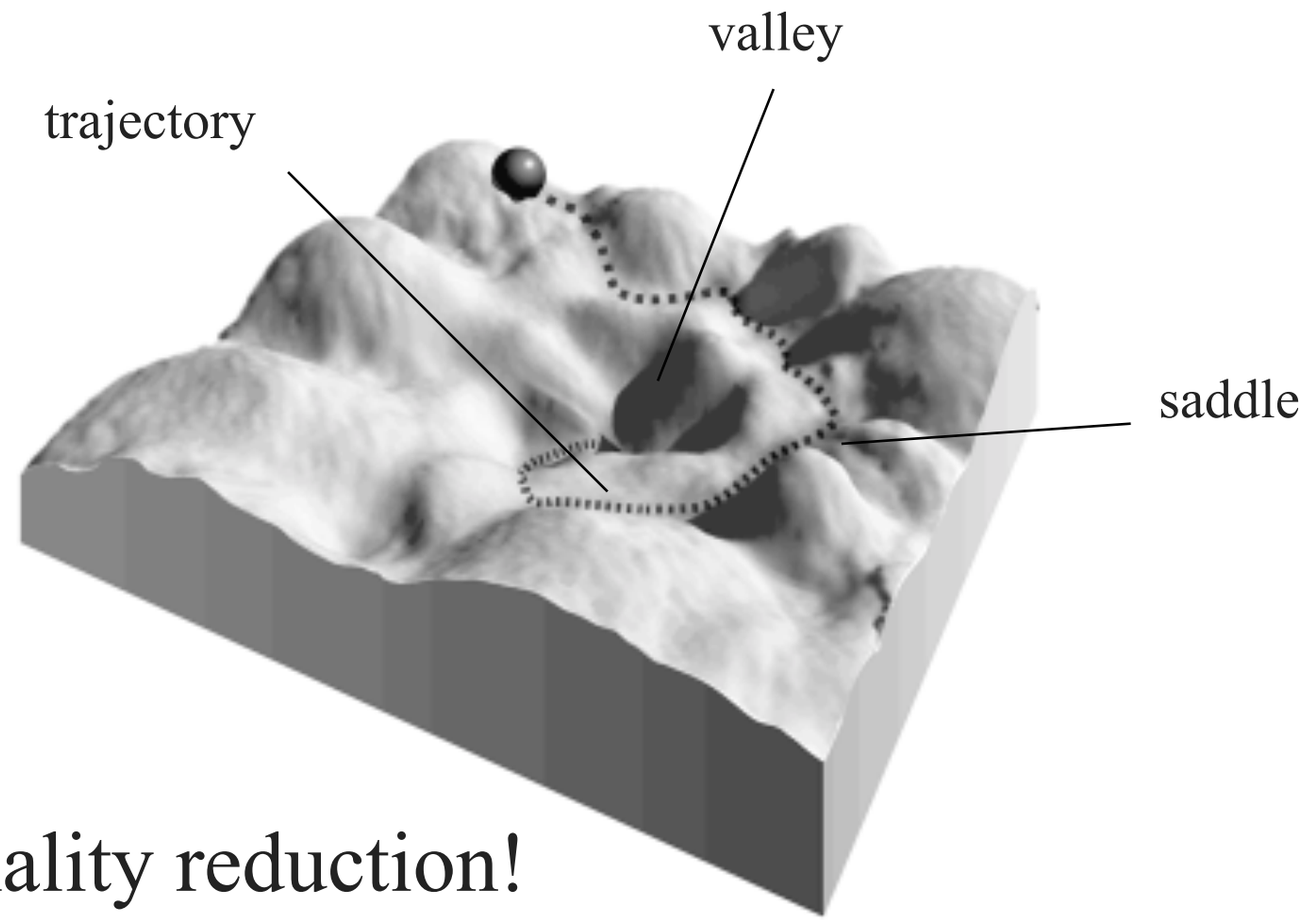
FREIBURG INSTITUTE
FOR ADVANCED STUDIES
ALBERT-LUDWIGS-
UNIVERSITÄT FREIBURG
SCHOOL OF
SOFT MATTER RESEARCH

protein dynamics

going beyond reaction coordinates

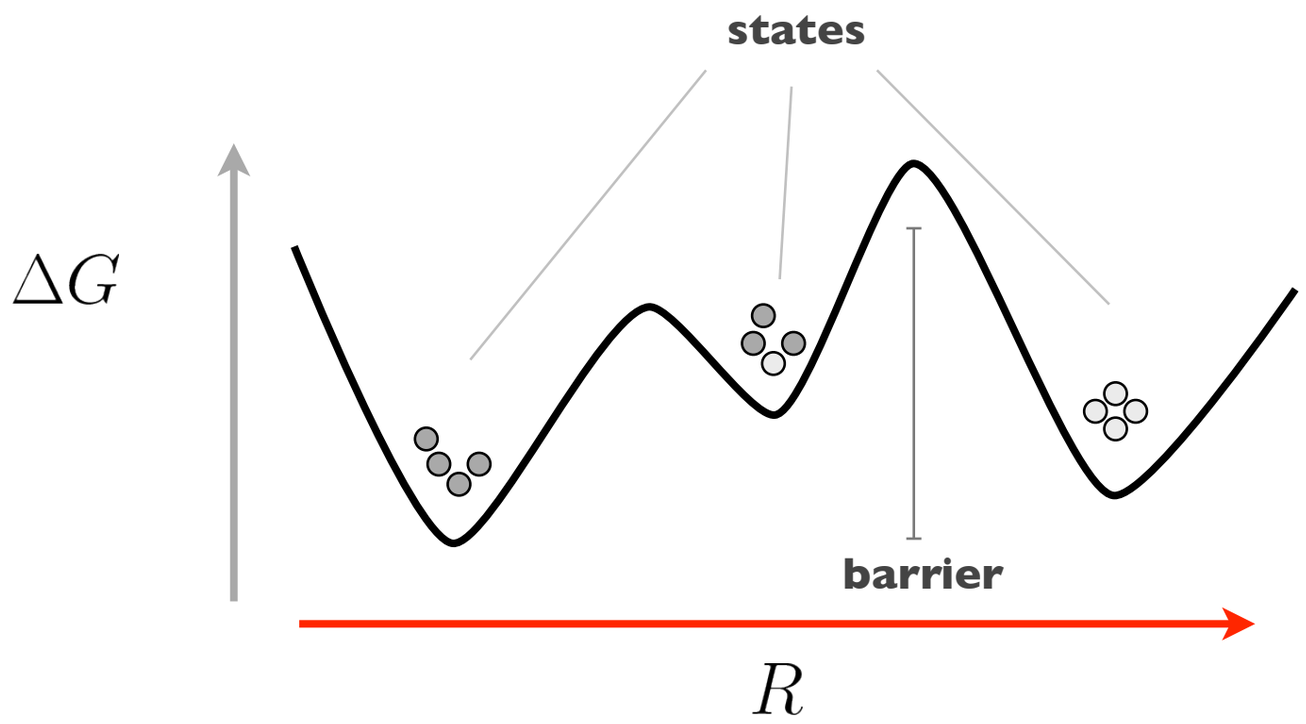
Protein Dynamics is described as the evolution of the system on the complex and multidimensional Free-Energy Landscape.



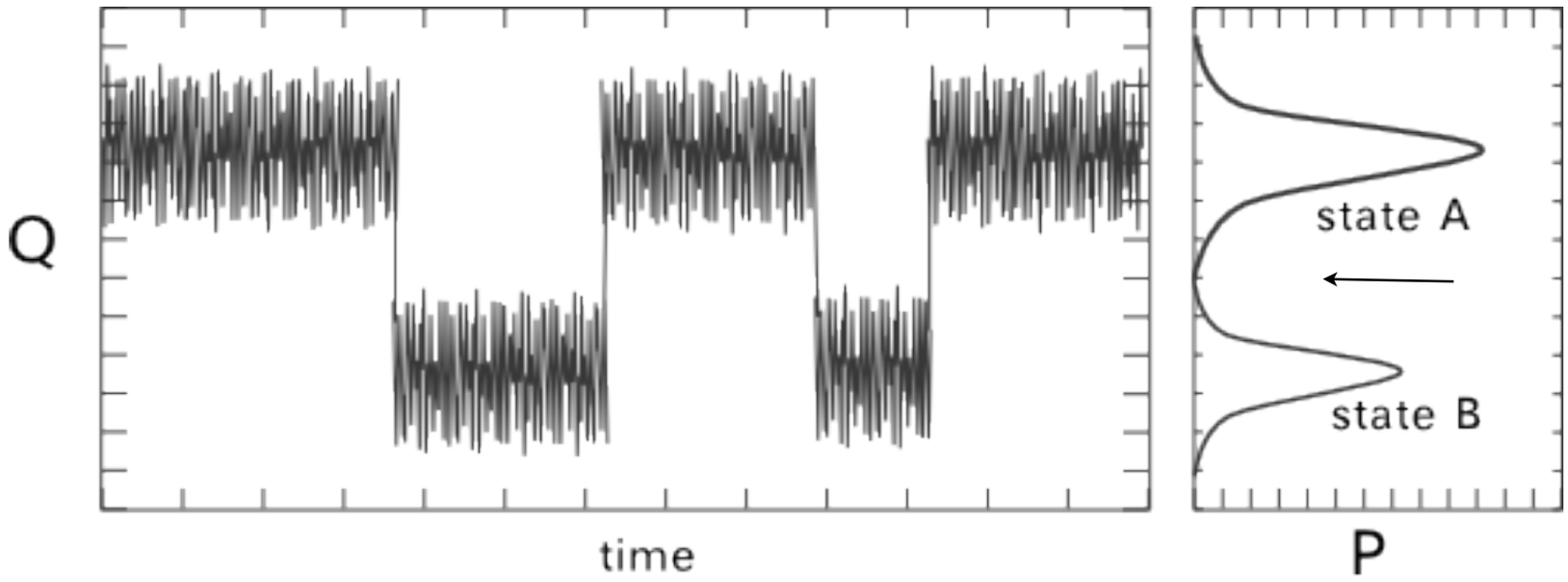
3N-hyperspace:
NEED a dimensionality reduction!

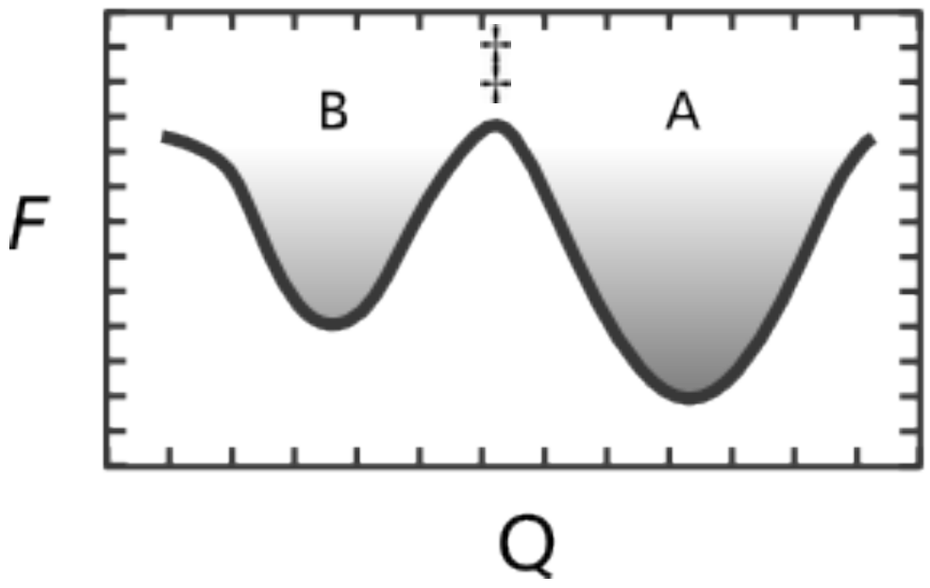
The Energy Landscape paradigm

Q is a GOOD order parameter if it identifies the different states as well as the barrier between them



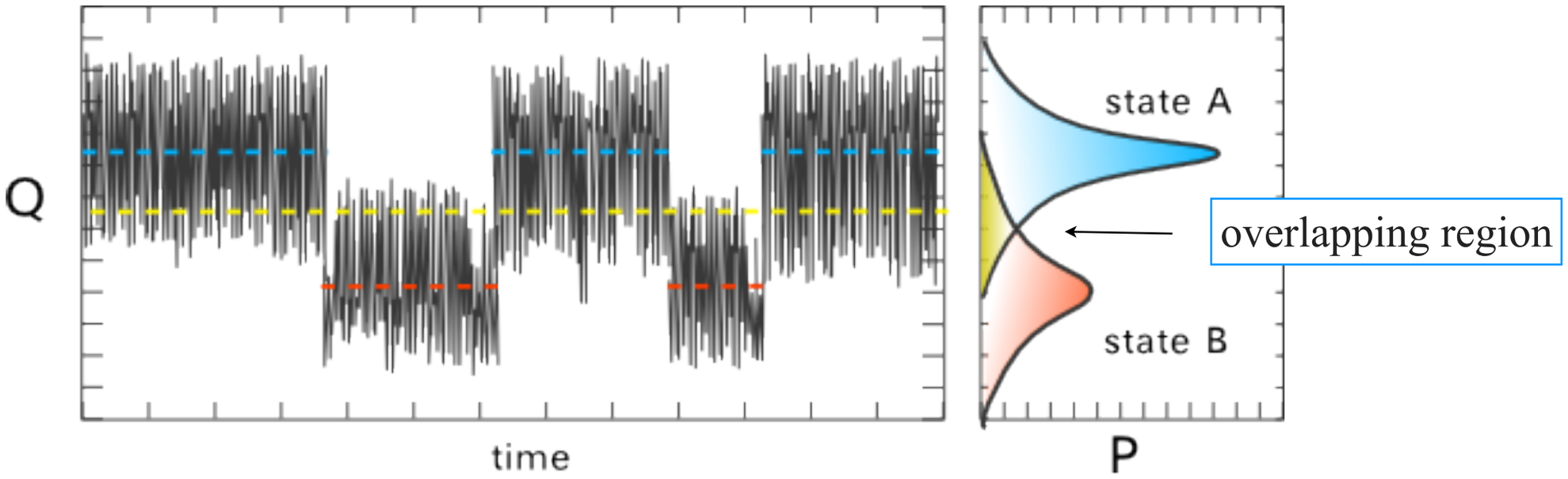
The histogram-based free-energy projection $\Delta F = -k_B T \log(P_i)$

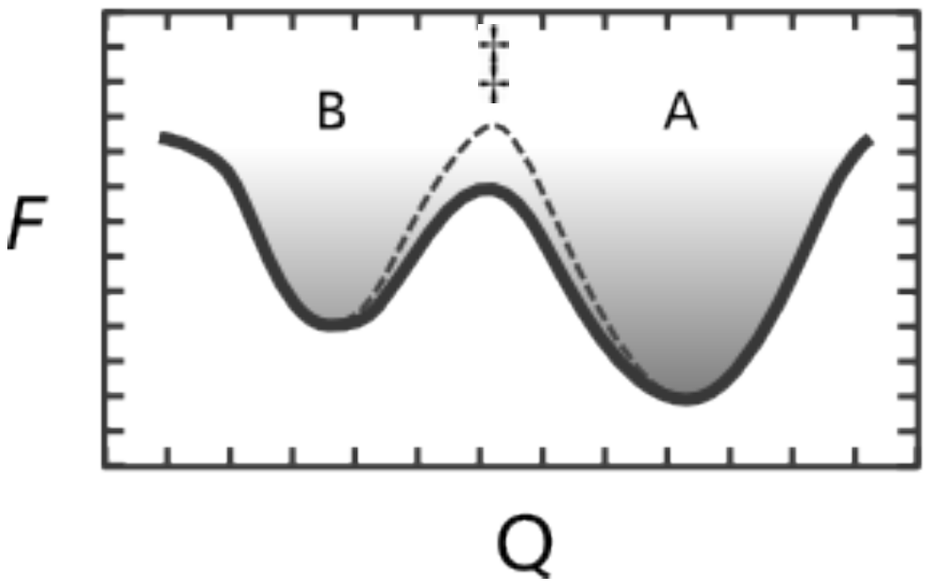




Free-energy projections (simple two-state)

The histogram-based free-energy projection $\Delta F = -k_B T \log(P_i)$



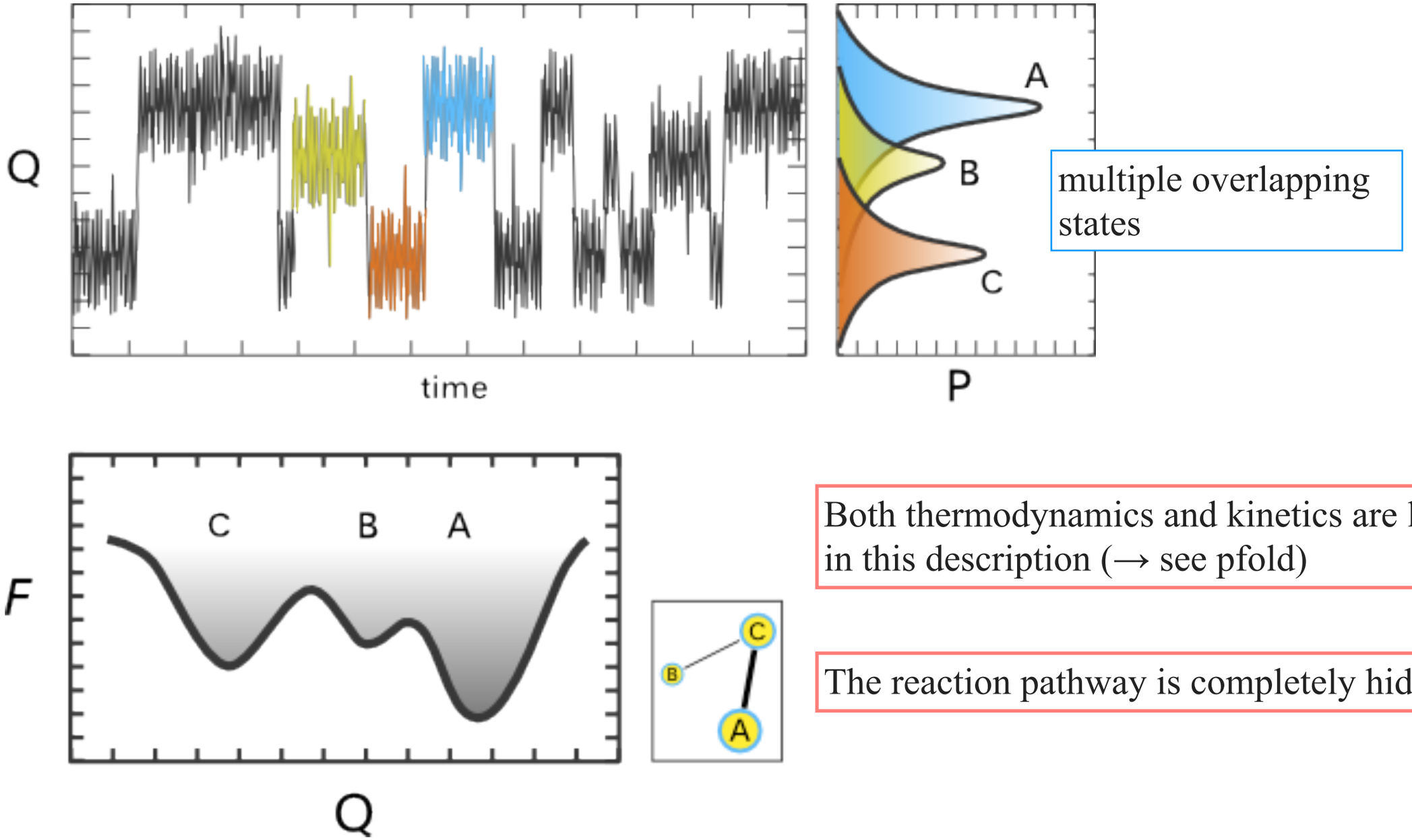


Artificial lowering of the free-energy barrier

The order parameter Q does not correctly discriminate the two states.

Free-energy projections (hard two-state)

The histogram-based free-energy projection $\Delta F = -k_B T \log(P_i)$



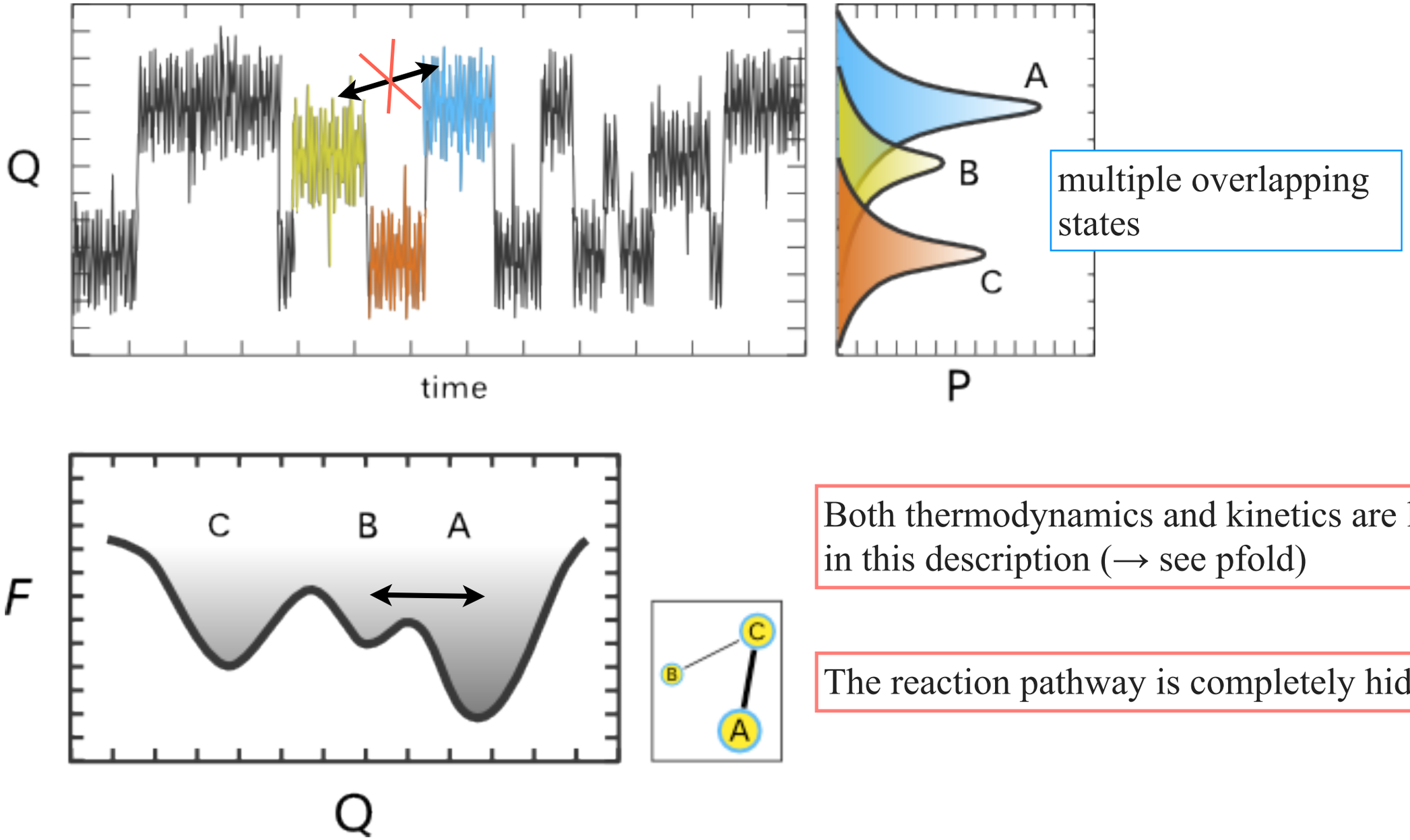
multiple overlapping states

Both thermodynamics and kinetics are lost in this description (→ see pfold)

The reaction pathway is completely hidden

Free-energy projections (multi-states)

The histogram-based free-energy projection $\Delta F = -k_B T \log(P_i)$



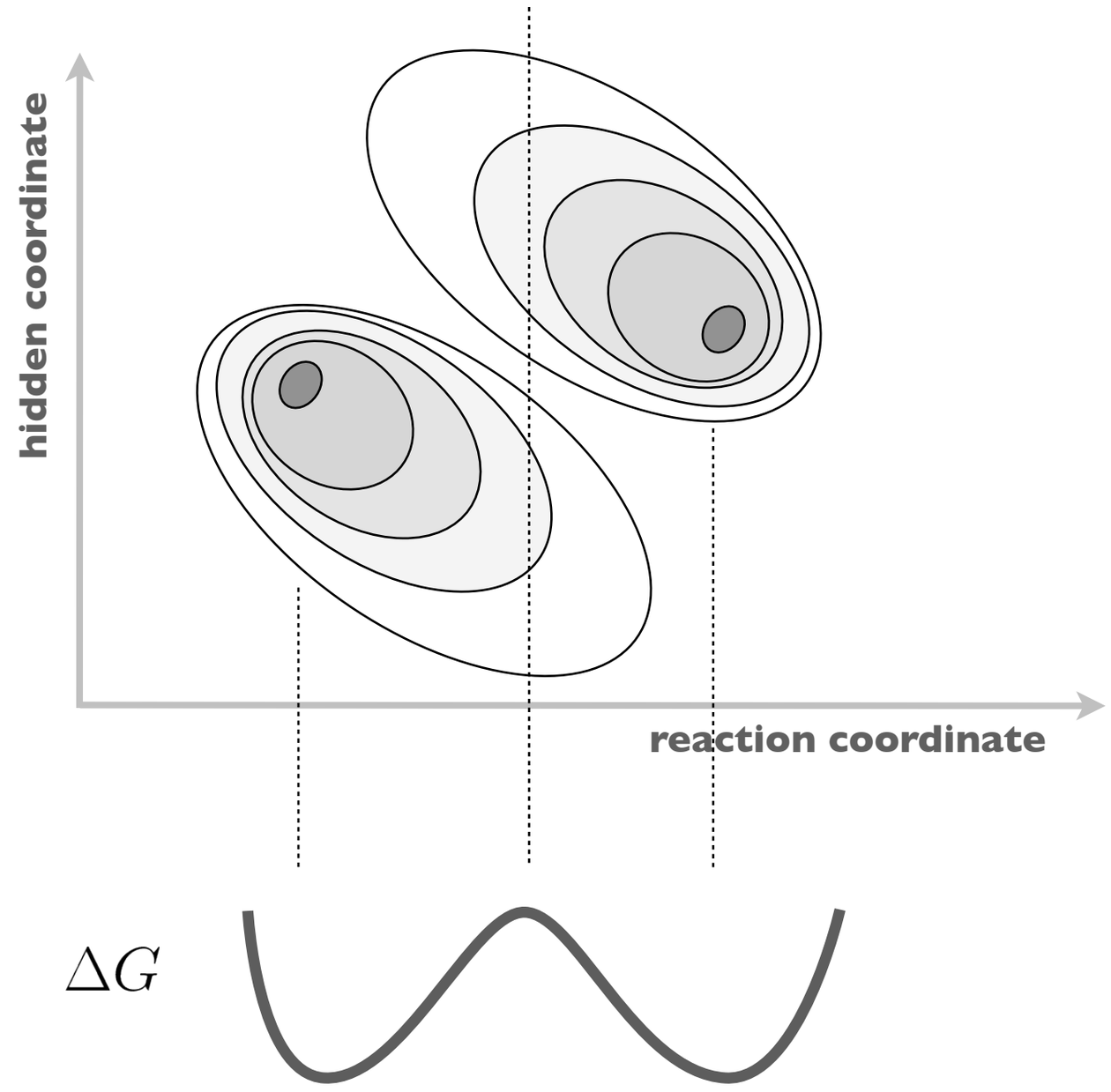
Free-energy projections (multi-states)

Hidden assumptions.

The order parameter is able to discriminate all the states of the protein.

Conformations belonging to the same minimum of the projection interconvert rapidly.

Dynamics is often slaved by hidden coordinates



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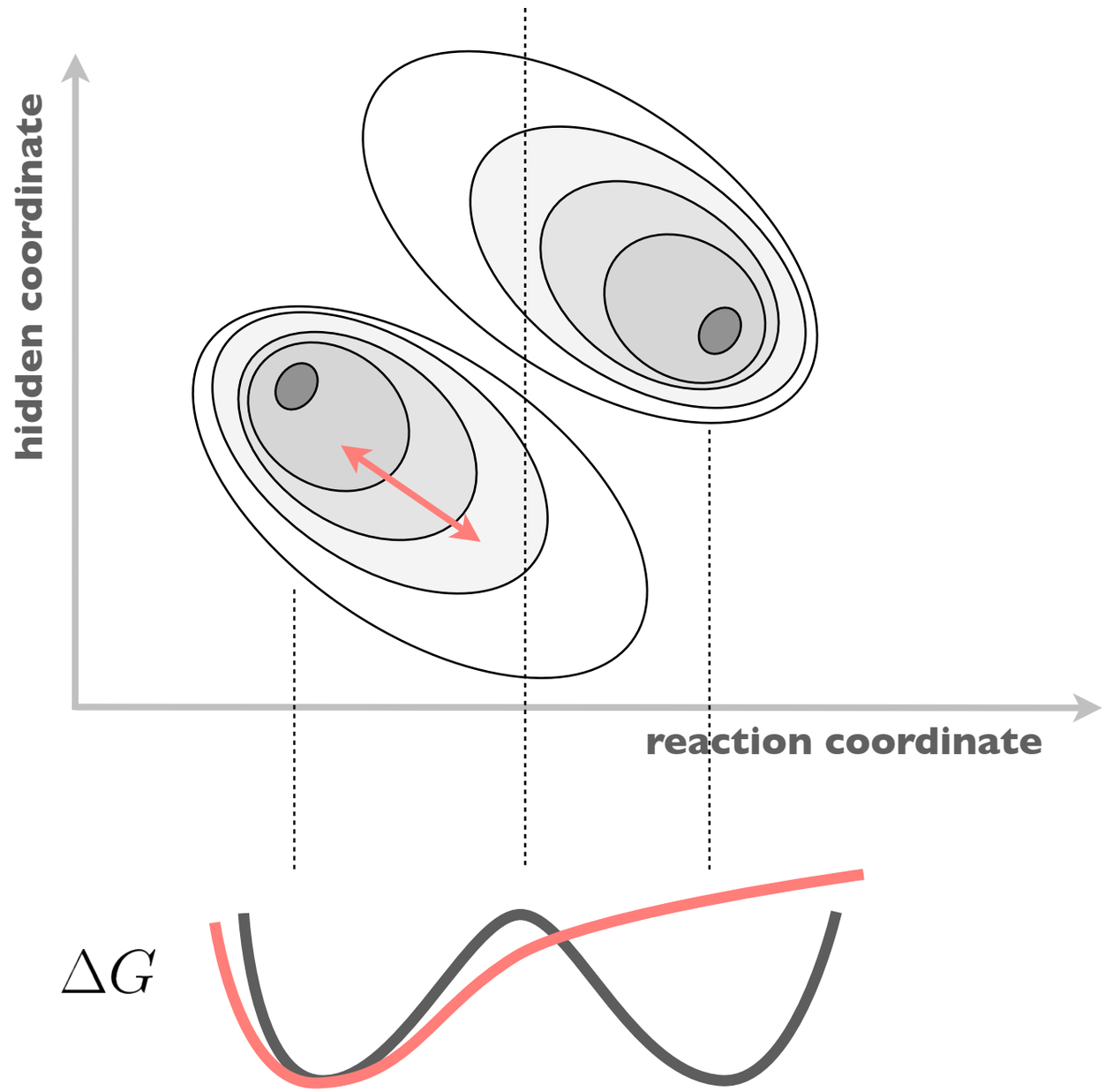

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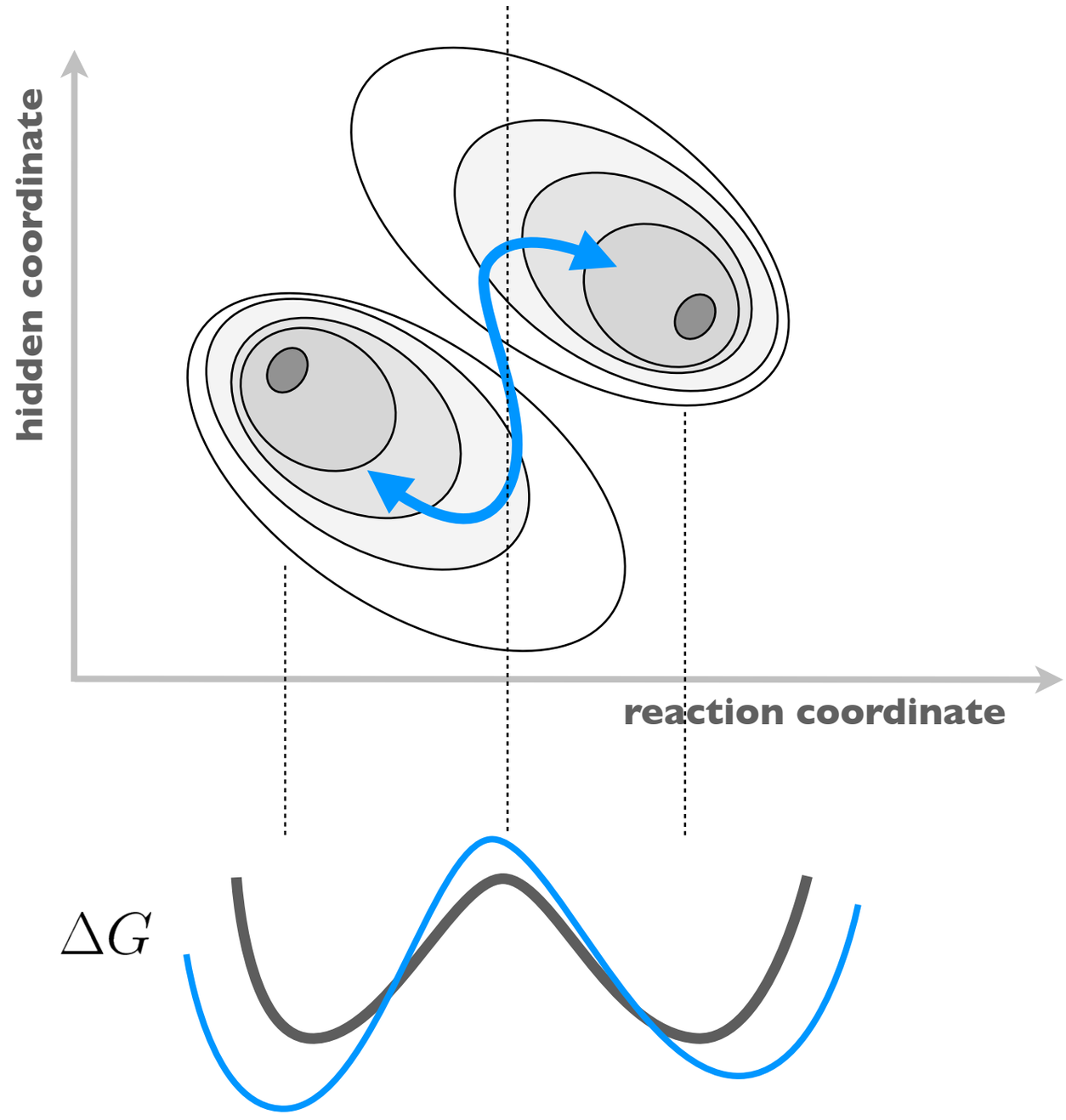
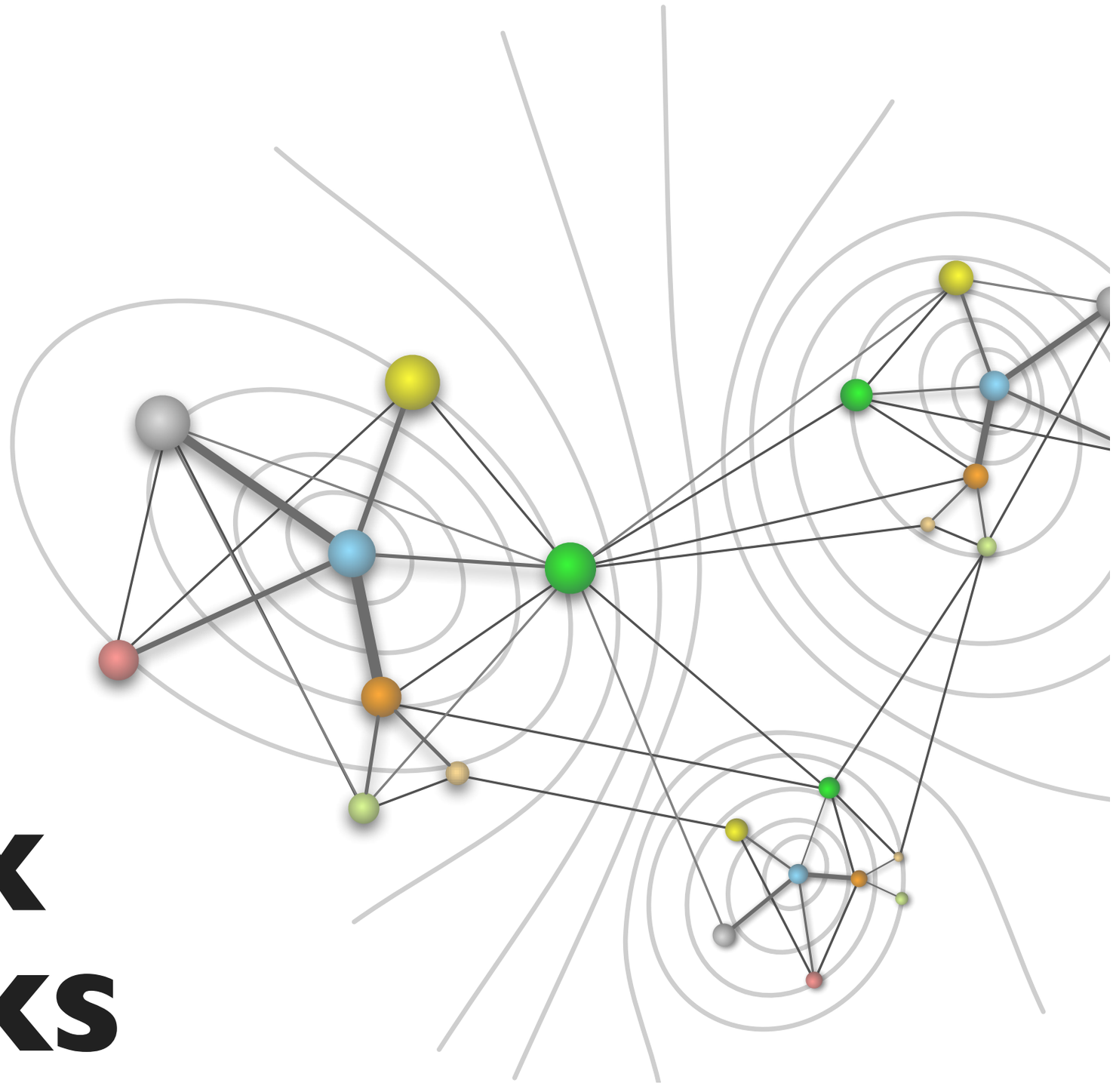
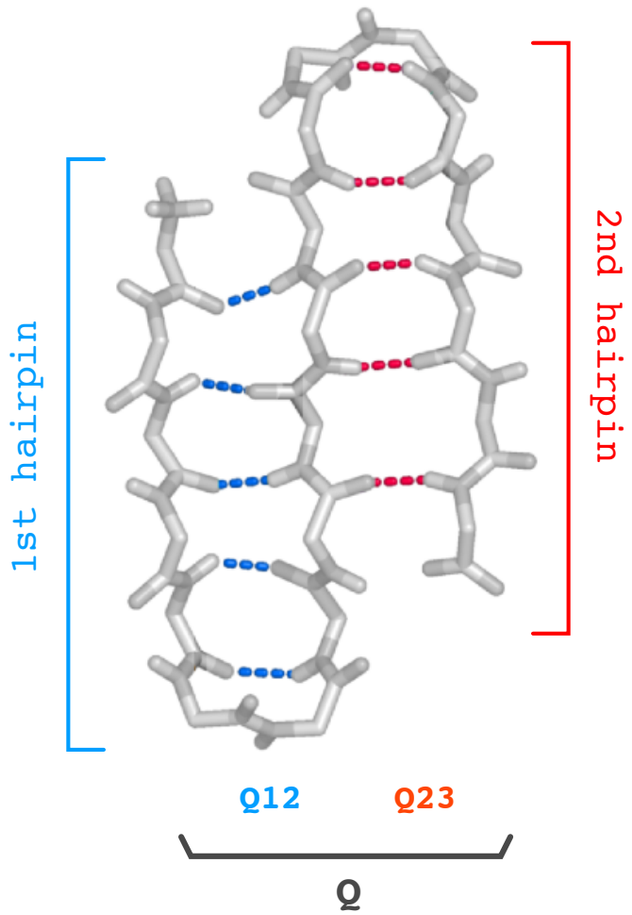
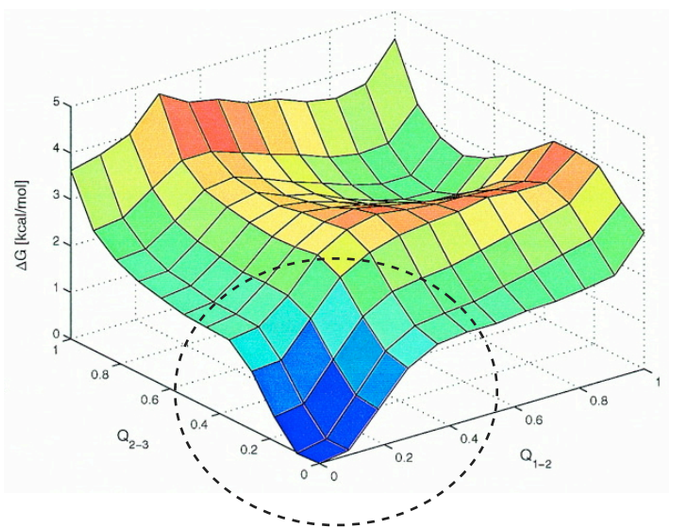


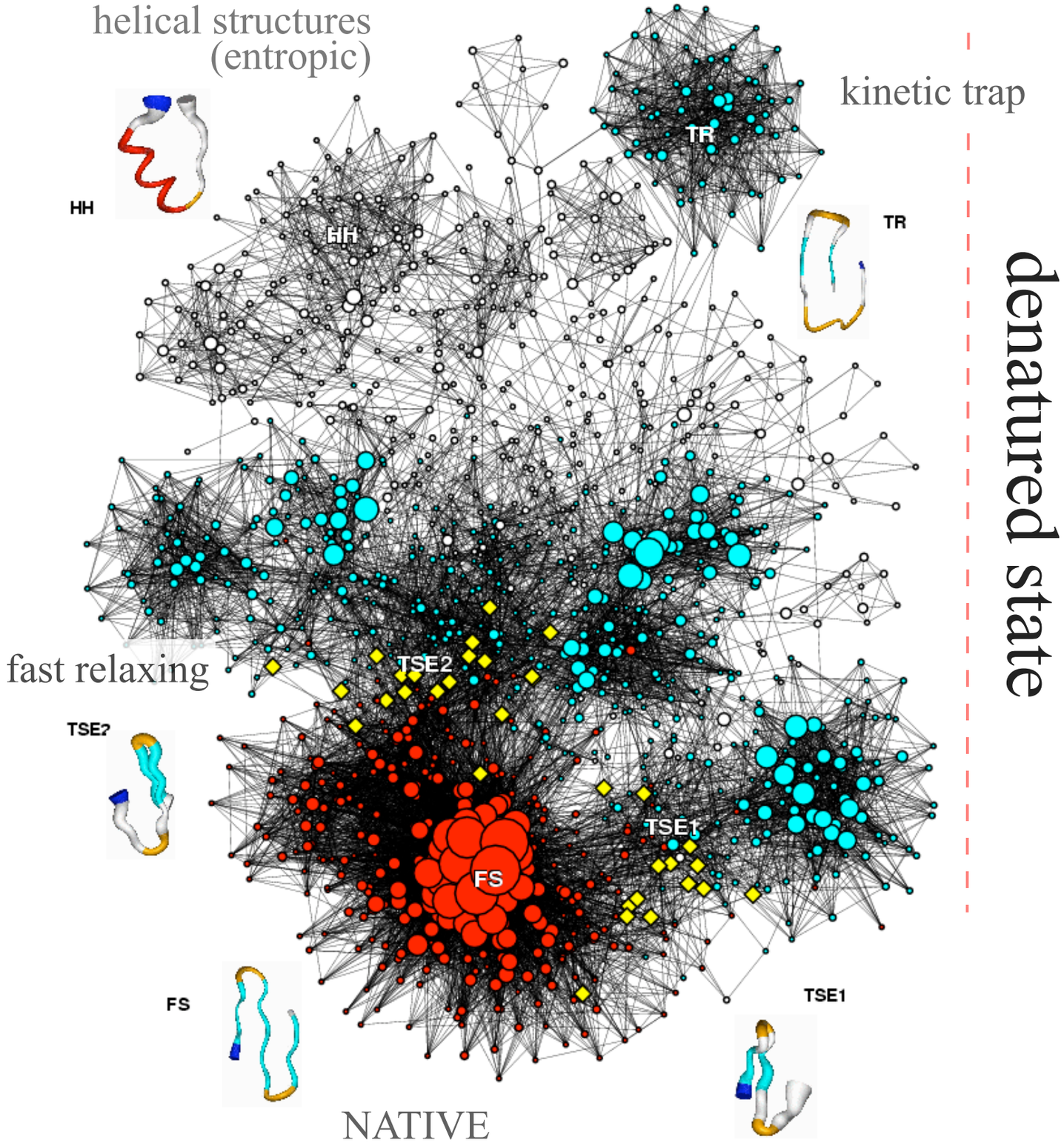


Complex Networks



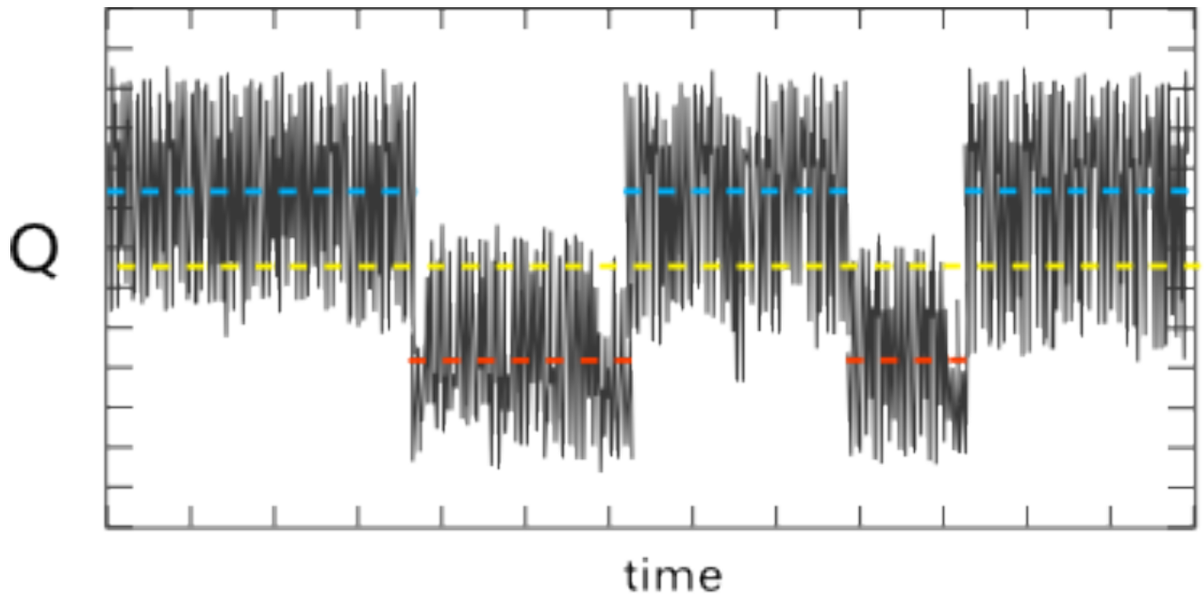


denatured state



Rao F & Caflisch A *JMB* 2004; Gfeller D *et al PRE* 2007; Gfeller D *et al PNAS* 2007; Rao F & Karplus M *PNAS* 2010

Avoid using arbitrarily chosen order parameters


Q
time

dynamics reading

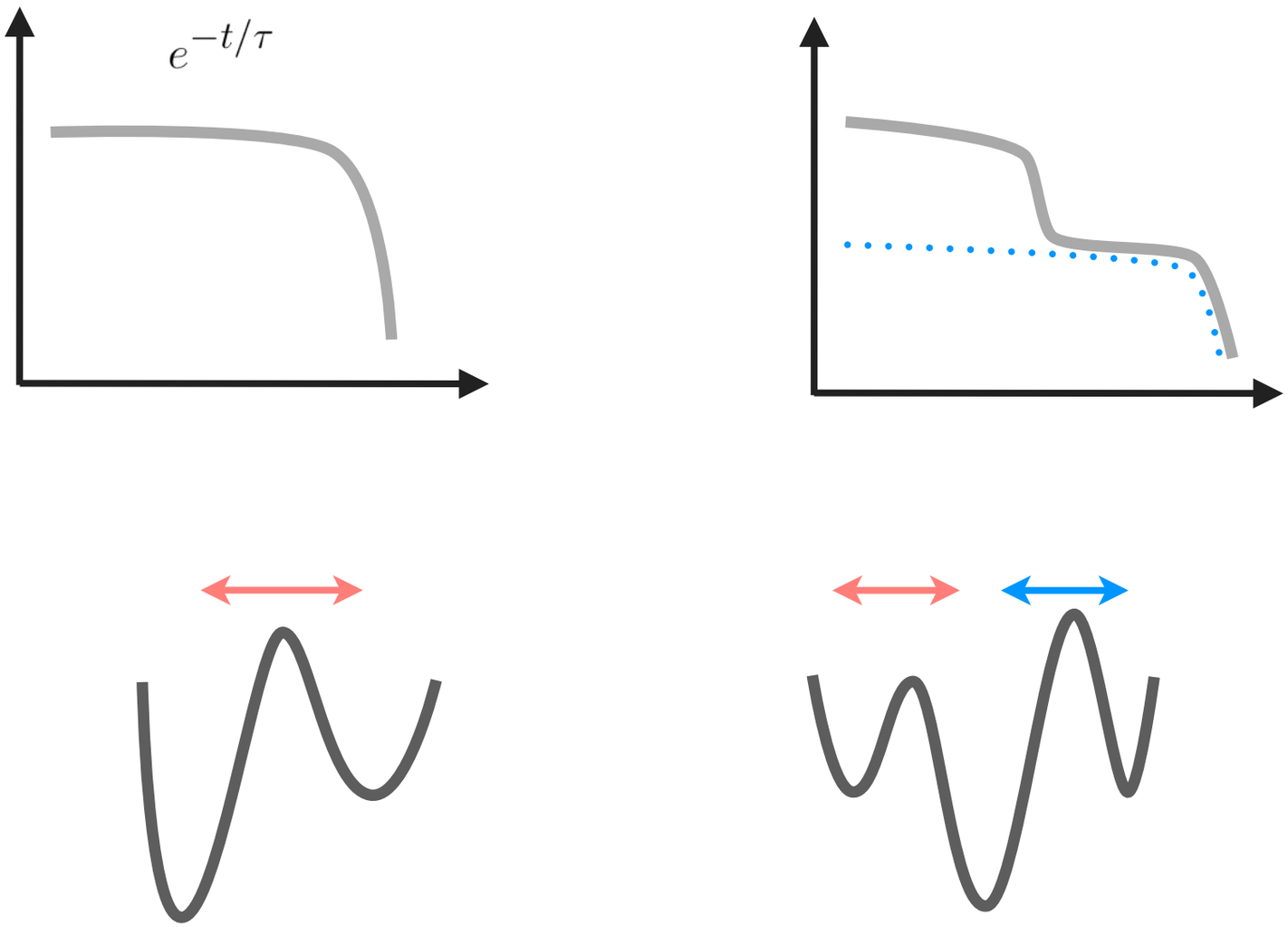
Hydrogen-bond kinetics as paradigm

it is apparently a simple two state process: **ON** or **OFF**

bound **unbound**

Consequently a simple exponential behavior is expected

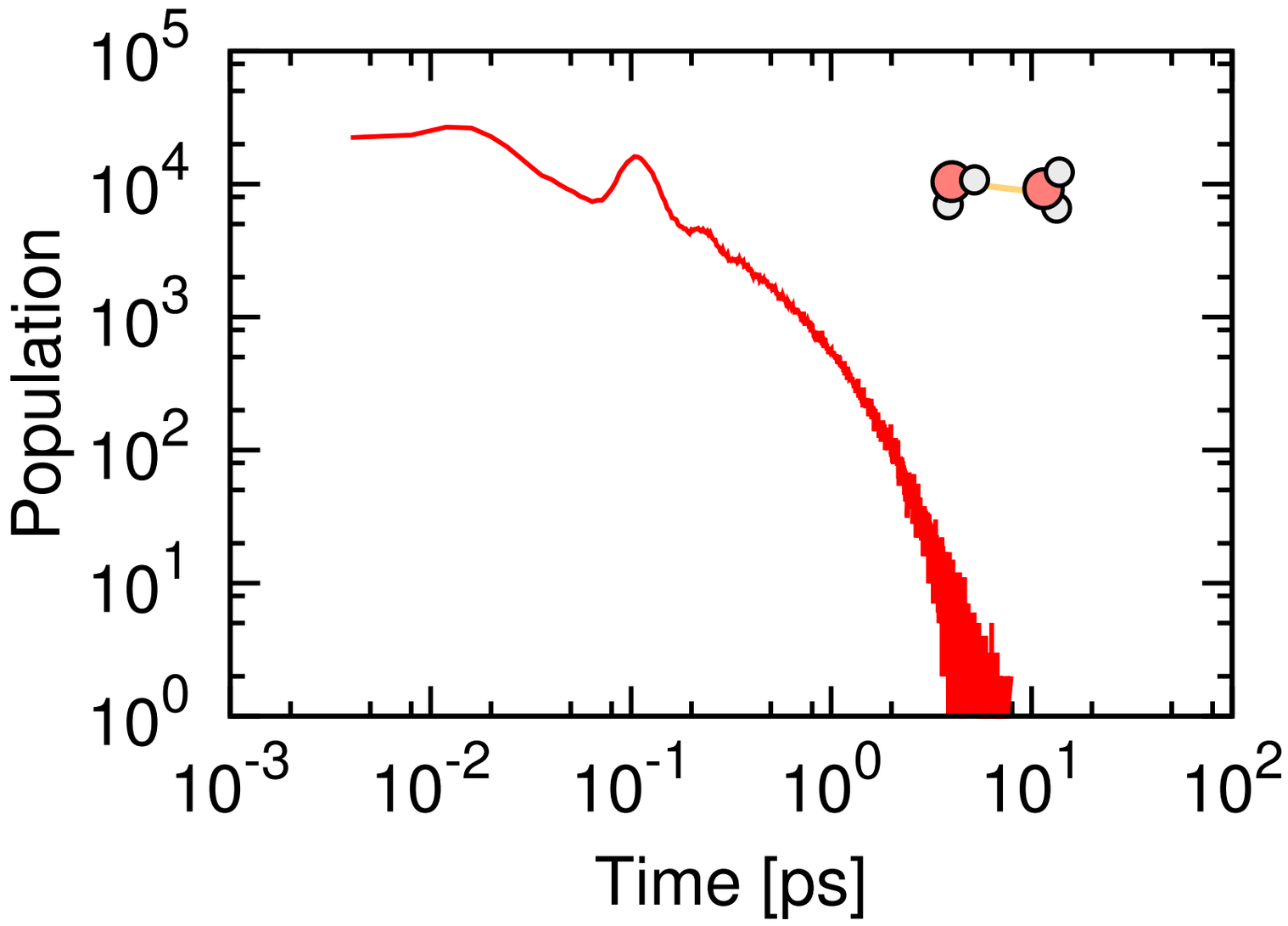
We know everything that is simple exponential kinetics



one time scale

two time scales

Bad-news a funky stretched exponential is observed instead



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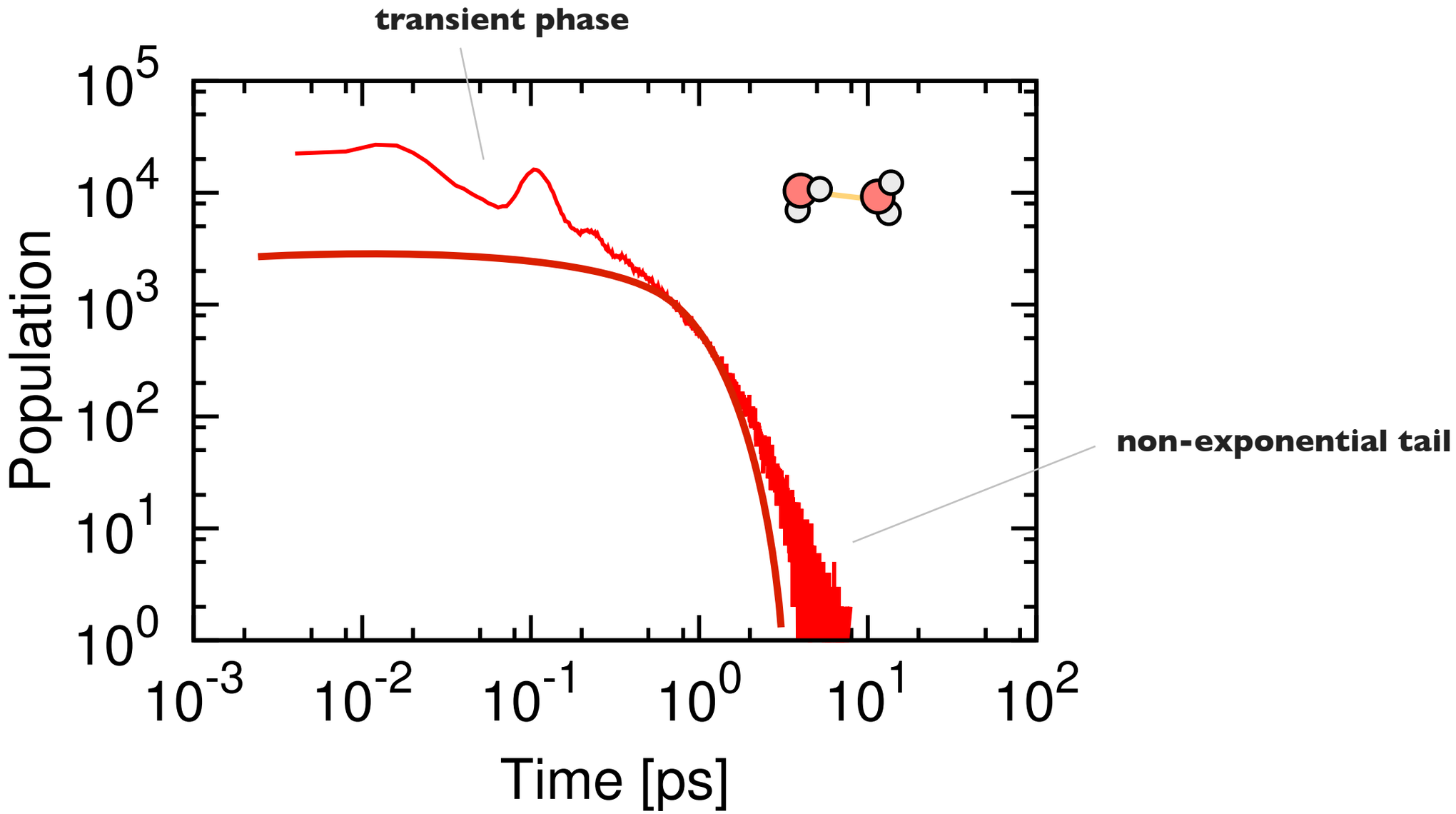
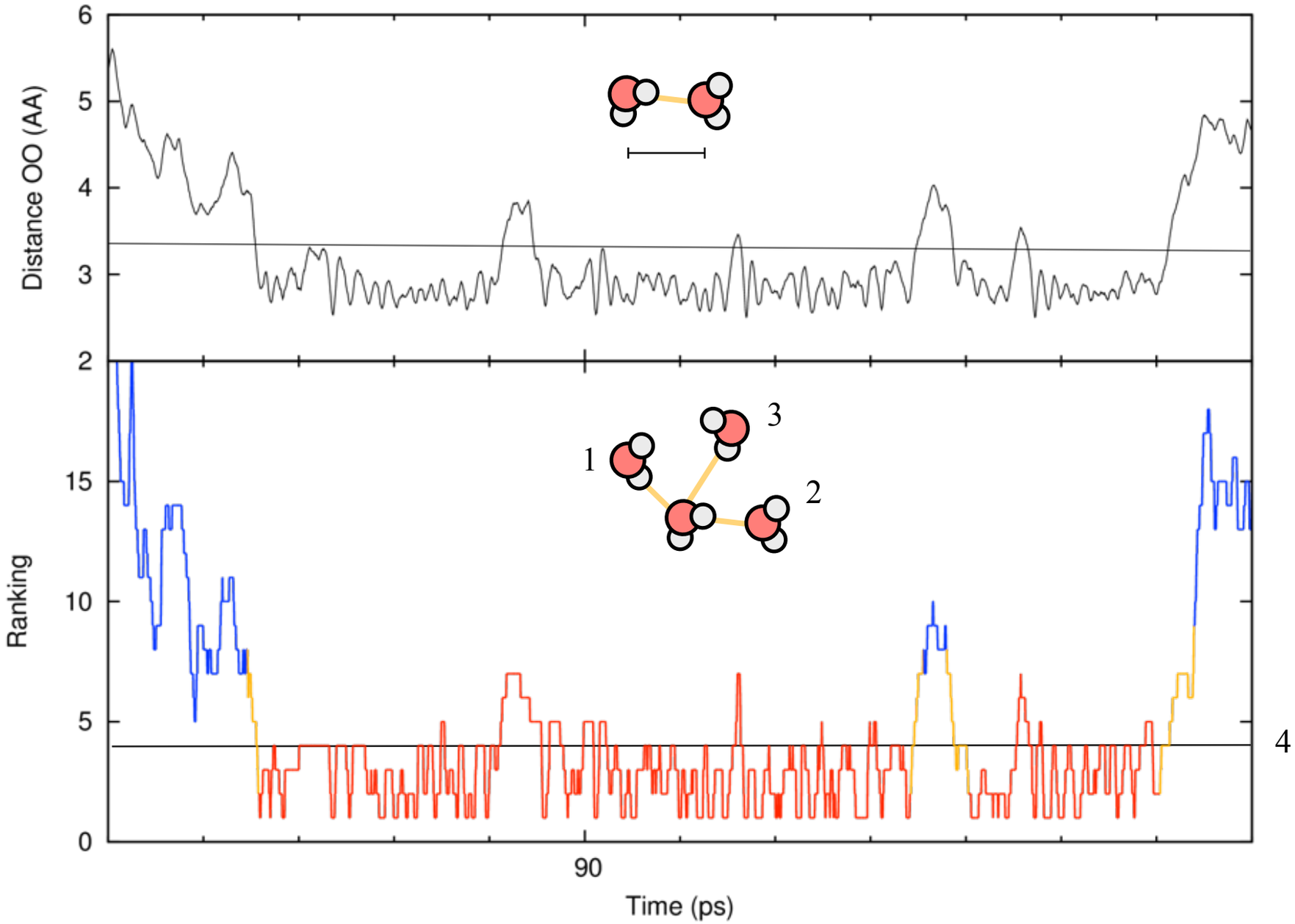


FACT: no characteristic time in hydrogen bonding

A molecular trajectory contains the information we're looking for



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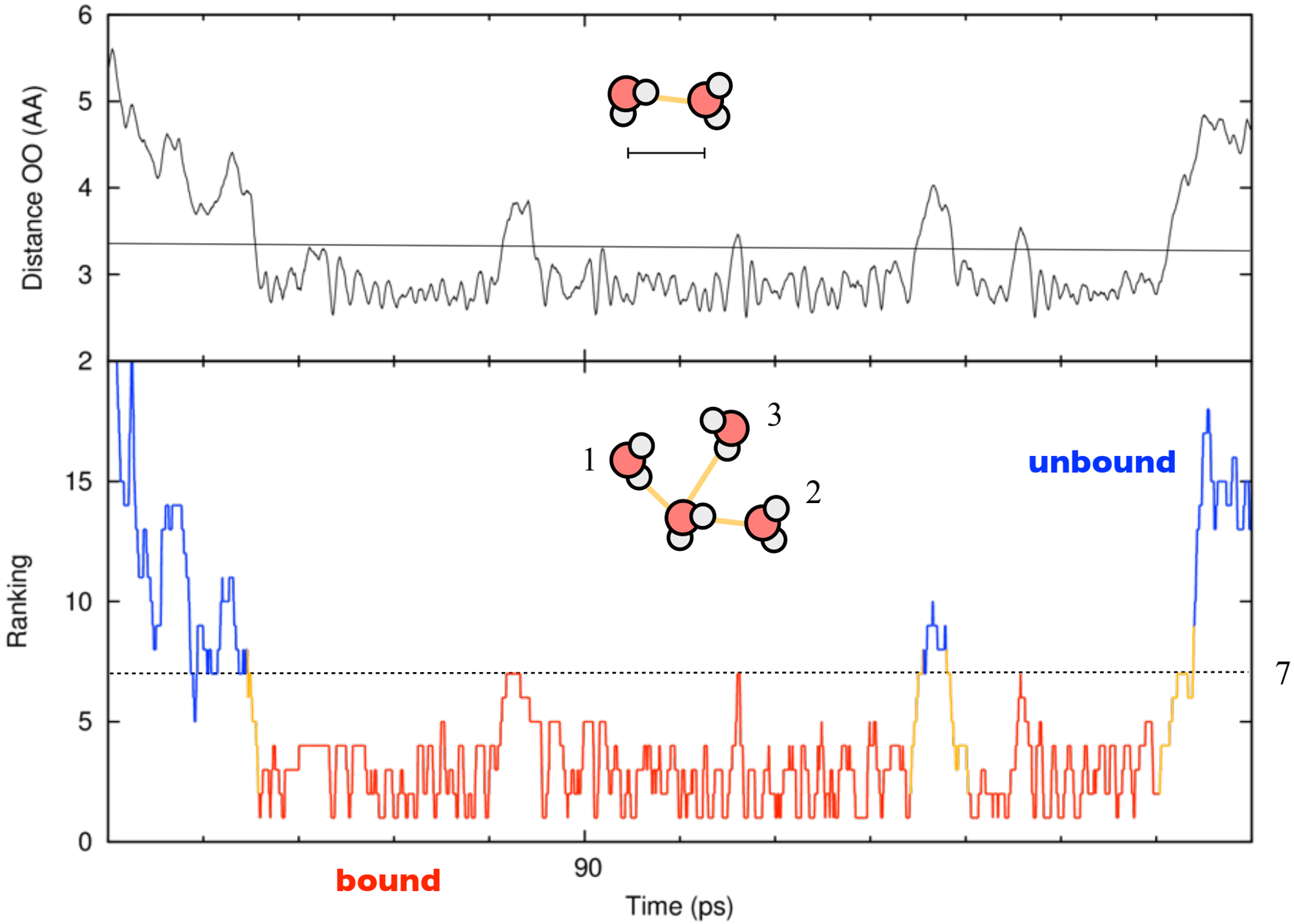

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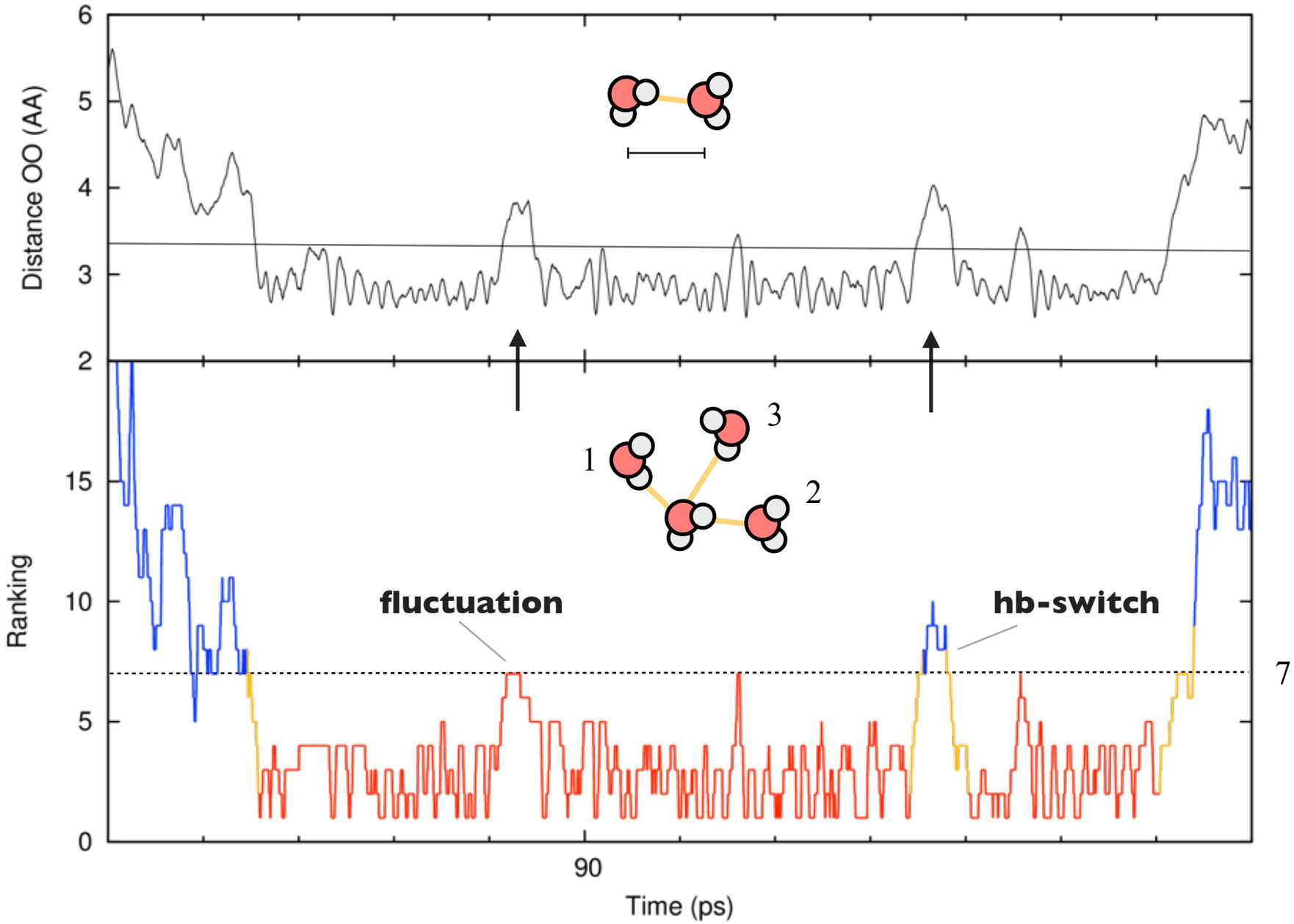
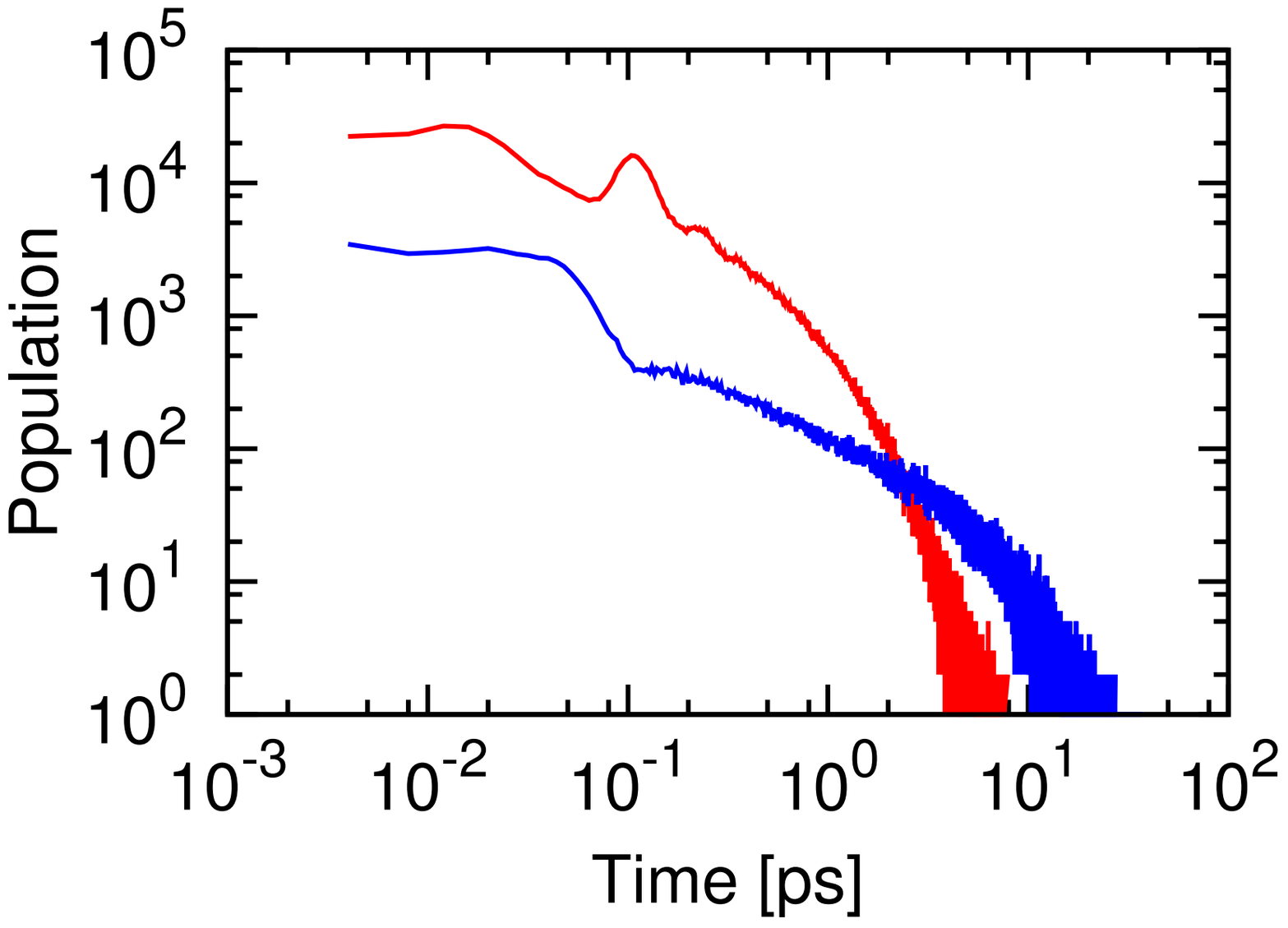


HB lifetime is (now) fitted by a multi-exponential



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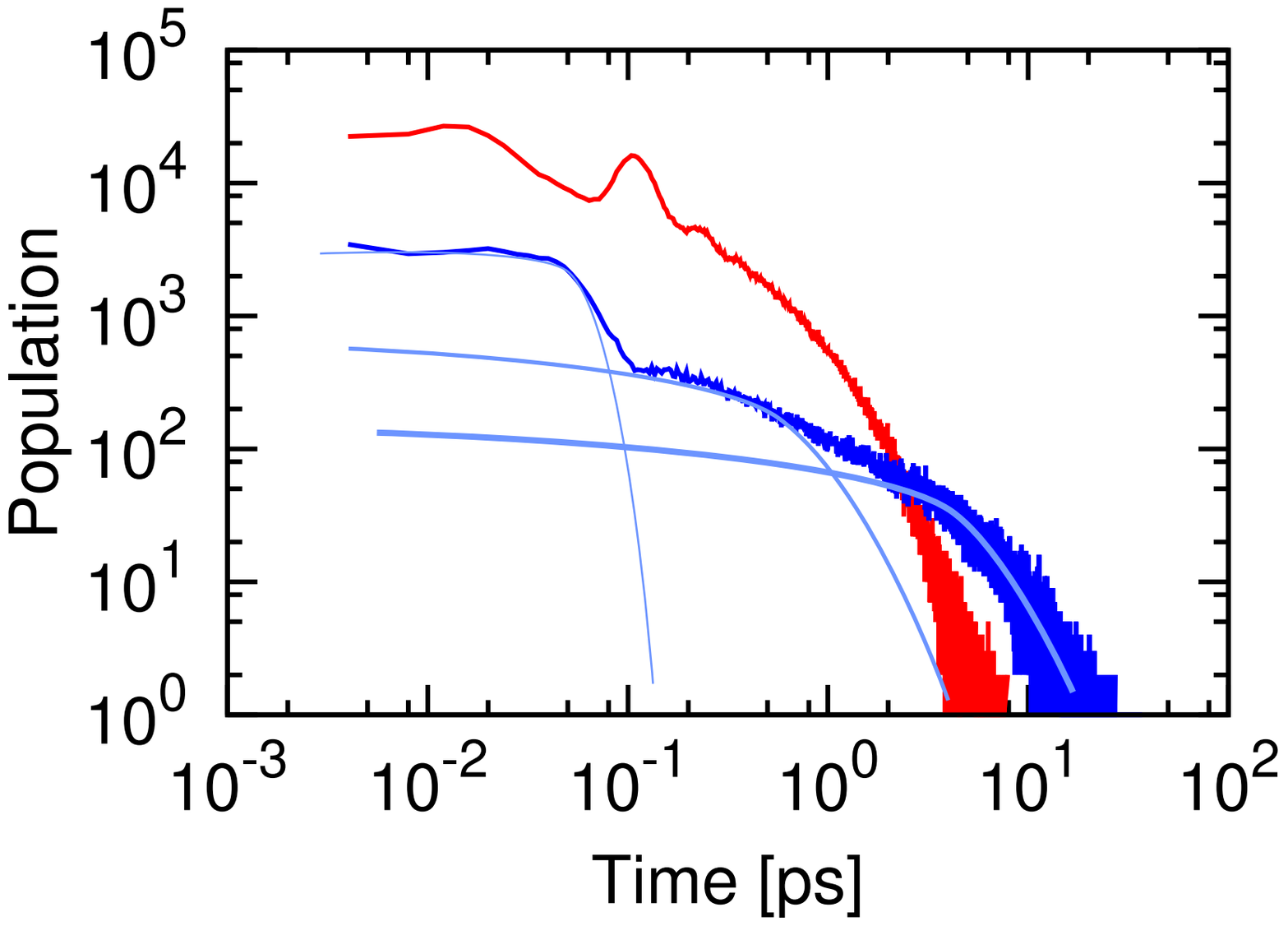

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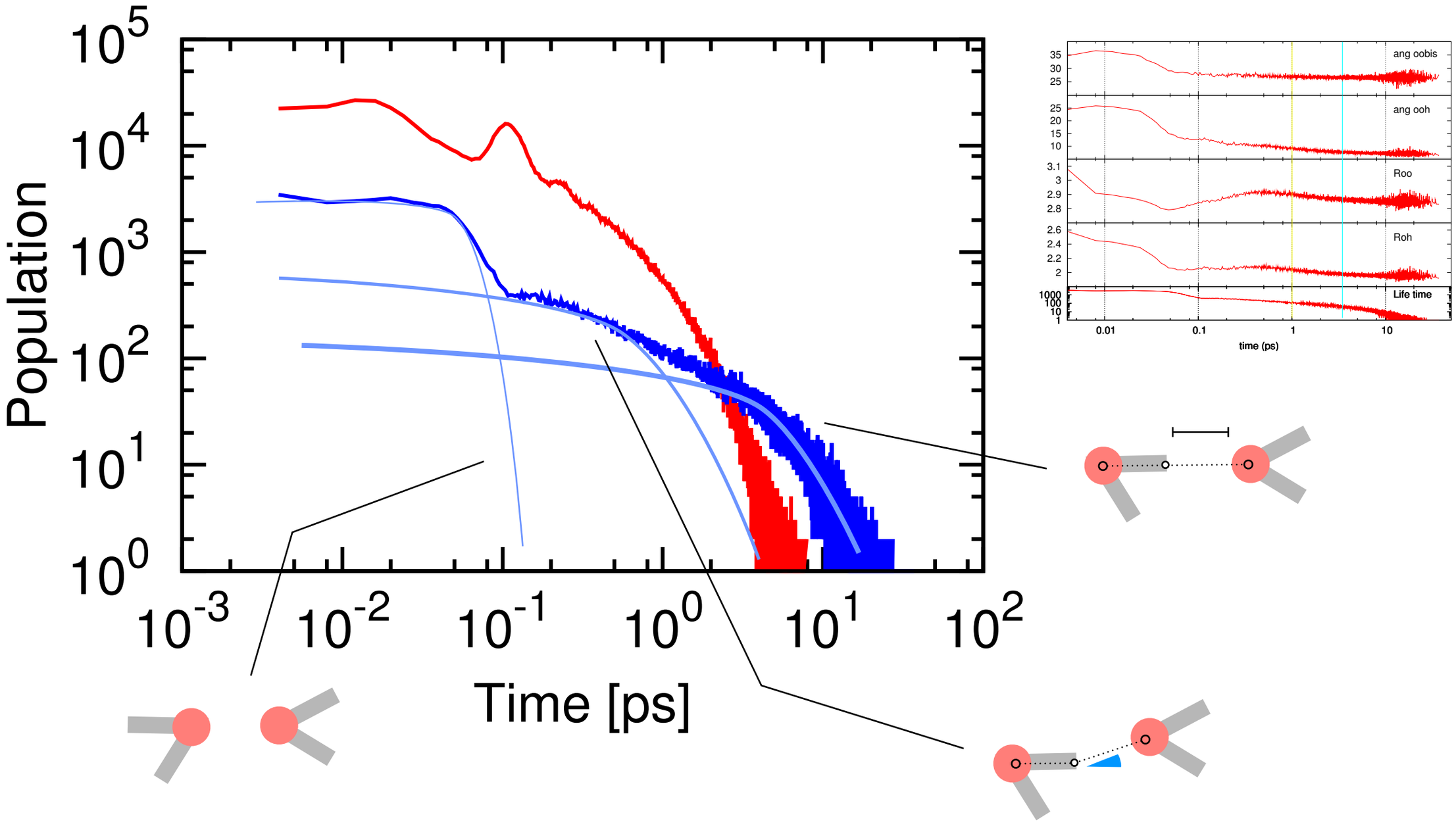
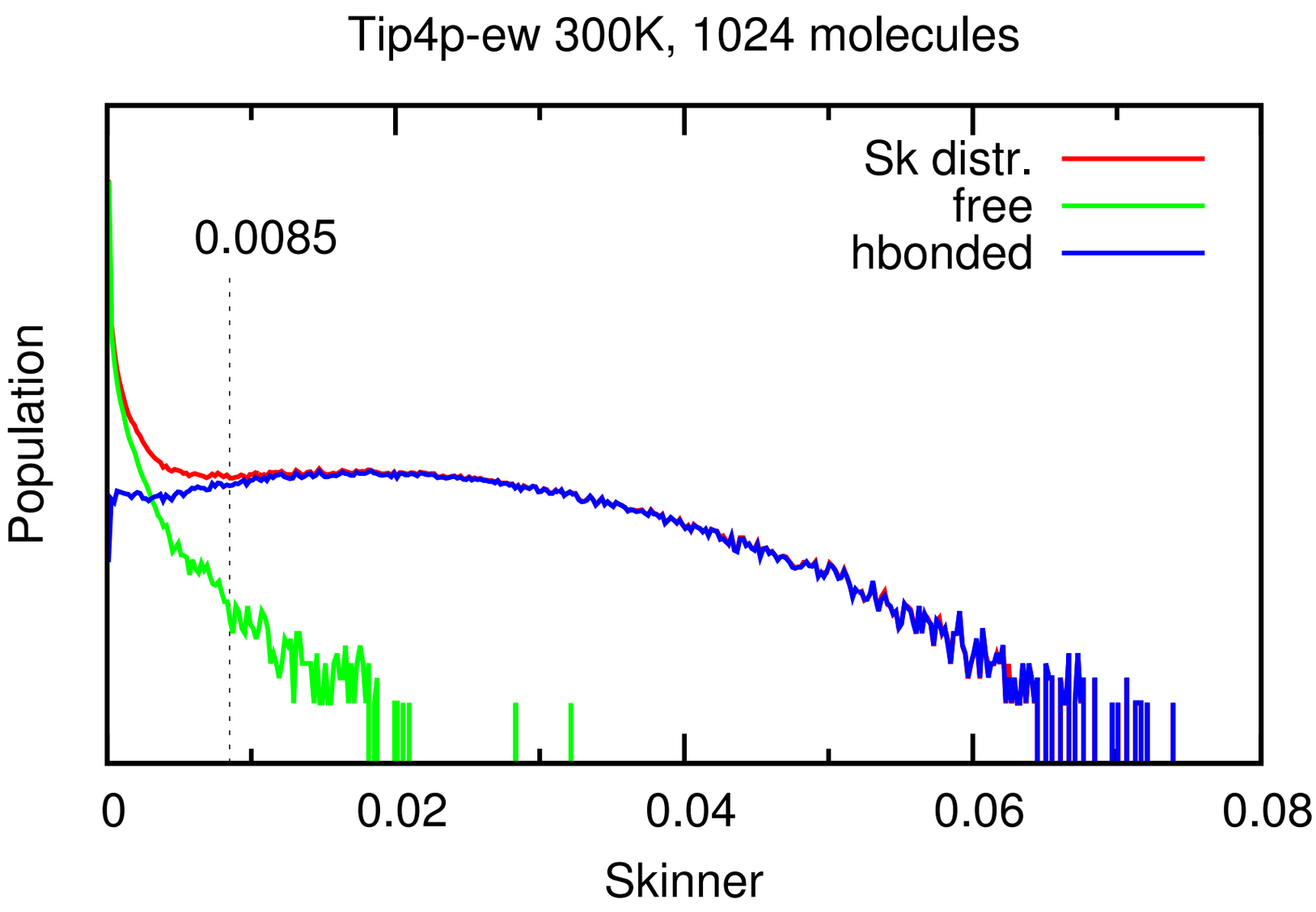


Dynamics provides smooth distributions of order parameters



Acknowledgments

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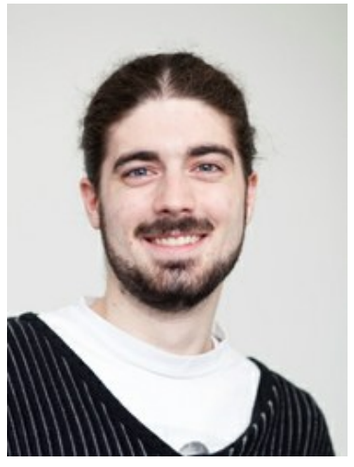

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