Finding Patterns and Drawing Maps in the Configuration Space of Materials and Molecules

Michele Ceriotti, EPFL-IMX-COSMO

ML 2015 - IPAM Los Angeles

Managing data from atomistic models

- Atomistic simulations provide **too much** information
- It is hard to decipher the essential features in structurally-complex compounds, materials, proteins, etc.

```
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ATOM     67  CA  LEU A  18      25.212  18.444  -9.785  1.00 17.64           C
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ATOM     79  CG  MET A  19
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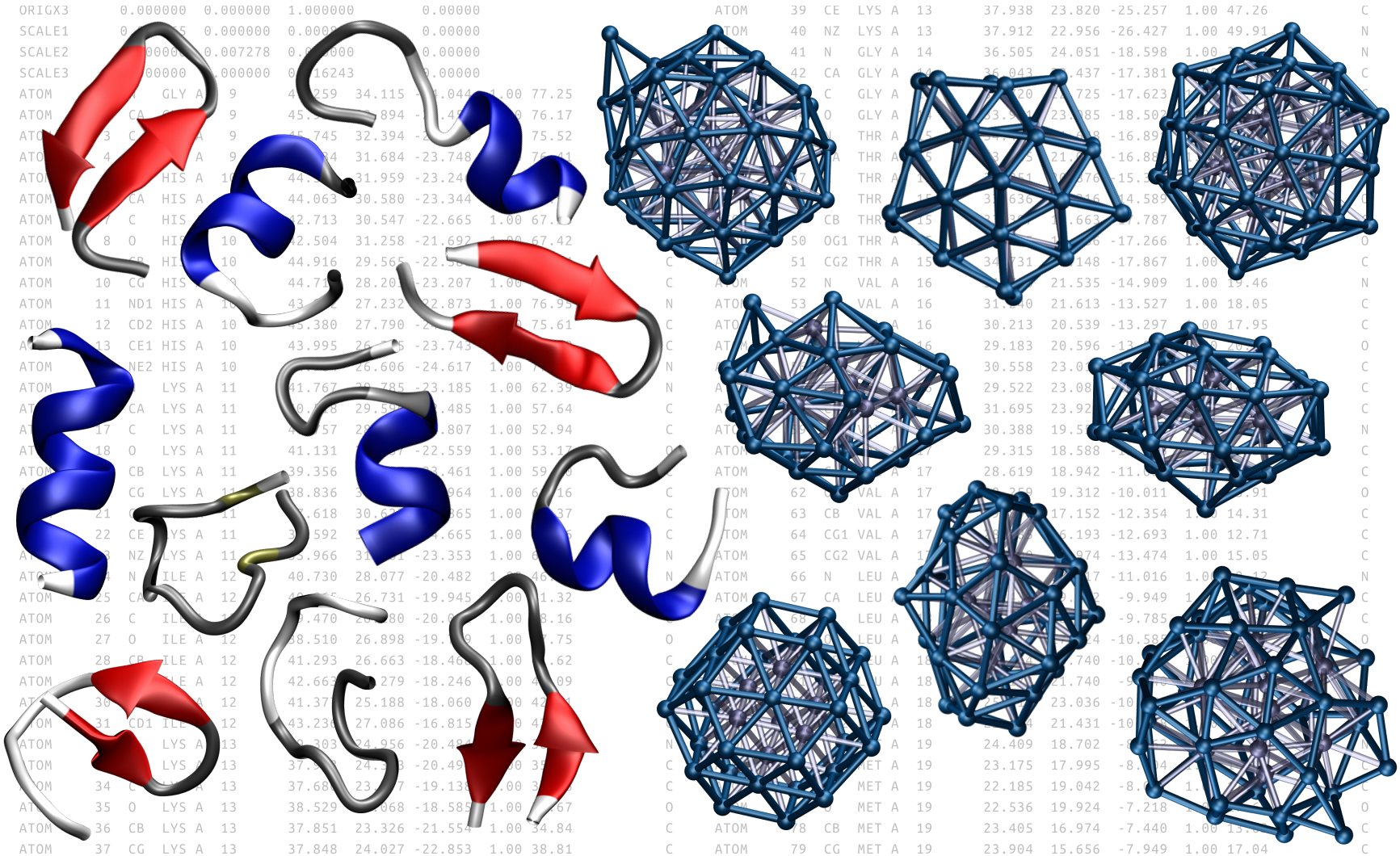
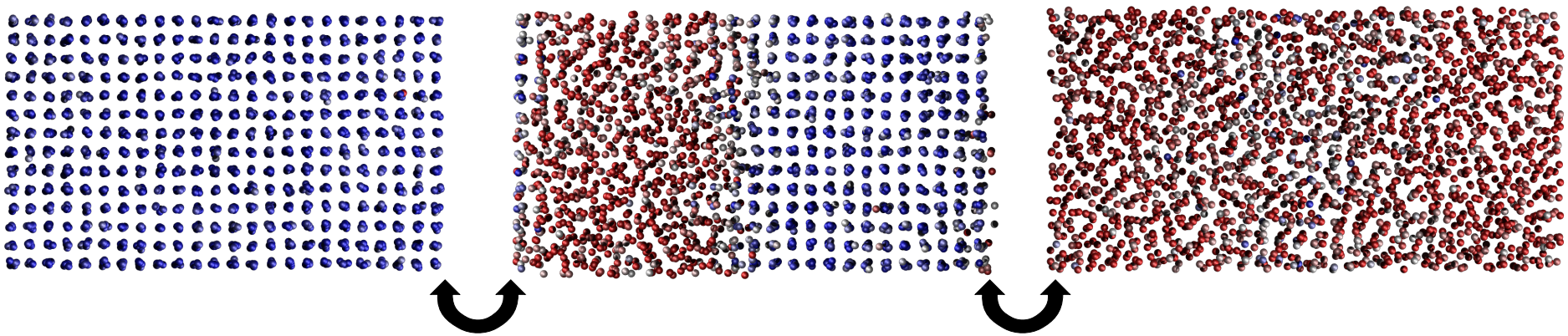


Describing structural complexity

- We are looking for **collective variables** that can describe this structural complexity
  - Discriminate between different structures
  - Follow the system across transitions
- Finding these variables is time-consuming and error-prone: can we **automate** the process?



Angioletti, Ceriotti, Lee, Finnis PRB 2010

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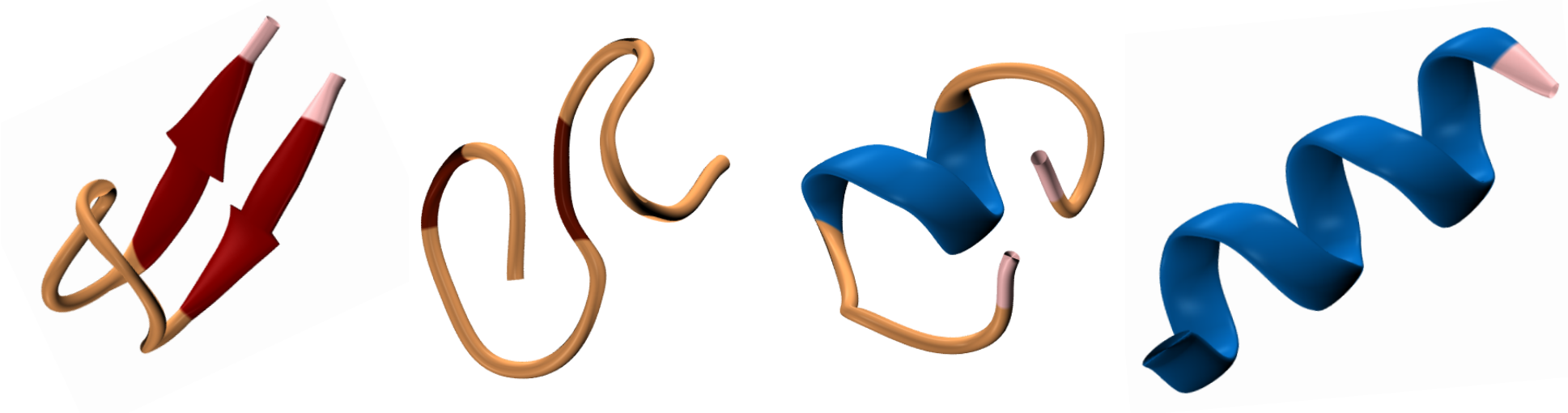
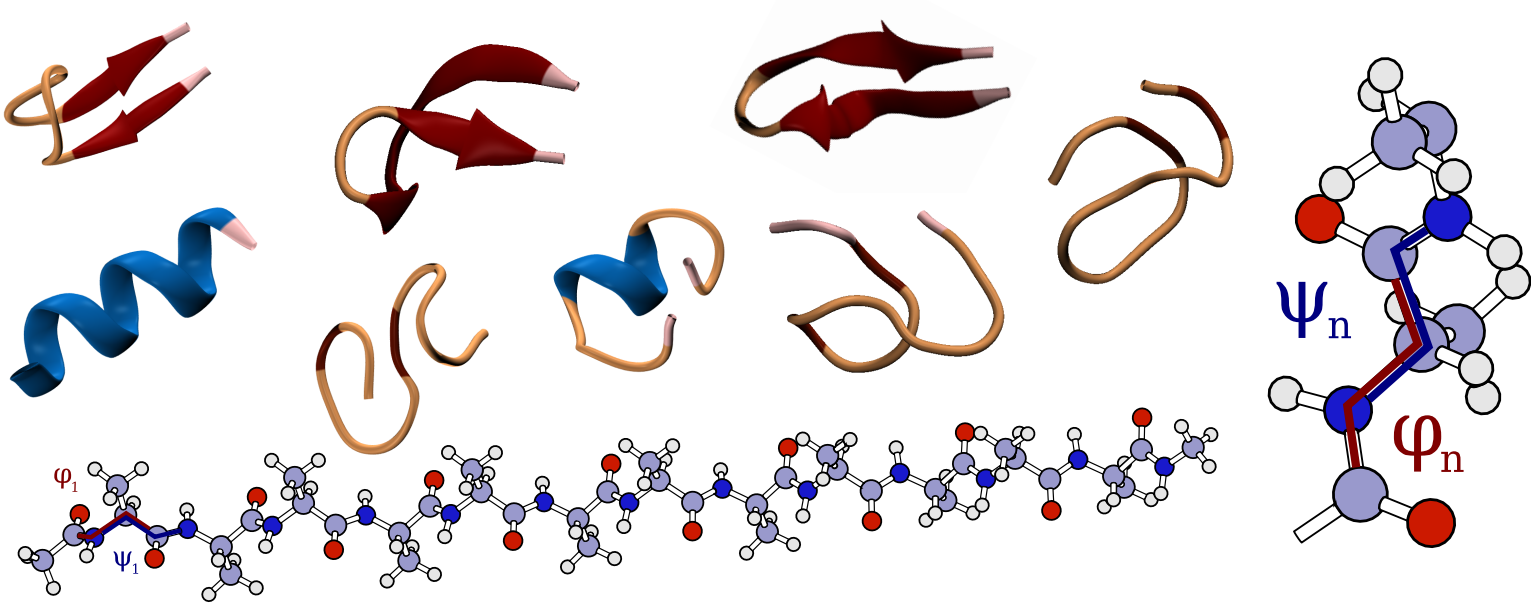


Tribello, Ceriotti, Parrinello PNAS 2010

Dimensionality reduction

- We can describe a complex atomistic structure as a point in a high-dimensional space. Then finding CVs means finding a low-dimensional **map** to describe the accessible configurations!
  - Take a set of configurations ⇒ high-dim. **landmark points**
  - Find the distances between the points
  - Arrange low-dim. points so that the distances are preserved
  - Locate other configurations with an **out-of-sample embedding**



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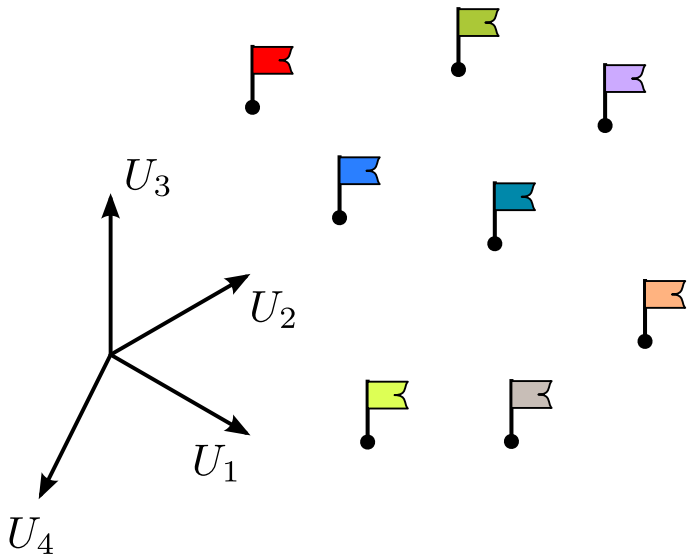

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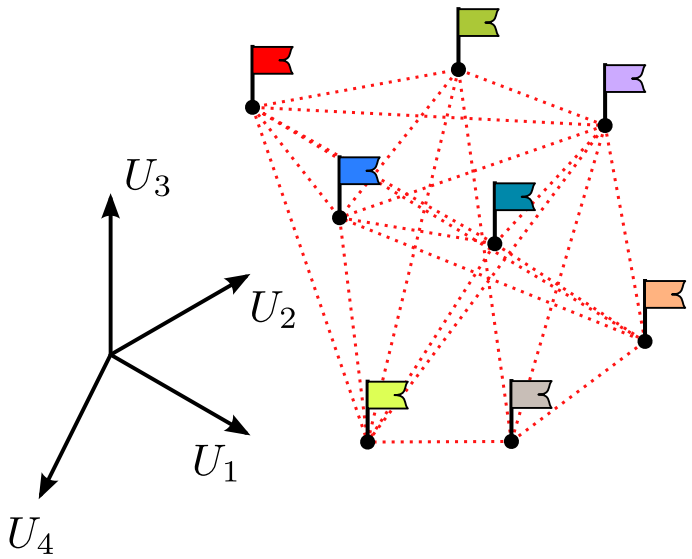

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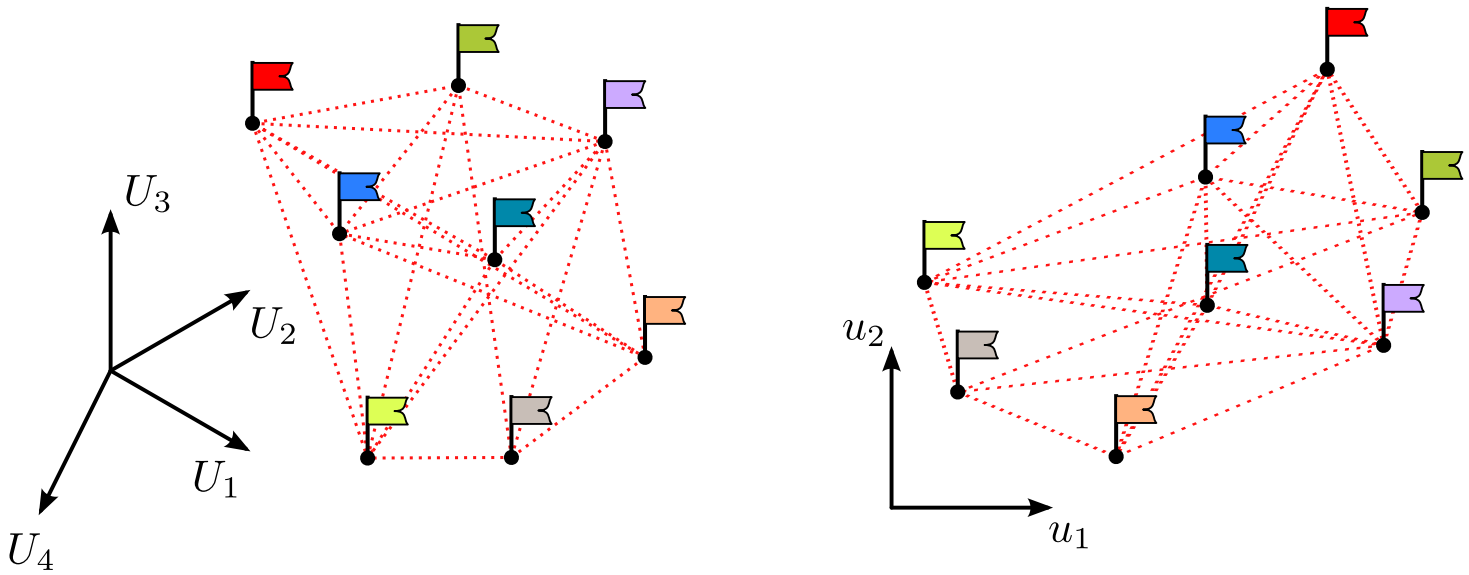

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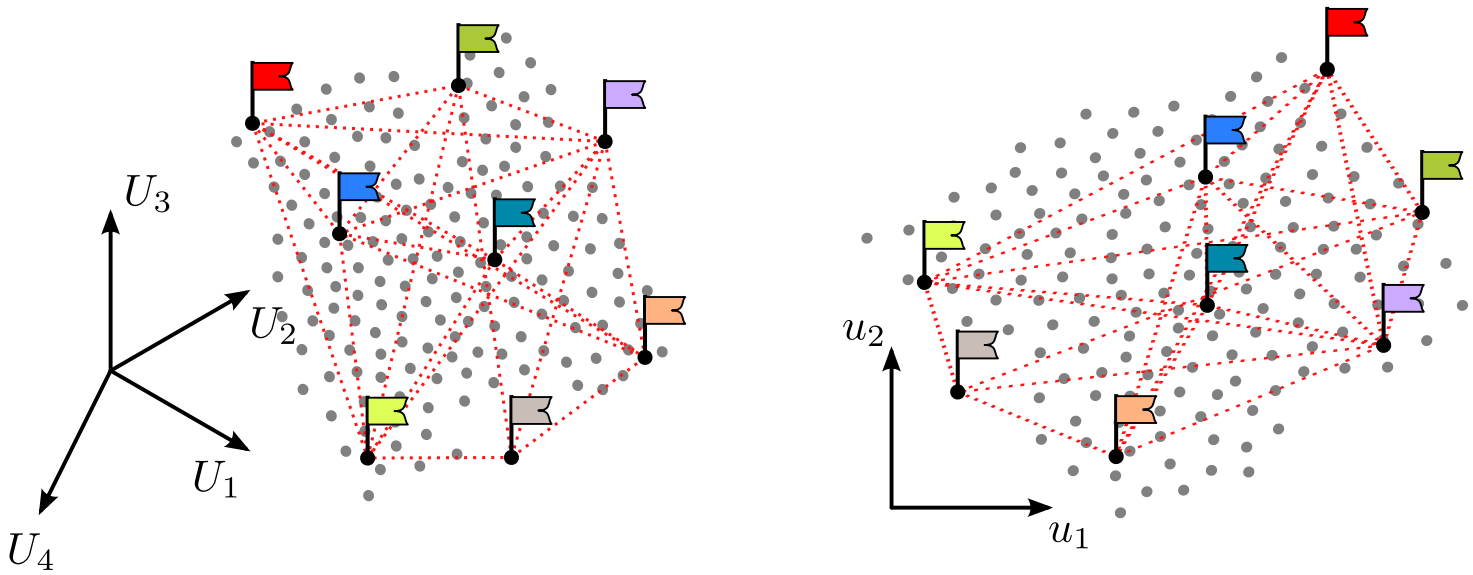

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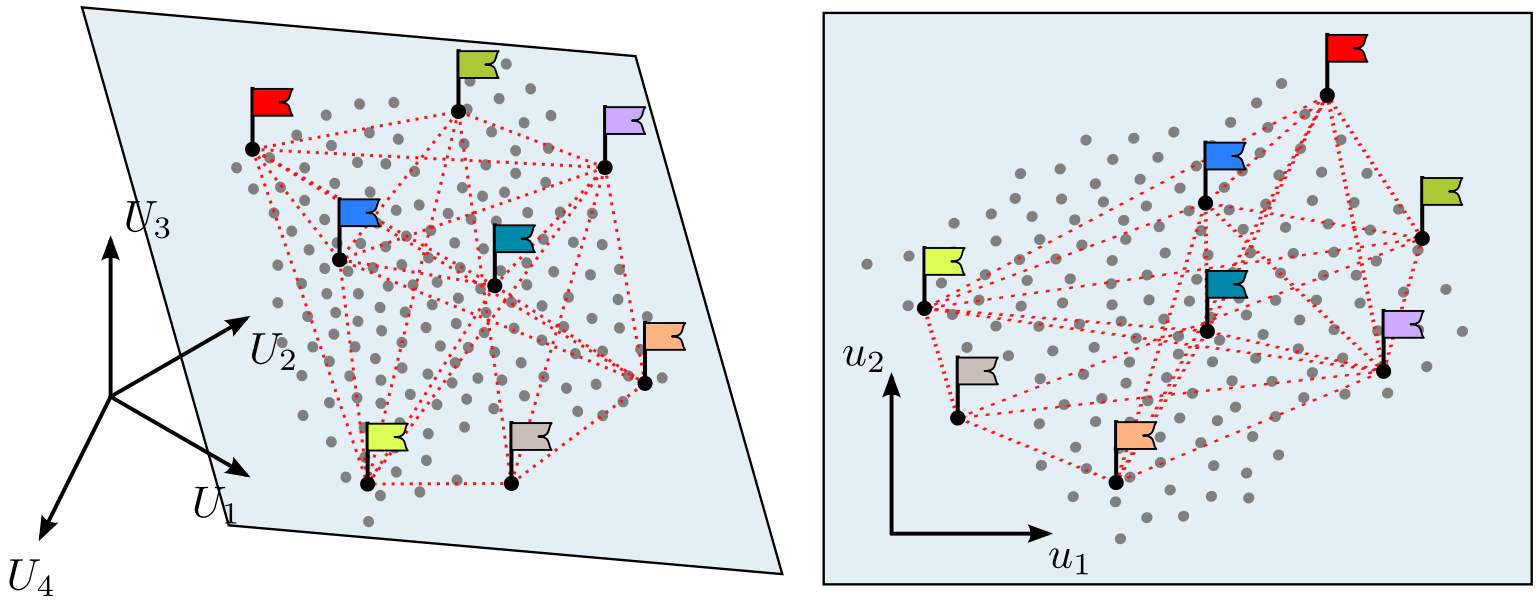
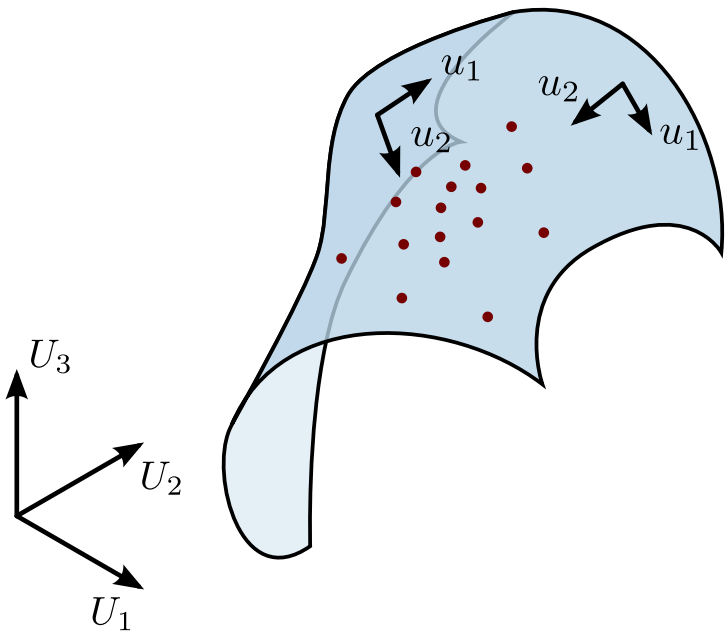
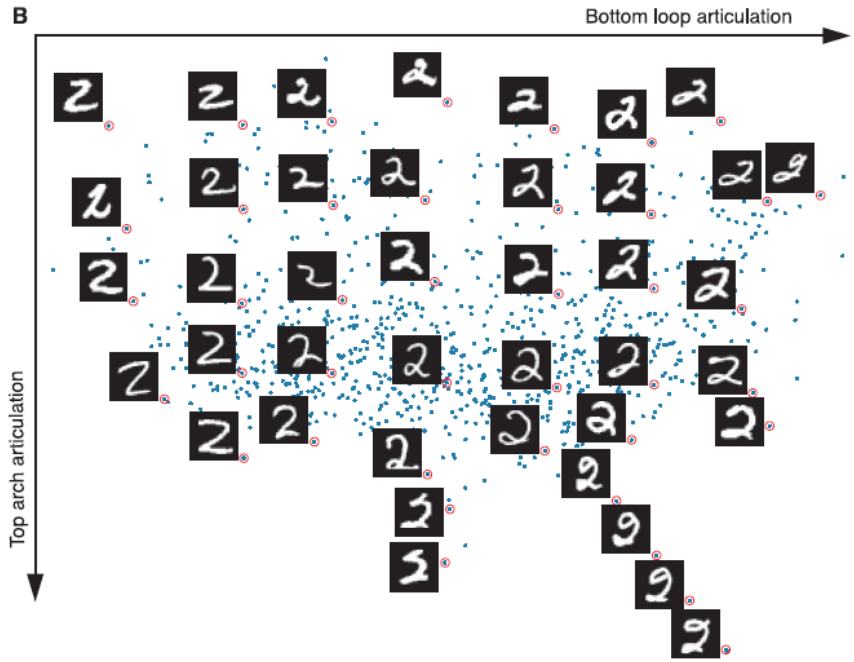


Non-linear dimensionality reduction

- Non-linear dimensionality reduction algorithms:
  - Describe curved, "locally-flat" manifolds
  - Developed by the CS community (image recognition)
  - Attempts to apply to chemical problems (PCA, ISOMAP, Diff. maps,...)
- Atomistic simulations are harder:
  - **Thermal fluctuations** are high-dimensional
  - A network of transition pathways with a complex topology





Tenenbaum *et al.*, Science (2000)

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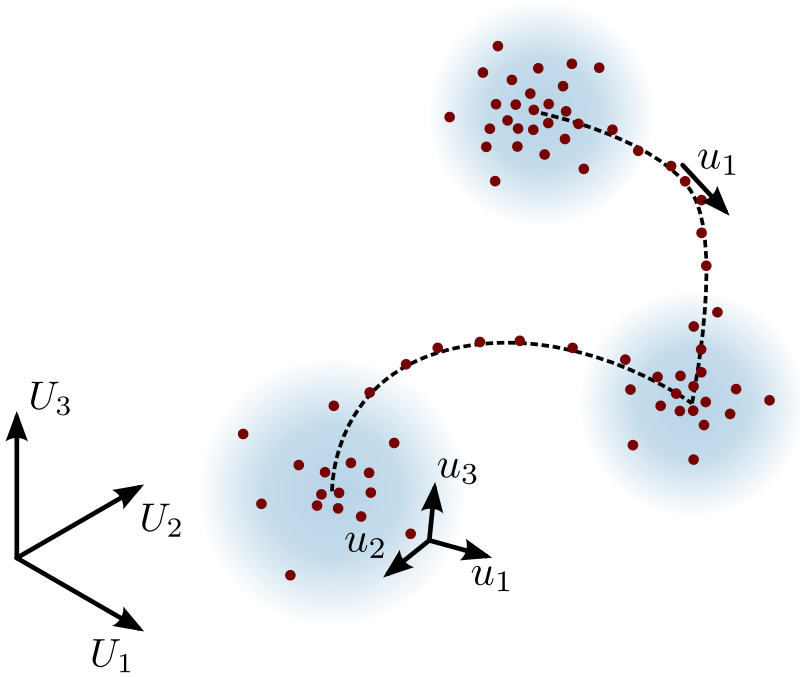

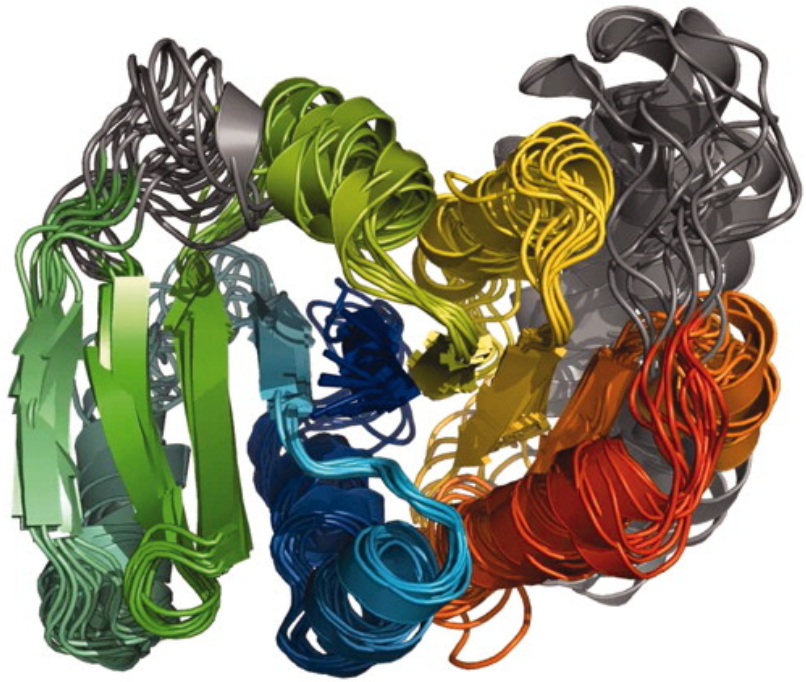

Introducing sketch-map

- Developing a more robust NLDR method
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  - We need the computational equivalent of a hand sketched map

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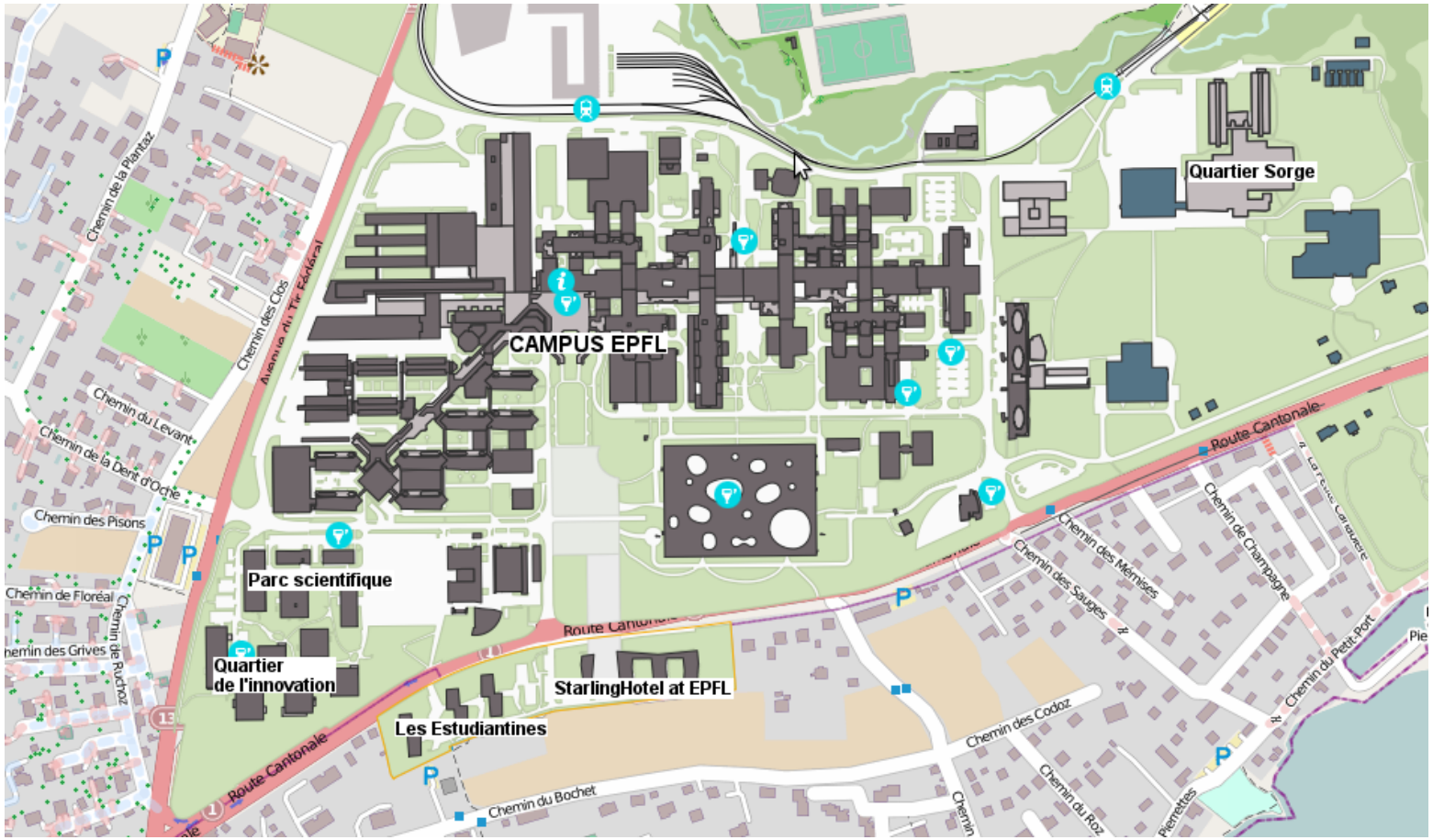

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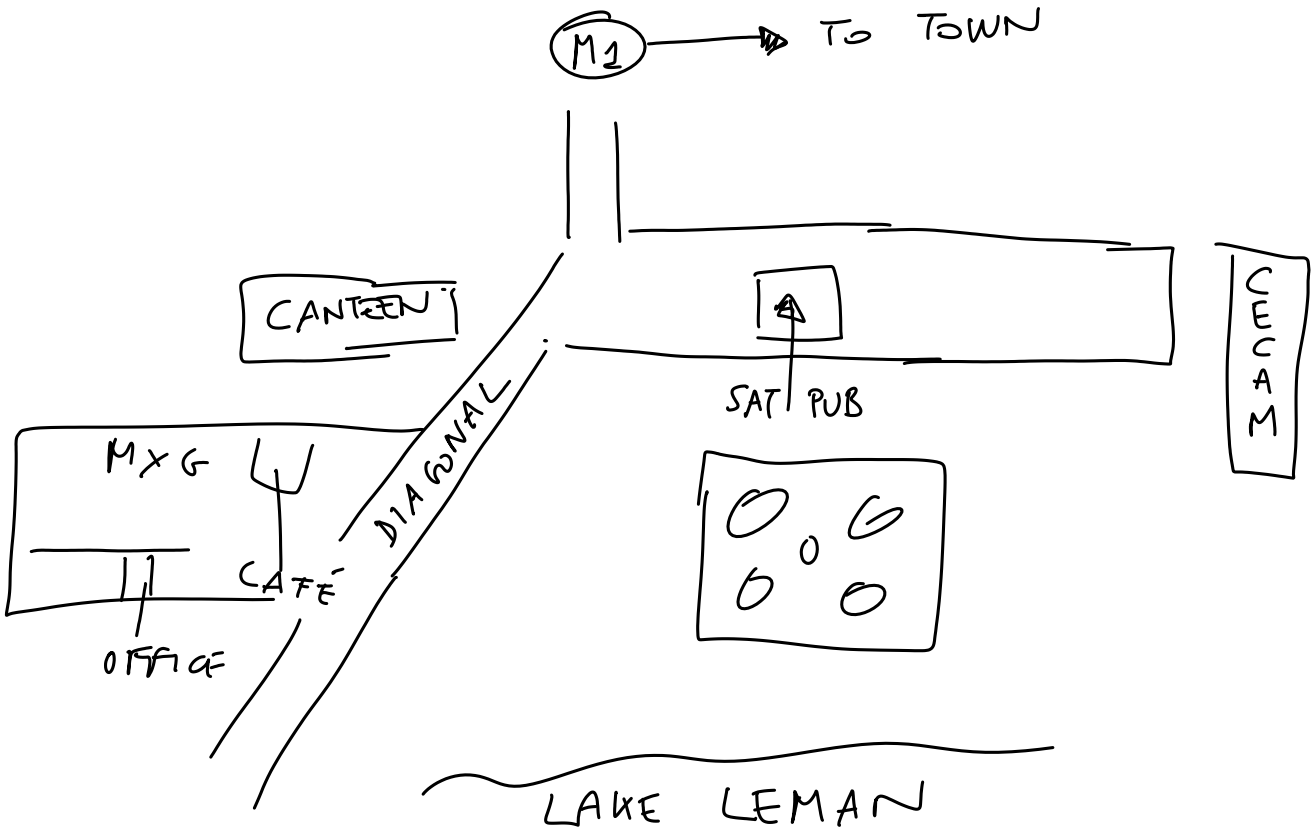
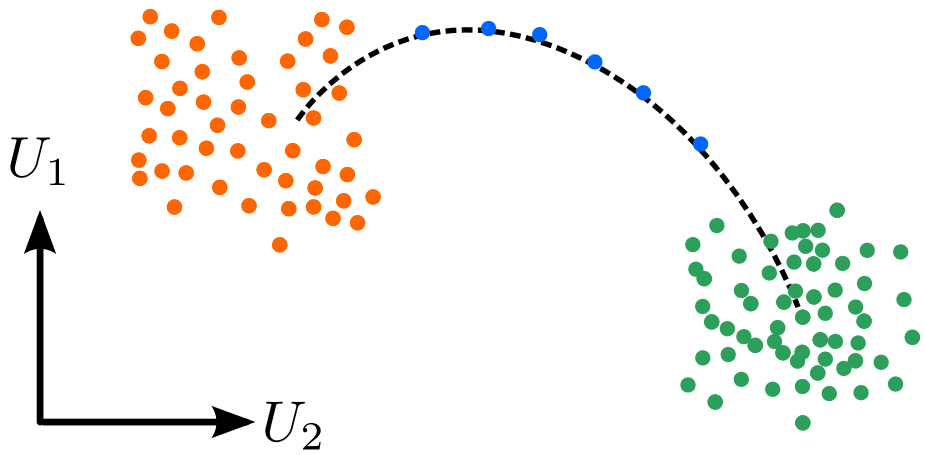


Proximity matching

- We would like to capture the low-dimensional structure of complex transitions
- Some portions of the landscape cannot be projected by matching high and low-dimensional distances. Thermal fluctuations exhibit inherent full dimensionality!
  - Idea: simplify the task, aim for proximity matching: close↔close, far↔far



Ceriotti, Tribello, Parrinello, PNAS 2011

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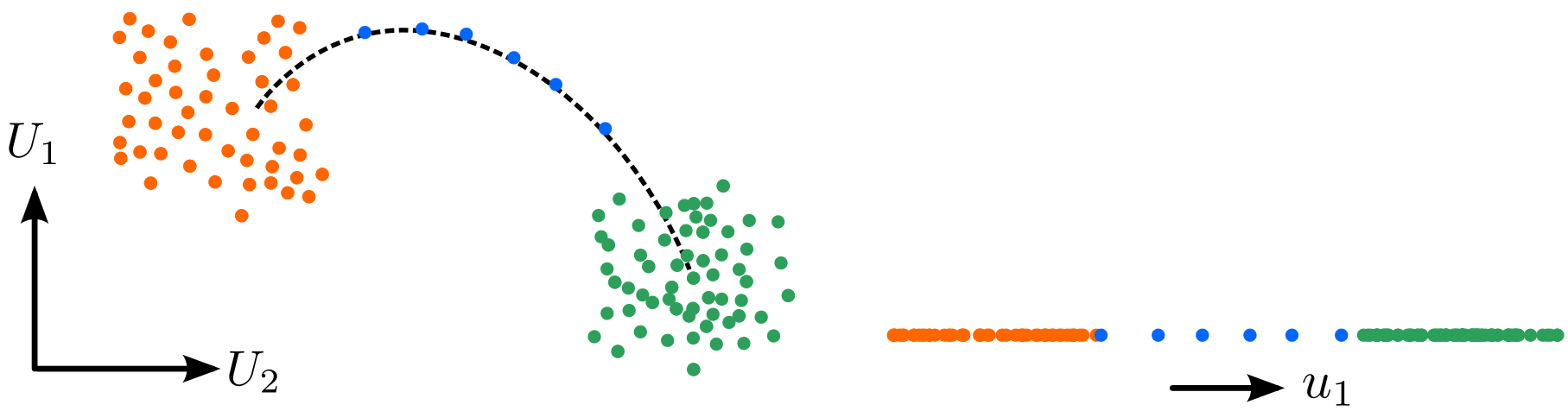

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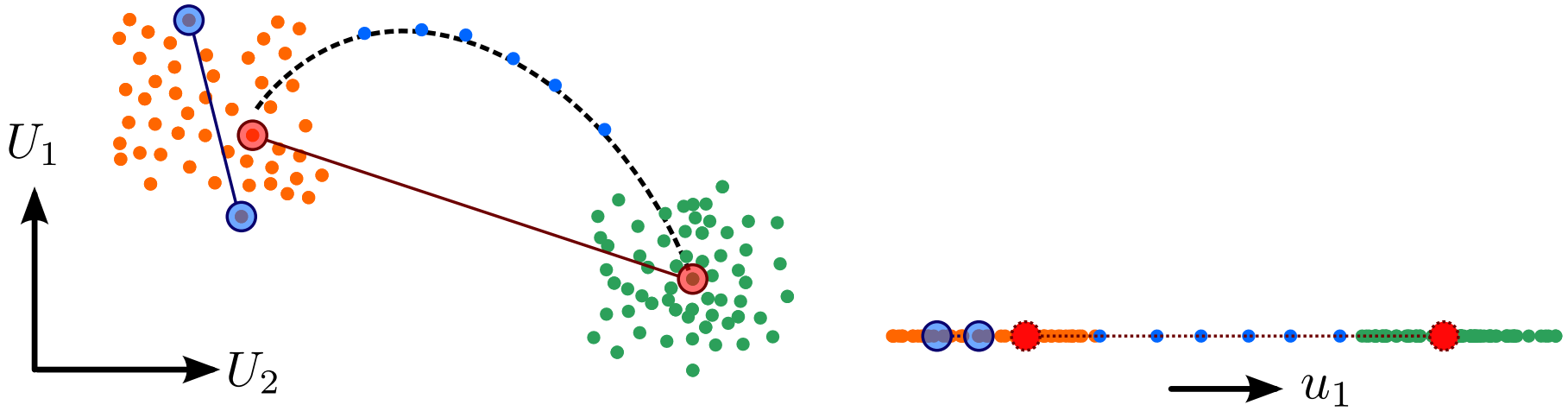

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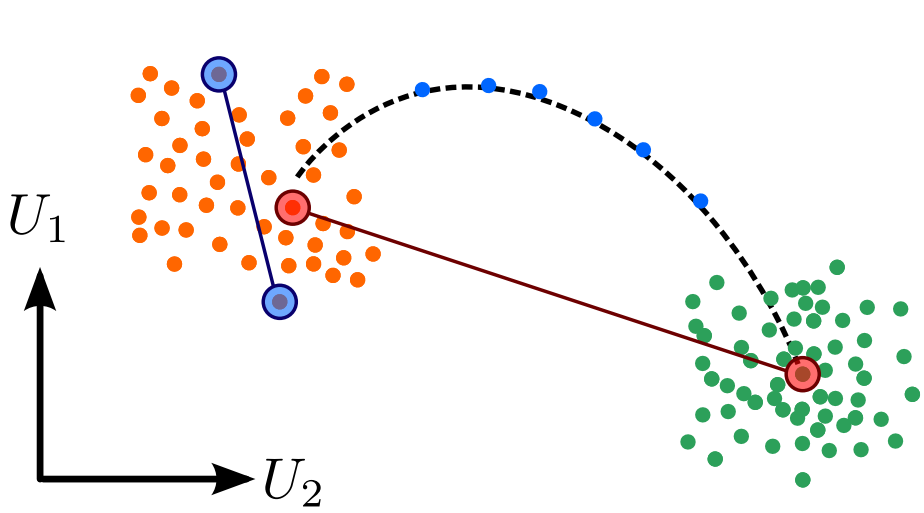

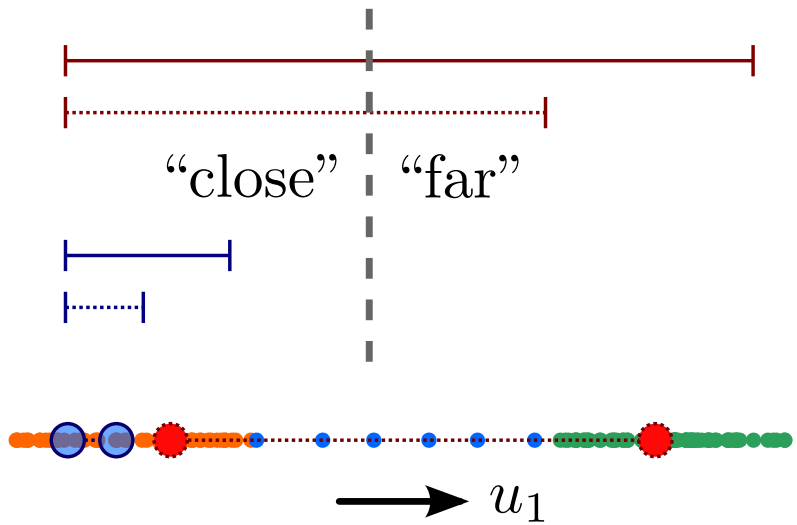

Ceriotti, Tribello, Parrinello, PNAS 2011

Sketch-map algorithm

- In "metric" MDS a **stress function** that measures how well distances are reproduced is minimized
- Modify the objective function to aim for **proximity matching**
  - Distances are transformed by **sigmoid functions** in both high and low dimension

$$\chi^2 = \sum_{i,j=1}^{N} [|X_i - X_j| - |x_i - x_j|]^2$$

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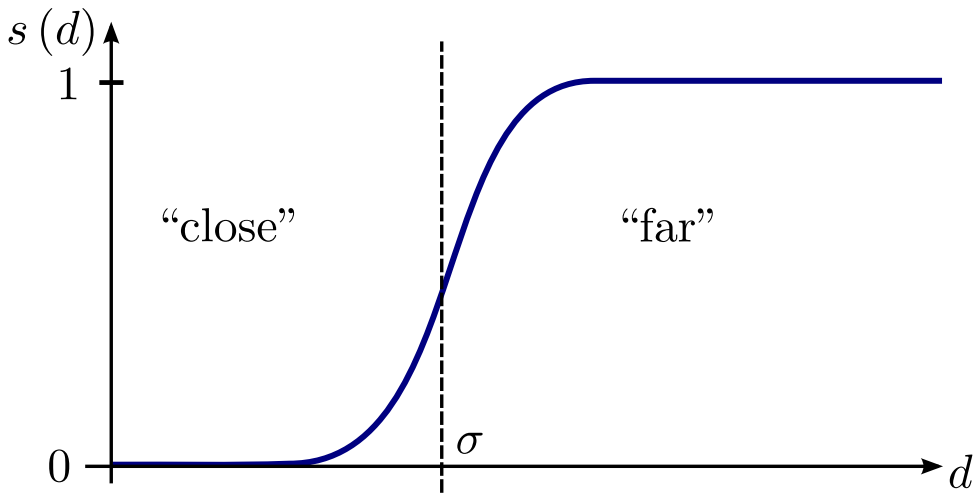
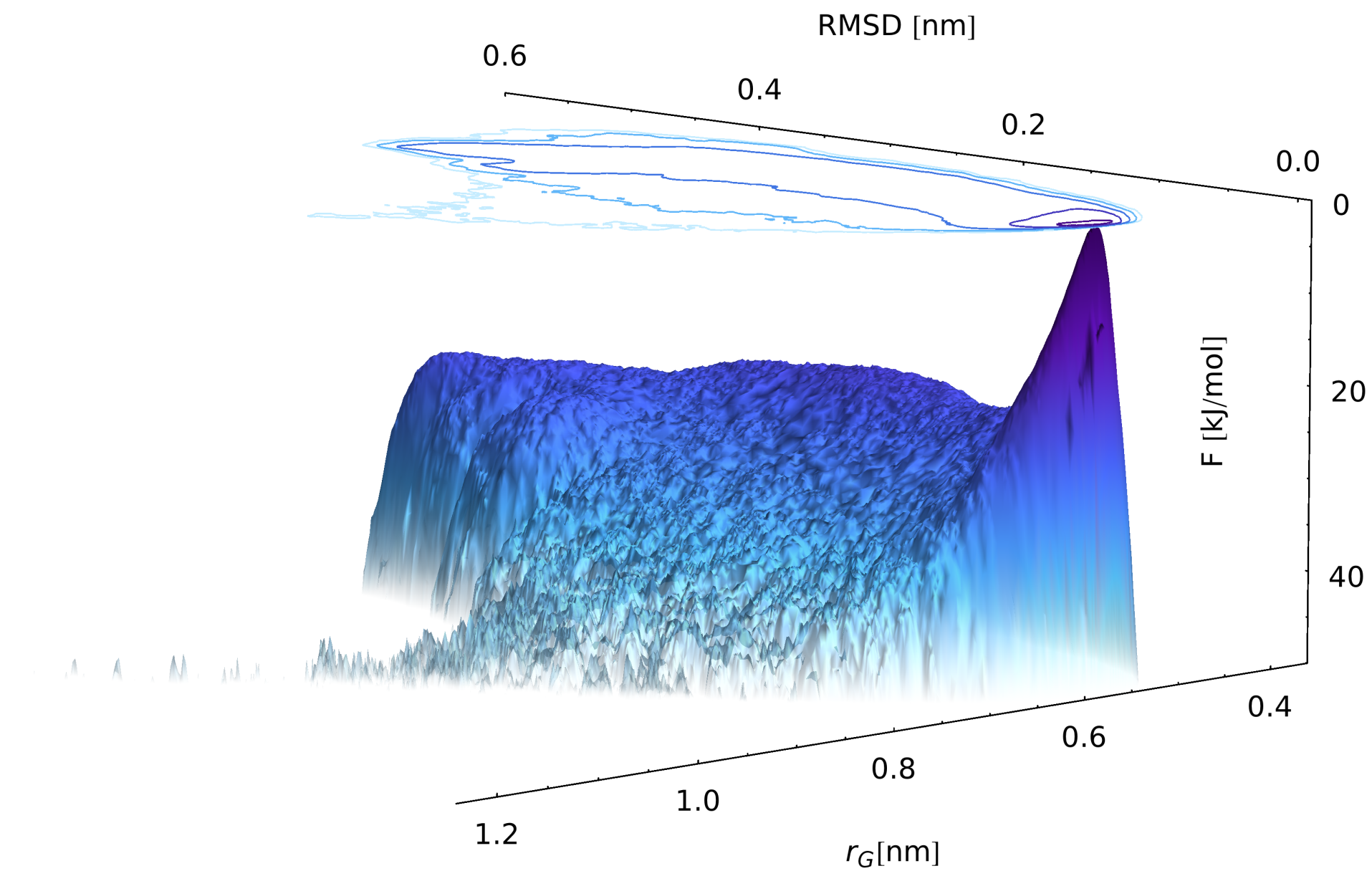


Sketch-mapping the folding landscape of a



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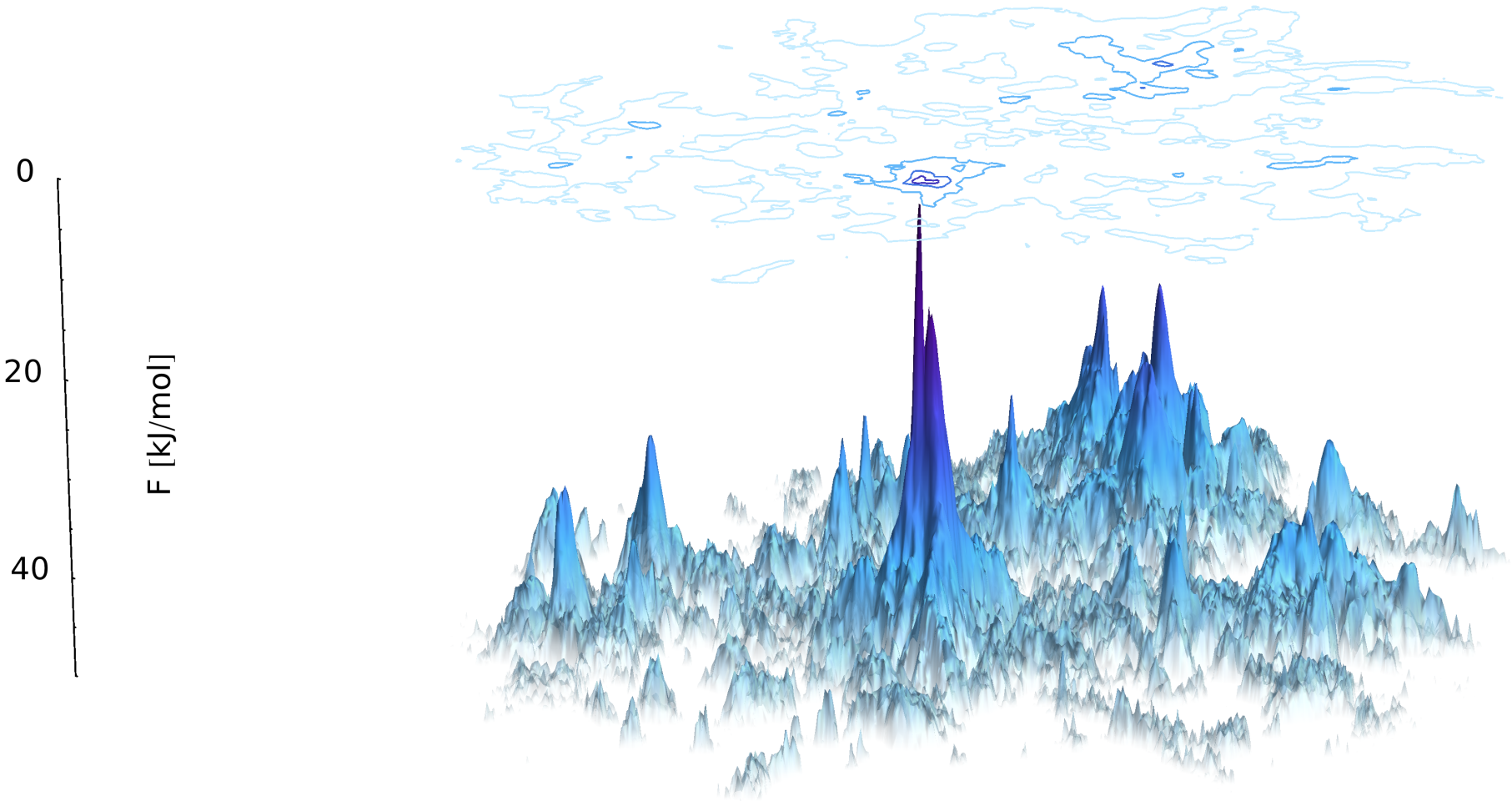
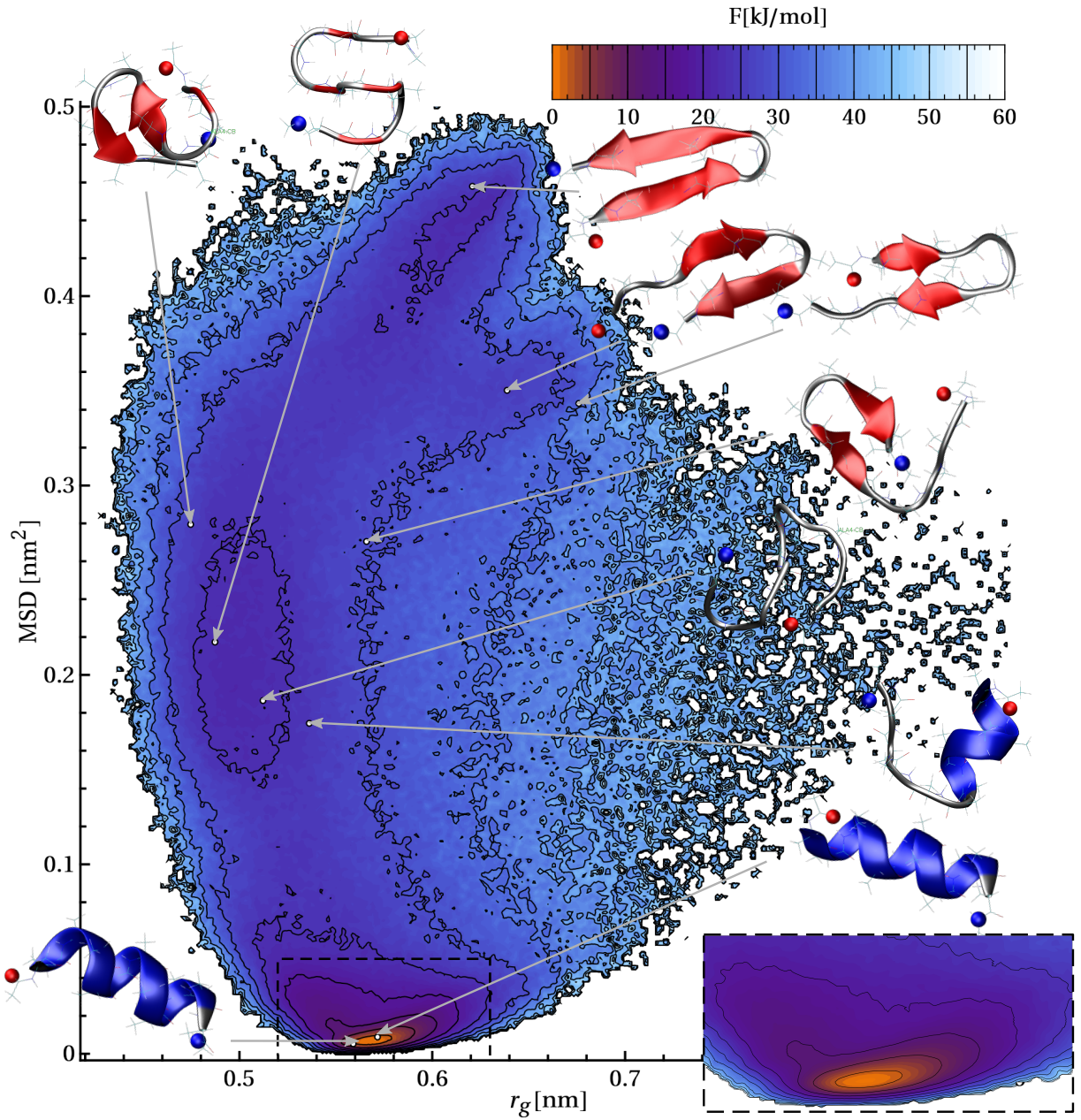


Sketch-mapping the folding landscape of a

"Conventional" CVs recognize the folded state, but many meta-stable structures overlap with each other



Ceriotti, Tribello, Parrinello, PNAS 2011

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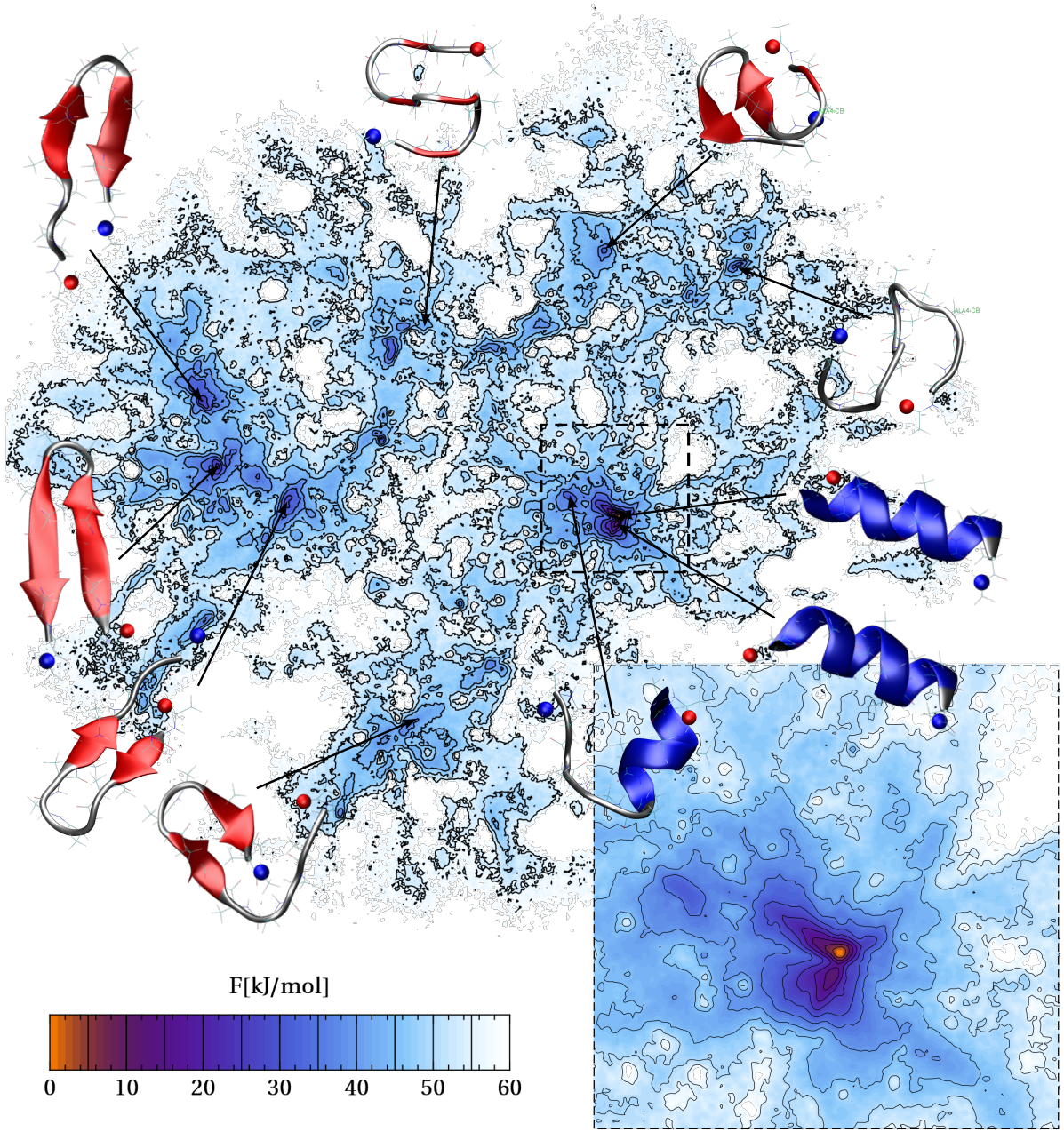
Sketch-map CVs give a very detailed picture, where each meta-stable configuration is clearly singled out



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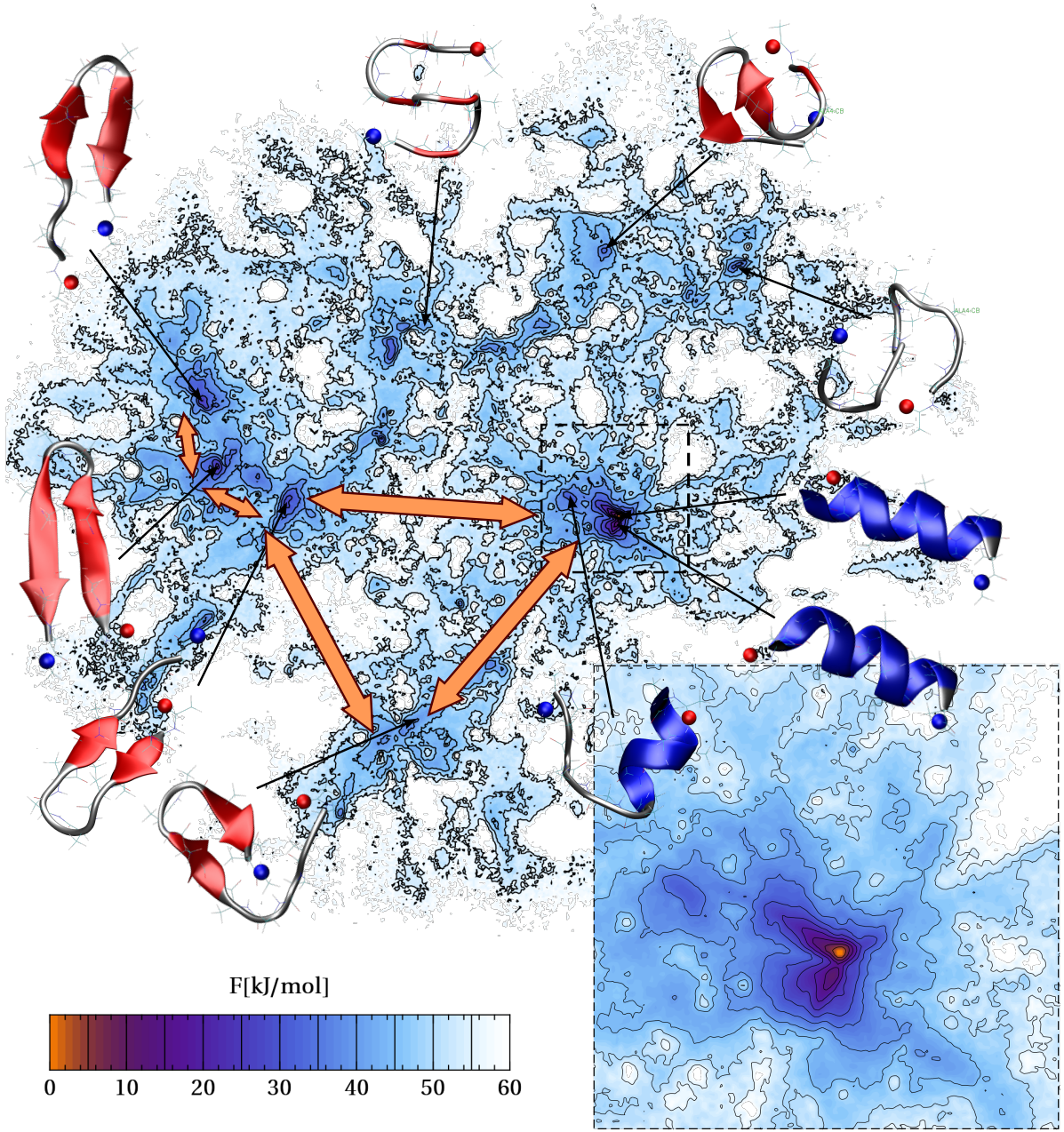
Can be used effectively for accelerated dynamics:
field-overlap metadynamics



Tribello, Ceriotti, Parrinello, PNAS 2012

Accelerating rare events

- When there are high **free energy barriers** it takes very long simulations to see interesting events
- Use a **bias** to discourage the system from staying in the same configuration and explore more efficiently (e.g. metadynamics)

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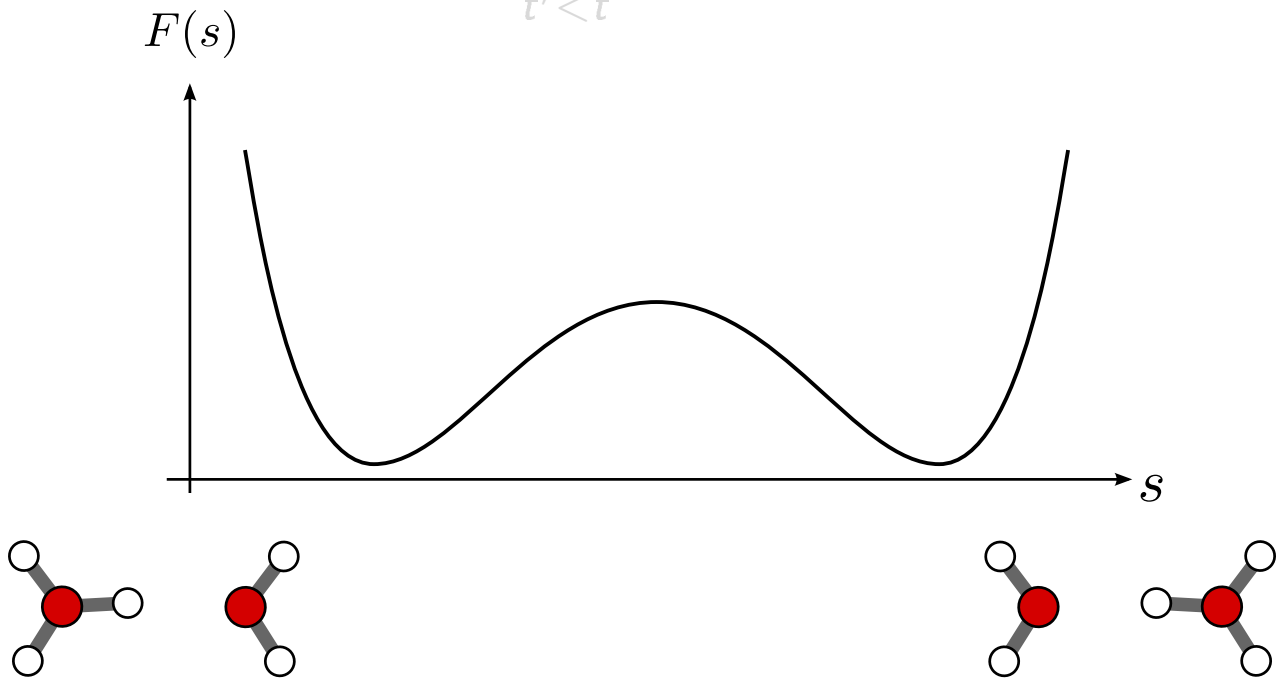

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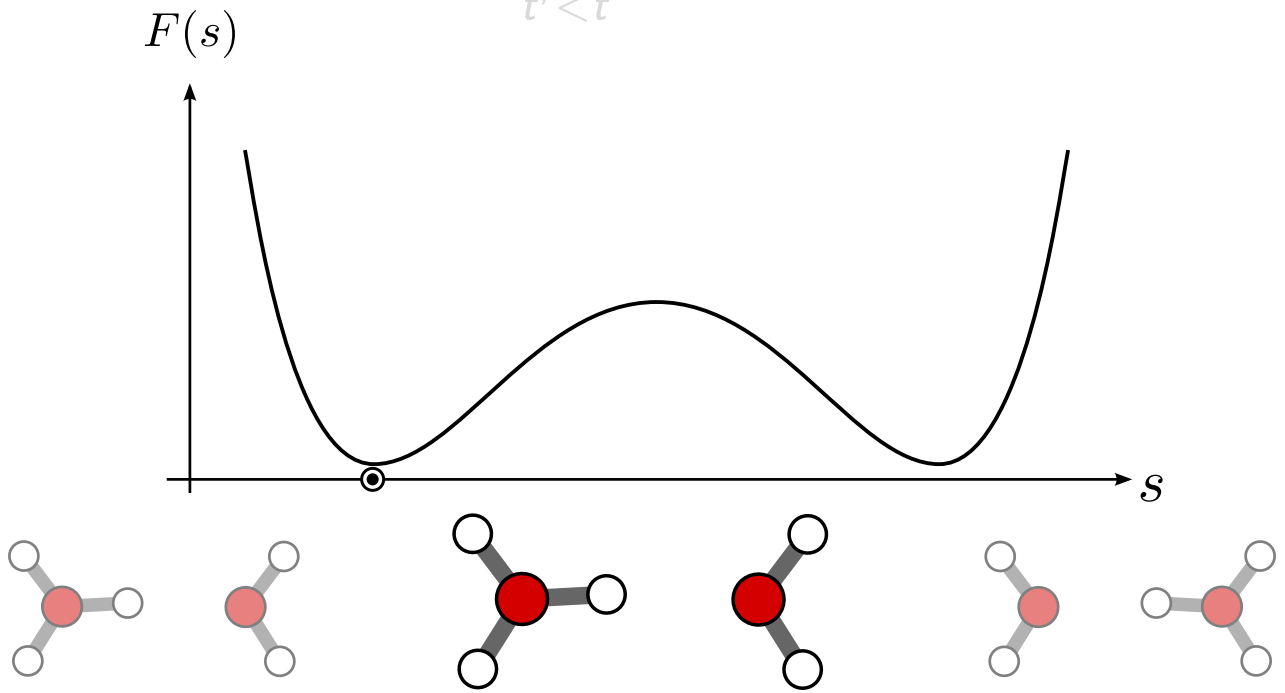

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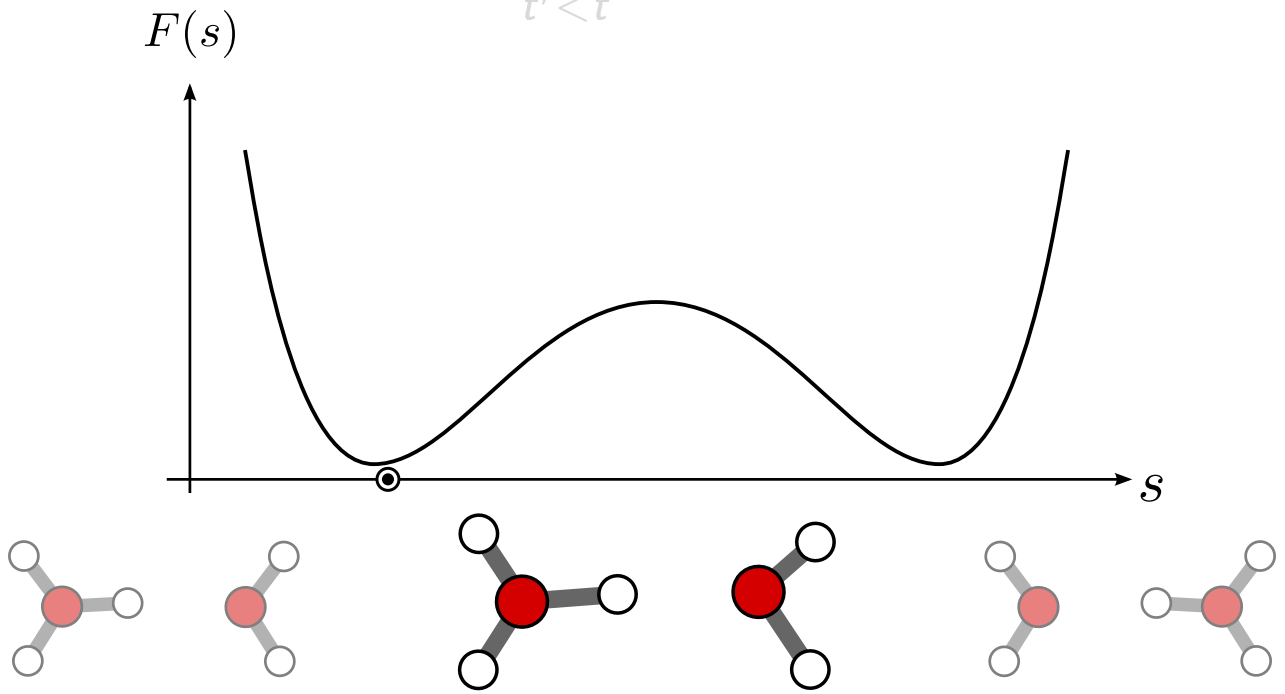

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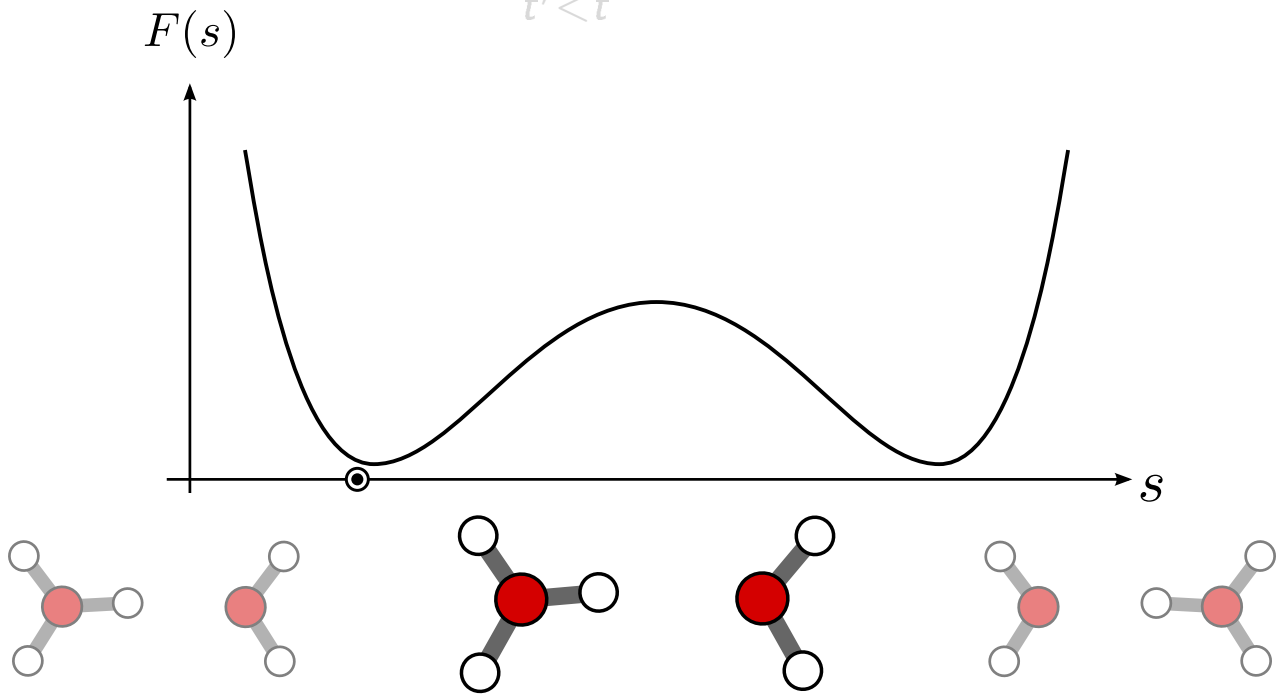

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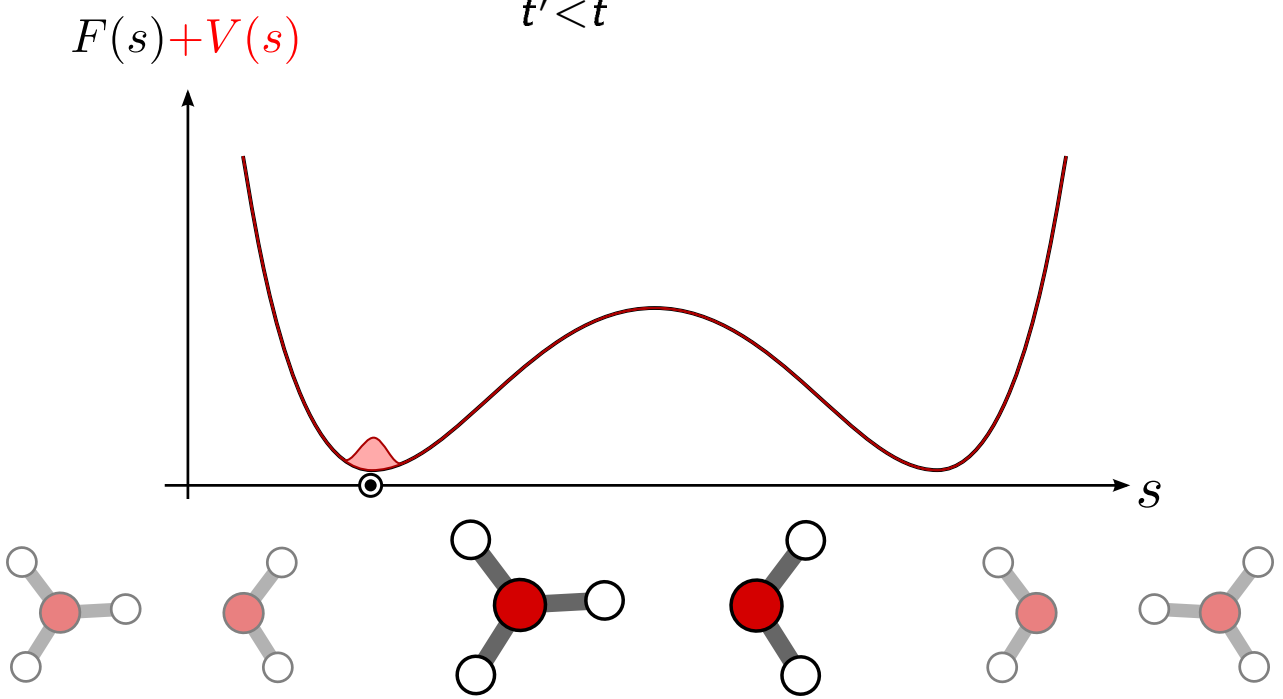

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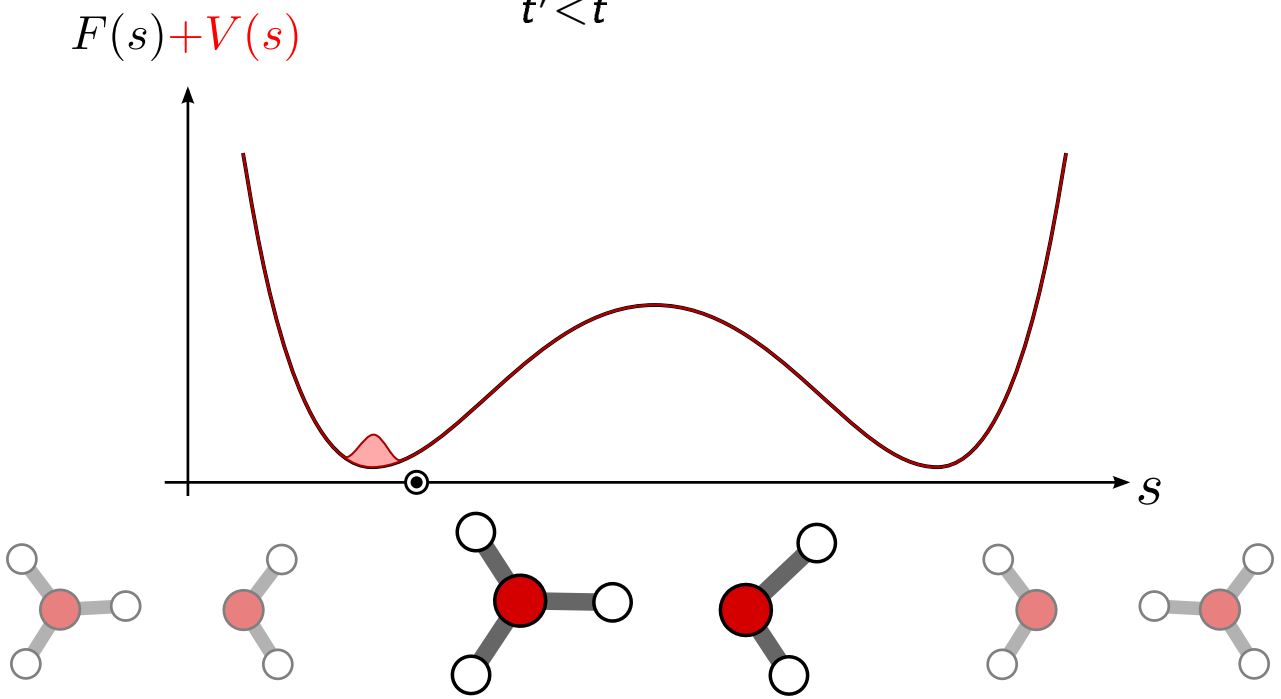

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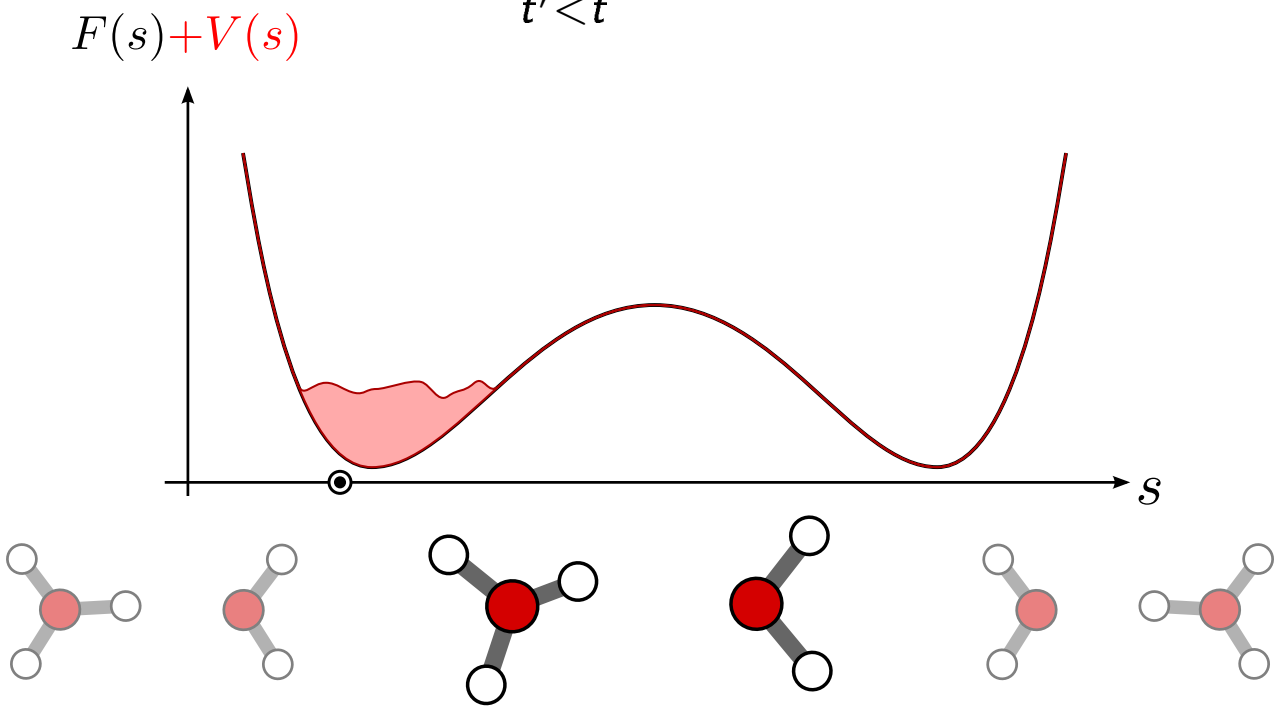

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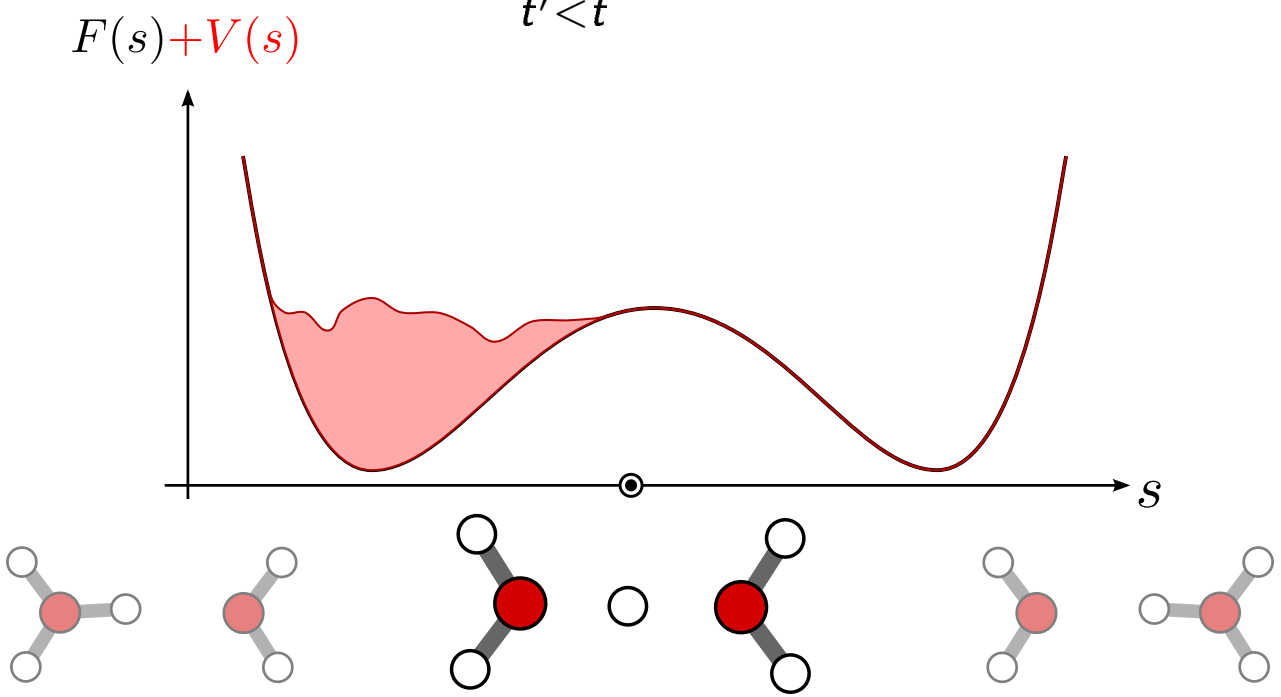

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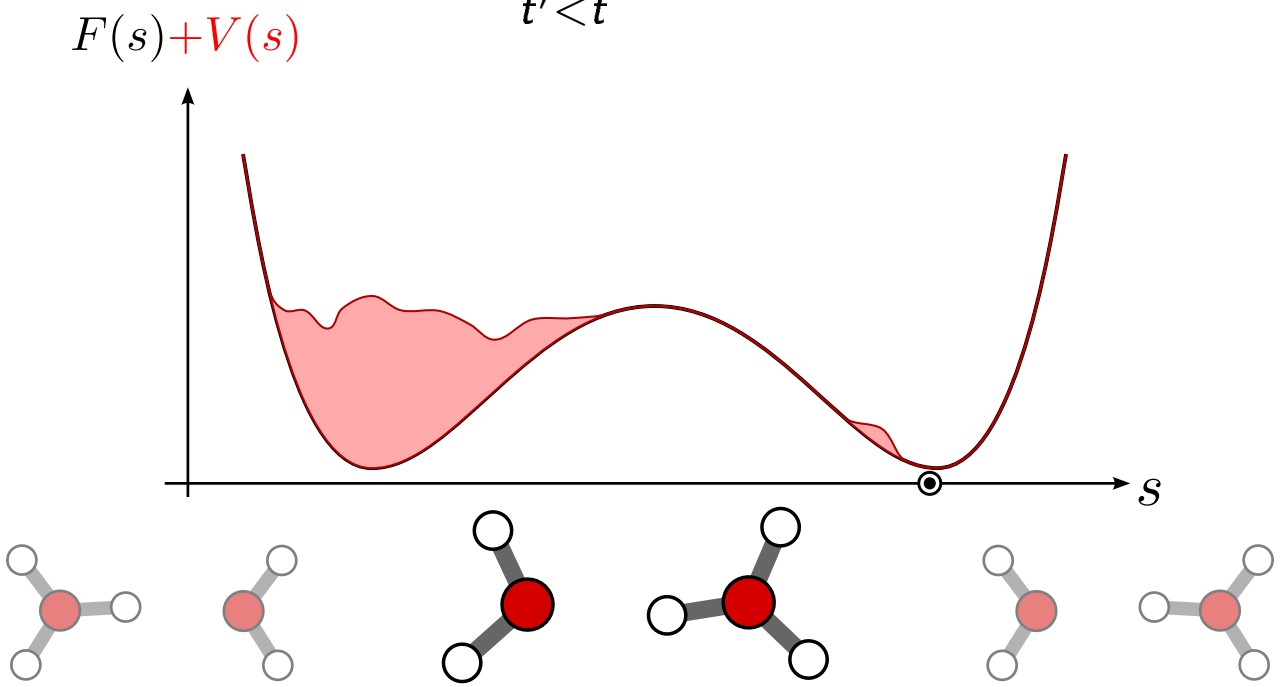

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Metadynamics and Hidden CVs

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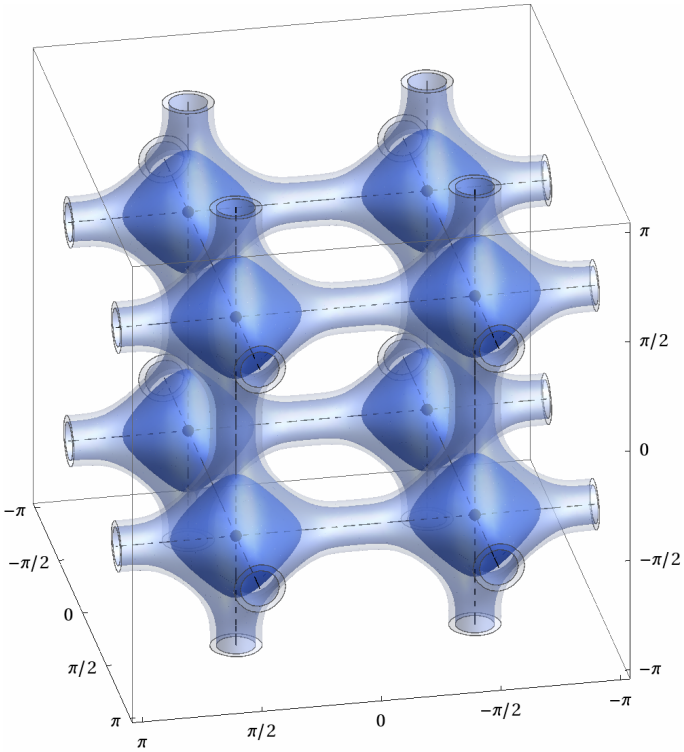
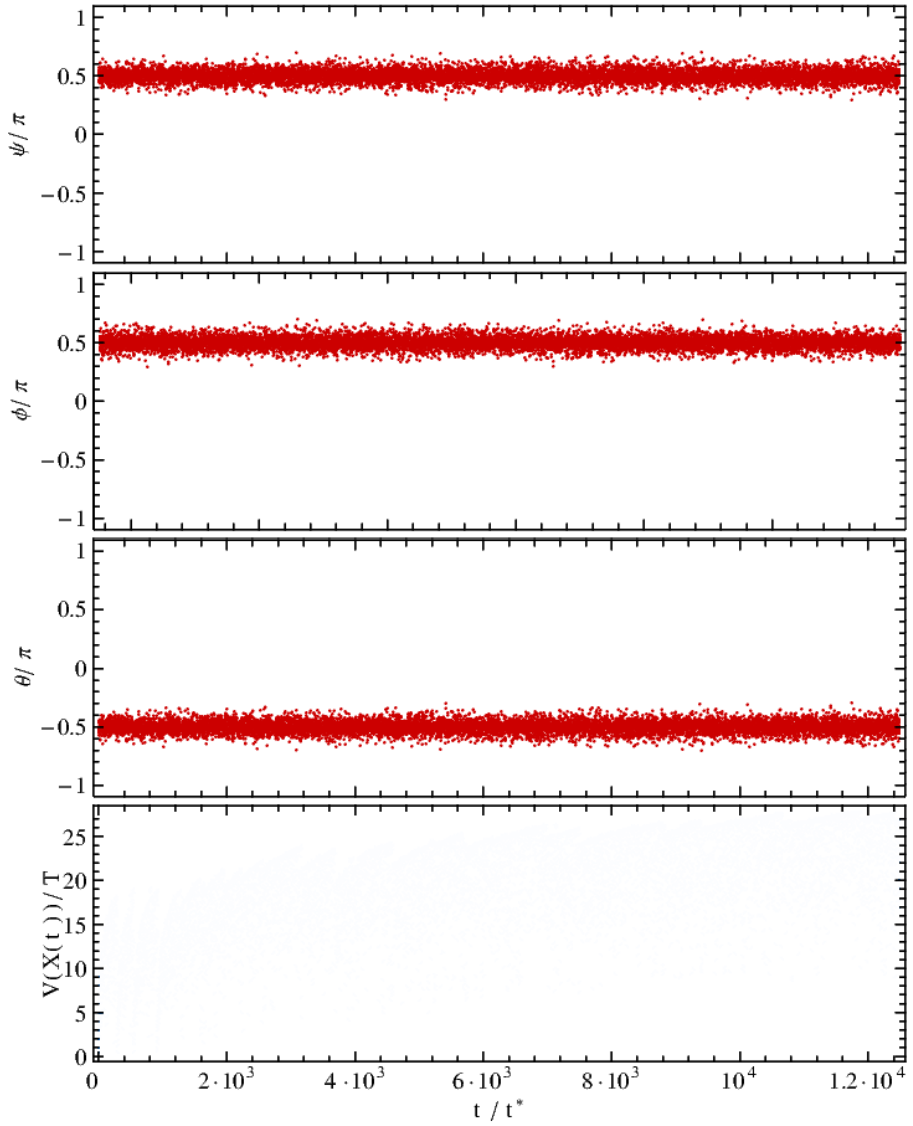
- **Field-overlap** using (2d!) **sketch-map** coordinates thoroughly samples in all directions





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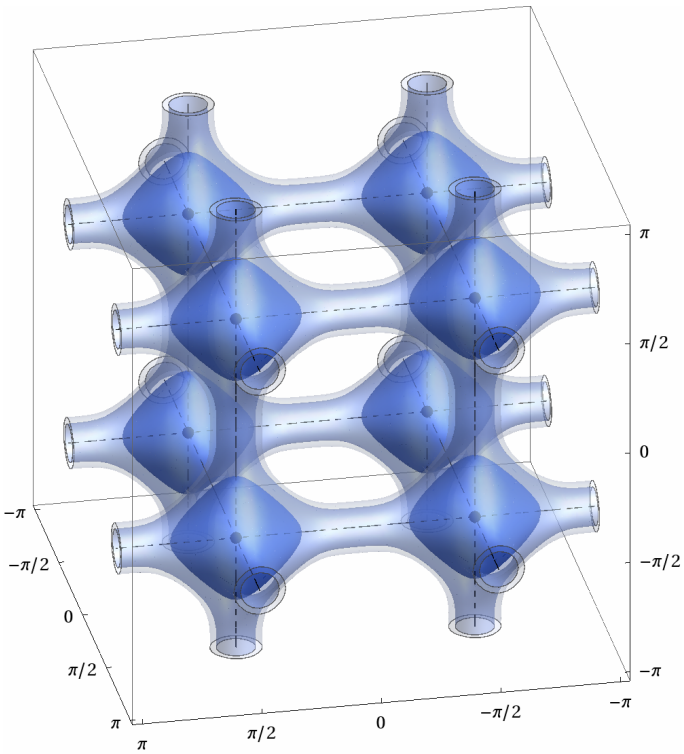

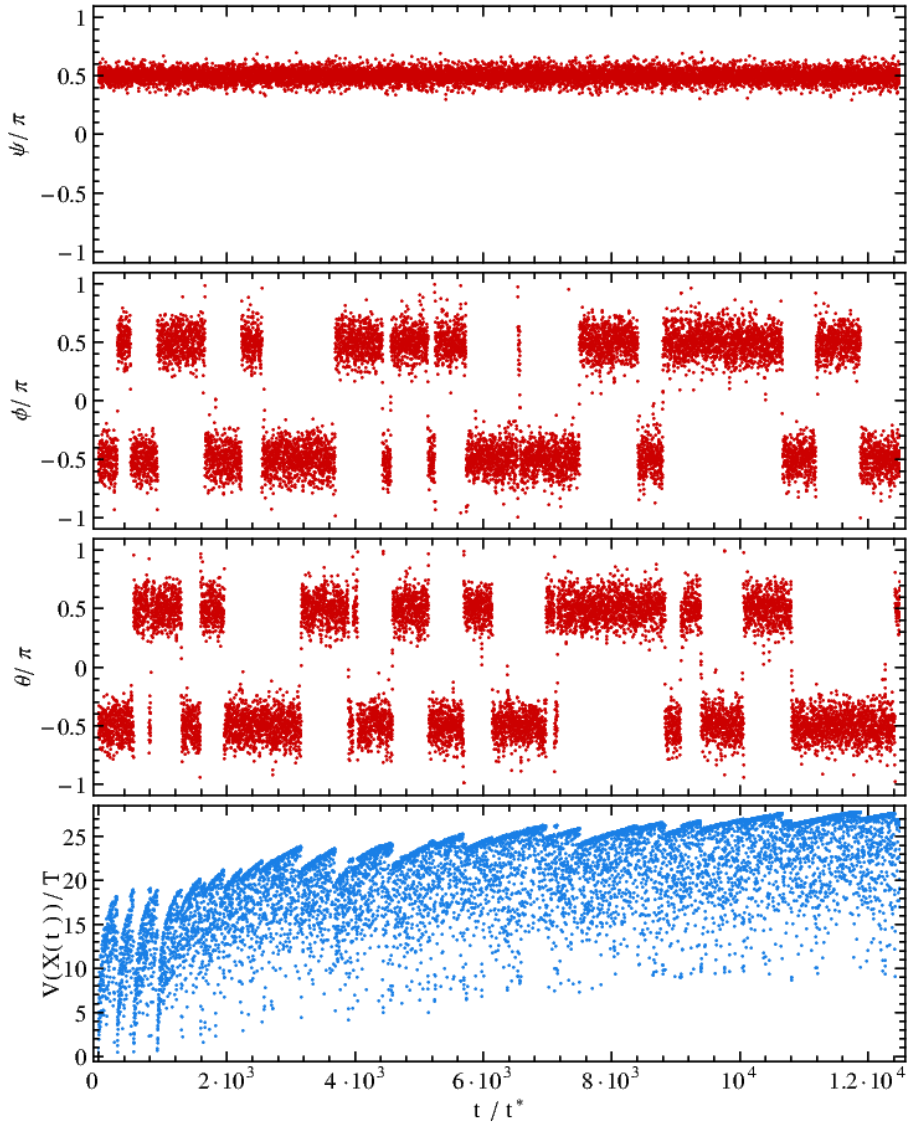

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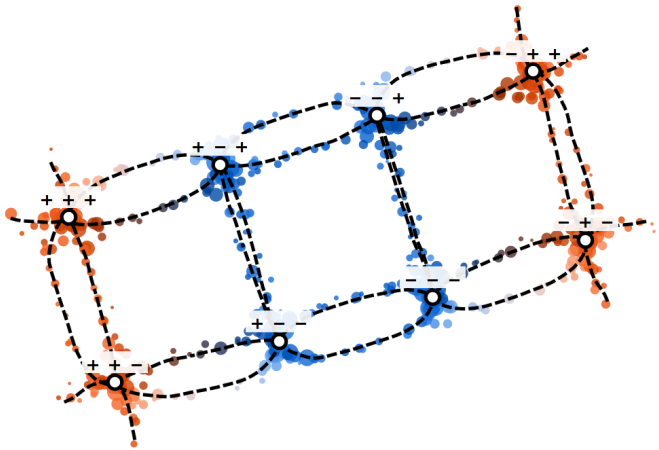
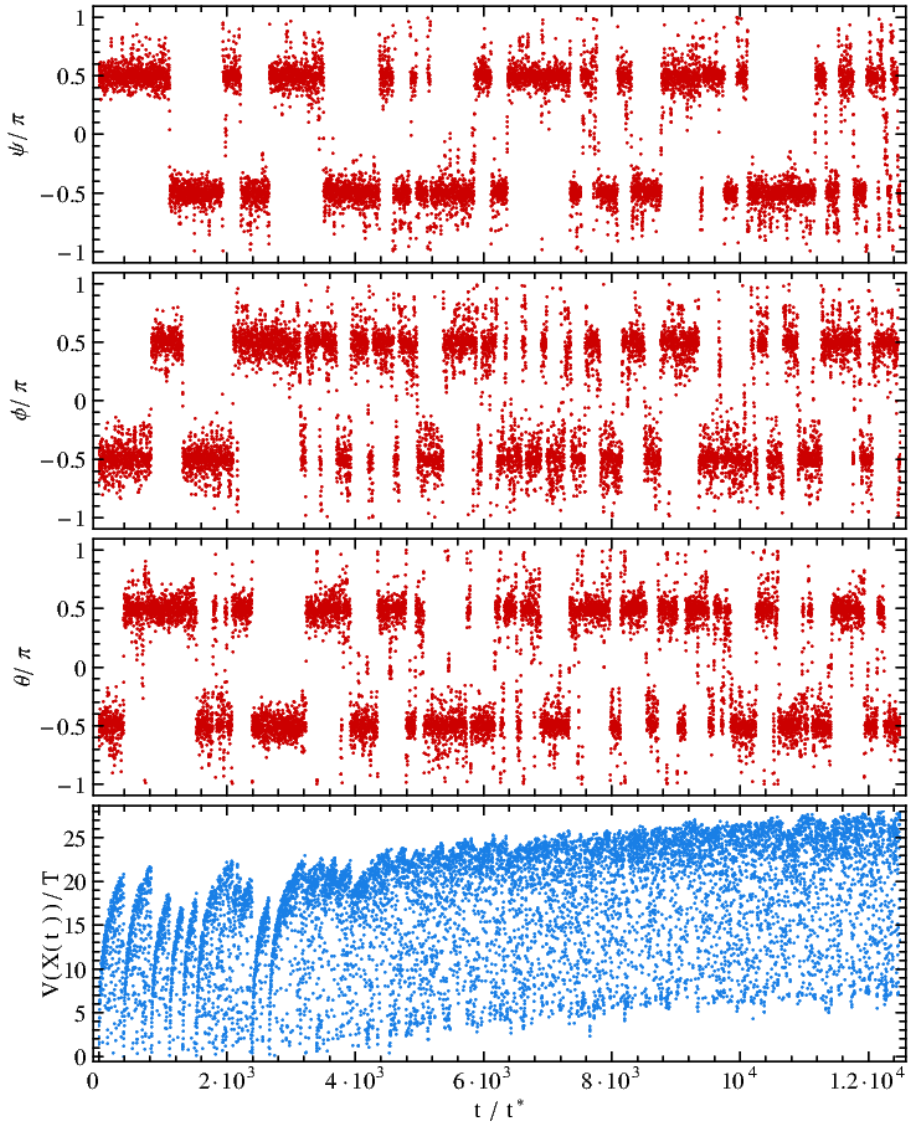
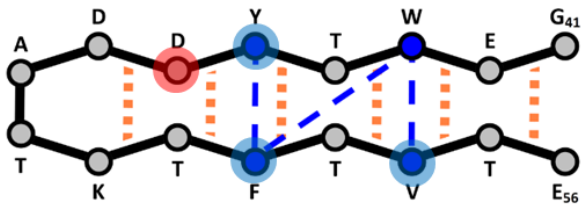




β-hairpin Mutants

- Sketch map can be used to compare the stability of different systems
- Consider a 16-residue hairpin-folding protein fragment
  - Many structures are locally stable other than the "folded" hairpin
  - We do a series of point mutations, and see how they affect stability



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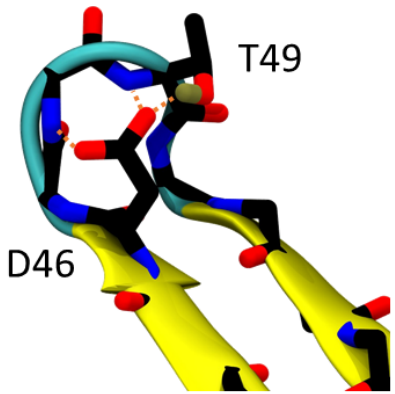

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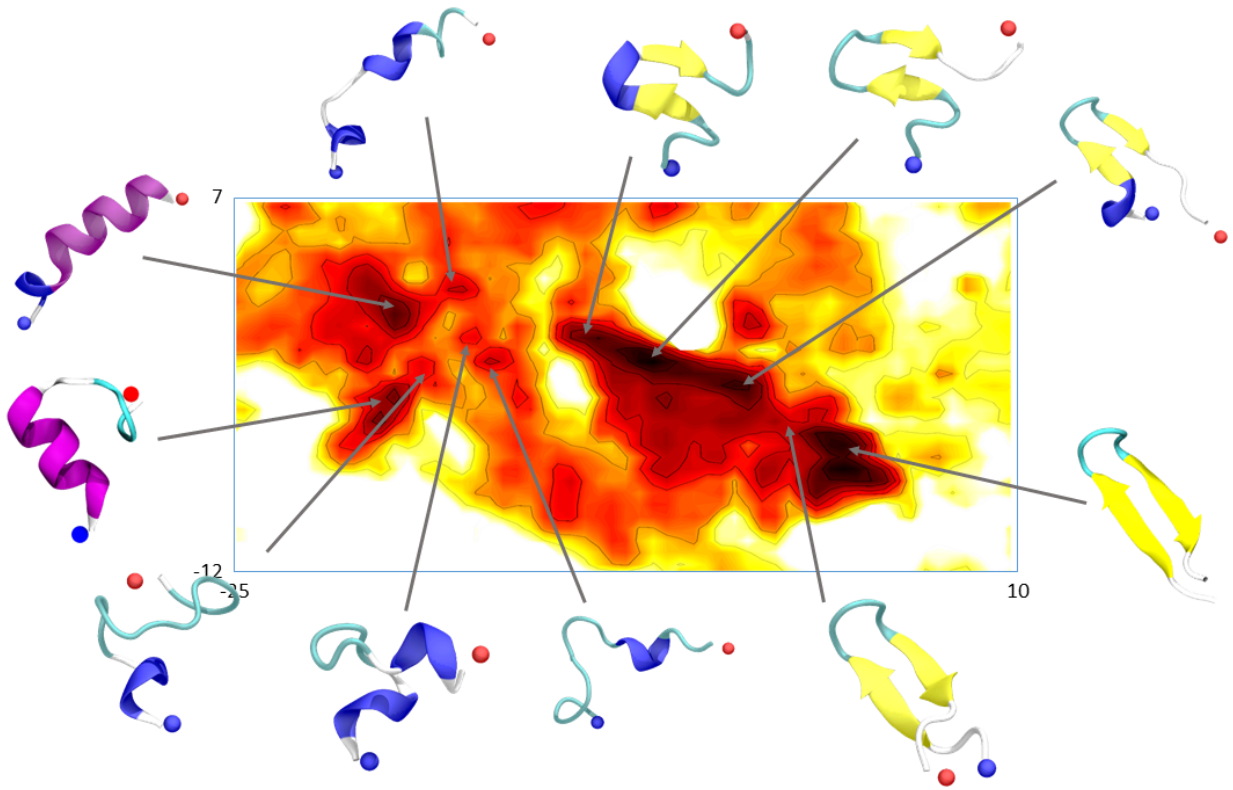

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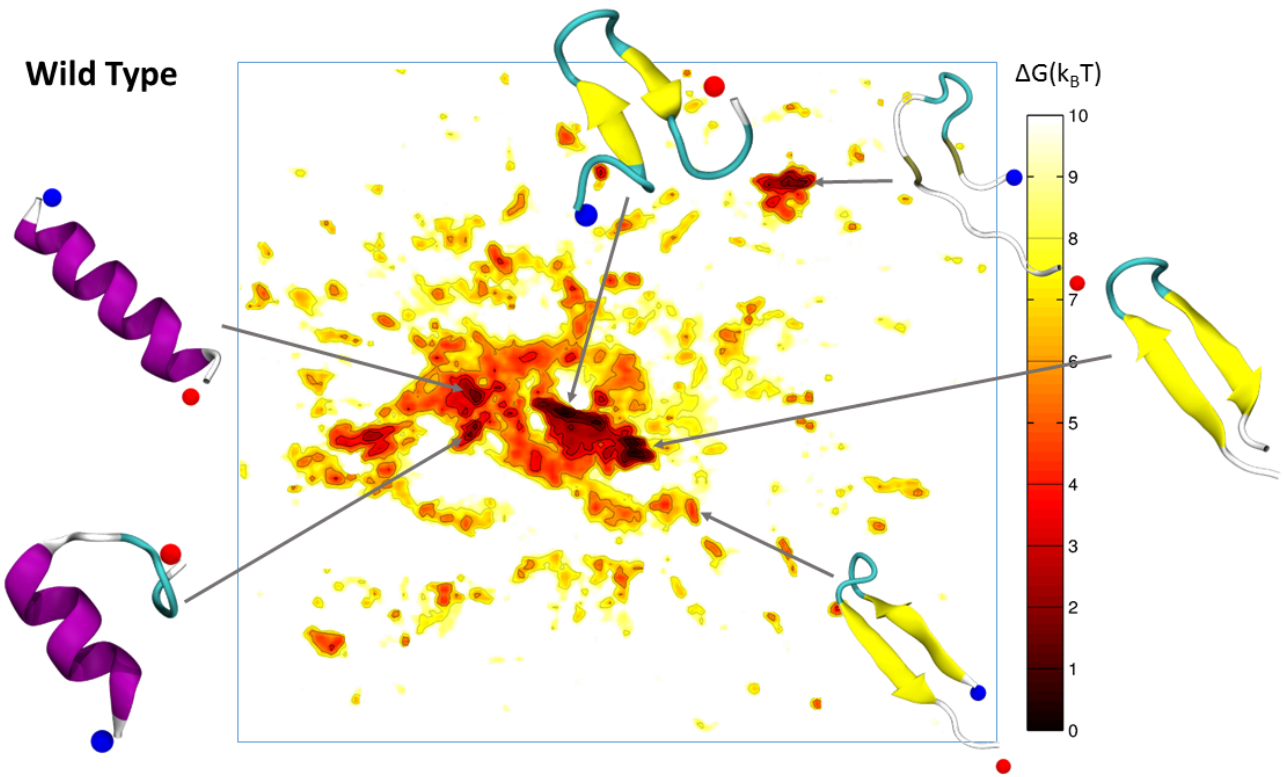

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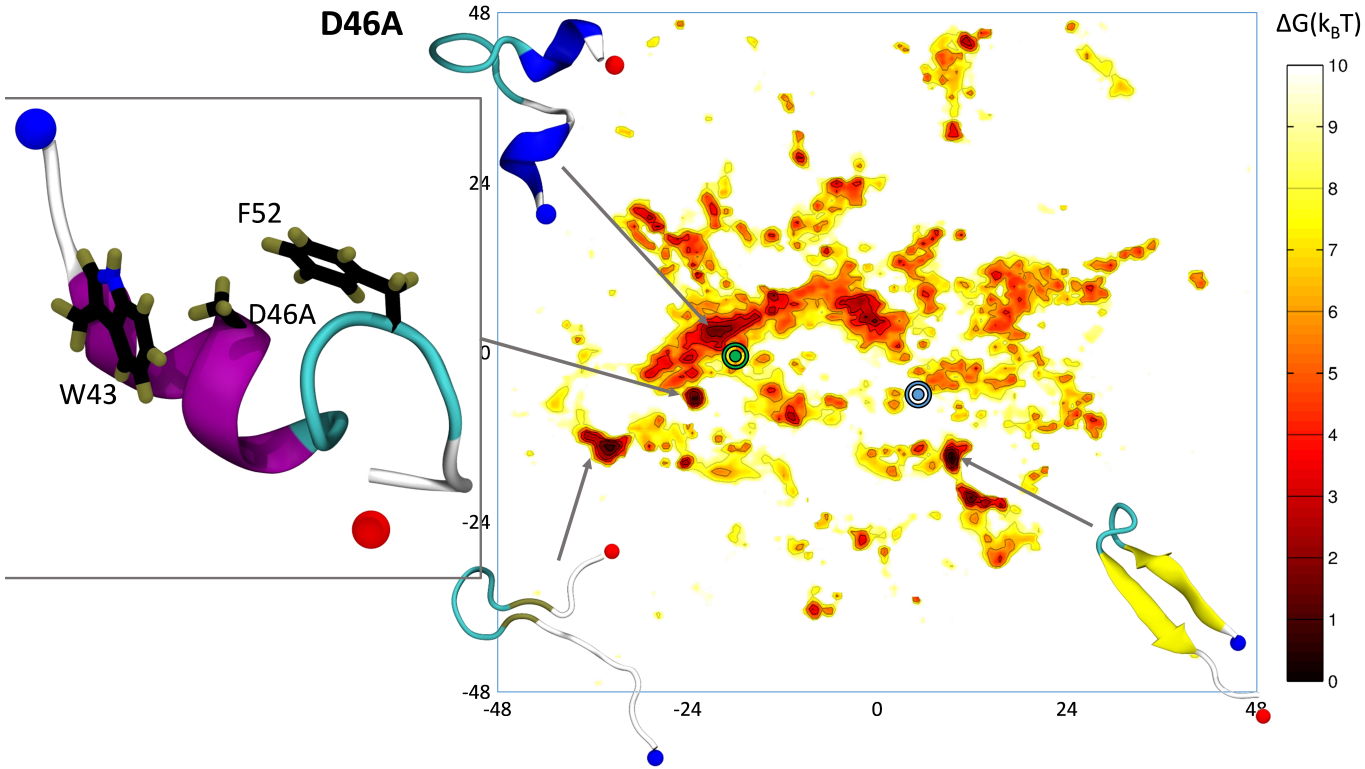

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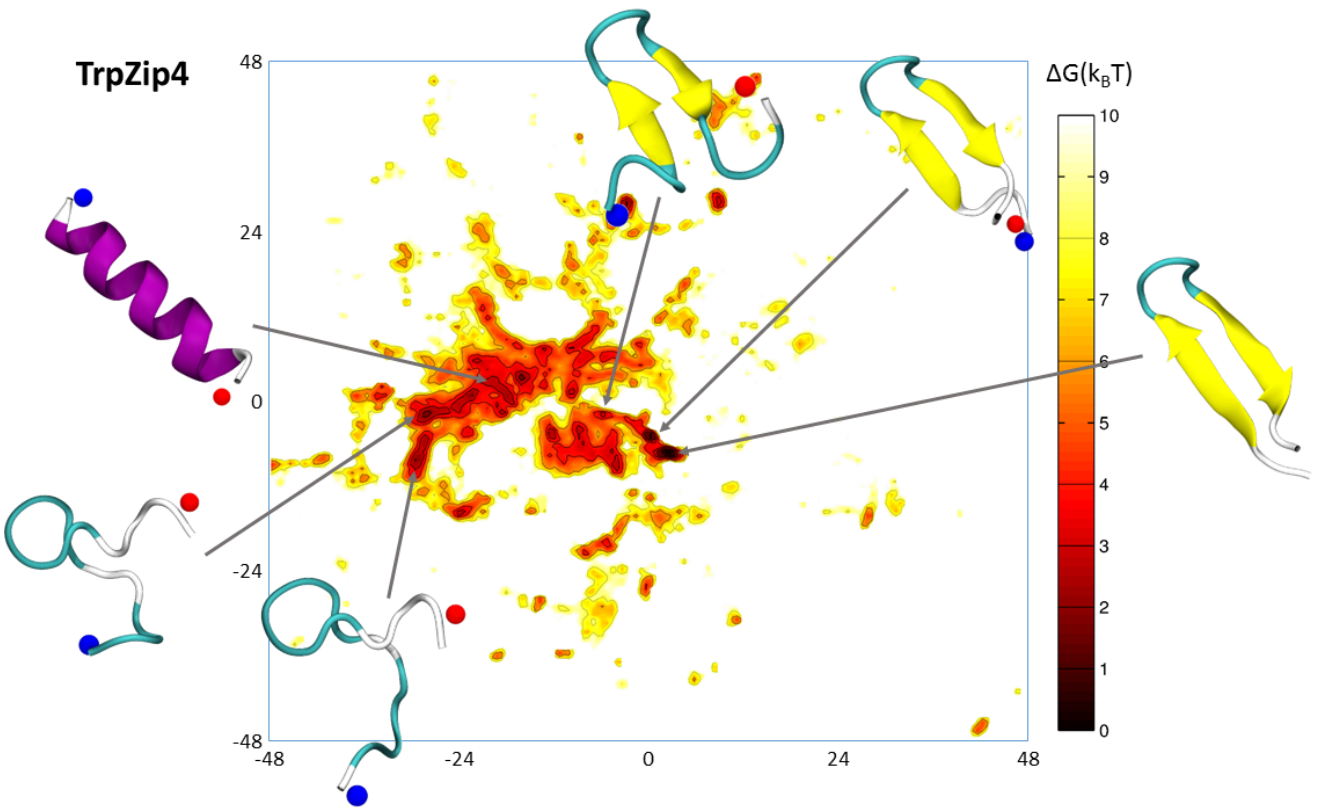

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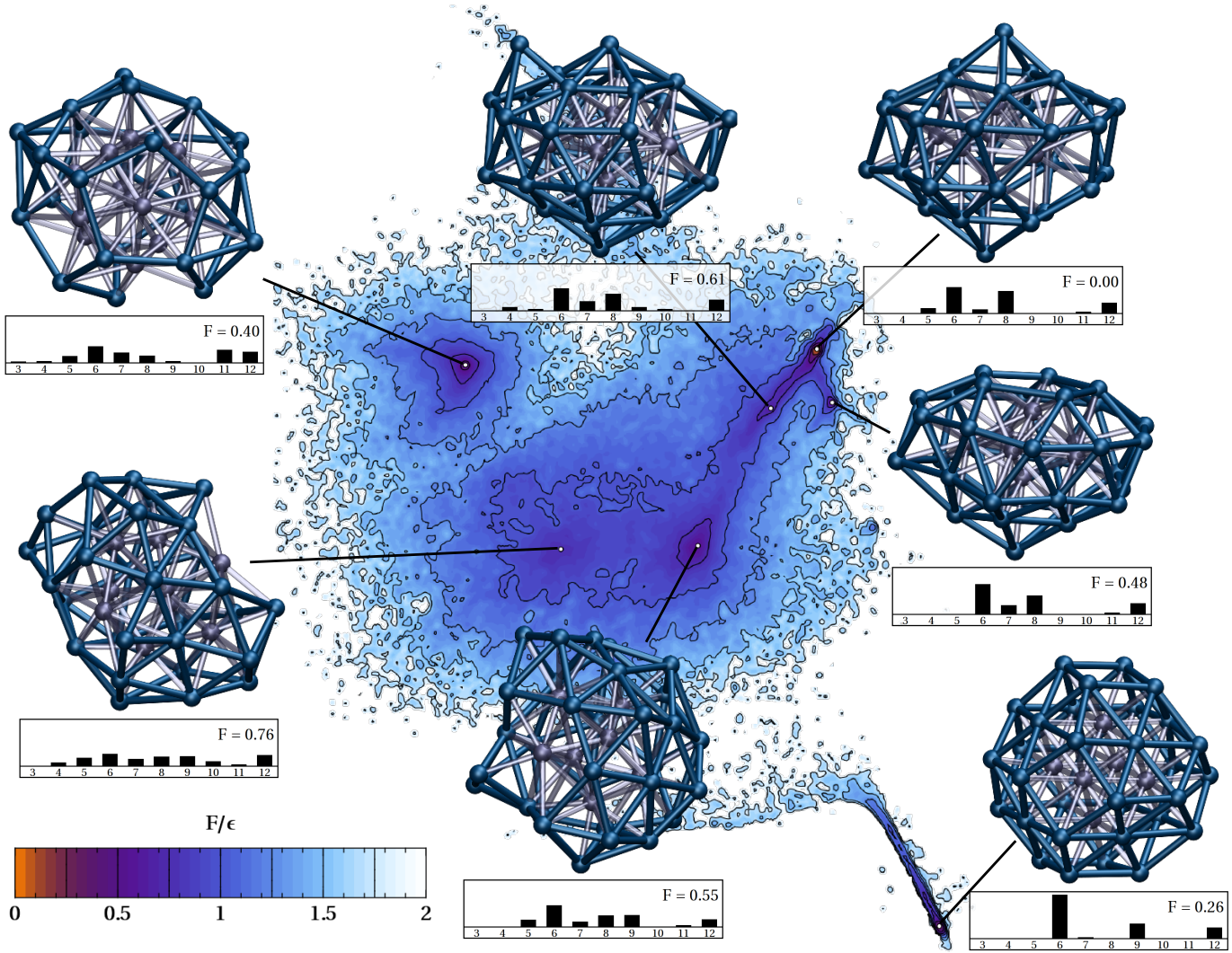
From clusters to defects in the bulk

- Start building a map for a Lennard-Jones cluster
- The same map describes the cluster across phase transitions
- ... and can even recognize the nature of defects in a bulk system!



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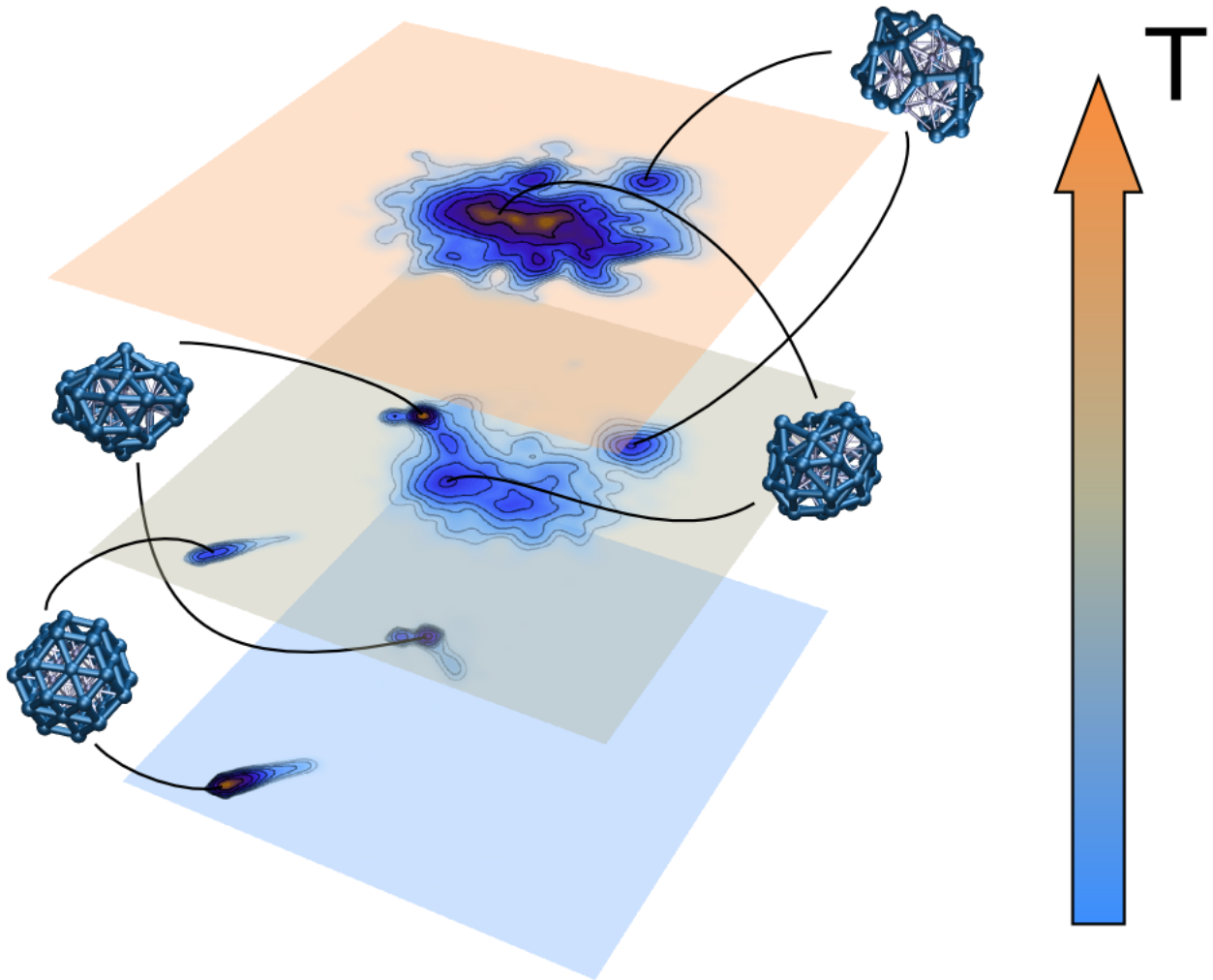

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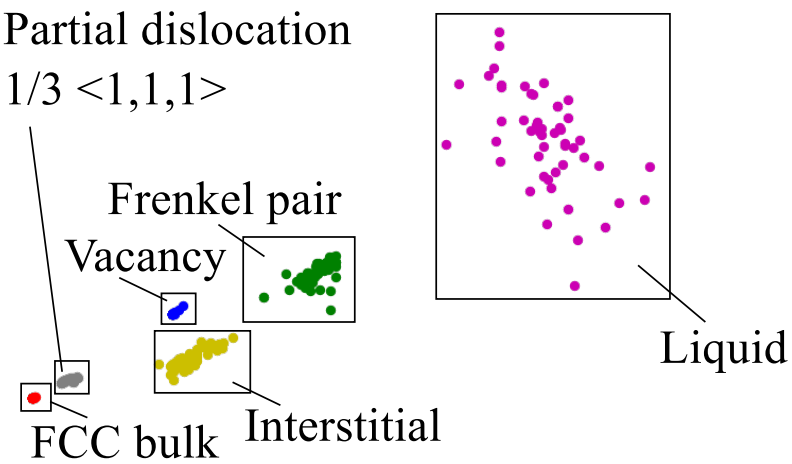
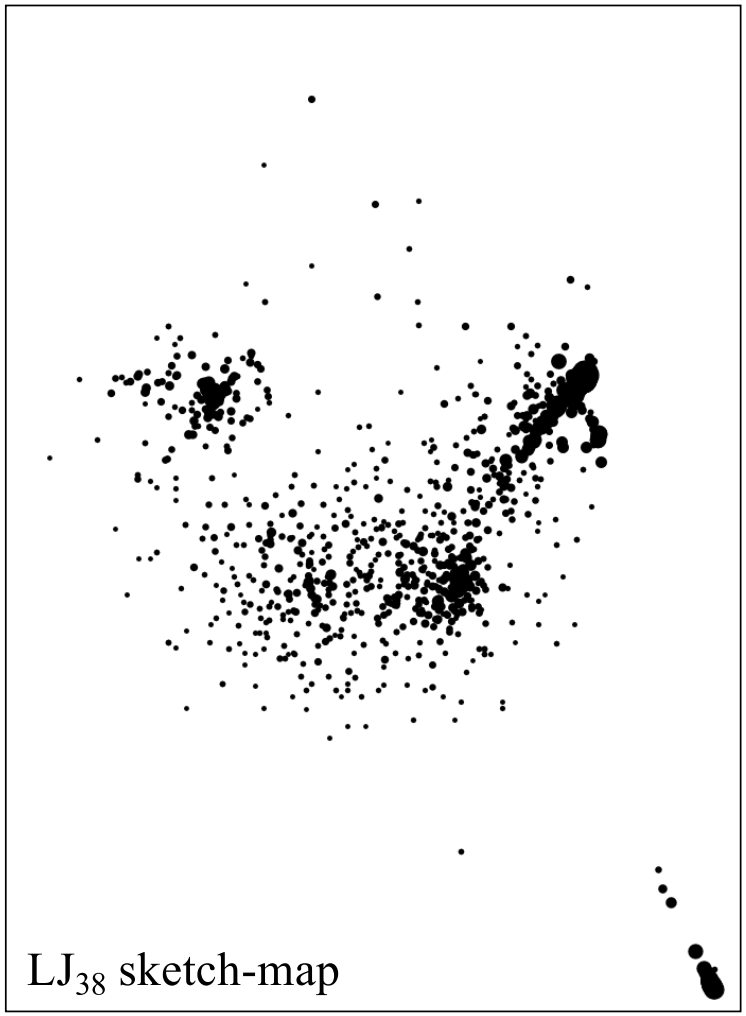
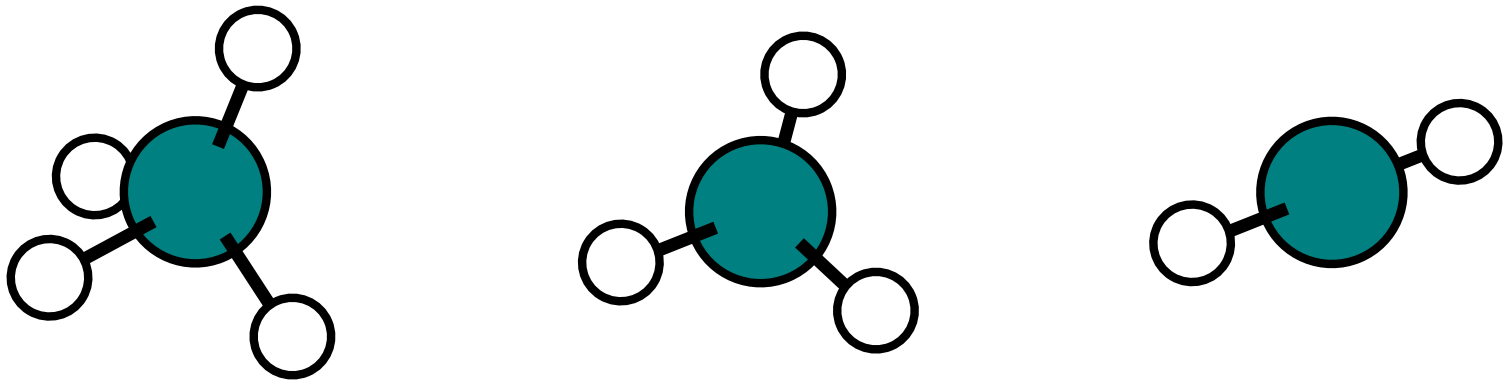




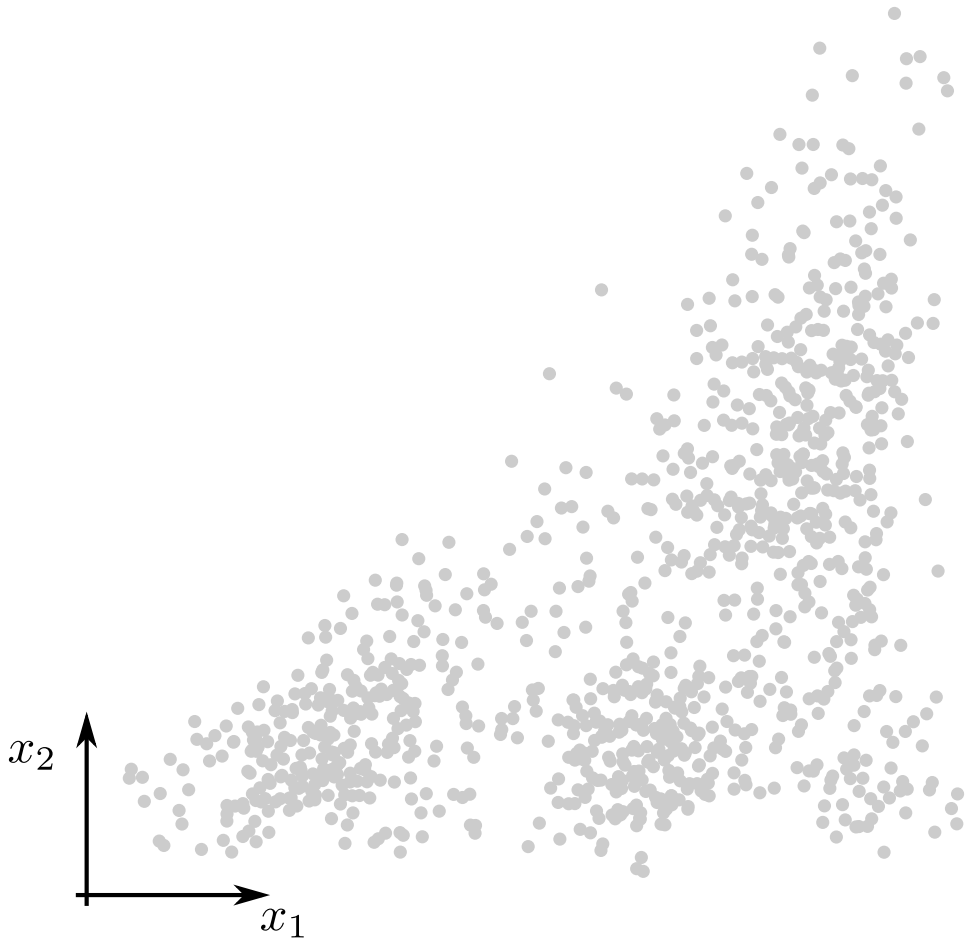
Recognizing molecular patterns

- We still need an effective high-dimensional description to start with
- "Chemical intuition" builds on recognizing recurring patterns in atomic configurations
- Automatic scheme to single out structural motifs in atomistic simulations



Probabilistic Analysis of Molecular Motifs

- Evaluate the probability distribution of molecular structures
- Cluster it around the modes of the distribution
- Naturally gives a fuzzy and continuous partitioning of configuration space



Piero Gasparotto & Michele Ceriotti, JCP 174110, 141 (2014)

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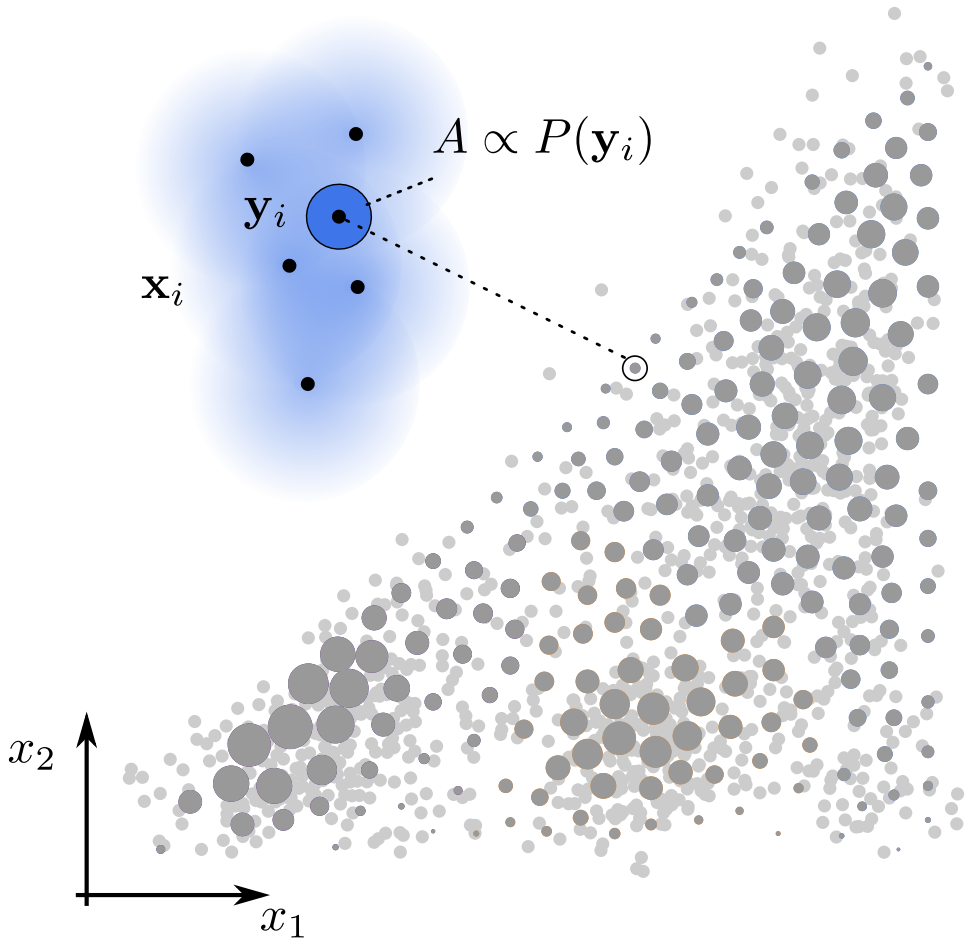

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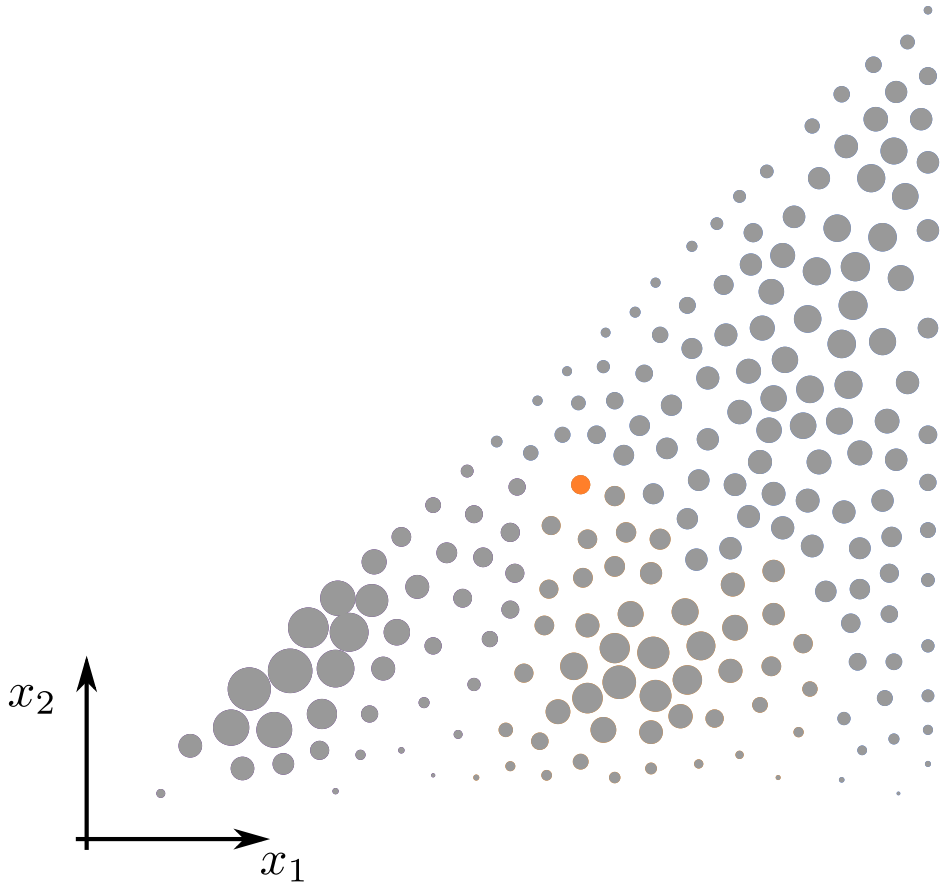

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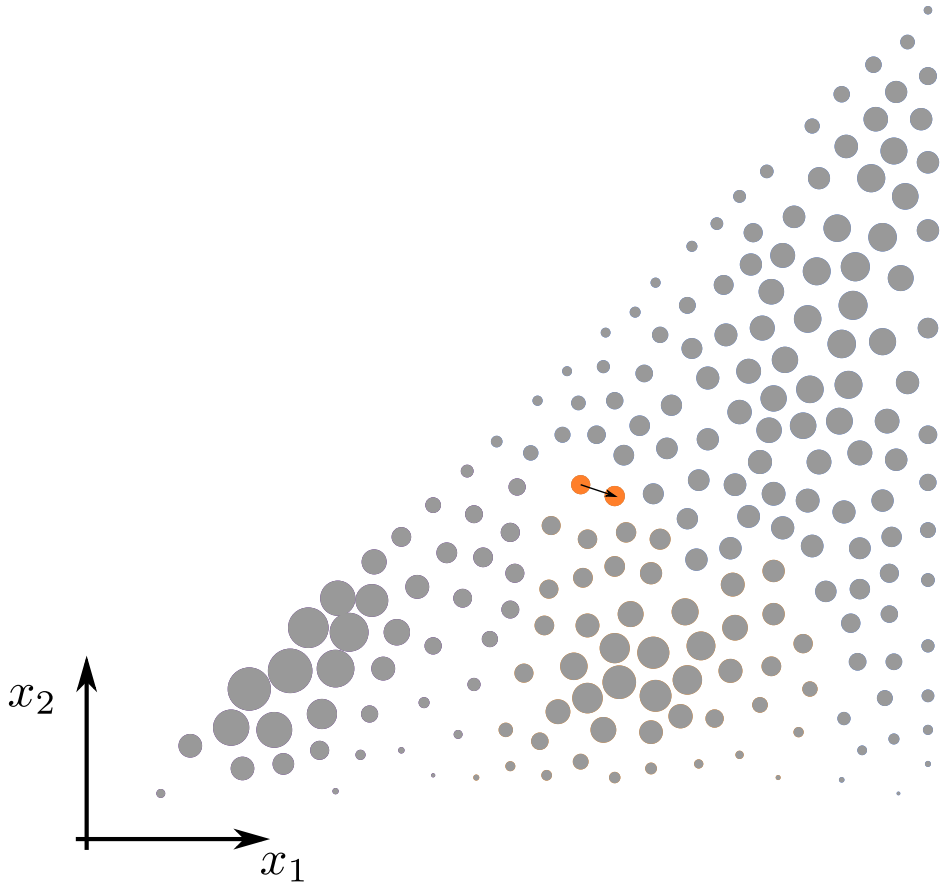

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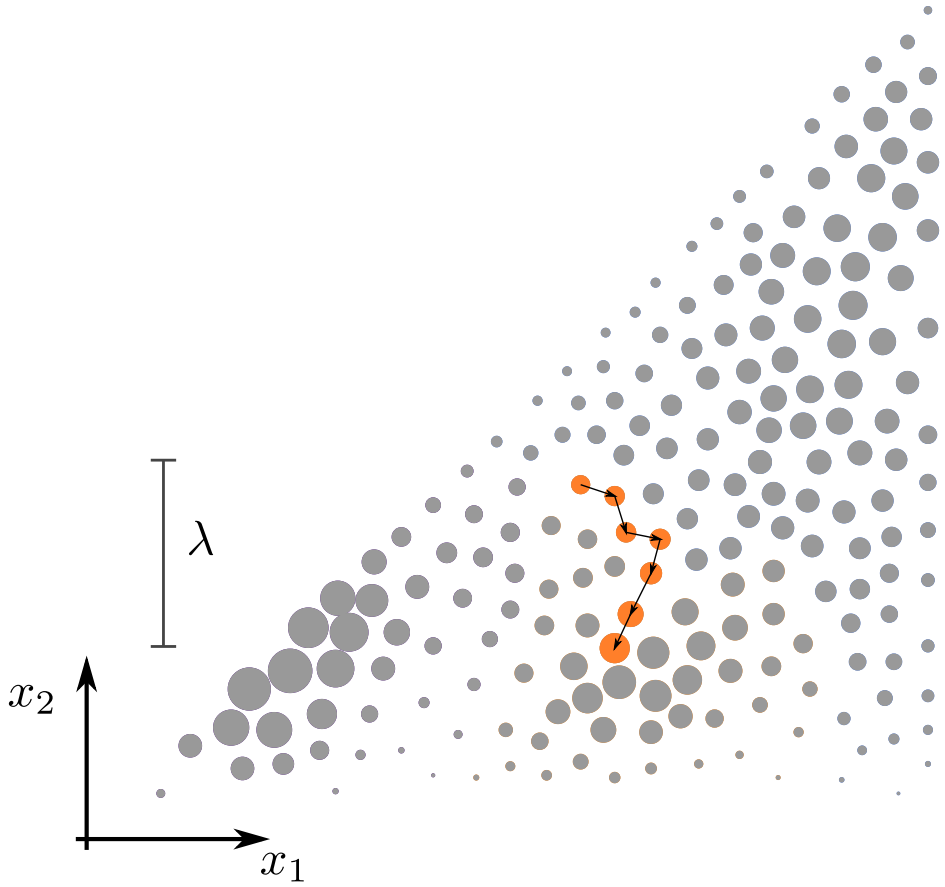

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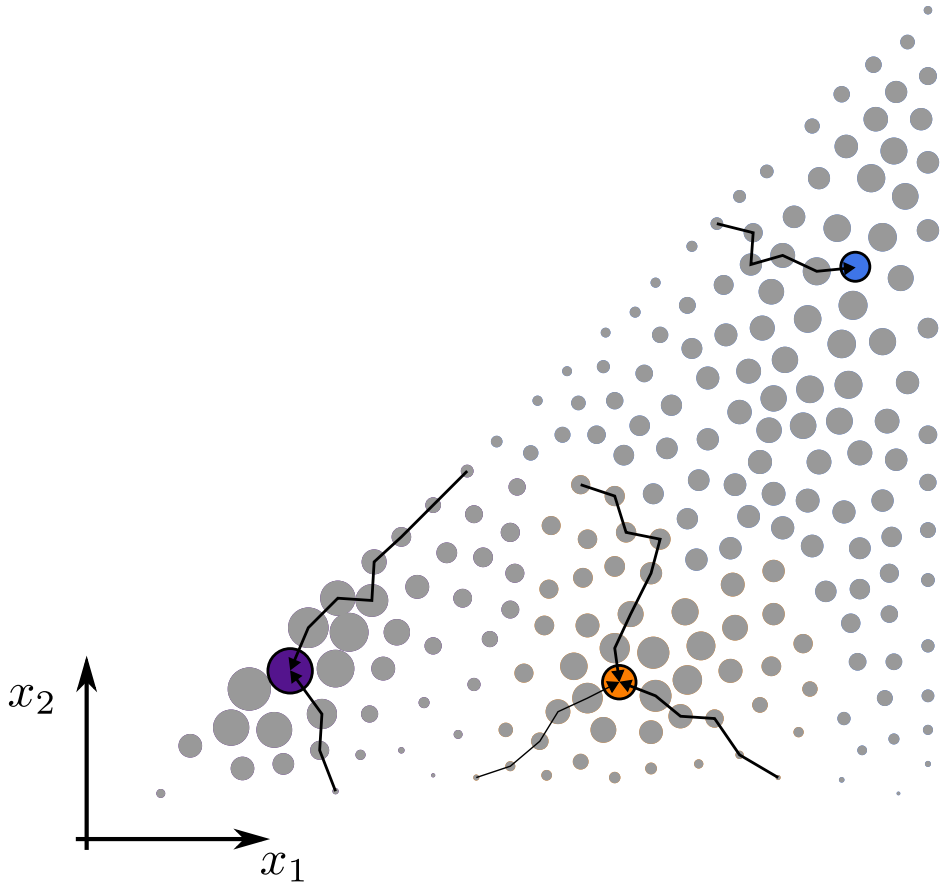

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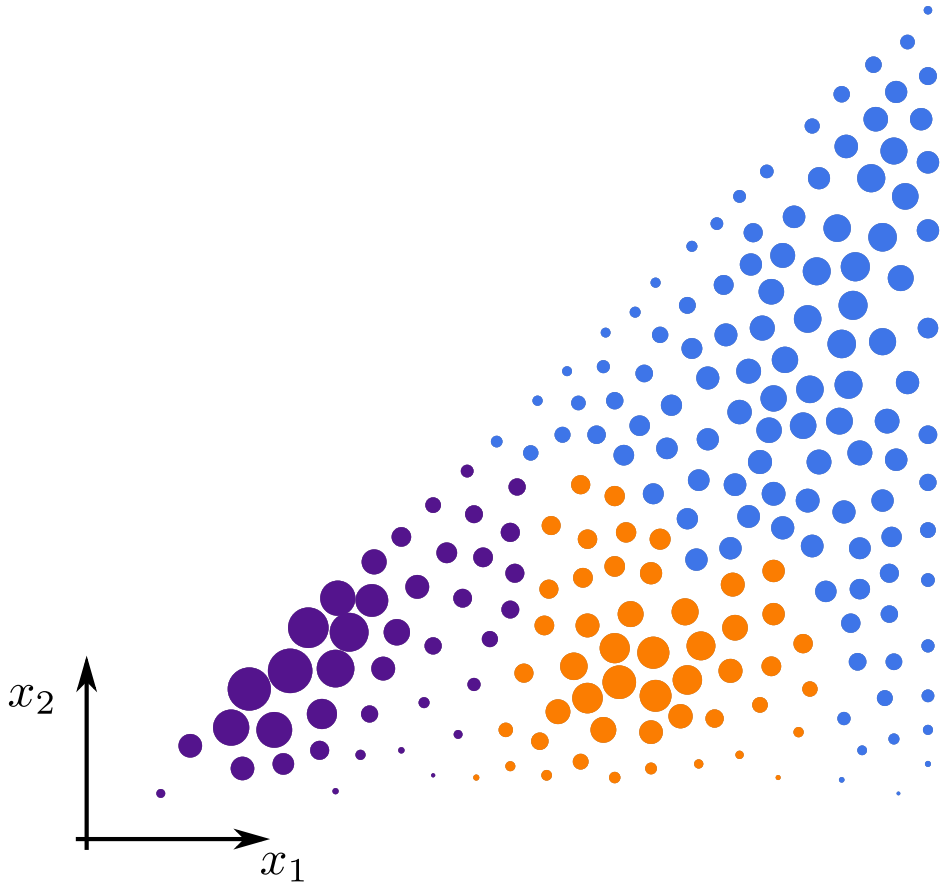

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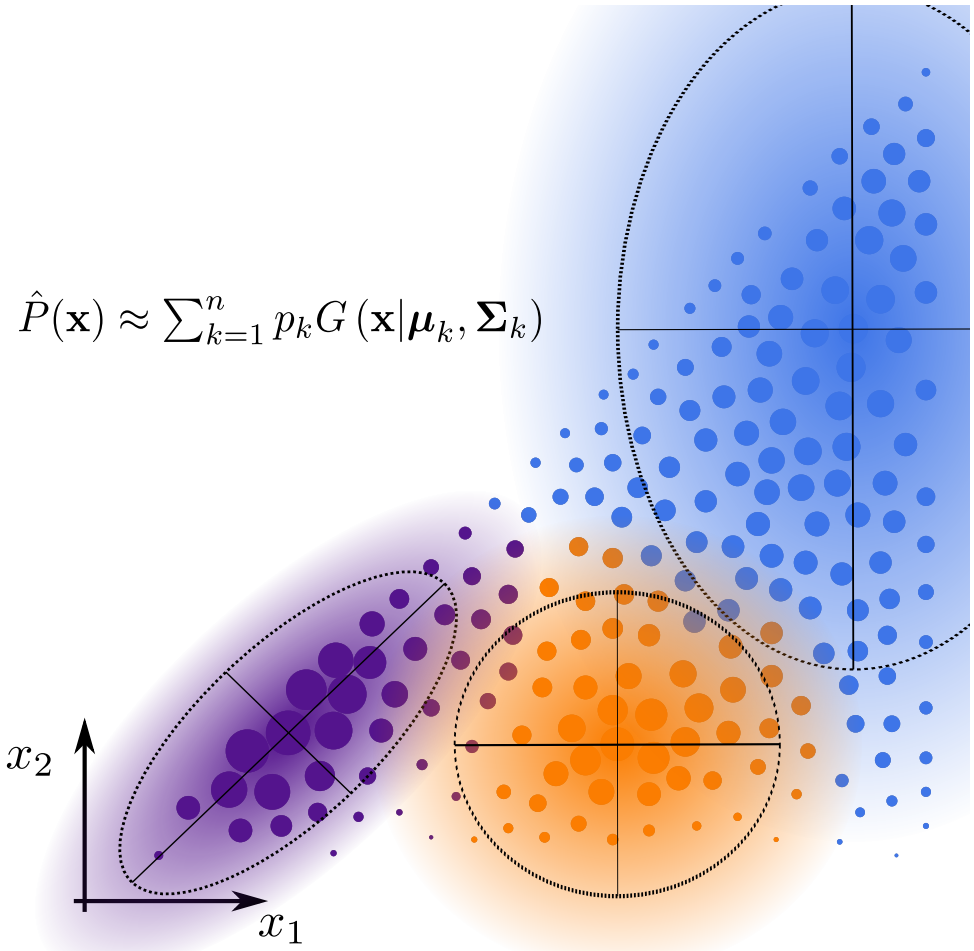

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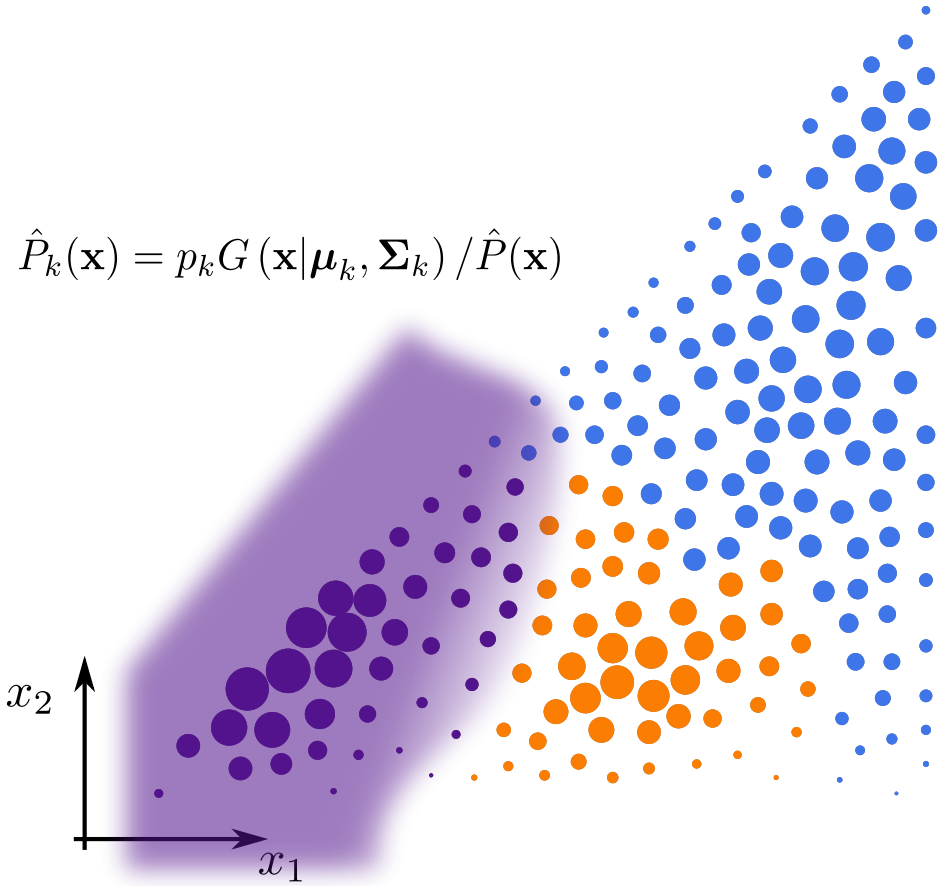

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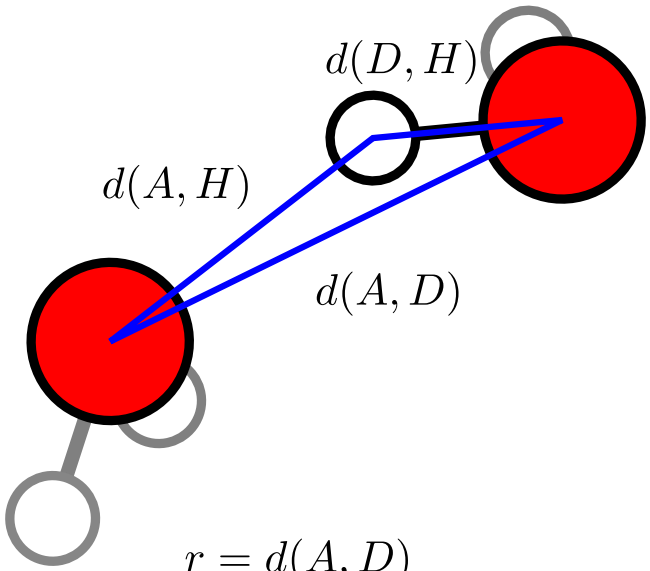
An Agnostic Definition of the H-Bond

- Most general description of a H-bond geometry: 3 distances
- PAMM recognizes multiple modes - one corresponds to the H-bond
- PAMM H-bond fingerprints can be used as HB counts, but are adaptive, unbiased and fuzzy



$$r = d(A,D)$$
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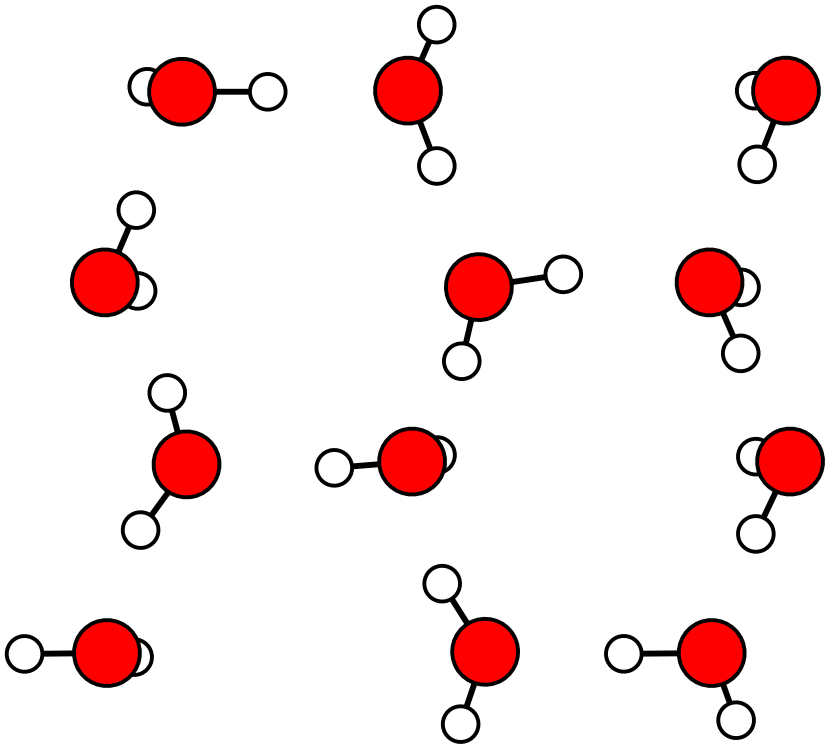

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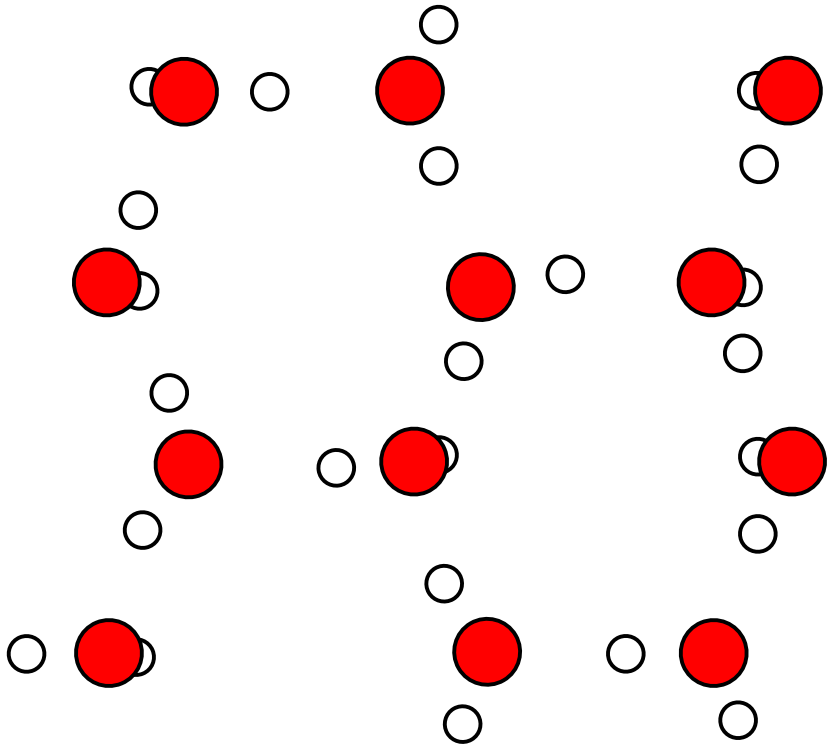

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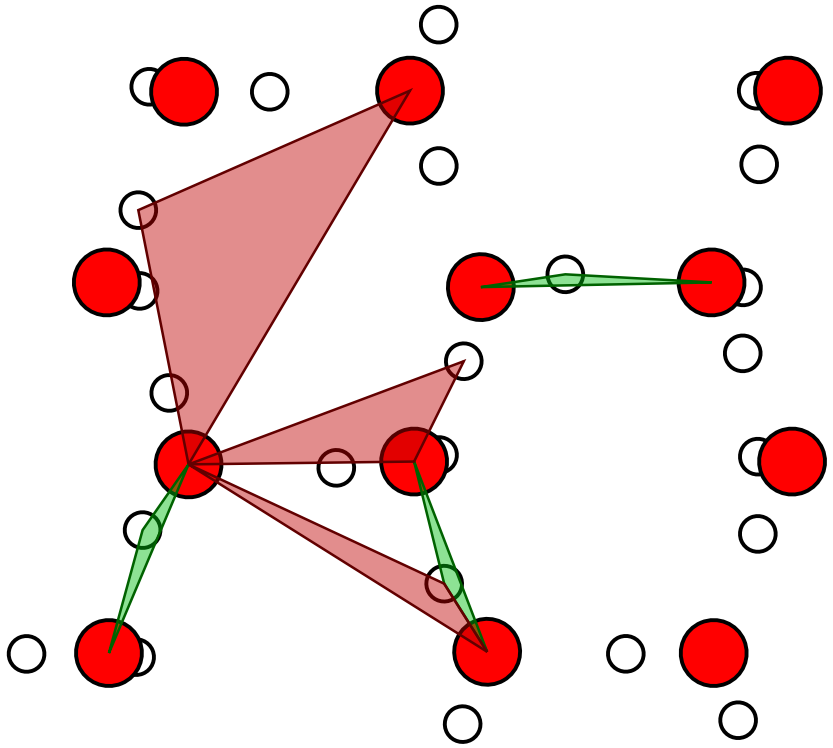

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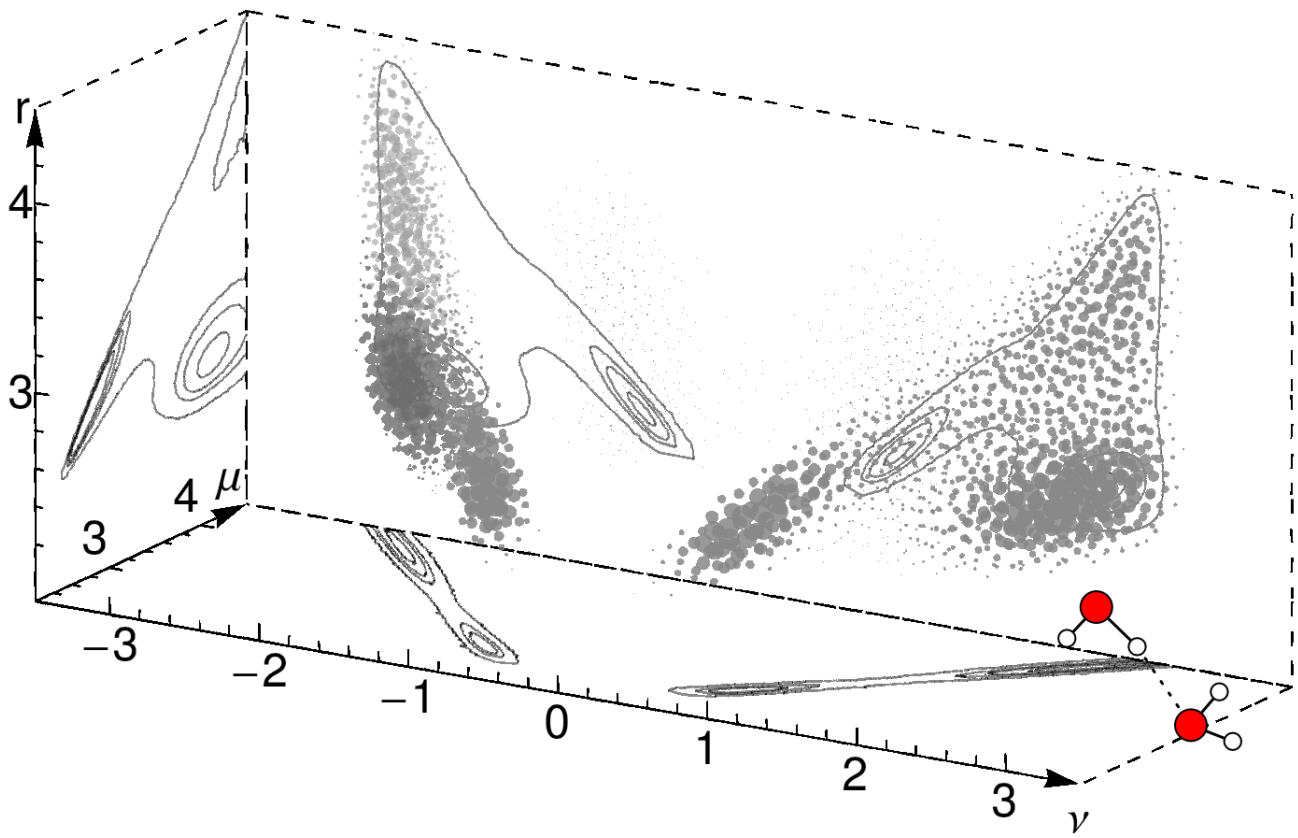

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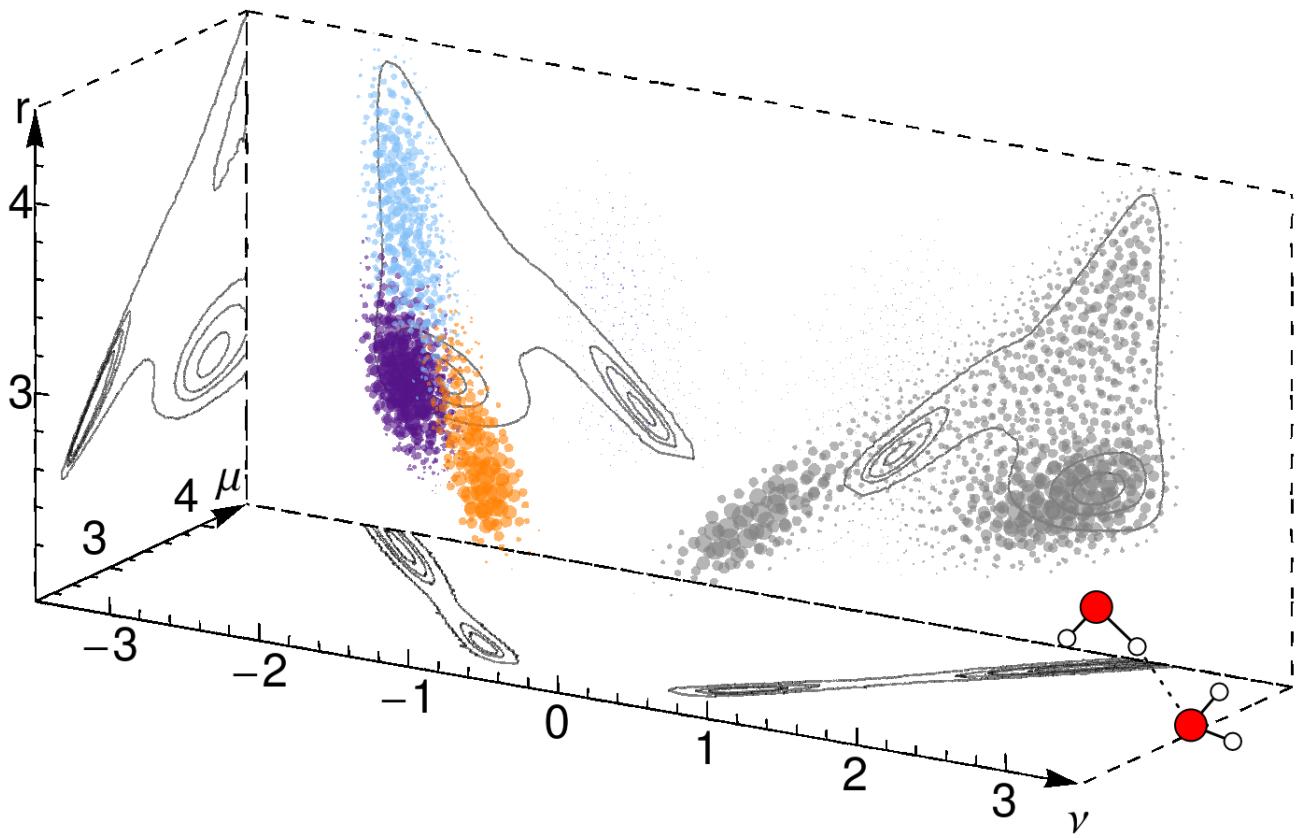

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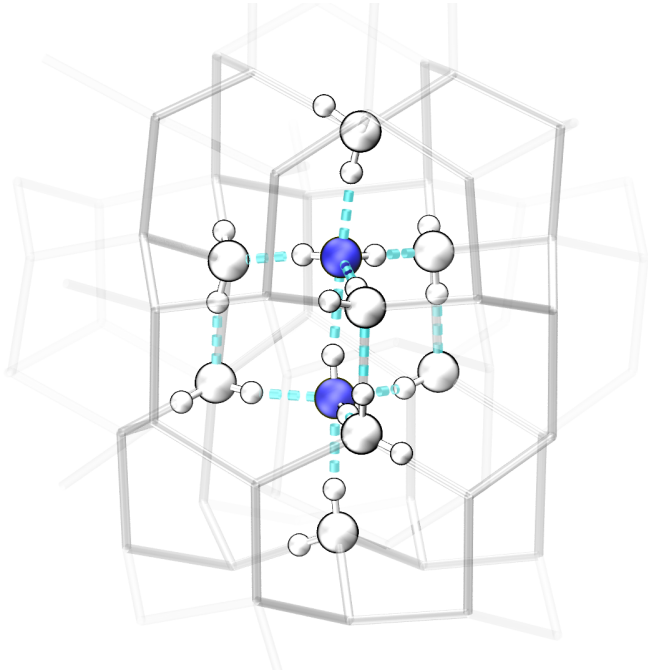

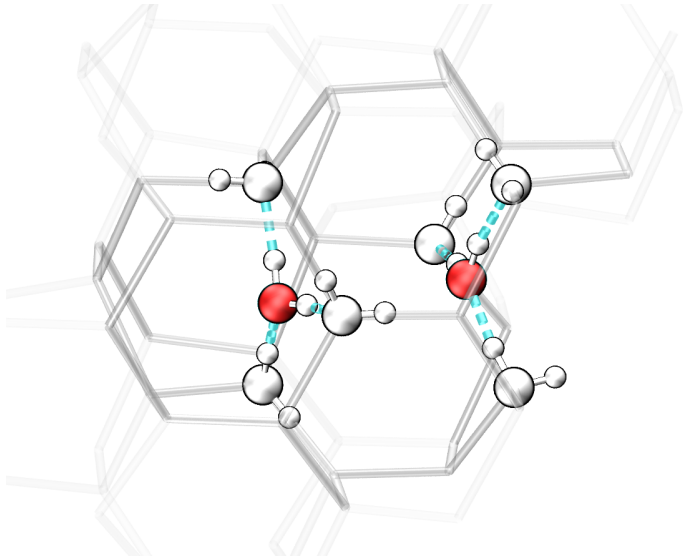

A H-bonding Environment Map

- PAMM gives for each (D, H, A) triplet a H-bond count s_{DHA}
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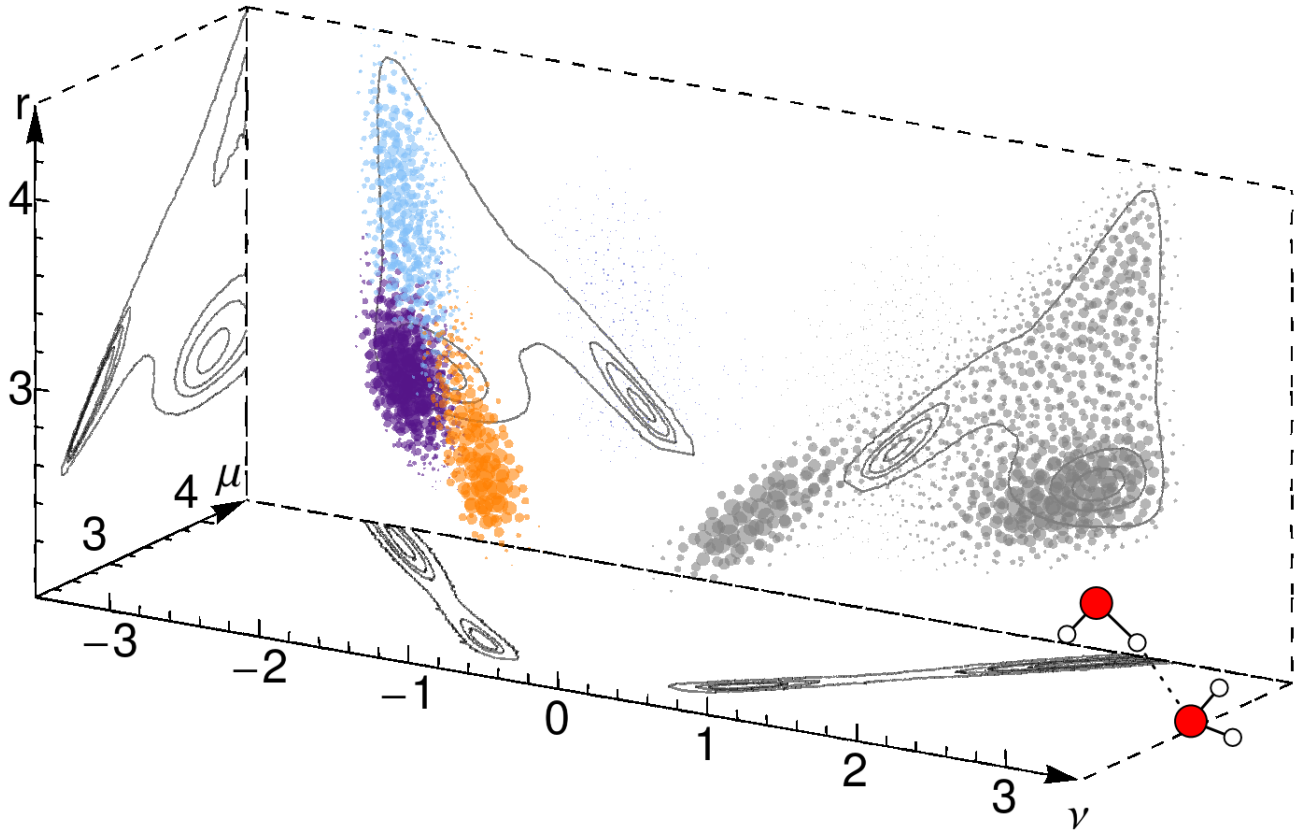

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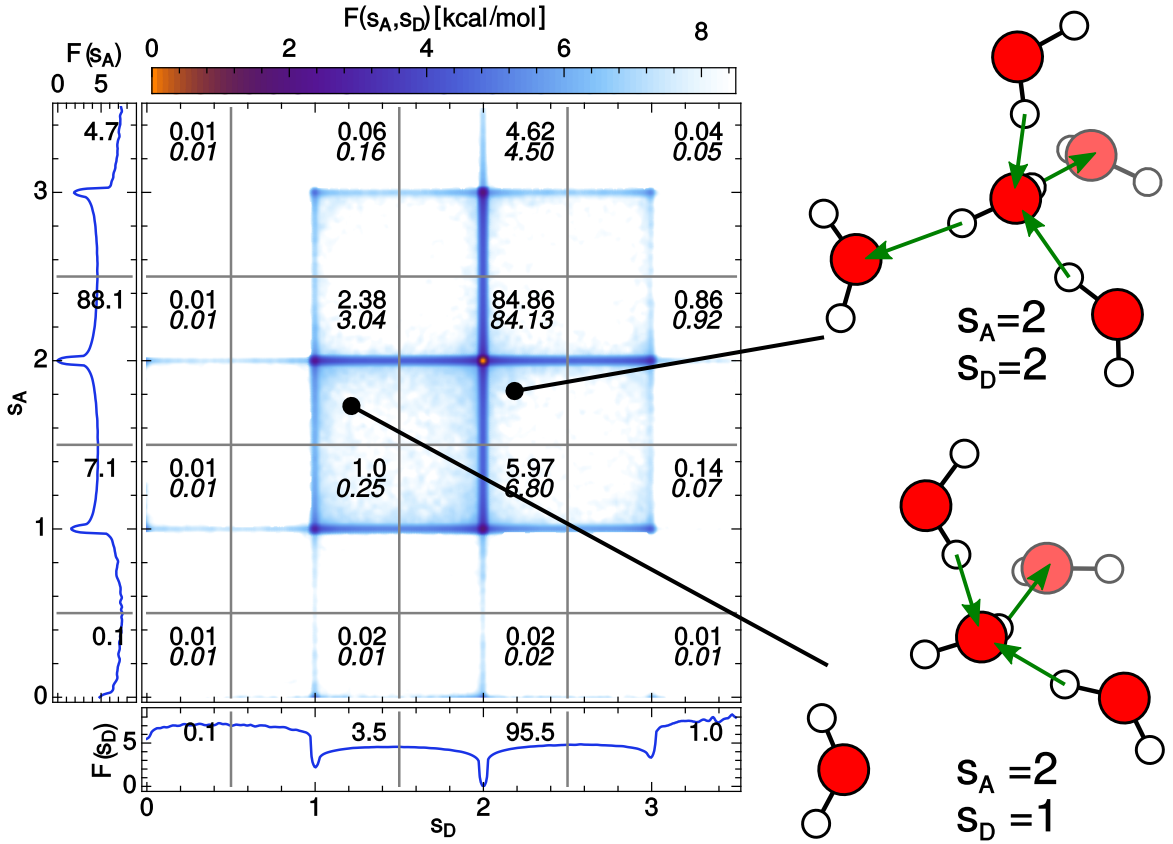

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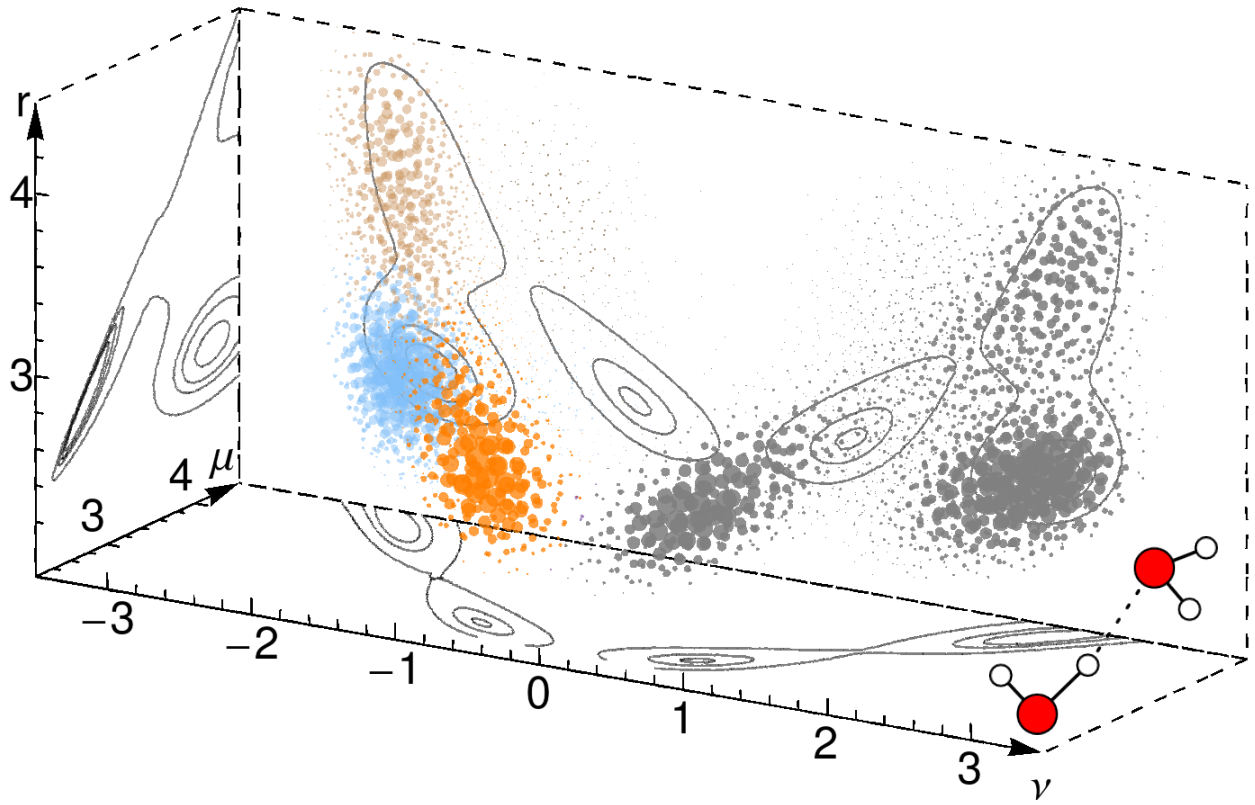

Ceriotti, Cuny, Parrinello, Manolopoulos, PNAS 110, 15591 (2013)

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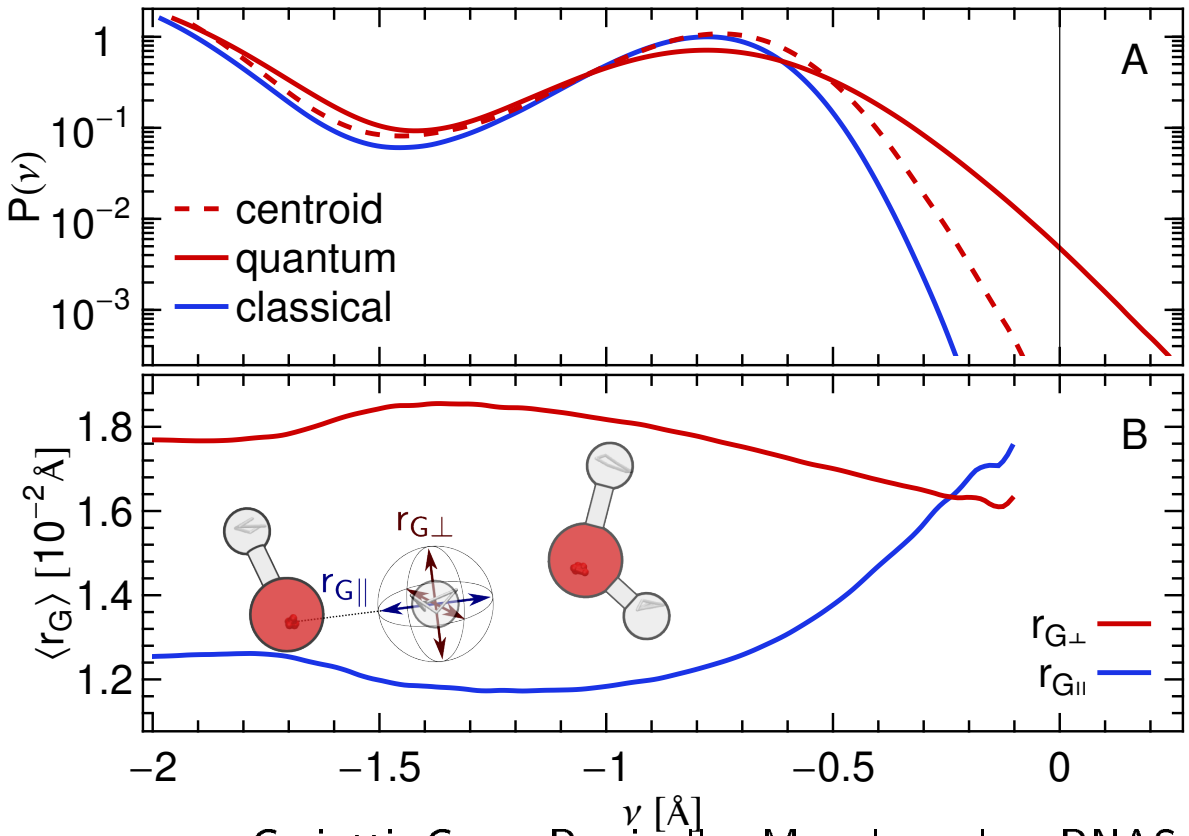

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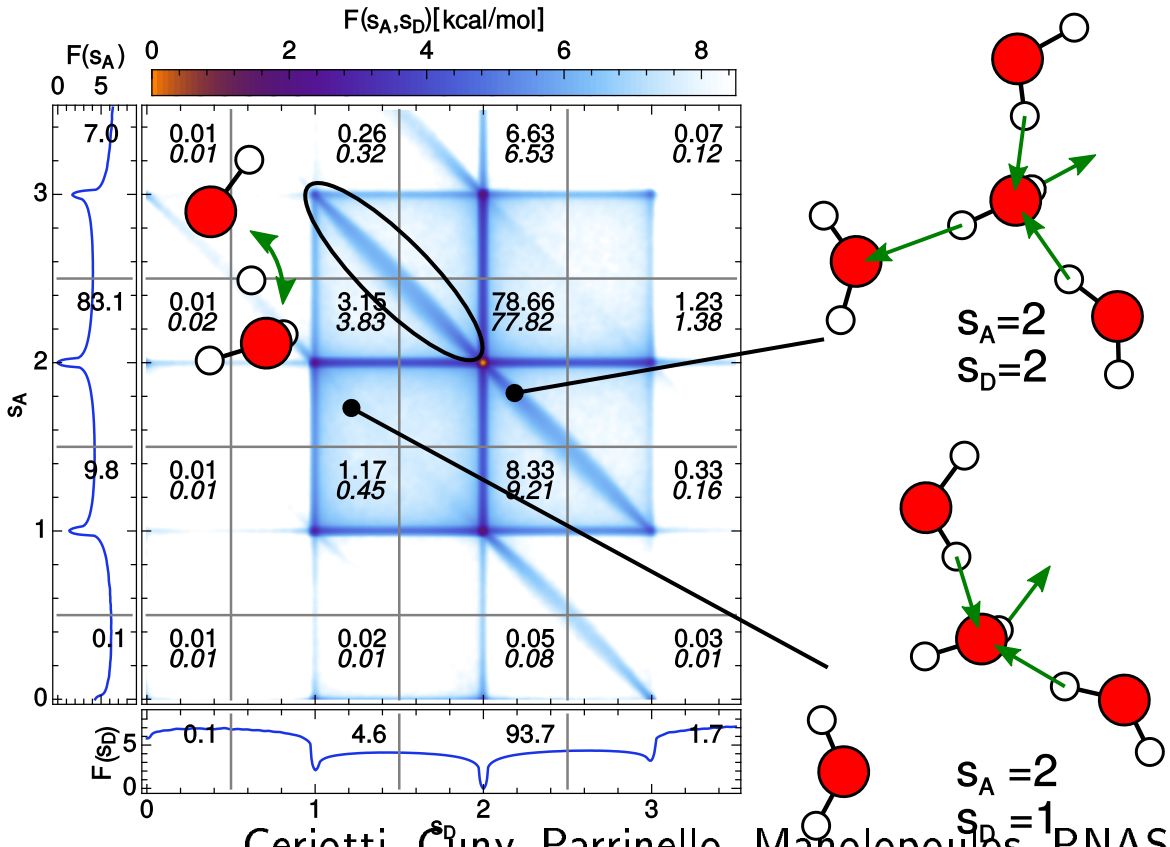

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What's an Excess Proton?

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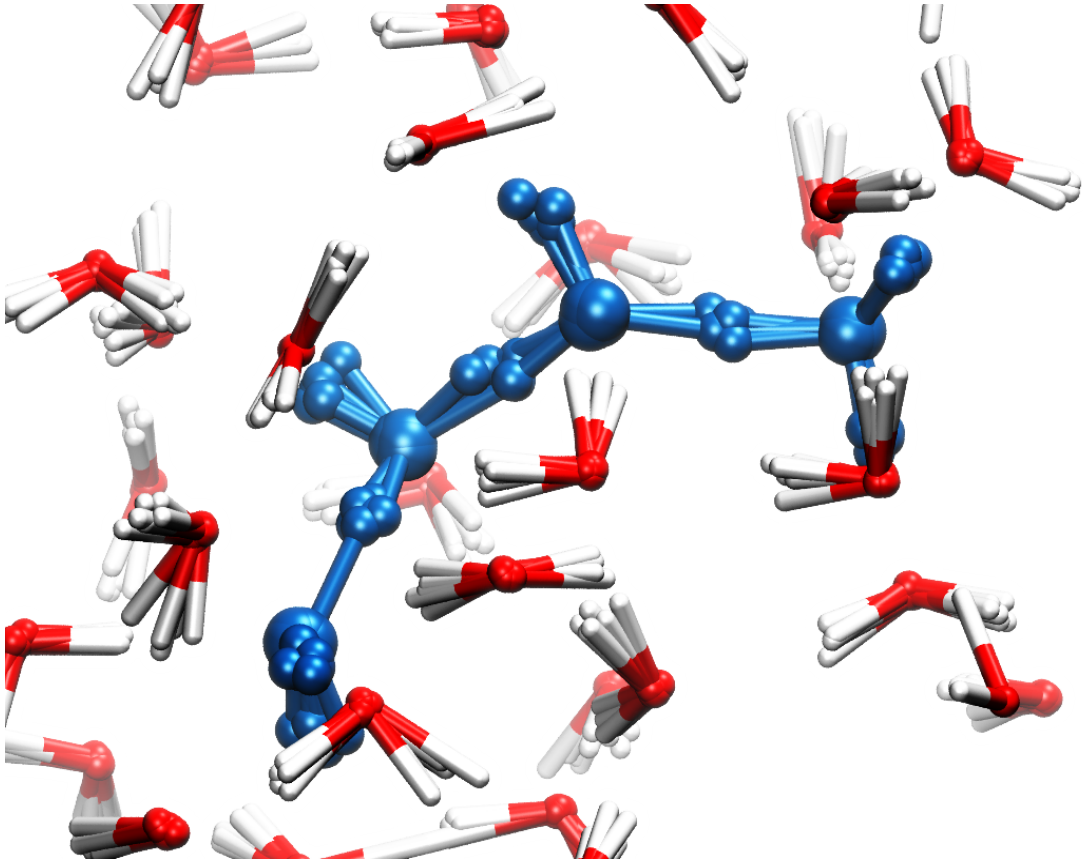

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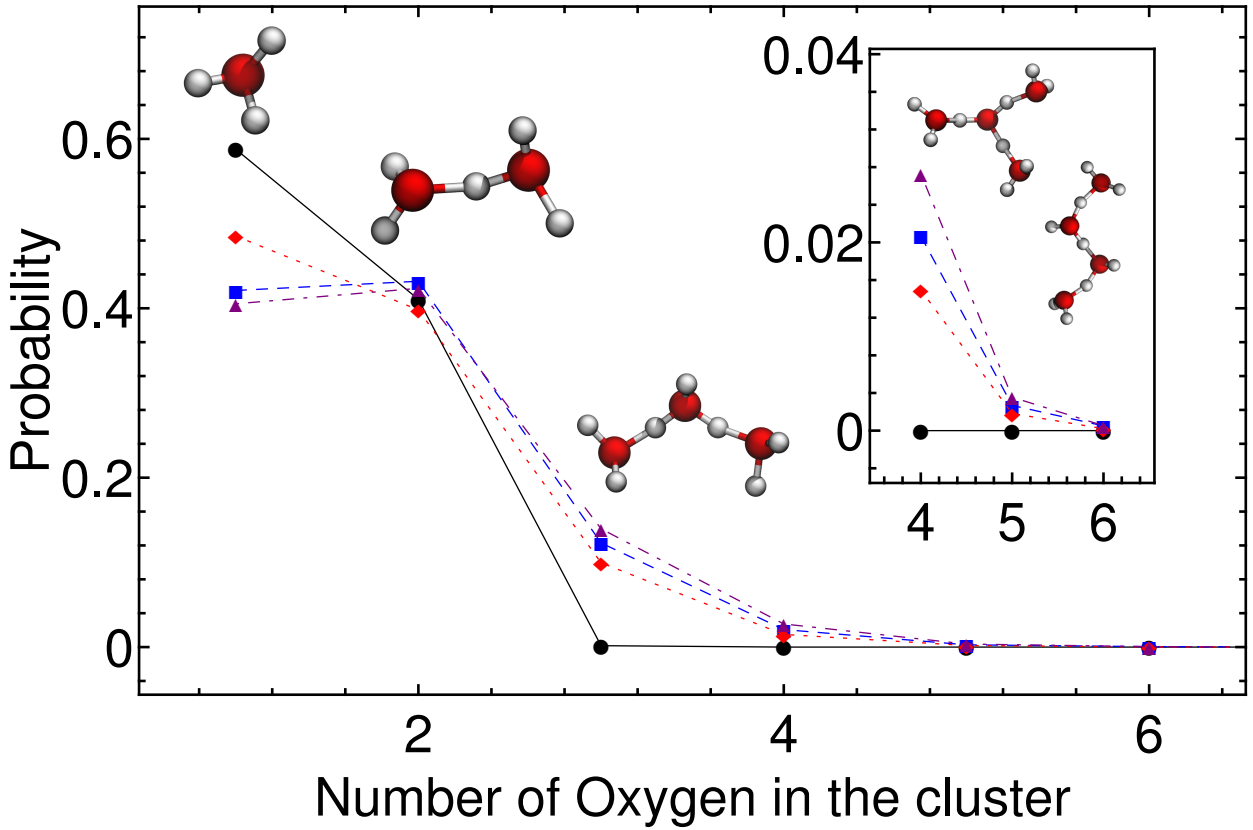

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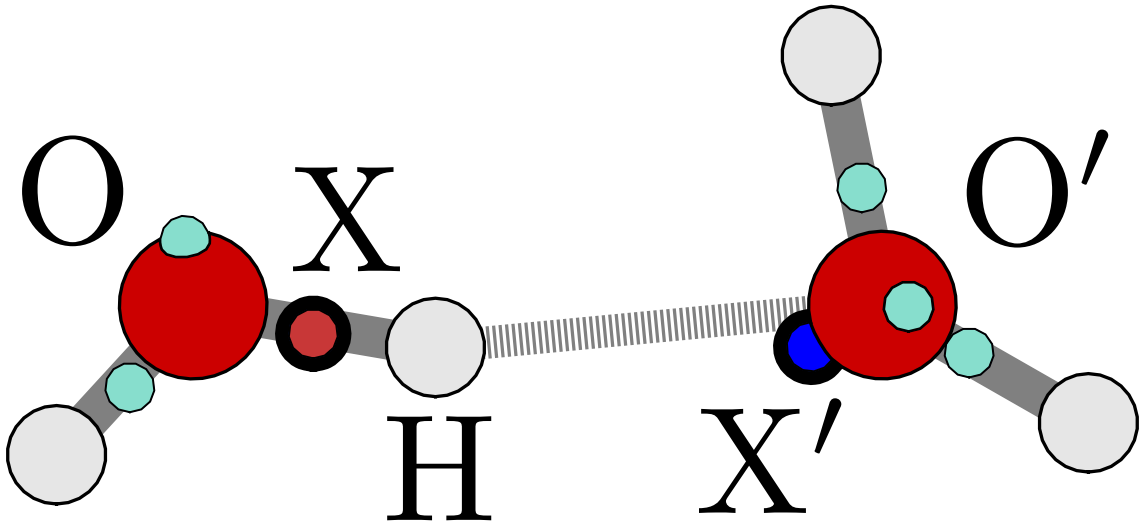

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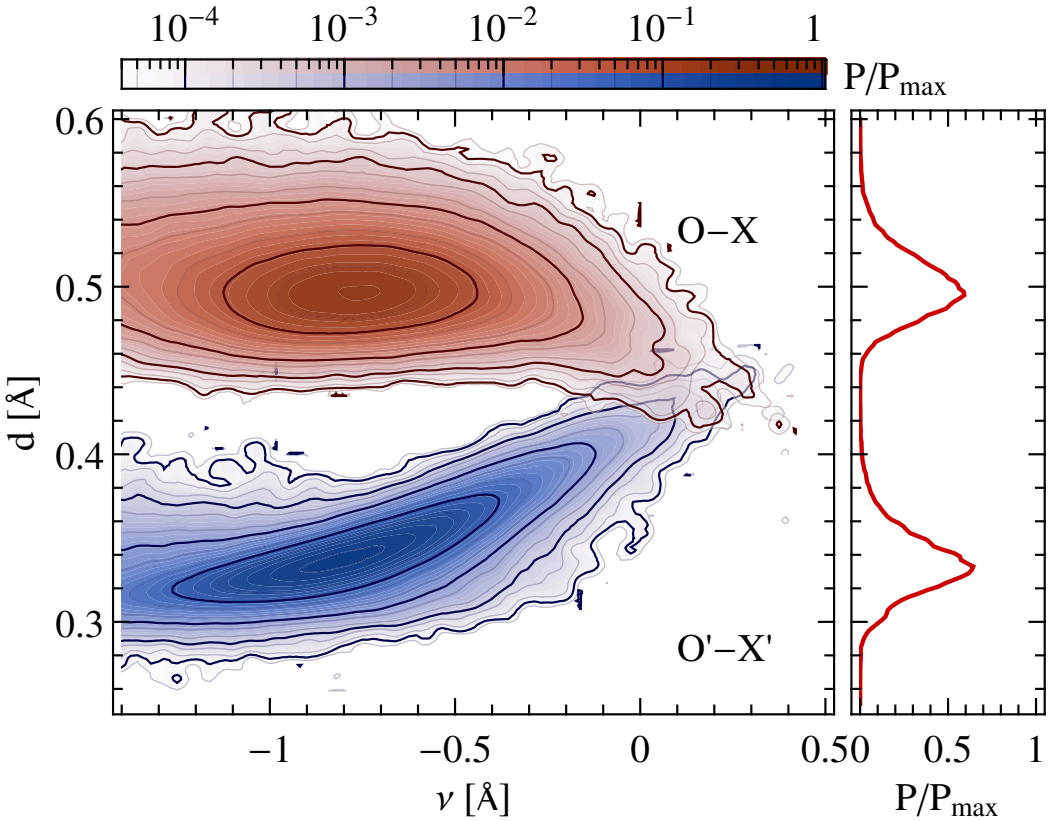

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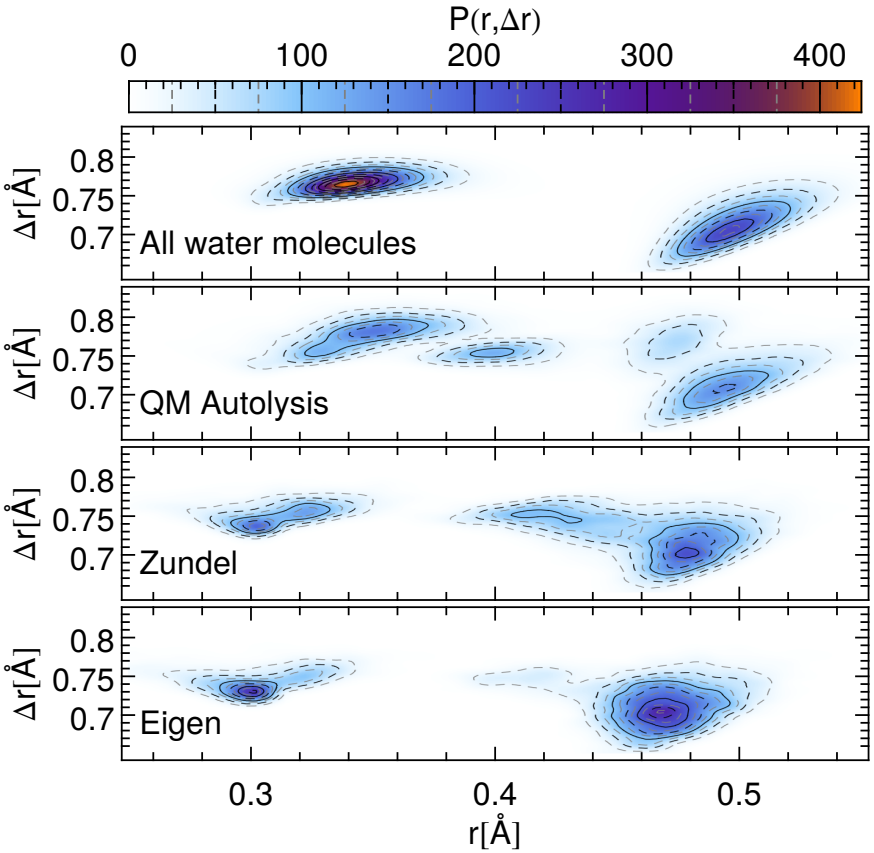

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PAMM Analysis of a Water Wire

- Can we use PAMM to identify proton-like water molecules in a wire?
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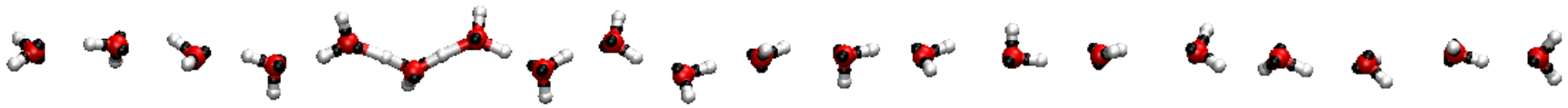

Mariana Rossi & MC, Work in Progress...

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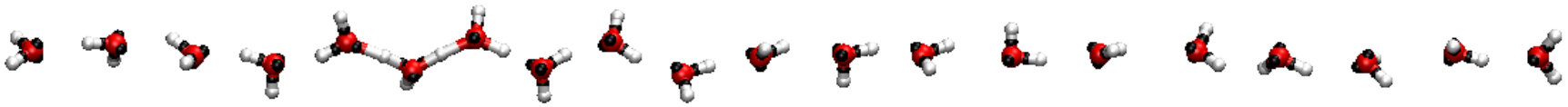

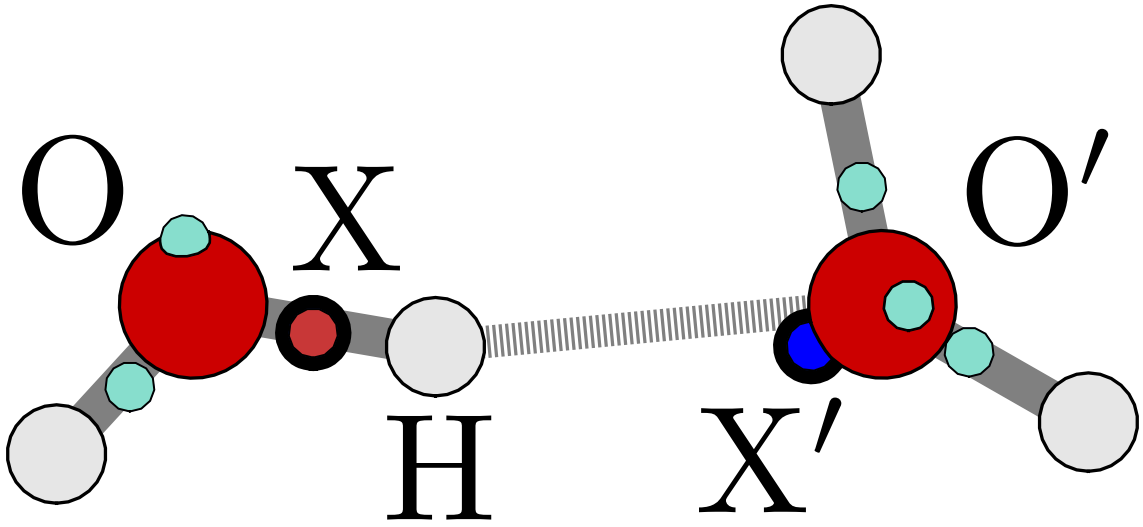

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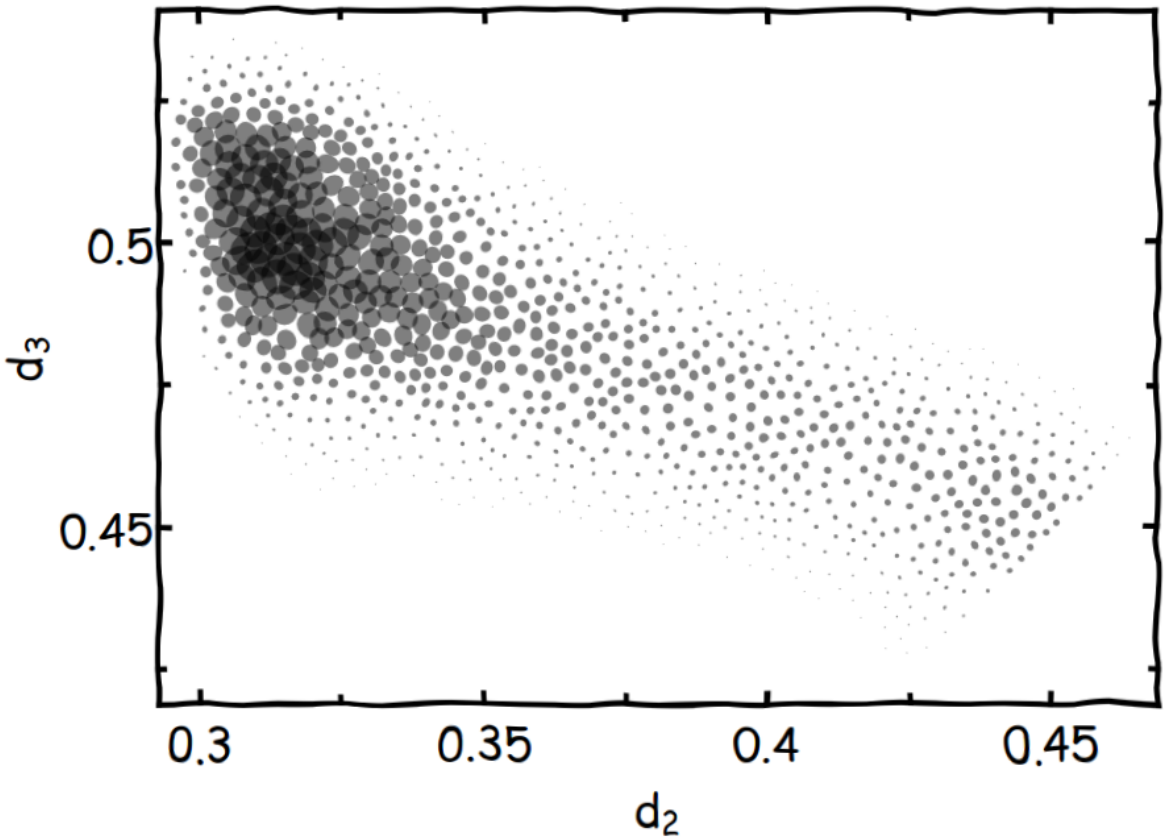

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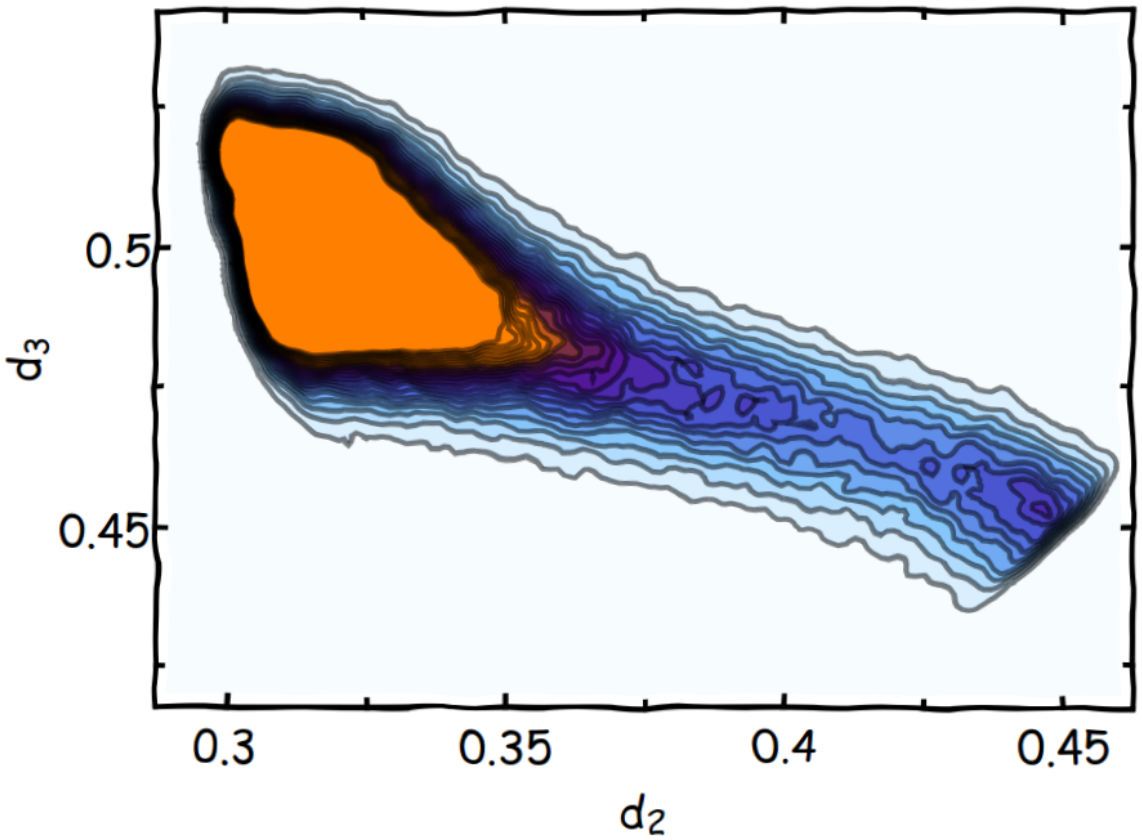

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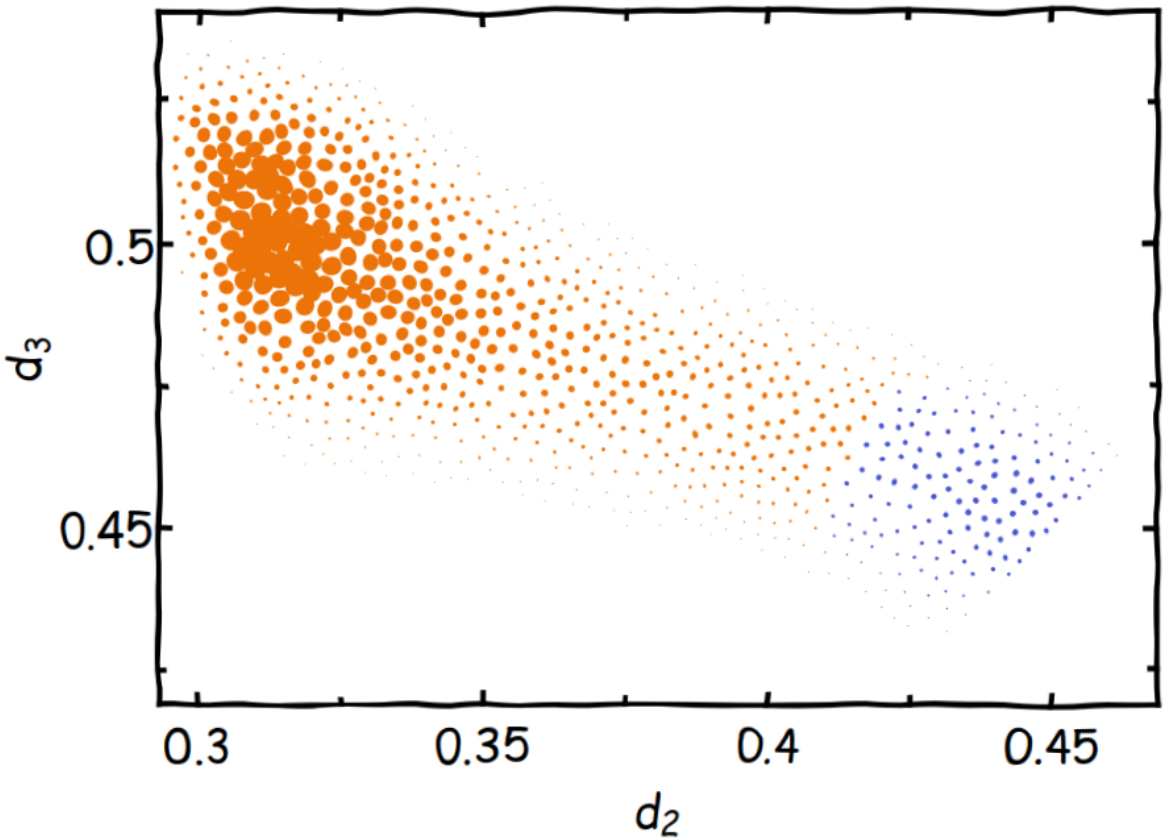

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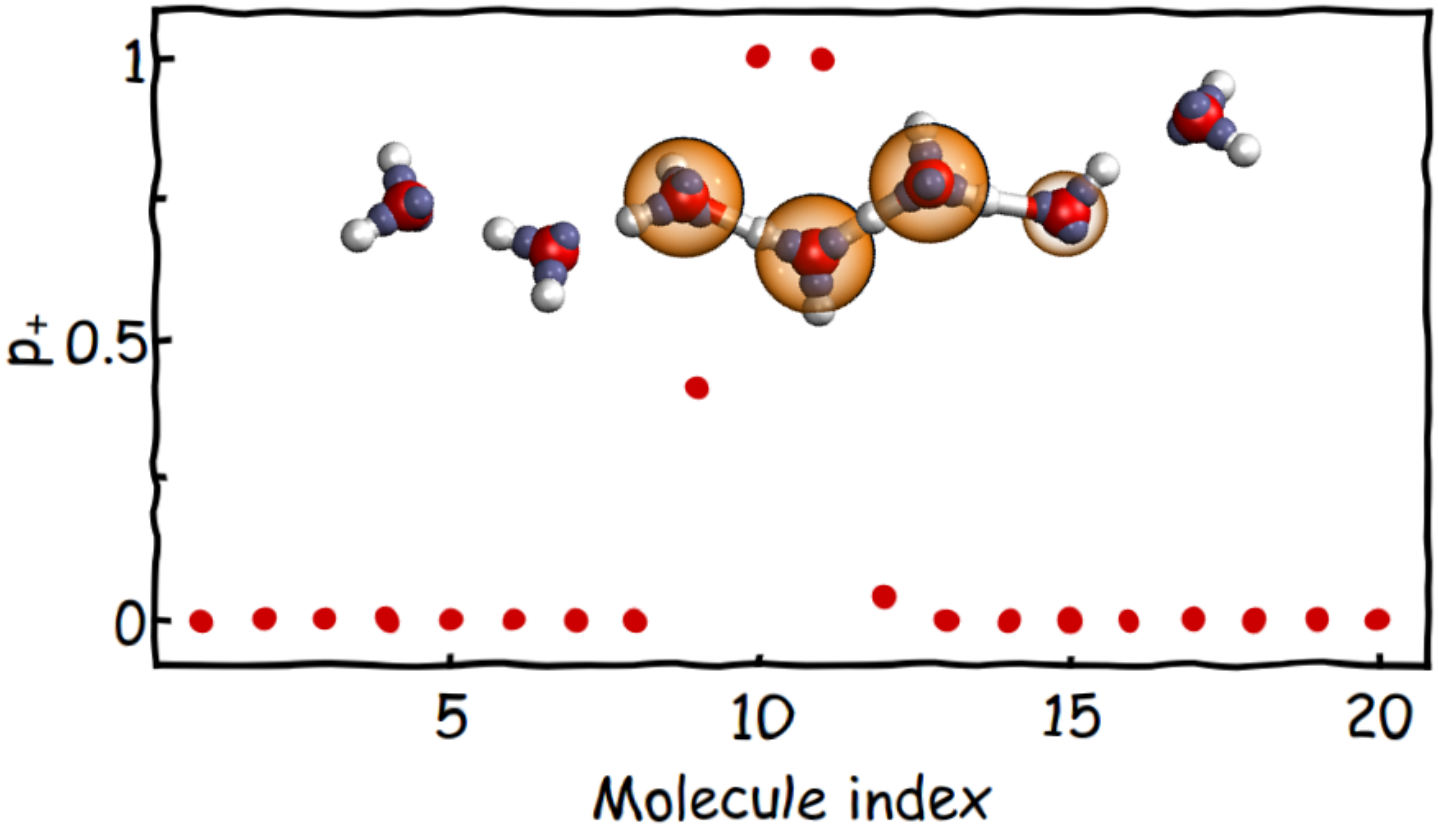

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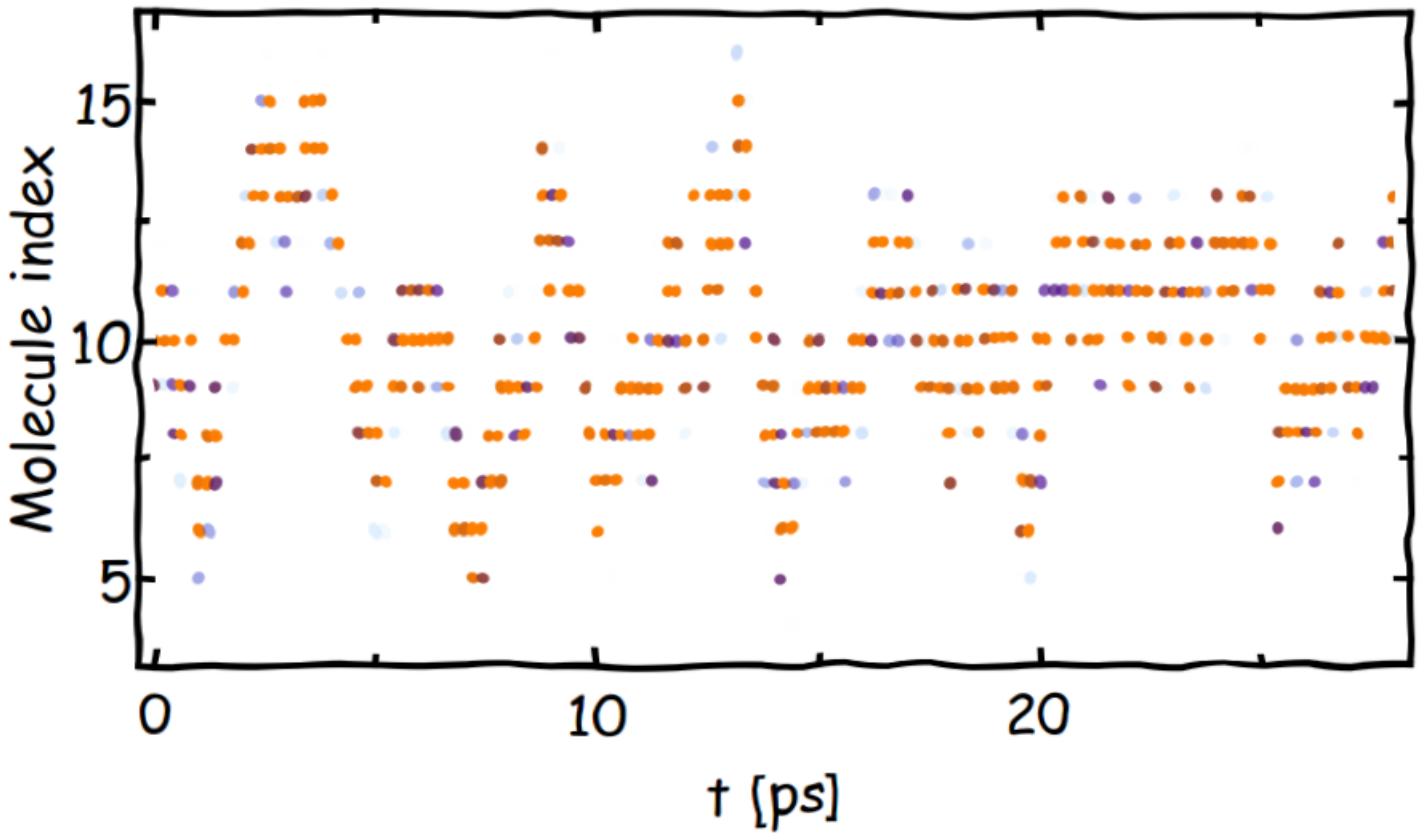

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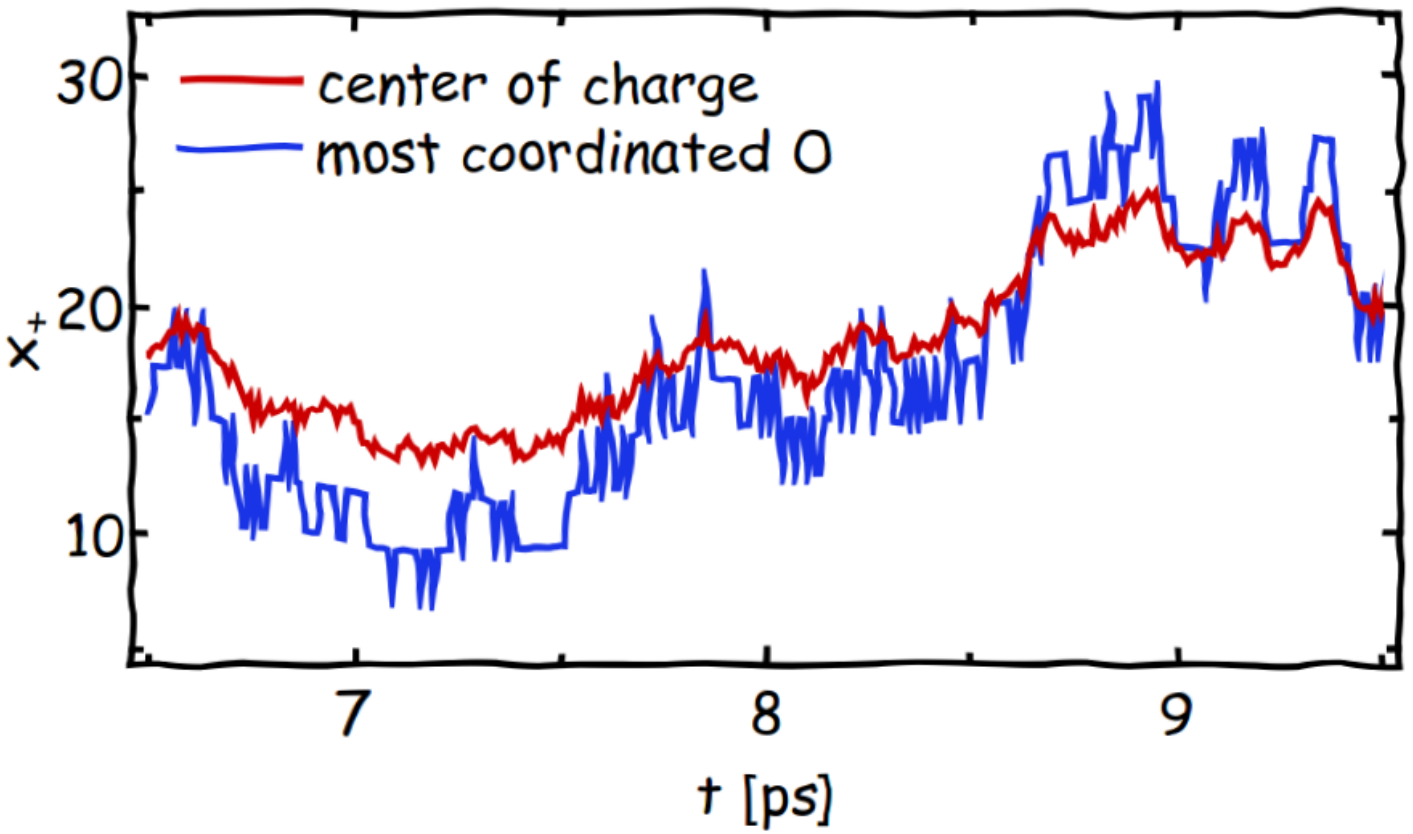

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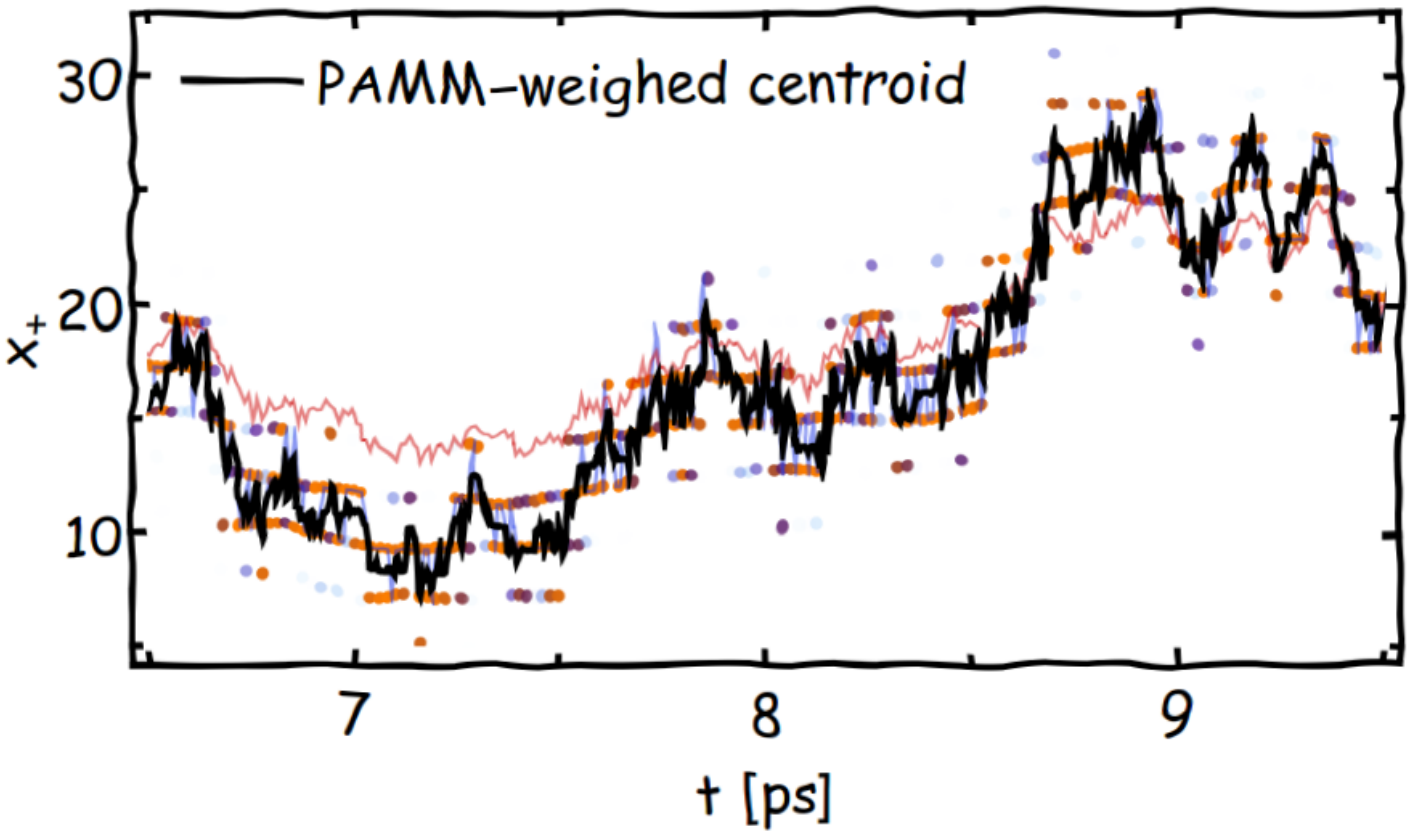
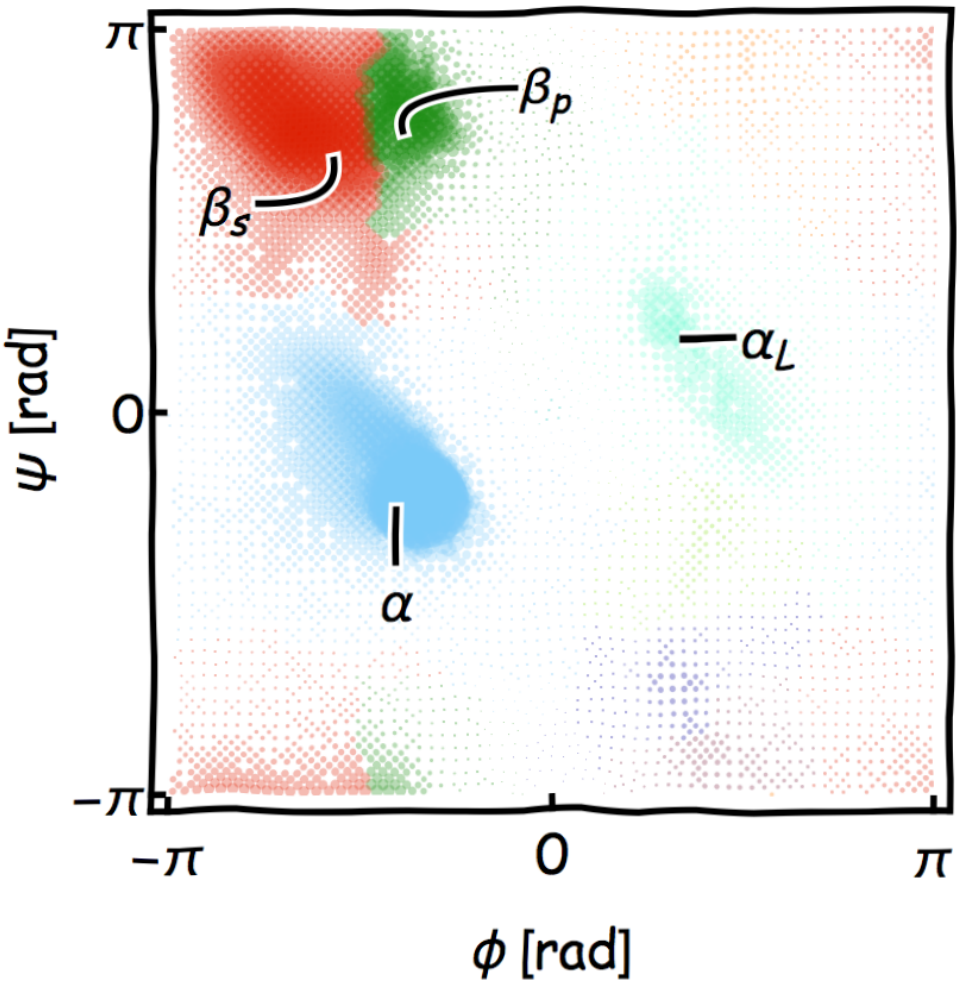


Machine-learning the Ramachandran plot

- Use data from the PDB, and "learn" with PAMM the stable patterns of proteins in dihedral space



Acknowledgements

Piero Gasparotto

CCMX
Competence Centre for
Materials Science and Technology

Michele Parrinello
Gareth Tribello

CSCS
Centro Svizzero di Calcolo Scientifico
Swiss National Supercomputing Centre

Mariana Rossi

Challenges for machine learning

- Machine learning can be used to process (large and/or high-dimensional) simulation data in a simpler-to-understand form
  - Use the ML description to improve simulations
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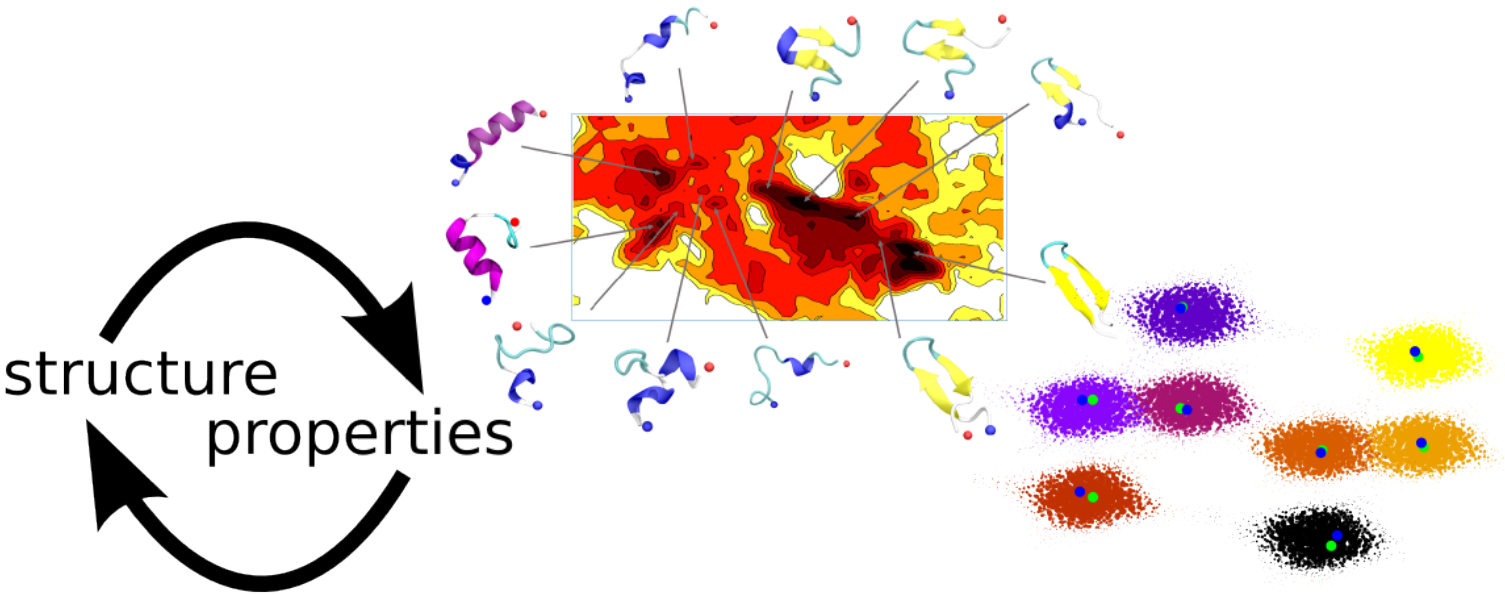

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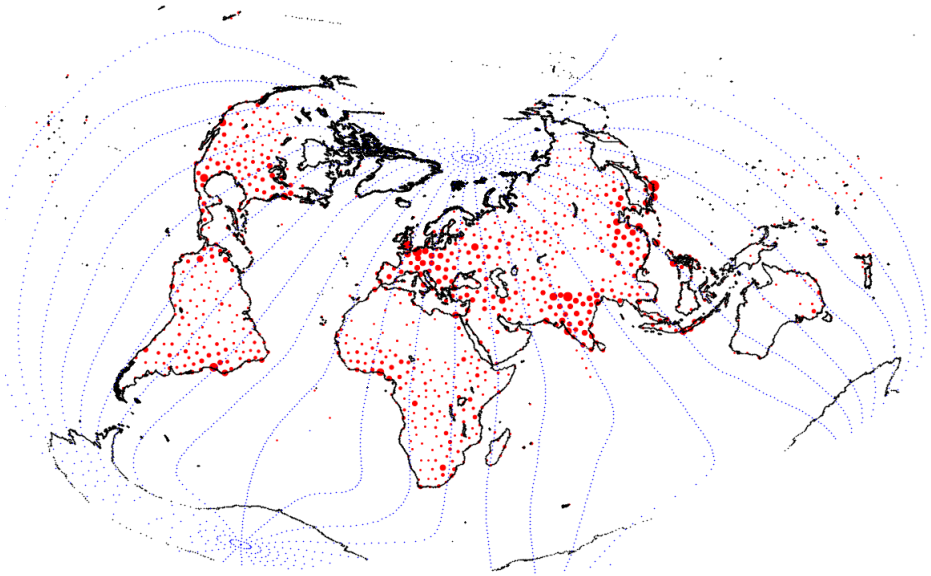

http://epfl-cosmo.github.io/sketchmap

http://github.com/epfl-cosmo/pamm