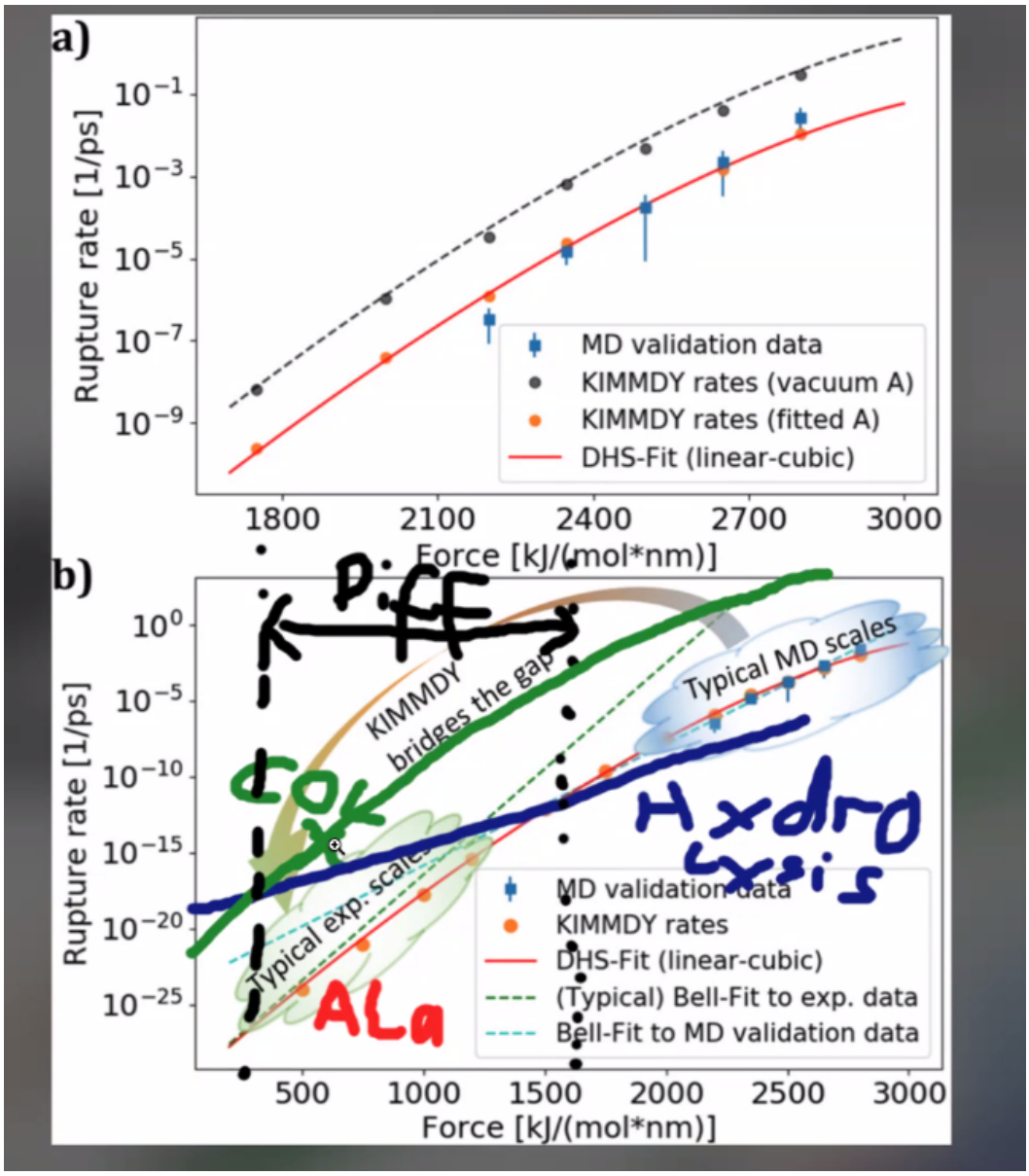
Using KIMMDY to simulate competing reactions in peptides

todo

- ☐ kimmdy xtc vs. trr: [ ] - parse mdp file [ ] - also pass delta t of both to the plugin [ ] - is the correct timeframe reported? [ ] - is the correct frame exported? [ ] - is it used?
- ☐ old ala system of benedict hyd vs. hom, validate hom rates with old implementation



–

☐ fix temperatures for hyd vs. hom

☐ hydrolysis vs. homolysis on collagen fibril, 1nN

☐ method, results etc.

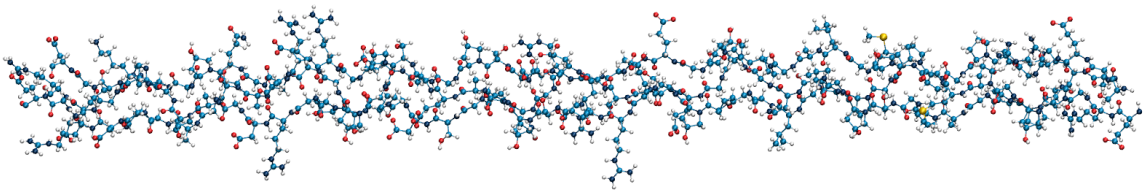
☐ nat com 23 benedict fibrille datapoints

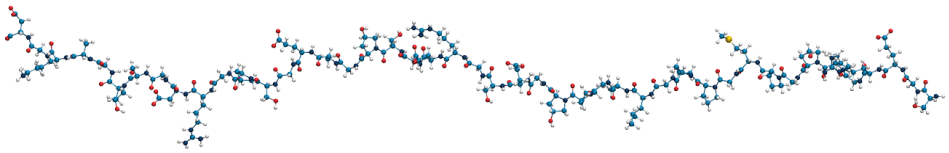
- kimmdy.utils WARNING: Did not find dissociation energy for atomtypes [‘N’, ‘CA’], residue general in ed issoc file, using standard value of 400.0 kimmdy.utils WARNING:

Did not find dissociation energy for atomtypes [‘CA’, ‘C’], residue general in ed issoc file, using standard value of 400.0 kimmdy.utils WARNING: Did not find dissociation energy for atomtypes [‘C’, ‘N’], residue general in edi ssoc file, using standard value of 400.0 kimmdy.utils WARNING: Did not find dissociation energy for atomtypes [‘N’, ‘CA’], residue GLY in edisso c file, using standard value of 400.0 kimmdy.utils WARNING: Did not find dissociation energy for atomtypes [‘CA’, ‘C’], residue GLY in edisso c file, using standard value of 400.0

Notes

- Hydrolysis vs. Homolysis
- Show multiple reactions
- Show topology modifications with simple graph example
- Show analysis of rates from different reactions
- System: Collagen triplehelix
  - equilibrated under different forces
  - show how the force affects the reaction rates
- Used PLUMED to write out
  - distances for `homolysis`
- SASA can be used as a proxy for the reaction rate, integrated per peptide bond over each MD window
  - relatable metric
  - discussion will mention shortcomings of SASA as a proxy for reaction rate (see Pill et al. (2019) and upcoming QM/MM work?), but this also nicely shows that KIMMDY itself is agnostic to where the reactions rates come from, so it can be continuously improved by having better data
  - k = k0 * A * e(delta X / kT) => take force dependence from pill et al paper!





Text

https://www.overleaf.com/project/67cae795c7c387cfc3fb1b21

TODO:

- Introduce collagen and homolysis (new suggestion by Eric)
- hydrolysis vs homolysis rate dependence plot
- distribution of reactions along z-axis to show sasa effect?
- comparison to experiment? h2o2?
- Test reference Pill et al. (2019) Rennekamp et al. (2020)

KIMMDY can execute arbitrary reactions with complex topology modifications

KIMMDY can combine multiple types of reactions in a single simulation

Results

Pill, Michael F., Allan L. L. East, Dominik Marx, Martin K. Beyer, and Hauke Clausen-Schaumann. 2019. "Mechanical Activation Drastically Accelerates Amide Bond Hydrolysis, Matching Enzyme Activity." https://doi.org/10.1002/anie.201902752.

Rennekamp, Benedikt, Fabian Kutzki, Agnieszka Obarska-Kosinska, Christopher Zapp, and Frauke Gräter. 2020. "Hybrid Kinetic Monte Carlo/Molecular Dynamics Simulations of Bond Scissions in Proteins." https://doi.org/10.1021/acs.jctc.9b00786.