Machine-Learned Committor Functions for Reactive Molecular Dynamics

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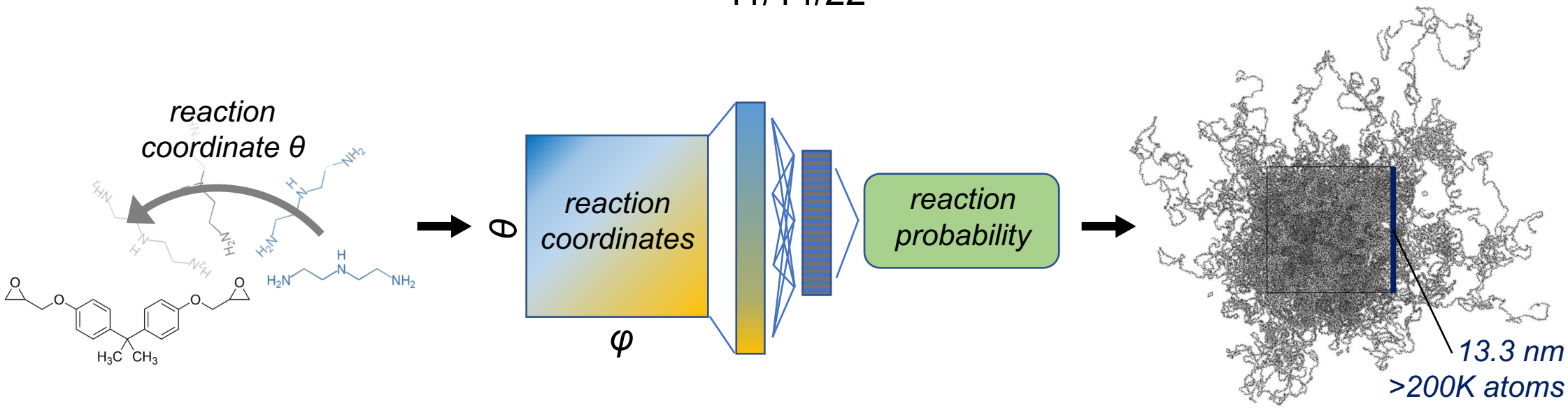
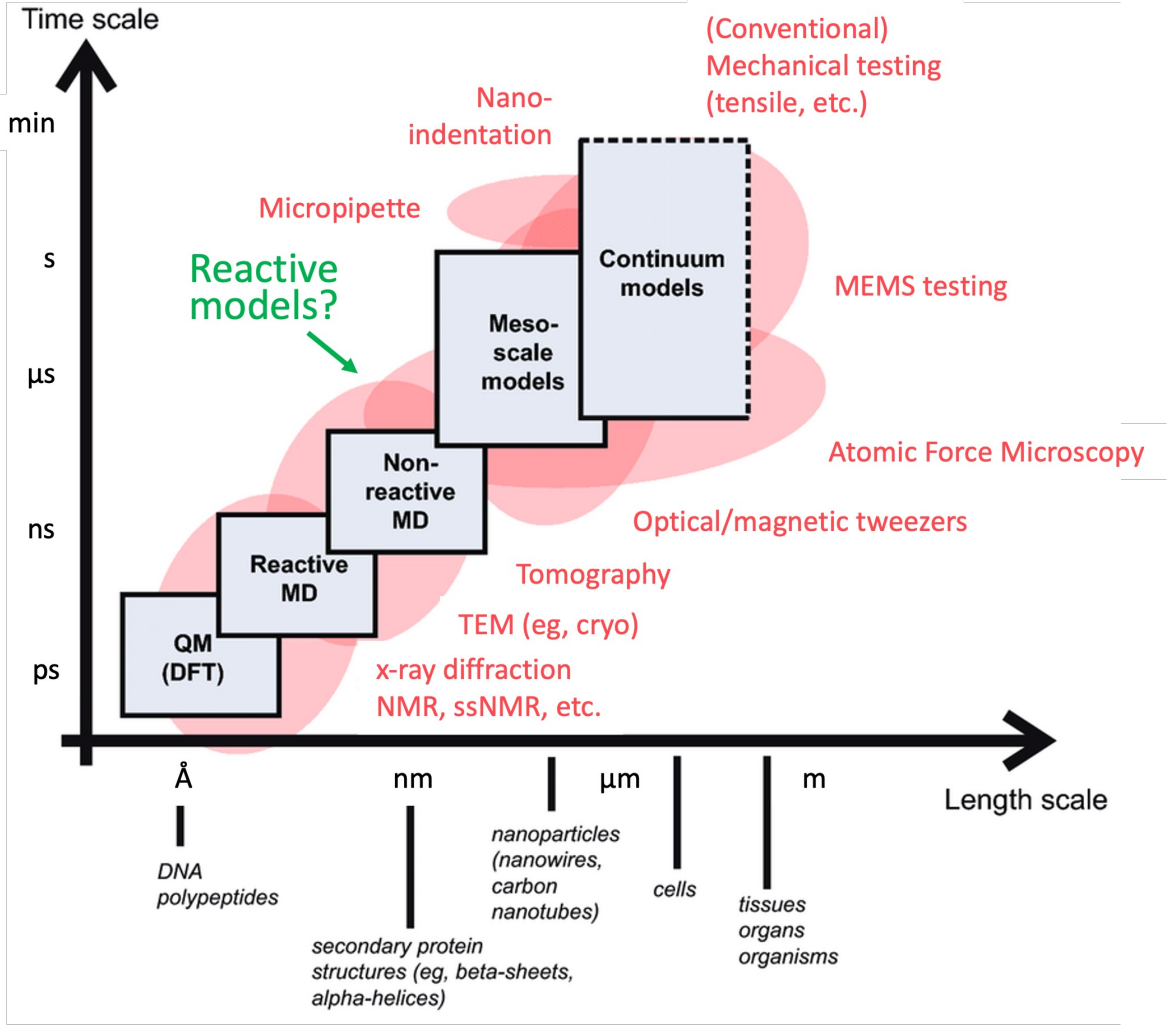


Modeling Organic Reactions at Scale is Hard

- Chemical reactions are quantum phenomena and depend on high-dimensional electron interactions
- Organic reactions often involve complex chemistry (radicals, resonance and other stabilization mechanisms, etc.)
- Solving for electron interactions is much slower than classical force fields, even with approximate methods like density-functional tight-binding (DFTB) method
- The objective of this work is to incorporate quantum-informed reaction probabilities into scalable molecular dynamics (MD)

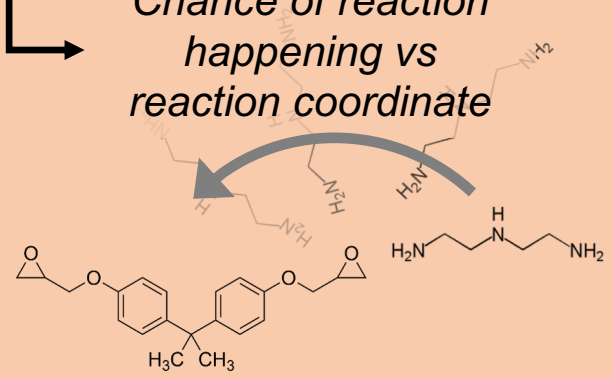


Jancar, J. et al. Polymer 2010, 51, 3321-3343.

Reactive MD Committors: Three-Step Approach

Step 1: Sample the Committor Function with Quantum Accuracy

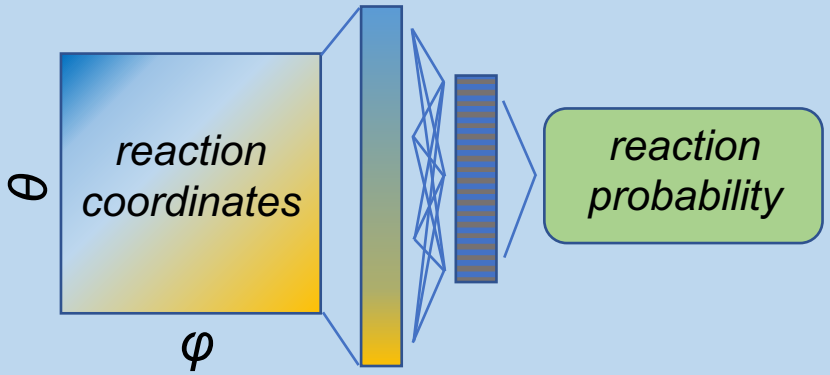
Chance of reaction happening vs reaction coordinate



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

dftbplus.org

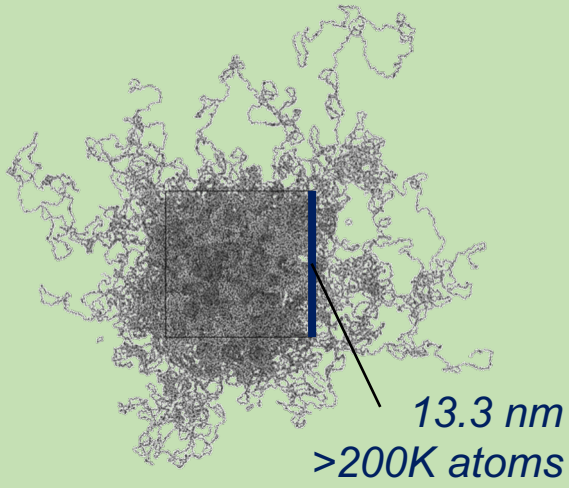
Step 2: Learn the Committor Function using a Deep Neural Net



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

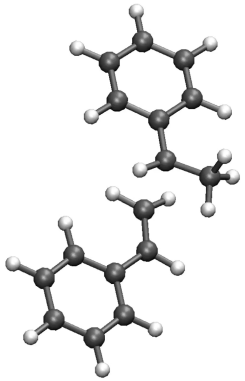


Python-enabled reaction constraints added to the REACTER protocol

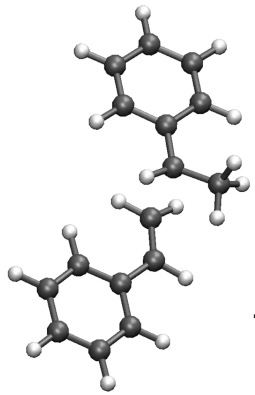
reacter.org

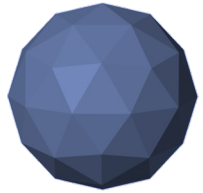
Step 1: Sampling the Committor Function

- 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 kcal/mol - 7.7 kcal/mol, Transition State (TS) bond length: 2.276 Å - 2.351 Å



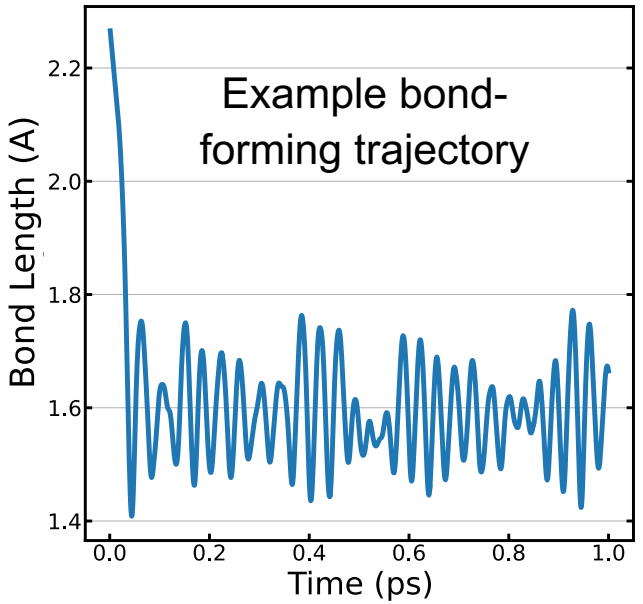
DFTB

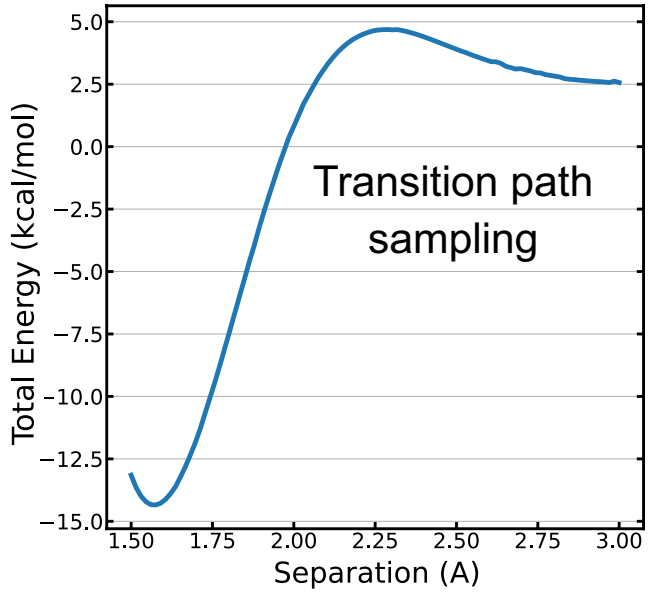




42-node icosphere used for rotations

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

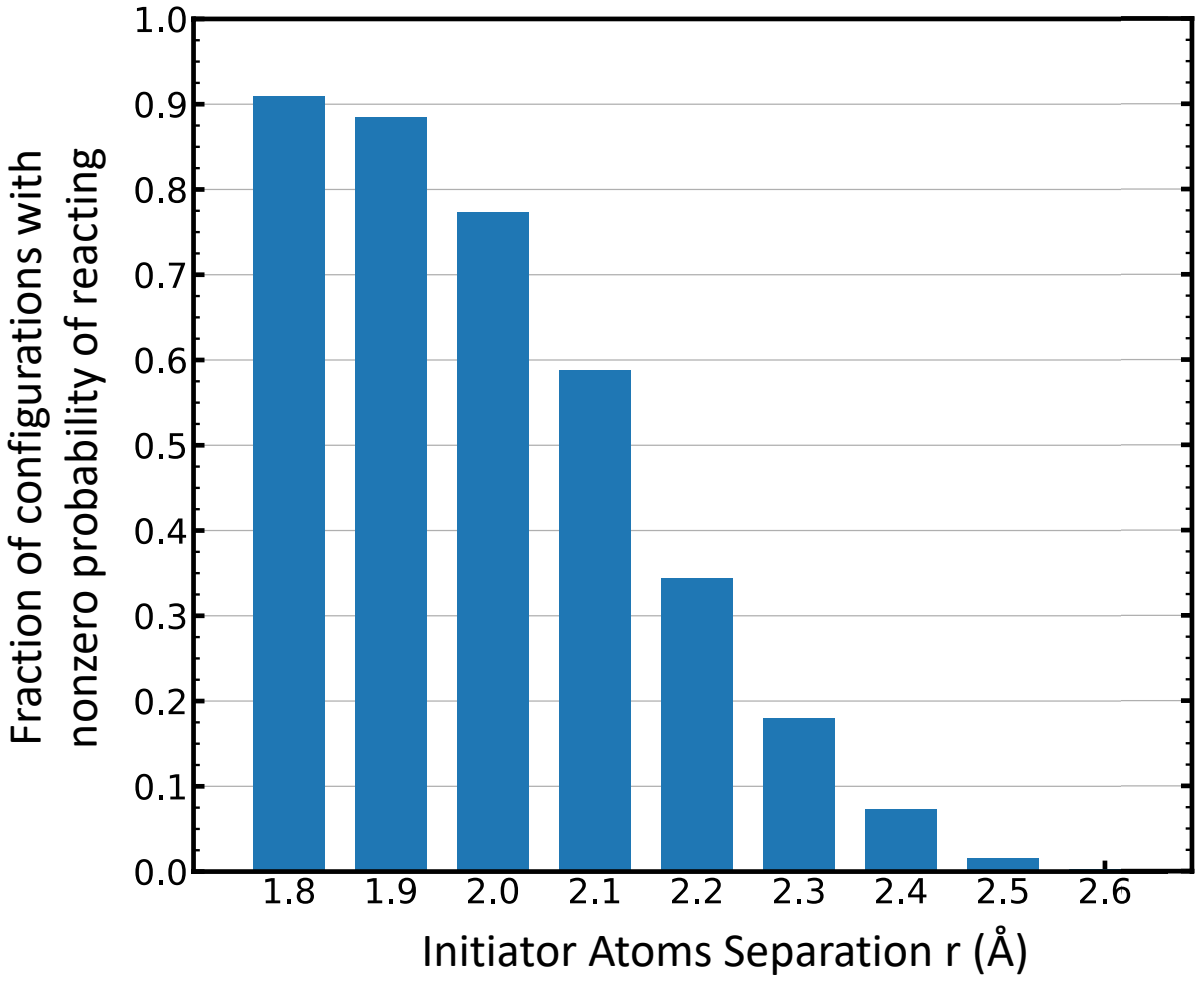




Khuong, K. S. et al. J. Am. Chem. Soc. 2005, 127, 1265-1277.

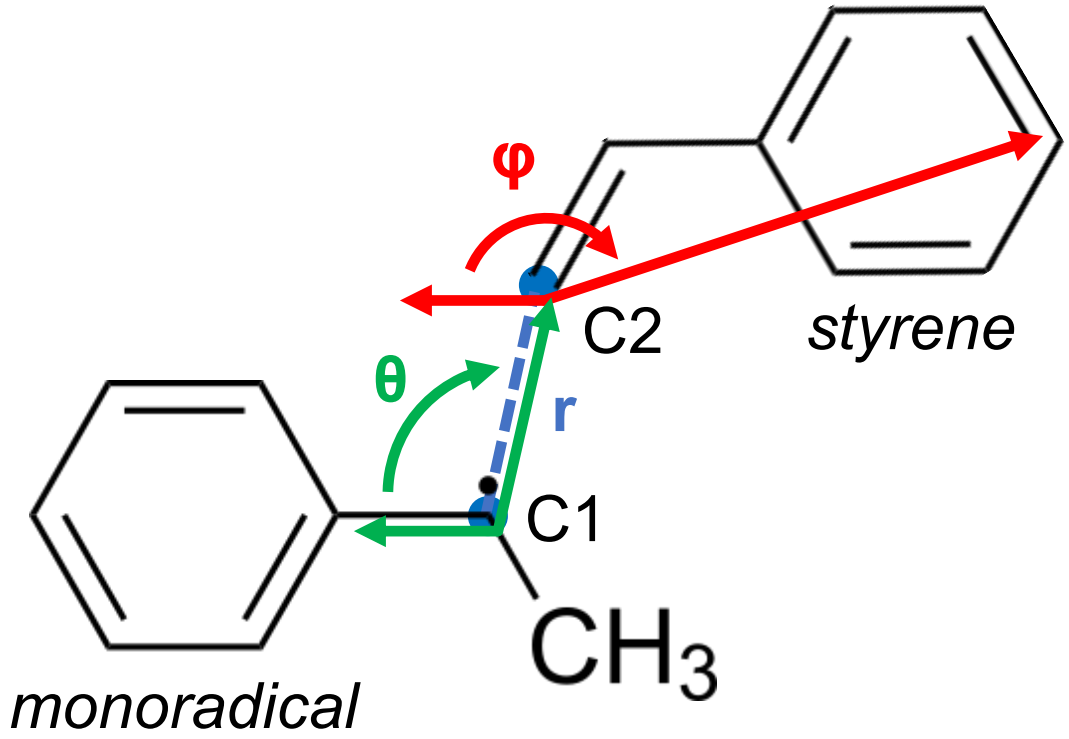
Analysis of DFTB Trajectories

- No bond-forming trajectories were found for initial bond separations r_i > 2.5 Å
- For r_i < 1.9 Å, ~75% of trajectories resulted in bond formation
- A refined data set was created for 1.75A < r_i < 2.5A at 0.05 Å increments
- 5236 configurations generated for r_i < 2.5 Å (> 250,000 MD runs)
- 80% of the 5236 configurations used for neural network training, 20% were saved for validation



Choice of Reaction Coordinates

- Reaction coordinates decrease the dimensionality of the problem
- Reaction Coordinates:
  - Three-dimensional (3D) position of less-substituted alkene carbon (C2) with respect to free radical carbon (C1)
  - 3D rotation of styrene molecule with respect to C2
- Five degrees of freedom in 3D
- These reaction coordinates were used for feature engineering during training of the neural net

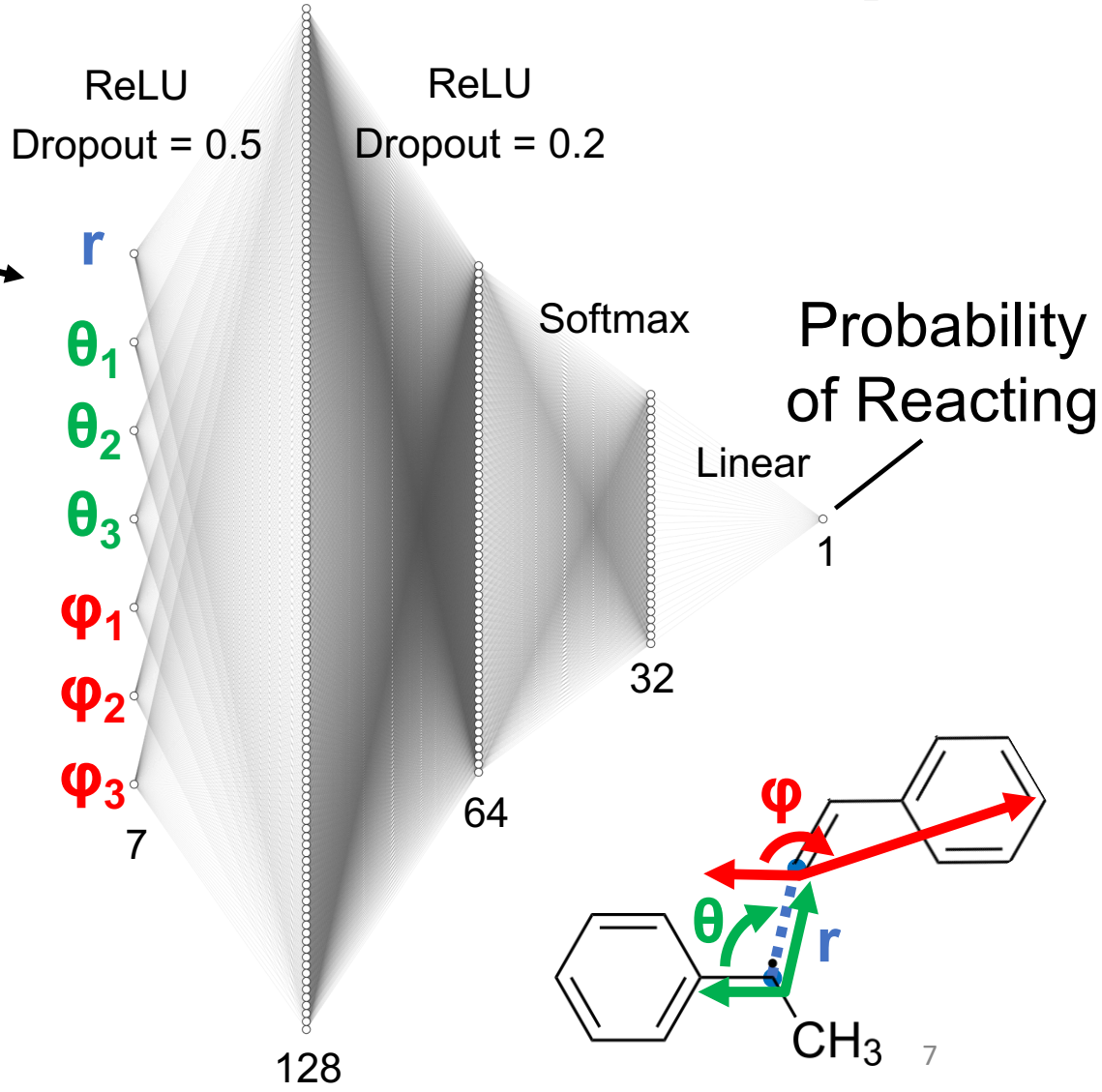


Two-dimensional projection of reaction coordinates

Step 2: Learning the Committor Function

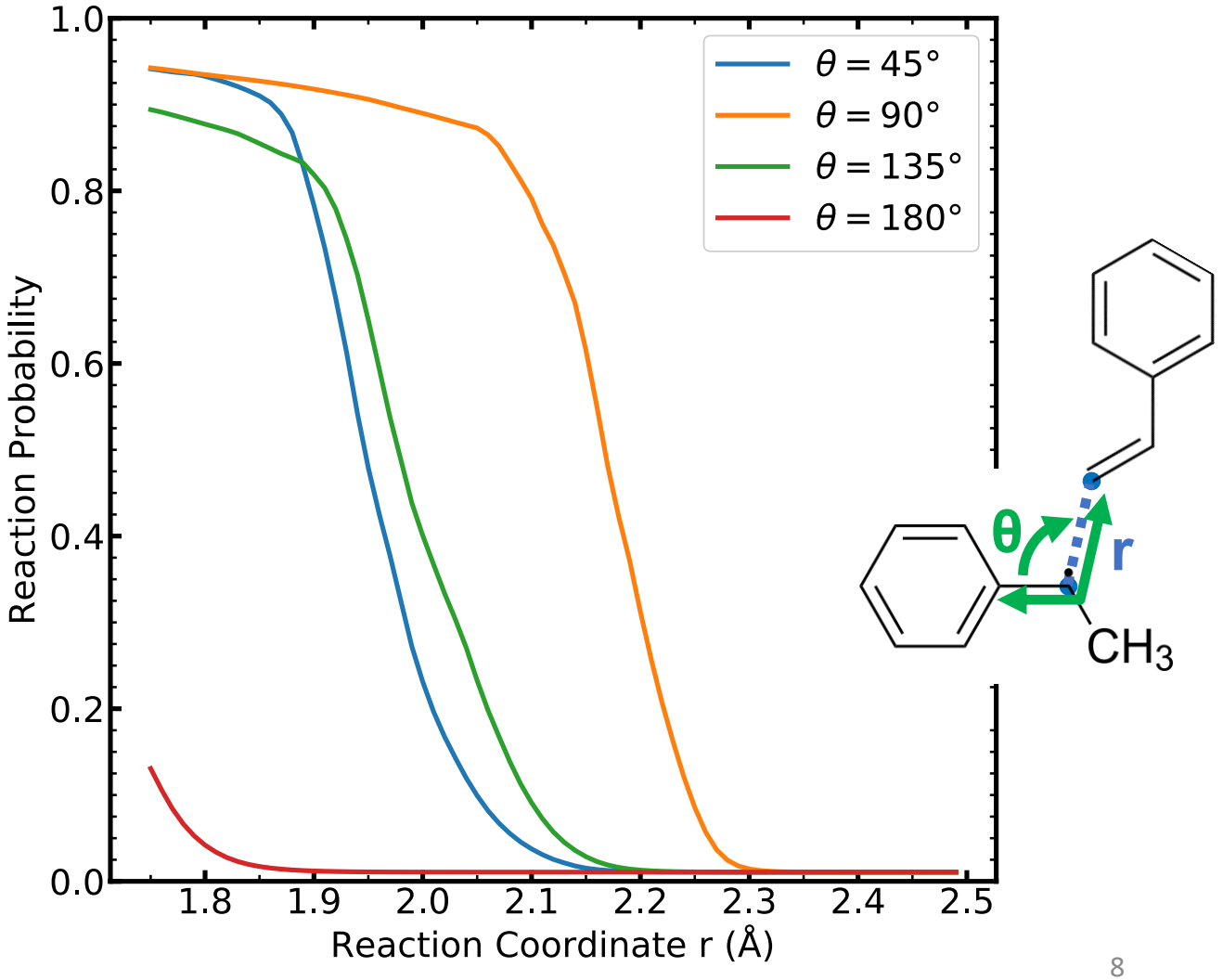
- Fully-connected deep neural net used to learn committor using reaction coordinates as input
- Three hidden layers (shown to right)
- Key optimizations of the model:
  - Using reduced reaction coordinates
  - Normalizing and centering input values
  - Continuous representation of rotations

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

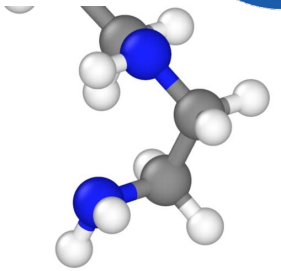


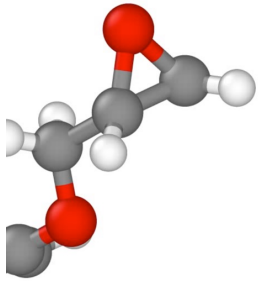
Analysis of the Learned Committor Function

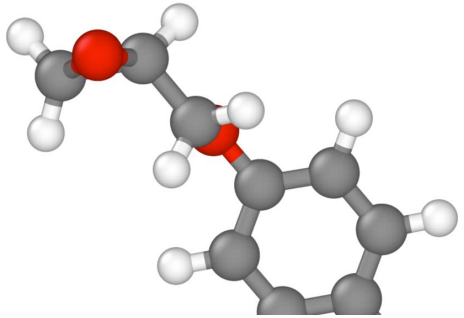
- Neural net enables real-time sampling of the styrene-monoradical committor surface
- Example in-plane results shown at right, demonstrating effect of bonding-atoms separation and angle $\boldsymbol{\theta}$
- For example, configurations are clearly disfavored when $\boldsymbol{\theta}$ = 180, an effect that would be ignored by simpler distance-based methods



REACTER: A Heuristic Method for Reactive MD







- A protocol for adjusting bond topology during classical MD
  - Add/remove specific bonds, angles, dihedrals, and impropers
  - Modify all force field types as well as atomic charges
  - Supports any fixed-valence force field
  - Enables complex mechanisms with stabilization
  - Reaction constraints, *now with Python support!*

- 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

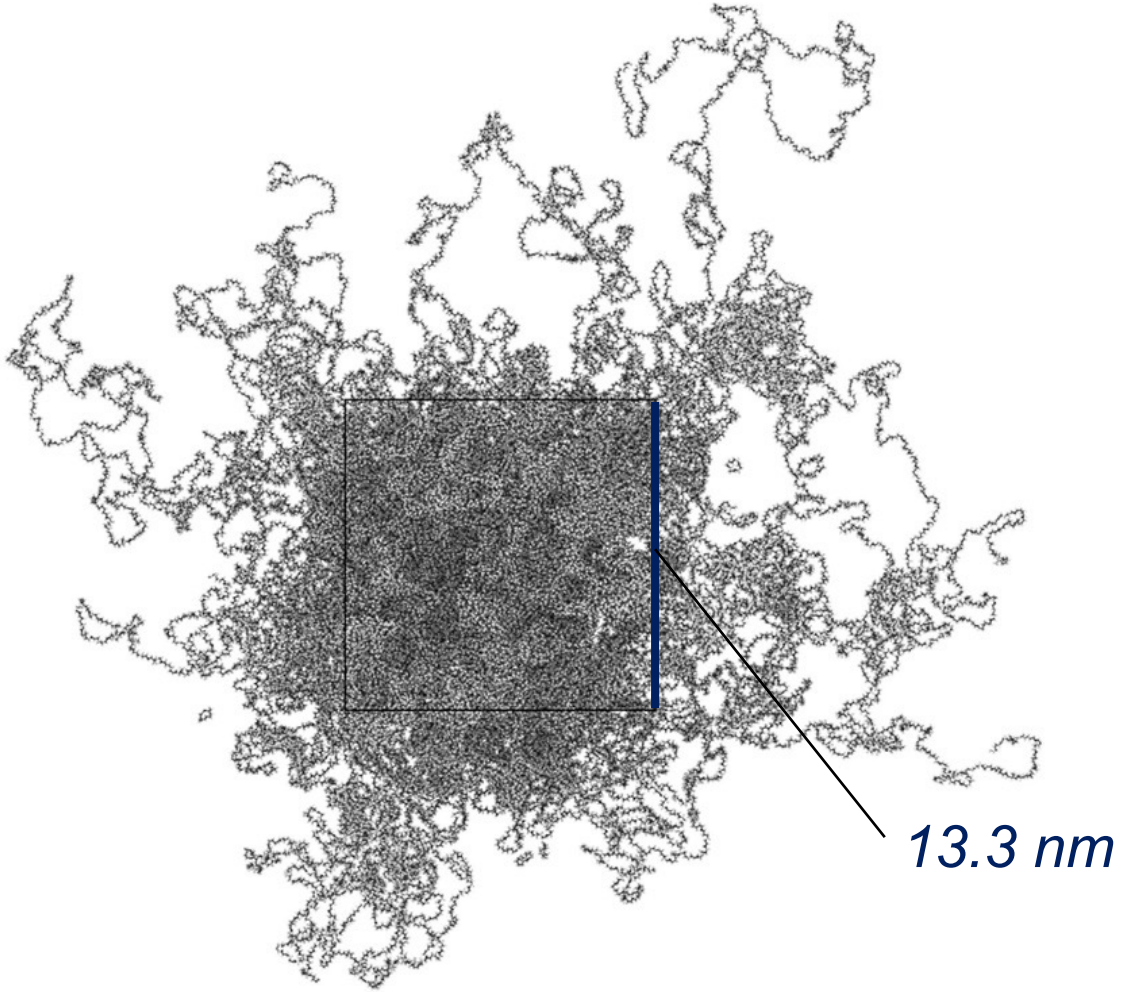
For more details:
Gissinger, J. R., et al. “REACTER: A Heuristic Method for Reactive Molecular Dynamics.” Macromolecules 2020, 53, 9953-9961

www.reacter.org

* LAMMPS is the Large-scale Atomic/Molecular Massively Parallel Simulator program

Step 3: Using the Committor Function

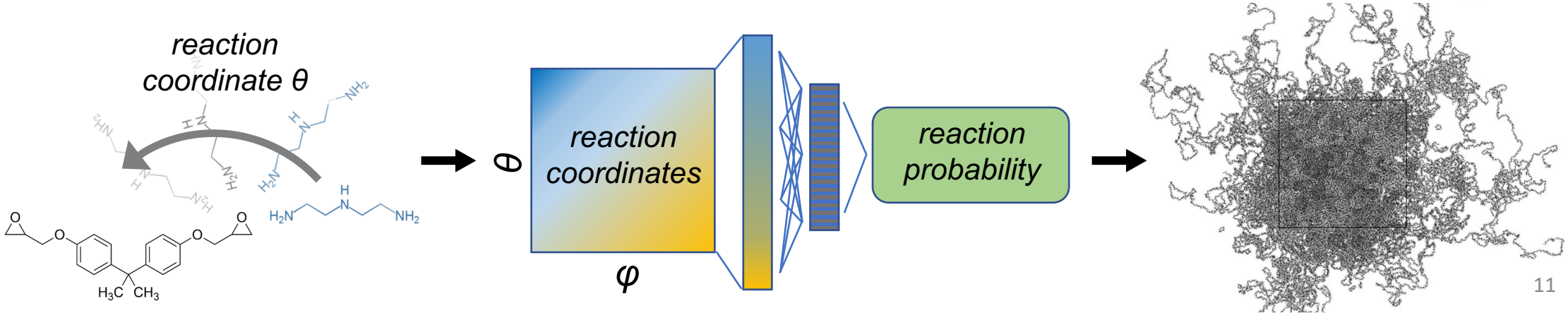
- Chain growth of polystyrene governed by Python-enabled reaction constraint
- Before every reaction attempt, reaction site coordinates exported to TensorFlow for evaluation of committor
- Soft Lennard-Jones potentials used to increase sampling of r < 2.5 Å
- Large-scale simulated polymerization completed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



Extent of Reaction: 68%

A Workflow for Modeling Organic Reactions at Scale

- 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
- Workflow used to model large-scale radical polymerization of polystyrene (>200K atoms)
- Future work: Improve DFTB sampling (e.g., metadynamics) and generalizability of the model
- Outlook: The technique is applicable to many types of reactions (catalysis, etc.)



Thank You!

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