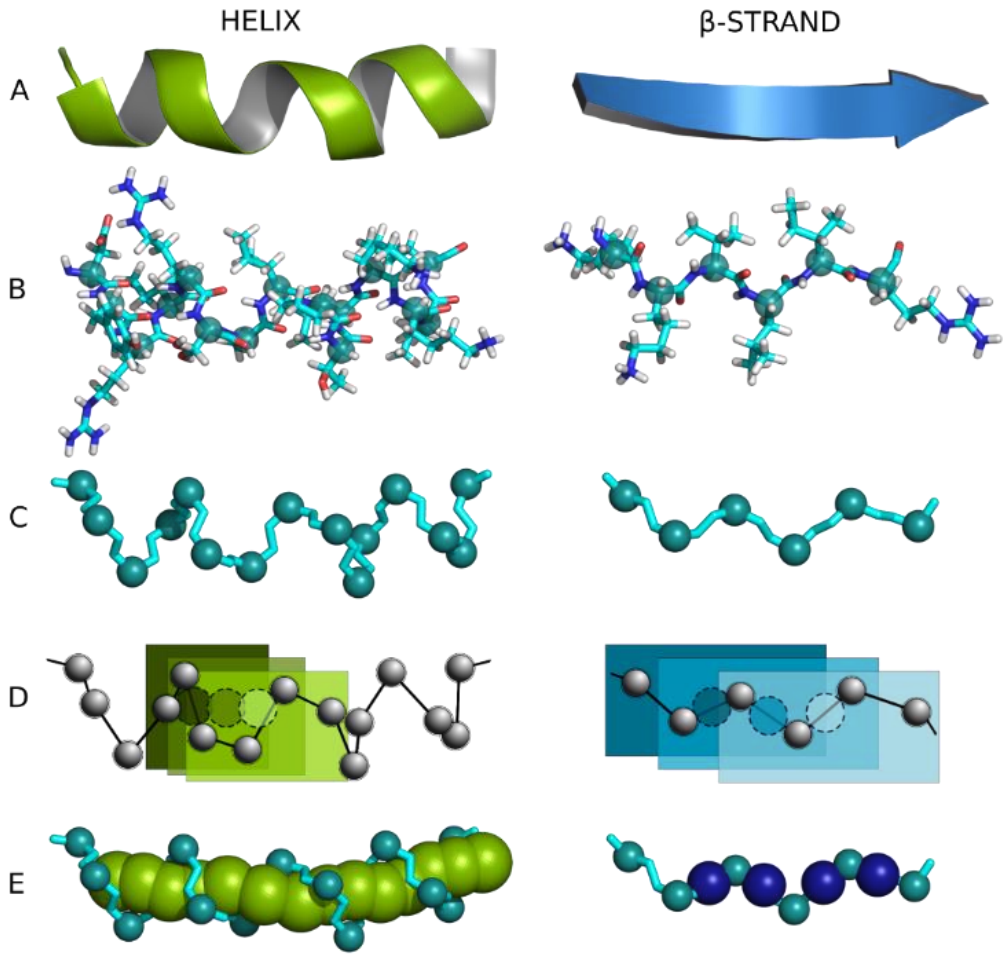
http://mw.concord.org/modeler1.3/mirror/documentation/UAFF.html

Coarse-graining further: Protein



http://inside.hlrs.de/htm/Edition_01_10/article_09.html

Example: a coarse-grained protein model SURPASS



http://biocomp.chem.uw.edu.pl/tools/surpass

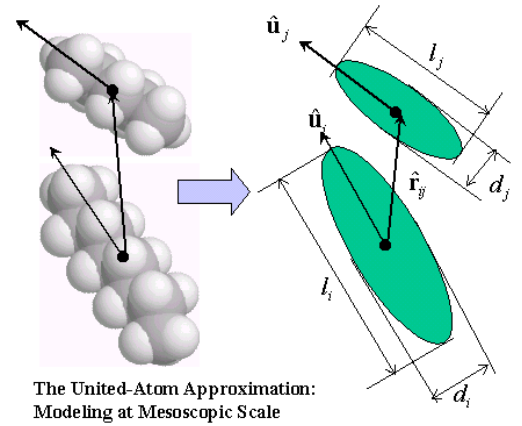
Coarse-grained models: basics

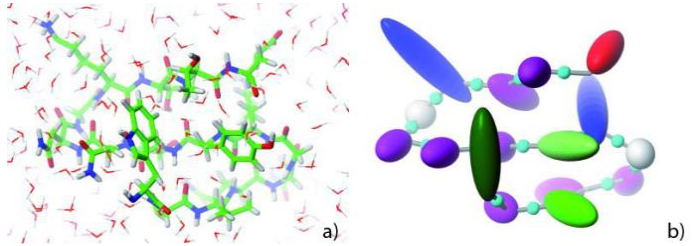
- Coarse-grained and mesoscale models fast
  - Soft, smooth potentials -> large timesteps in MD
- Capable of capturing phenomenological behaviour (details obscure)
- Loose detail to a varying degree
  - Several atoms in a blob
  - Entire molecules as rods, spheroids (elogated spheres)
- Typically parametrized to reproduce partitions, phase and structural transitions
- Especially used in macromolecular modelling (polymers, proteins, ...); liquid crystals

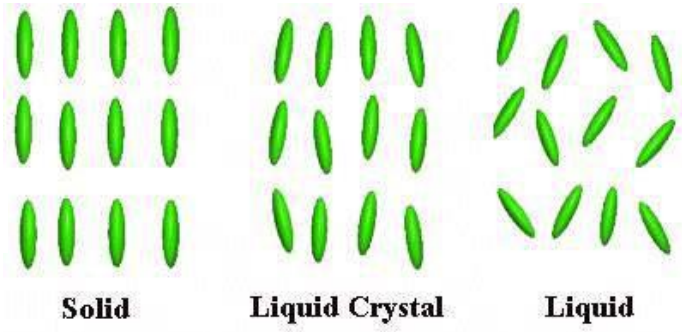
http://mw.concord.org/modeler1.3/mirror/documentation/UAFF.html

http://inside.hlrs.de/htm/Edition_01_10/article_09.html

http://plc.cwru.edu/tutorial/enhanced/files/lc/intro.htm

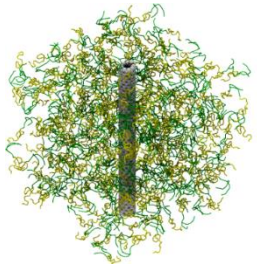


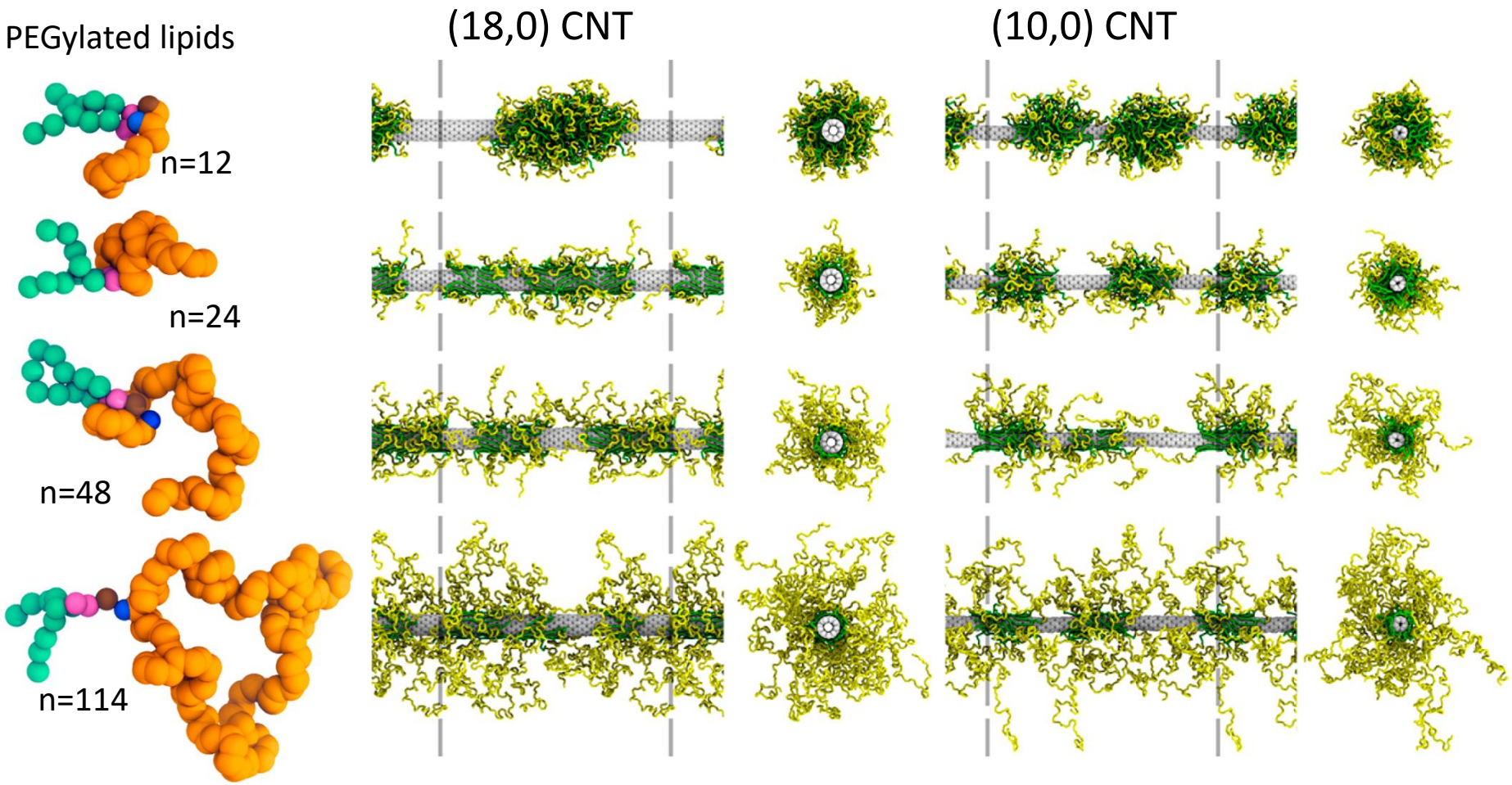




Research example of coarse-grained molecular modelling:

Carbon nanotube dispersion via surfactants





Aslan, Määttä, Haznefaroglu, Pfefferle, Elimelich, Pauthe, **Sammalkorpi**, Van Tassel, Soft Matter 9, 2136 (2013).
Määttä, Vierros, Van Tassel, **Sammalkorpi**, J. Chem. Eng. Data **59**, 3080 (2014).

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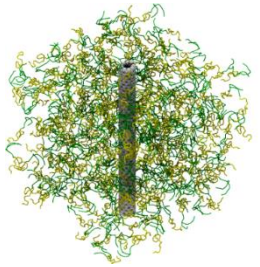
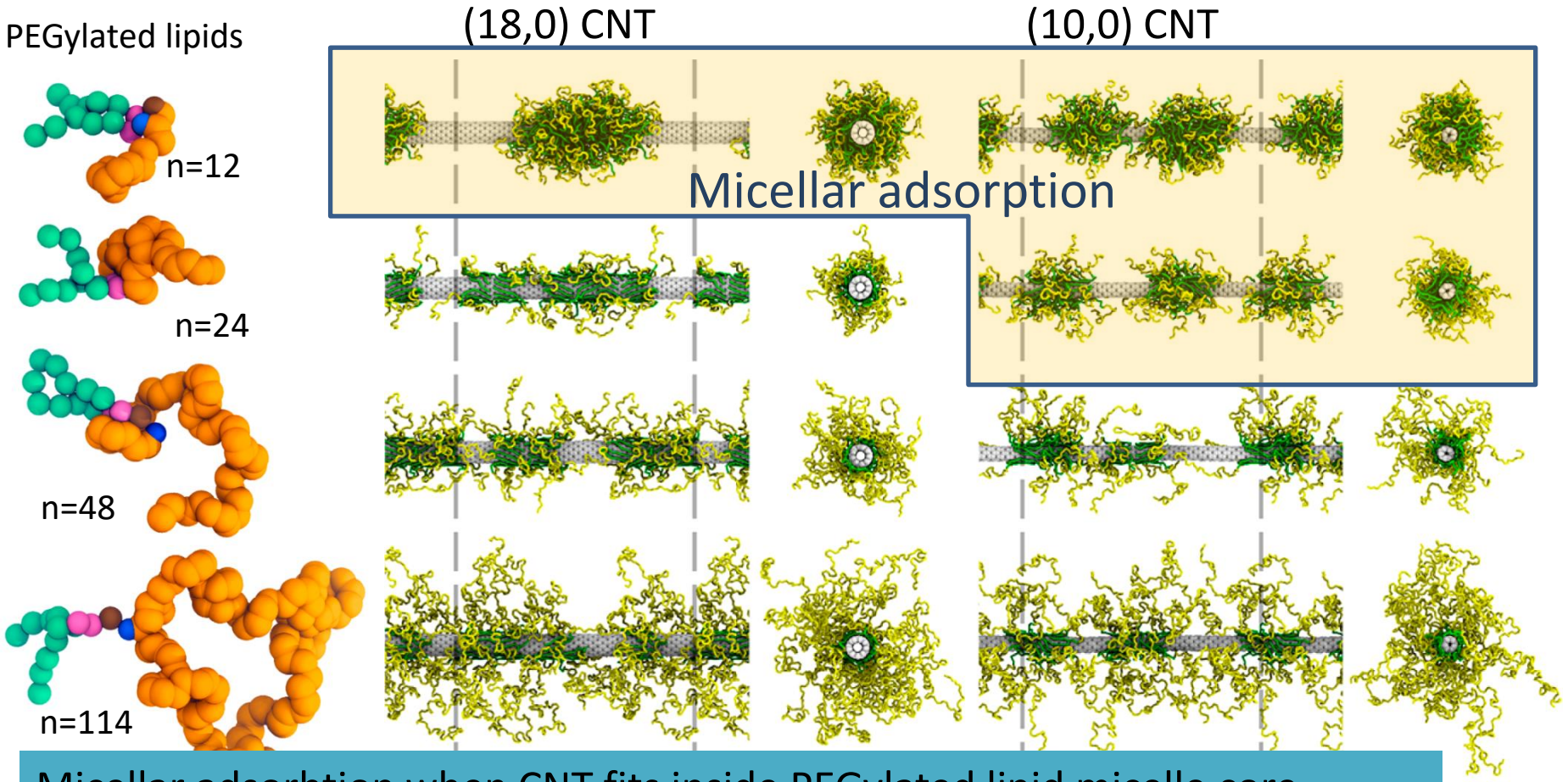




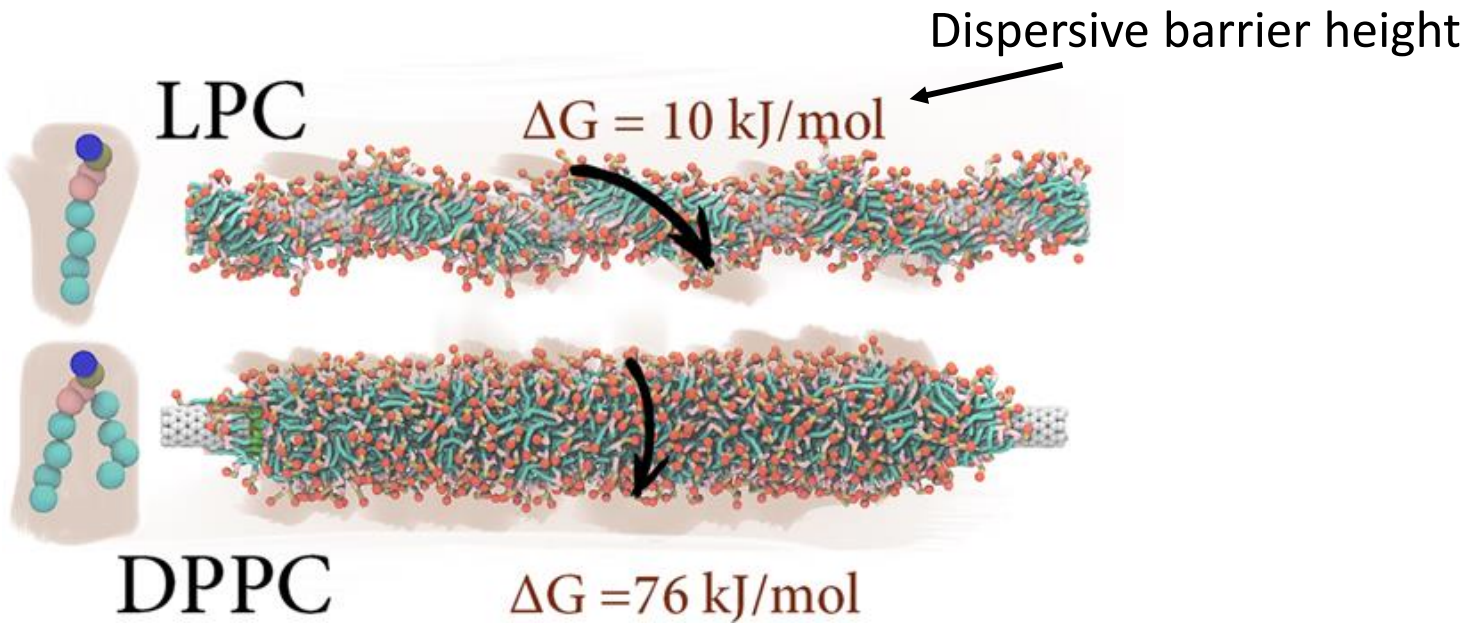
Micellar adsorbtion when CNT fits inside PEGylated lipid micelle core
Adsorption morphology influences dispersion efficiency (micelles effective)

Aslan, Määttä, Haznefaroglu, Pfefferle, Elimelich, Pauthe, **Sammalkorpi**, Van Tassel, Soft Matter 9, 2136 (2013).
Määttä, Vierros, Van Tassel, **Sammalkorpi**, J. Chem. Eng. Data **59**, 3080 (2014).

Research example of coarse-grained molecular modelling:

Carbon nanotube dispersion via surfactants

- Lipids: Dispersive coating regardless of object size or form



Lipid and substrate curvature control adsorption morphology
Head group **density** and **distance from CNT surface** dictate dispersion efficiency: Complete cylindrical coating more effective than spirals

Määttä, Vierros, **Sammalkorpi**, J. Phys. Chem. B 119, 4020 (2015).

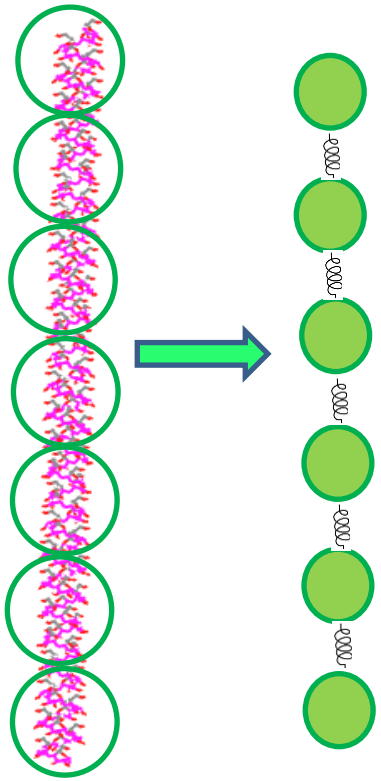
Non-equilibrium MD (NEMD)

- Any MD simulation of a system which is not in thermodynamic equilibrium.
- Usually some perturbative term is added to the equations of motion.
- For instance for simulating viscosity, heat conductivity and atomic diffusion there are special NEMD algorithms.
- At its simplest, the perturbation can be an external force acting on some of the atoms.
- **Time development is now the object of interest, not a steady state property**
- The external force heats the system up, which can be compensated by temperature control
  - Careful! Thermostat / barostat may influence the perturbation

https://www.eurekalert.org/multimedia/pub/141040.php
http://bionano.physics.illinois.edu/node/133

Dissipative particle dynamics

- In 1992 Hoogerbrugge and Koelman introduced a new coarse-grained method for fluid dynamics simulation coined Dissipative Particle Dynamics (DPD). From a technical point of view, DPD differs from Molecular Dynamics (MD) in two respects:
  - The conservative pairwise forces between DPD particles (which represent clusters of microscopic particles) are soft--repulsive, which makes it possible to extend the simulations to longer time scales.
  - Second, a special ``DPD thermostat'' for the canonical ensemble is implemented in terms of dissipative as well as random pairwise forces such that the momentum is locally conserved, which results in the emergence of hydrodynamic flow effects on the macroscopic scale.



Dissipative force

$$f_i = \sum_{j \neq i} (F_{ij}^C + F_{ij}^D + F_{ij}^R)$$

Random force (fluctuations)

Conservative force

Dissipative particle dynamics (DPD)

- To get hydrodynamic behaviour, one must implement random and dissipative forces while preserving proper mass and momentum transport through simulation → DPD
- hydrodynamic time and space scales beyond those available with molecular dynamics
- particles moving in continuous space and discrete time (like molecular dynamics), but
  - Particles represent whole molecules or fluid regions, rather than single atoms
  - Atomistic details are not considered relevant to the processes addressed: particles' internal degrees of freedom are integrated out and replaced by simplified pairwise dissipative and random forces. These conserve momentum locally and ensure correct hydrodynamic behavior.

Dissipative particle dynamics (DPD)

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Dissipative force

$$f_i = \sum_{j \neq i} (F_{ij}^C + F_{ij}^D + F_{ij}^R)$$

Conservative force

Random force (fluctuations)

- conservative force gives beads a chemical identity
- dissipative and random forces together form a thermostat
- DPD forces conserve momentum locally: **hydrodynamic modes of the fluid emerge even for small particle numbers**
- All forces, including the random force between two interacting beads must be antisymmetric for momentum conservation (Difference to Brownian dynamics)

Dissipative particle dynamics (DPD)

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Dissipative force

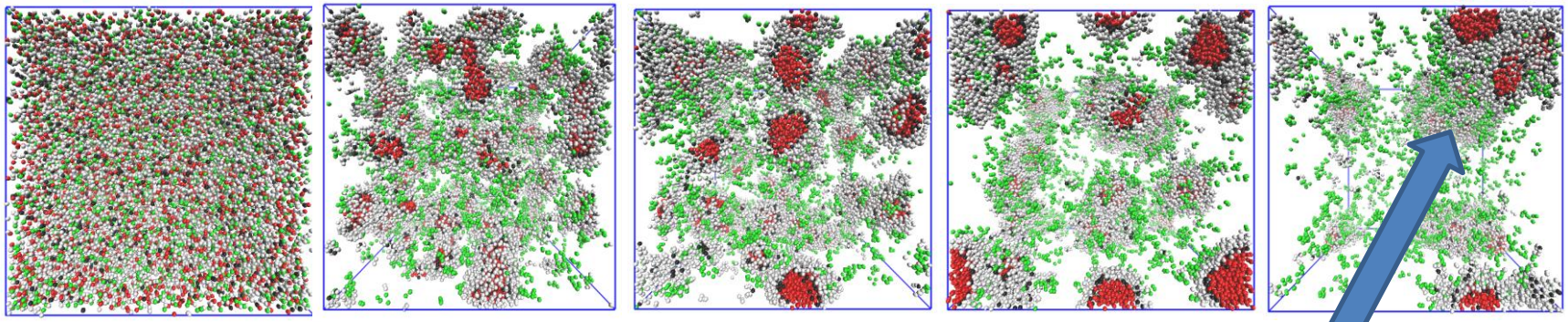
$$f_i = \sum_{j \neq i} (F_{ij}^C + F_{ij}^D + F_{ij}^R)$$

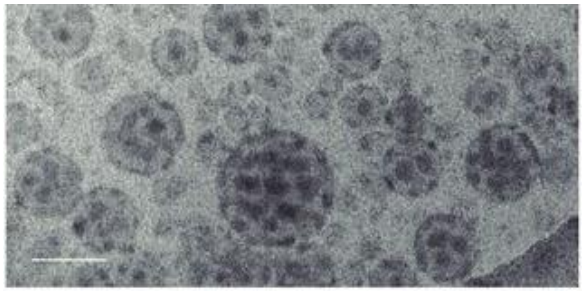
Conservative force

Random force (fluctuations)

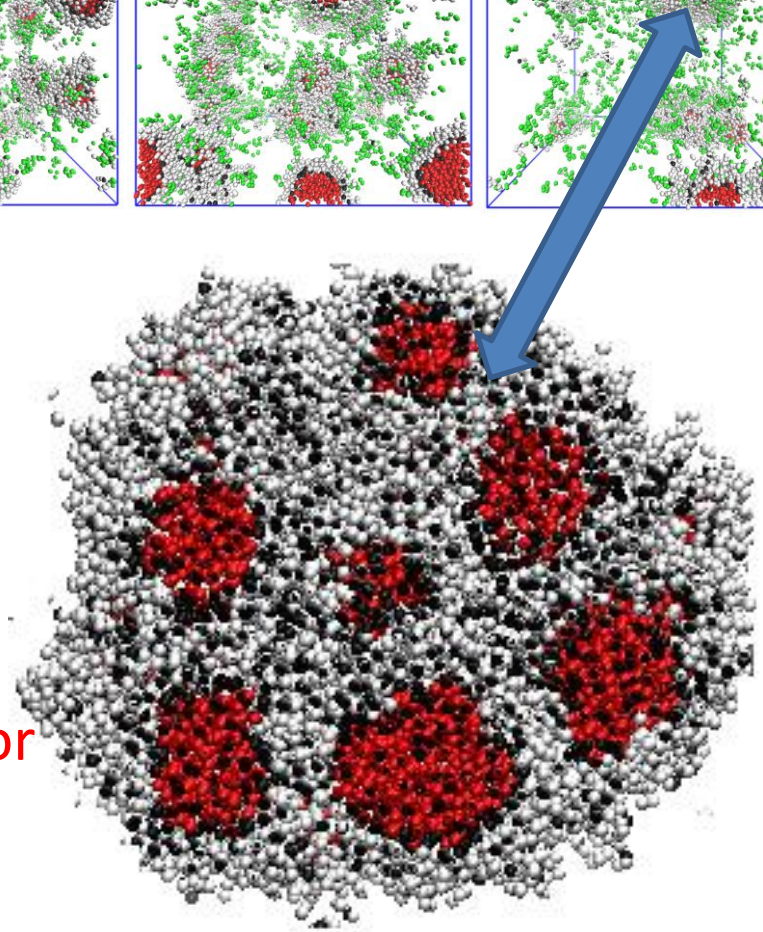
- conservative force gives beads a chemical identity
- dissipative and random forces together form a thermostat
  - related via the fluctuation-dissipation theorem and can be thought of as a random energy kick for all the particles, with an associated viscous drag term to remove an equal amount of energy from the system.
- The softness of the potential prevents the energy from diverging if a long time step is employed; the short-ranged character makes the force routine efficient

DPD Time evolution of a polymer core-shell particle system



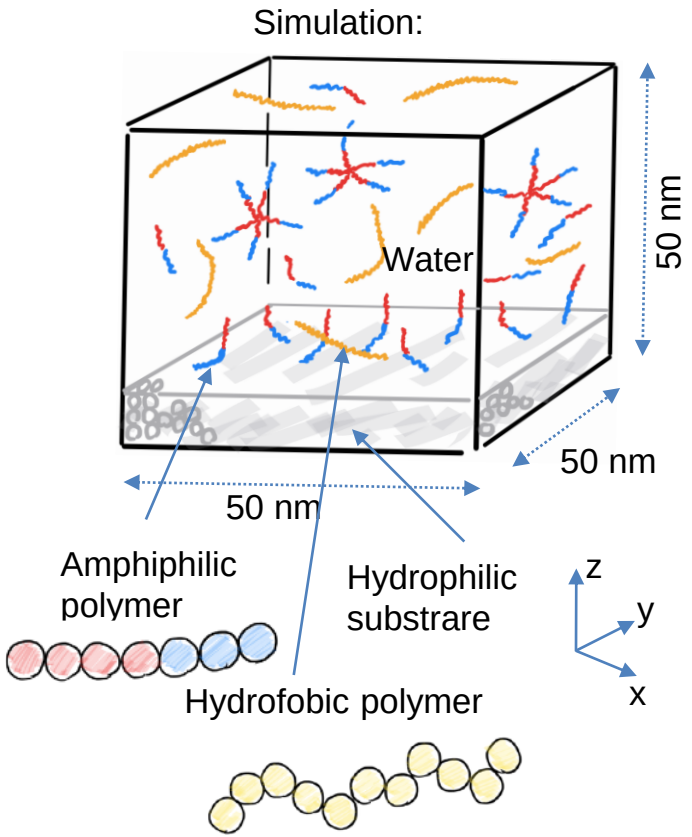


Nanoscale 7(28), 11841-762015 (2015)

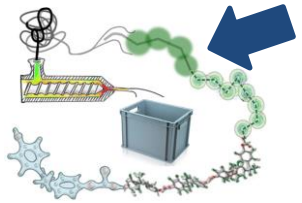


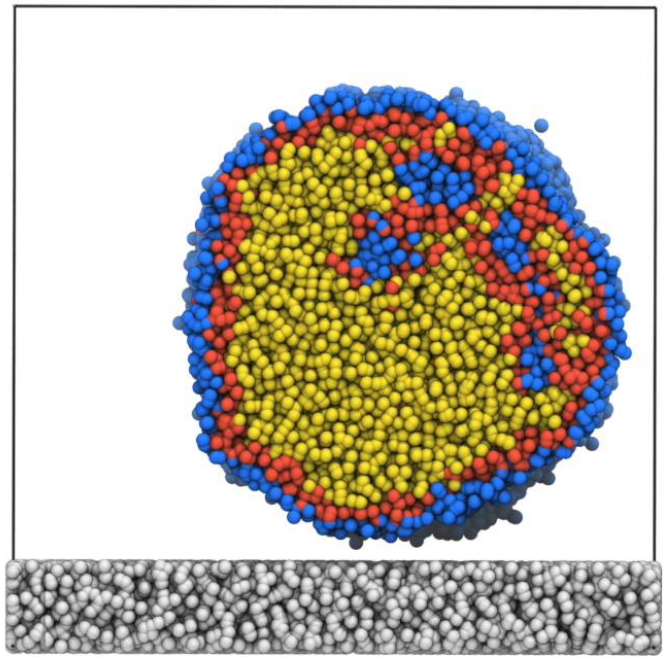
DPD length scale is long enough for overlap with electron microscopy

DPD modelling of polymer film formation



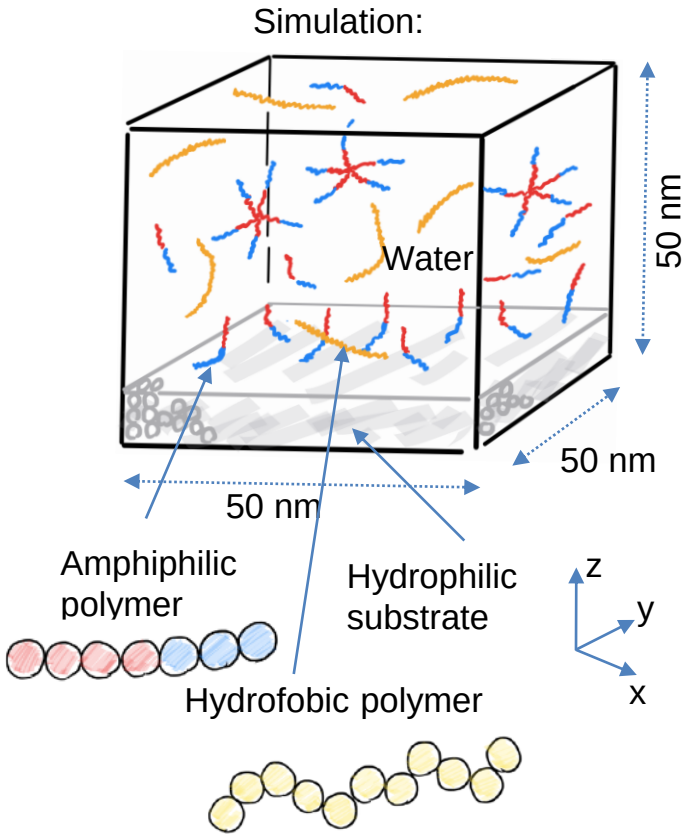
Target: moisture protecting film

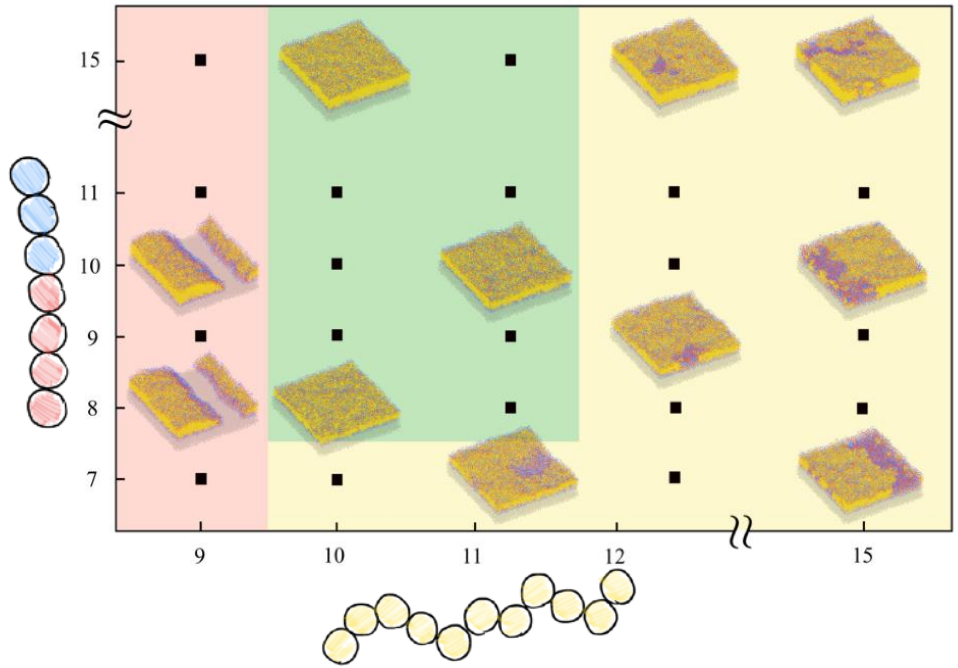




SJ Nikkhah and **M Sammalkorpi**, J. Colloid Interface Science (2023).
K Hasheminejad, A Scacchi, SJ Nikkhah, and **M. Sammalkorpi** (2022).

DPD modelling of polymer film formation





SJ Nikkhah and **M Sammalkorpi**, J. Colloid Interface Science (2023).
K Hasheminejad, A Scacchi, SJ Nikkhah, and **M. Sammalkorpi** , Applied Surface Science (2024).

Brownian dynamics or Langevin dynamics

- Langevin dynamics

$$M\ddot{X} = -\nabla U(X) - \gamma M\dot{X} + \sqrt{2\gamma k_B T M}R(t)$$

- Brownian dynamics: acceleration is zero

$$0 = -\nabla U(X) - \gamma M\dot{X} + \sqrt{2\gamma k_B T M}R(t)$$

- Random $\dot{X}(t) = -\nabla U(X)/\zeta + \sqrt{2D}R(t).$
- Brownian motion: random motion of particles in a fluid, diffusion or transport phenomena
- Langevin dynamics: particles in viscous solvent

Animations: https://en.wikipedia.org/wiki/Brownian_motion

Molecular modelling across different length and time scales: Beyond particle methods

What to do when particle based length and time scales are not appropriate descriptions?

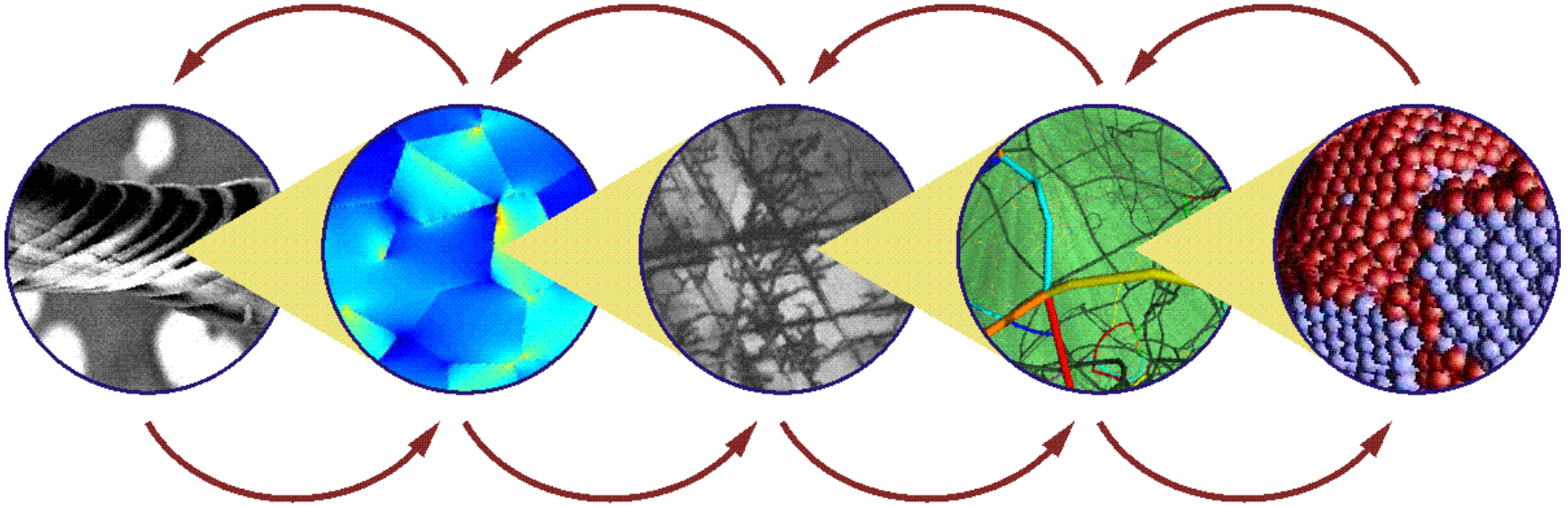
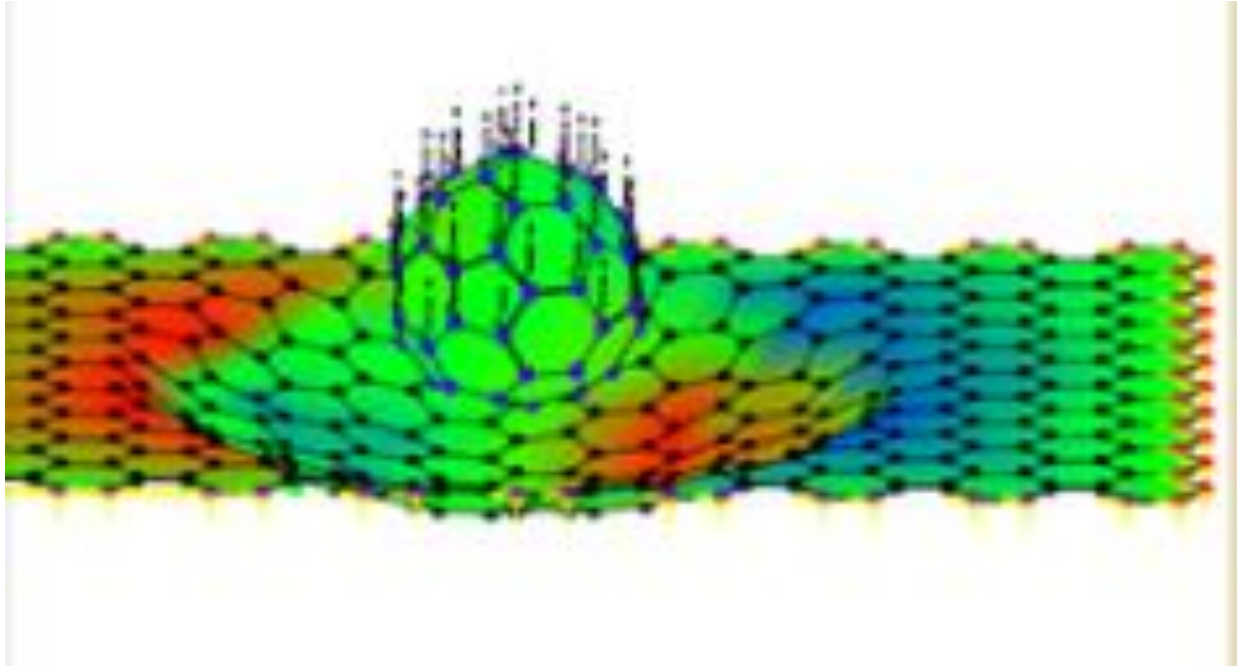


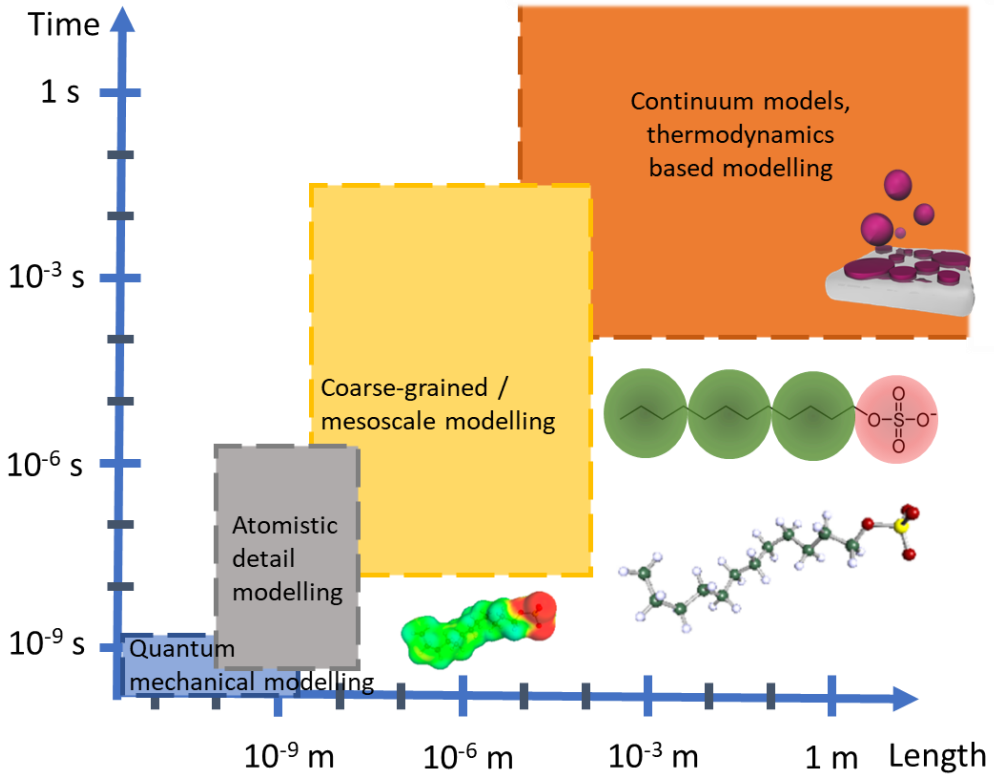
Figure:
http://www.kochmann.caltech.edu/research_multiscale.html

Example: The finite element method (FEM)

- Describe the molecular system by partial differential equations (PDE) or integral equations
- Eliminate or integrate numerically



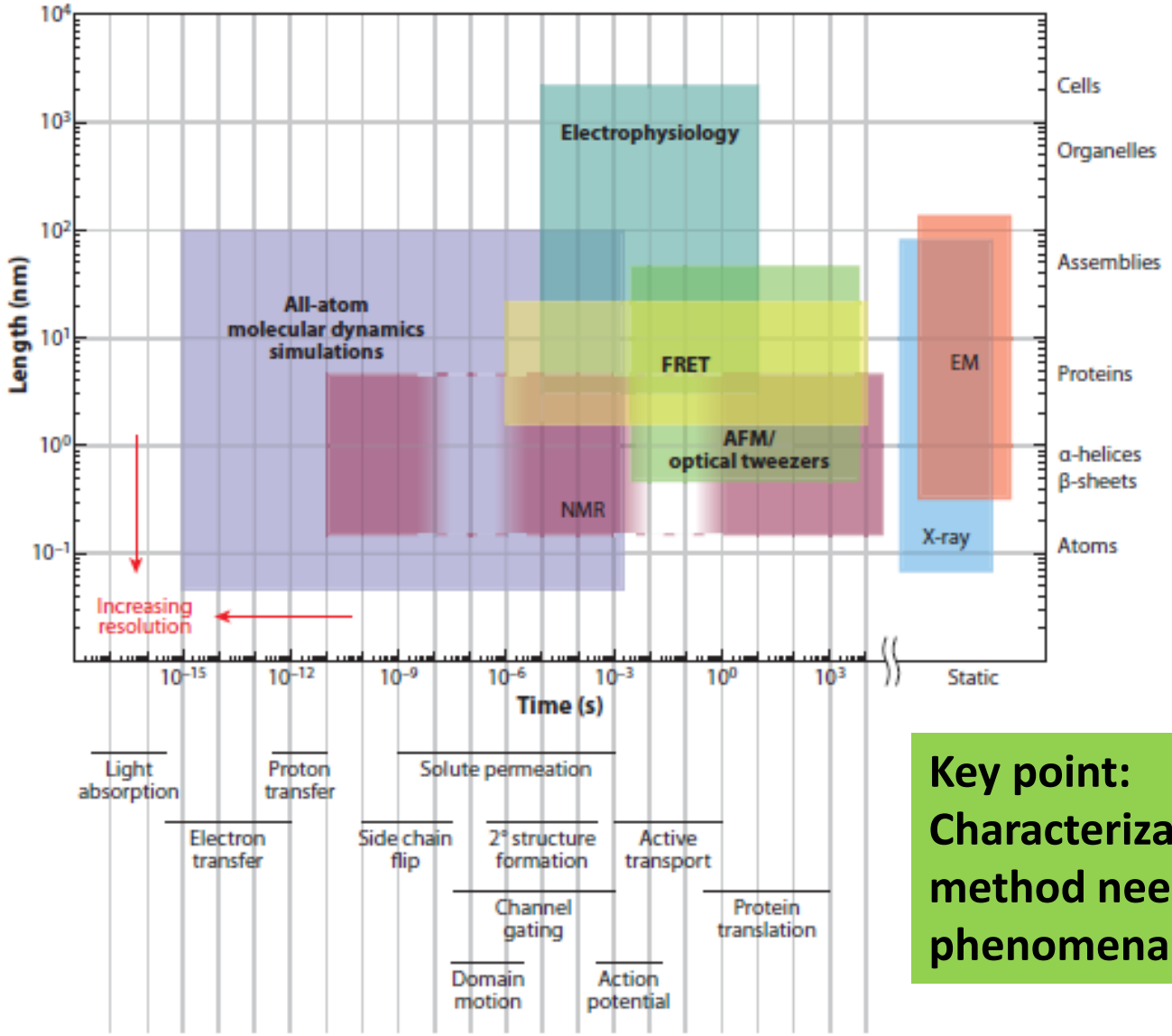
Molecular modelling: Summary



	Common experimental characterization methods
Macroscopic mechanical and structural properties, dynamic evolution at macroscopic scale	Rheometry, tensile tester, mechanical analysis, direct imaging, …
Assembly and morphology (structural and dynamical properties); some chemical specificity	Optical, confocal and Raman microscopy, light scattering methods, …
Chemically specific molecular and aggregate level structure and dynamics, mechanical properties	SAXS, XRD, NMR, FTIR, …
Electronic structure dependent properties and molecule structure: chemical reactions, band structure, electron level charge transfer, …	Spectroscopy, NMR, FTIR, electrochemical methods, …

Key point:
No modelling approach is valid for everything!
Length and time scale need consideration!

Spatiotemporal resolution of various biophysical techniques.

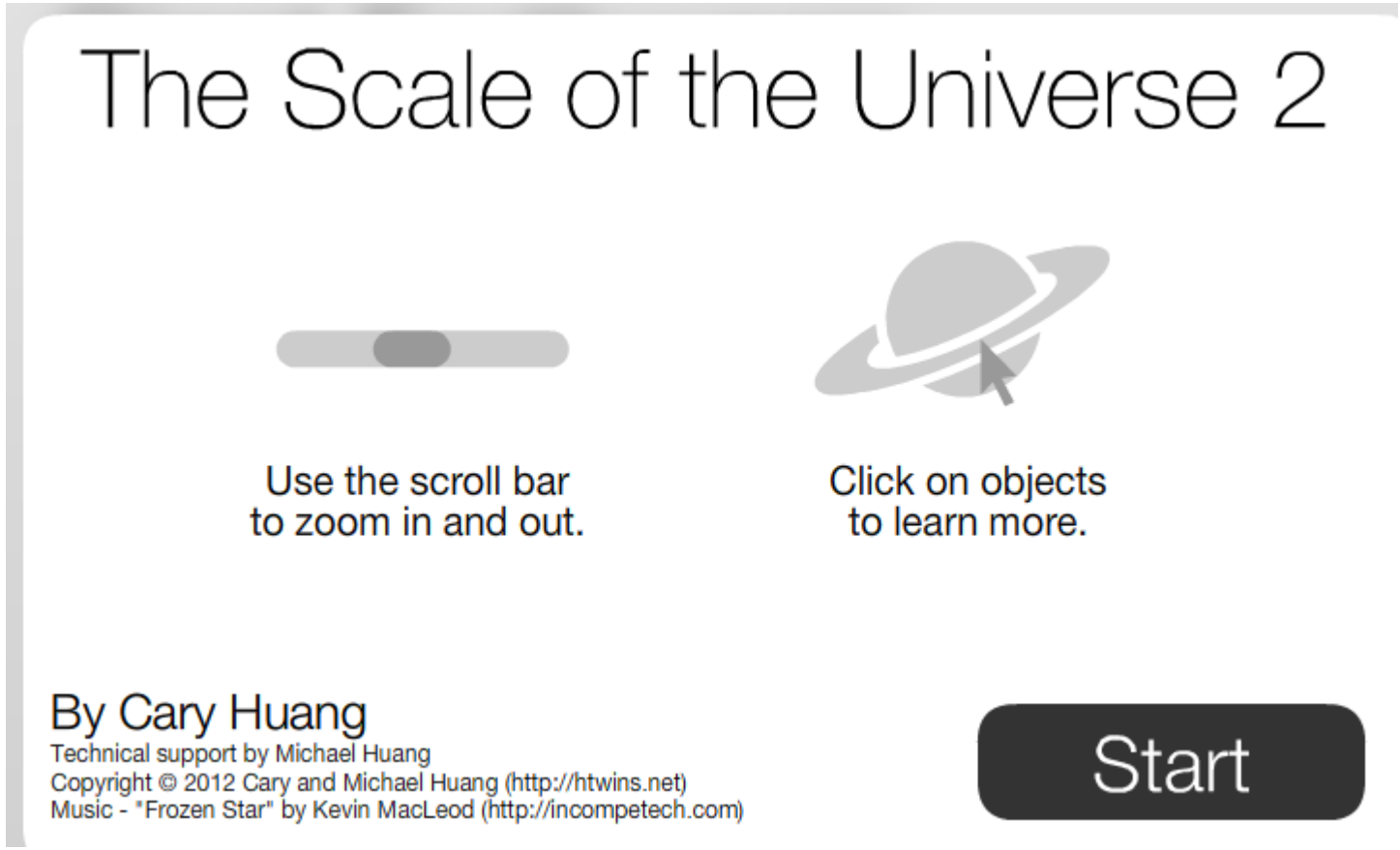


Key point: Characterization method needs to match phenomena of interest

Annu. Rev. Biophys. 2012. 41:429–52

Appropriate ending to a physical modelling course: An animation of the scale of the Universe

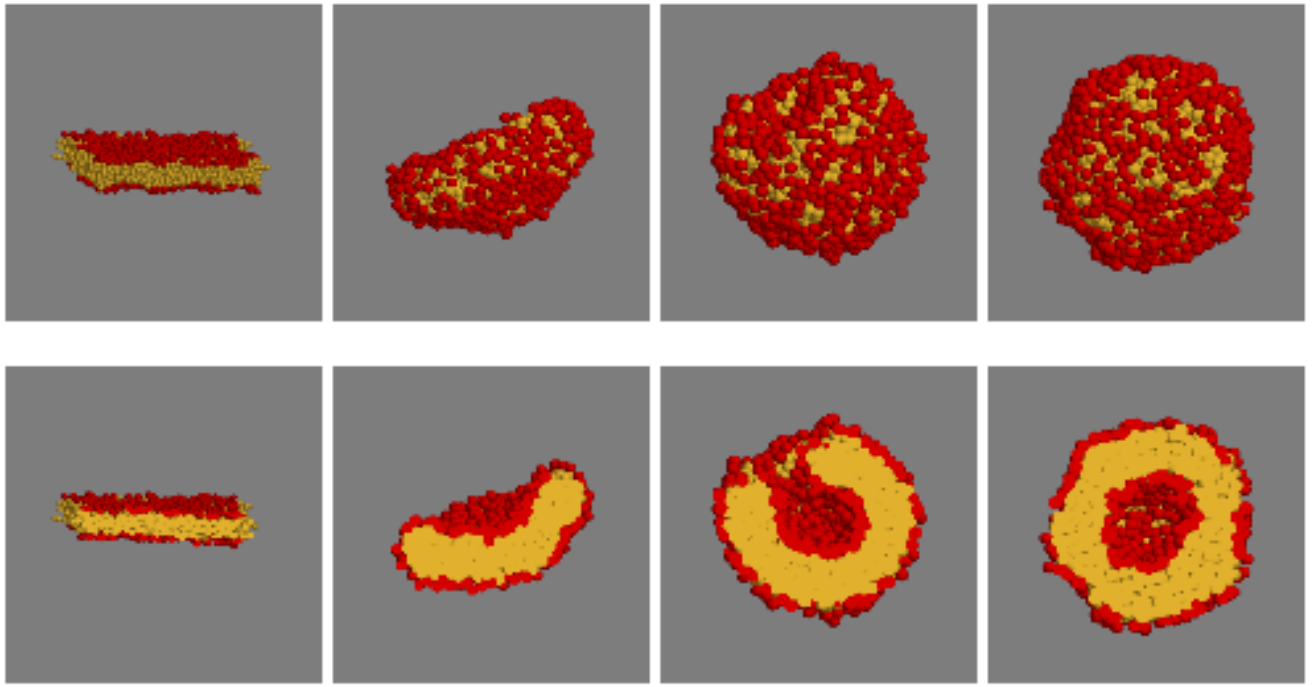
- Go to this link: http://htwins.net/scale2/



Dissipative particle dynamics in practice 2

DPD Simulation of liposome formation:

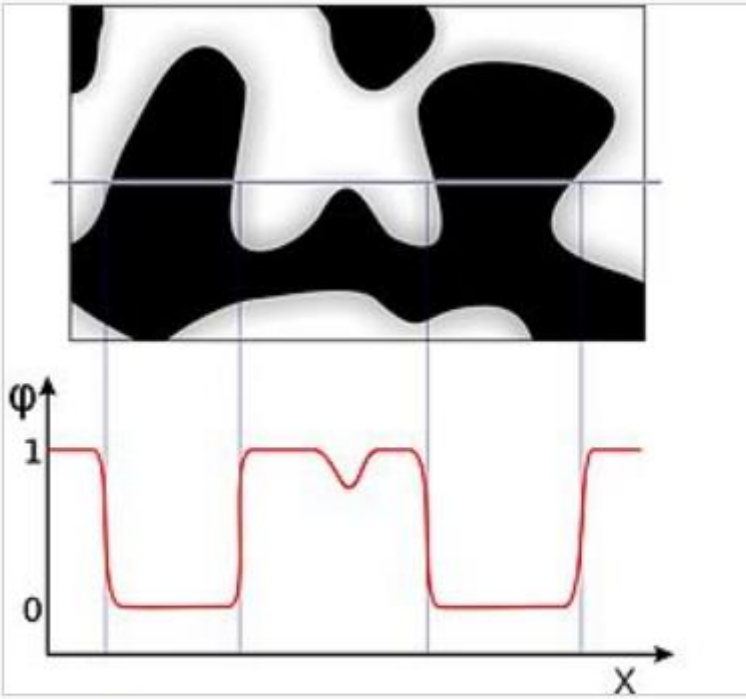
- Below are snapshots of a DPD simulation of liposome formation (Nikunen, Karttunen & Vattulainen). The second row shows a cross-section of the system. Water has been removed for clarity.
- The system has roughly 86000 particles.



Movie: http://www.softsimu.net/formation.mpg http://www.softsimu.net/dpd.shtml

Example: Phase-field modelling I

- a mathematical model for solving interfacial problems
  - Examples: Domain formation, solidification dynamics, viscous fingering, fracture dynamics, vesicle dynamics, …
  - substitutes boundary conditions at the interface by a partial differential equation for the evolution of an auxiliary field (the phase field) that takes the role of an order parameter. This phase field takes two distinct values (for instance +1 and −1) in each of the phases, with a smooth change between both values in the zone around the interface.



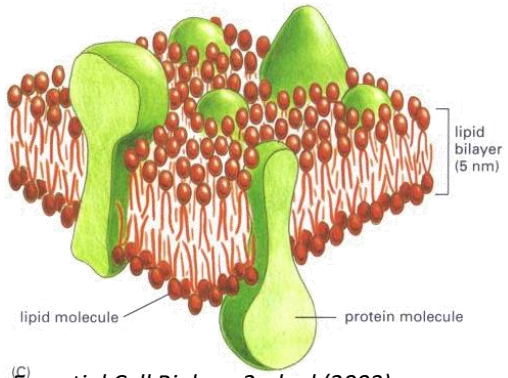
A two phase microstructure and the order parameter ϕ profile is shown on a line across the domain. Gradual change of order parameter from one phase to another shows diffuse nature of the interface.

http://en.wikipedia.org/wiki/Phase_field_models

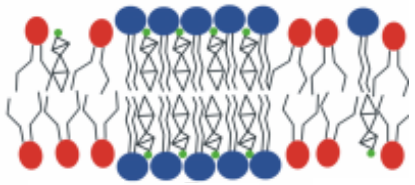
Phase-field modelling II

- Typically models based on a free energy functional that depends on the order parameter (the phase field) and a diffusive field
- Permits solving the problem (the functional) by integrating a set of partial differential equations for the whole system
- Avoids explicit treatment of the boundary conditions at the interface
- Equations of the model obtained by using general relations of statistical mechanics
- Computational: integration of partial differential equations to solve the interfacial dynamics

Example of Phase-field modelling
Modelling Lipid Rafts in Cell membranes

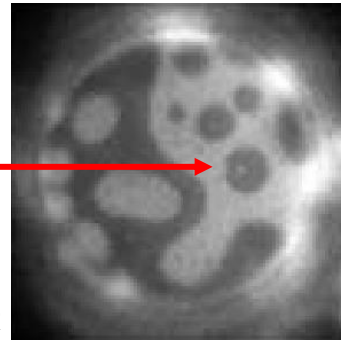


Essential Cell Biology 2nd ed (2003)



L_d L_o L_d

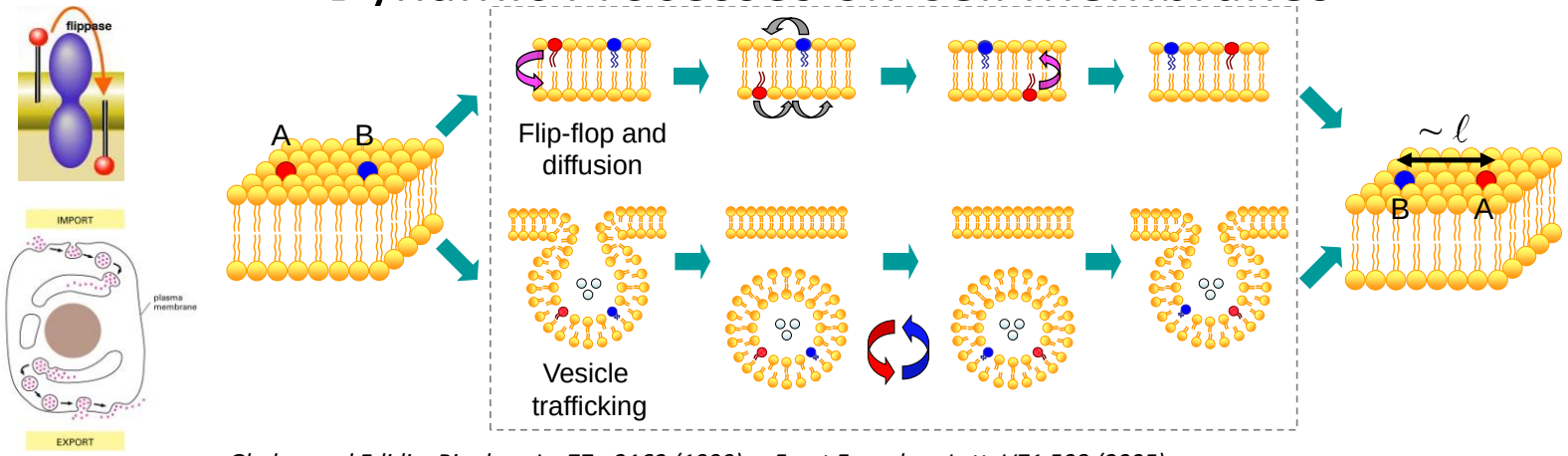
In vitro



Veatch & Keller Biophys. J. v85 p3074 (2003)

- Importance of Lipid Rafts:
  - Signal transduction, Protein Sorting & Virus Entry

Example of Phase-field modelling
Modelling Lipid rafts in Cell membranes
Dynamic Processes on Cell Membranes



Gheber and Edidin, Biophys. J. v77 p3163 (1999) Foret Europhys. Lett. V71 508 (2005)
Turner, Sens and Socci, Phys. Rev. Lett v95 p168301 (2005)

- Recycling Rate ***H*** & Recycling Length ***l***

$$\frac{\partial c(\vec{r},\tau)}{\partial \tau} = \nabla \cdot [M \nabla(-\nabla^2 c - c + c^3)] + \xi(\vec{r},\tau)$$

$$H^2 \sim p/[D(T_c - T)^2]$$

$$\left\langle \hat{\xi}(\vec{q}_1,\tau_1)\hat{\xi}(\vec{q}_2,\tau_2)\right\rangle = \frac{H^2 l^2}{1+l^2 q_1^{\,2}} q_1^{\,2}\delta(\vec{q}_1+\vec{q}_2)\delta(\tau_1-\tau_2)$$

In vivo

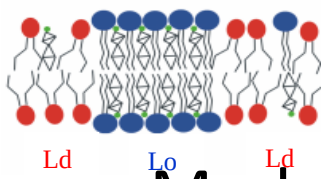
$$\left\langle \hat{\eta}(\vec{q}_1,\tau_1)\hat{\eta}(\vec{q}_2,\tau_2)\right\rangle = 2k_B T M q_1^{\,2}\delta(\vec{q}_1+\vec{q}_2)\delta(\tau_1-\tau_2)$$

In vitro

Epithelial Cell

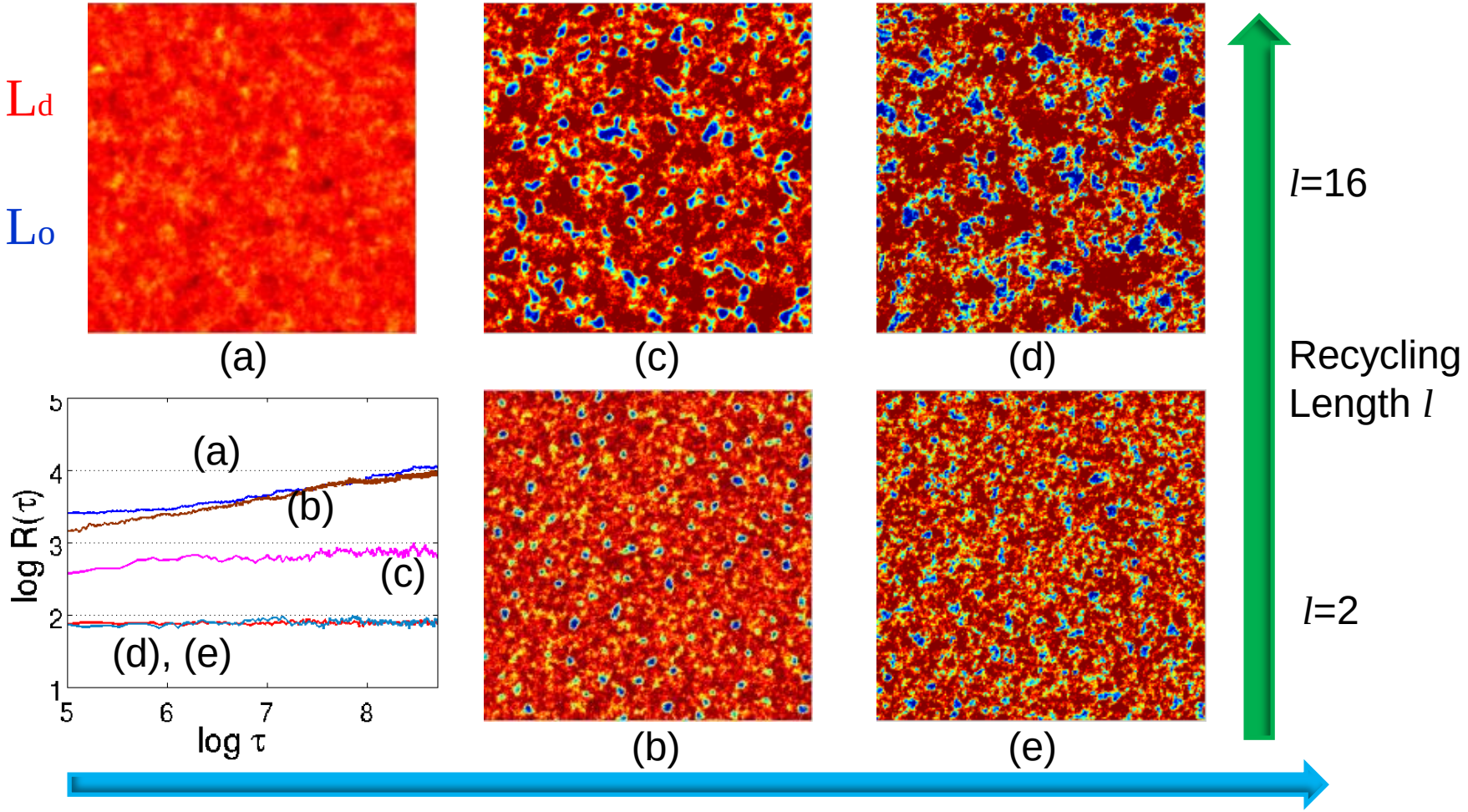
Essential Cell Biology 2nd ed (2003)

J. Fan, M. Sammalkorpi, and M. Haataja, *Phys. Rev. Lett.* v104, 118101 (2010); Phys. Rev. E **81**, 011908 (2010); *Phys. Rev. Lett.* v100, 178102 (2008)



Example of Phase-field modelling

Modelling Lipid rafts in Cell membranes: Critical *Hl*

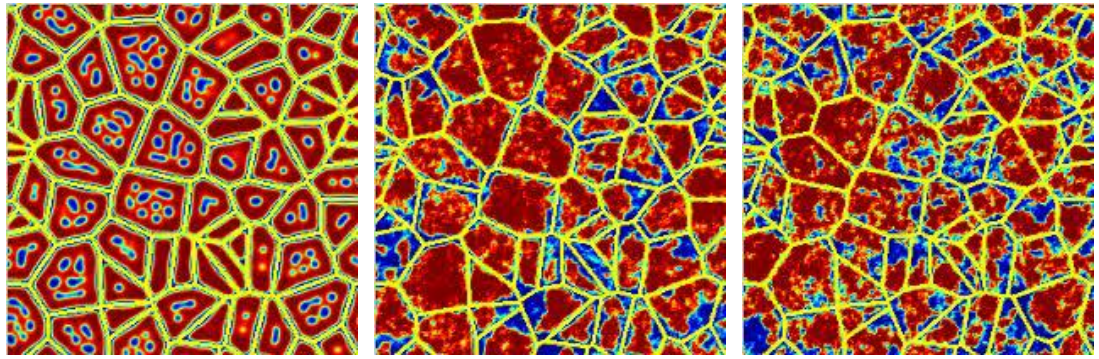


J. Fan, M. Sammalkorpi, and M. Haataja, *Phys. Rev. Lett.* v104, 118101 (2010); Phys. Rev. E **81**, 011908 (2010); *Phys. Rev. Lett.* v100, 178102 (2008)

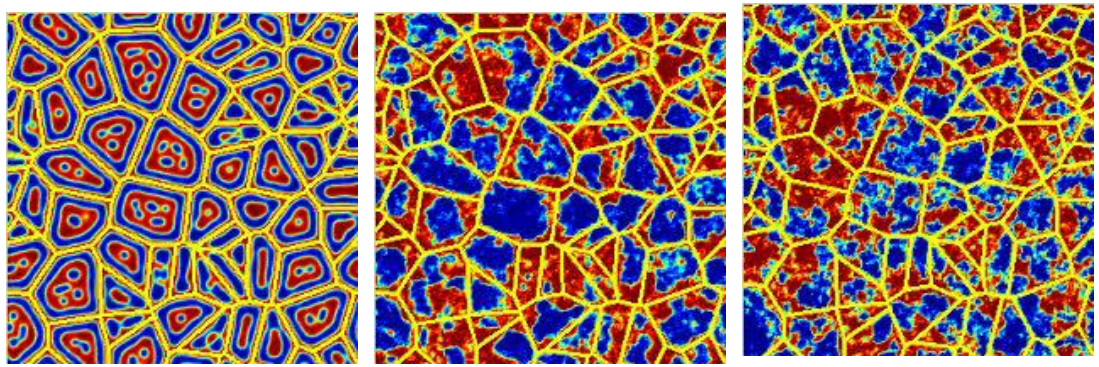
Example of Phase-field modelling: Modelling Lipid rafts in Cell membranes: The local interaction can regulate both the raft size and the raft spatial distribution.

- Local membrane-cytoskeleton interaction $\frac{\partial c(\vec{r},\tau)}{\partial \tau} = \nabla^2(-\nabla^2 c - c + c^3 + g(\vec{r})) + \xi(\vec{r},\tau)$

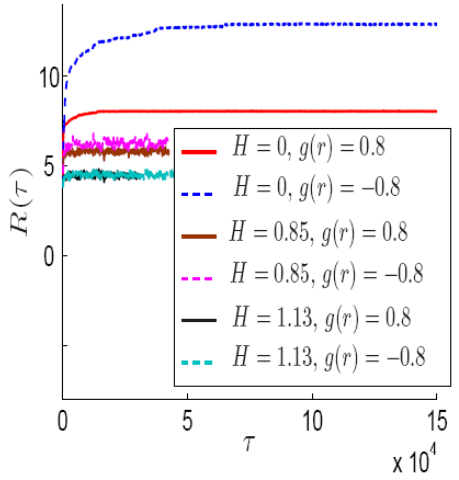
  - Local attractions (yellow meshes g(r)>0)

Ld 

  - Local repulsions (yellow meshes g(r)<0)

Lo 

H=0 *H*=0.85 *H*=1.13



The local interaction can regulate both the raft size and the raft spatial distribution.

J. Fan, M. Sammalkorpi, and M. Haataja, *Phys. Rev. Lett.* v104, 118101 (2010); Phys. Rev. E **81**, 011908 (2010); *Phys. Rev. Lett.* v100, 178102 (2008)