Phase space dynamics of biomolecular systems: the structure of chaos and role of water in conformational transitions

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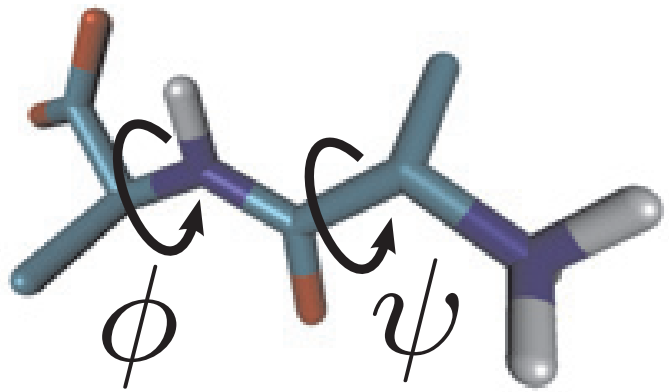
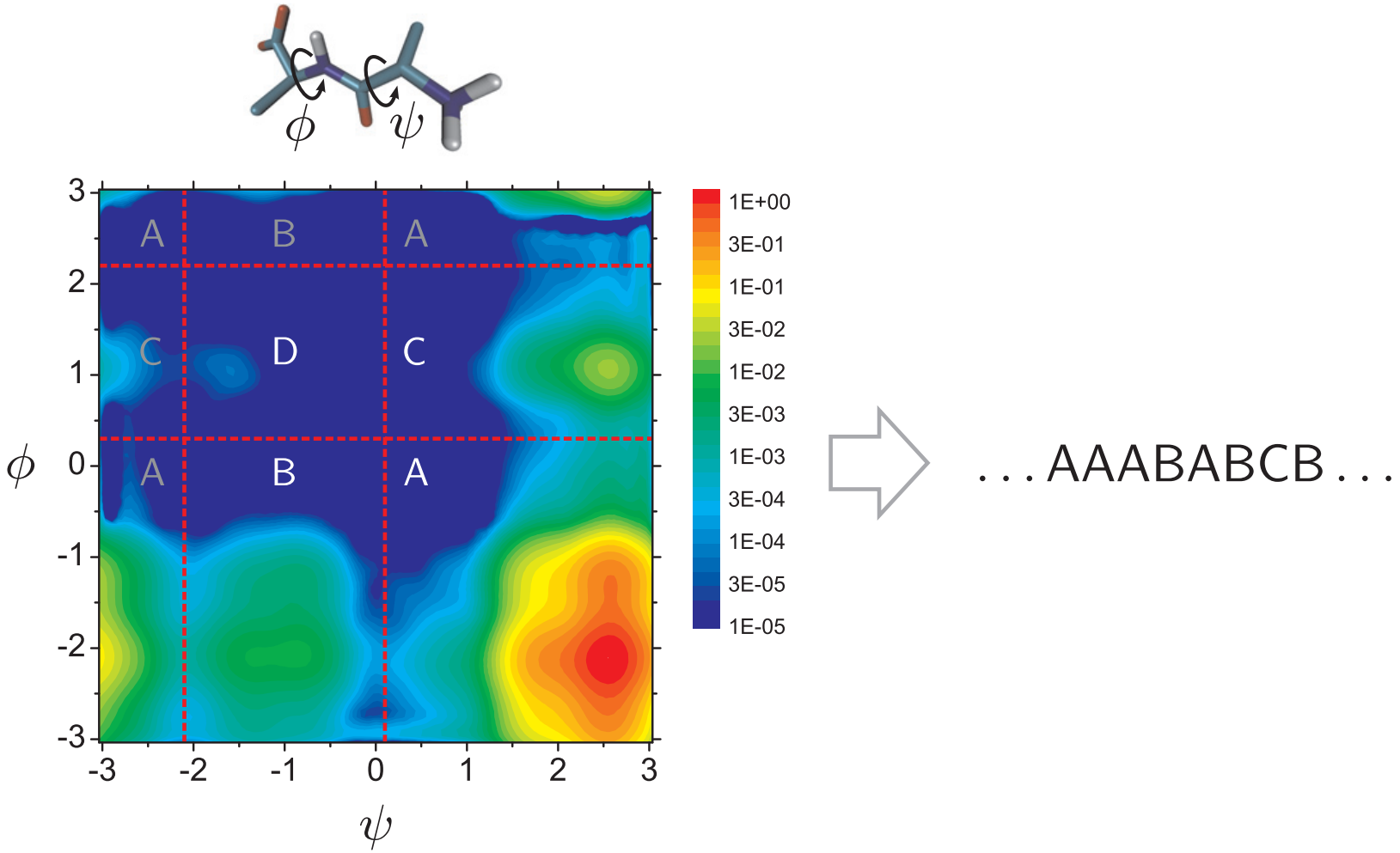
21 Jun 2011

Dialanine conformational dynamics

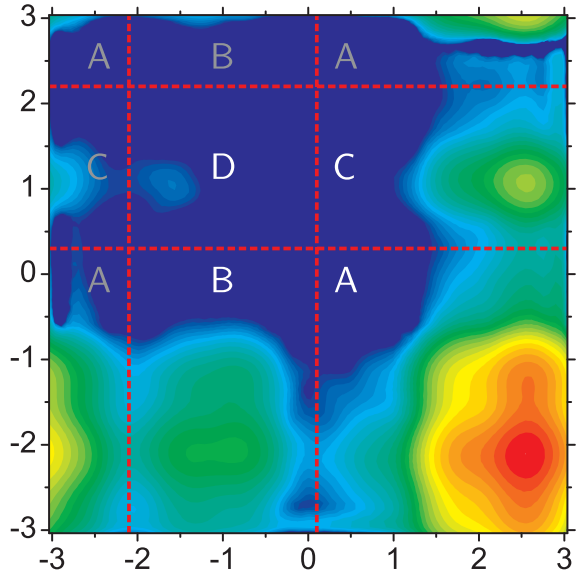


Dialanine conformational dynamics



Density of conformations for a 1μs trajectory and its symbolisation

Markov State Model



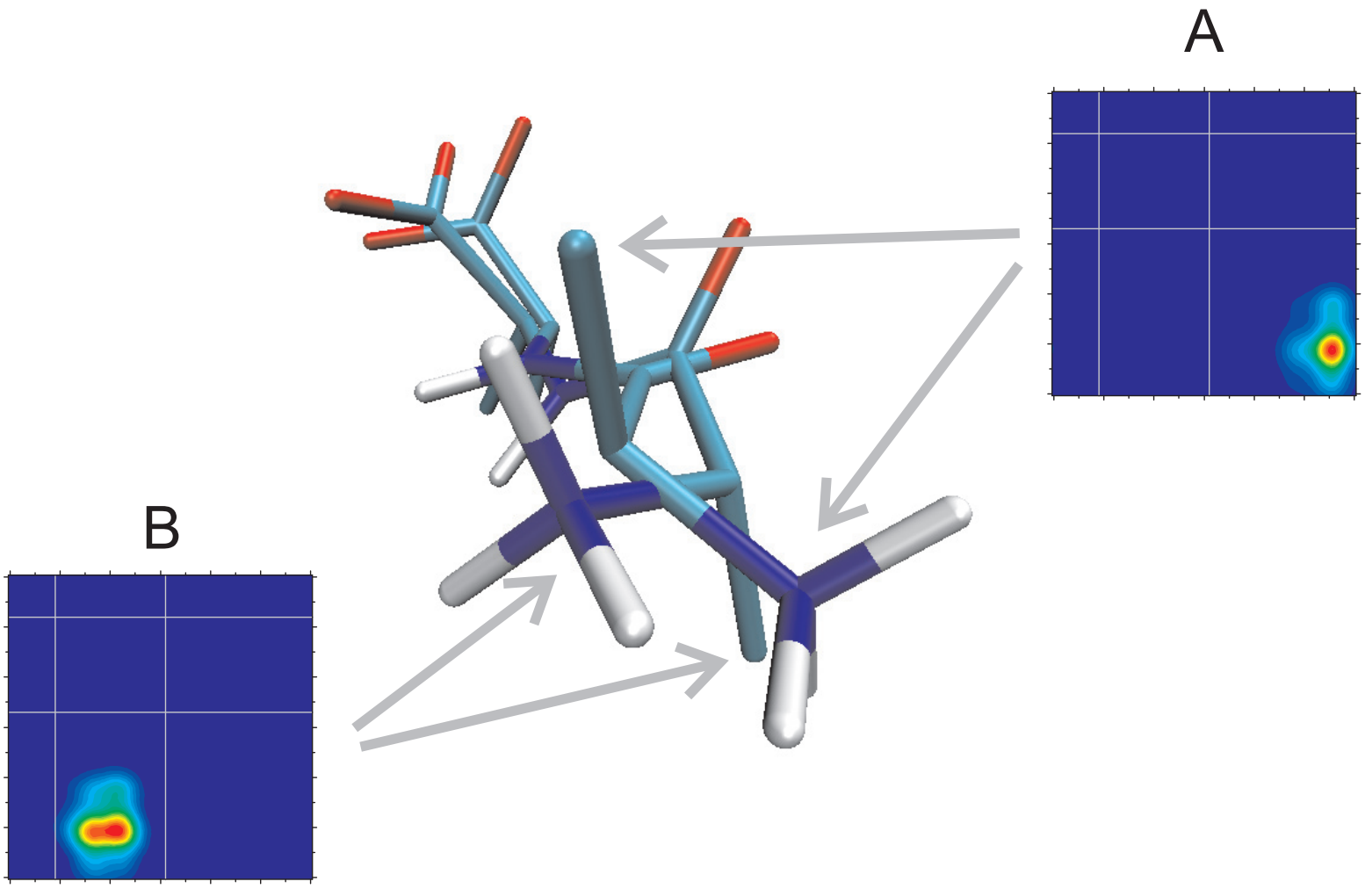
$\Delta t = 5ps$:

	A	B	C
A	0.997	0.002	0.001
B	0.261	0.737	0.002
C	0.097	0.001	0.901

Markov State Model

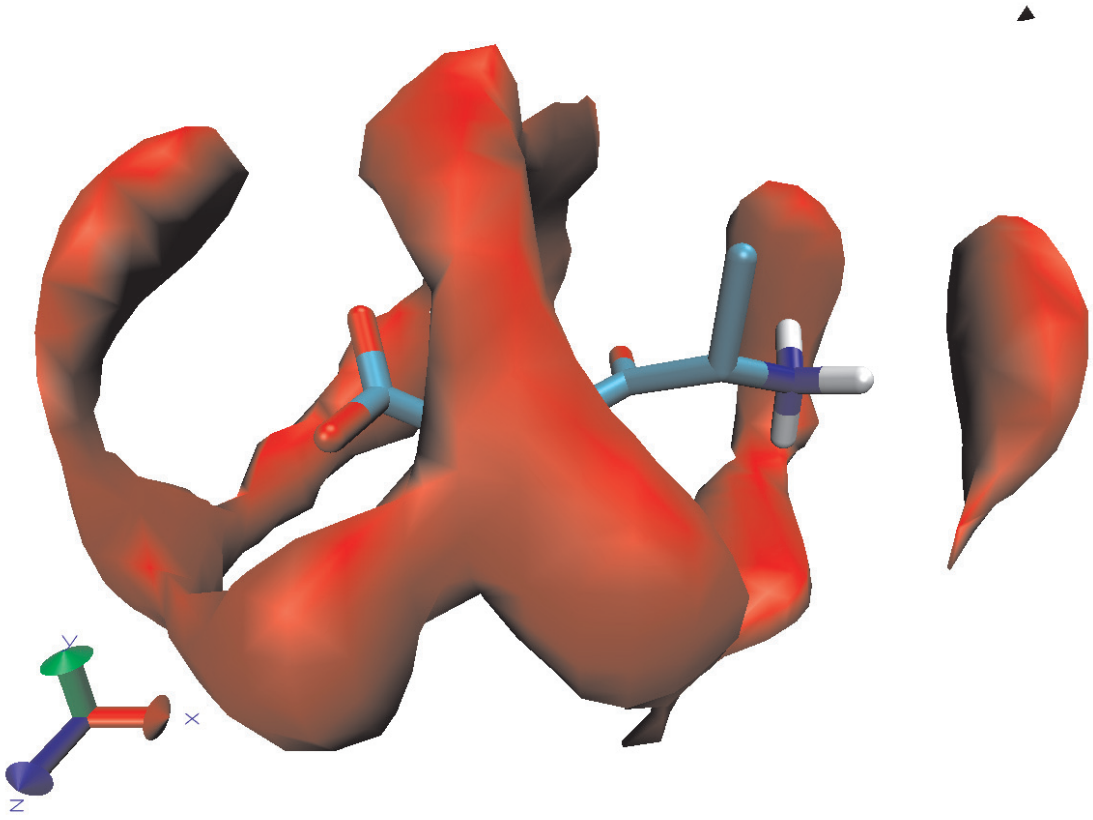
The probabilities do not say anything about *how* and *why* the transitions happen.

How water contributes to the transition from A to B



Transition from A to B corresponds to almost 180° flip

How water contributes to the transition from A to B

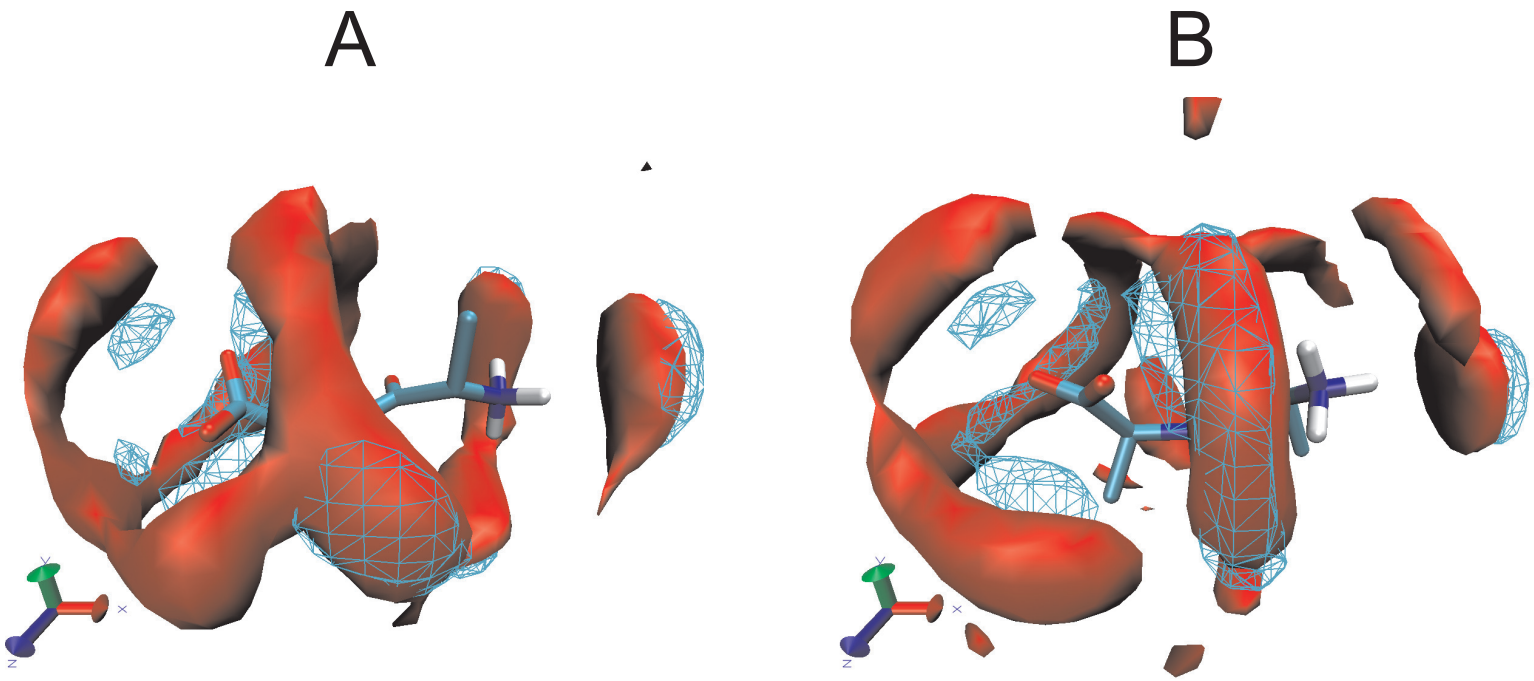


Density isosurface at 0.7 $\frac{am}{A^3}$ (average: 0.5) of oxygen of state A

How water contributes to the transition from A to B

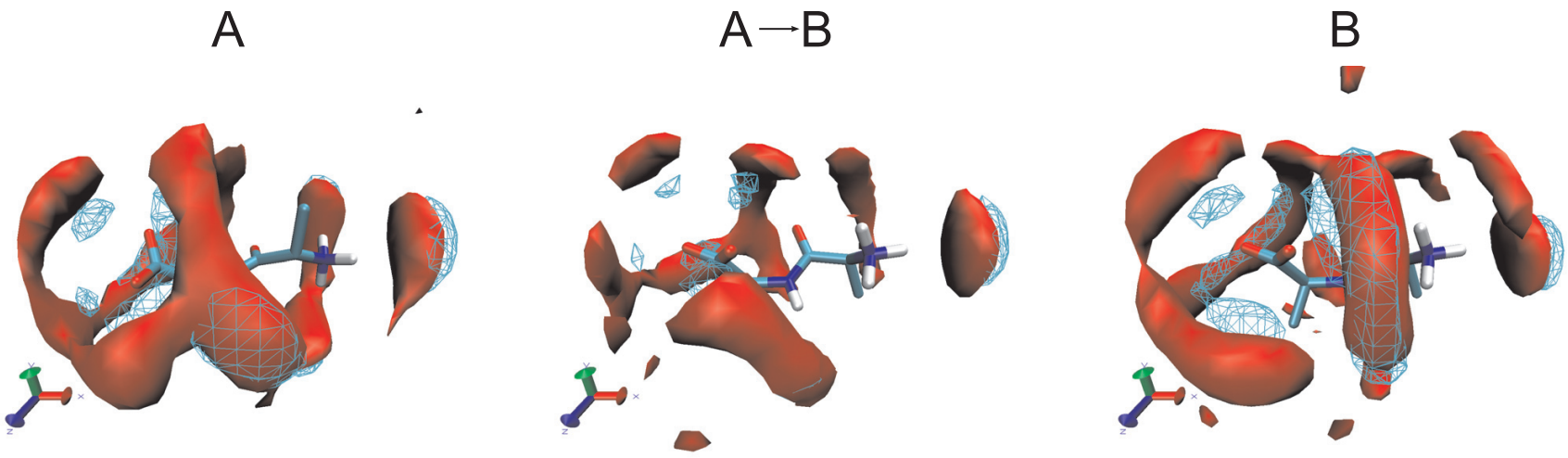
Dense areas of water correspond to *more stable structure*,
that is a more rigid hydrogen bonds network.

How water contributes to the transition from A to B

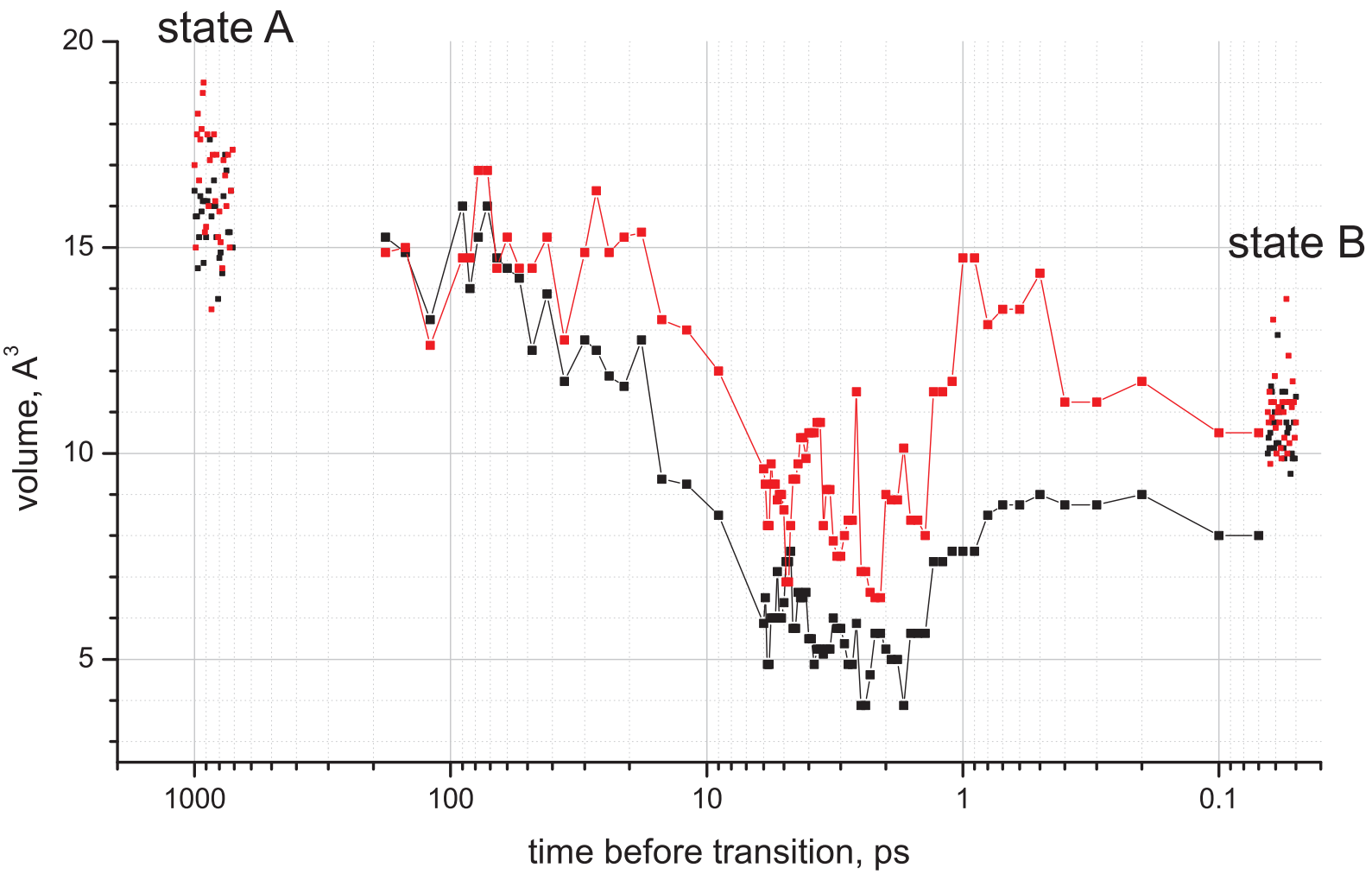


Density isosurfaces for states A and B

How water contributes to the transition from A to B

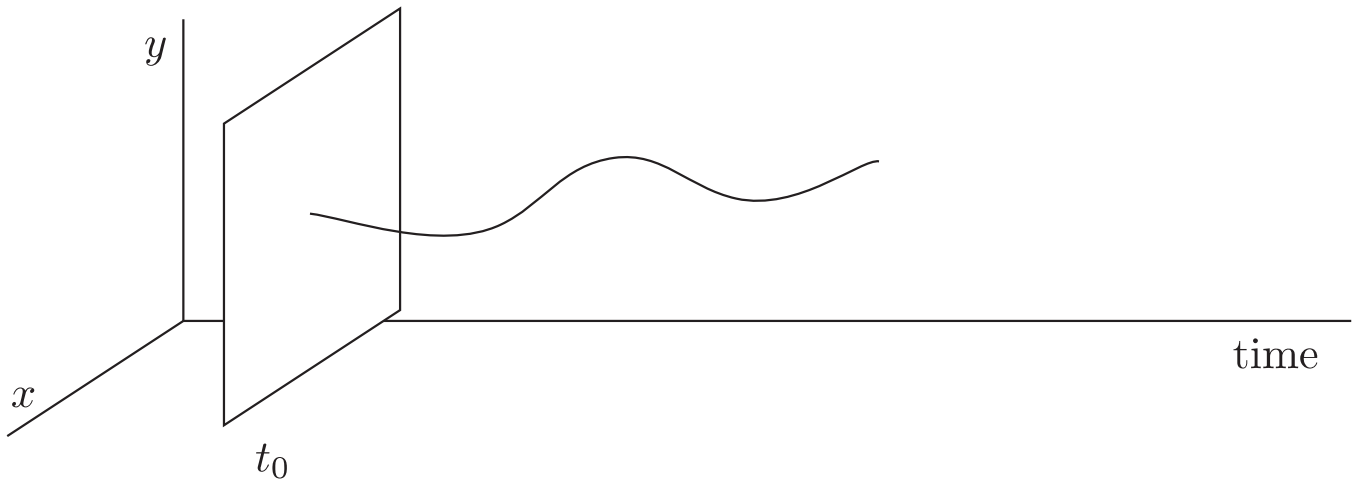


Water hydrogen bond network dynamics



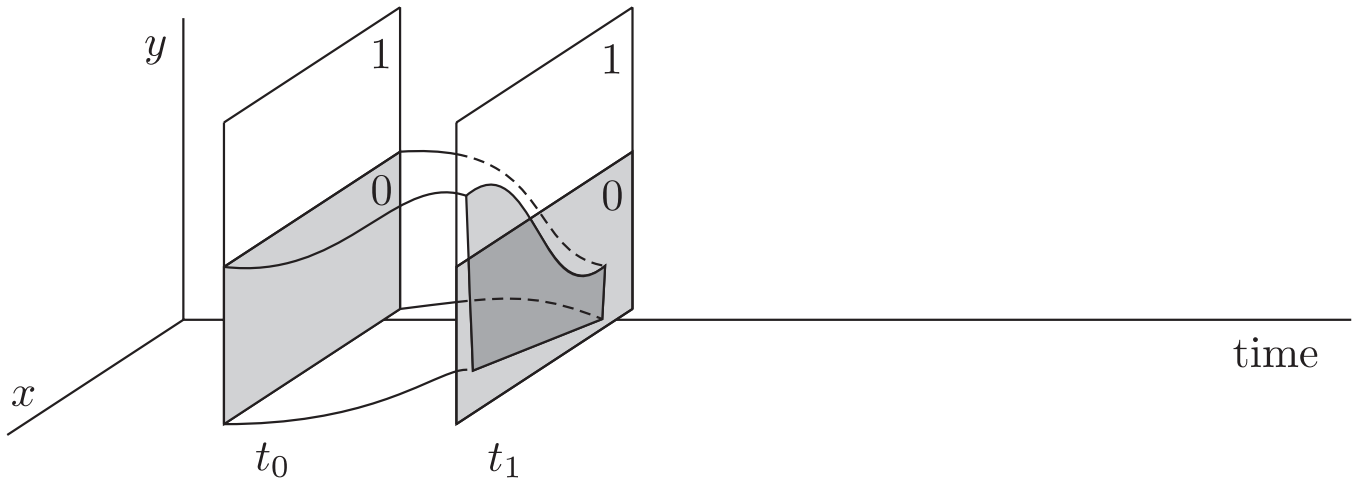
Volume of high oxygen and hydrogen density during the transition from state A to state B

Symbolic sequences carry information about the phase space



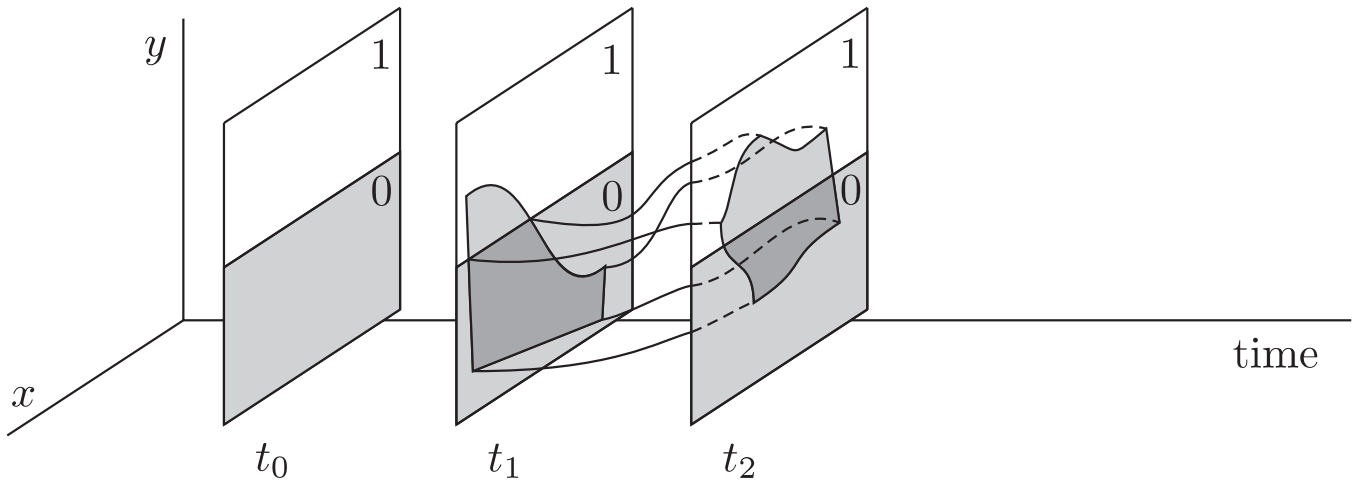
Two-dimensional system with a trajectory

Symbolic sequences carry information about the phase space



Symbolic sequence: 00

Symbolic sequences carry information about the phase space



Symbolic sequence: 000

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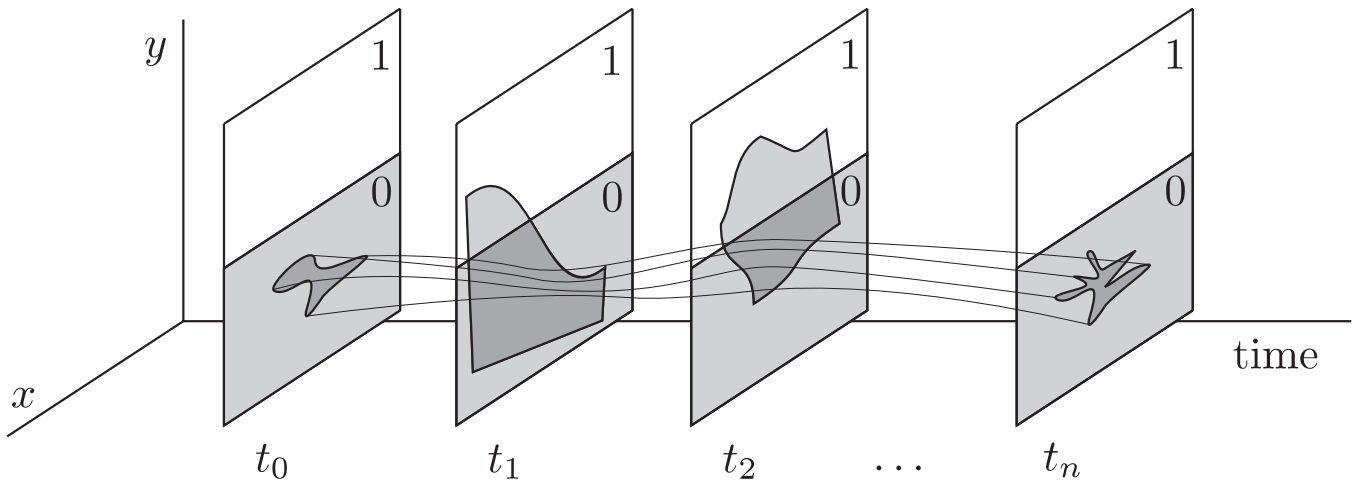
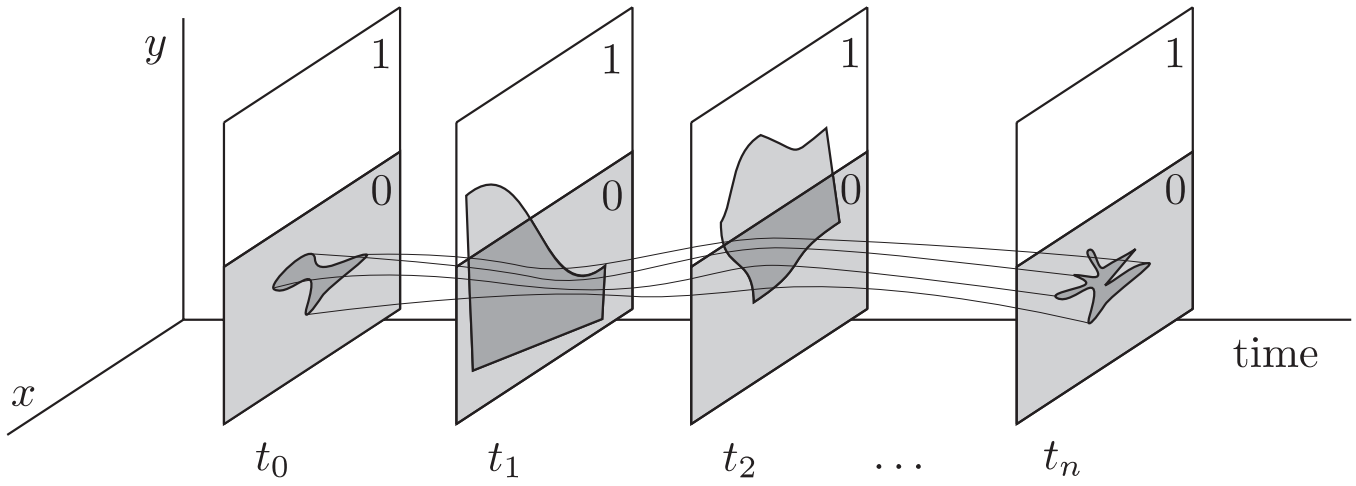


Symbolic sequence: $000\ldots0$

Symbolic sequences carry information about the phase space



- for an initial $\mathbf{x}_0$, the trajectory $\{\mathbf{x}_i\}_{i=-n}^{n}$ visits the partition elements $B_{\mathbf{x}_i}$
- for a *generating partition* the intersection of all images and pre-images in the limit $n \to \infty$ is a single point: $\cap_{i=-n}^{n} \mathbf{f}^{(-i)}(B_{\mathbf{x}_i})$

[VM Alekseev and MV Yakobson, *Physics Reports* **75**, 290 (1981)]

The Standard Map

$$H(x, p, t) = \frac{p^2}{2} + K \cos x \delta_1(t)$$

Represented as a map:

$$\begin{aligned} p_{n+1} &= p_n + K \sin x_n \\ x_{n+1} &= x_n + p_n + K \sin x_n \end{aligned}$$

The Standard Map

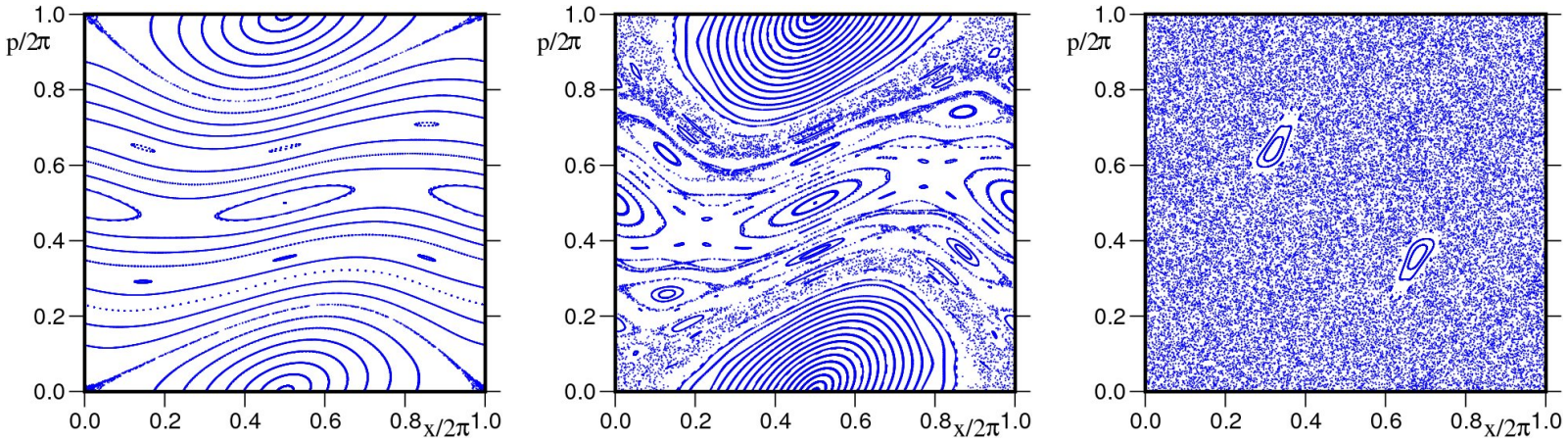


Figure: $K = 0.5$, $K = 0.971635$, $K = 5$

The Standard Map

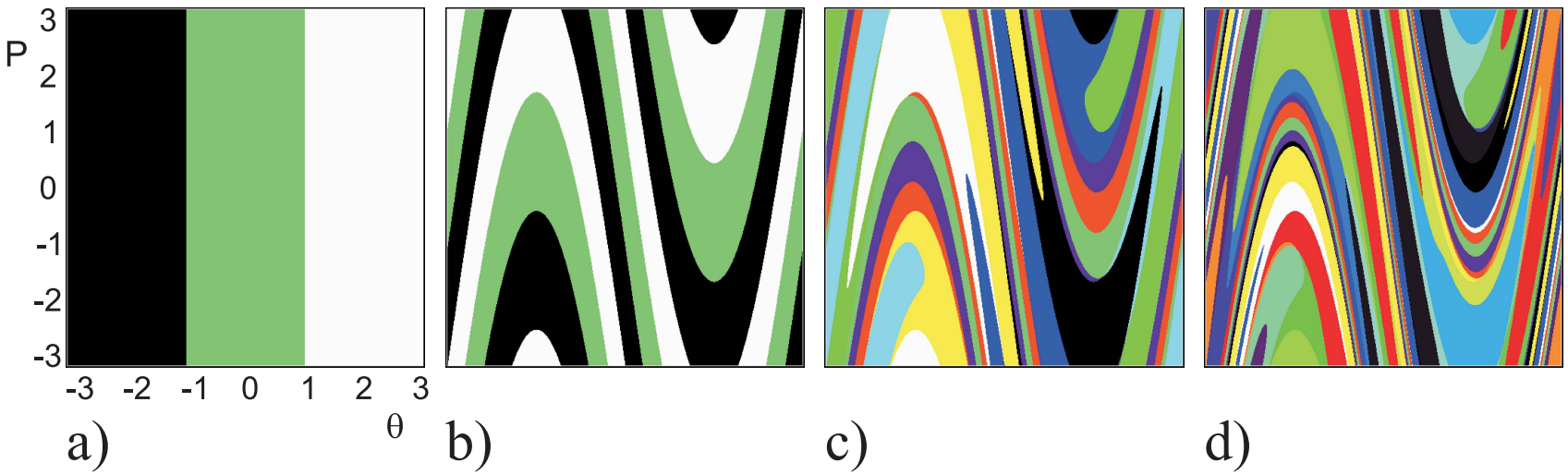


Figure: The refinement of a partition caused by considering longer symbolic sequences for the Standard map. a) the original three symbol partitioning corresponding to the one time step history; b) - d) two to four symbol histories induced partitioning

Back to dialanine

Time scales of the transitions: 0.25 ns

Problem: none of the molecular properties exhibit this long time scale.

Partition the ψ - ϕ map

Divide the A basin into $3^8 = 19683$ parts $\overleftarrow{s}_i \equiv \{\ldots s_{i-2}s_{i-1}s_i\}$

For each part analyse the statistic $P(s_{i+1}|\overleftarrow{s}_i)$

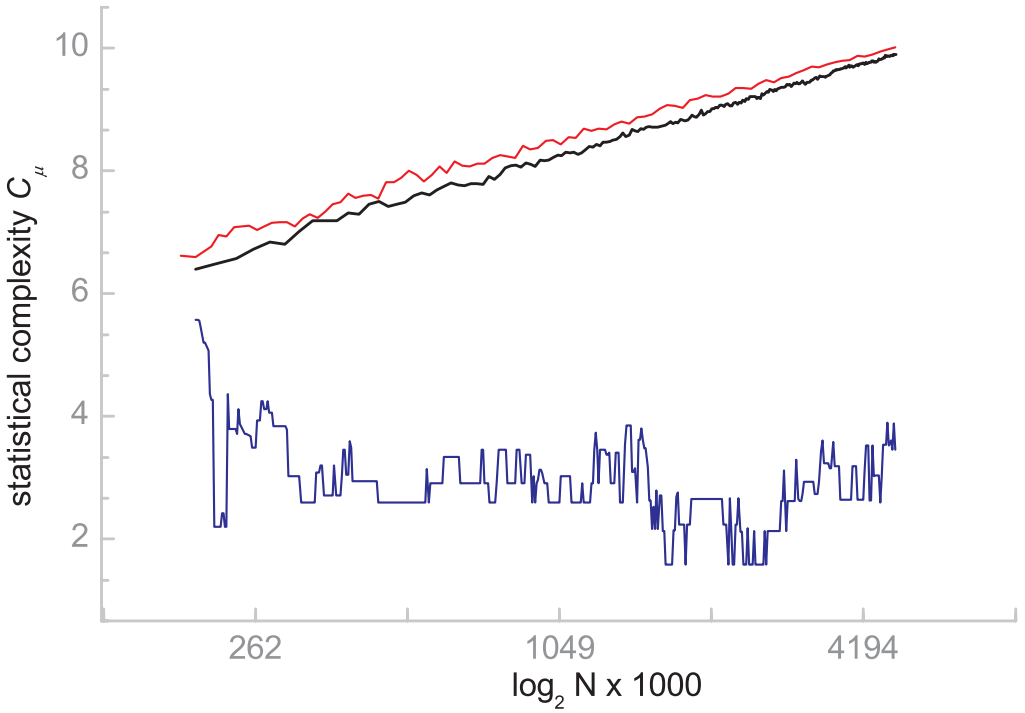
Partition the ψ - ϕ map

For the first few hundred picoseconds the probabilities for all parts are the same.

Then, some start deviating from the rest. By the end of the 1μ simulation $\approx 5\%$ of the trajectories are different from the rest and between each other.

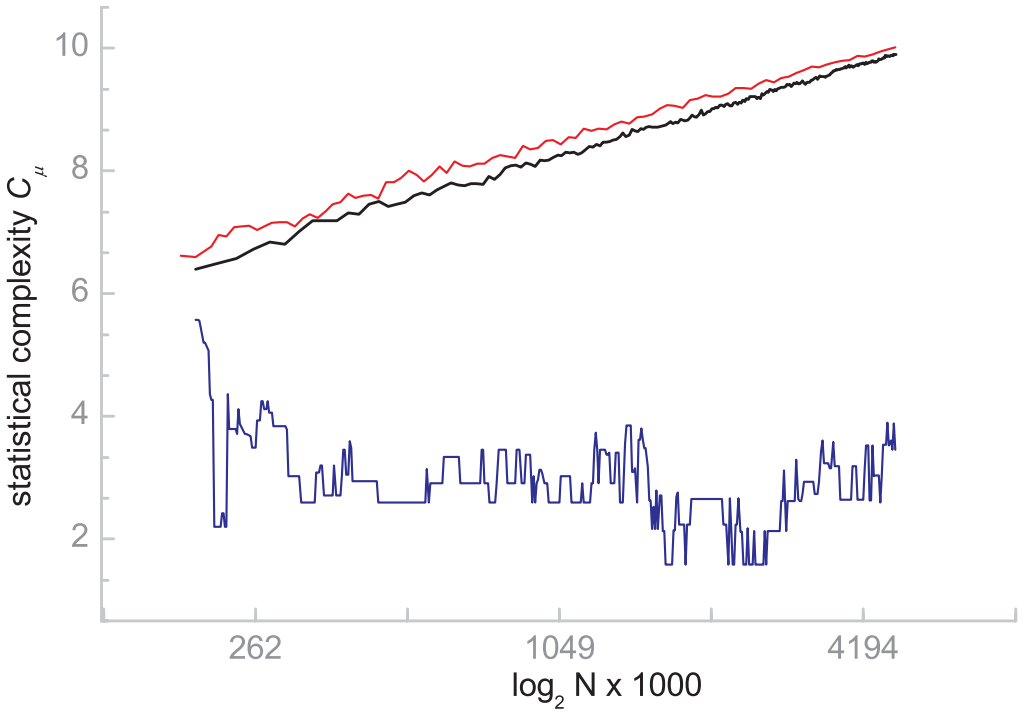
The number of these different trajectories grows logarithmically.

Consequences of slowly changing $P(s_{i+1}|\overleftarrow{s}_i)$



The number of special trajectories for original time series (black), and two simulated time series of stationary (blue) and non-stationary (red) Markov chain models

Consequences of slowly changing $P(s_{i+1}|\overleftarrow{s}_i)$



The number of special trajectories for original time series (black), and two simulated time series of stationary (blue) and non-stationary (red) Markov chain models

$P(0) = P(1) = P(2) = 1/3;$
$P(00) = P(10) = \cdots = 1/9;$
$P(0|00) \neq P(0|10)$

Special trajectories behave the same for any partition

Different projections: ψ - ϕ, coordinates or velocities of different atoms of the peptide, give the same grows of the number of these special trajectories.

Physical meaning: because the trajectories passing through the areas 'cut out' by symbolisation are influenced by the other degrees of freedom, the neighbouring atoms.

This rate of appearance of the special trajectories is *the same for dialanine and water*!

The special trajectories for a 21-residue peptide

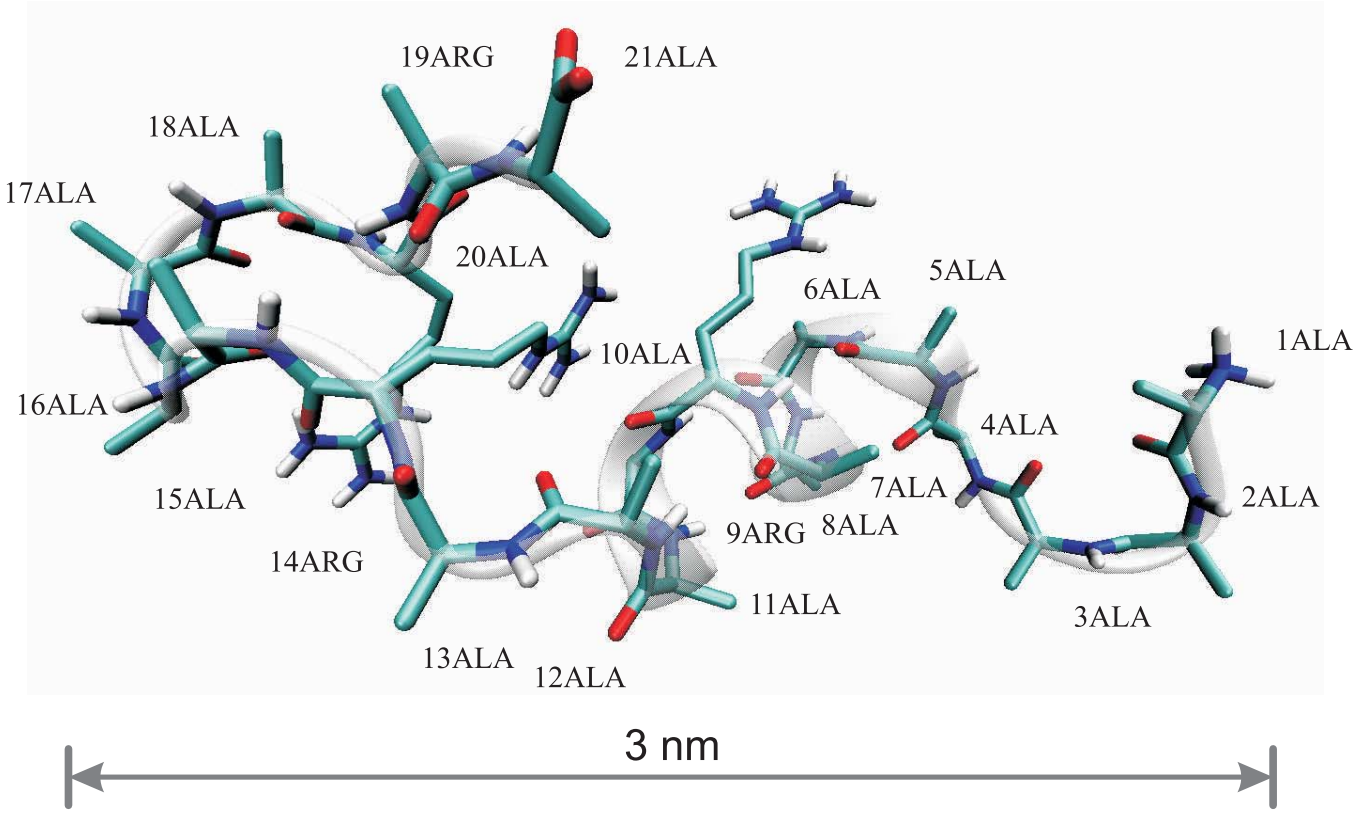
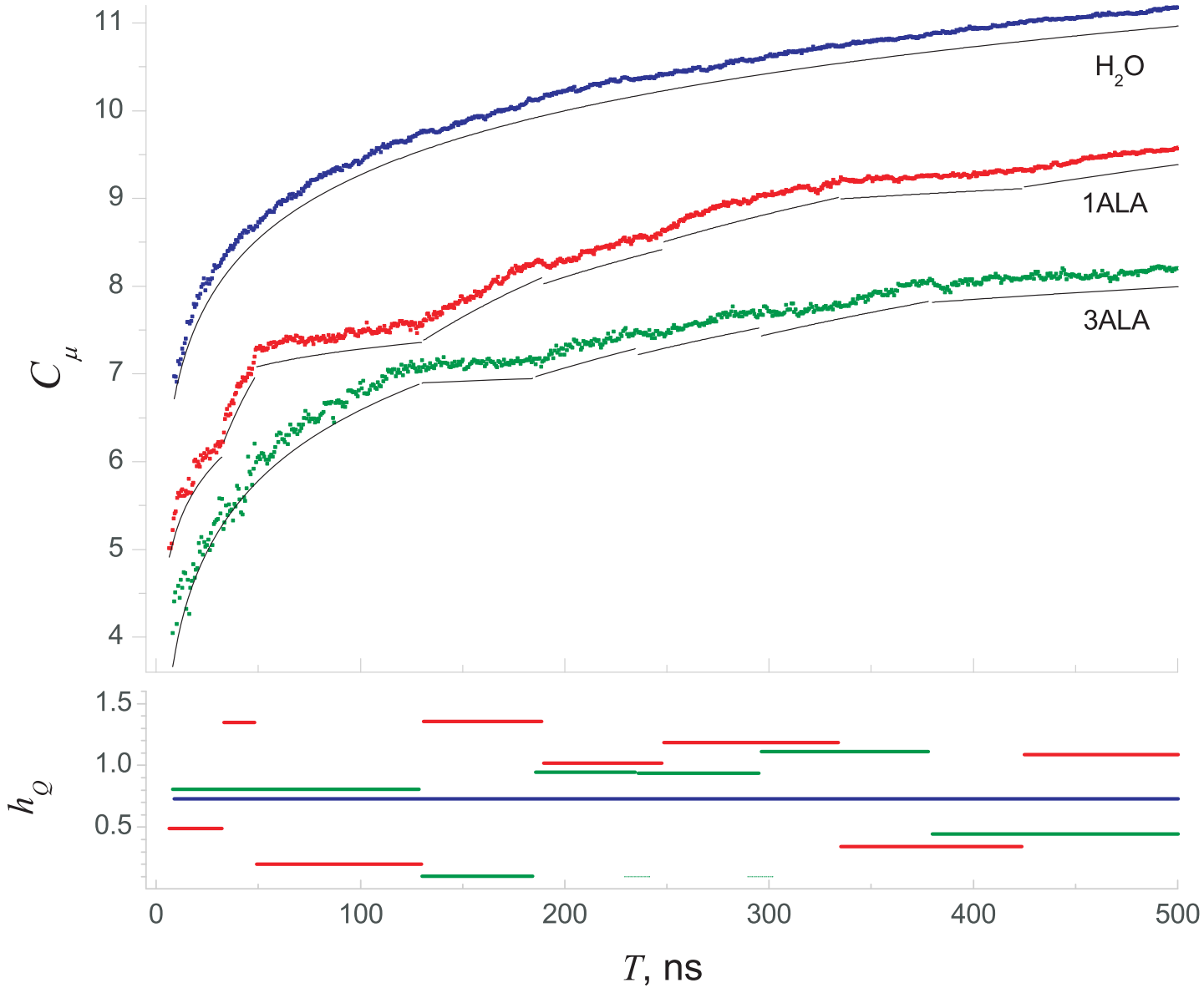


Figure: The A5(A3RA)3A molecule

The special trajectories for the 21-residue peptide



Conclusion

- Water drives the conformational changes in peptides (proteins).
- There is a *very slowly changing* process(s) in water that is collective and related to conformational transitions.