KIMMDY 2.0
A Monte Carlo Reactive Molecular Dynamics Framework

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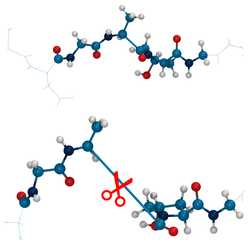
Abstract

Forcefield based molecular dynamics simulations allowed us to reach biologically relevant timescales and system sizes. A fundamental limit of this molecular mechanics approach is a lack of reactivity. We present a framework for combining classical molecular dynamics simulations with a kinetic Monte Carlo approach to bridge timescales and allow reactions to occur within a simulation. This is a generalization of our previous approach specifically targeted at bond breakages (1). It is implemented as a user-friendly, extensible python module based on the open-source high-performance molecular dynamics software suit GROMACS (2).

Problem

Chemical **reactions** occur on **many timescales**. And while those happening within femtoseconds can feasibly be simulated by quantum mechanical calculations, those that reach up to micro-, milli- or even full seconds can not. Forcefield-based molecular mechanics gets us into the microsecond timescale, but can not execute reactions. Even if it could, some reactions would still be inaccessible to our sampling due to their low rate.

KIMMDY **skips ahead** in time by querying possible reactions about their rates and choosing a reaction based on (rejection free) **kinetic Monte Carlo**. It then adjusts the topology of the system according to the reaction results and continues the MD simulation.



Implementation

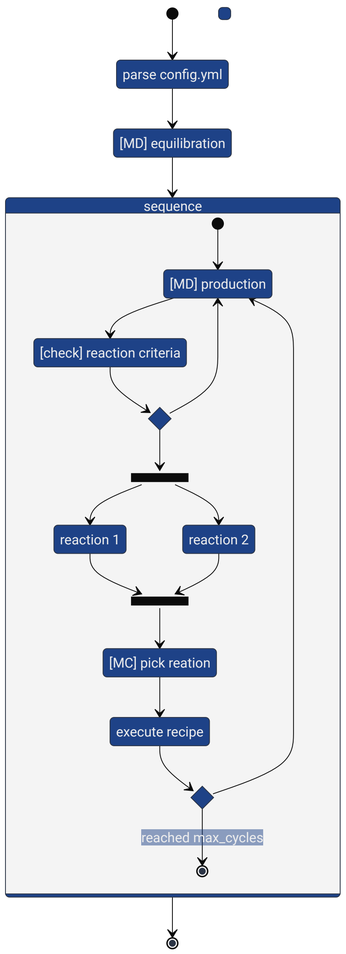


Figure 1: State diagram of KIMMDY 2.0

```python
class ConversionType(Enum):
    BREAK = auto()
    MOVE = auto()
    CONNECT = auto()


@dataclass
class ConversionRecipe:
    type: list[ConversionType]
    atom_idx: list[tuple[int, int]]


@dataclass
class ReactionResult:
    recipes: list[ConversionRecipe]
    rates: list[float]
```

Figure 2: A simplified version of the standardized output for reactions.

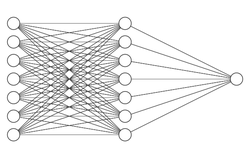
KIMMDY is designed to be **extensible** with new reactions via a simple python plugin architecture. All a new reaction needs is a way of returning rates for possible reactions and the corresponding changes that need to be performed on the topology on acceptance.

For example, the bond rupture reaction (**homolysis**) estimates transition state energies with a bond stretching potential and then uses the Arrhenius equation Equation 1 to return rates.

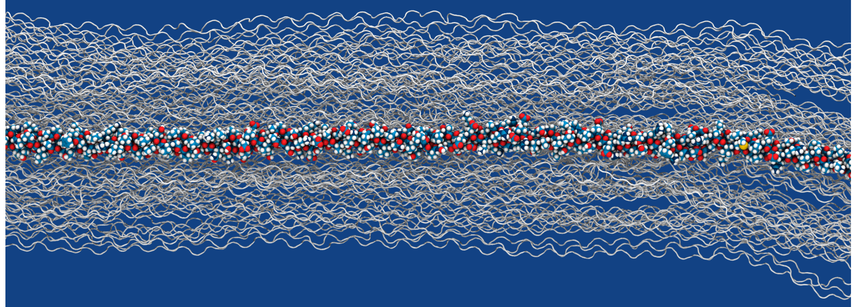
$$k = Ae^{\frac{-\Delta E^{\ddagger}}{RT}} \tag{1}$$

(3)

Other reactions require more sophistication. Once a bond is ruptured, the remaining radicals can "jump" via **Hydrogen Atom Transfer** (HAT), for which you want to head over to the poster of Kai Riedmiller to see our **Machine Learning** solution for rate prediction.



Bridging Timescales in Reactive Molecular Dynamics



Follow the QR code or visit
https://github.com/hits-mbm-dev/kimmdy-poster
for the repository of this poster.
Or even better yet, talk to me in front of the poster!

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Heidelberg Biosciences International Graduate School

HITS
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```
# kimmdy.yml
dryrun: false
out: 'out-dir
ff: 'amber99sb-star-ildnp.ff'
top: 'topol.top'
gro: 'npt.gro'
idx: 'backbone.ndx'
plumed:
  dat: 'plumed.dat'
  distances: 'distances.dat'
equilibration:
  mdp: 'eq.mdp'
production:
  mdp: 'pull-f1500.mdp'
reactions:
  homolysis:
    edis: 'edissoc.dat'
    bonds: 'ffbonded.itp'
  dummyreaction: default
  hat:
    model: default
sequence:
  - equilibration
  - mult: 2
    tasks:
      - production
      - reactions
```

Figure 3: A kimmdy.yml input file.

Usage

- specify the files necessary for your simulation
- include special requirements for further reactions
- specify a sequence of steps
- run KIMMDY

Current Challenges

- tune a generalized `topology changer`
  - that also handles large systems
  - works with additional forcefield parameters and atom types
- include further reactions
  - Hydrogen Atom Transfer (HAT)
  - Hydrolysis

Validation

The first version of KIMMDY (1) is used to predict bond ruptures in collagen (the most abundant protein in connective tissue). Those are validated in experiments using **Electron Paramagnetic Resonance** (EPR), which detects the radicals produced by homolytic bond ruptures. Other reactions are harder to measure *in vitro*.

Further results will be validated with **QMMM simulations** using GROMACS(2) and CP2K(4). Together they can act as a molecular magnifying glass. Once KIMMDY has identified a region of interest and potential reactions, we can further investigate this site as a QM region within the context of a MM simulation.

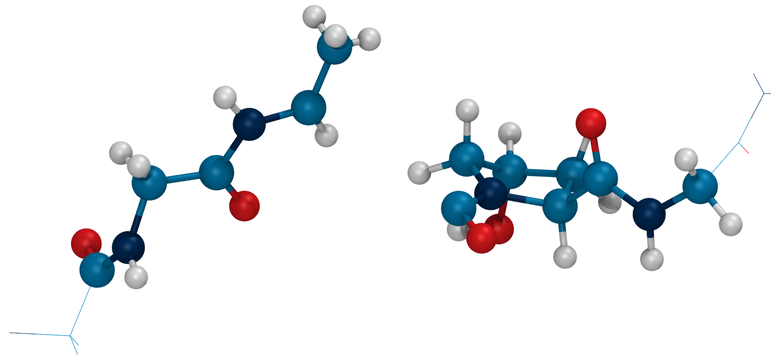

Figure 4: Snapshot from a QMMM simulation. QM atoms are shown as spheres, MM atoms and bonds shown as faint lines

Availability

KIMMDY 2.0 is not ready just yet, but expect to find the actively developed version here **soon**:
https://github.com/hits-mbm-dev/kimmdy.

Acknowledgments

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FAST. FLEXIBLE. FREE. GROMACS

CP2K

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