Micaela Matta
Lecturer (Assistant Professor) in Computational Materials Chemistry
King's College London, Department of Chemistry

SwiftPol: RDKit and cheminformatics for polymer building

Drug discovery toolkits

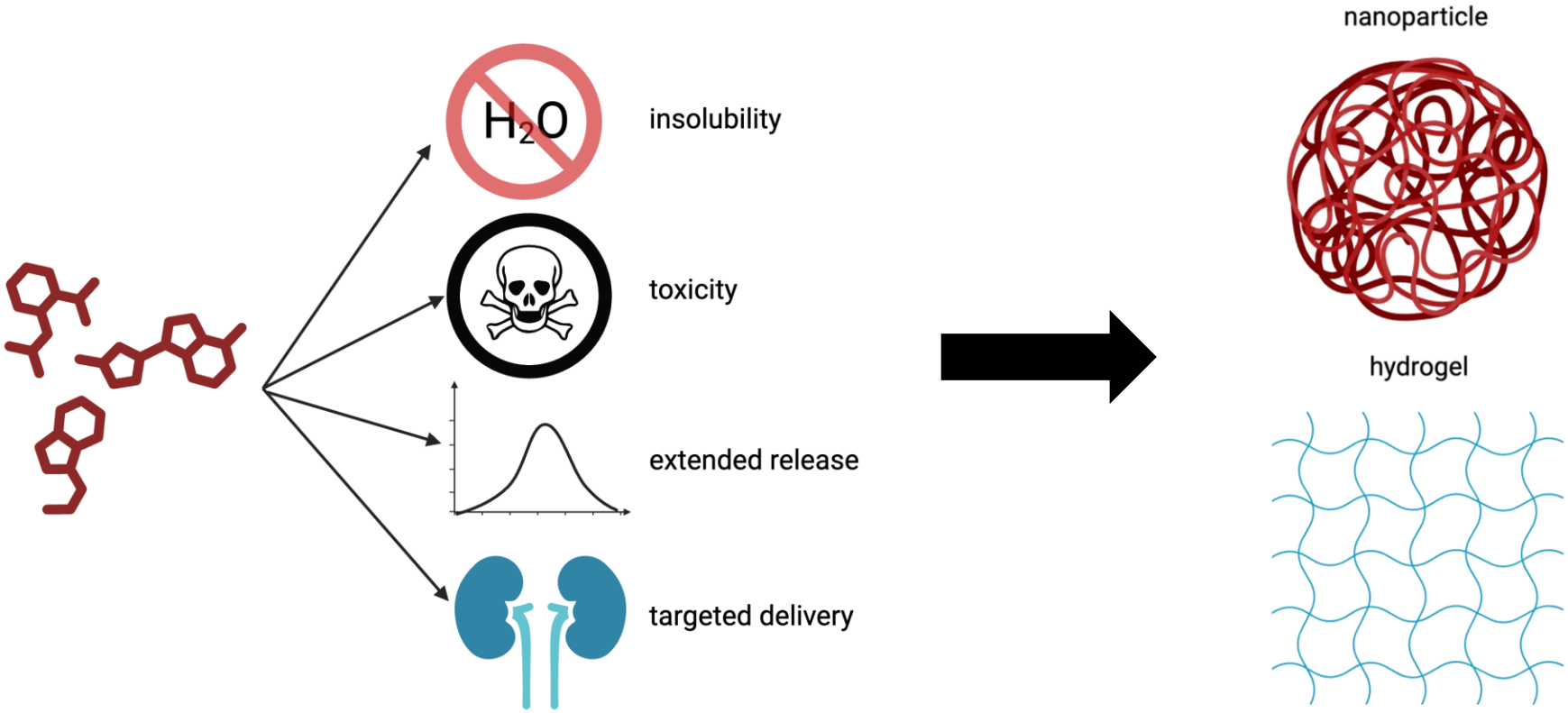
Materials discovery, polymer simulations

LIDo London Interdisciplinary Doctoral Programme
open forcefield
Johnson&Johnson Innovative Medicine
UKRI Biotechnology and Biological Sciences Research Council

Image created with Biorender.com

Polymer excipients for drug delivery/controlled release

‘Difficult’ drugs – how do we deliver to the target tissue?



How do variations in polymer structure influence downstream drug delivery?

Chatterjee M, Chanda N. Mater Adv. 2022 Jan 24;3(2):837–58.

Main bottlenecks in polymer simulations

Polymer building

Parameterization

Melt equilibration

?

1. (How) should we account for polymer heterogeneity in simulated materials, to approximate real systems?

2. Can we build complex 3D polymer topologies (dendrimers, polymer brushes, crosslinked networks) using cheap cheminformatics tools?

H. Turney, M. Matta. *Recent advances and challenges in polymer modelling workflows*.
ACS* Macromolecules, *under review.

Polymer building: which tool?

Tool	Co-polymers?	Branched Polymers?	Tacticity?	Dispersity?	Bespoke monomer input (format)	Actively maintained (commits within 2y)?
CHARMM Polymer Builder	✓·	X	✓·	X	X (pre-defined monomer library)	X
EMC	✓·	✓·	✓·	X	✓ (monomer and terminal SMILES)	✓·
mBuild	✓·	✓·	✓·	X	✓ (monomer SMILES)	✓·
Moltemplate	✓·	✓·	✓·	X	✓ (monomer PDB or xyz)	✓·
PolyCostruct	✓·	✓·	✓·	X	✓ (monomer PDB or itp)	✓·
Polymatic	✓·	✓·	✓·	X	✓ (monomer pdb/xyz and monomer parameters)	X
PolyPly	✓·	✓·	✓·	X	X* (pre-defined monomer library, new monomers must be added to library first)	✓·
PySIMM	✓·	✓·	✓·	✓·	✓ (monomer SMILES or mol file)	X
PySoftK	✓·	✓·	✓·	X	✓ (monomer SMILES)	✓·
RadonPy	✓·	✓·	✓·	X	✓ (monomer SMILES)	✓·
SwiftPol	✓·	✓·	✓·	✓·	✓ (monomer SMILES + Reaction SMARTS)	✓·

FAIR & realistic polymer simulations

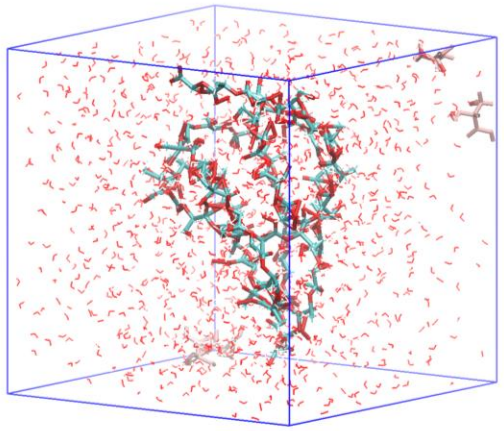
With Hannah Turney, Lukasz Sekula

SwiftPol

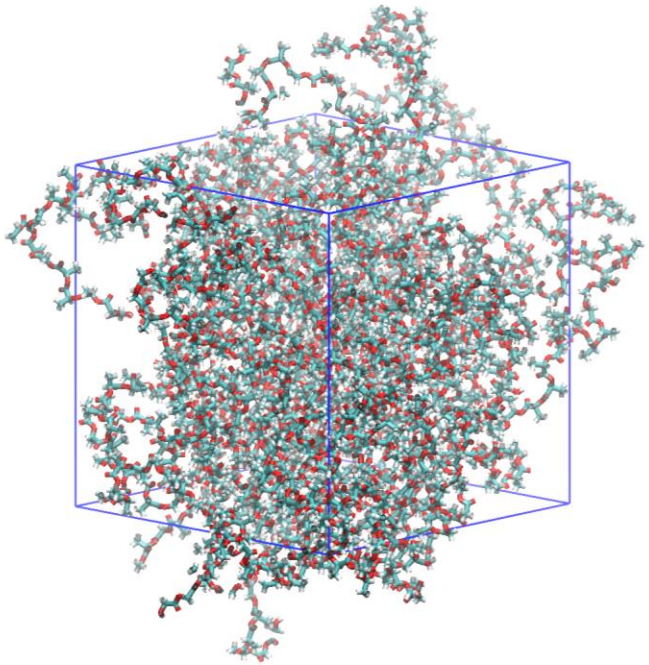
Journal of Open Source Software, 10(110), 8053,
https://doi.org/10.21105/joss.08053

Findable
Accessible
Interoperable
Reusable

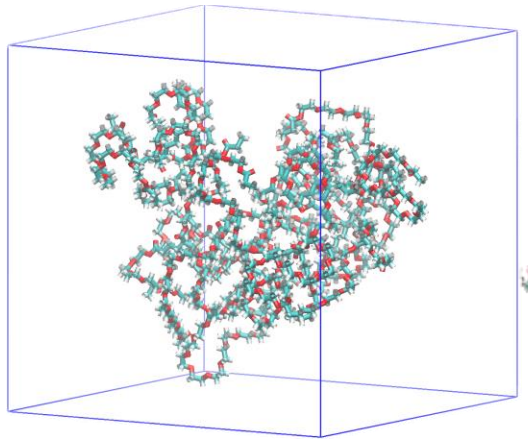
Polymers in solution



Polymer melts



Crosslinked polymers



Polymer-API mixtures

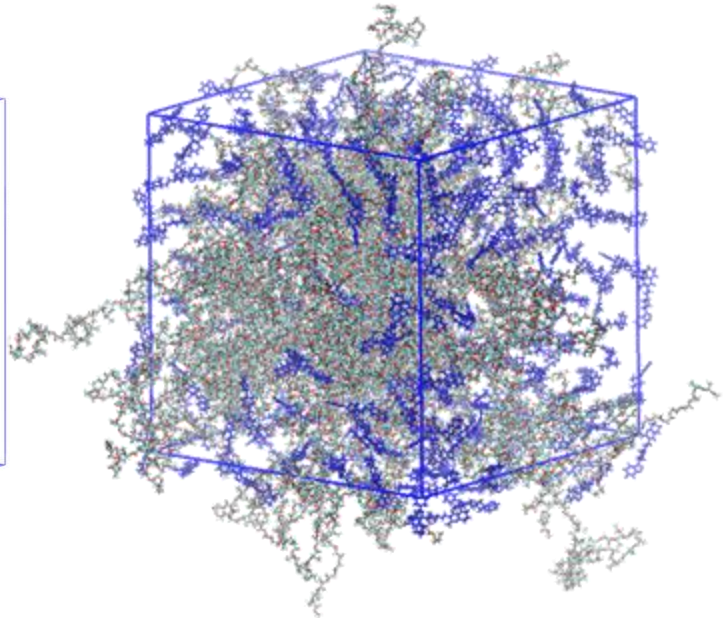
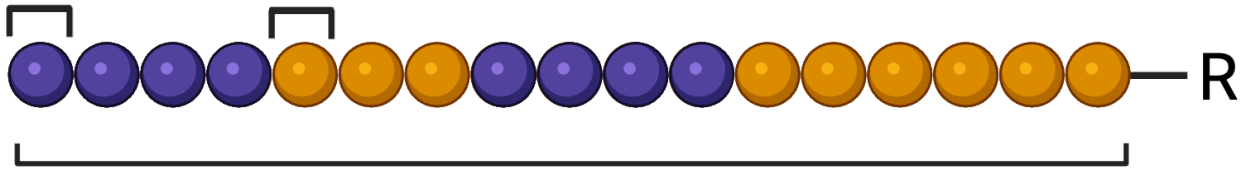
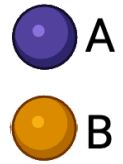


Image created with Biorender.com

Polymers are statistical objects





R =

Hydroxyl —OH

DOP = $\bar{x}$(nA+nB)

Ester —O

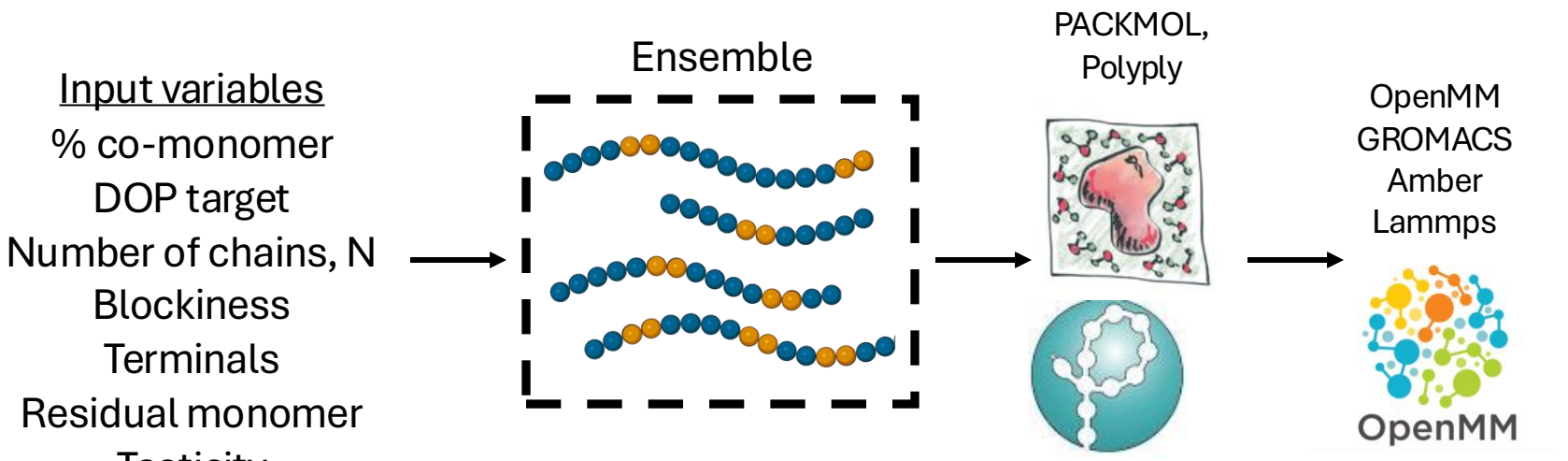
Carboxyl O OH

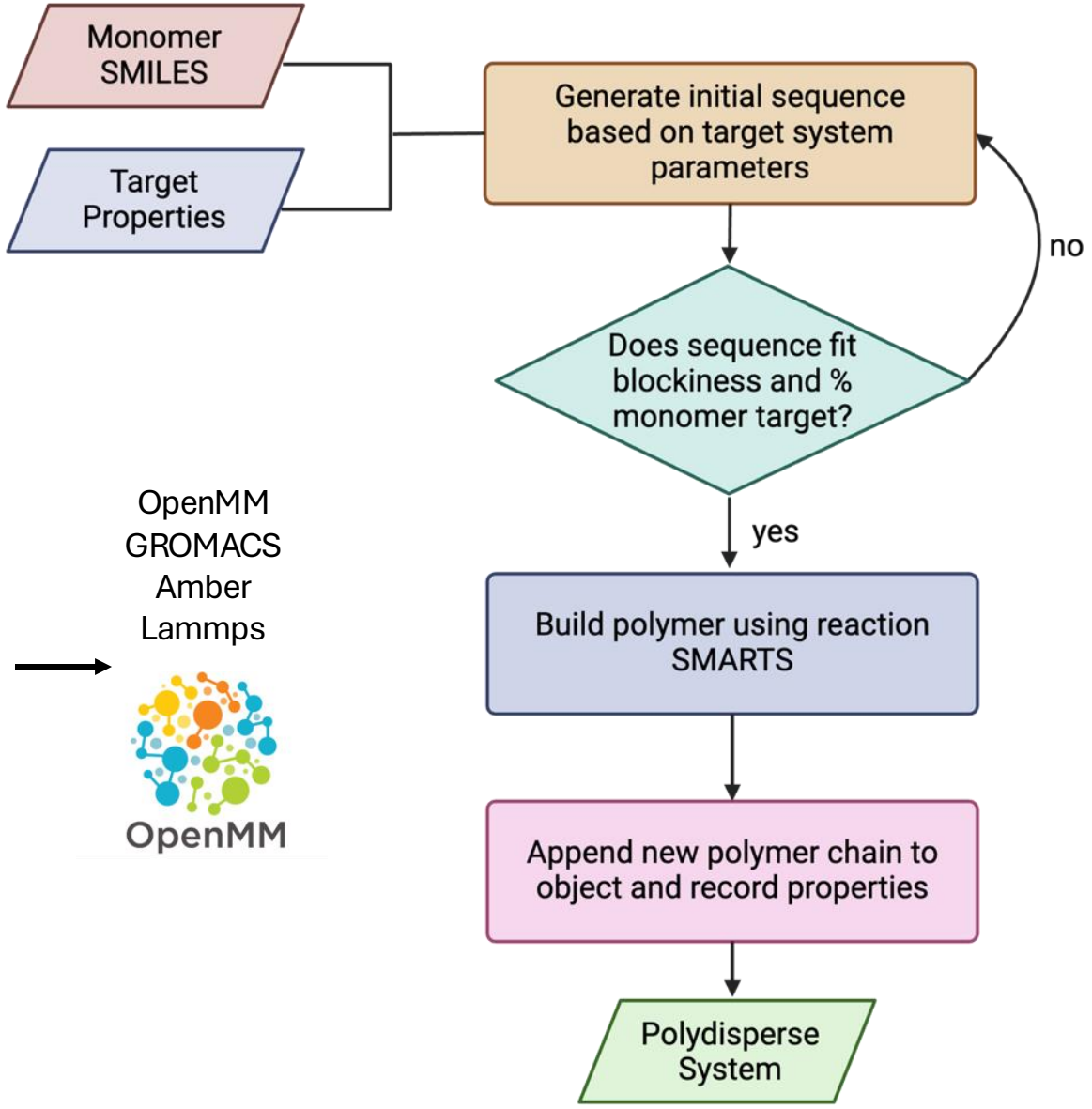
Multicomponent polymer ensembles

With Hannah Turney

SwiftPol

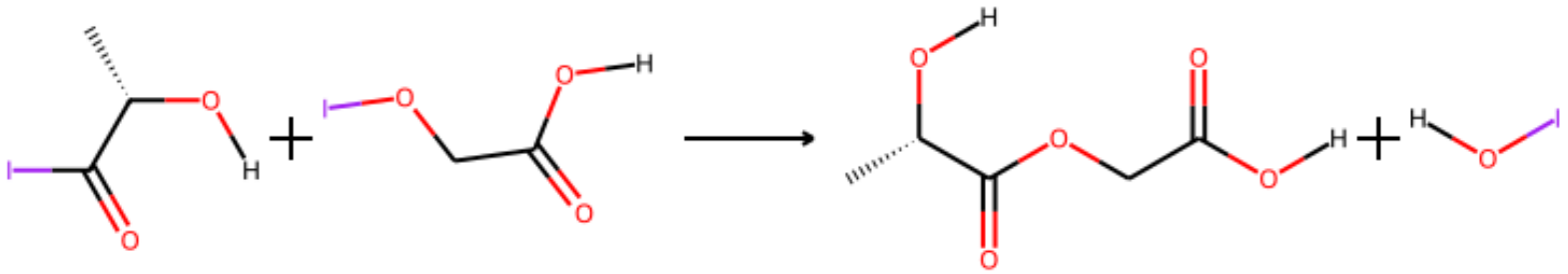
Journal of Open Source Software, 10(110), 8053,
https://doi.org/10.21105/joss.08053





Getting started with SwiftPol

PLGA polymerization



[C:1][O:2][H:3].[I:4][O:5][C:6]>>[C:1][O:2][C:6].[H:3][O:5][I:4]

% monomer A = 75
% acceptance window = 10
DOP = 50-mer
Terminals = hydroxyl
Blockiness index = 1.0

Zoladex® (goserelin implant)

RisperdalCONSTA® risperidone Long-Acting Injection 12.5mg, 25mg, 37.5mg, 50mg

Eligard® (leuprolide acetate) for injectable suspension

TRELSTAR (triptorelin pamoate for injectable suspension)

Getting started with *SwiftPol*

KING'S College LONDON

Demo of Build tools from SwiftPol

- Build a short linear co-polymer chain (PLGA)
- Create a small SwiftPol PLGA ensemble, assign partial charges to the chain, and inspect the chains in the system
- Solvate the PLGA ensemble with water, NaCl and residual monomer

[3]:
```
# Print SwiftPol Version
from swiftpol.__version__ import __version__
__version__
```

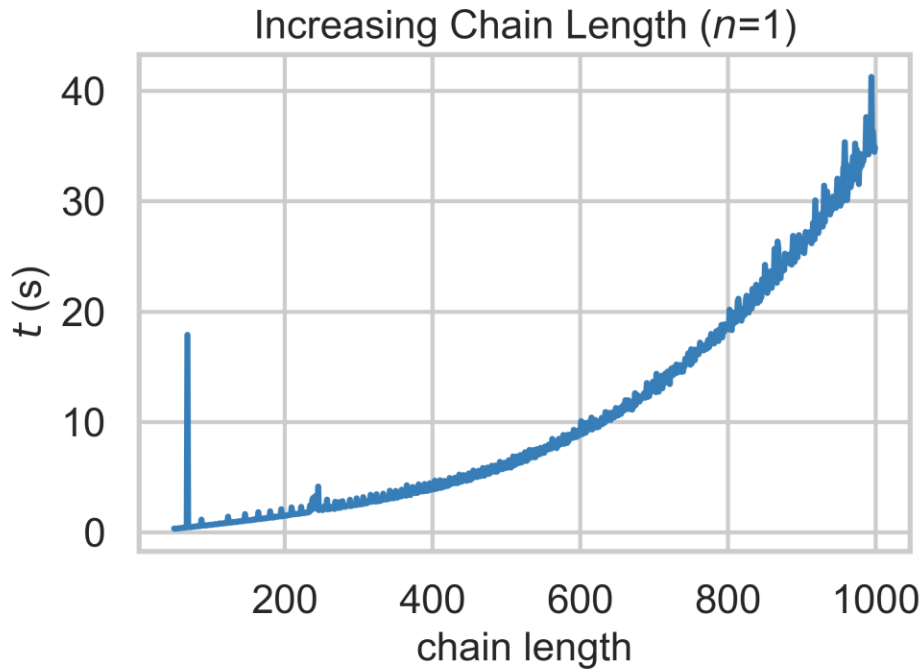
[3]:
```
'0.1.1'
```

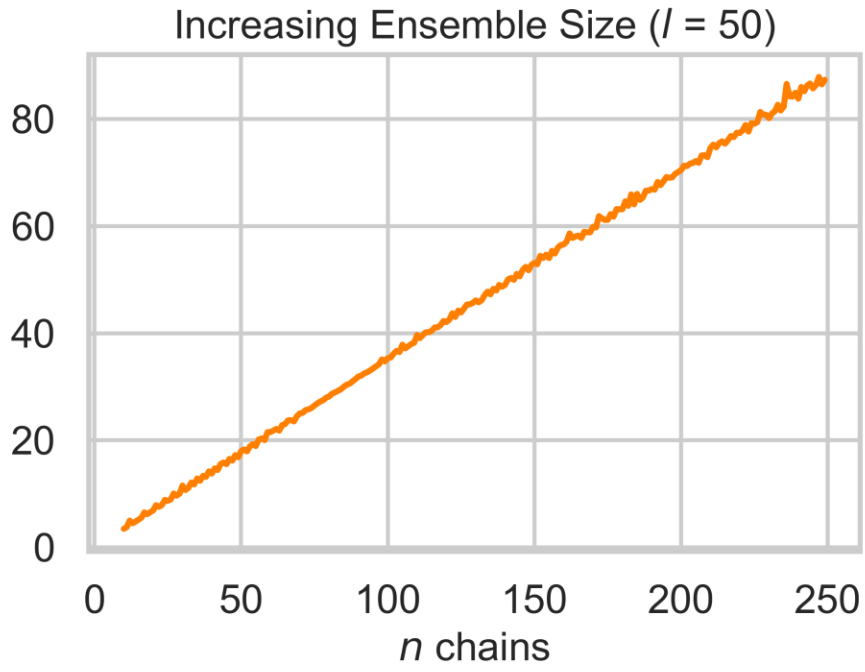
[4]:
```
# Import monomers to build PLGA and visualise using RDkit
from rdkit import Chem
from rdkit import RDLogger
```

Speed test: ensemble size and chain length

Macbook Pro M2 chip, 8 cores

RDKit 2025.03.2

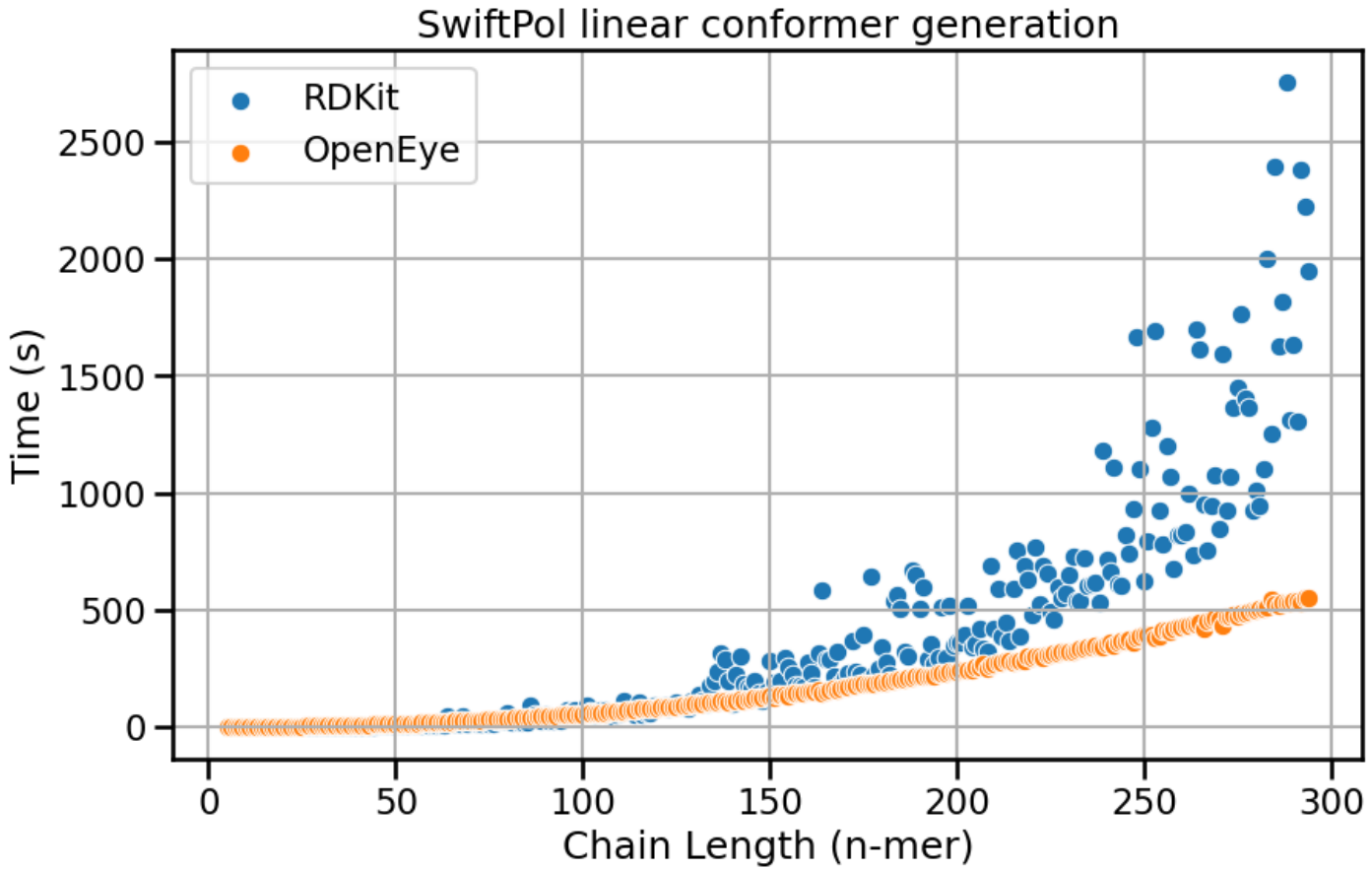




Speed test: conformer generation

Macbook Pro M2 chip, 8 cores

RDKit 2025.03.2
OEToolkits 2024.2.1



We acknowledge the use of a free academic license provided by OpenEye, Candence Molecular Sciences, Santa Fe, NM. J. Chem. Inf. Model. 2010, 50 (4), 572–584.

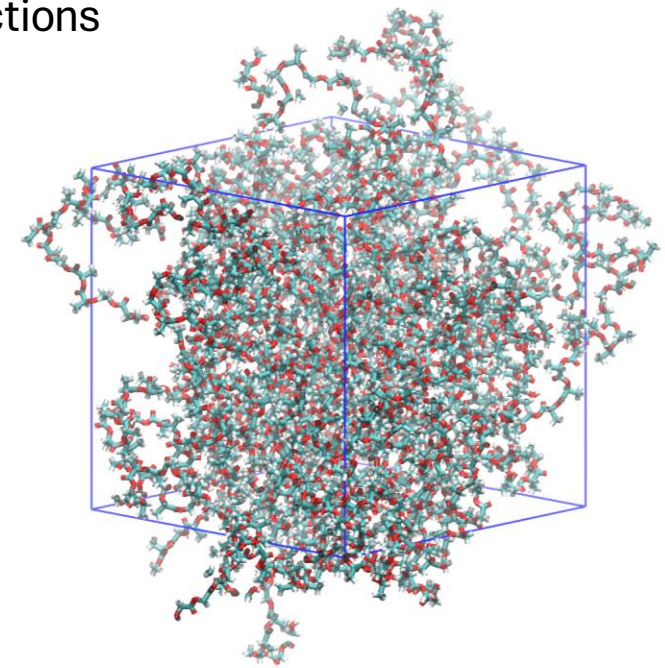
Case Study: Poly(lactide-co-glycolide)

Evonik Resomer® Select 7525 DLG 2CA @ 0.37x M_w

PLGA 75:25, ester terminated

Polymer melt configuration generated with PolyPly using integrated SwiftPol export functions

	% Lactide (1:1 D:L)	Blockiness	Residual monomer (% w/w)	Dispersity (M_w/M_n)
Experimental	74.38	0.40	1.94	1.74 (+-0.04)
SwiftPol	73.85	0.39	1.84	1.70



M_w (mean) = 3580 Da/chain

International Journal of Pharmaceutics 2021, 607, 120907.
Nat Commun 2022, 13 (1), 68.

Building crosslinked, hyperbranched polymer systems, gels

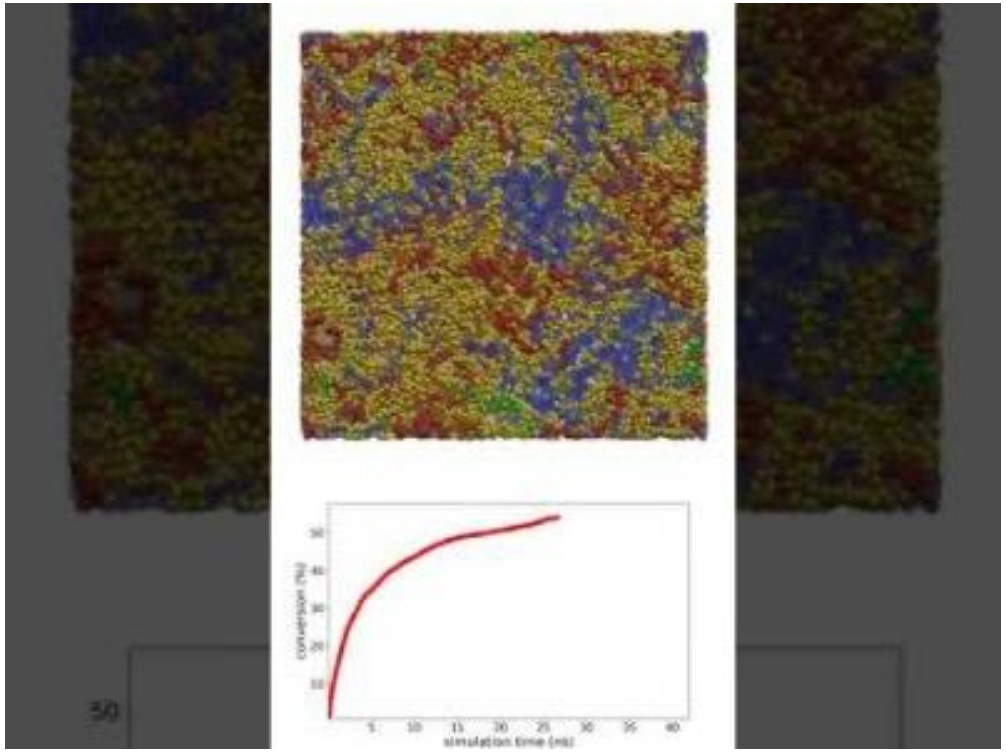
State of the art: building complex polymer structures requires 3D, expensive MD-based protocols.

3 alternatives:

1. ReaxFF (old school, limited parameters)
   npj Comput Mater 2, 15011 (2016)

2. Topology rebuilding MD protocols
   (requires careful reaction definition, topologies)
   Computer Physics Communications, 304, 2024, 109287

3. Neural Network Potentials (accurate, but expensive)

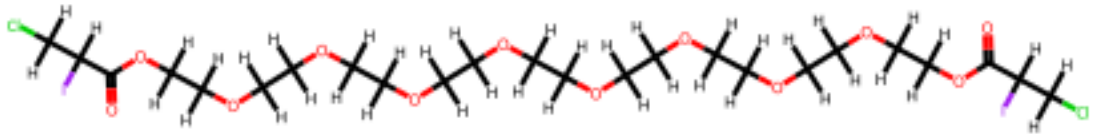


Reacter.org

Building crosslinked polymer systems with SwiftPol

KING'S College LONDON

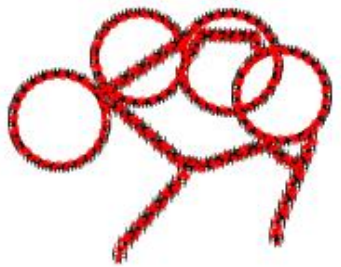
Example: PEGDA (PEG diacrylate). The addition of a 2nd PEGDA chain occurs across the acrylate C=C double bond.



We define reactions for branched and linear chain addition, their probabilities, and how much crosslinking

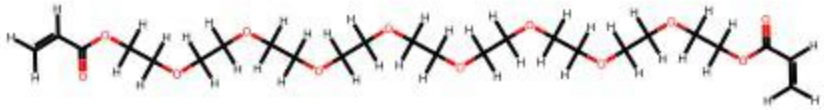
```
# Build up a larger branched system to a target molecular weight
branched_mw = crosslink.build_branched_polymer(starting_polymer = polymer,
                                               reaction_templates = reaction_templates,
                                               target_mw=10000,
                                               probability_of_branched_addition=0.8,
                                               probability_of_linear_addition=0.2)

# Crosslink chains and clean up halogens
crosslinked_network = crosslink.crosslink_polymer(branched_mw, percentage_to_crosslink=80)
crosslinked_network
```



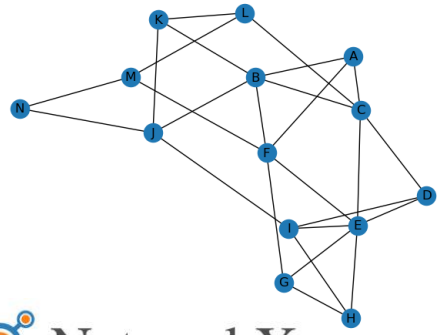
Building crosslinked polymer systems with SwiftPol

1D



<u>Input variables:</u>
Reax scheme
target Mw
X-linking %

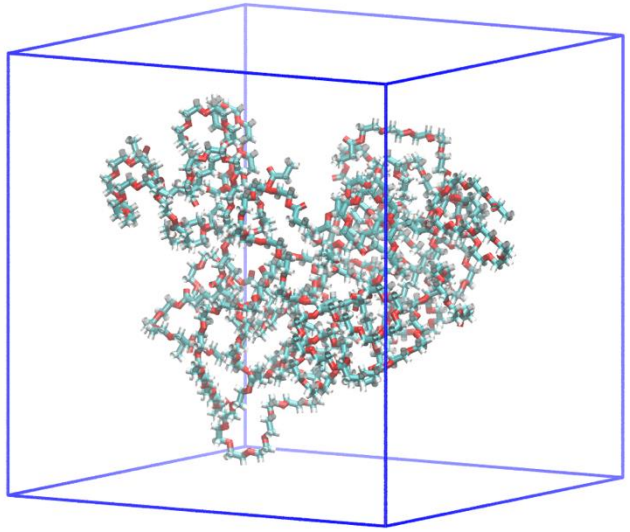
2D



NetworkX
Network Analysis in Python

<u>Output:</u>
RDKit object
network metrics

3D

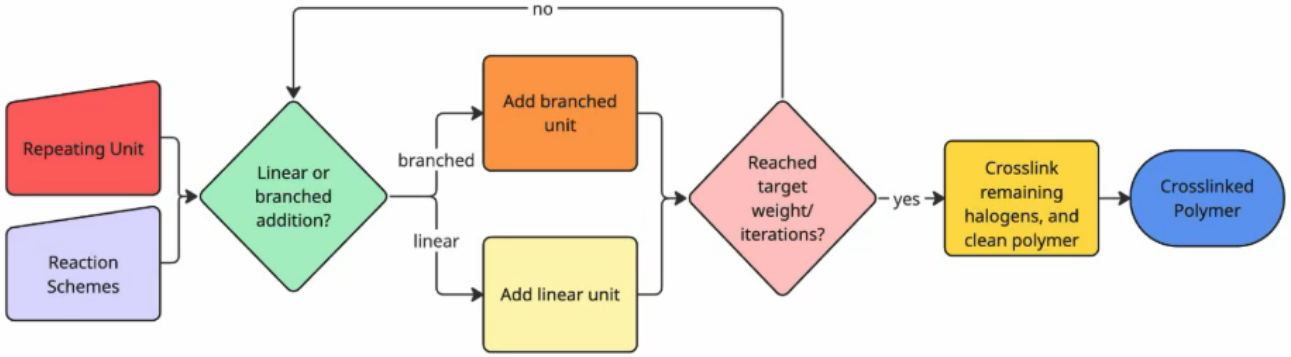


Export to MD build
(further reactions can occur)

Getting started with *SwiftPol*

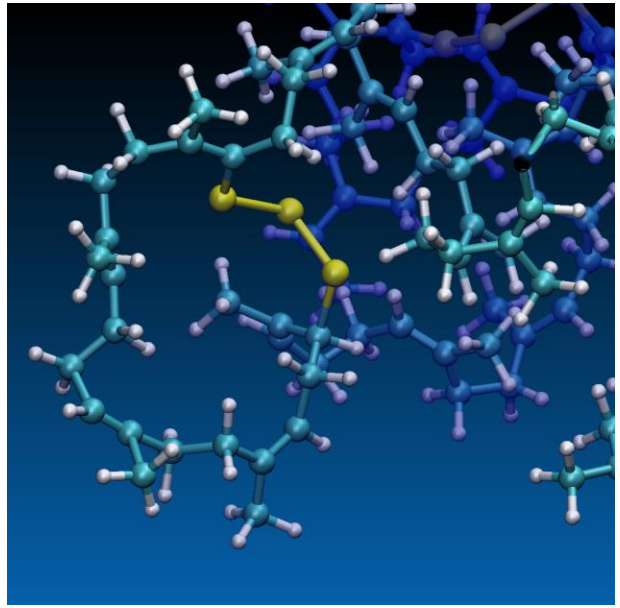
Creating crosslinked polymers with SwiftPol.crosslink

This code uses SwiftPol's framework to build a chain of Polyethylene Glycol Diacrylate (PEGDA) and build a large crosslinked polymer network.



[2]:
```
# Imports
from rdkit import Chem
from rdkit.Chem import AllChem
import random
# Import SwiftPol
from swiftpol import build, crosslink
```

[ ]:
```
# Build linear PEGDA chain using SwiftPol
monomer = ["IC=CC(=O)OI", "IOCCOI"] # PEGDA monomers with iodinated polymerization points
```



Sulphur crosslinks in vulcanized rubber.
Built with Swiftpol v.0.1.4 (Hannah Turney)

Growing pains and work in progress

Conformer generation is slow (stress tests ongoing).. But not slower than running reactive MD

We use different halogen tags for reaction SMARTS, we will explore other notations

Documentation

It works

Check out example notebooks:

swiftpol

Search docs

CONTENTS:

- Getting Started with Swiftpol
- swiftpol
- swiftpol.build
- swiftpol.parameterize
- swiftpol.crosslink

Welcome to SwiftPol's documentation! View page source

Welcome to SwiftPol's documentation!

SwiftPol

About SwiftPol

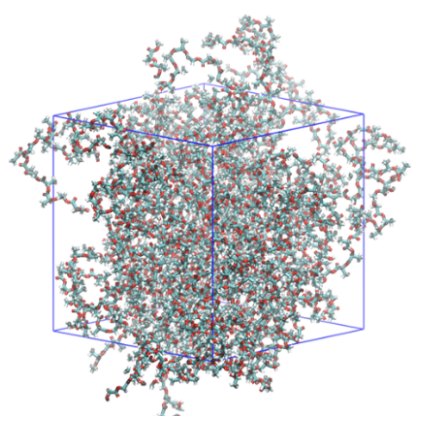
A polymer sample contains a natural degree of variation in its structure and non-uniformity between its chains, which is often disregarded in MD systems.

SwiftPol uses a statistical approach to build polydisperse polymer systems, allowing for a more realistic representation of polymer systems in MD.

SwiftPol.build.polymer_system takes as an input:

- The simplified molecular-input line-entry system (SMILES) string of all co-monomers.
- Values of the target average properties of the ensemble: monomer % composition (for copolymers), length, number of chains, blockiness (for blocky copolymers), terminals, residual monomer.
- Reaction SMARTS which describes the polymerization reaction associated with their polymer chemistry.

...and builds a polydisperse chain ensemble.



Conclusion

Polymer building

1. (How) should we account for polymer heterogeneity in simulated materials, to approximate real systems?

More realistic systems are possible. But does this change our AA-MD results? Stay tuned.

Parameterization

2. Can we build complex 3D polymer topologies (dendrimers, polymer brushes, crosslinked networks) using cheap cheminformatics tools?

Definitely! Significant advantages over other methods.

Melt equilibration

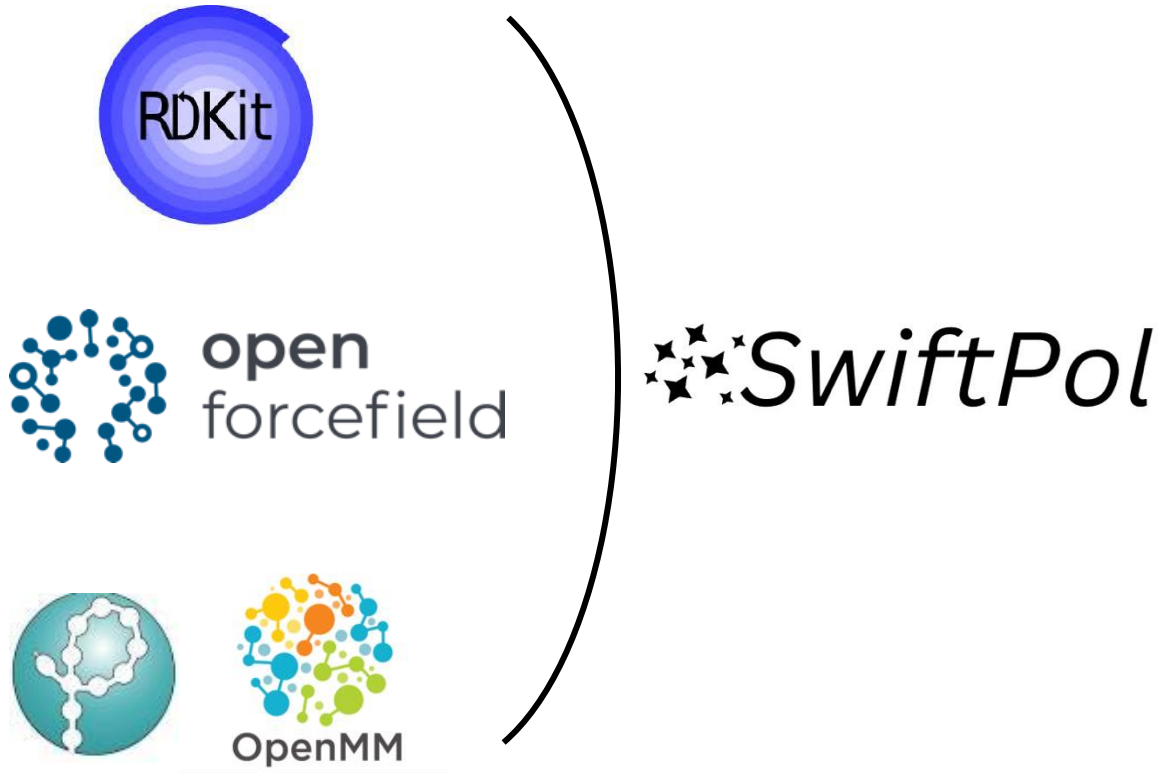
H. Turney, M. Matta. *Recent advances and challenges in polymer modelling workflows*.
ACS* Macromolecules, *under review.

Conclusion

Polymer building

Parameterization

Melt equilibration



H. Turney, M. Matta. *Recent advances and challenges in polymer modelling workflows.*
ACS* Macromolecules, *under review.

micaela.matta@kcl.ac.uk
@micaelamatta.bsky.social
mattaresearch.com

Swiftpol Team:

Hannah Turney

hannah.turney@kcl.ac.uk

Lukasz Sekula

J&J

David Hahn

Anusha Lalitha

Gary Tresadern

OpenFF

Jeff Wagner

London Interdisciplinary Doctoral Programme
open forcefield
Johnson&Johnson Innovative Medicine
UKRI Biotechnology and Biological Sciences Research Council