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Multiscale modelling of polymer aggregates

Paola Carbone

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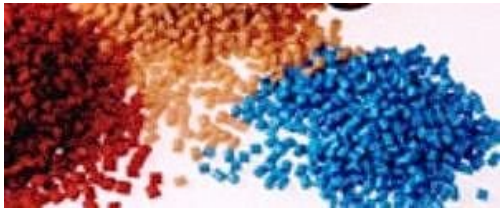
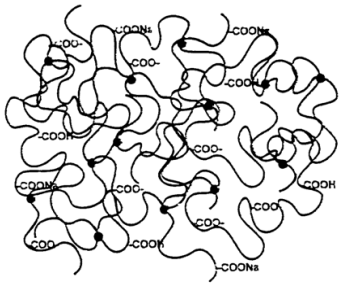
School of Chemical Engineering and Analytical Science

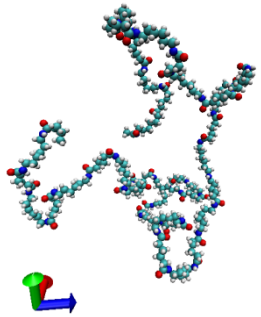
Polymers: Length and Time Scales

Polymers can be studied at different length scales

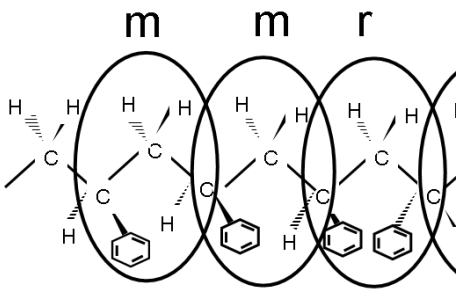




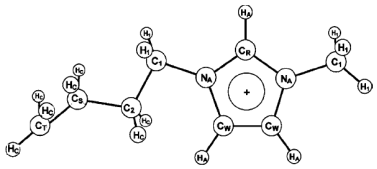
Macro L 100-1000 Å
T 1 sec



Meso
L 10-50 Å
T 10^{-8} 10^{-4} sec



Micro L 3-10 Å
T 10^{-13} sec



Nano L 1-3 Å
T 10^{-15} sec

Multiscale modelling approaches

- **Passing Parameters :**

Obtain data from models at one length scale and pass this information to a model in a different length scale (example: force field development):

"A CFD/MD model for polymer nanoparticles precipitation "

N. DiPasquale, D. Marchisio, P. Carbone, A. Barresi, Chem. Eng. Res. and Des. 2013, 91, 2275-2290

- **Integrating parameters:**

Merge data obtained from models at different length scales (hybrid models).

"Developing hybrid model for polymer bulks"

N. DiPasquale, D. Marchisio, P.C, J. Chem. Phys. 137: 164111-164119 (2012)
N. DiPasquale, R. Gowers, P. Carbone, J. Comp. Chem. 2014, 35, 1199

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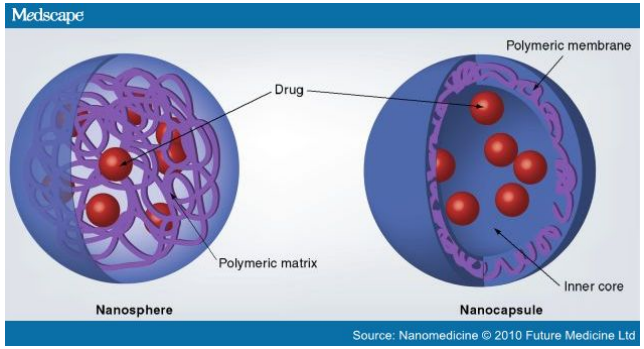
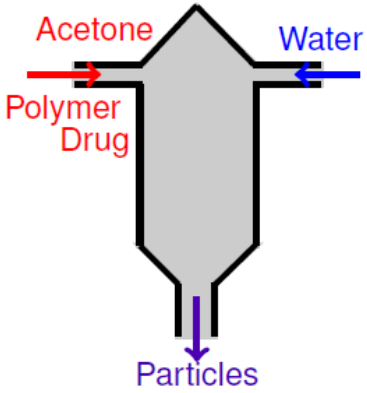
Parameters passing models : When are they useful?

Polymer nanoparticles for biological applications



Polymer (PCL) nanoparticles: production (Confined Impinging Jets Mixer)



Particles are produced with solvent displacement by mixing of a solvent (acetone) containing the polymer and the drug, and the anti-solvent (water), inducing the formation of polymer particles entrapping drug molecules inside.

Parameters passing models: application

The model must account for:

- turbulent mixing
- effect of turbulent fluctuations on particle formation
- effect of molecular growth and aggregation on the final particle characteristics

The calculation of the nucleation rate (J) for polymer particles is related to the polymer concentration on the different position in the mixer and its volume and area.
CFD provides information about the polymer concentration and **MD** about the polymer size and shape as a function of the solvent quality and mixture.

$$J^s = \left(\sum_{n=u}^{v} \frac{d^2}{24Nn^{2/3}D \exp\left(-(\Delta G_V(n) + \Delta G_A(n) - \Delta G_1)/(2k_BT)\right)} \right)^{-1},$$

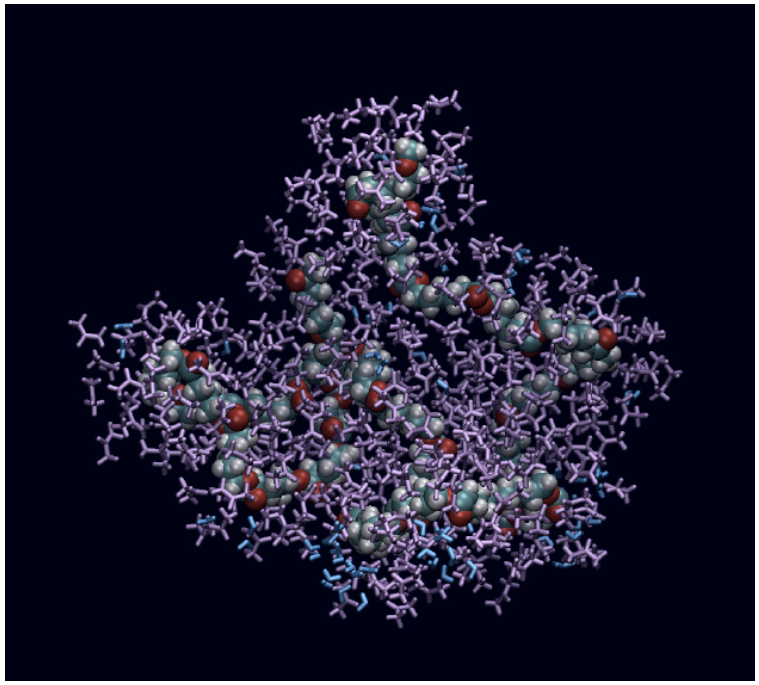
$$\Delta G_A(n) = A_s(n)\sigma,$$

A_s surface characterizing one nucleus parameter obtained from **MD** simulations

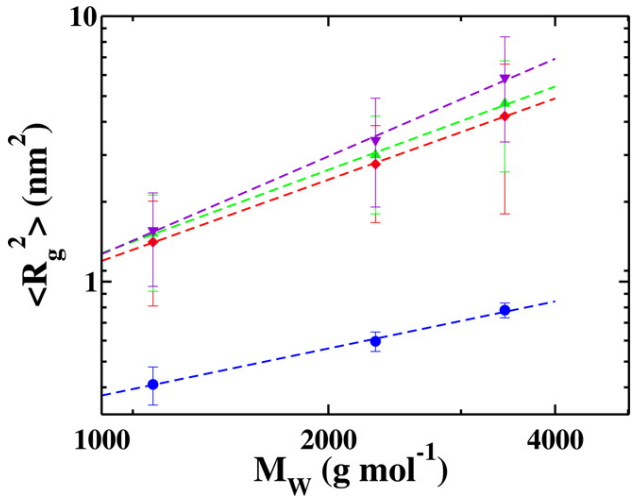
N. DiPasquale, D. Marchisio, P. Carbone, A. Barresi, Chem. Eng. Res. and Des. 2013, 91, 2275-2290

Parameters passing models : application

MD revealed that the PCL chain structure is almost identical in all acetone concentration.



	$\langle R_g^2 \rangle$	$\langle R_{g,x}^2 \rangle$	$\langle R_{g,y}^2 \rangle$	$\langle R_{g,z}^2 \rangle$
$x_A = 1$	1.56 ± 0.60	1.24 ± 0.60	0.24 ± 0.10	0.07 ± 0.03
$x_A = 0.75$	1.52 ± 0.60	1.21 ± 0.60	0.24 ± 0.10	0.07 ± 0.03
$x_A = 0.50$	1.41 ± 0.50	1.10 ± 0.50	0.23 ± 0.10	0.07 ± 0.03
$x_A = 0$	0.41 ± 0.07	0.23 ± 0.08	0.12 ± 0.02	0.07 ± 0.01



N. DiPasquale, D. Marchisio, A. Barresi, P. Carbone, J. Phys. Chem B, 118, 46, 13258-13267 (**2015**)

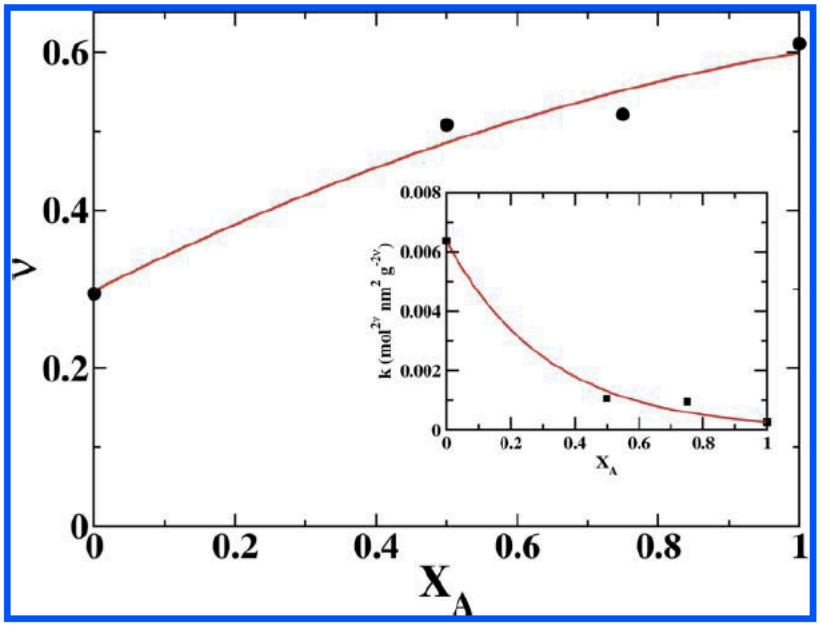
Parameters passing models : application

The Flory parameter υ changes with the acetone concentration X_A

$$\langle R_g^2 \rangle = k M_W^{2\nu}$$

$$\nu(x_A) = 0.30 + 0.45x_A - 0.15x_A^2$$

$$k(x_A) = 0.0064 \exp(-3.15x_A)$$



$$\langle R_g^2 \rangle = [0.0064 \exp(-3.15x_A)] M_W^{(0.60+0.90x_A-0.30x_A^2)}$$

N. DiPasquale, D. Marchisio, A. Barresi, P. Carbone, J. Phys. Chem B, 118, 46, 13258-13267 (**2015**)

Parameters passing models : application

The Diffusion coefficient, D, changes with the acetone concentration X_A

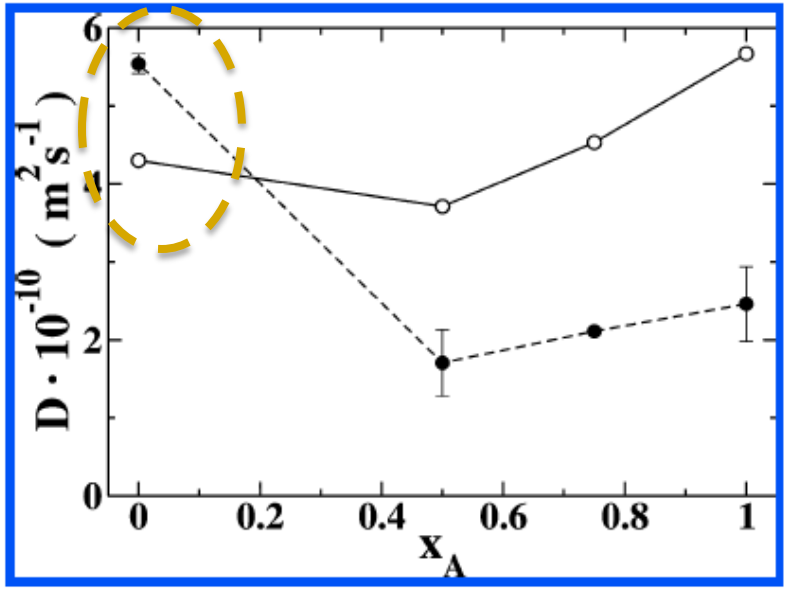


Figure 11. Diffusion coefficients for PCL-10 versus the composition of the water–acetone mixture (x_A) as simulated with MD (●) and as predicted with the Stokes–Einstein theory (○) of eq 6. Lines are provided only as a guide to the eyes.

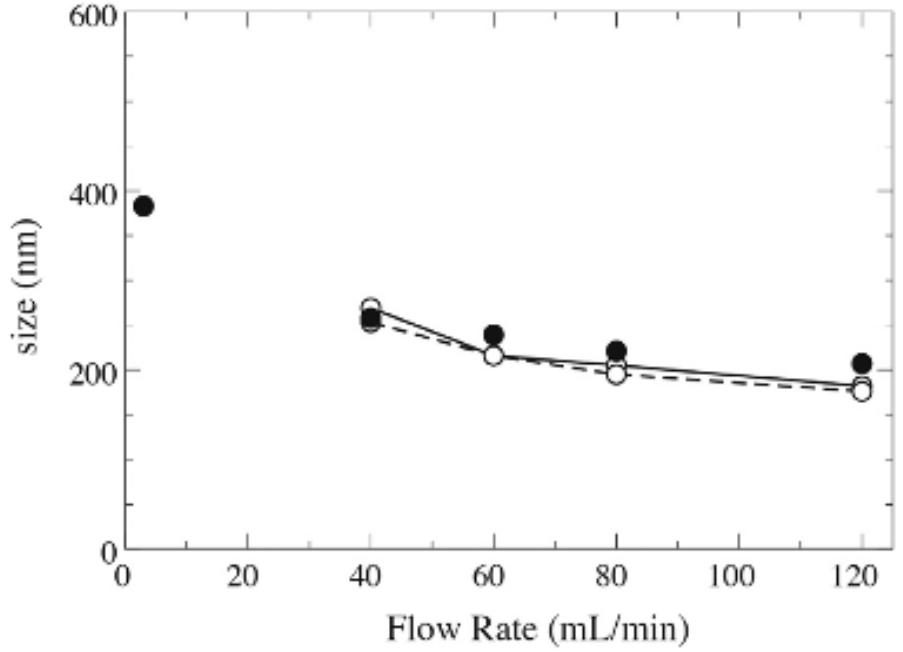
$$\mathcal{D}_{SE} = \frac{k_B T}{6\pi\mu R_h}$$

$$\mu = \exp(x_A \ln(\mu_A) + (1 - x_A)\ln(\mu_W))$$

N. DiPasquale, D. Marchisio, A. Barresi, P. Carbone, J. Phys. Chem B, 118, 46, 13258-13267 (**2015**)

Parameters passing models : application

Comparison between experimental results (black filled circles) and simulation results (open circles)



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Merge data obtained from models at different length scales (hybrid models).

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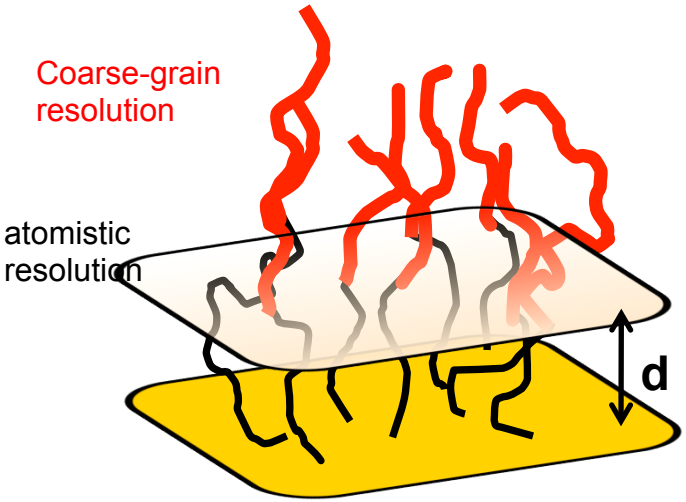
R. Gowers, P. Carbone, J. Chem. Phys 142: 224907 (2015)

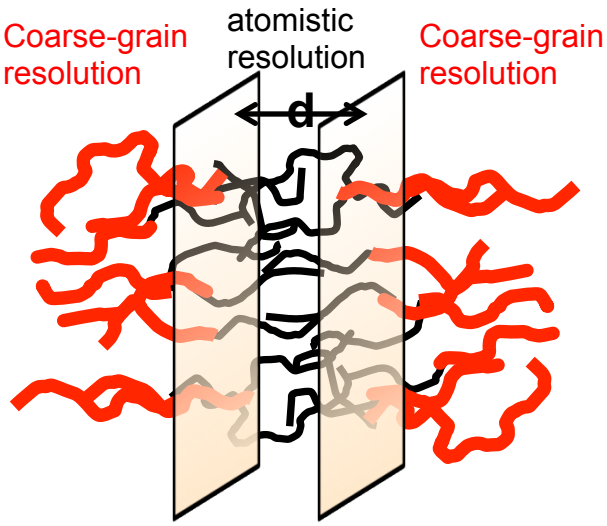
Hybrid models: when are they useful?

When will an hybrid model be useful?

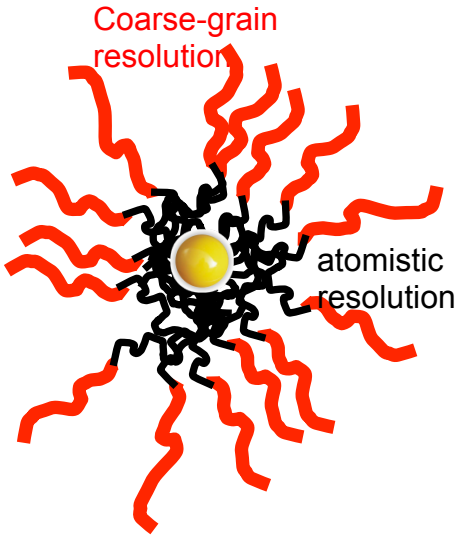
Solid-soft interfaces



Soft-soft interfaces



Diffusion of particles



Developing hybrid models: challenges

If the CG force field is derived from atomistic simulation,
is it possible to describe a macromolecule with a dual resolution?

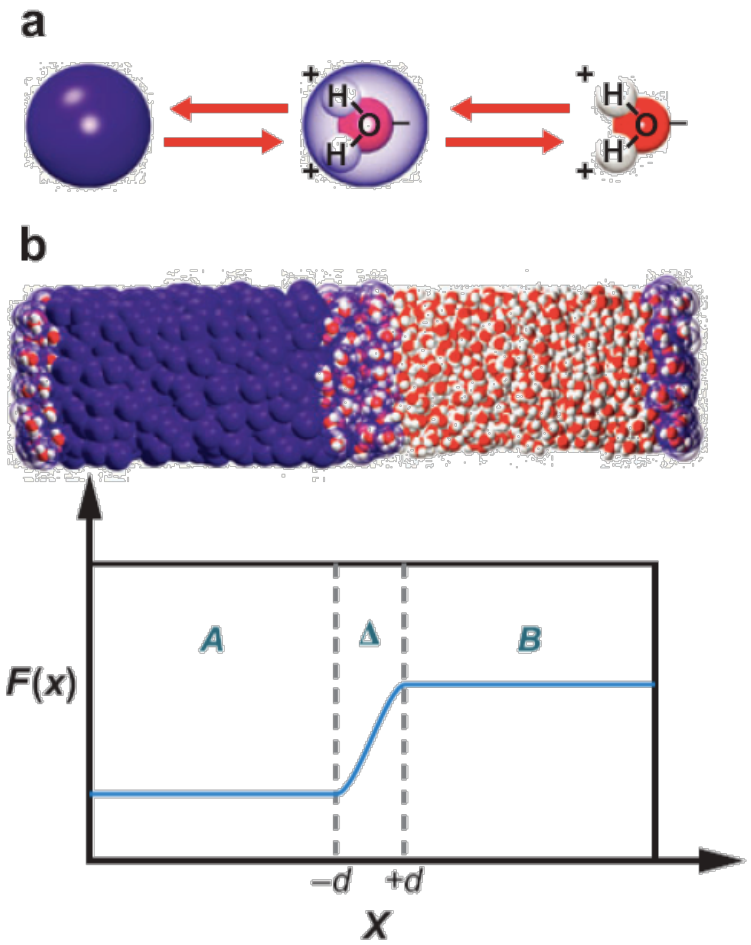
Requirements/characteristics

1) The CG potential needs to represent the same atomistic thermodynamic state

2) The two force fields need to be mixable

3) temperature gradient maybe the present and should be taken care of

Adaptive resolution for water



M. Praprotnik, L. Delle Site, K. Kremer, Annu. Rev. Phys. Chem. **2008**. 59:545–71

Developing hybrid models: polymer melts

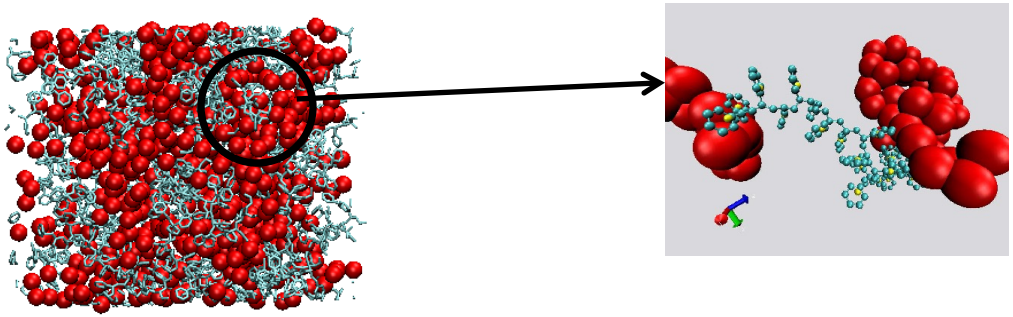
At equilibrium, conditions analogous to two-phase coexistence, it should be:

$$\mu_{AA} = \mu_{CG},\ p_{AA} = p_{CG},\ T_{AA} = T_{CG}$$

Therefore no-physical mass transfer through the interface

For polymer melts

1) A single molecule needs to be model at different level of resolution
2) The mixing of CG and atomistic potential is needed for both the bonded and non-bonded interactions



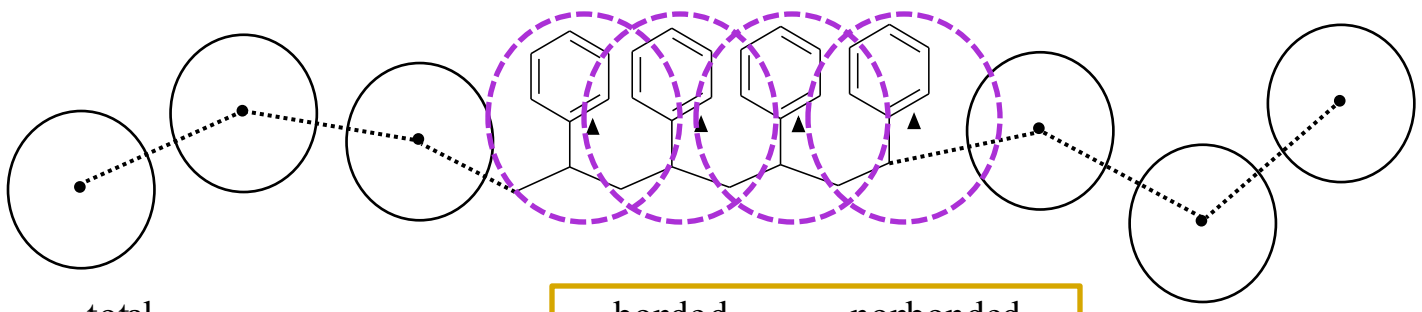
Hybrid model: Developing the force field

Two possible strategies are possible

1) Take existing atomistic and coarse-grained force fields and devise a way to mix them together

2) Develop directly the “hybrid” atomistic/coarse-grained potential using one of the existing method to optimize coarse-grained force fields

Hybrid model: Developing the force field Strategy 1



$$V^{total} = V_{AA} + V_{CG} + V^{bonded}_{AA\text{-}CG} + V^{nonbonded}_{AA\text{-}CG}$$

$$V^{bonded}_{AA\text{-}CG} = V^{str}_{AA\text{-}CG} + V^{bend}_{AA\text{-}CG} = \frac{1}{2}K_s\left(\left|\mathbf{R}_{A_i} - \mathbf{R}_{B_j}\right| - d^0_{A_iB_j}\right)^2 + \frac{1}{2}K_b\left(\vartheta_{AB} - \vartheta^0_{AB}\right)^2$$

Extracted from the atomistic simulations

From the fitting of the IBI potentials

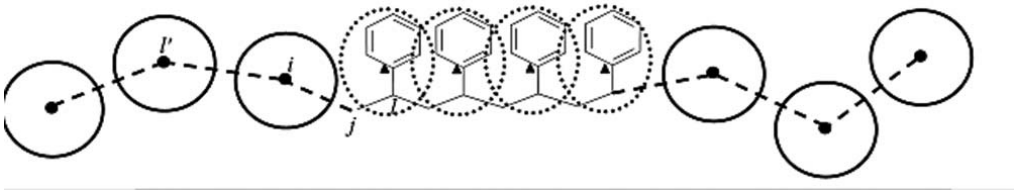
Cross terms

$$V^{nonbonded}_{AA\text{-}CG} = V^{nonbonded}_{CG\text{-}CG}$$

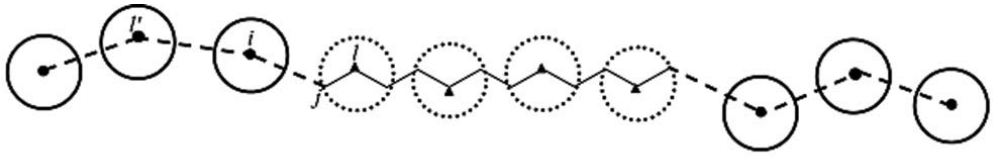
$$f_j = \frac{m_j}{\sum_{i=1}^{N_A} m_i} F_i$$

N. DiPasquale, D. Marchisio, P.Carbone, J. Chem. Phys. 137: 164111-164119 (2012)

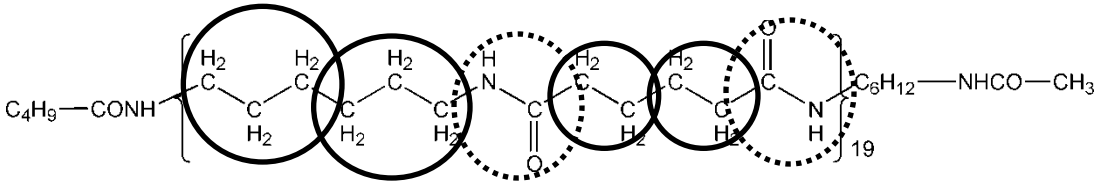
Systems investigated



Atactic Polystyrene



Polyethyelene



Polyamide-6,6

IBIsCO

H. A. Karimi-Varzaneh, H. J. Qian, X. Y. Chen, P. Carbone and F. Muller-Plathe, *J. Comp. Chem.*, 2011, **32**, 1475-1487.

Single Chain Structural properties

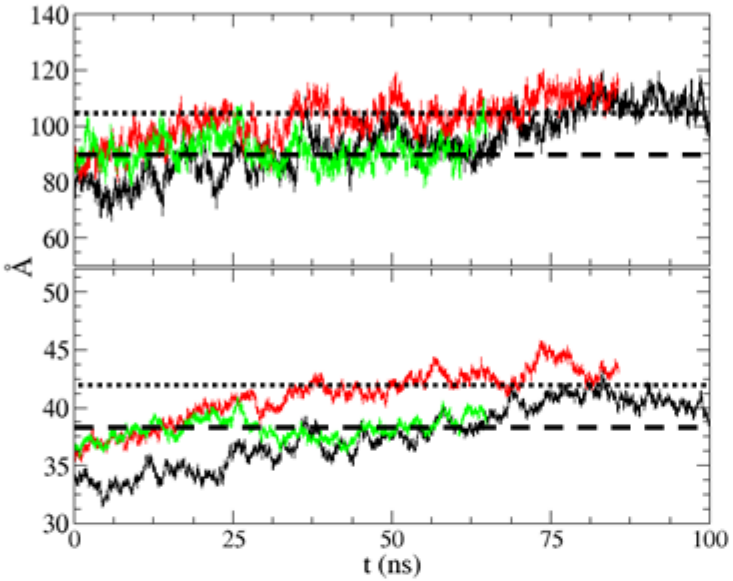
How well the structure properties are reproduced?

Comparison between the end-to-end distance and radius of gyration between the hybrid and mono-resolved model (_ _ _ : All-Atom [*]
..... : CG)

More atoms

More beads

50% atoms and beads



Polyethylene

R_{ee}

R_g

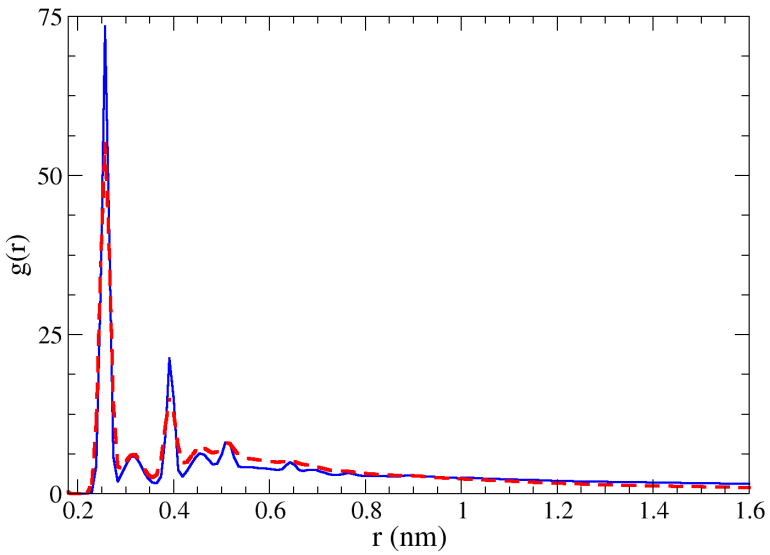
[*] P. Carbone, H. A. Karimi-Varzaneh and F. Muller-Plathe, *Faraday Discuss.*, 2010, **144**, 25-42.

Structural properties

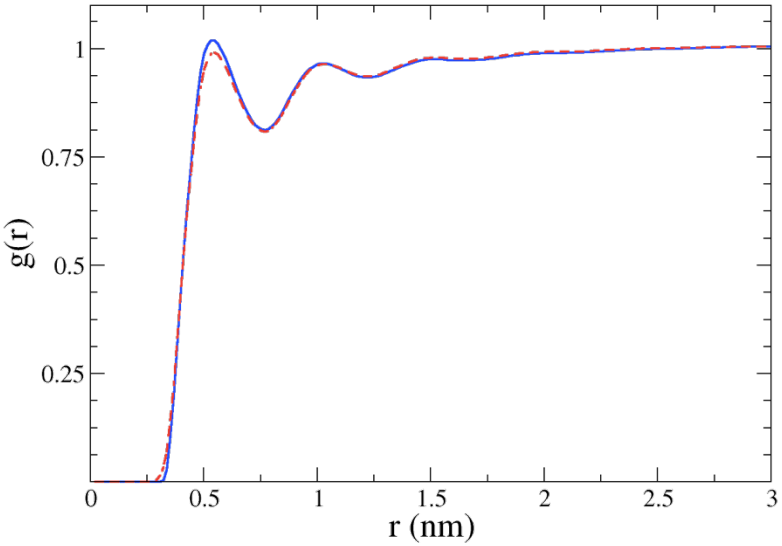
How well the atomistic and global structure is reproduced?

Intra and inter -chain radial distribution function

Atomistic reference Hybrid models



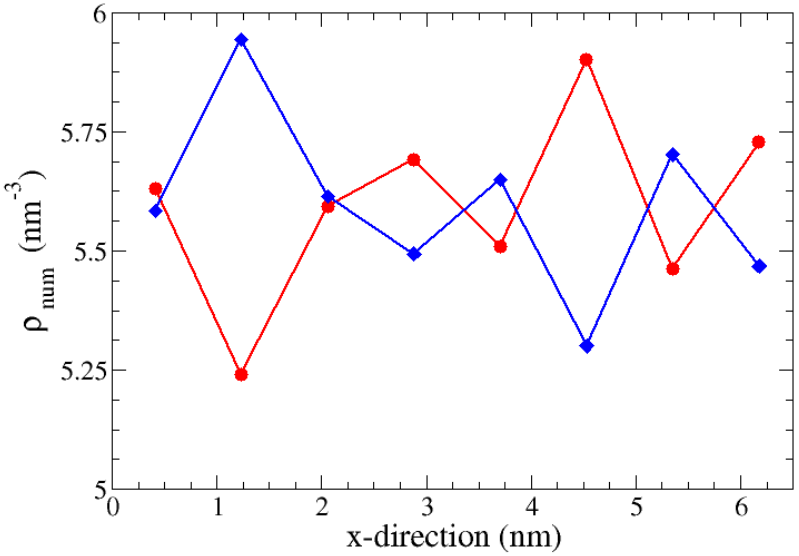
Intra-chain



Interchain

Is there an interface in the model?

Numerical density profile across the simulation box along the *x*-axis calculated separately for the **coarse-grained beads** (blue line) and **virtual sites** (red line)



Polyethylene

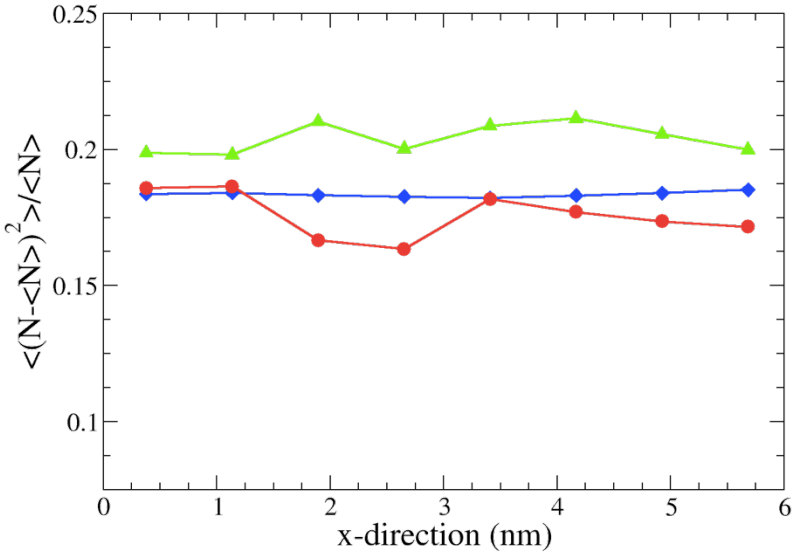
No bias in the potential

Interface: density fluctuations

If the compressibility predicted by the two models is different, unphysical mass transfer can occur in the system.

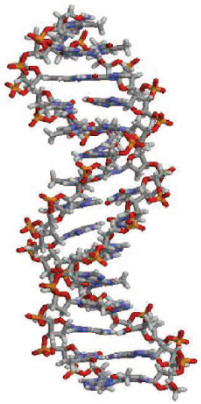
Particle number (N) fluctuation across the simulation box along the *x*-axis for **pure atomistic** (red dotted line), pure **coarse-grained** (solid blue line) and **hybrid** (green dashed line) model

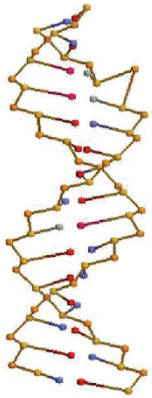
Polyethylene



No visible interface in the model

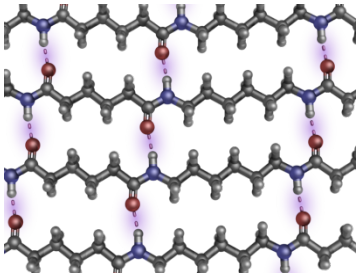
Importance of hydrogen bonds



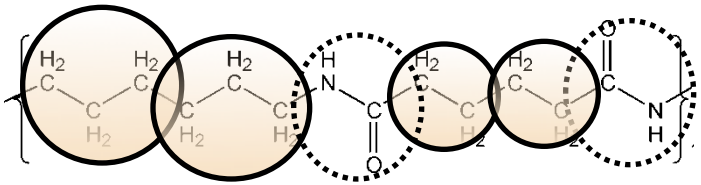


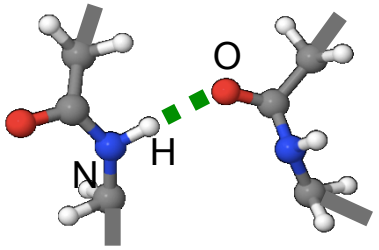
Duplex DNA structures

M. McCullagh et al. *J. Phys. Chem. B* **2008,** *112,* 10388–10398
Knotts, T. A. t.; Rathore, N.; Schwartz, D. C.; de Pablo, J. J. *J. Chem. Phys.* **2007**, *126*, 084901.



HB are responsible for the crystallization and transition temperature in PA

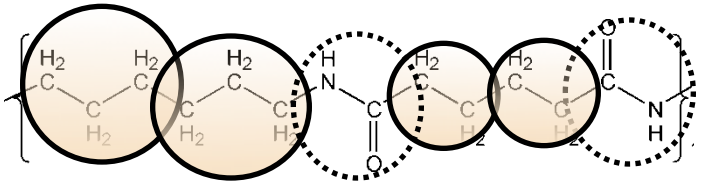


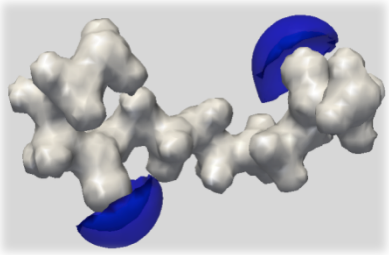


Hossein Ali Karimi-Varzaneh, Paola Carbone, and Florian Müller-Plathe, *Macromolecules* **2008** *41* (19), 7211-7218

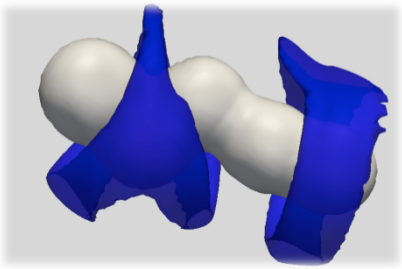
PA: formation of hydrogen bonds

Can the hybrid model form hydrogen bonds?

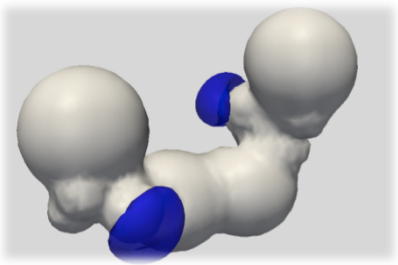




Atomistic model
# of pairs: 4,087,000



CG model
# of pairs: 114,000



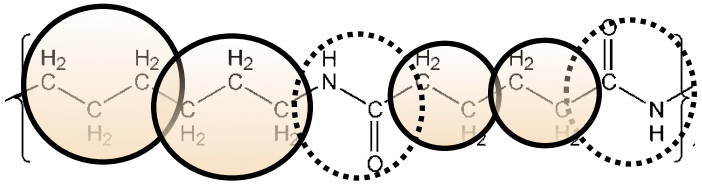
Hybrid model
# of pairs: 671,000

Directionality is maintained

Electrostatic is included via Coulomb interactions and Reaction field

R. Gowers, P. Carbone, J. Chem. Phys 142: 224907 (2015)

PA: Is the system equilibrated?



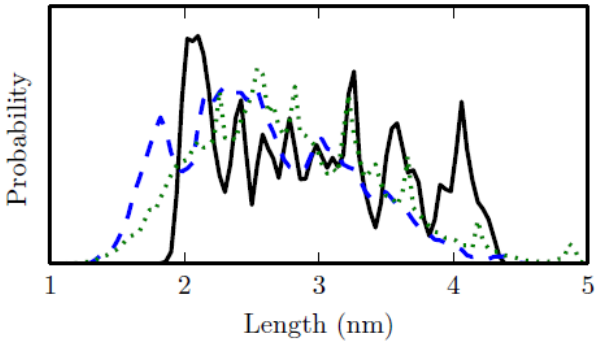
Simulation details

0.001 ps timestep
NPT at 101.3 kPa

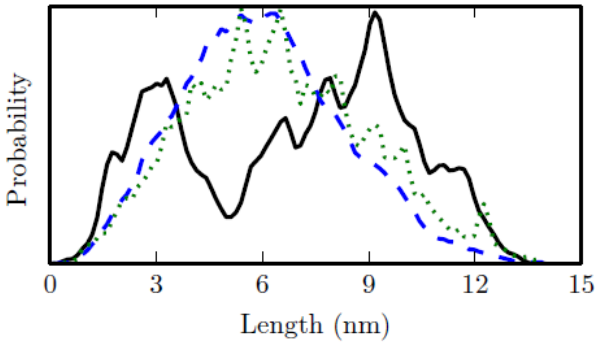
atom-atom cut-off: 0.9 nm
bead-bead cut-off: 1.2 nm

time: 300ns
T=400K

Atomistic
Hybrid
CG

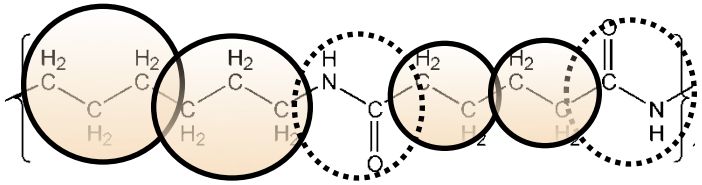


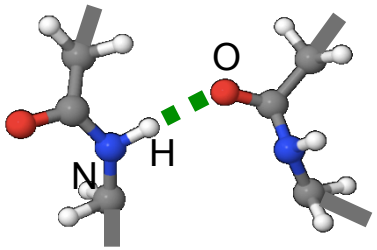
(a) Radius of gyration



(b) End to end distance

PA: formation of hydrogen bonds





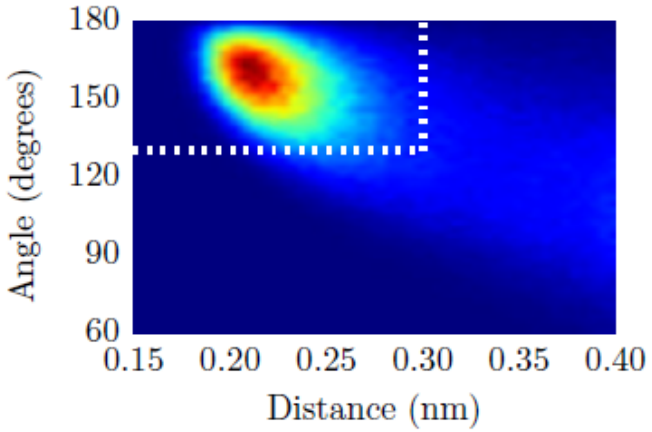
Geometrical criterion

$$d \leq 0.297 \text{ nm}$$

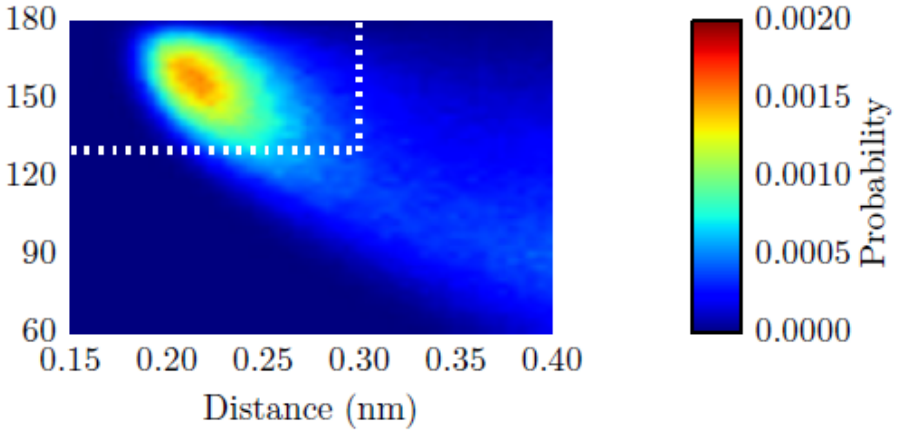
$$\theta_{N-H\cdots O} > 130^0$$

T=400K

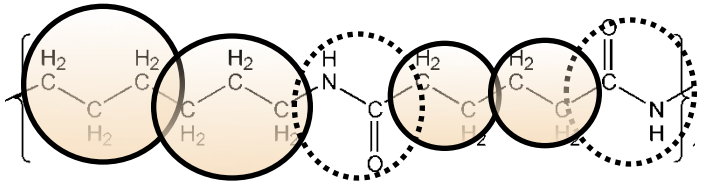
Atomistic



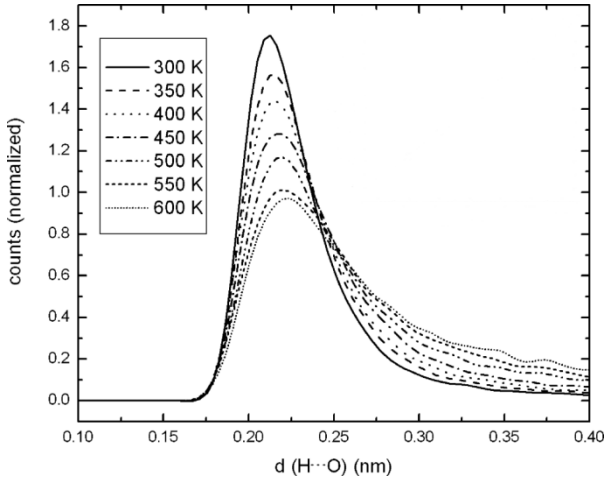
Hybrid model



PA: Thermodynamics of hydrogen bonds

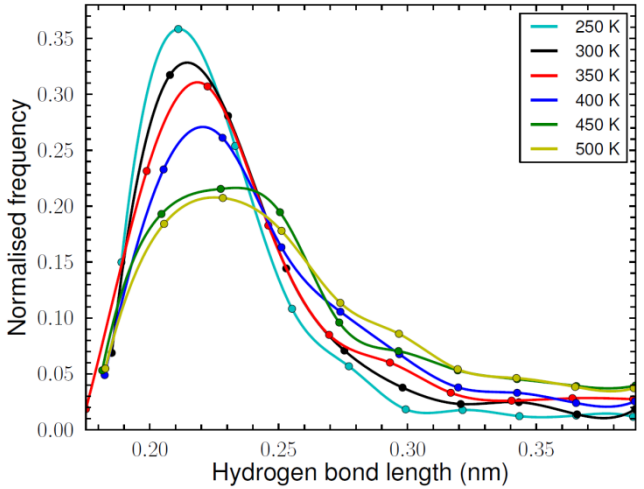


AA-model



Hossein Ali Karimi-Varzaneh, Paola Carbone, and Florian Müller-Plathe, *Macromolecules* **2008** *41* (19), 7211-7218

Hybrid AA-CG model



R. Gowers, P. Carbone, J. Chem. Phys 142: 224907 (2015)

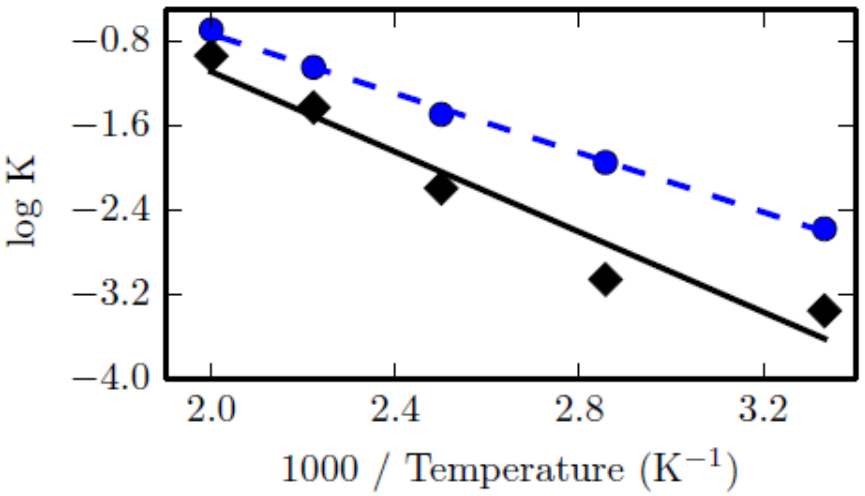
Polyamide: formation of hydrogen bonds

$$\log K = -\frac{\Delta H}{RT} + \frac{\Delta S}{R}$$

$$(NH\ldots O)_{bonded} \overset{K}{\rightleftharpoons} (NH)_{free} + (O)_{free}$$

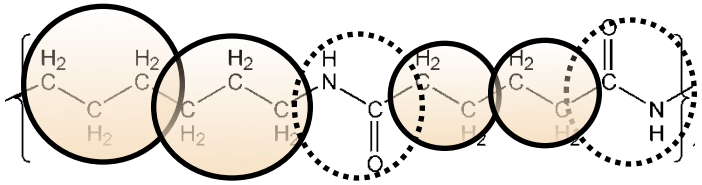
$$K = \frac{\left[(NH)_{free}\right]\left[(O)_{free}\right]}{\left[(NH\ldots O)_{bonded}\right]} \approx \frac{(1-X)^2}{X}$$

Atomistic
Hybrid

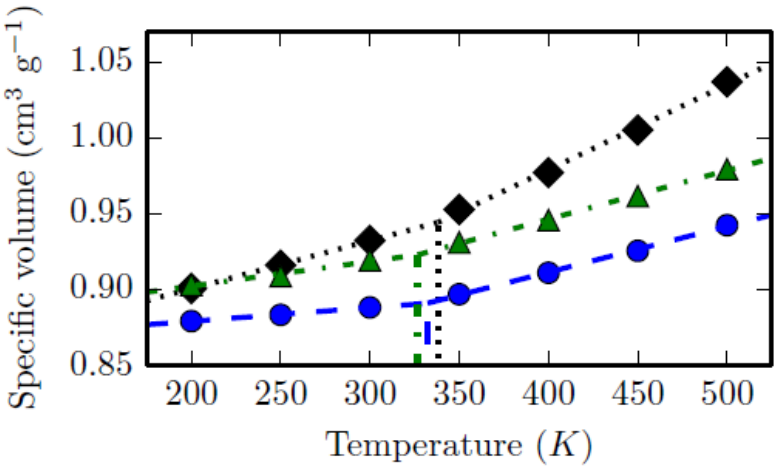


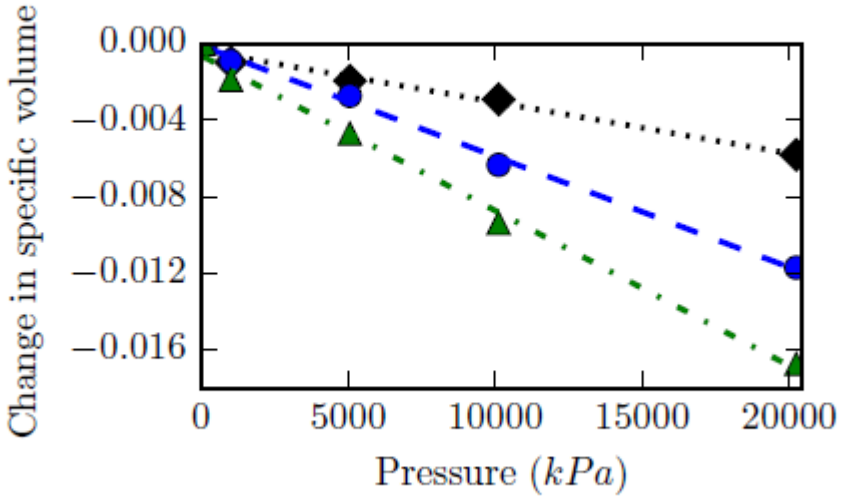
	Exp	Sim At	Sim CG/At
ΔH [kJ/mol]	29÷59 (high M_w)	15.4 ± 0.6	11.7 ± 0.5
	14.5÷27 (Low M_w)		
ΔS	--	21.7 ± 1.2	17.4 ± 1.3

PA: Transferability of the model

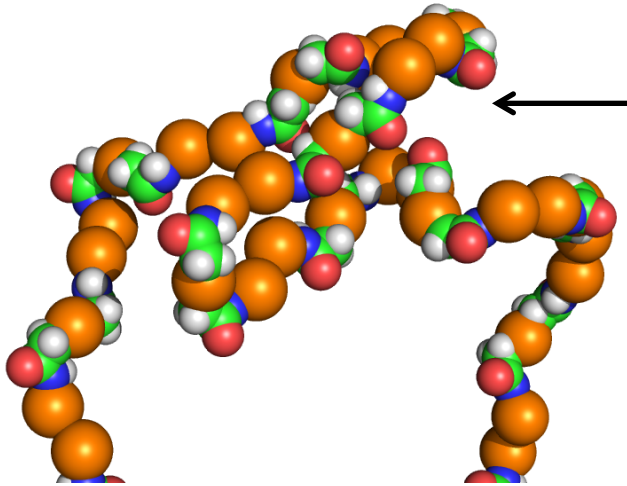


Atomistic
Hybrid
CG





Transferability of the model

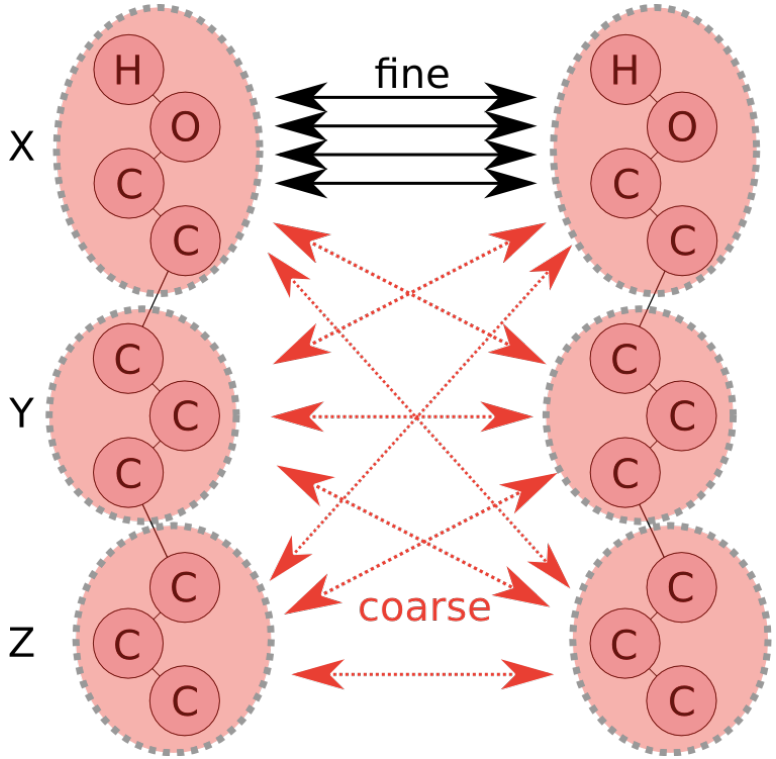


Onset of the folding of the chain?

	Atomistic*	CG*	Exp*	Hybrid
T_g (K)	330	380	330	313
α_{rubber} (K^{-1})	5.4E-4	5.6E-4	6.6E-4	4.8E-4
α_{glass} (K^{-1})	2.8E4	2.1 E-4	3.4E-4	2.4E-4
B (kPa^{-1})	2.7E-07	7.9E-7K^{-1}	7.3E-7	5.8E-7

* P. Carbone, H. Karimi, X. Chen, F. Müller-Plathe J. Chem. Phys, 128, 64904 (2008)

Hybrid model: Developing the force field Strategy 2

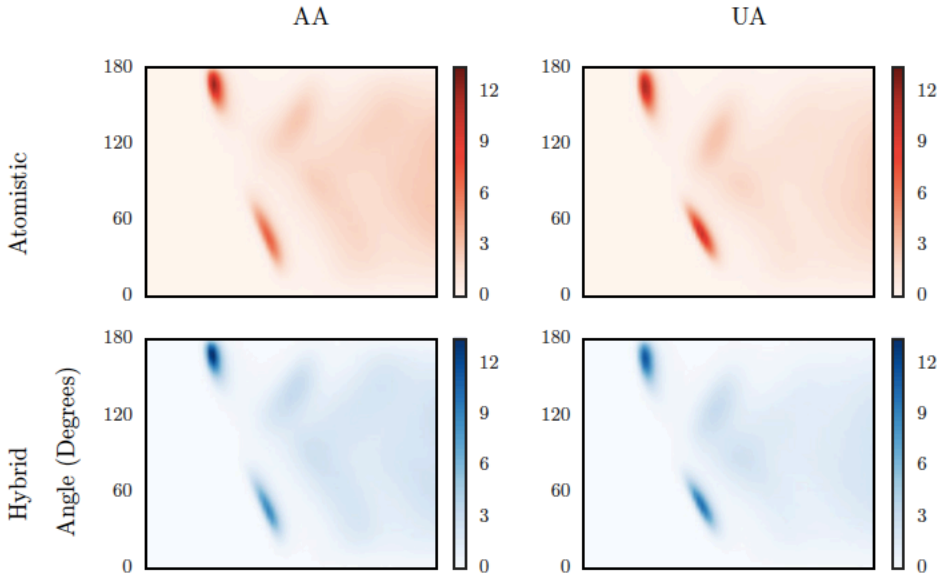


1) We use the IBI inversion to develop only the interactions between the beads of the carbon tail
2) The “head” polar group are modelled with atomistic interactions
3) We still use the VS to collect all the forces from the CG beads
4) All the bonded interactions are treated at atomistic level

R. Gowers, P. Carbone unpublished data

Hybrid model: Developing the force field Strategy 2

Hydrogen bonds are reproduced



R. Gowers, P. Carbone unpublished data

Developing a Multiple time steps scheme

We can further reduce the time of the simulation developing a MTS scheme which integrate the equation of motion between AA and bead-beads (BB) with a different timestep

$$\mathrm{F}_{BB}(t_n + k\Delta t) = \sum_{i=0}^{h} \frac{(k\Delta t)^i}{i!} \left(\frac{\partial^{(i)} F_{BB}}{\partial t^{(i)}} \right)_{t_0} \qquad \text{with} \quad k = 1, \ldots . m$$

F_{BB} is the force acting between two CG beads, and m is the maximum number of time steps to approximate, i is the Taylor series expansion order (h=1)

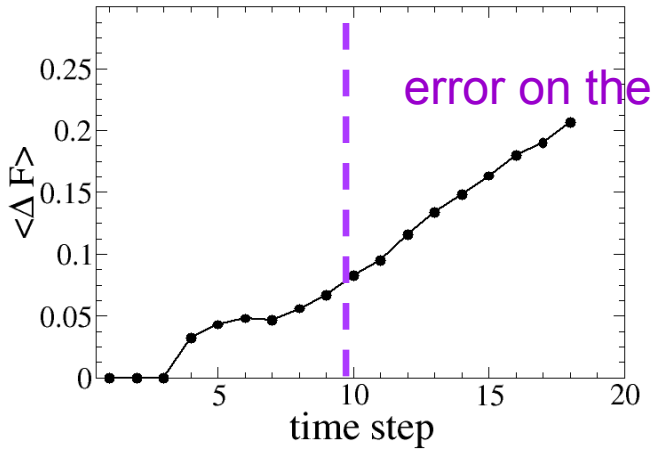
N. DiPasquale, R. Gowers, P. Carbone, J. Comp. Chem. **2014**, 35, 1199

Developing a Multiple time steps scheme

How many time steps can be approximated?

They can be estimated by calculating the weighted average fractional deviation between the approximated bead–bead forces and their true values through performing a very short preliminary simulation.

$$\langle \Delta F \rangle = \frac{1}{3} \sum_{i=1}^{N_{CG}} \sum_{\alpha=x,y,z} \left(\left| \frac{F_{i\alpha}^{t} - F_{i\alpha}^{a}}{\sum_{i=1}^{N_{CG}} |F_{i\alpha}^{t}|} \right| \right)$$



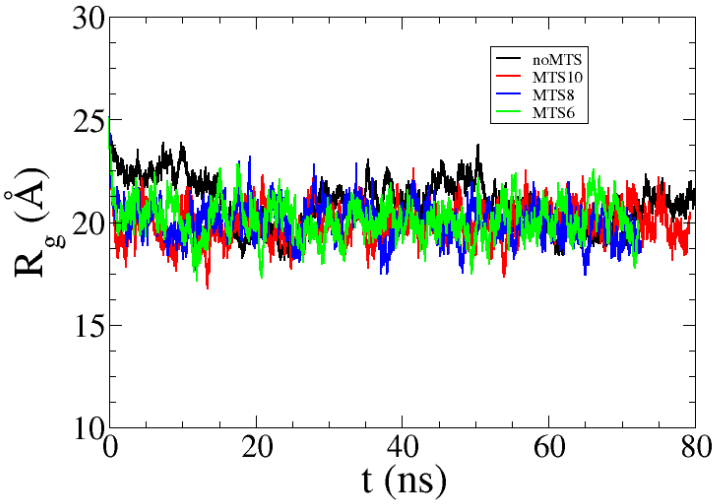
error on the force less than 15%.

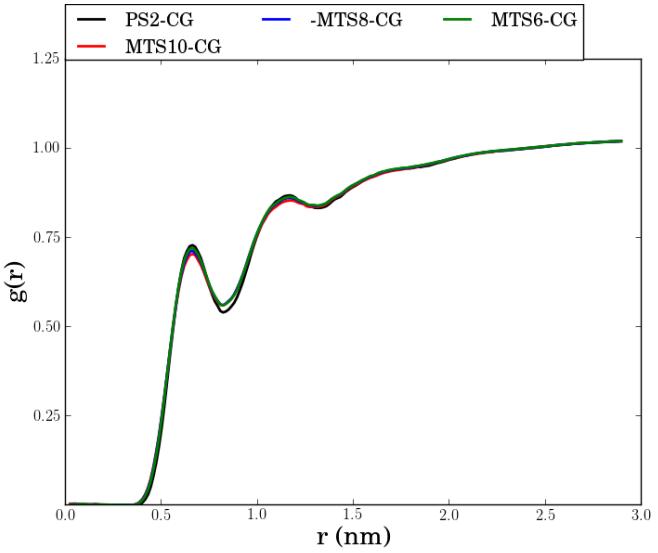
N. DiPasquale, R. Gowers, P. Carbone, J. Comp. Chem. **2014**, 35, 1199

Developing a Multiple time steps scheme

Effect of the MTS scheme on the structural properties

Atactic Polystyrene





Developing a Multiple time steps scheme

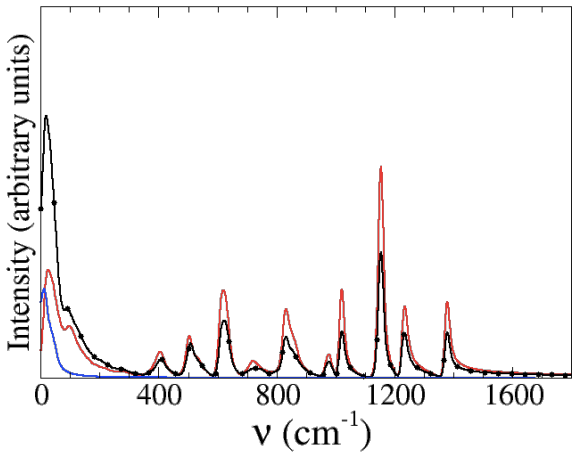
Effect of the MTS scheme on the dynamical properties.

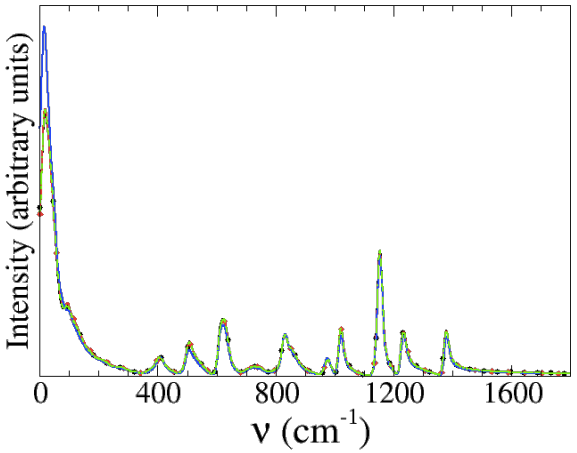
The spectral density $I(v)$:

$$I(v) = \frac{1}{\pi}\int_0^{+\infty} C_{\mathrm{vv}}(t)\cos(vt)\,dt \qquad C_{\mathrm{vv}}(t) = \frac{\langle \mathrm{v}(0)\cdot \mathrm{v}(t)\rangle}{\langle \mathrm{v}(0)\cdot \mathrm{v}(0)\rangle}$$

The spectrum obtained contains all the system vibration frequencies (v) that our MD simulations are able to capture considering that a timestep of 1 fs is used

CG, **AA**, **hybrid model**





Computational performances

TABLE II. Comparison of the computational cost of the models examined.

Model	Number of pairs	Normalised execution time
Atomistic	4 087 000	1.0
Hybrid	863 000	0.20
CG	188 000	0.057

On the MTS scheme:

The computational gain in using the MTS scheme depends on two factors: the number of time steps approximated and the number of CG beads in the model. In the specific case studied here, the computational gain turns out to be around 20%.

Conclusions

- For polymers it is possible to combine models of different length scales via parameters passing or parameters integration.

- Data from atomistic MD can be passed to continuum models (CFD) to get obtain a fully predictive model for polymers self-assembly

- The development of hybrid AA-CG model for polymer melts is possible

- The IBI force field can be mixed with the atomistic one from which it has been developed

- The structural properties of the system are maintained

- There is no interface in the model that behaves as a homogeneous system

- Directional properties such as HBs are maintained

- MTS scheme to better integrate the two time scales can be developed

Future directions

CFD/MD model

- Develop a multiscale model to couple DPD and CFD

CG/AA model

- Investigate the dynamic properties of the dual resolved model
- Construct a new AA-CG model that can keep the atomistic structure within the model

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