Folding kinetics and unfolded state dynamics of the GB1 hairpin from molecular simulation

Supporting information

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Calculation of the rate matrix K

As described in the main text the rate matrix **K** is calculated using the approximate expression

$$k_{ji} \approx \begin{cases} t_{ji}(\Delta t)/\Delta t & \text{for } i \neq j \\ -\sum_{j \neq i} k_{ji} & \text{for } i = j \end{cases} \tag{1}$$

In this expression we use the transition probability matrix $\mathbf{T}(\Delta t)$ for a given "lag time" Δt, which is obtained using the maximum likelihood estimator[1]

$$t_{ji}(\Delta t) = n_{ji}(\Delta t) / \sum_j n_{ji}(\Delta t). \tag{2}$$

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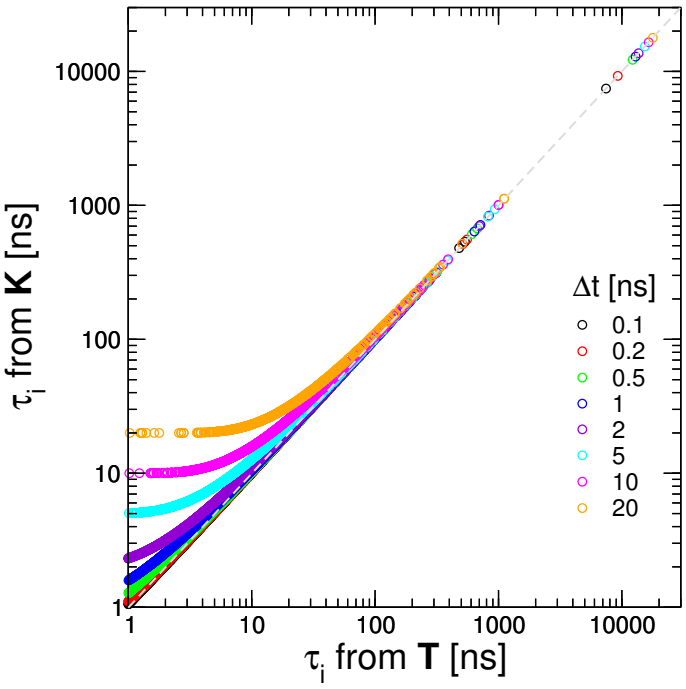

Figure 1: **Comparison of relaxation times from the transition matrix and the approximated rate matrix**. We show a comparison of relaxation times for different lag times Δt used to count transitions. The dashed gray line is the $y = x$.

Here $n_{ji}(\Delta t)$ are the elements of the transition count matrix $\mathbf{N}(\Delta t)$, determined from the simulation trajectories as the number of transitions from microstate i to microstate j after a specified lag Δt. This approximation in Eq. (1) becomes exact in the limit $\Delta t \to 0$. In S.I. Figure 1, we compare the relaxation times for the transition matrix and those of the rate matrix. We see that the relaxation times from both methods agree quantitatively up to time-scales approximately equal to the lag time used for counting transitions.

Lumping of microstates into macrostates

In Table 1 we list the most populated states found in each of the macrostates of the 9-macrostate model (see Figure 7 A-B, bottom, in the main text).

Table 1: Equilibrium populations and epresentative sets of torsional states lumped into the different clusters for the 9-macrostate model.

Macrostate	P_{eq}	Representative microstates
1	7.52e-03	EEEEEAAALEEAEE
		AEEEEAAALEEAEE
		EEEEEAAALEEAEA
2	3.02e-03	EAEAAEAALEEEEE
		EAEAAEAALEAEEE
		EEEAAEAALEEEEE
3	4.85e-03	EEEAAAAAAAALAEE
		EEEAAAAAAAALAEA
		AEEAAAAAAAALAEE
4	3.90e-04	EAAAEAAEEELEEE
		EAAAEAAEEELEEA
5	2.63e-01	EAAAAAAAAAAAEE
		EAAAAAAAAAEEEE
		EAAAAAAAAAEEEE
6	5.57e-02	EEEEAEAAAEEEEE
		EEEEAEAAEEEEEE
		EAAAAEAAAEEEEE
7	3.90e-01	EEEEEAAALEEEEE
		EEEEEAAALEEEEA
		AEEEEAAALEEEEE
8	1.44e-01	EEEAAAAAAAAAEE
		EEEAAAAAAEEEEE
		EEEAAAAAAAEEEE
9	1.32e-01	EAAAEAAAAAAAEE
		EAAAEAAAAAAEEE
		EEEEEAAEAEEEEE

References

(1) Prinz, J.-H.; Wu, H.; Sarich, M.; Keller, B.; Senne, M.; Held, M.; Chodera, J. D.; Schutte, C.; Noe, F. *J. Chem. Phys.* **2011**, *134*, 174105.