The Markovian time scale of peptide conformational dynamics

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The assumption of Markovian property transitions between protein conformational states is critical in the framework of Transition State Theory. We test this assumption by analysing the transitions obtained directly from the dynamics of an MD simulated peptide VPAL (Valine - Proline - Alanine - Leucine). The conformational states of the peptide are defined phenomenologically using clustering in dihedral space. We find that the transitions are Markovian at the time scale of ≈50ps and longer. However, at the time scale of ≈40ps the dynamics can not be adequately represented in the Markovian framework. Instead, at least two previous time steps are required. Our methodology reveals the mechanism of such correlations and demonstrates the existence of recrossing between a pair of conformational states. Using this methodology we suggest an approach which defines additional conformational states that now posses the required Markovian property of their dynamics.

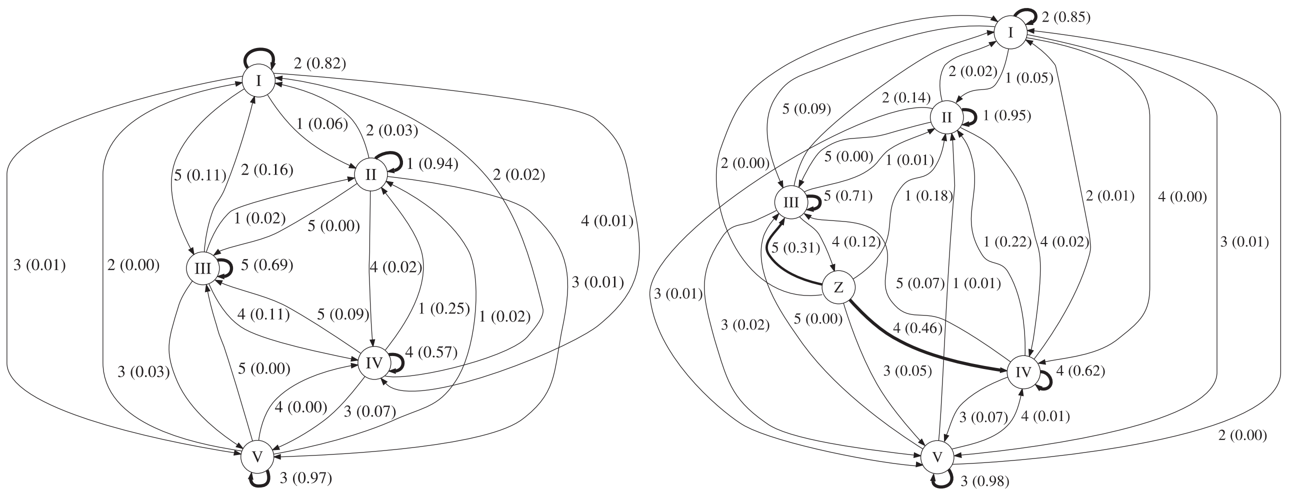

FIG. 1: **Left**: ϵ-machine for the Markovian regime of the peptide's dynamics; the time step of the data is 50ps; **right**: An additional causal state Z compared to the Markovian ϵ-machine (left) signifies the non-Markovian property of the transition from the configurational state 5 to 4; the time step of the data is 40ps

The methodology adopted is "Computational Mechanics" (CM) [Crutchfield et al, *Phys. Rev. Lett.*, **63**, 105 (1989)]. CM builds a statistic on "pasts" of symbols s_i representing the state of the system at times t_i, $\overleftarrow{s}_i \equiv \{\ldots s_{i-2}s_{i-1}s_i\}$, by analysing the "futures" $\overrightarrow{s}_i \equiv \{s_{i+1}s_{i+2}\ldots\}$ following each past and groups the pasts into classes called "causal states" ϵ_j. The collection of the causal states together with the transition probabilities between them is called an "ϵ-machine".

The transitions between the causal states I-V (the arcs on Fig. 1) describe the configurational transitions that have the probabilities given by the off-diagonal elements of the transition matrix. At the time scale of ≈40ps a fundamentally different situation is observed: an additional causal state is required to adequately describe the dynamics. This indicates that the dynamics becomes non-Markovian. The additional causal state Z makes the usual Markovian transition matrix picture invalid, which is confirmed by the differences between the corresponding causal states transitions (T^{ϵ}) and the Markovian transition matrix (T^{40ps}):

$$T^{50ps} = \begin{bmatrix} 0.9391 & 0.0622 & 0.0189 & 0.2401 & 0.0207 \\ 0.0251 & 0.8209 & 0.0027 & 0.0143 & 0.1550 \\ 0.0132 & 0.0080 & 0.9717 & 0.0804 & 0.0250 \\ 0.0195 & 0.0050 & 0.0059 & 0.5456 & 0.1298 \\ 0.0031 & 0.1039 & 0.0008 & 0.1195 & 0.6695 \end{bmatrix}; (T^{\epsilon} - T^{40ps})/T^{40ps} = \begin{bmatrix} 0.0 & 0.8 & -7.6 & 6.9 & -17.4 \\ 0.2 & 0.1 & -5.0 & -2.4 & 1.1 \\ -6.5 & -16.4 & 0.1 & 2.5 & 2.9 \\ 2.6 & -61.1 & 0.5 & 4.0 & 2.7 \\ -10.9 & 2.2 & 4.5 & -35.2 & -0.4 \end{bmatrix}.$$

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