Modeling Nonequilibrium Reactive Systems with REACTER

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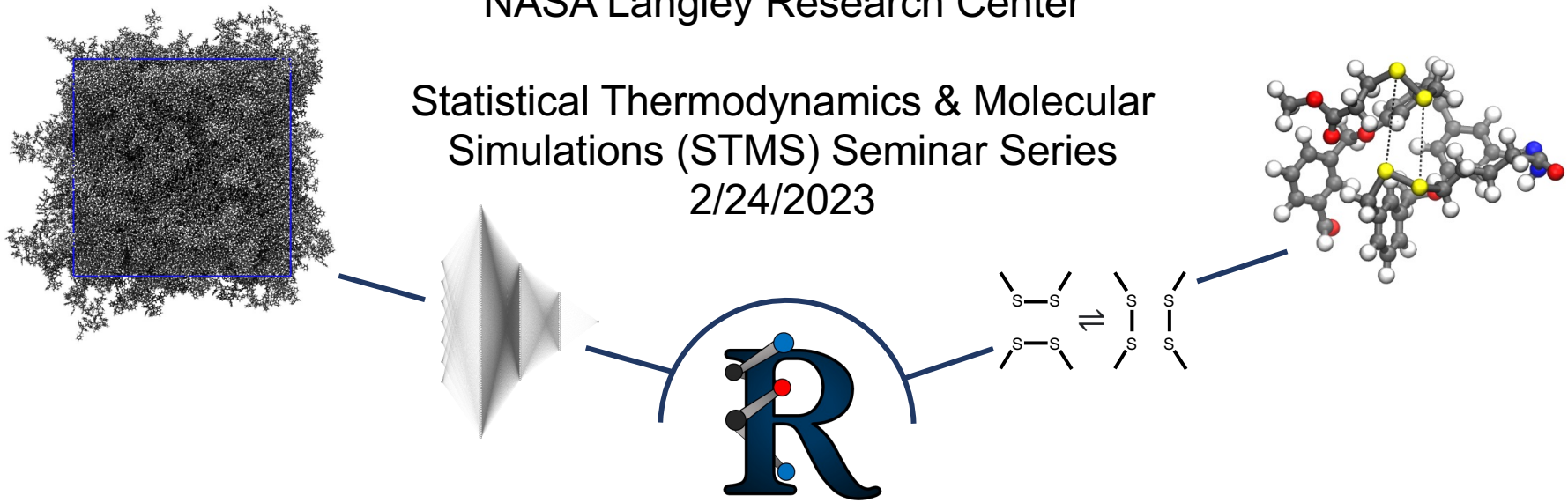
All Images Credit NASA unless otherwise indicated

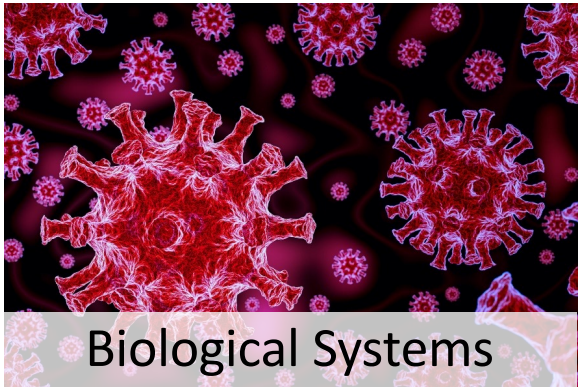
Statistical Thermodynamics & Molecular Simulations (STMS) Seminar Series
2/24/2023

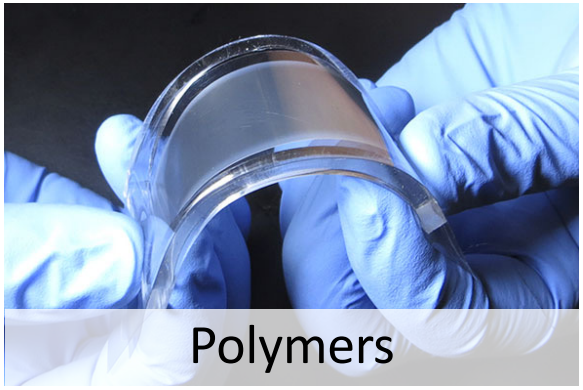


Chemical Reactions are Everywhere


Industrial Processes


Pharmaceuticals

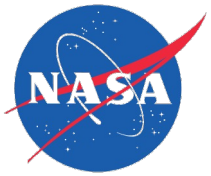

Biological Systems


Polymers

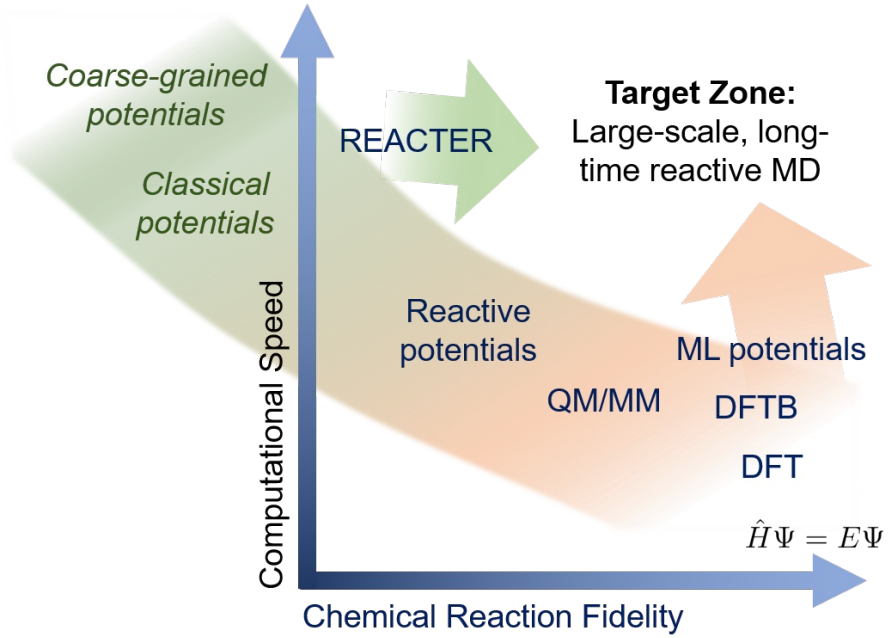

Extreme Materials


Energy

There was a Missing Scale for Reaction Modeling

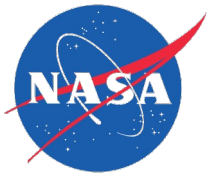


- Quantum mechanics can model reactions from first principles
- Levels of abstraction come with a tradeoff: accuracy *vs.* speed
- Reactive force fields can achieve near-DFT accuracy
  - Much faster than DFT, much slower than classical MD
- Can a heuristic description of reactions allow for reactive modeling at much greater scales?

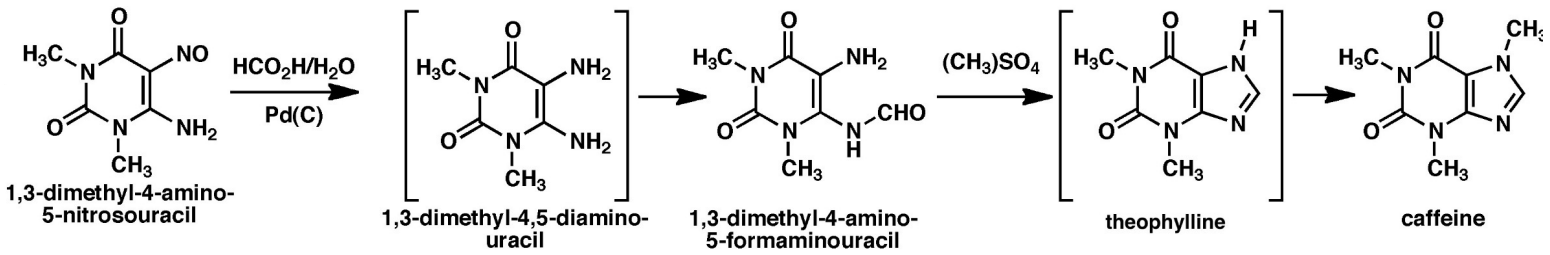


DFT: Density Functional Theory

There is Much Heuristic Knowledge in Chemistry



- Many relevant reaction pathways are already well characterized
  - Polymer chemistry, organic chemistry, materials science
  - Reaction pathways available in literature, textbooks, and online databases
- Dynamic modeling of products forming from reactants allows:
  - Creation of realistic initial configurations for further study
  - Large-scale, computationally-efficient simulations of reactive systems



Example of a sequence with complex but well-characterized reactions (artificial synthesis of caffeine).

Temple NJ, Wilson T (2003). *Beverages in Nutrition and Health*. Totowa, NJ: Humana Press. p. 172.

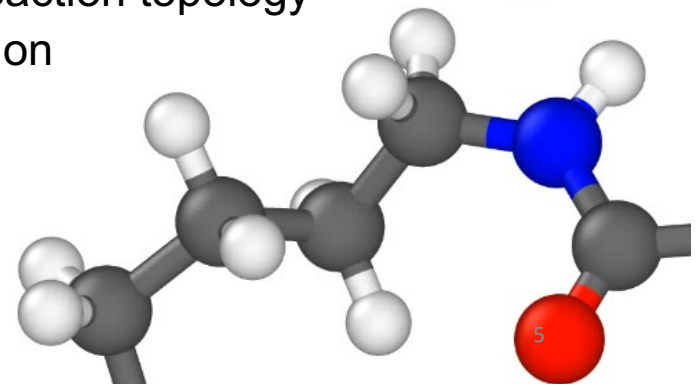
What is REACTER?

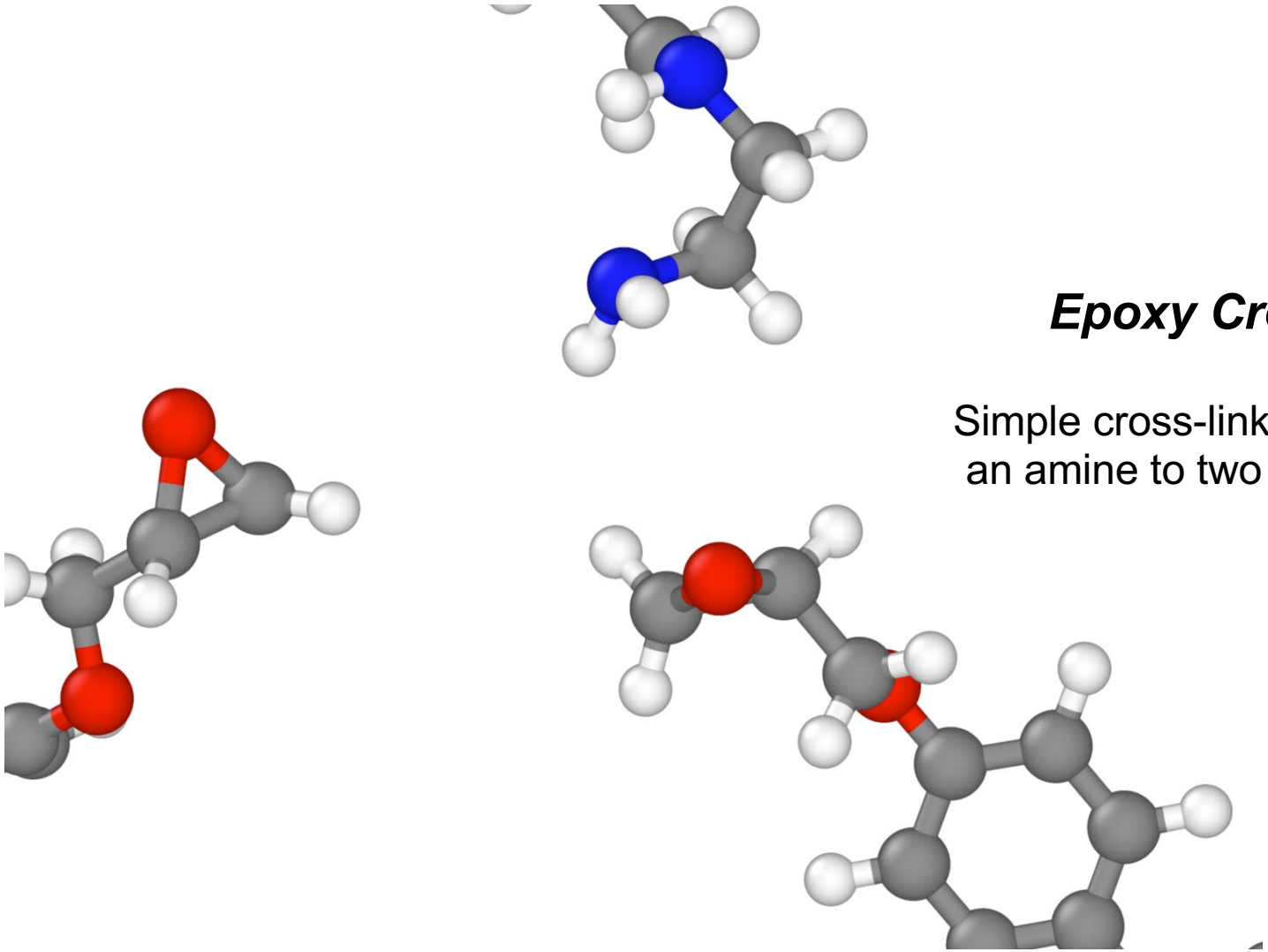
- **A protocol for modeling reactions during classical MD**
  - Add/remove specific bonds, angles, dihedrals, etc.
  - Modify all force field types as well as atomic charges
  - Supports any fixed-valence force field (PCFF, OPLS, etc.)
  - Reaction stabilization

- Parallel implementation in LAMMPS as ***fix bond/react***
  - User inputs: molecule templates of pre- and post-reaction topology
  - A map file relating atoms before and after the reaction

REACTER: A Heuristic Method for Reactive Molecular Dynamics.
Gissinger, Jensen & Wise. Macromolecules 53, 22, 9953–9961 (2020).

www.reacter.org



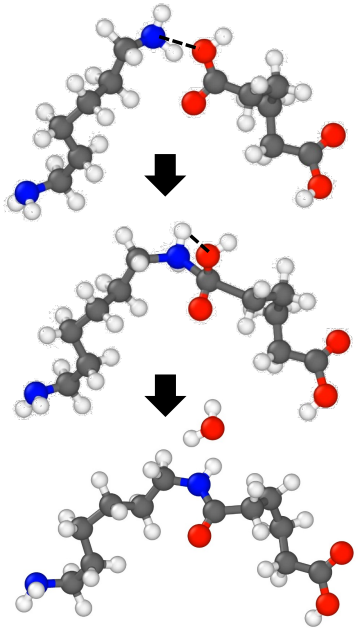


Epoxy Crosslinking

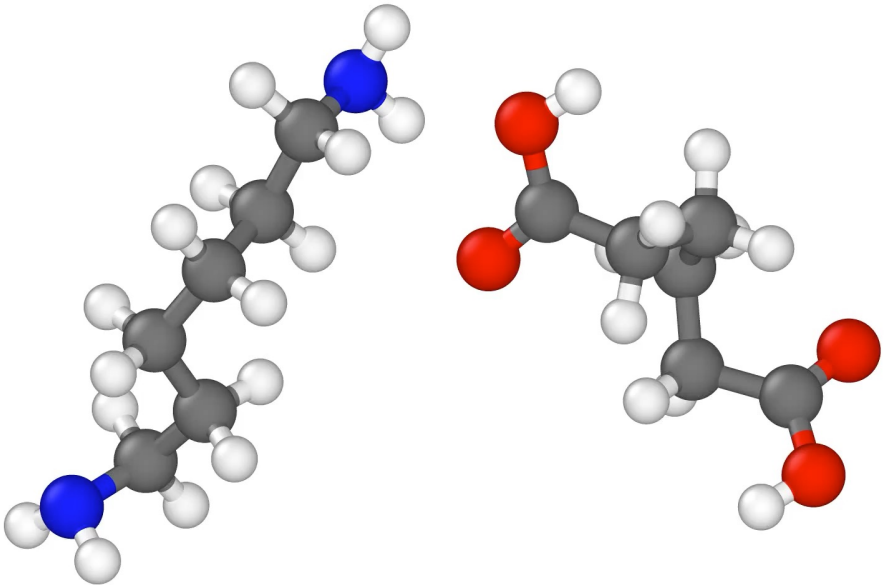
Simple cross-linking mechanism of an amine to two epoxy molecules

Delete Atoms Based on Topology

1) Delete unwanted reaction by-products
2) Remove specific molecules based on topology (such as small rings)



nylon polycondensation



deletion of condensed water molecule

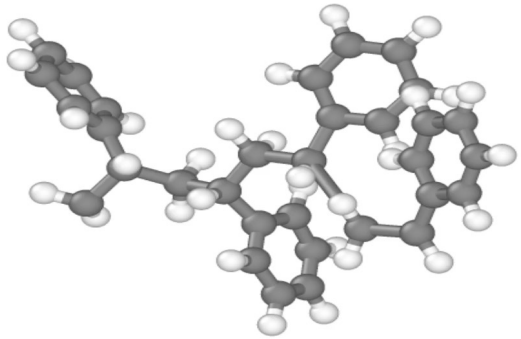
Create Atoms (and their Bonds)

Example:

- Dynamic growth of polystyrene by creating monomers

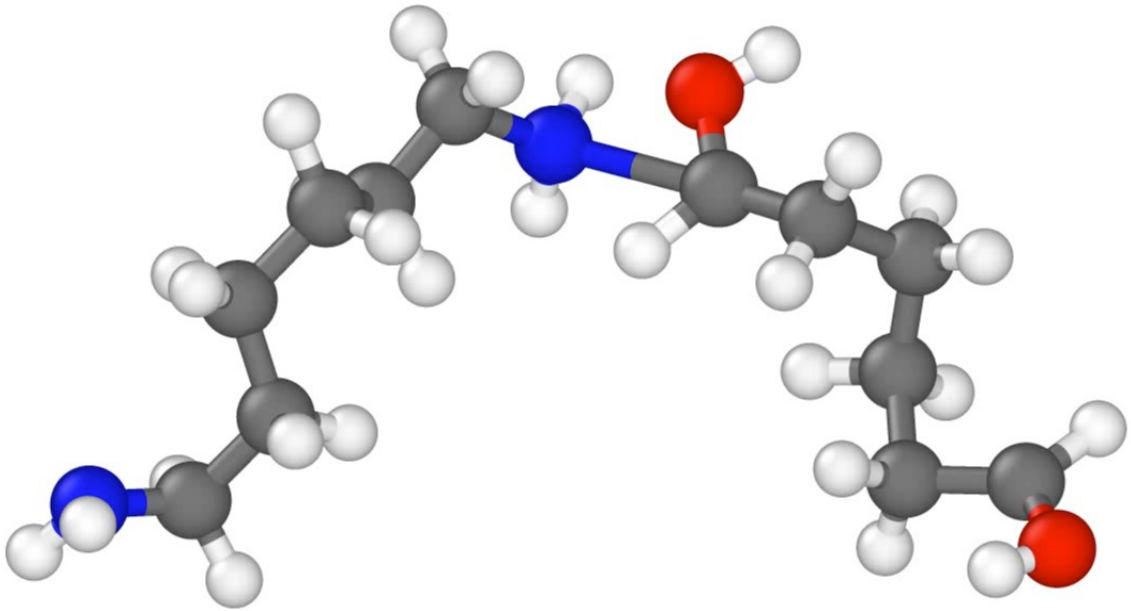
Features:

- Place new atoms using best-fit between template and reaction site
- Prevent created atoms from overlapping with existing atoms

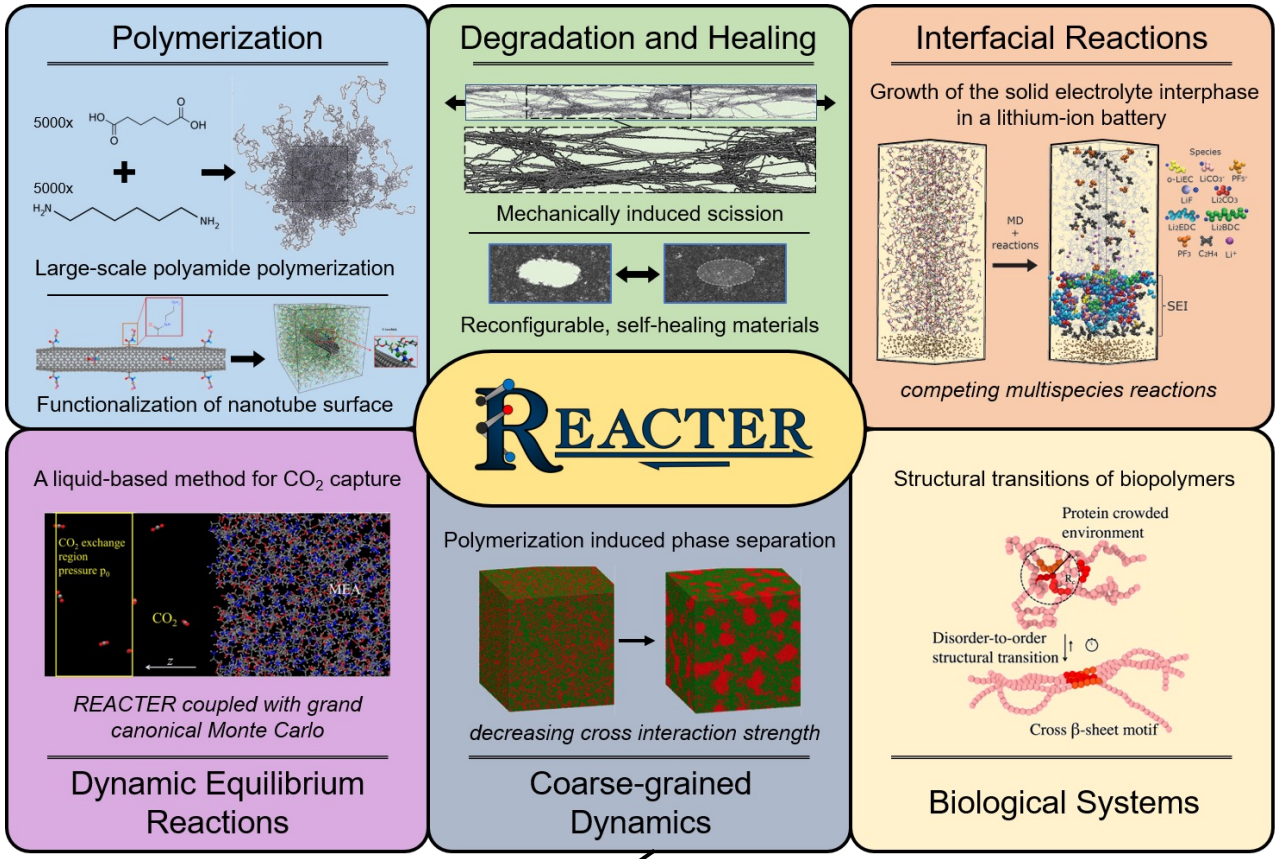


Bond-Breaking Reaction Trigger

- Simple criterion for mechanically-induced chain scission
- Or, if using custom criteria, REACTER can be used to reorganize topology



REACTER has Applications in a Variety of Fields



Gissinger et al. *Macromolecules* ***2020,*** *53.22*, 9953.

Song et al. *Composites Science and Technology* **2021**, *209*, 108790.

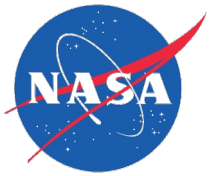
Yeganeh et al. *Science Advances* **2022**, *8.6,* eabm0144.

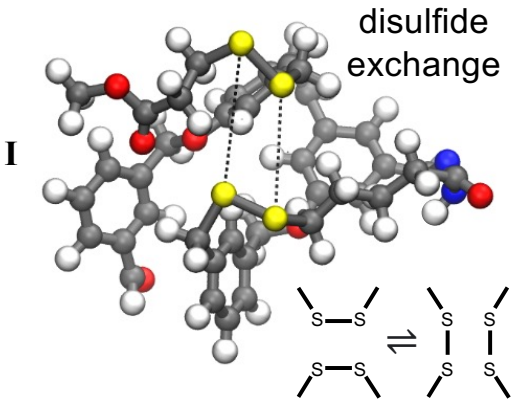
Alzate-Vargas et al. *The Journal of Physical Chemistry C* **2021,** *125.34*, 18588.

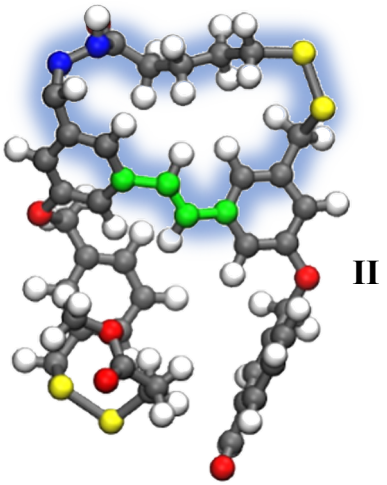
Tejedor et al. *Nature Communications* **2022**, *13.1*, 5717.

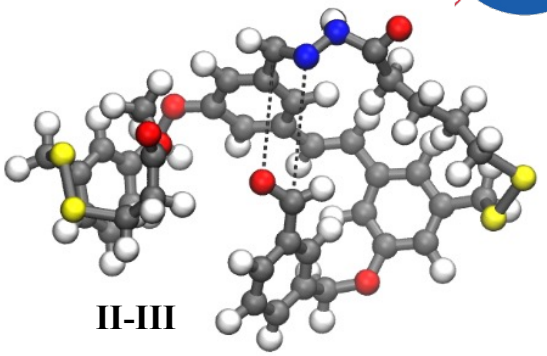
Stevens, *The Journal of Chemical Physics* **2021**, *155.5,* 054905.

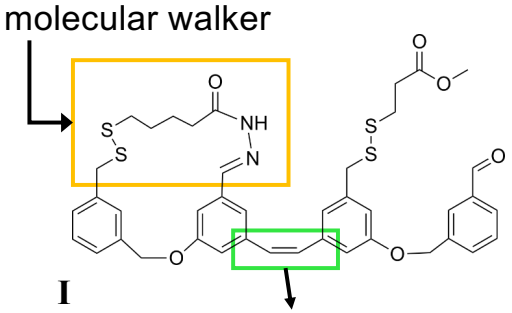
Dynamic Modeling of Molecular Machines



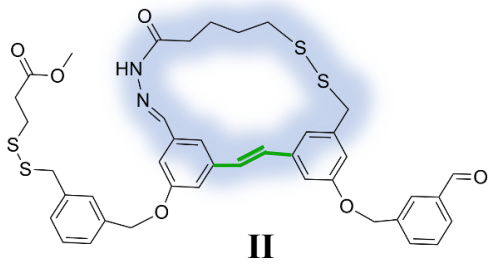




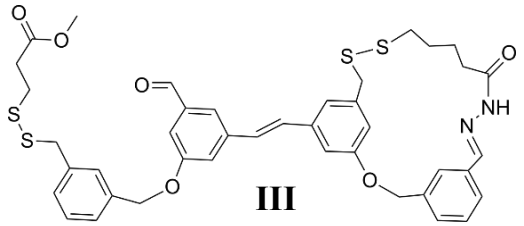




Stilbene linkage can undergo photoisomerization.

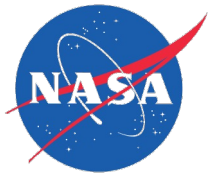


Z-E stilbene transition



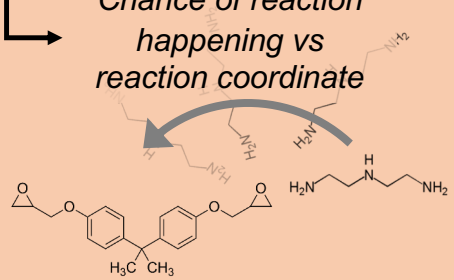
A hydrazone exchange completes the molecular walker's journey.

REACTER-ML Framework: Three-Step Approach



Step 1: Sample the Committor Function with Quantum Accuracy

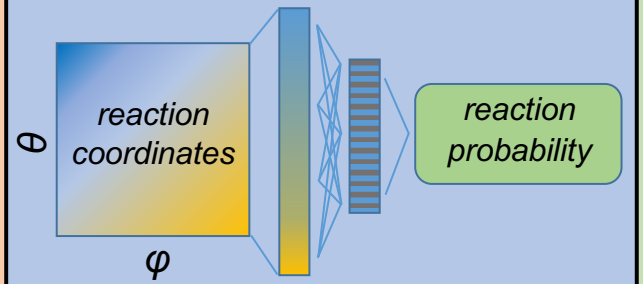
Chance of reaction happening vs reaction coordinate



Tight-binding density functional theory (DFTB) used for efficient sampling

dftbplus.org

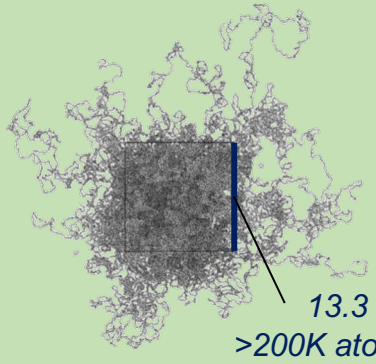
Step 2: Learn the Committor Function using a Deep Neural Net



TensorFlow used to optimize a deep learning framework trained on DFTB data

tensorflow.org

Step 3: Interface the Neural Net with Large-Scale Reactive MD

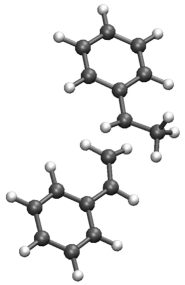


Python-enabled reaction constraints added to the REACTER protocol

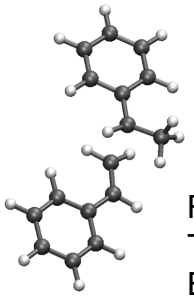
reacter.org

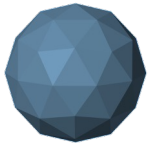
Step 1: Sampling the Committor Function

- DFTB with spin polarization and solvation model (toluene)
- Swarm of trajectories approach used to generate a probability of reaction for a given configuration
- 50 trajectories (500 fs) launched from a given configuration (temperature = 530 K)
- Bond-forming trajectories were identified if bonding atoms were separated by < 1.8 Å at end of run
- Khuong et al.: Reaction barrier: 6.0 - 7.7 kcal/mol, Transition State (TS) bond length: 2.276 - 2.351 Å



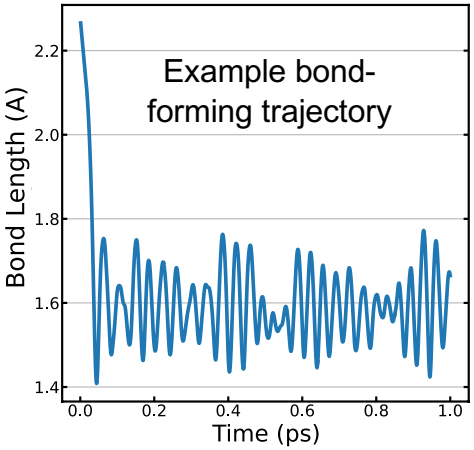
DFTB

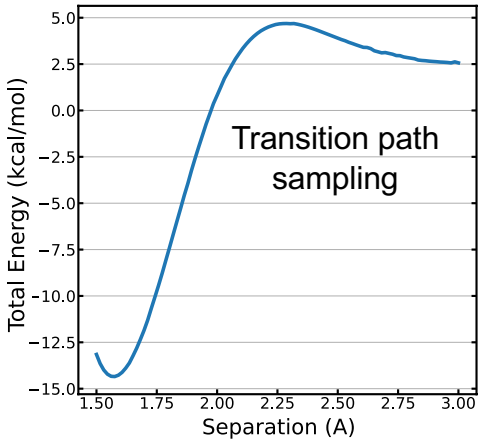




42-node icosphere used for rotations

Reaction barrier: 4.7 kcal/mol
TS bond length: 2.29 Å
Equilibrium bond length: 1.57 Å



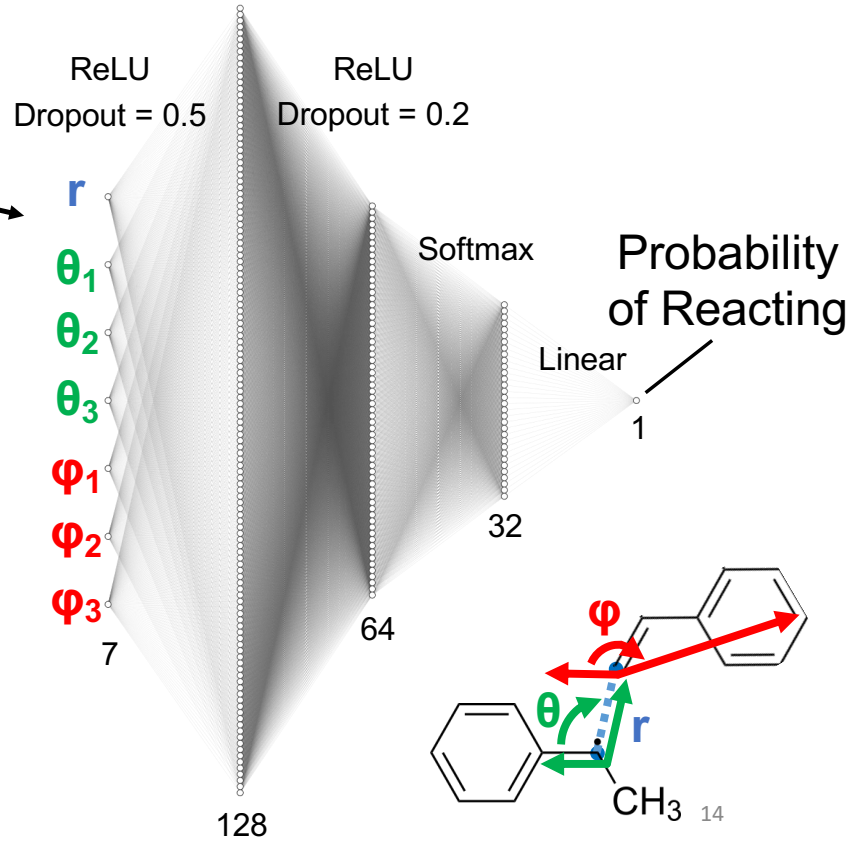


Khuong, K. S. et al. J. Am. Chem. Soc. 2005, 127, 1265-1277.

Step 2: Learning the Committor Function

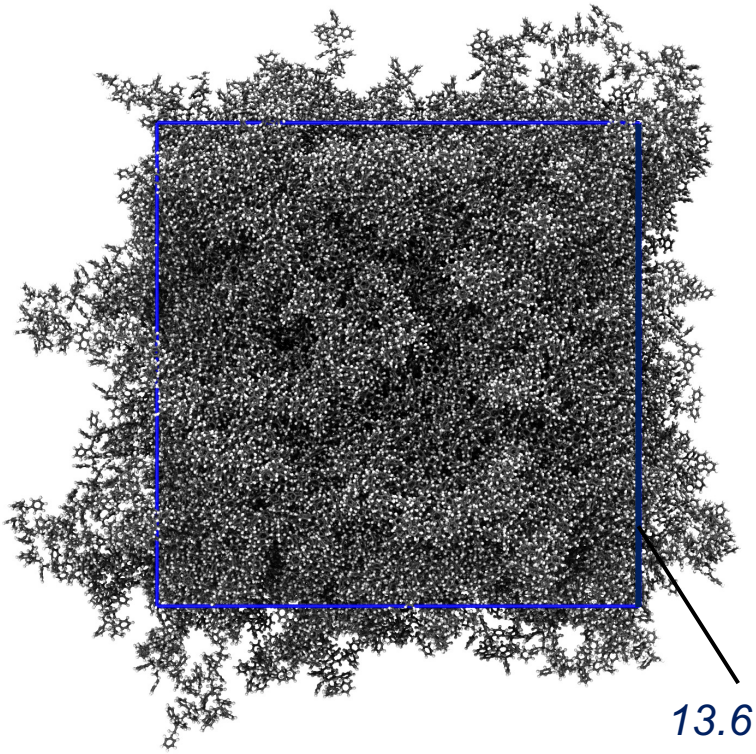
- Fully-connected deep neural net used to learn committor using reaction coordinates as input
- Three hidden layers (shown to right)
- Key optimizations of the model:
  - Using reduced reaction coordinates
  - Normalizing and centering input values
  - Continuous representation of rotations

    E.g., rather than Euler angles, use 2D coordinates on unit circle (adds one dimension)
- Mean Absolute Error of Predicted Reaction Probabilities: 0.087



Step 3: Using the Committor Function

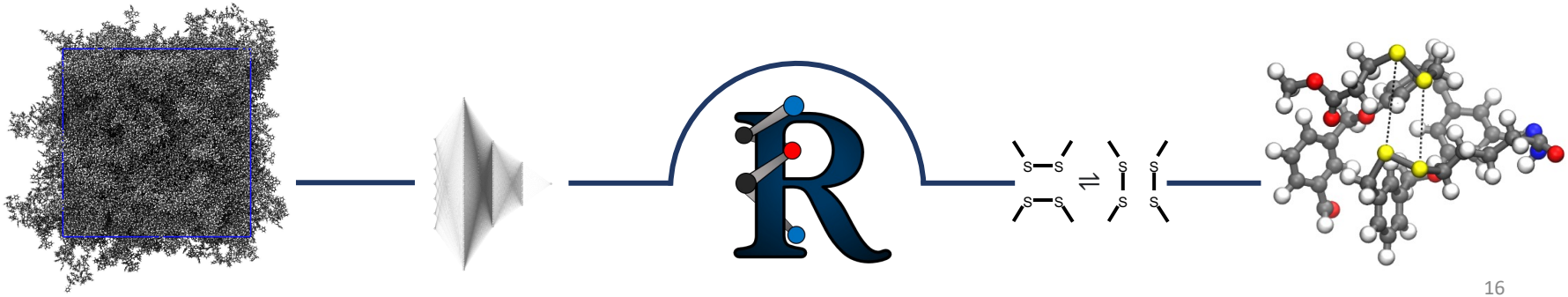
- Chain growth of polystyrene governed by Python-enabled reaction constraint
- Before every reaction attempt, reaction site coordinates exported to TensorFlow for evaluation of committor
- Soft Lennard-Jones potentials used to increase sampling of r < 2.5 Å
- Large-scale simulated polymerization completed (200K atoms)
- Simulated polymerization reaction rate agrees with previous distance-based reactive MD results



Extent of Reaction: 95%

A Framework for Modeling Organic Reactions at Scale

- REACTER is a versatile tool for reactive molecular dynamics simulations
  - Nonequilibrium reactive systems from battery interfaces to biomolecules
- A committor function was incorporated into classical molecular dynamics:
  1. Sampling the committor - DFTB and swarm of trajectories method
  2. Learning the committor - deep neural network using reduced reaction coordinates
  3. Using the committor - REACTER with Python-enabled reaction constraint
- Future work: Improve REACTER-ML interface; automatic typing of new interactions



Thank You!

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