HELPING CHEMICAL INDUSTRY IN ITS GREEN AND DIGITAL TRANSITION

NEXTMOL

Dr. Monica de Mier, CEO

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About us

NEXTMOL

We are an awarded startup company specialized in **computational chemistry**.

We offer digital solutions to **accelerate the R&D** of best-in-class and more sustainable **specialty chemicals** based on **molecular modeling** and **artificial intelligence**.

Spin-off company of:

BSC Barcelona Supercomputing Center
Centro Nacional de Supercomputación

With the support of:

REPSOL Fundación

aws

NVIDIA INCEPTION PROGRAM

Funding and awards:

GOBIERNO DE ESPAÑA
MINISTERIO DE CIENCIA E INNOVACIÓN

ACCIÓ
Generalitat de Catalunya

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e-dci
European Extreme Data & Computing Initiative

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European Innovation Council

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SOUTH SUMMIT

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ISO 27001
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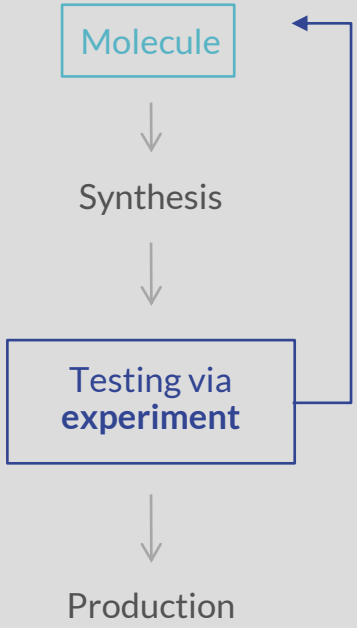
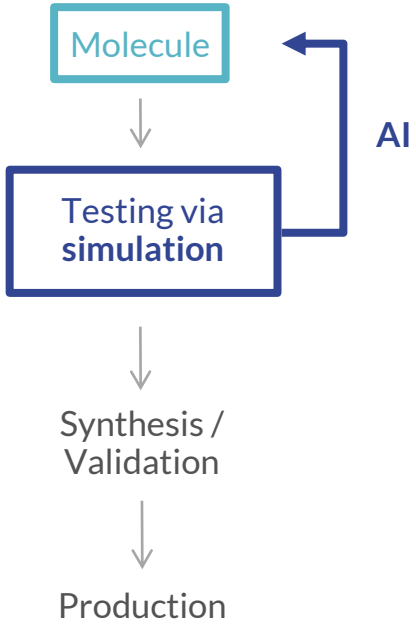
Traditional Lab



Lab with Nextmol

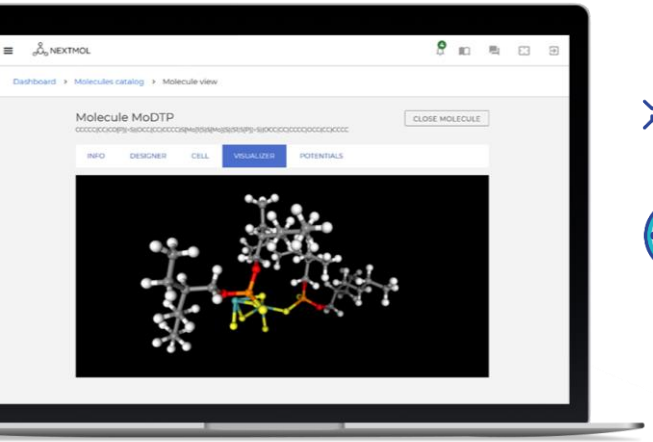


Computational lab for chemical R&D

- Molecules characterized directly on the computer
- Automated idea-testing loop
- Only the most promising candidates go to the lab
- Guides and complements the experimental work

Computational and green lab for chemical R&D

- Reduced synthesis and waste
- Rapid replacement of raw materials, ingredients or formulations by green alternatives (biobased, biodegradable, etc.)
- Targeted functionalities and properties



Polymers

Surfactants

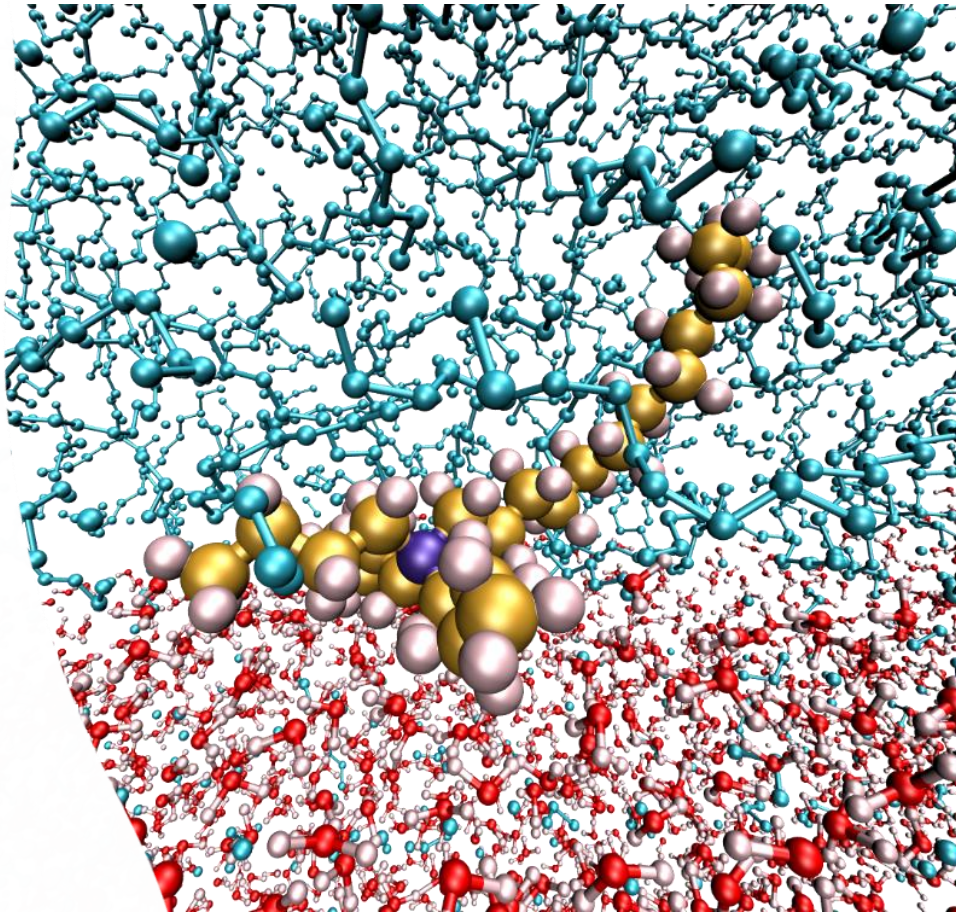


Image: Anti-agglomerant additive, © Nextmol

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Use case:

Biodegradable polymers for hair care applications

Polymers – a key ingredient of hair care products

- Polymers are ubiquitous in hair care products: Viscosity modifiers, emulsifiers, “hold” in hair gels and sprays, conditioners to improve combing, etc.
- Polymer in liquid formulations are ingredients used in millions of products, but they cannot be recovered and thus create a large pollution problem.
- **Goal:** substitute established hair care polymers with biodegradable alternatives that exhibit the same (or even better) performance.

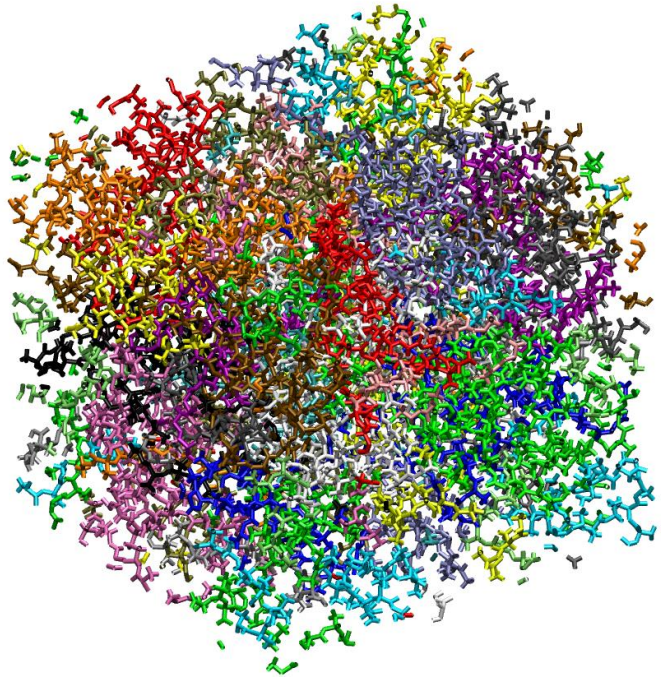
https://www.rsc.org/policy-evidence-campaigns/environmental-sustainability/sustainability-reports-surveys-and-campaigns/polymers-in-liquid-formulations-plfs/

Molecular modeling

The first step is to generate the polymer from its monomers:

- Inputs to provide consist of the SMILES of the repeating units and the capping groups.
- Copolymers can be either random or block, controlled by respective specification of the ratios and block sizes of the monomers.
- The final density of the generated polymer blends is then reached after a short MD equilibration.

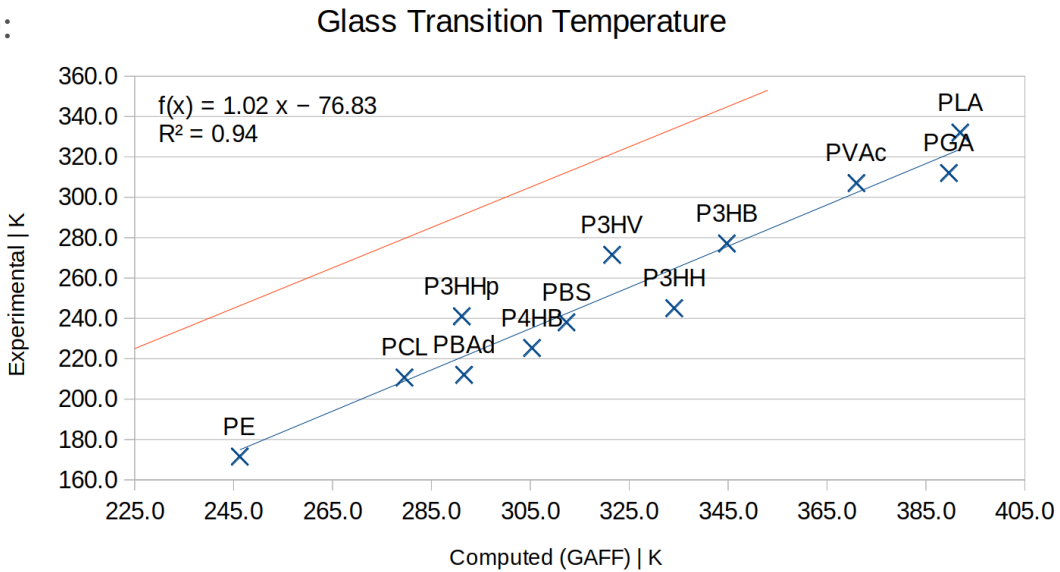
Density (g/cm^3)	Polymer Database	Nextmol builder
Poly(4-hydroxybutyrate)	1.22-1.28	1.283



Computational characterization

We characterize the polymers by calculating computational physico-chemical descriptors of polymer blends via Molecular Dynamics (MD):

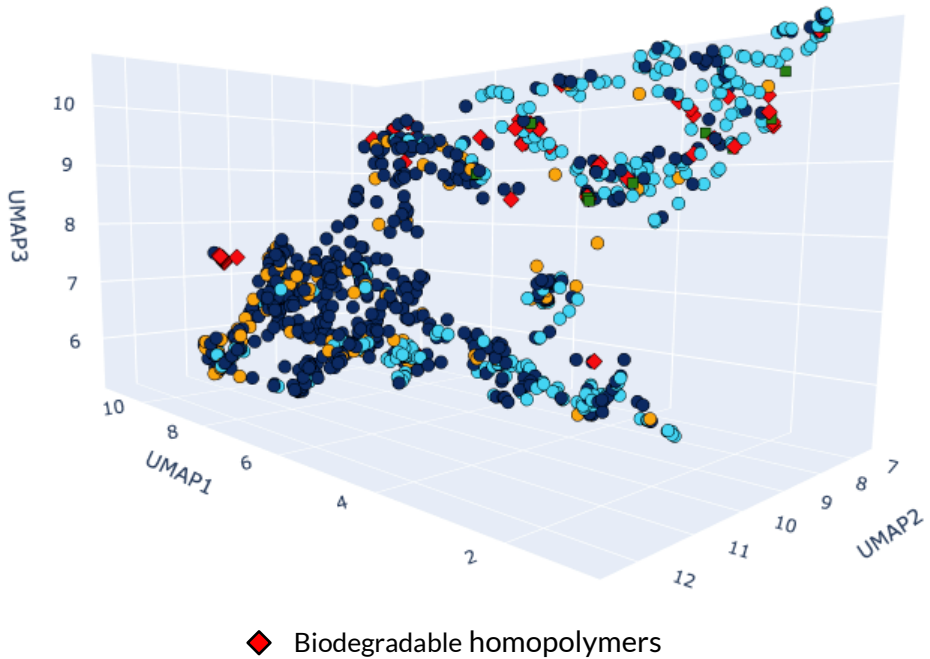
- Properties: Glass transition temperature, Hansen solubility parameters, persistence length, radius of gyration, …
- Good agreement with experimental reference values – we can rank the polymer blends against each other.
- Possibility to perform a virtual high-throughput screening.



Selecting biodegradable polymers via ML

Combining ML and MD allows us to focus on the most interesting candidates:

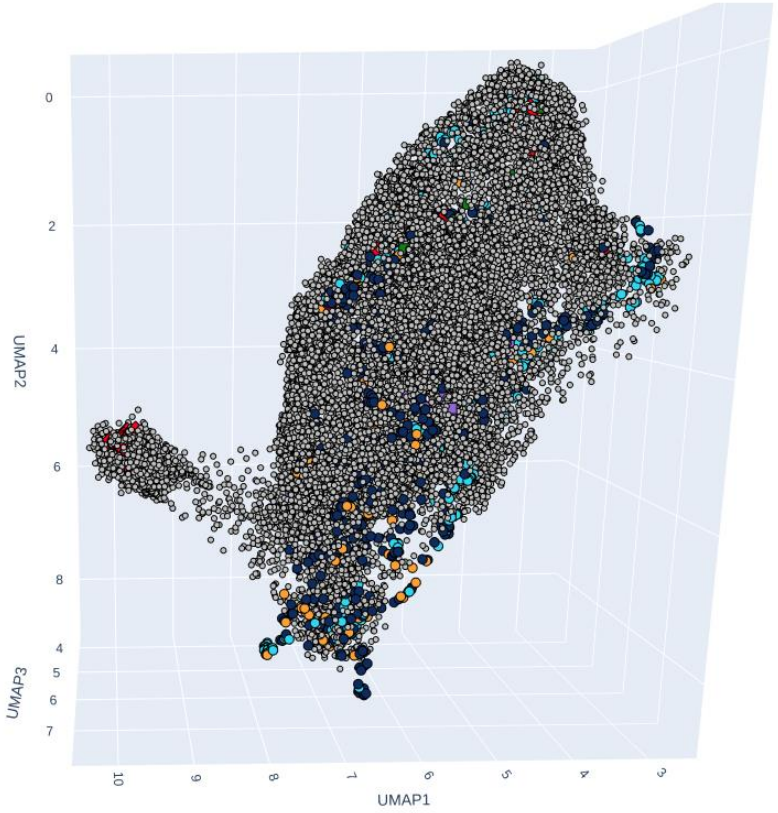
- We collected a dataset of 1,044 homopolymers from the literature.
- We analyzed the chemical space: molecular descriptors and dimensionality reduction.
- We selected those polymers that are close to the known biodegradable ones to contribute to our ML models → Focus of the subsequent MD calculations.
- These homopolymers of interest will be combined into copolymers for property tuning.



Biodegradable polymers

Polymer informatics with copolymers

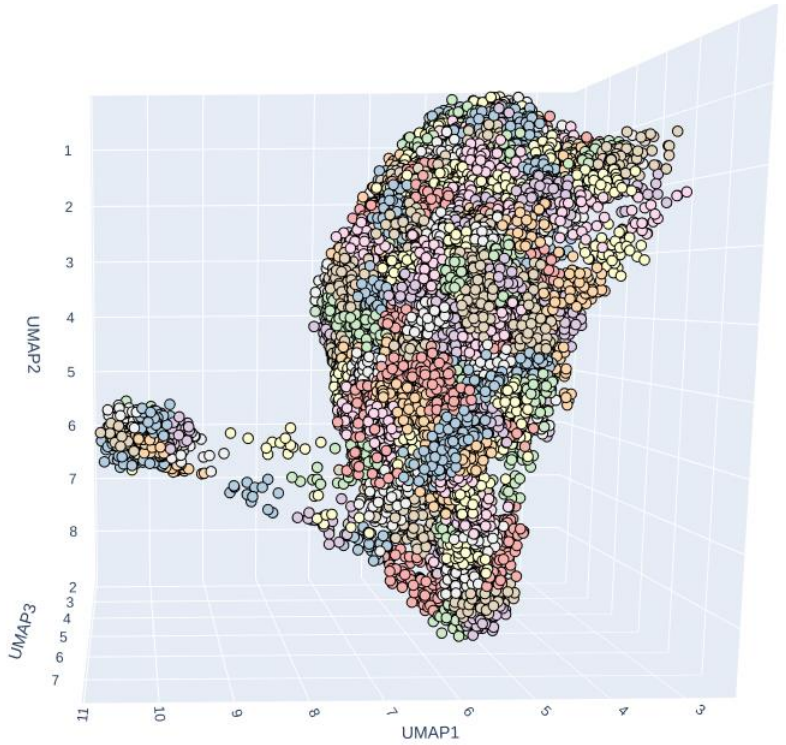
- 20,000 hypothetical copolymers have been generated by binary combinations of 67 biodegradable monomers at different ratios.
- These hypothetical copolymers are represented in grey in the figure. They permit to densely cover the chemical space of interest.
- Evaluation of their physico-chemical properties, such as Tg, will permit to train predictive ML model in order to accelerate the identification of promising candidates.



Polymer informatics with copolymers

As this is a huge number, it is necessary to prioritize the sampling of the chemical space that is relevant to our problem. For that purpose, we have adopted the following strategy :

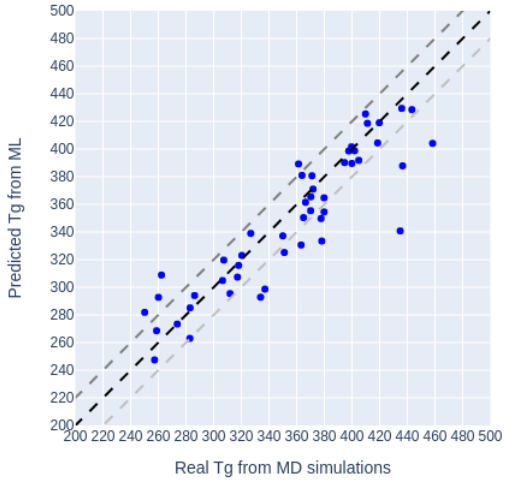
- Perform an unsupervised K-means clustering to identify 500 cluster of similar structures.
- Select the closest copolymer compositions to the cluster centroids.
- The selected structures are built, and their physico-chemical properties are evaluated via MD simulations.

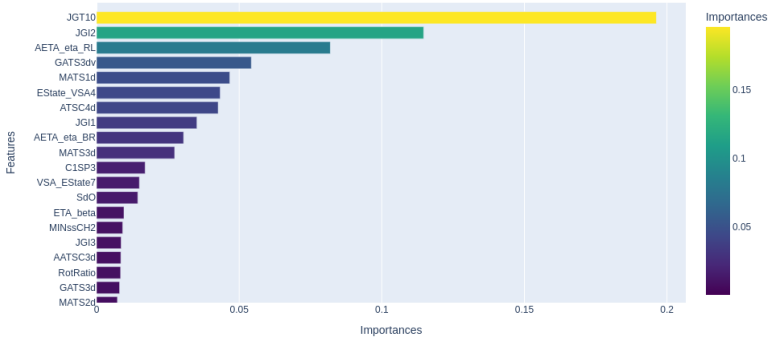


Machine Learning model

- We have trained supervised Machine Learning models on 500 polymers for which properties had been calculated via Molecular Dynamics simulations of 4 replicas:
  - Homopolymers, including hyaluronic acid, cellulose, starch, alginate and pectin
  - Copolymers, including copolymers with polysaccharides
- Properties: Glass transition temperature, Hansen solubility parameters
- 2D molecular descriptors, Random Forest
- 90/10 train-test split

Mean absolute error of 18 K and a R^2 of 0.8





Most important features

Biodegradable polymers

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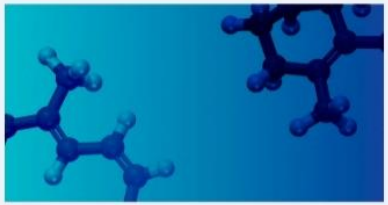
Logout



Polymers

SMILES of monomer #1

O(C(*)(C(*)))

SMILES of monomer #2

*OC(CCCCCC)CC(*)(=O)

Ratio of monomer #1

0.50 − +

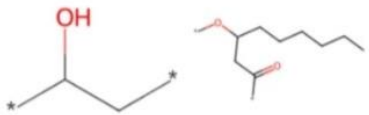
Model 1: Machine Learning prediction of Tg and HSP

The main outcome of these models is the prediction of the glass transition temperature (Tg).

The following solubility parameters are also predicted:

- Hildebrand: obtained from the total cohesive energy of the system
- Dispersion: obtained from the Lennard-Jones vdW contributions to the cohesive energy
- Electrostatic: obtained from the Coulombic contributions to the cohesive energy Use the sidebar to input the polymer of your interest.

Predictions



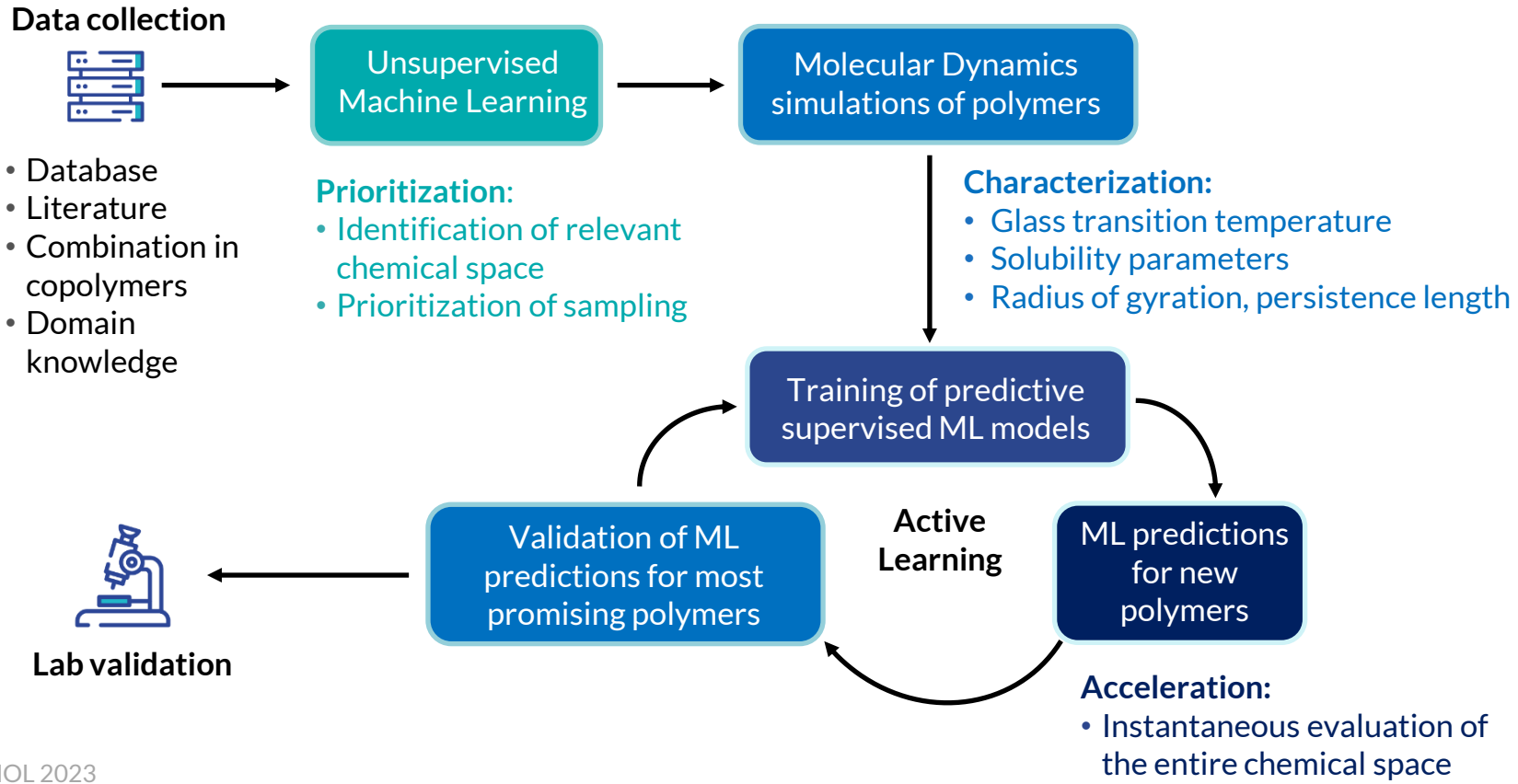
Ratio monomer #1: 0.5 | Ratio monomer #2: 0.5

Prediction

		ratio 2	Applicability Domain	vs AD threshold	rescaled Tg [K]	Tg [K]	Hildebrand [J/cm³]^(1/2)	Dispersion [J/cm³]^(1/2)	Electrostatic [J/cm³]^(1/2)
0	(=O)	0.5	inside	0.99	223.73	323.09	22.12	18.39	9.71

Download polymer predictions as CSV

Summary



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Thank you!

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Application to hypothetical polymers

- We analyzed the chemical space of a dataset of one million hypothetical polymers (PI1M) and compared with the known biodegradable ones.
- The biodegradable polymers are concentrated in two specific regions.
- 8,621 (out of 1 million) hypothetical polymers are located close to known biodegradable polymers and will therefore be studied in more detail.
- Acceleration of more than x100 compared to a brute force analysis of all polymers.