CLPdyn: a cheap and reliable tool for molecular dynamics studies of organic molecules in condensed phase

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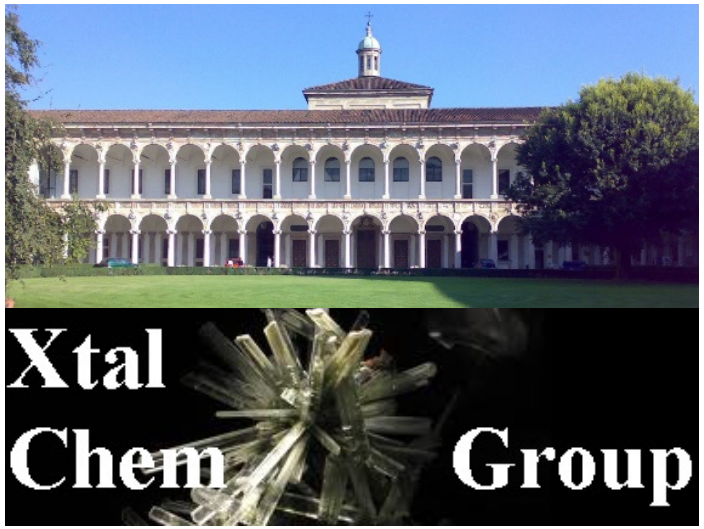

Università degli Studi di Milano

22.08.2019, ECM32, Wien, Austria

Outline

(i) Motivation

(ii) The method

(iii) The program CLP-dyn

(iv) Applications and results

(v) Conclusions

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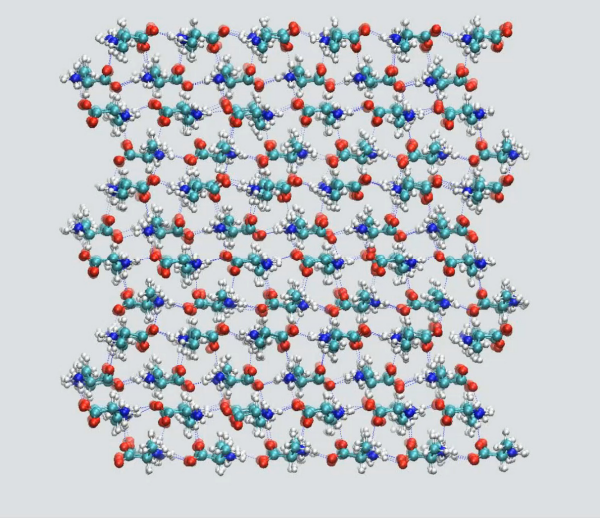
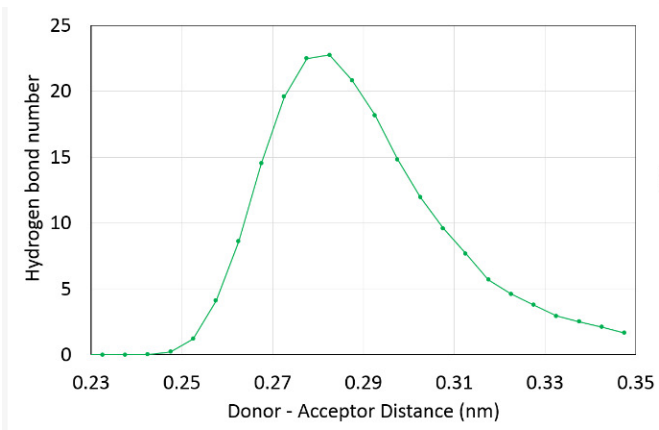
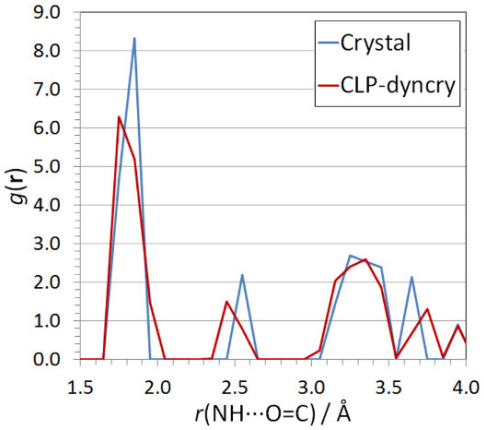
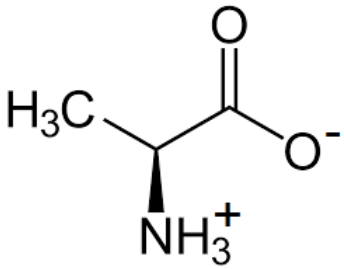
Dynamics



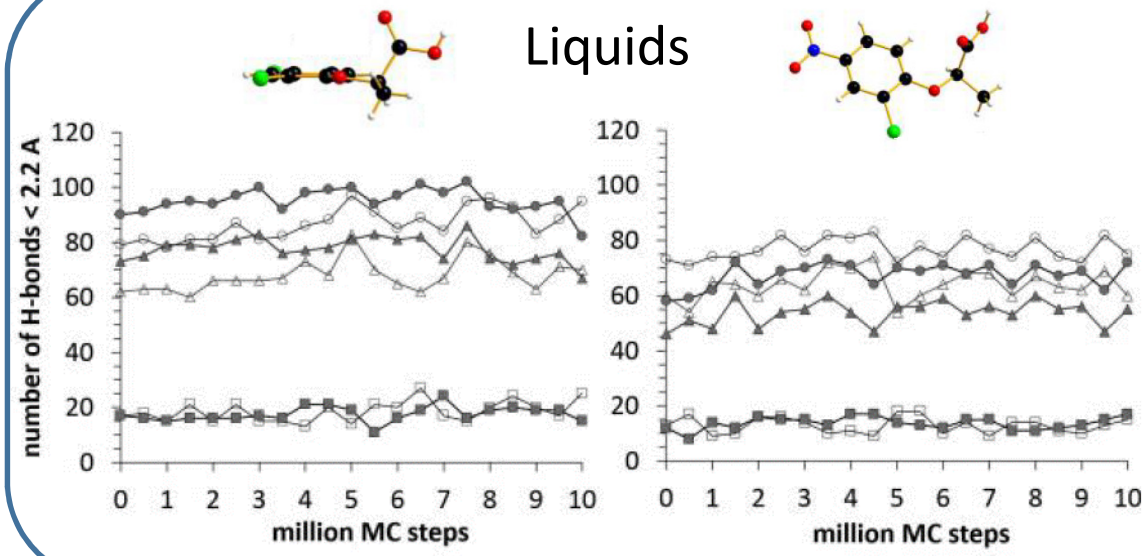




Solids



Liquids



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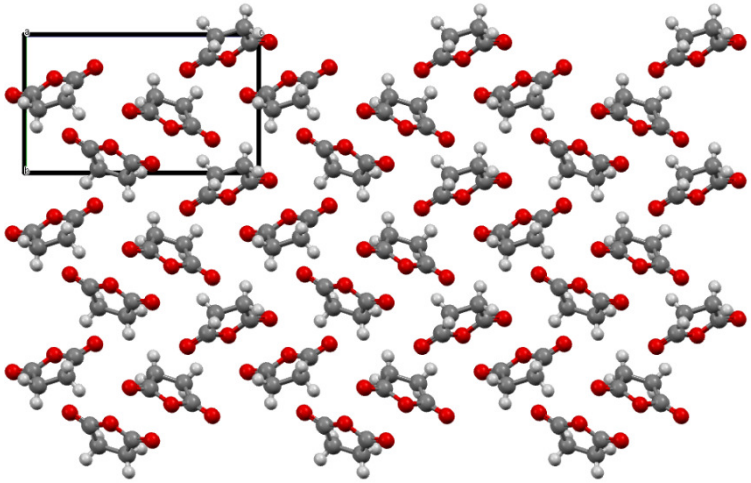
Why a new MD software?

Popular MD programs (AIMD, GROMACS…) **are not specifically oriented** toward **crystallographic problems**

Other programs are mostly used to simulate **hard matter systems** (oxides, metals, semiconductors…)



…and molecular crystals?

Force fields that perform very well for biopolymers (AMBER, CHARMM, OPLS-AA…) are often not well suited to deal with **small organic molecules**

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(i) Motivation

(ii) The method

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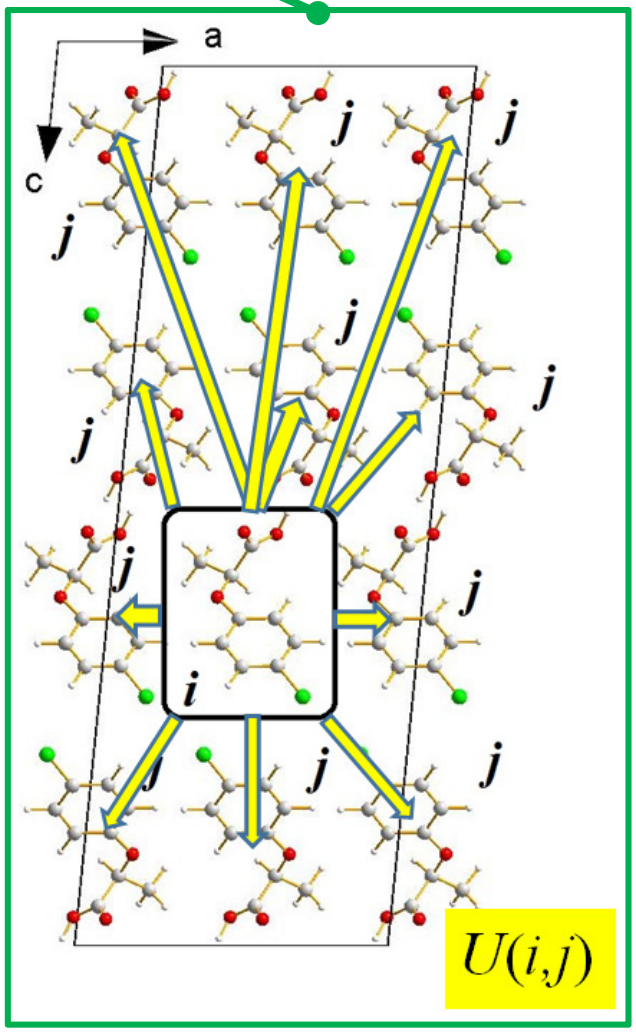
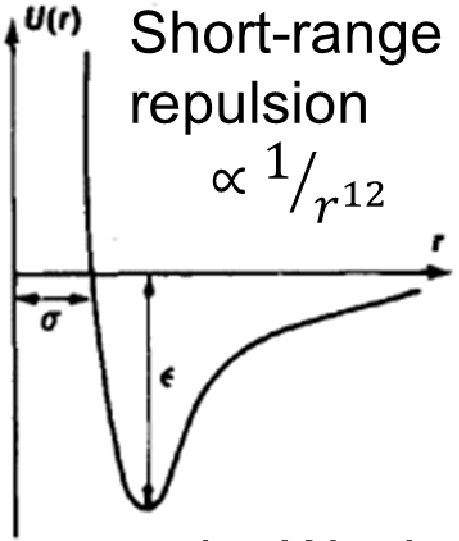
(iv) Applications and results

(v) Conclusions

The method

$$U(i,j) = E_{rep}(i,j) + E_{vdW}(i,j) + E_{el}(i,j) + E_{pol}(i) + E_{pol}(j)$$





Short-range repulsion

$$\propto 1/r^{12}$$

van der Waals

$$\propto -1/r^{6}$$

$$E_{el}(i,j) = \frac{1}{4\pi\varepsilon_0}\frac{q_i q_j}{r_{ij}}$$

$$E_{pol}(i) = -\frac{1}{2}\alpha_i \varepsilon_{i\leftarrow j}^2$$

$$E_{pol}(j) = -\frac{1}{2}\alpha_j \varepsilon_{j\leftarrow i}^2$$

$$\varepsilon_i = \frac{1}{4\pi\varepsilon_0}\sum_j \frac{q_j(\mathbf{r}_i - \mathbf{r}_j)}{|\mathbf{r}_i - \mathbf{r}_j|^3}$$

$$PPE = \sum_{i=1}^{N} PPE(i)$$

$$PPE(i) = \sum_j U(i,j)$$

Packing Potential Energy

The method

Lattice Energy, Packing Energy

$$E_{latt} = PE = U(crystal) = \frac{1}{2}PPE$$

$$\Delta H = -PE - 2RT$$

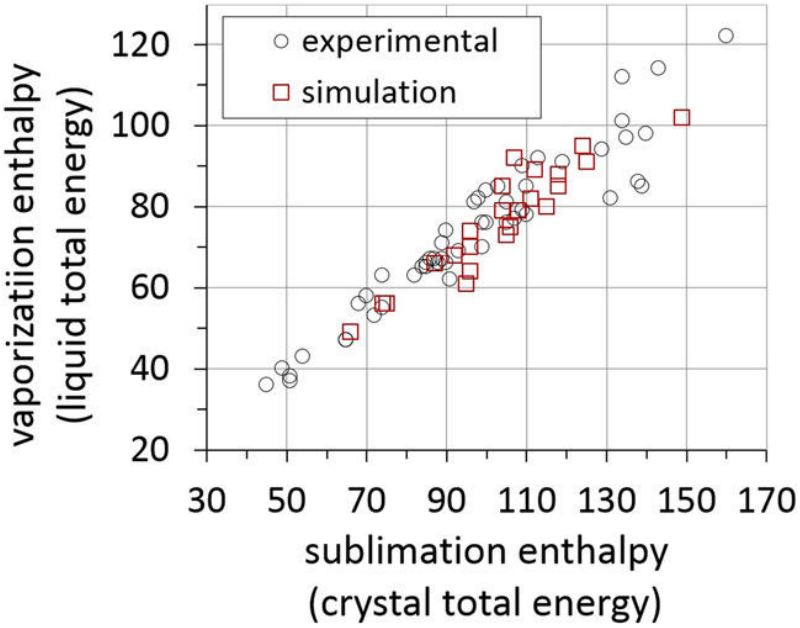
Ignoring zero-point and molecular relaxation corrections

Parametrization

(i) Enthalpies of sublimation (solids) and of evaporation (liquids);

(ii) Observed lattice parameters (solids) and specific volumes (liquids);

(iii) *U*(i,j) from MP2 calculations



Gavezzotti & Lo Presti, Cryst. Growth Des. ***2015****, 15, 3792–3803*

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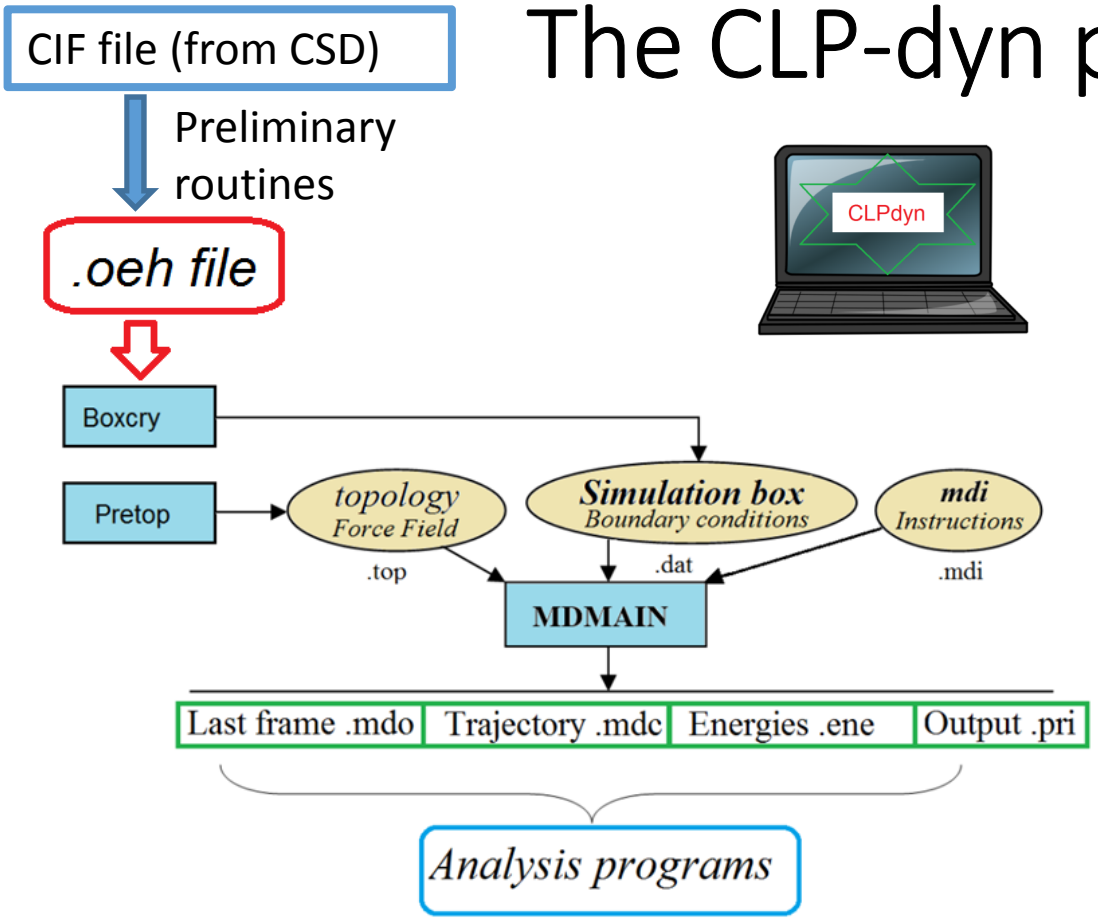
The CLP-dyn package



- For **bulk crystals**, periodicity is determined by repetition of the crystallographic unit cell. **Bulk liquids** use cubic simulation boxes. Also **non-periodic clusters** (nanocrystals and droplets) can be treated.
- Leap-Frog integrator.
- Berendsen (T, p) (anisotropic) rescaling allowed (**NpT ensemble**).
- **Heterogeneous mixtures** (liquids+solids) are allowed.

$$V(t + 1/2\Delta t) = V(t - 1/2\Delta t) + \frac{\Delta t}{M} F(t)$$
$$r(t + \Delta t) = r(t) + \Delta t \cdot V(t + 1/2\Delta t)$$

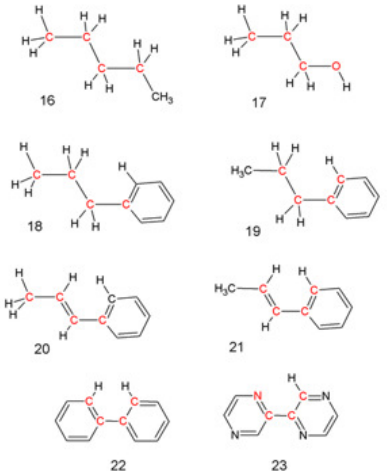
$$\lambda(t) = \left[1 + f\left(\frac{T_{set}}{T} - 1\right)\right]^{1/2}$$

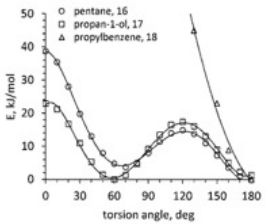
$$P_{ii} = \frac{2}{3V}\left(E_{kin,ii} - W_{ii}\right)$$

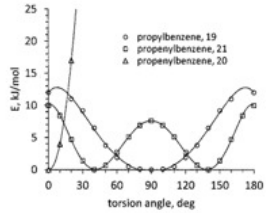
$$\mu_i = [1 - c(P_{set} - P_{ii})]^{1/3}$$

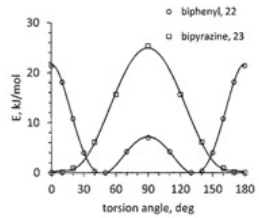
Intramolecular force field

$$E(\text{str}) = 1/2 \cdot k_{str}(R - R^0)^2$$
$$E(\text{bend}) = 1/2 \cdot k_{bend}(\cos\vartheta - \cos\vartheta^0)^2$$
$$E(\text{tors}) = k_{tors}[1 + f \cdot \cos(m\varphi)]$$









k_{str} and k_{bend} from MP2/6-31G** ab initio calculations on the corresponding deformation of prototypic compounds (Gavezzotti, New J. Chem. **2016**, *40*, 6848)

k_{tors} calibrated by fitting against MP2/6-31G** potential curves of ~ 50 organic compounds *in vacuo* (Gavezzotti & Lo Presti, J. Appl. Cryst. **2019**, submitted)

Intramolecular potentials here serve only as restraints to avoid undue molecular bond and angle distortions

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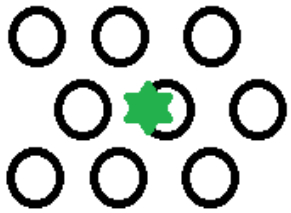
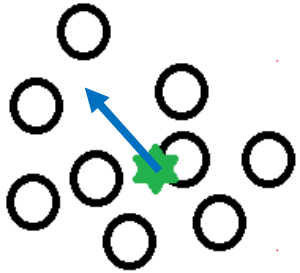
Isolated clusters: suppression of net momenta



Centre of mass (COM)

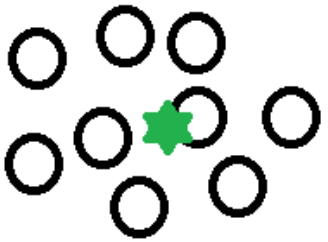
Isolated cluster

Starting configuration



Back-translation

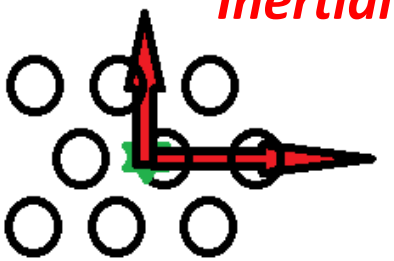
After 1-2 ps



Ending configuration

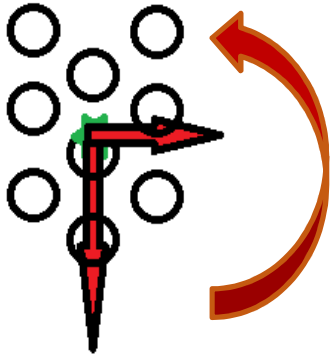
Starting configuration

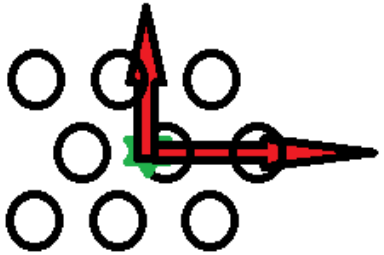
Inertial axes



Isolated cluster

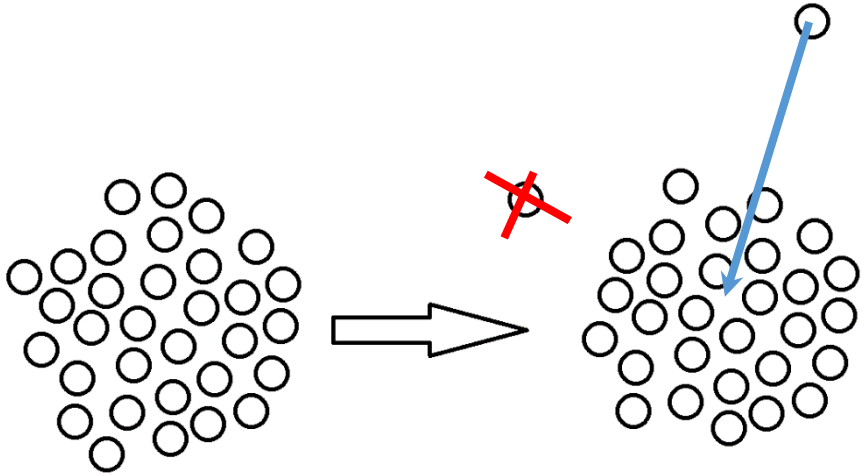
Back-rotation (search of the rotation matrix that minimizes individual COM distances)





Ending configuration

Isolated clusters: Evaporation



(1) *Tethering*: if the COM of a give molecule is more distant than a given threshold (for example ~ 2*cluster radius) from the cluster COM, the distance is reduced by a user-defined factor $0<F_{ev}<1$, usually 0.9.

(2) *Deletion*: if the COM of a give molecule is more distant than a given threshold (for example ~ 2*cluster radius) from the cluster COM, the molecule is deleted.

Quantification of symmetries

$$\Sigma_{(1)} = \frac{1}{N_{at}} \cdot \sum_{ij} |x_i + x_j|$$
$$\Sigma_{(2)} = \frac{1}{N_{at}} \cdot \sum_{ij} |x_i - x_j|$$
$$\Sigma_{(3)} = \frac{1}{N_{at}} \cdot \sum_{ij} |y_i + y_j|$$
$$\Sigma_{(4)} = \frac{1}{N_{at}} \cdot \sum_{ij} |y_i - y_j|$$
$$\Sigma_{(5)} = \frac{1}{N_{at}} \cdot \sum_{ij} |z_i + z_j|$$
$$\Sigma_{(6)} = \frac{1}{N_{at}} \cdot \sum_{ij} |z_i - z_j|$$

symmetry relationship		$\Sigma_{(i)}$					
	(i)	(1)	(2)	(3)	(4)	(5)	(6)
x, y, z	T	any	0	any	0	any	0
$-x, y, z$	G,M	0	any	any	0	any	0
$x, -y, z$	G,M	any	0	0	any	any	0
$x, y, -z$	G,M	any	0	any	0	0	any
$-x, -y, z$	S,A	0	any	0	any	any	0
$-x, y, -z$	S,A	0	any	any	0	0	any
$x, -y, -z$	S,A	any	0	0	any	0	any
$-x, -y, -z$	I	0	any	0	any	0	any

Translation

Planes

Axes (screws and C_2)

Inversion

Symmetry indices

$$g_{ij} = \sum_{i=1}^{3} \min(\Sigma_i)$$

For each molecular pair

Average symmetry index of the whole array

$$G = \frac{1}{N_{pairs}} \cdot \sum_{i<j} g_{ij}$$

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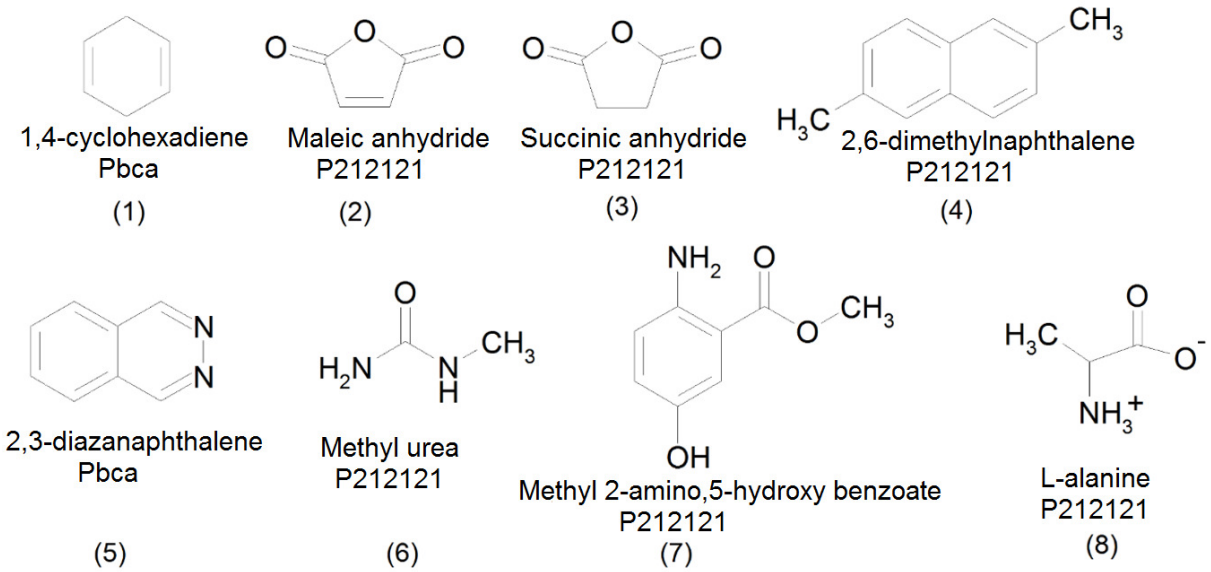
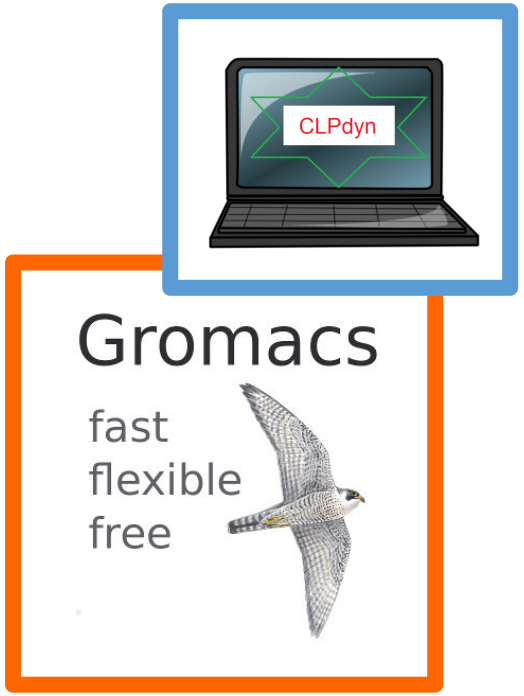
Bulk crystals





- Simulation boxes ~ 30-40 Å large
- 14 Å cutoff for long range non-bonded interactions
- NpT runs
- Intramolecular non-bonded energy terms NOT included

All the results were compared with analogue calculations with GROMACS as a well-established benchmark

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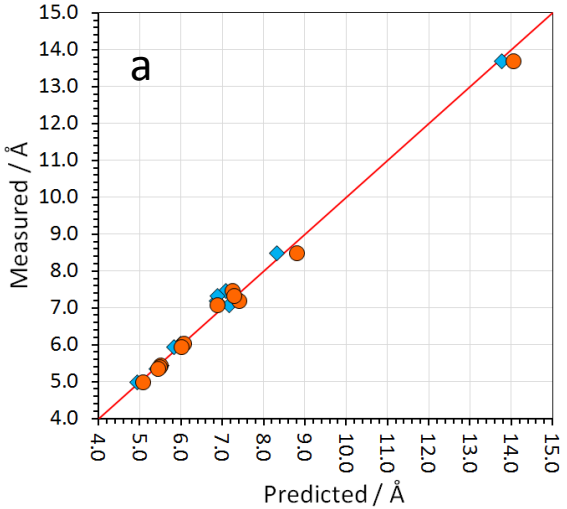
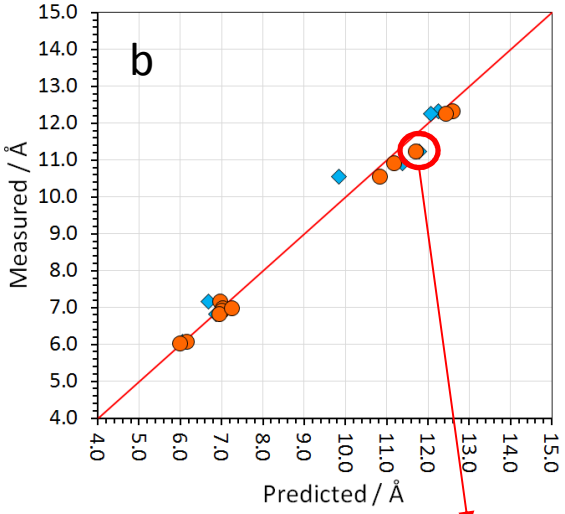
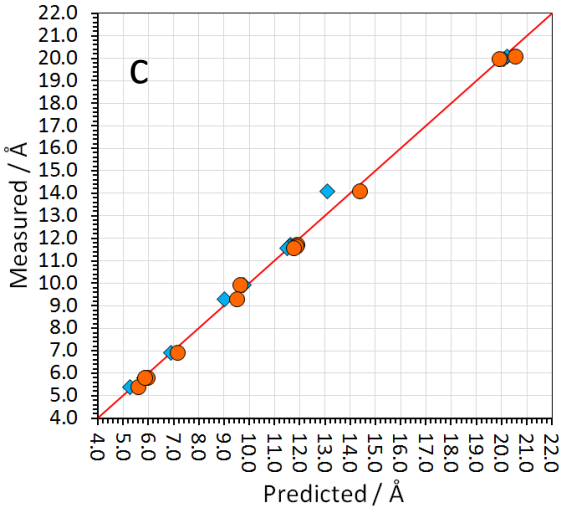
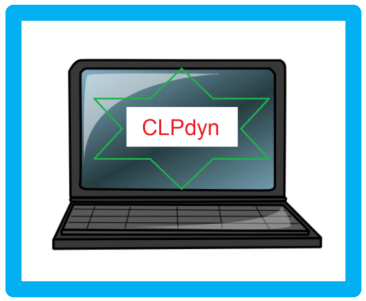
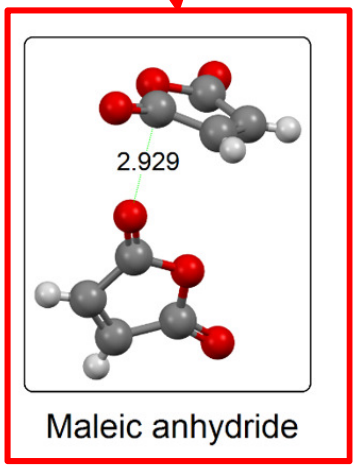
Bulk crystals











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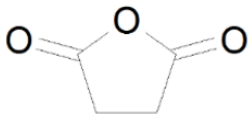
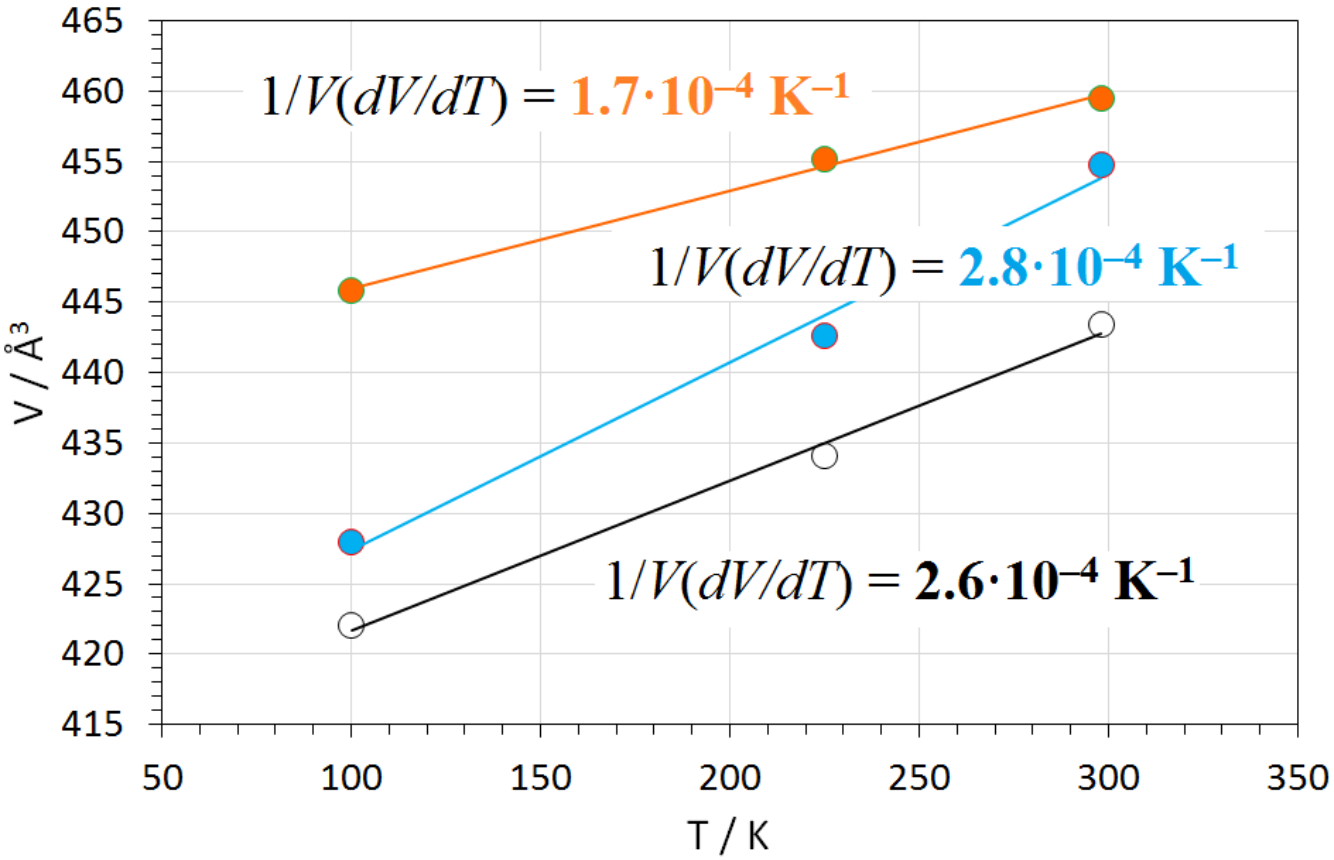
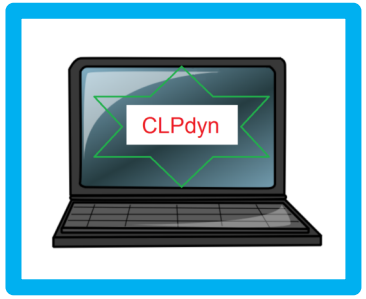


Succinic anhydride





Experimental

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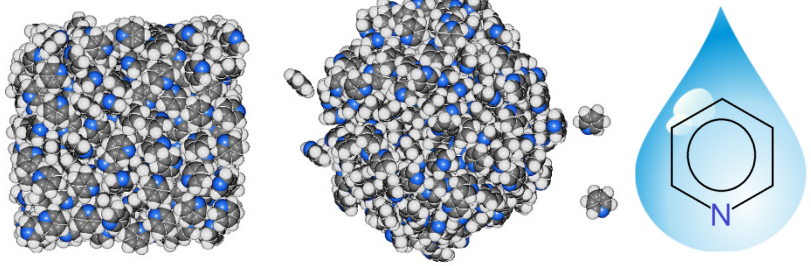
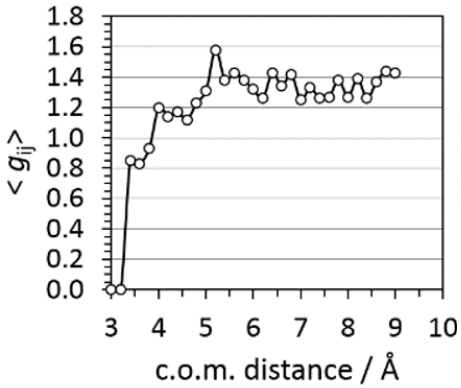
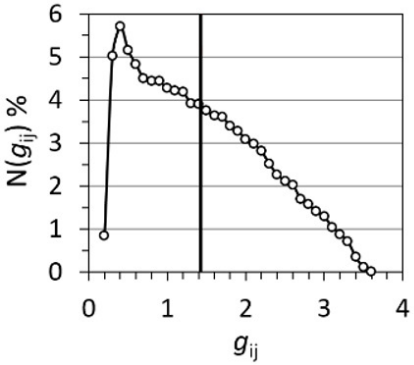
Liquid clusters

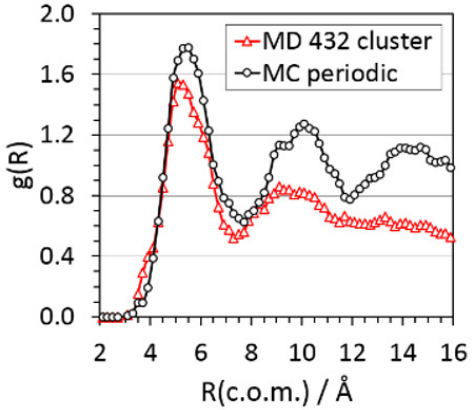
Start

End









Surface tension effects are correctly reproduced

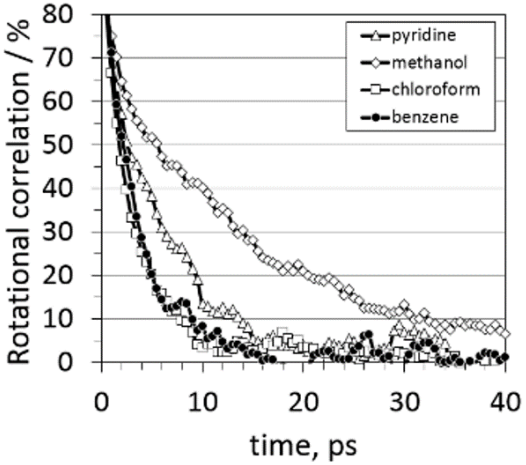
Inner droplets resemble bulk liquids

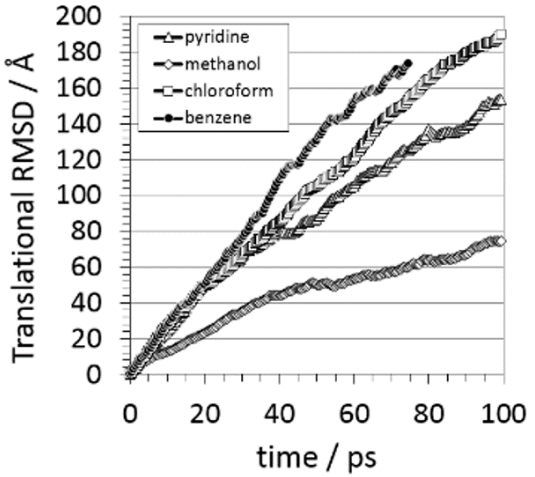
Closer molecular pairs tend to have higher symmetry relationships

$$g(R_k) = \frac{N(R_k)}{4\pi R_k^2 \mathrm{d}R} \cdot \left(\frac{N}{V}\right)^{-1}$$

$$C(\mathbf{u}) = 100 \cdot \langle \mathbf{u}(t) \cdot \mathbf{u}(0) \rangle$$

$$D = \frac{1}{6\Delta t} \cdot \langle \mathbf{d}(t) - \mathbf{d}(0) \rangle$$





Chasing nucleation

nature
International journal of science

Letter | Published: 04 April 2018

Molecular nucleation mechanisms and control strategies for crystal polymorph selection

Alexander E. S. Van Driessche, Nani Van Gerven, Paul H. H. Bomans, Rick R. M. Joosten, Heiner Friedrich, David Gil-Carton, Nico A. J. M. Sommerdijk & Mike Sleutel

Nature **556**, 89–94 (05 April 2018) | Download Citation

Van Driessche, Sleutel et al., Nature, 2018, **556**, 89-94

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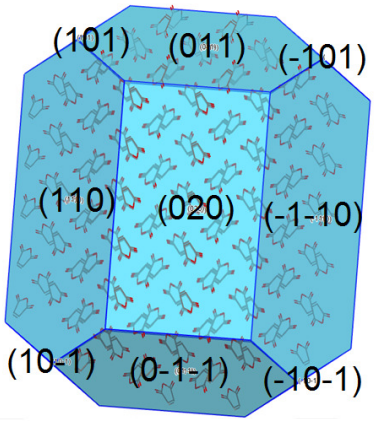
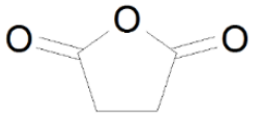
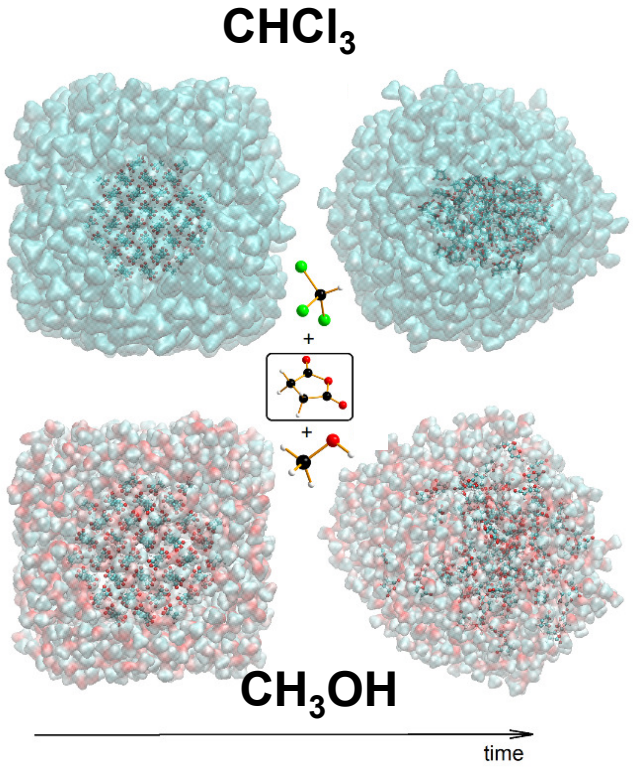
Chasing nucleation

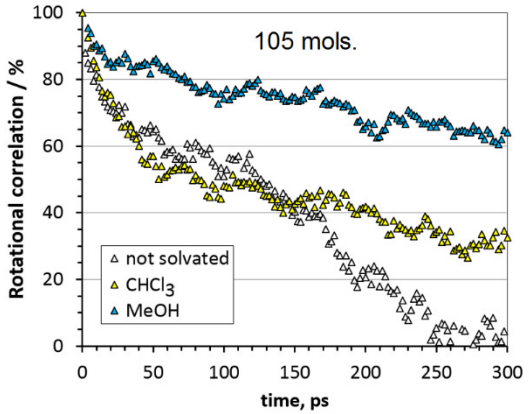




Succinic anhydride

105-mol cluster





$$C(\mathbf{u}) = 100 \cdot \langle \mathbf{u}(t) \cdot \mathbf{u}(0) \rangle$$

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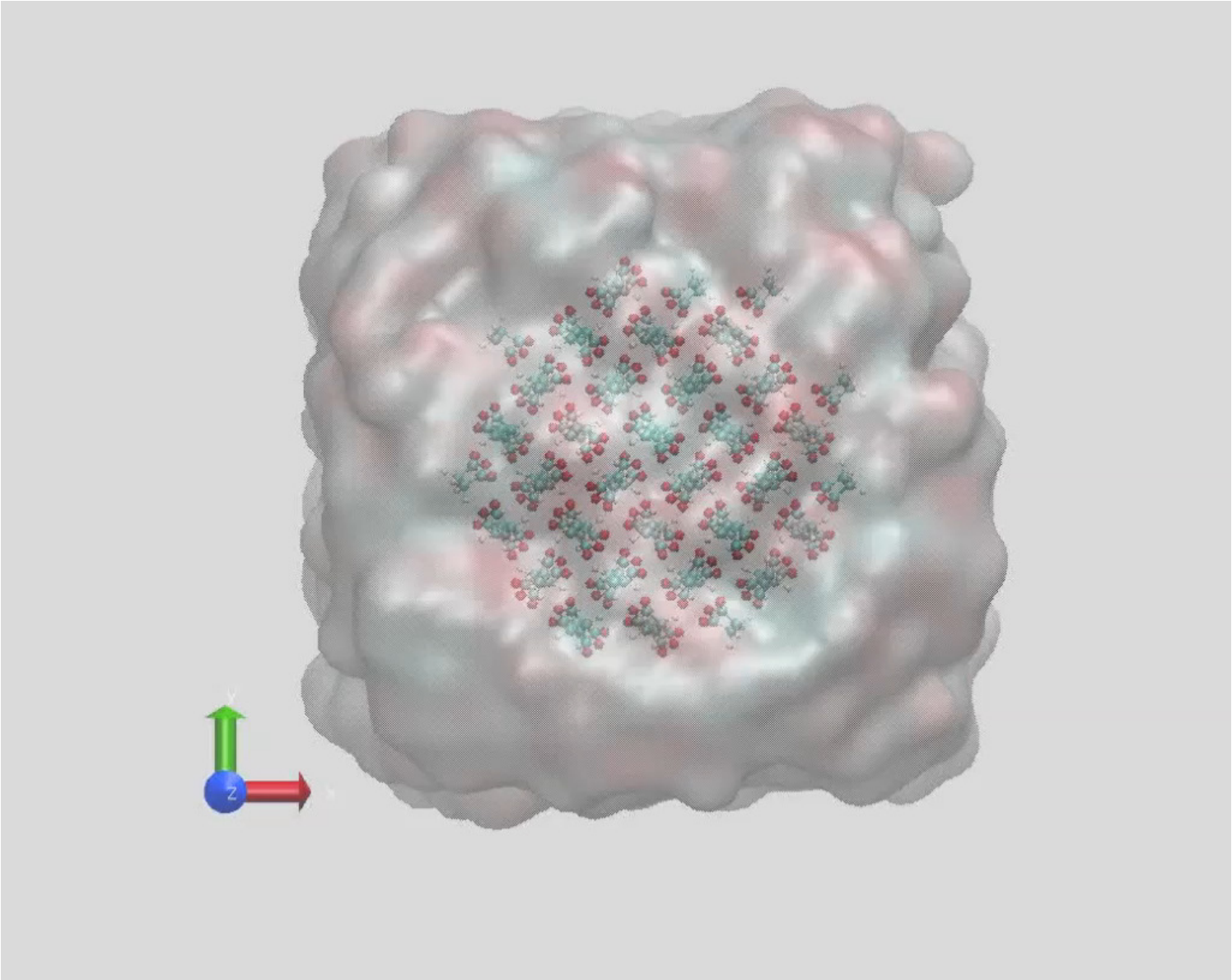
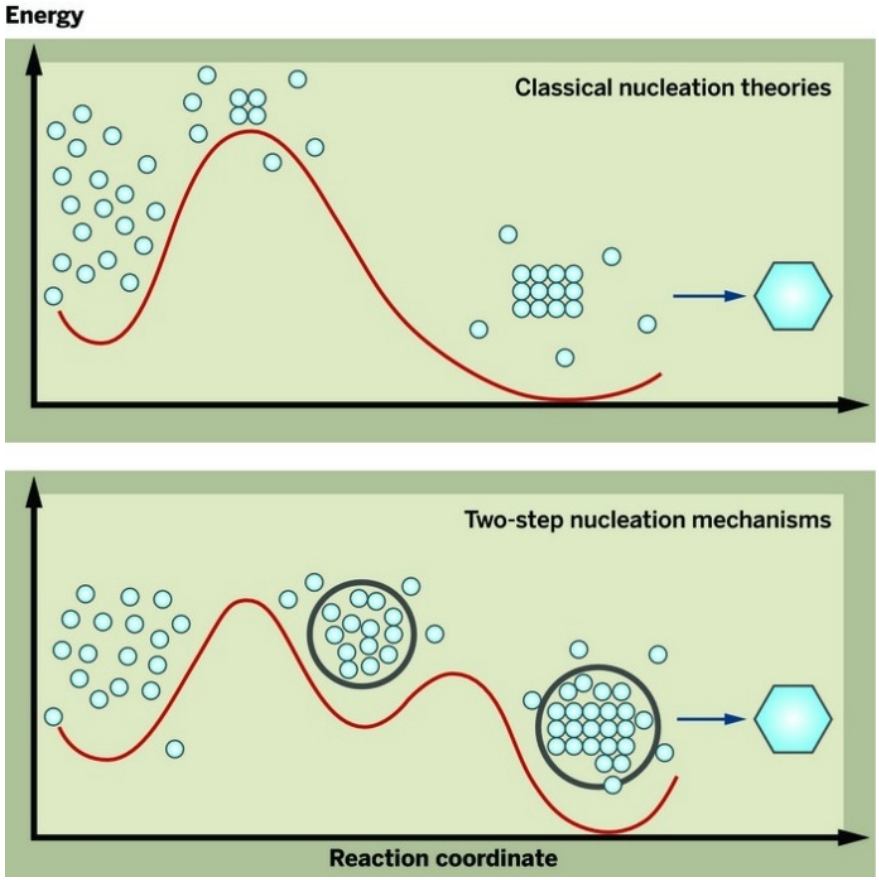
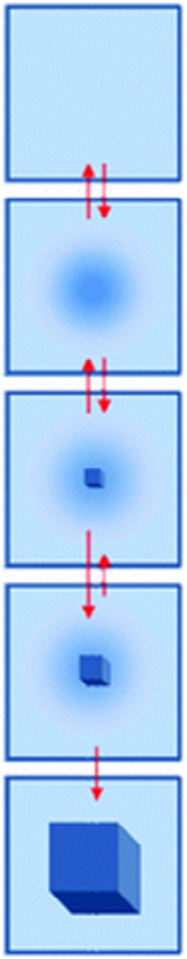
Chasing nucleation



Chasing nucleation





Vekilov, ***Nanoscale***, 2010,**2**, 2346-2357

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Outline

(i) Motivation

(ii) The method

(iii) The program CLP-dyn

(iv) Applications and results

(v) Conclusions

Conclusions

CLP-dyn can afford reliable simulations of crystals, liquids and finite-size clusters. It is equipped with *ad-hoc* procedures to **dampen unwanted global momenta**, **take into account evaporation** and **monitor the evolution of symmetry**

The **agreement with other MD methods and experimental estimates** is good

Liquid droplets show a **inner bulk-like structure**, tempered by strong **surface tension** effects.

Next neighbour molecules tend to aggregate in (partly) **symmetric arrangements** already in a full liquid state.

Nevertheless, ***large clusters up to 100-200 molecules are unstable against dissolution***, posing into question the validity of the classical one-step model for nucleation.

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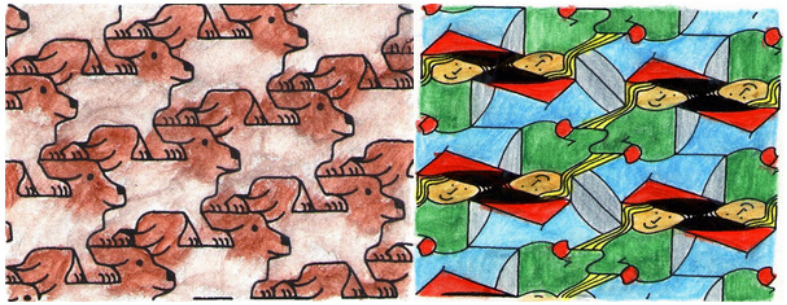
Availability

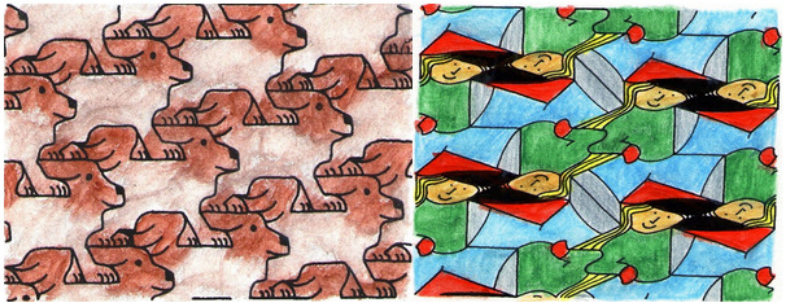
Version June, 2019: freely available (GNU General Public Licence)

A. Gavezzotti and L. Lo Presti, New J. Chem. **2019**, 43, 2077
A.Gavezzotti and L. Lo Presti, J. Appl. Cryst. **2019**, submitted

www.angelogavezzotti.it

click ENTER to access
links to programs and data





* ENTER

notice theory download PIXEL-CLP download CLP-dyn

Source codes, instructions, pre-compiled macros and worked I/O examples

Thank you for your kind attention

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Support slides

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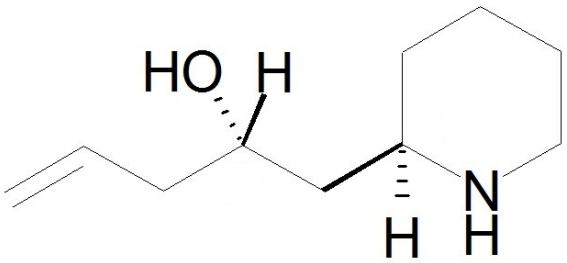
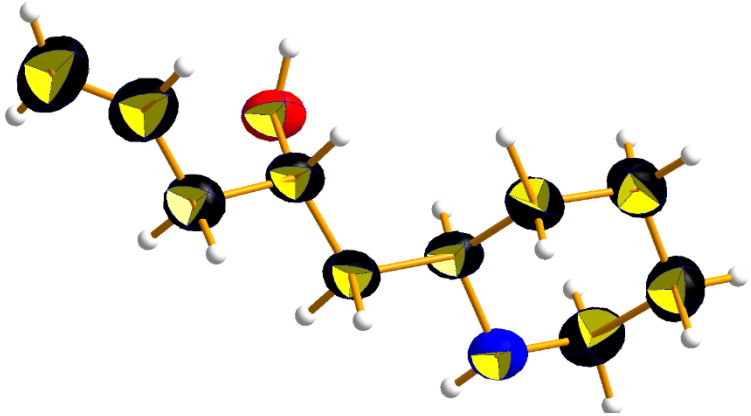
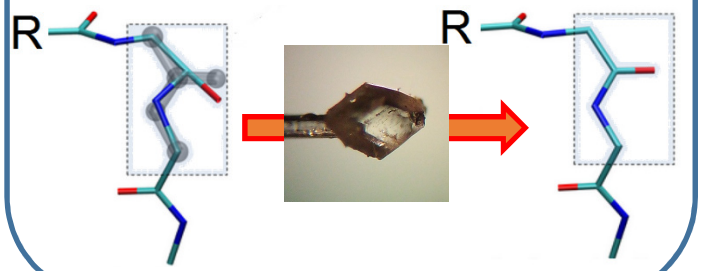
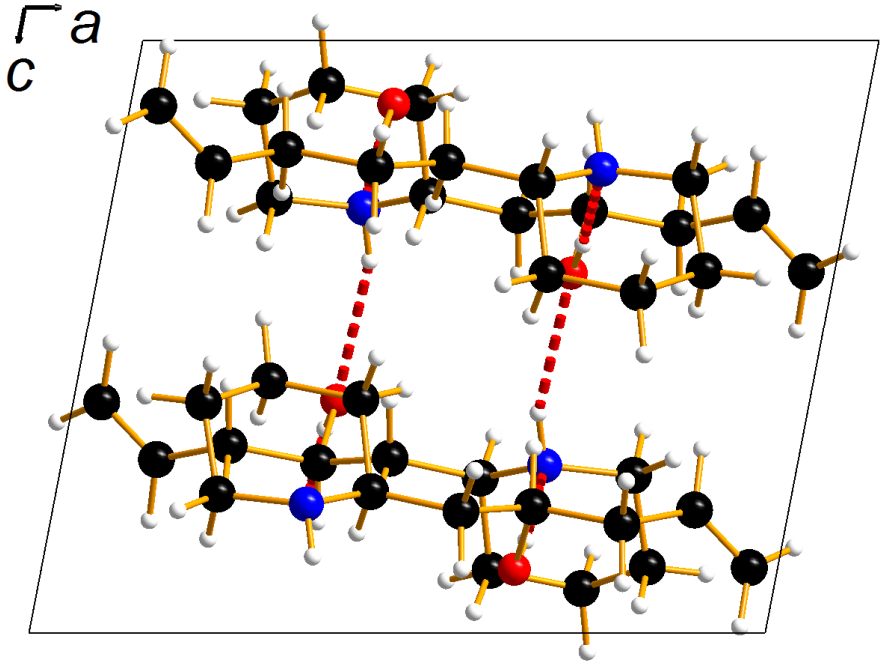
Structure…





$$\langle \mathbf{R} \rangle = \frac{1}{\Delta t} \int_{t_1}^{t_2} \mathbf{R}(t) d\mathbf{r}$$





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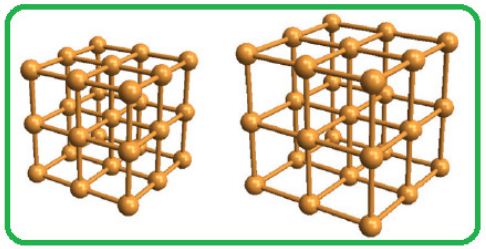
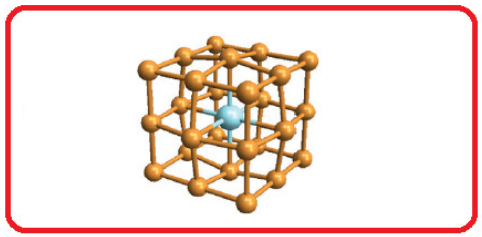
Molecular dynamics in materials science

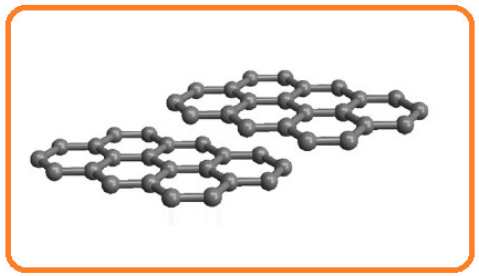
Response to (T,p)



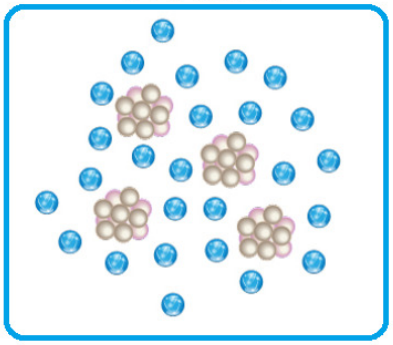
Lattice defects



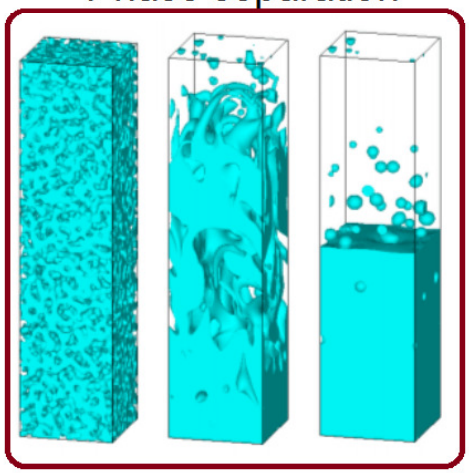
Interfaces



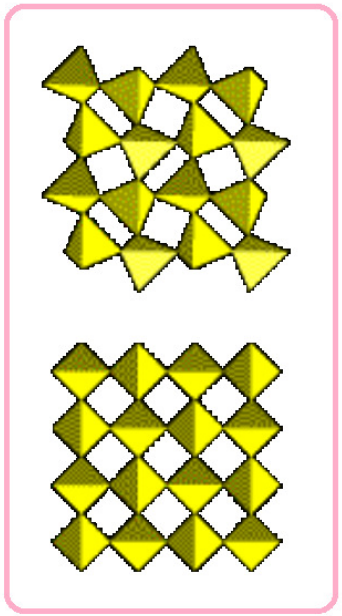
Solvation



Phase separation



Phase transitons



Gavezzotti, *Synlett*, **2002**, 2, 201–214

Hermann, Di Stasio, Tkatchenko, *Chem. Rev.* **2017**, 117, 4714-4758

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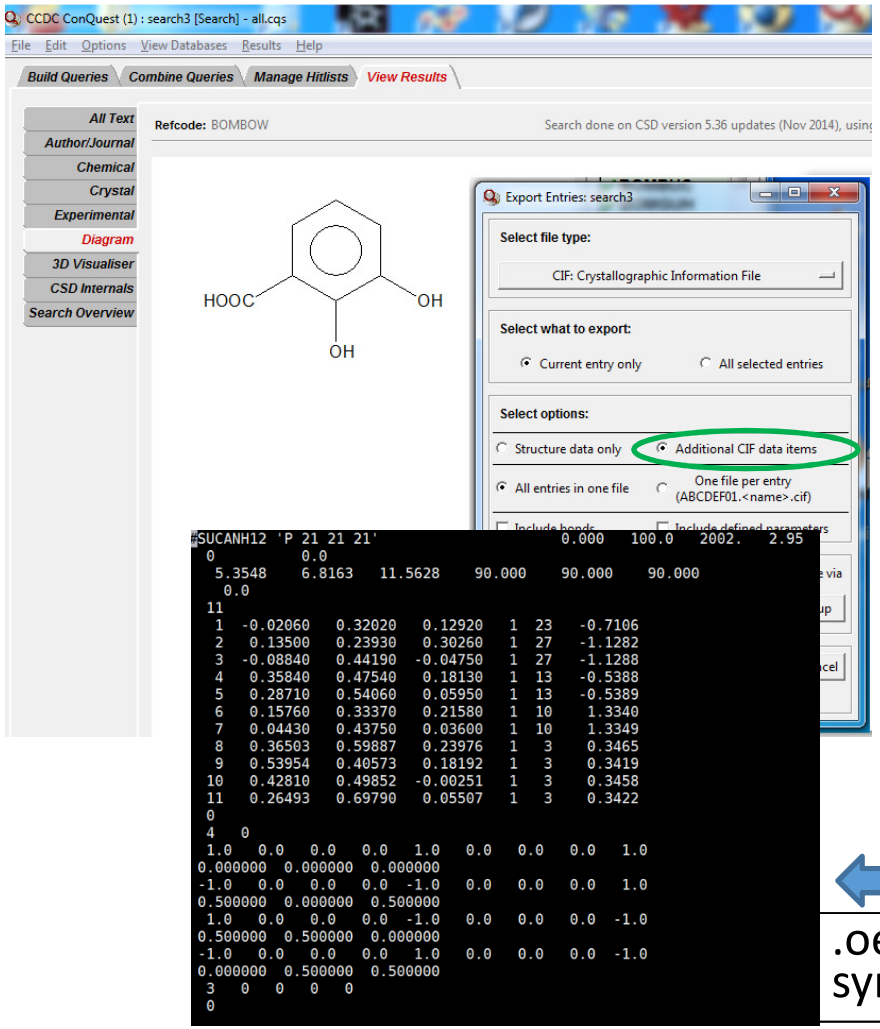
Retrieving structures




```
#SUCANH12 'P 21 21 21'                          0.000   100.0   2002.   2.95
 0          0.0
  5.3548     6.8163    11.5628     90.000     90.000     90.000
   0.0
 11
  1  -0.02060   0.32020   0.12920   1  23   -0.7106
  2   0.13500   0.23930   0.30260   1  27   -1.1282
  3  -0.08840   0.44190  -0.04750   1  27   -1.1288
  4   0.35840   0.47540   0.18130   1  13   -0.5388
  5   0.28710   0.54060   0.05950   1  13   -0.5389
  6   0.15760   0.33370   0.21580   1  10    1.3340
  7   0.04430   0.43750   0.03600   1  10    1.3349
  8   0.36503   0.59887   0.23976   1   3    0.3465
  9   0.53954   0.40573   0.18192   1   3    0.3419
 10   0.42810   0.49852  -0.00251   1   3    0.3458
 11   0.26493   0.69790   0.05507   1   3    0.3422
 0
 4   0
 1.0   0.0   0.0   0.0   1.0   0.0   0.0   0.0   1.0
0.000000  0.000000  0.000000
-1.0   0.0   0.0   0.0  -1.0   0.0   0.0   0.0   1.0
0.500000  0.000000  0.500000
 1.0   0.0   0.0   0.0  -1.0   0.0   0.0   0.0  -1.0
0.500000  0.500000  0.000000
-1.0   0.0   0.0   0.0   1.0   0.0   0.0   0.0  -1.0
0.000000  0.500000  0.500000
 3   0   0   0   0
 0
```

(1) Retrieve your entry from CSD in cif format (make sure to include also additional data items)

RETCIF

(2) Interprets structural data

RETCOR

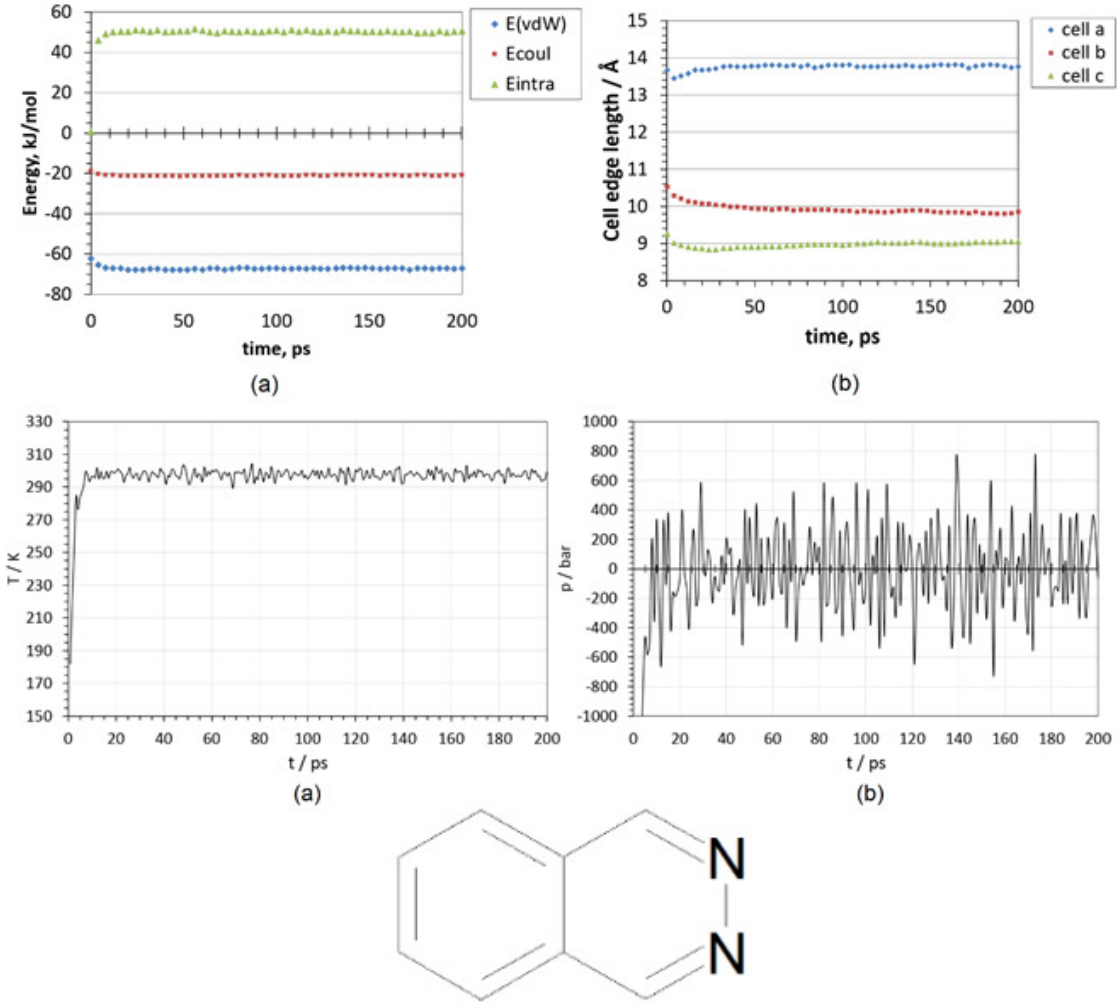
(3) Renormalizes H atom positions, check cell and Wyckoff symmetry

RETCHA

(4) Assigns atom point charges with the Extended Hückel method

.oeh ASCII file: lattice, coordinates, charges and symmetry

Equilibration



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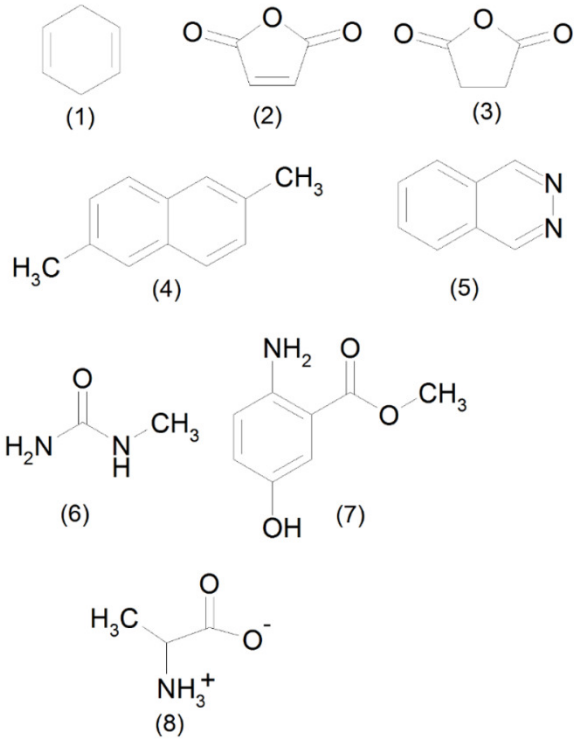
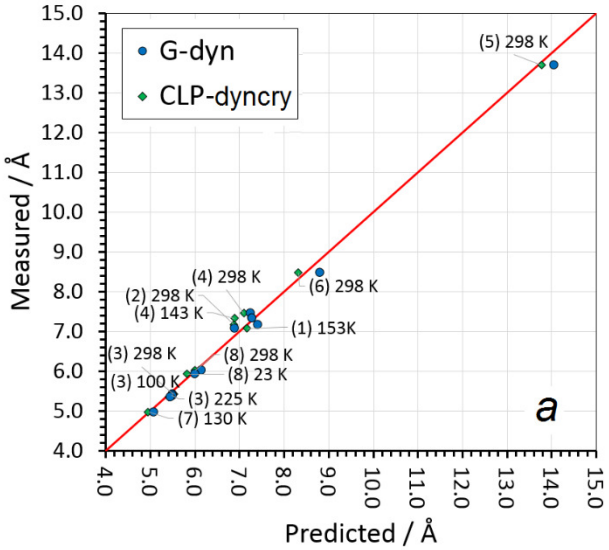
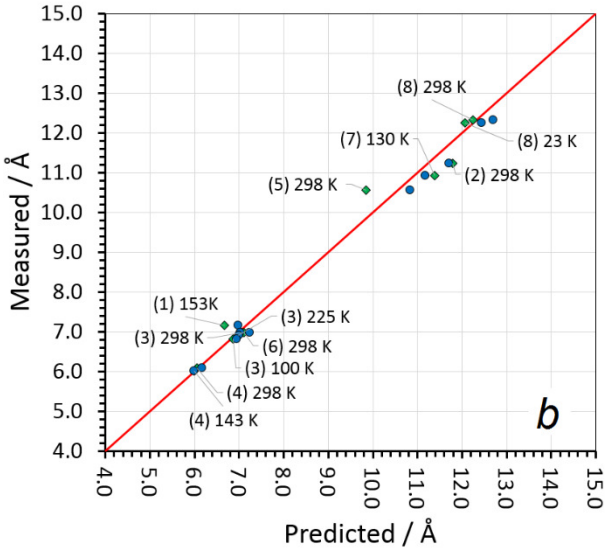
Bulk crystals

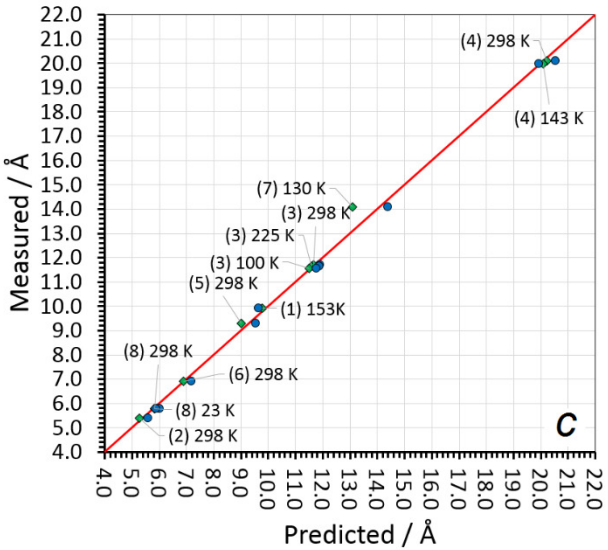




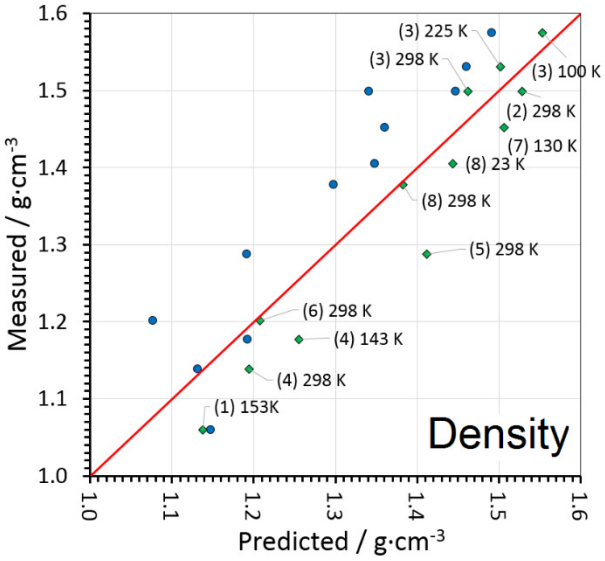
(a)



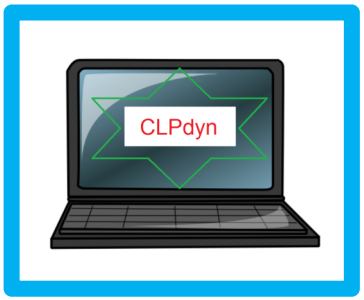
(b)



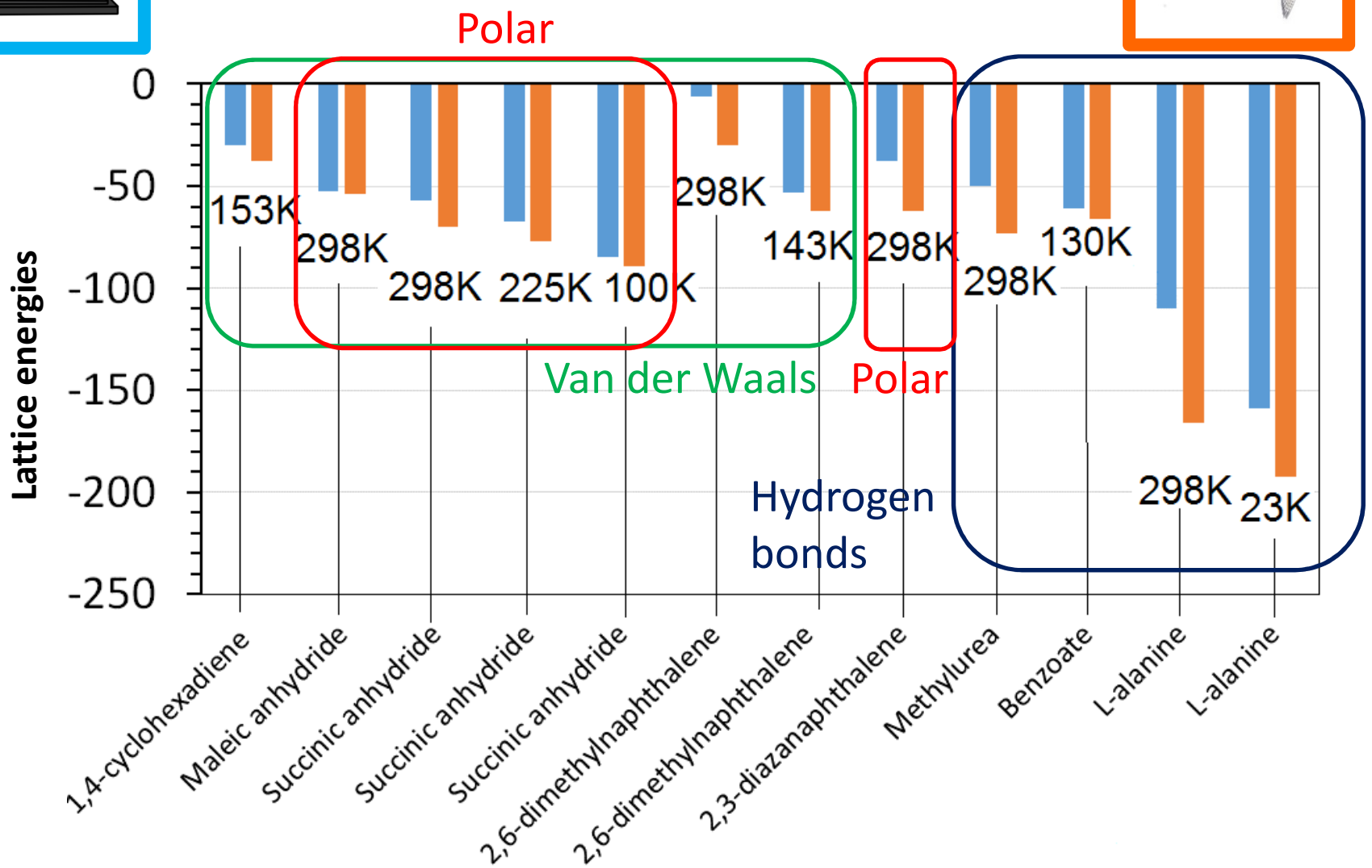
(c)



(d)



Bulk crystals



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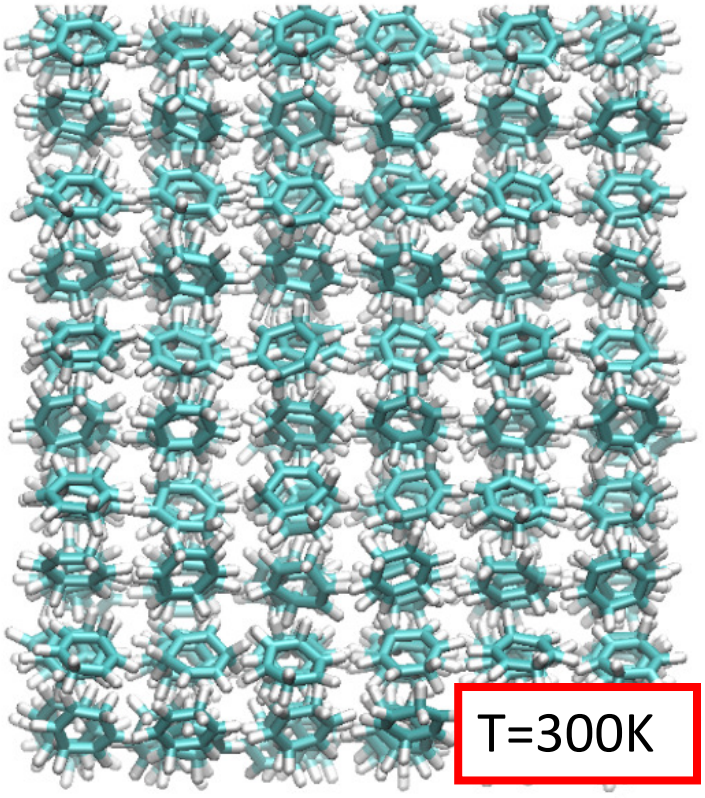
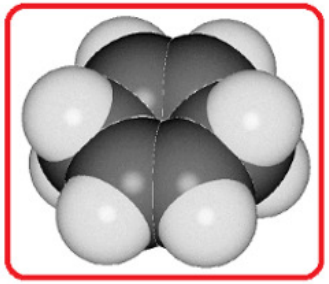
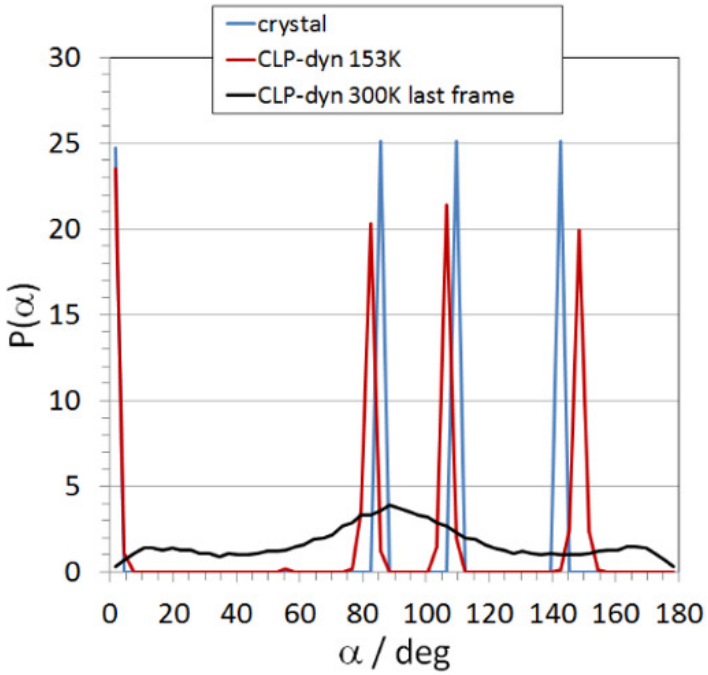
Bulk crystals

1,4-cyclohexadiene



T=300K





T_{melt} = 224 K

Pre-melting?

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Bulk Liquids

Substance	Method	Energies / kJ·mol^{-1}		Density / g·cm^{-3}		n
		CE[a]	exptl $\Delta_{vap}H$[b]	Calc	Exptl	
benzene	MC	31.6(2)	34	0.897(2)	0.87	686
	MD	32.5(5)		0.917(9)		250
chloroform	MC	26.8(1)	31	1.410(2)	1.47	1458
	MD	26.4(3)		1.451(10)		432
methanol	MC	37.8(1)	37	0.770(1)	0.79	1458
	MD	42.6(5)		0.799(10)		432
pyridine	MC	39.2(2)	40	1.047(5)	0.982	432
	MD	38.9(7)		1.040(13)		250

Cohesive energies and **densities** of bulk liquids, compared with Monte-Carlo (**MC**) results. n = number of molecules in the simulation box.

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Evaporation rates of liquid clusters

n	radius,	$t(20)^a$	RMSD(10)[b]	E_{coh}[c]	Evaporation rate	
					mol/ps	$10^5 \cdot$ mol/(ps Å^2)
$CHCl_3$						
102	13	3.2	40	16	0.05	2.3
260	19	3.7	44	20	0.08	1.7
514	24	4.5	43	22	0.08	1.4
998	31	5.2	27	26	0.11	0.9
bulk	–	4.7	–	26	–	–
C_6H_6						
149	17	6.1	41	24	0.09	2.5
278	21	5.7	40	26	0.04	0.8
479	26	5.1	28	27	0.04	0.5
bulk	–	6.7	–	33	–	–

[a]Time (ps) for rotational correlation to decay from 100 to 20 % .

[b]Root–mean–square center–of–mass displacement after 10 ps simulation (starting diffusion; Å).

[c]Cohesive intermolecular energy (kJ/mol).

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