Simulation of aggregation phenomena in solution

Leonardo Lo Presti

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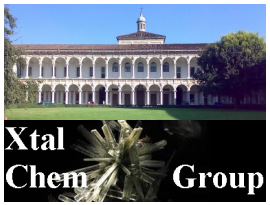

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Outline

(i) Motivation
(ii) Method
(iii) Applications and Results
(iv) Conclusions

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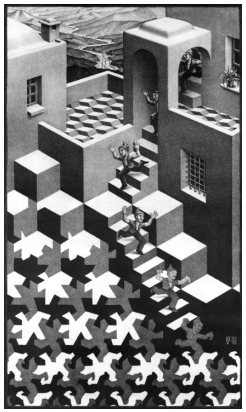
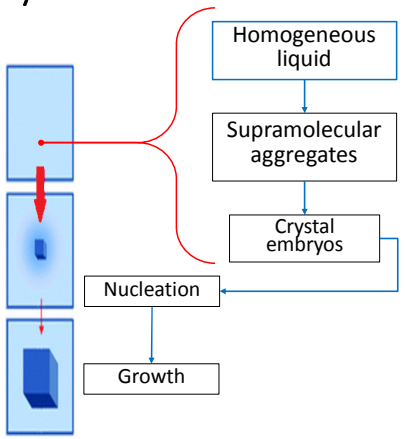
Crystallization





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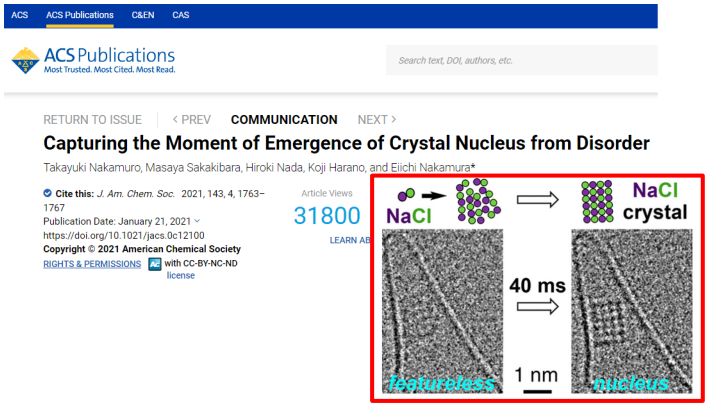
Chasing nucleation



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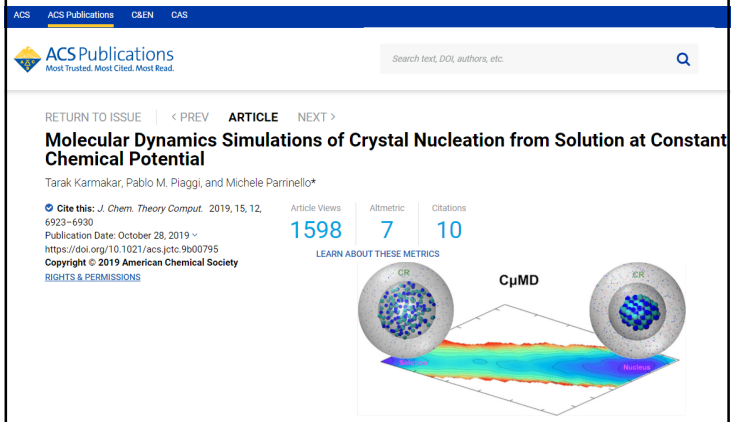
Chasing nucleation



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The Kinetic-Biased algorithm

$$T_i^b = g \cdot T_i$$

$$\Delta T_i = T_i^b - T_i = T_i \cdot (g - 1)$$

$$\Delta T_{i,a} = \frac{\Delta T_i}{N_i} = T_{i,a}^{new} - T_{i,a} < 0$$

$$\Delta T_k = -\Delta T_i / N_k > 0$$
$$T_k^b = T_k + \Delta T_k = B \cdot T_k$$
$$B = 1 + \frac{\Delta T_k}{T_k}$$
$$\pm v_{k,a,s}^{new} = \pm\sqrt{B} \cdot v_{k,a,s} \ , s = x, y, z$$

$$T_i^b = \sum_a^{N_i} T_{i,a}^b = \sum_a^{N_i} \frac{1}{2} m_{i,a} v_{i,a,b}^2 = g \cdot T_i$$

$$\sum_a^{N_i} \frac{1}{2} m_{i,a} v_{i,a,b}^2 = g \cdot \sum_a^{N_i} \frac{1}{2} m_{i,a} v_{i,a}^2 = \sum_a^{N_i} \frac{1}{2} m_{i,a} g\left(v_{i,a}^2\right)$$

$$\pm v_{i,a,s}^b = \pm\sqrt{g} \cdot v_{i,a,s} \ , s = x, y, z$$

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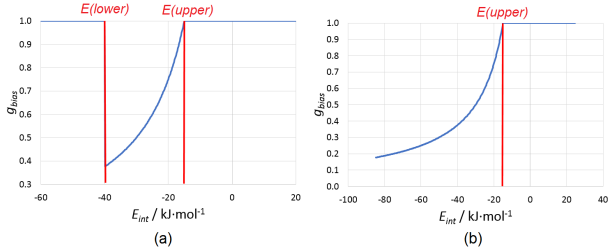
The Kinetic-Biased algorithm



$$g = 1 - \frac{|E_{ij} - E_{bias}(upper)|}{|E_{ij}|} \quad \text{if } E_{bias}(lower) < E_{ij} < E_{bias}(upper)$$
$$g = 1 \quad otherwise$$

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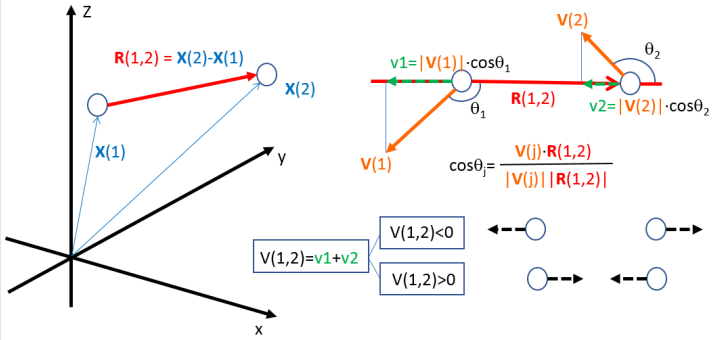
Relative forces and velocities



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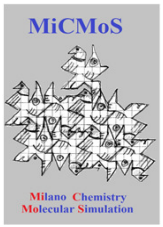
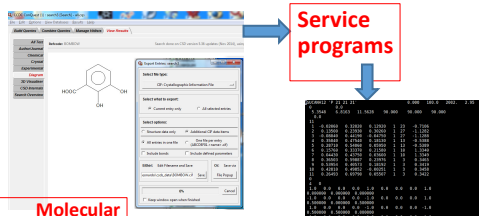


https://sites.unimi.it/xtal_chem_group/index.php

- *New J. Chem.* 2019, 43, 2077–2084
- *J. Appl. Cryst.* 2019, 52, 1253–1263
- *Cryst. Growth Des.* 2020, 20, 11, 7421–7428

Free!



Service programs

Molecular topology and simulation box

MD

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

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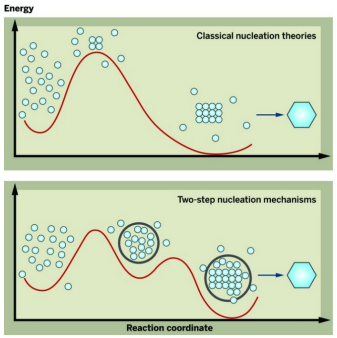
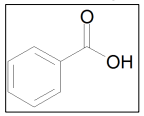
Nucleation theories

Classical Nucleation Theory

Multi-step theory



Case study



Benzoic acid (*Bza*)

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

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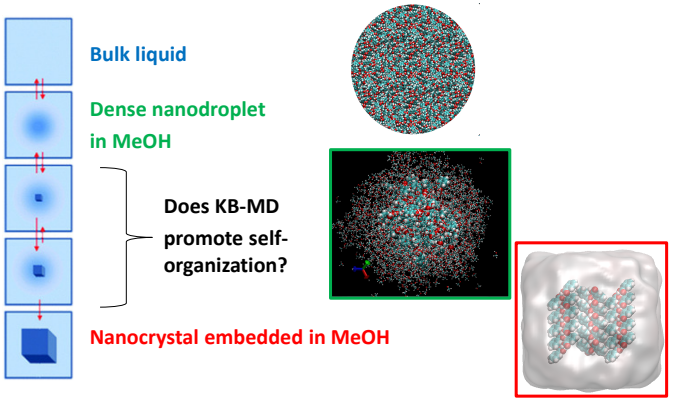
Following the path of Bza to crystallization



Bulk liquid

Dense nanodroplet in MeOH

Does KB-MD promote self-organization?

Nanocrystal embedded in MeOH

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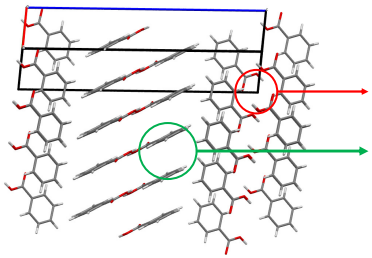
Bza crystal structure

BENZAC02, Feld et al., Z. Kristallogr. 1981, 157, 215



Cyclic HBs, E_{ij} ~ 80-90 kJ/mol

Stacking, E_{ij} ~ 10-20 kJ/mol

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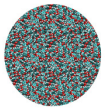
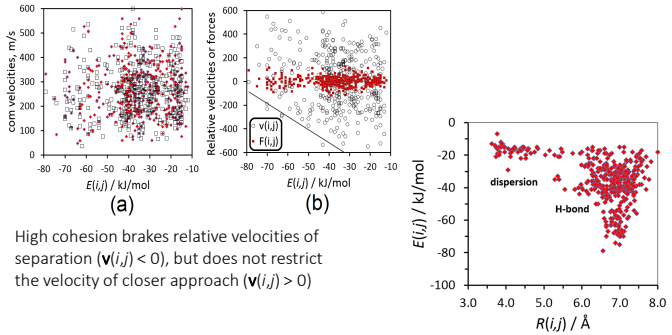
Unbiased liquid





High cohesion brakes relative velocities of separation ($\mathbf{v}(i,j) < 0$), but does not restrict the velocity of closer approach ($\mathbf{v}(i,j) > 0$)

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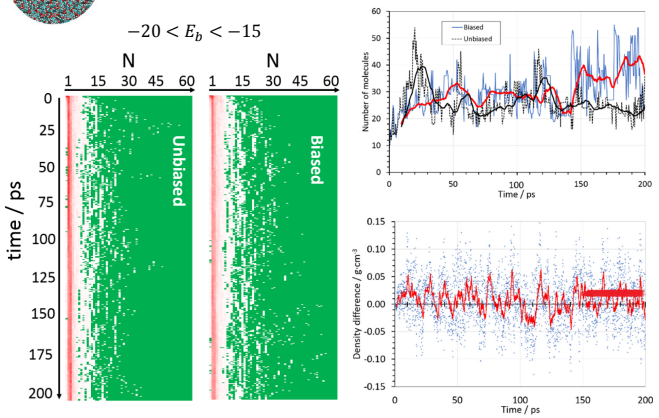
Cluster dimension in the liquids

$-20 < E_b < -15$



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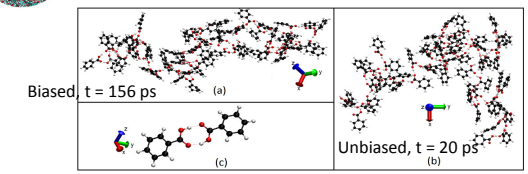
Cluster energy in liquids



Cluster	$E_{cohesive}$	$E_{Dispersion}$	$E_{coulomb}$
Biased	–60.6	–5.3	–55.3
Unbiased	–61.3	–2.8	–58.5
Cyclic dimer	–47.3	+7.8	–55.1
Bulk liquid, biased	–77(3)	–22(5)	–55(5)
Bulk liquid, unbiased	–76(3)	–23(5)	–53(5)
Bulk crystal	–88(1)	–38.9(9)	–49(1)

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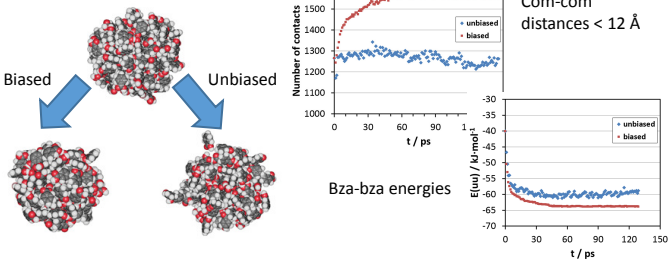
Nanodroplet

	E(bza-bza)	E(solv-solv)	E(bza-solv)	Bza disp.	Bza Coul	n. of HB
biased	-63.7	-46.3	-58.7	-25.0	-38.8	61
unbiased	-59.6	-40.0	-53.8	-15.6	-42.8	79



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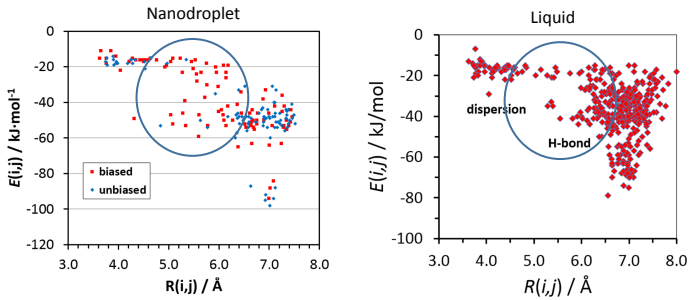
Nanodroplet



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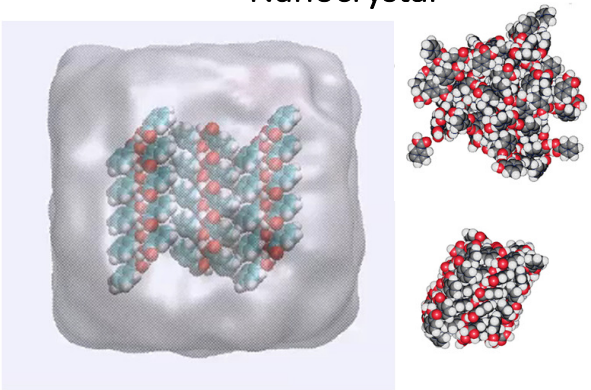
Nanocrystal



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Conclusions

Under the biasing restrictions, pure liquid benzoic acid condenses by increasing its density and forming hydrogen-bonded clusters of irregular shape and multiform size

A solvated liquid droplet freezes to an amorphous semi-solid, into a compact form held together mainly by the dispersive potentials.

A microcrystal slab preserves its symmetric stability under biased dynamic conditions, while an unbiased simulation quickly runs into a liquid drop.

This last point strongly suggests (one could say demonstrates) **that isolated clusters cannot be crystalline**, contrary to hypotheses embedded into classical nucleation theory

The KB algorithm drives the system toward aggregation, not symmetrization (at least at these very short time scales)

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Thank you for your kind attention

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Support slides

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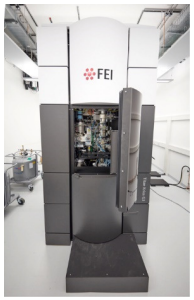
Chasing nucleation



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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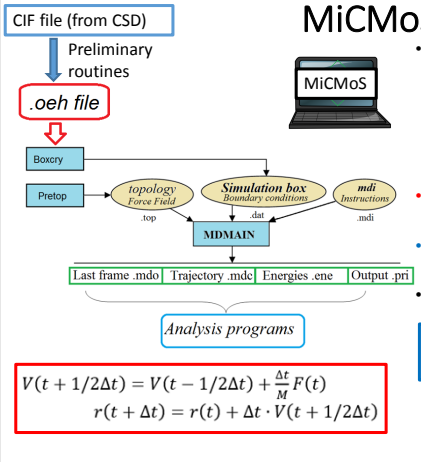

- For **bulk crystals**, periodicity is determined by repetition of the crystallographic unit cell. **Bulk liquids** use cubic simulation boxes. Also **non-periodic clusters** (nanocrystals and droplets) can be treated.
- Leap-Frog and celocity-Verlet integrator.
- Berendsen (T, p) (anisotropic) rescaling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

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

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

$$P_{ii} = \frac{2}{3V}\left(E_{kin,ii} - W_{ii}\right)$$
$$\mu_i = [1 - c(P_{set} - P_{ii})]^{1/3}$$

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The method

Lattice Energy, Packing Energy

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

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

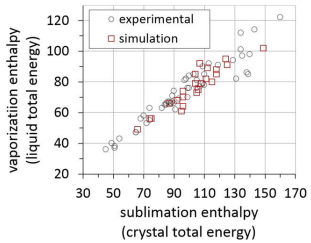
Ignoring zero-point and molecular relaxation corrections

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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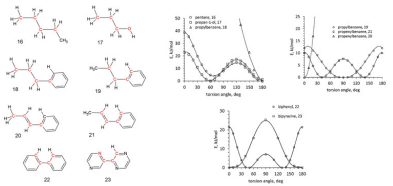
Intramolecular force field

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



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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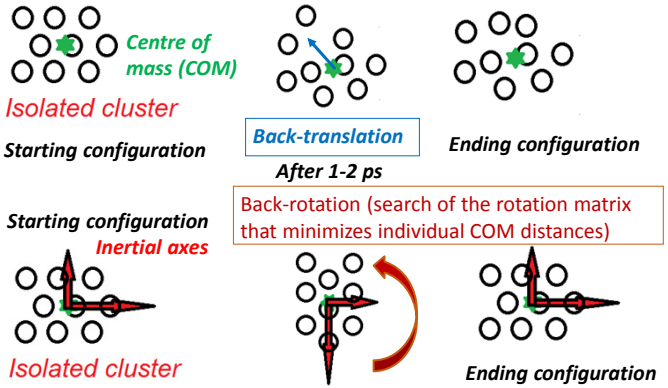
Isolated clusters: suppression of net momenta



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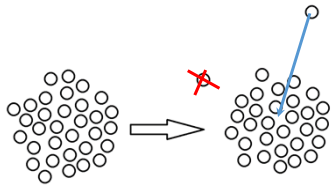
Isolated clusters: Evaporation



(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.

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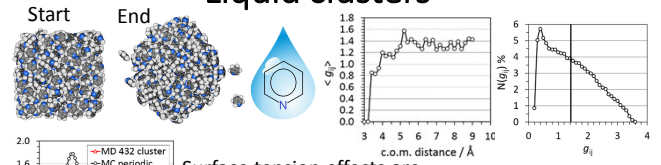
Liquid clusters



Surface tension effects are correctly reproduced

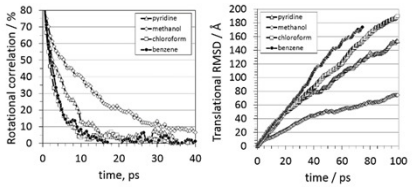
Inner droplets resemble bulk liquids

Closer molecular pairs tend to have higher symmetry relationships

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

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

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



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