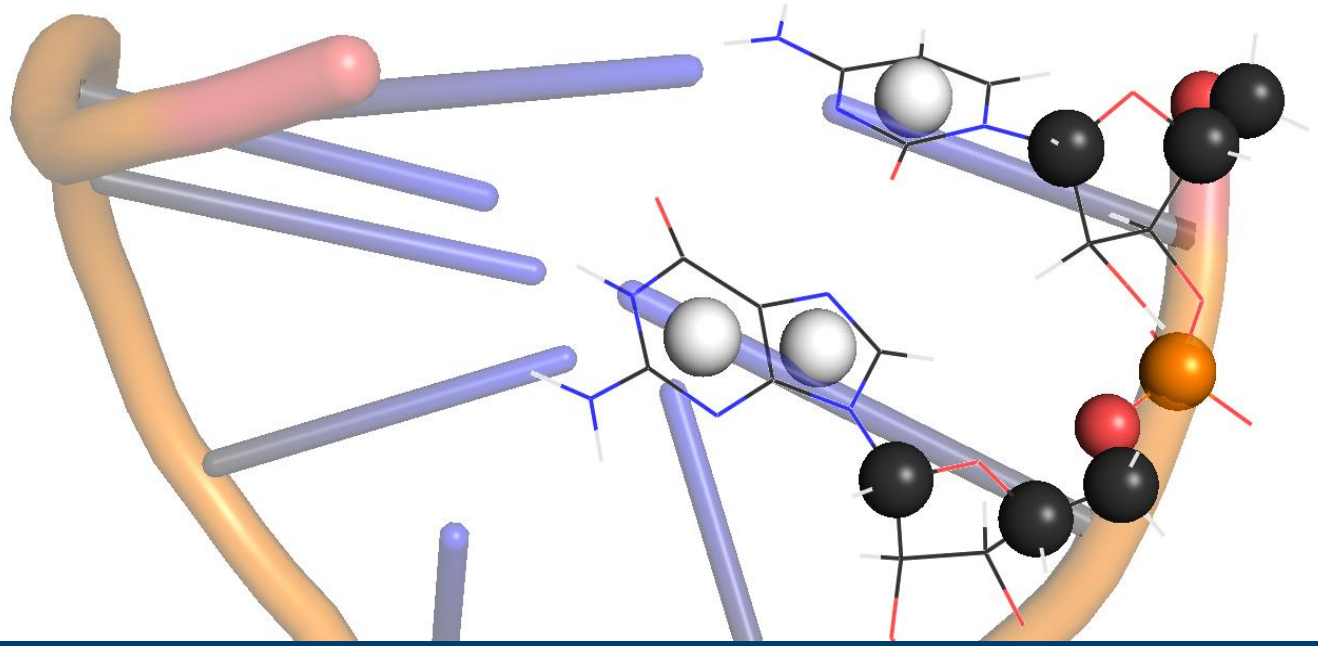


MADRNA:
COARSE GRAINING RNA FORCE FIELDS VIA ML

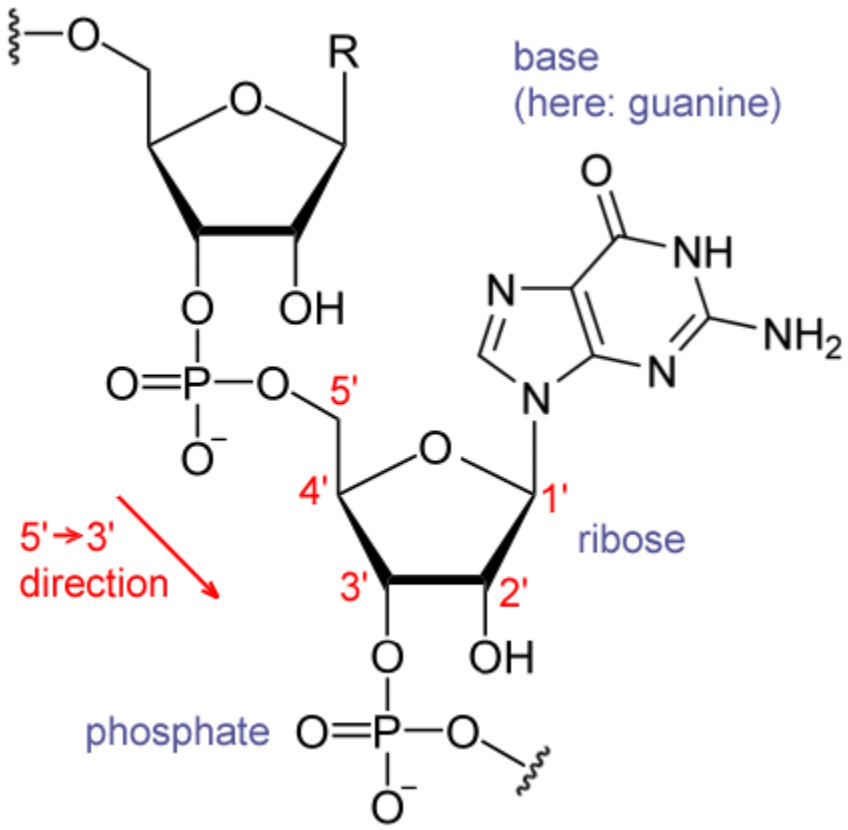
15.07.25 I ANTON DORN

UNIVERSITÄT GÖTTINGEN

JÜLICH Forschungszentrum

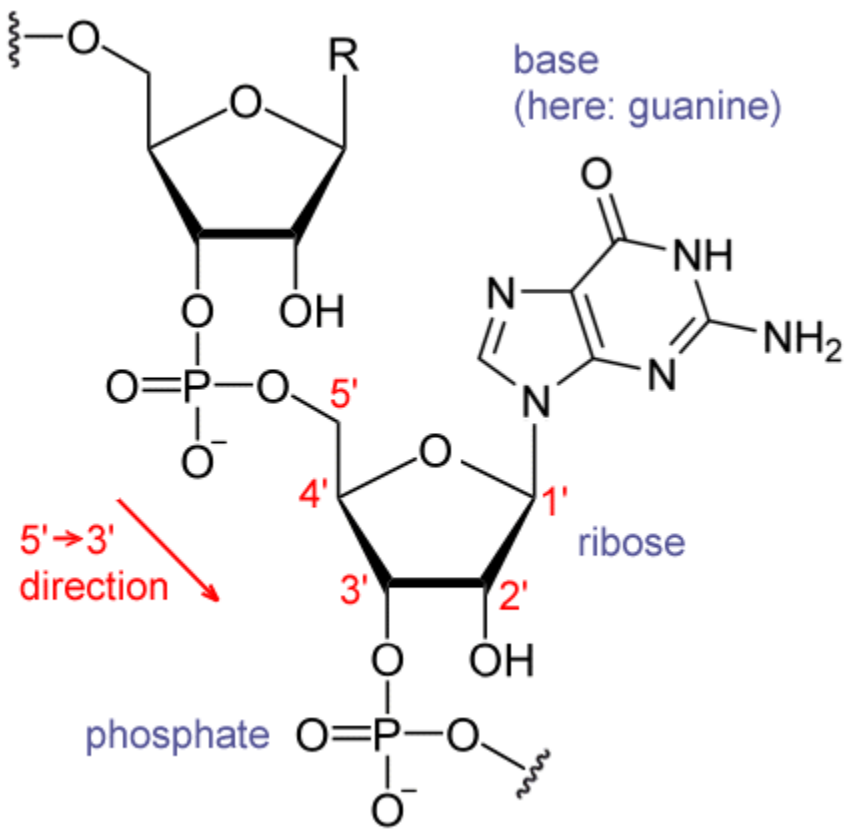
WHAT IS RNA?

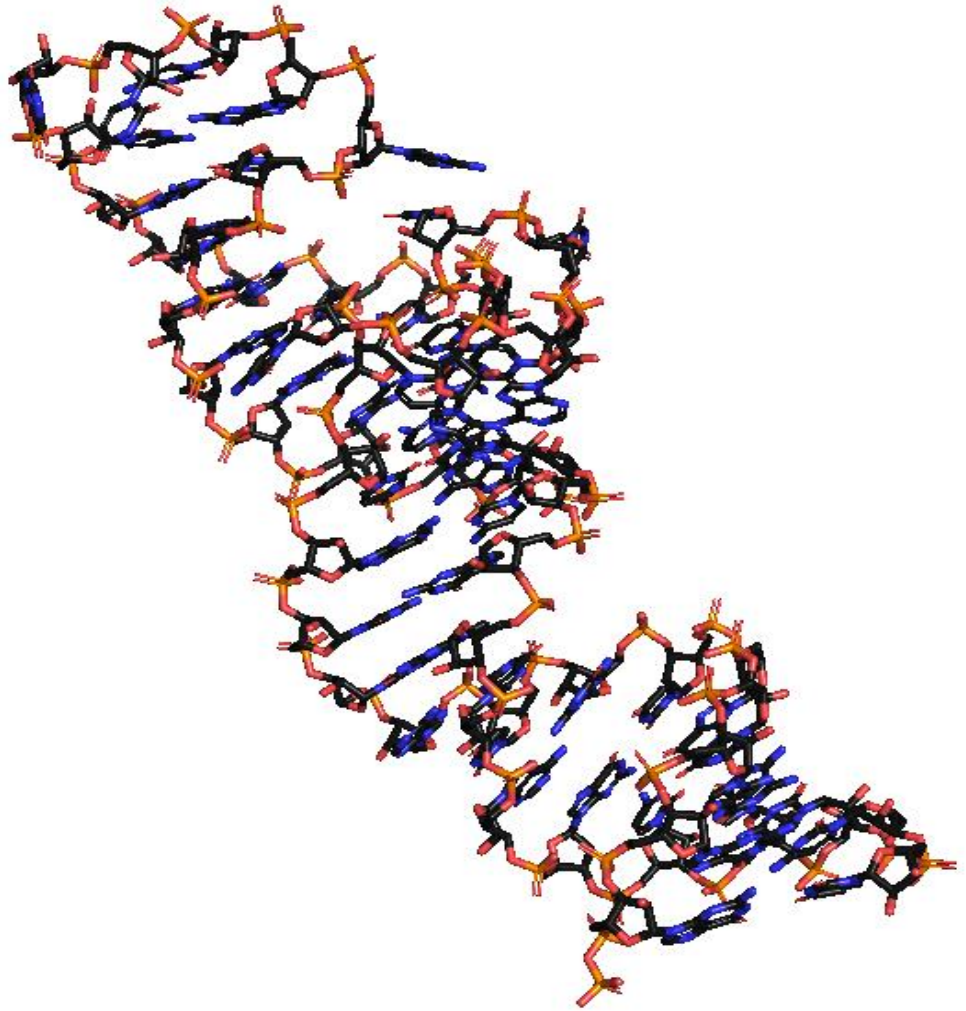
Ribonucleic Acid



WHAT IS RNA?

Ribonucleic Acid

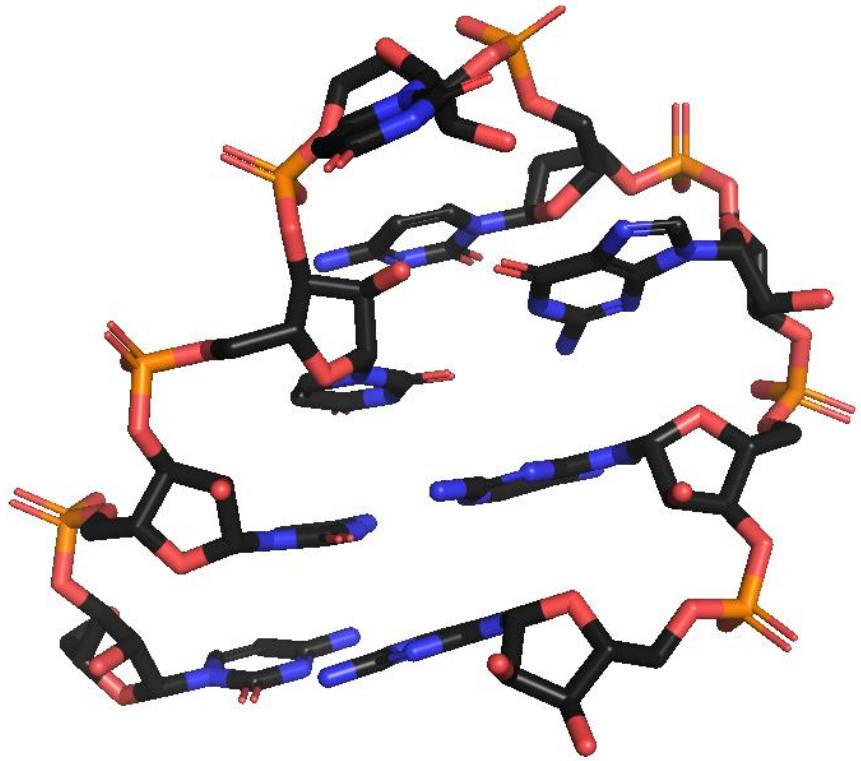




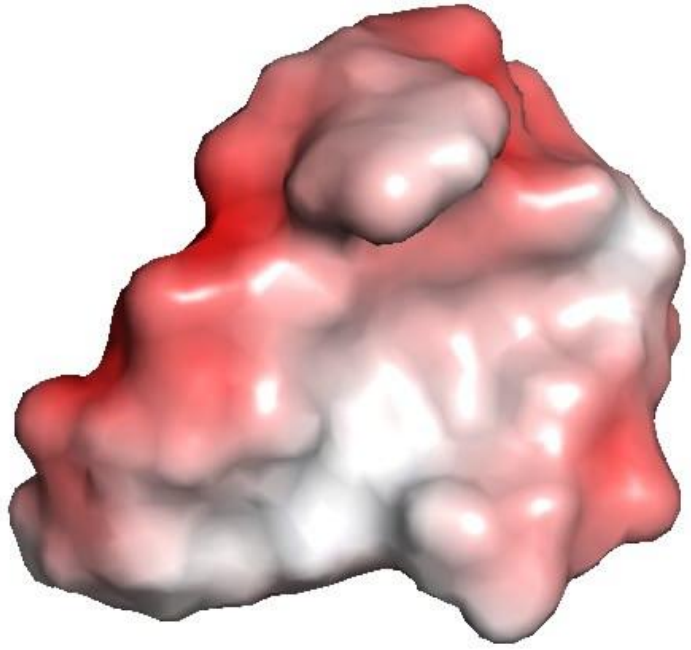
[8XZK]

SIMULATION CHALLENGES

Base Stacking, (Non-) Canoncial Basepairing, Backbone

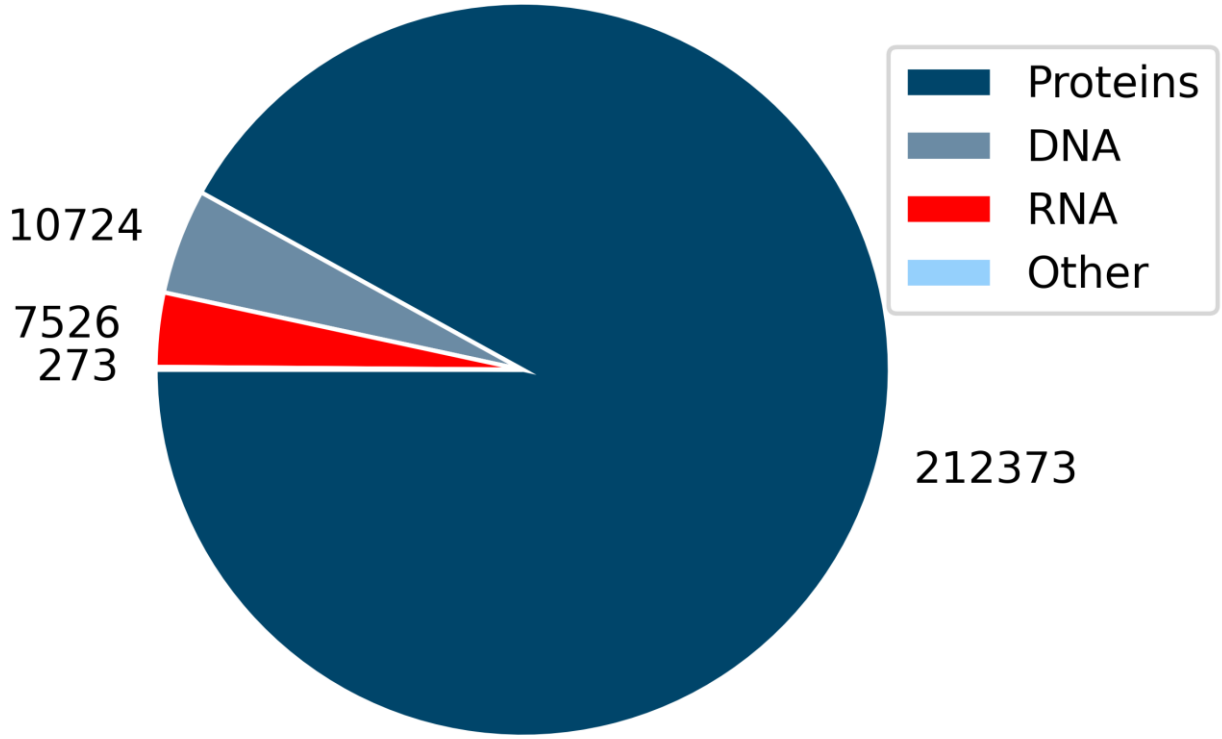


[1F7Y Tetraloop]



DATA SPARSITY

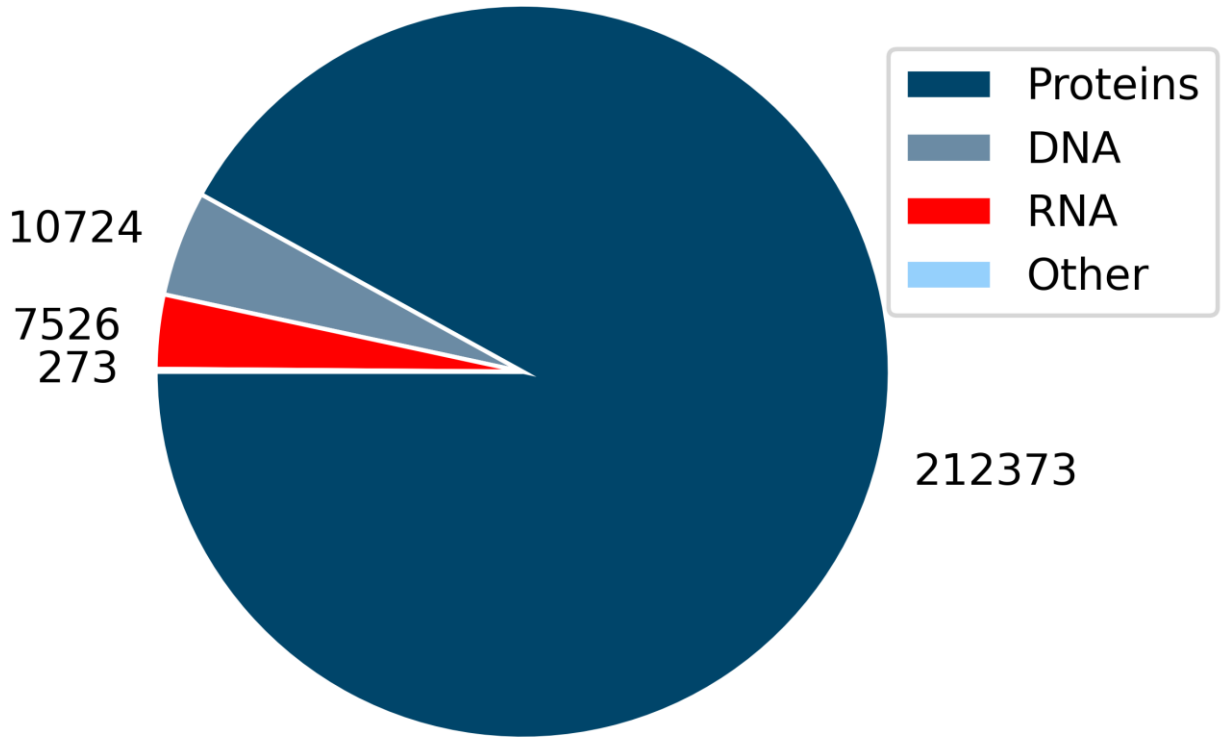
Of Experimental Structural Data



PDB-Database, 2023

DATA SPARSITY

Of Experimental Structural Data



PDB-Database, 2023

E.g. Pucci et al, 2020:

> 40 Nucleotides

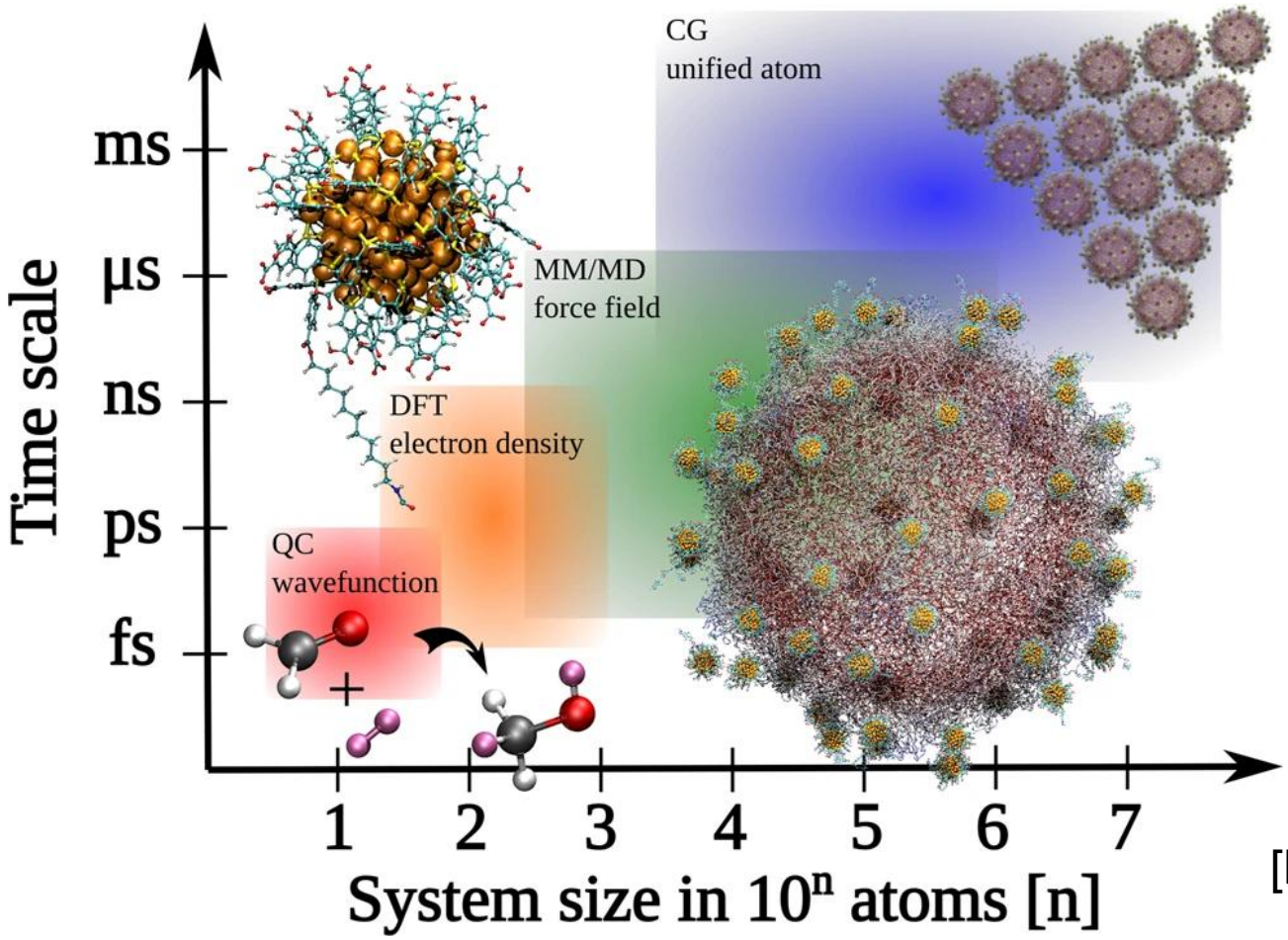
< 50% Sequence Identity

< 3.6 Å X-ray resolution

→ 69 Structures

SIMULATION OF MOLECULES

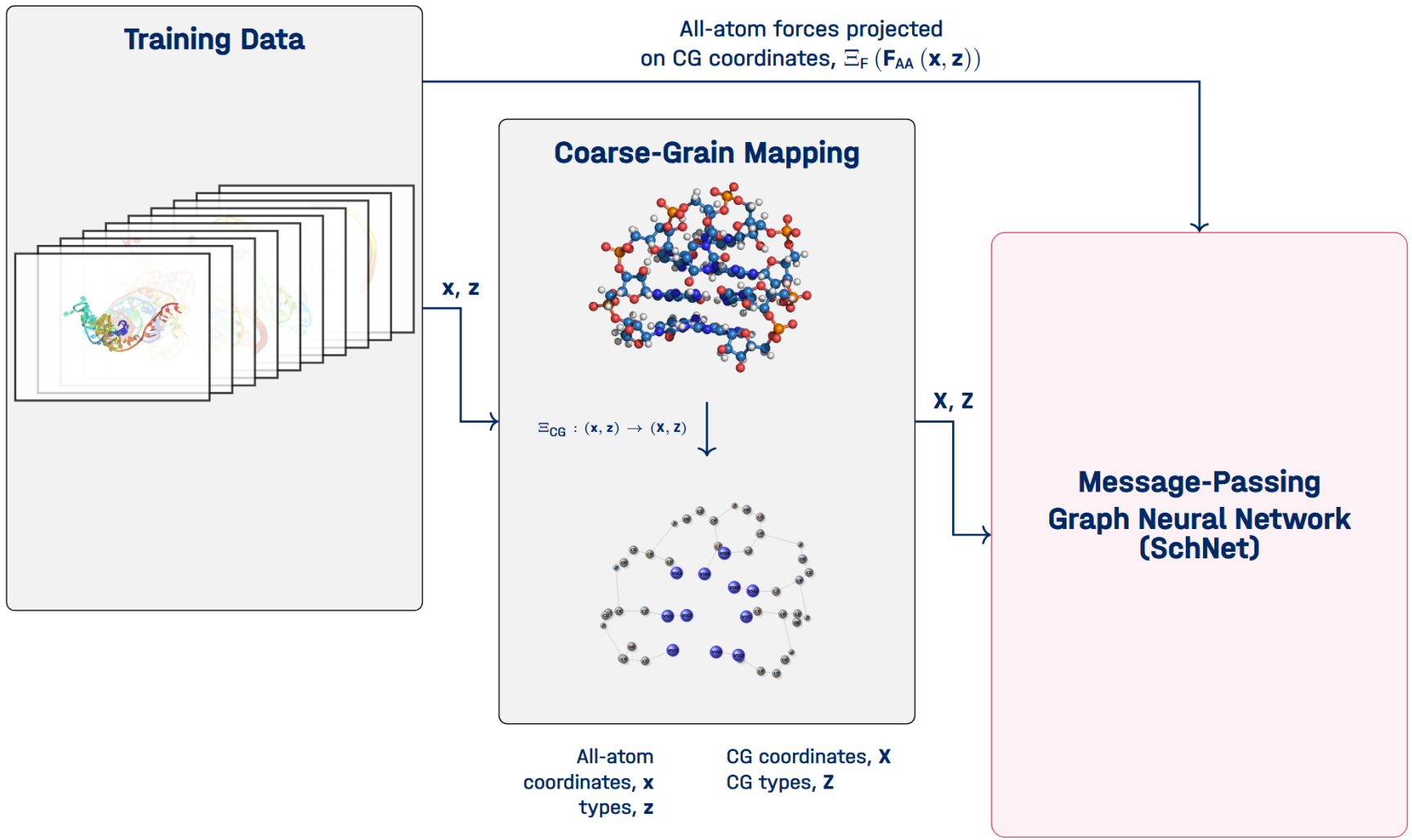
From Small and Accurate to Large and Fast



[Malola, Häkkinen, 2021]

ARCHITECTURE

Inputs

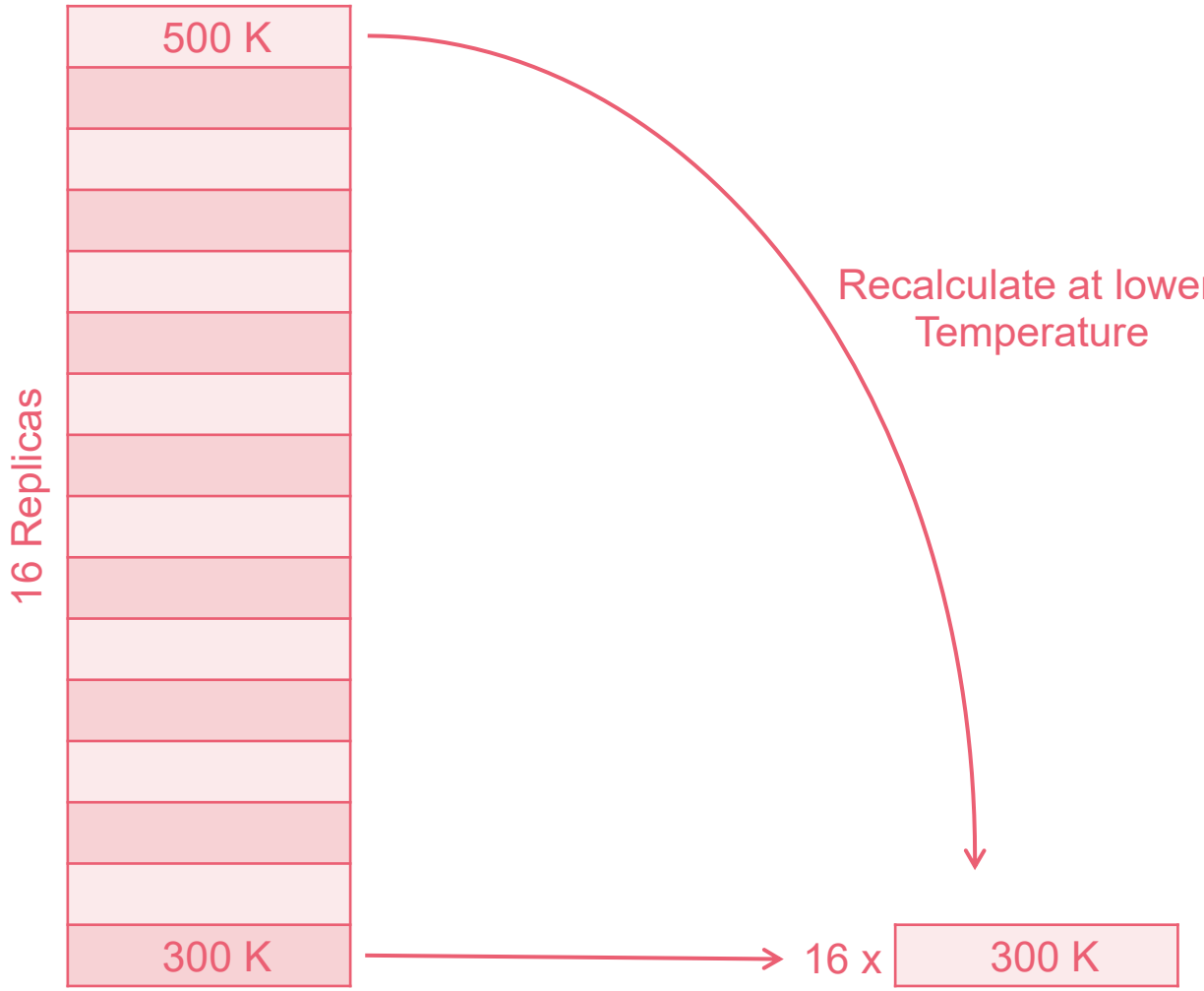


[Adapted from Clementi Group]

TRAINING DATA

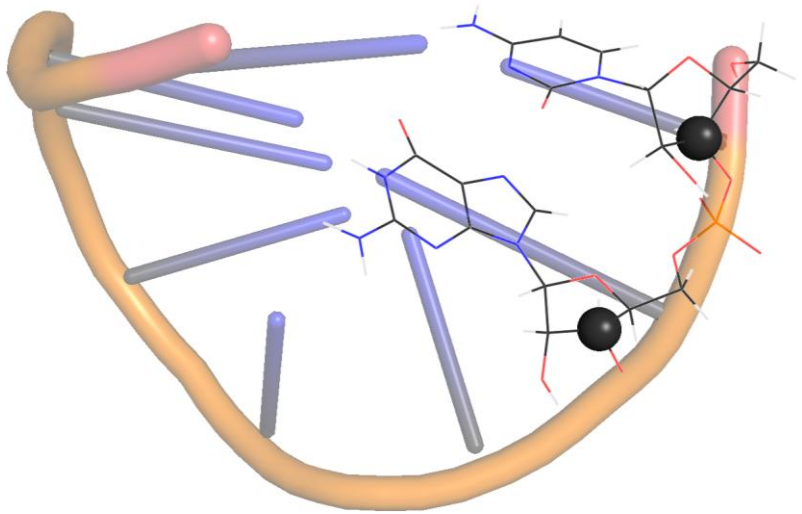
All Atom Simulations

- GROMACS
- Replica Exchange (REST2)
- 16-32 Replicas
- 100 ns
- Testset: 8 Tetraloops



COARSE-GRAINING MAPPING

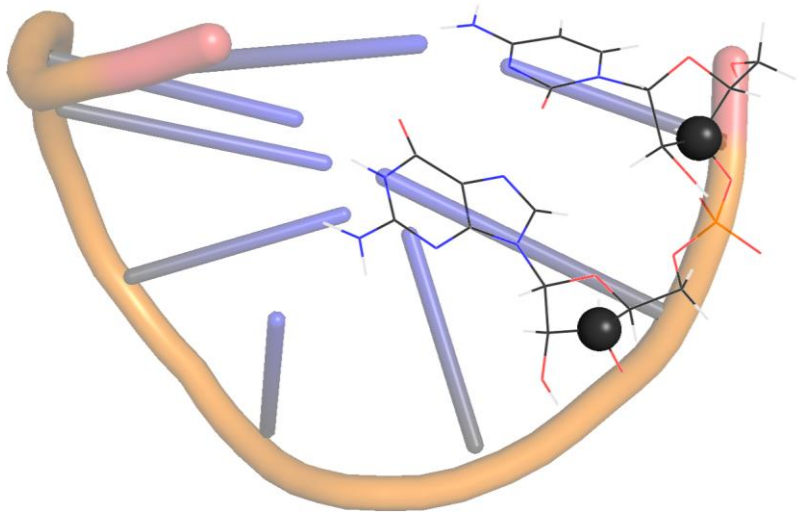
Different Bead Models



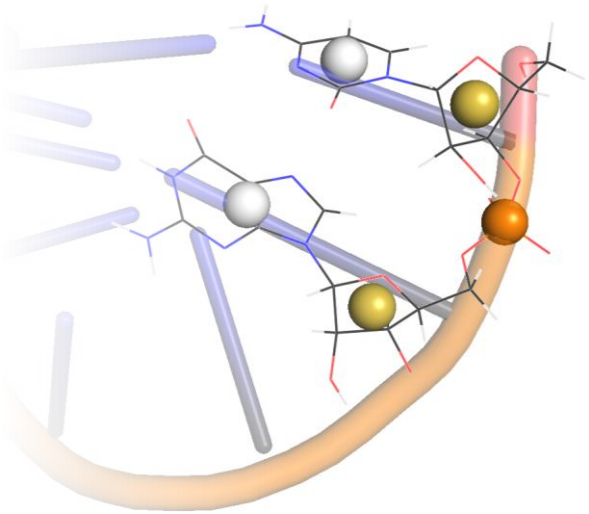
1 Bead

COARSE-GRAINING MAPPING

Different Bead Models



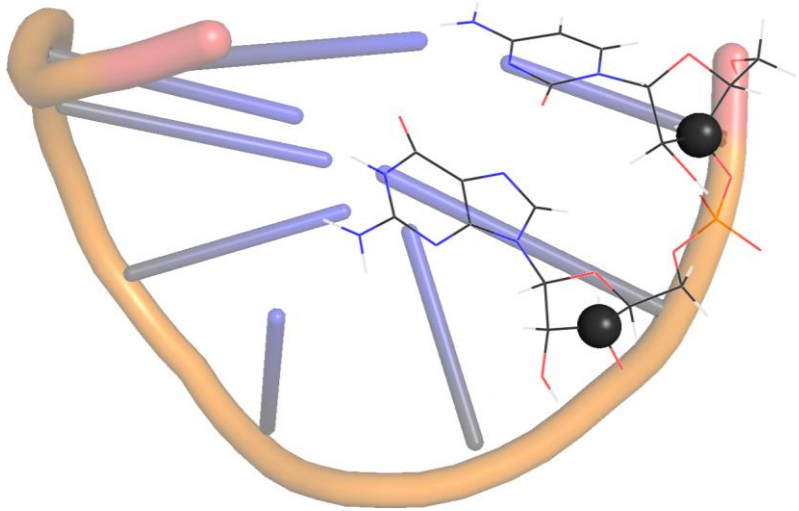
1 Bead



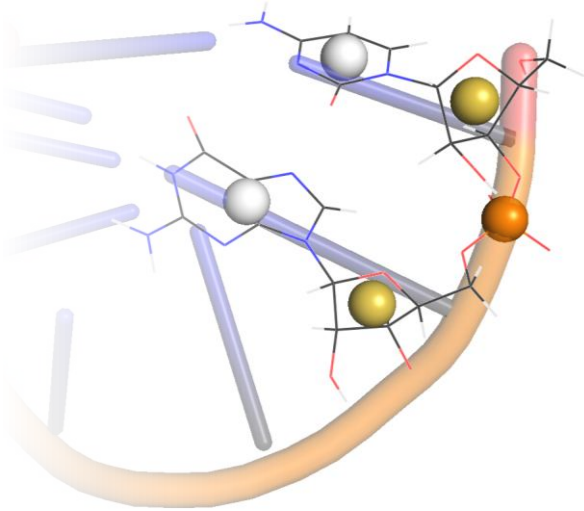
3 Beads

COARSE-GRAINING MAPPING

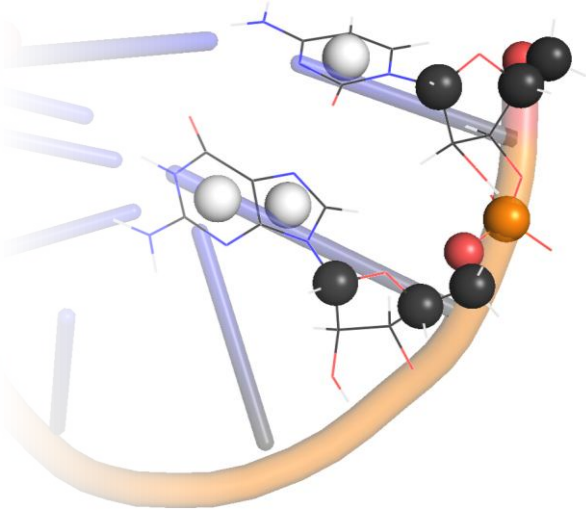
Different Bead Models



1 Bead



3 Beads

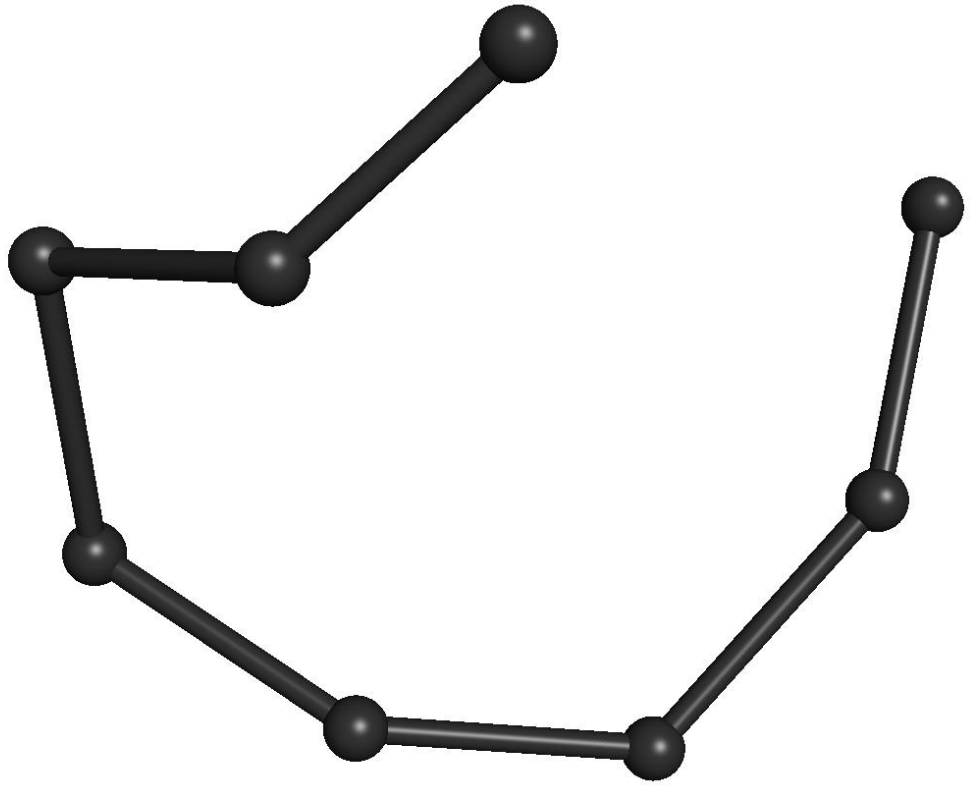


6/7 Beads

[Cragnolini, 2015]

COARSE-GRAINING MAPPING

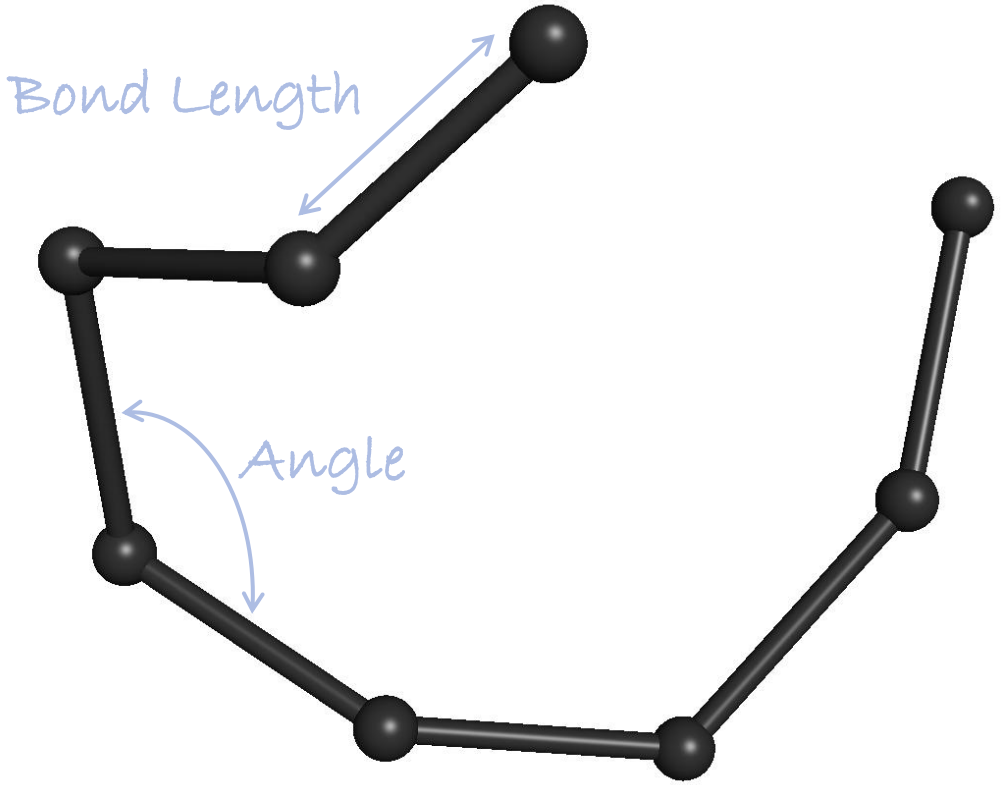
Priors



COARSE-GRAINING MAPPING

Priors

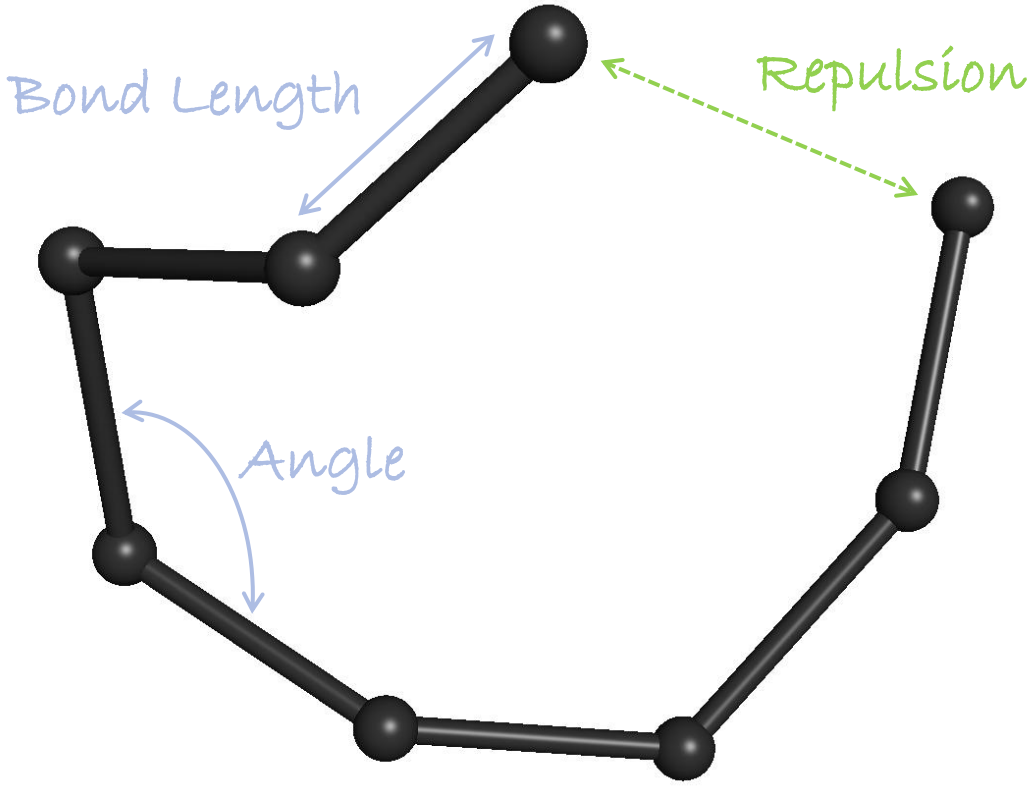
- Bonds, Angle:
  Harmonic



COARSE-GRAINING MAPPING

Priors

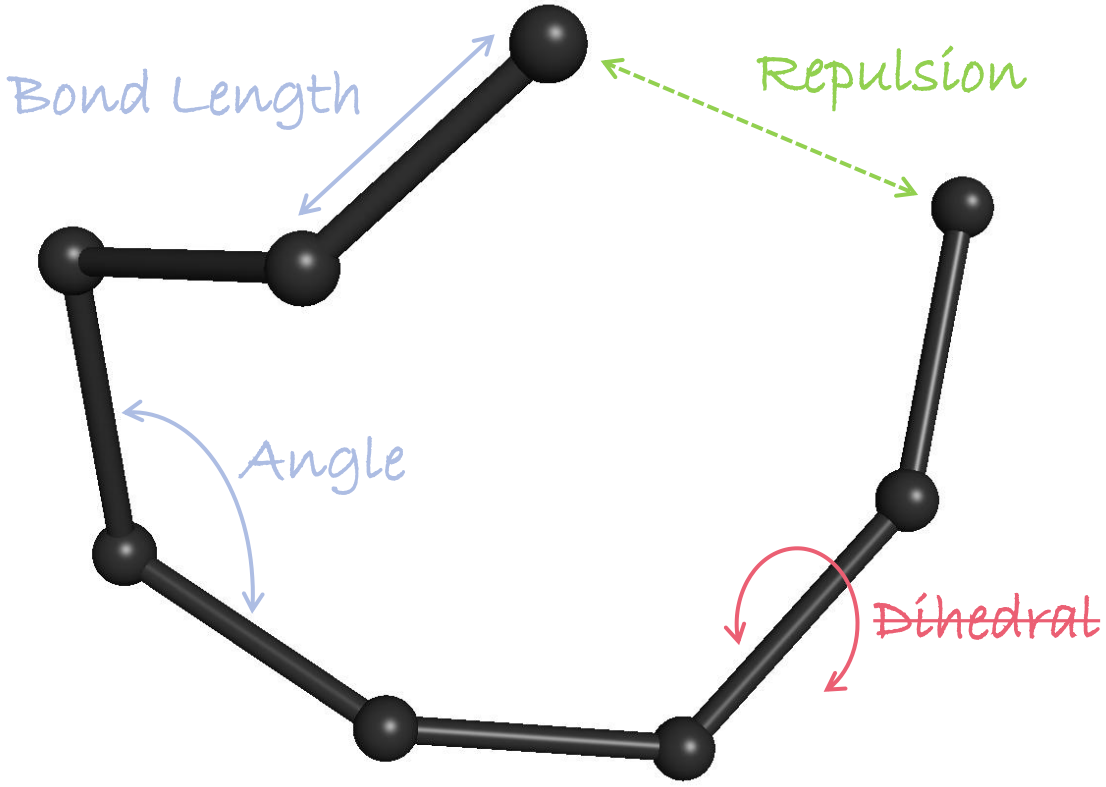
- Bonds, Angle: Harmonic
- Repulsion: Exponential



COARSE-GRAINING MAPPING

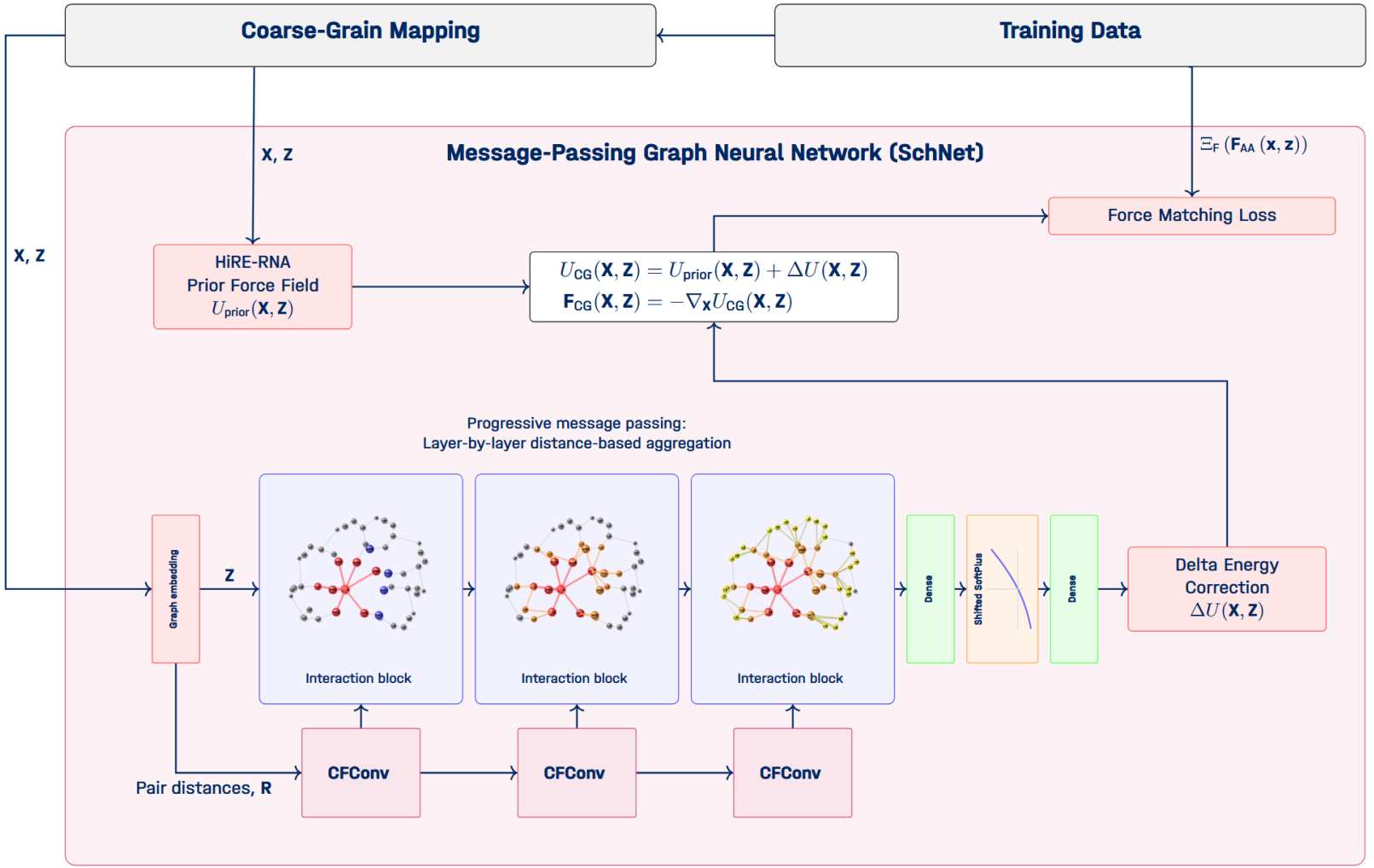
Priors

- Bonds, Angle:
  Harmonic
- Repulsion:
  Exponential
- Dihedral:
  ~ 100x
  Simulation cost



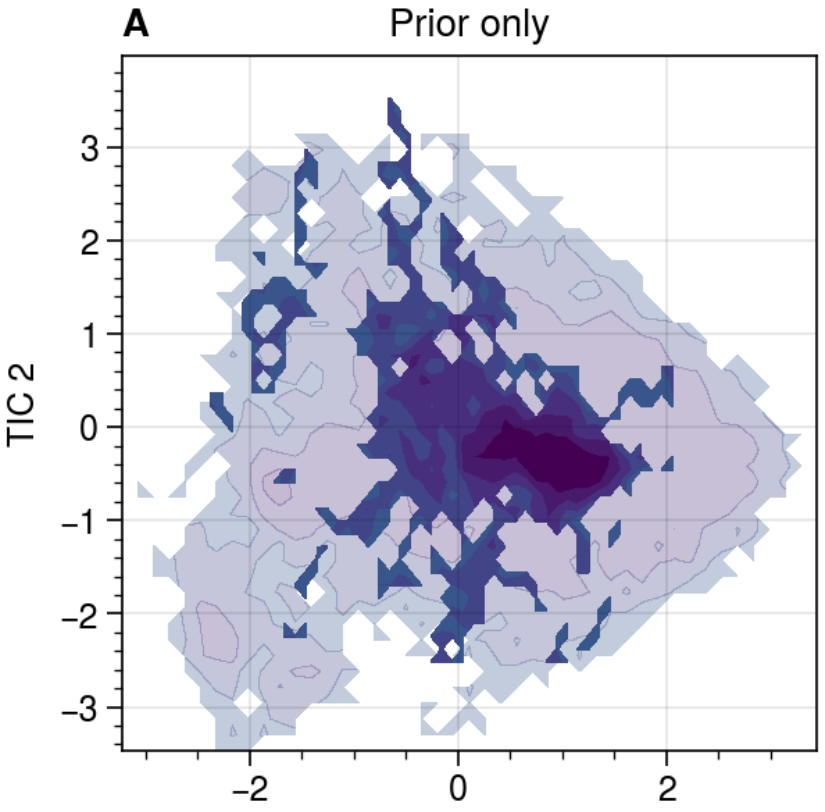
ARCHITECTURE

Graph Neural Network



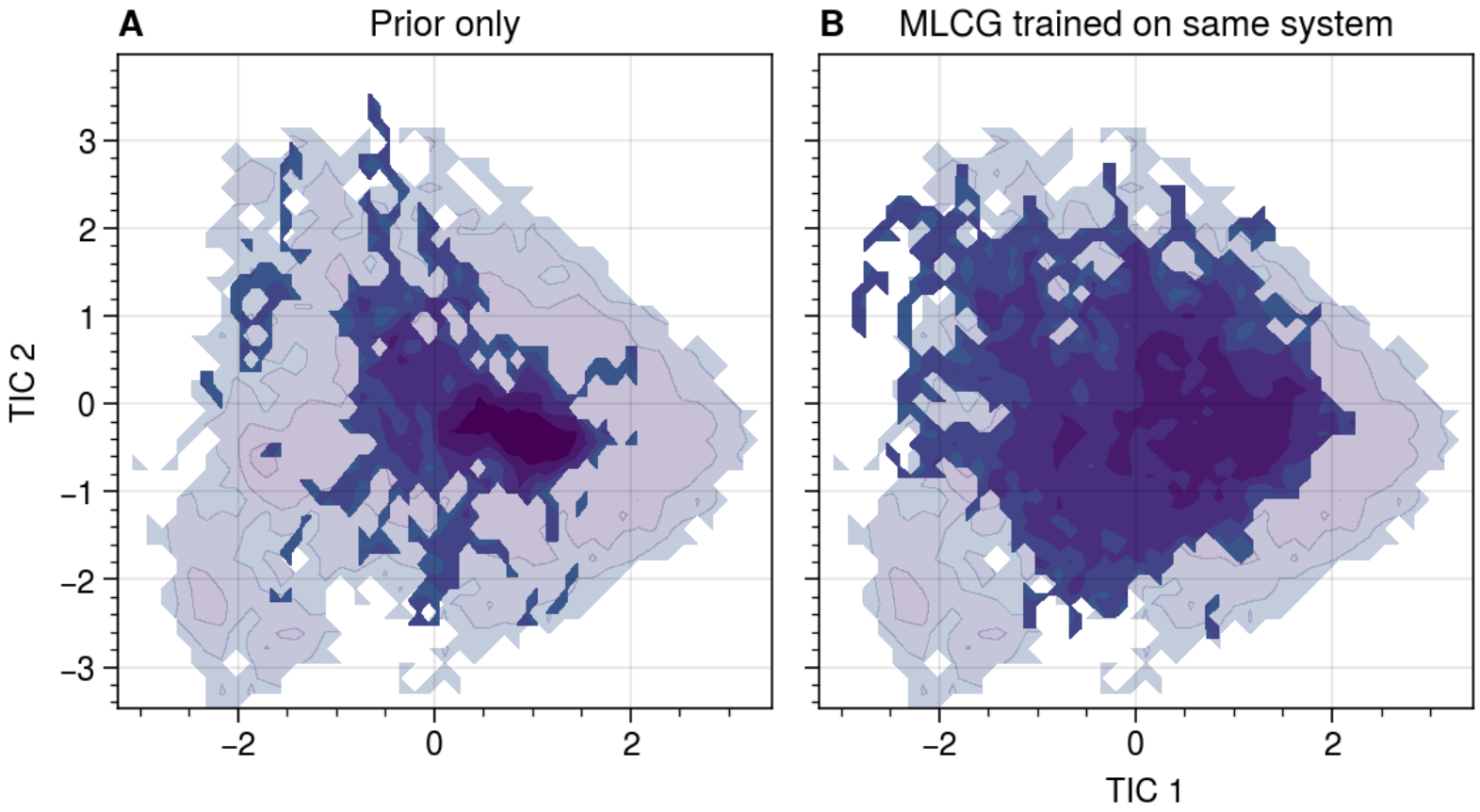
FREE ENERGY LANDSCAPES

1RNG Tetraloop



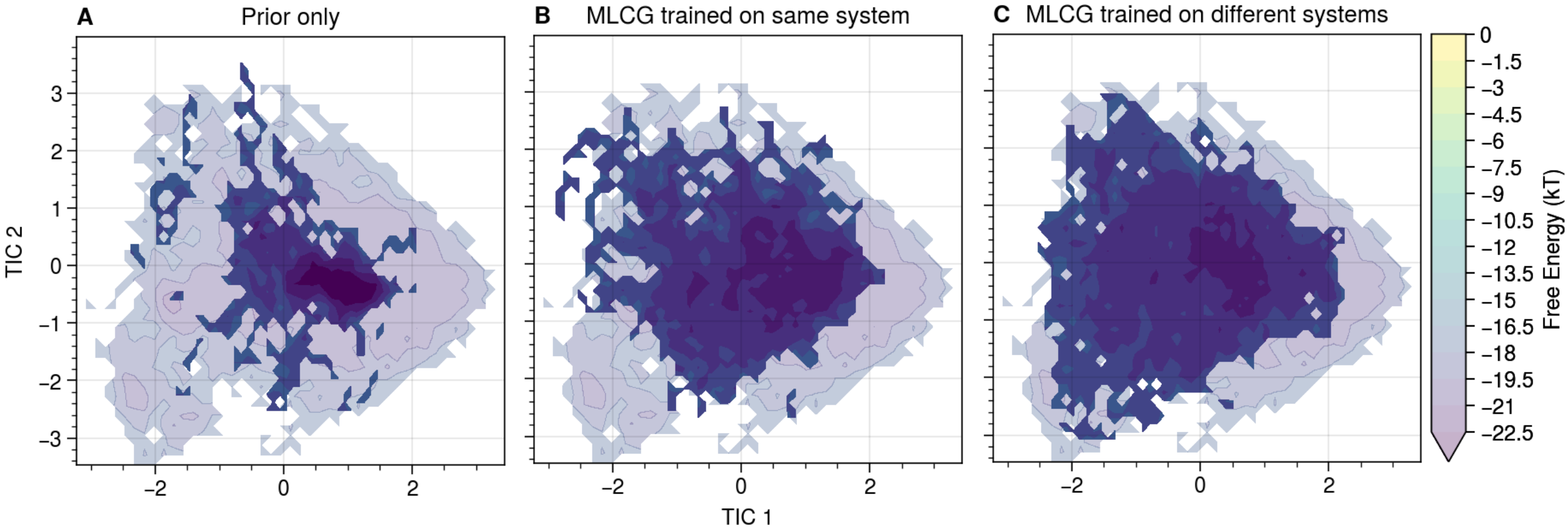
FREE ENERGY LANDSCAPES

1RNG Tetraloop



FREE ENERGY LANDSCAPES

1RNG Tetraloop



OUTLOOK

Where to go from here

- Tetraloops -> Larger Systems

OUTLOOK

Where to go from here

- Tetraloops -> Larger Systems
- Incorporate Contact predictions?

OUTLOOK

Where to go from here

- Tetraloops -> Larger Systems
- Incorporate Contact predictions?
- Better Parallelisation?

FIN

Acknowledgments:

Alex Schug, Comp. Struct. Bio. Group, JSC, FZ Jülich

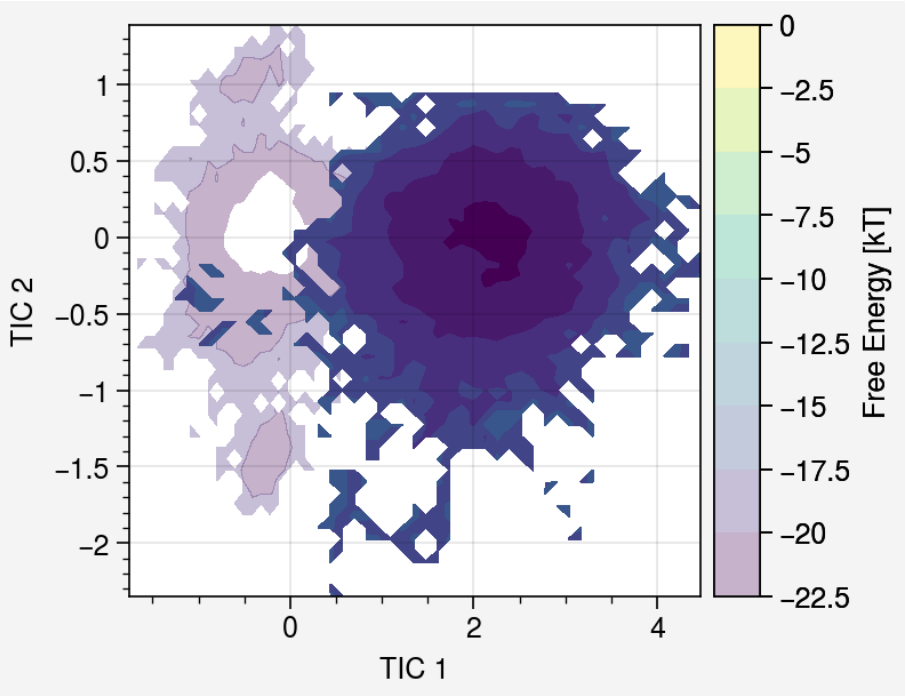
Emile de Bruyn, Stefan Kesselheim, JSC

Fabrice von der Lehr, Philipp Knechtges, DLR Cologne

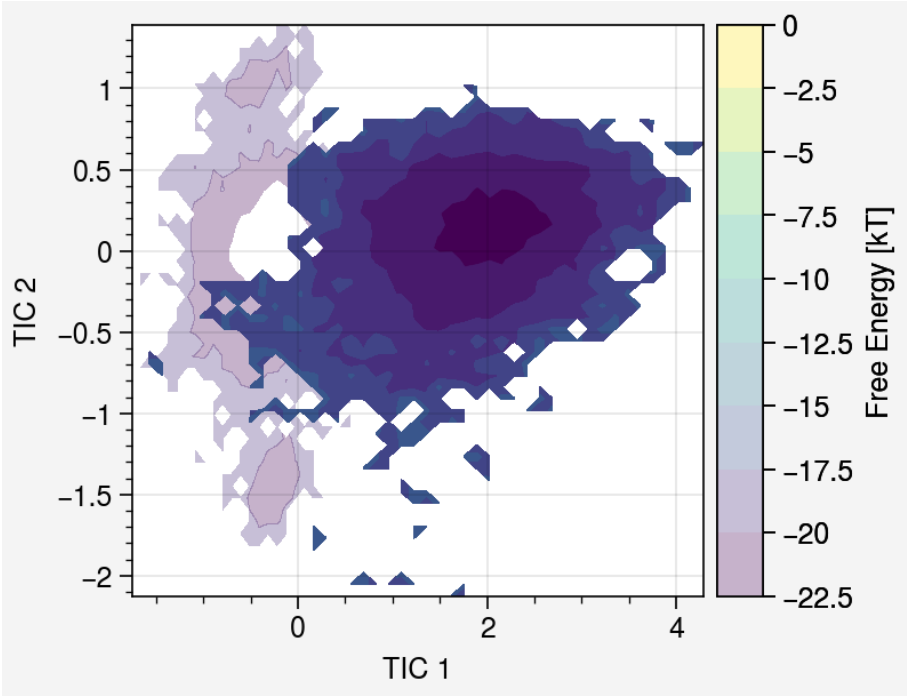
Stefan Klumpp, GA Universität Göttingen

FREE ENERGY LANDSCAPES

1 Bead Model



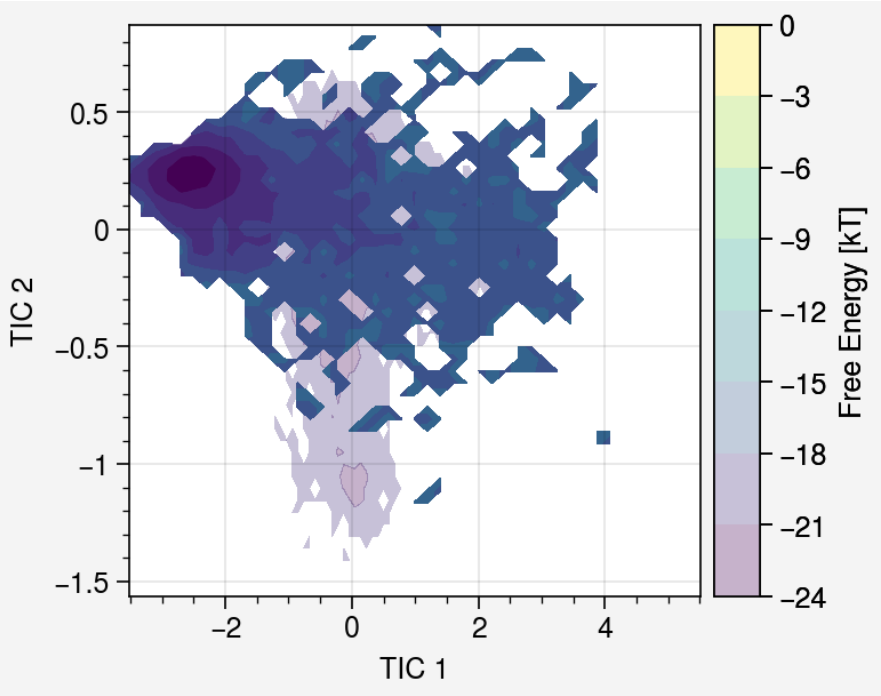
Prior



Trained

FREE ENERGY LANDSCAPES

3 Bead Model



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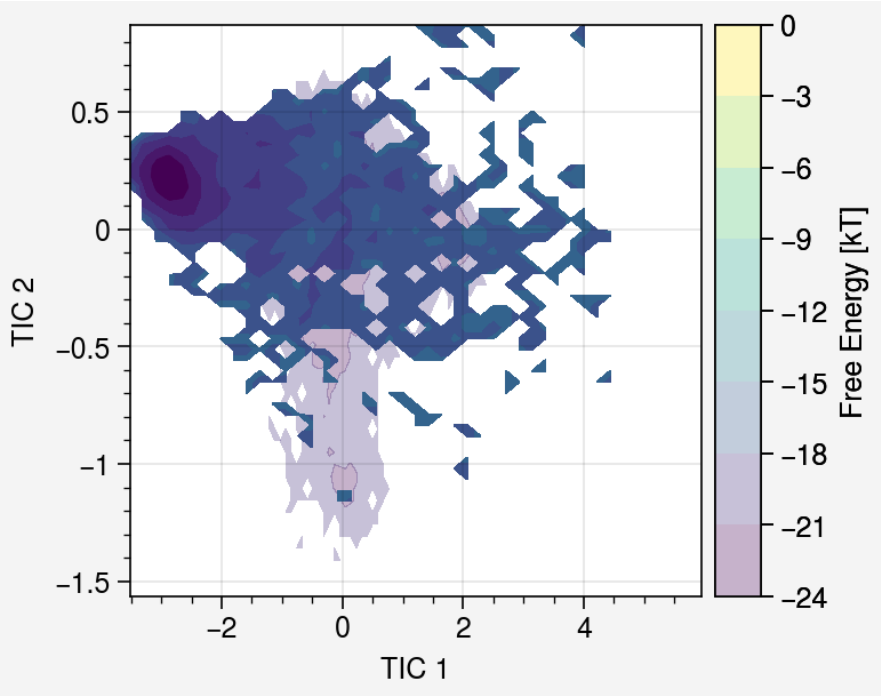

Trained