Simultaneous computation of dynamical and equilibrium information using a weighted ensemble of trajectories

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Supporting Information

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S1. Reference coordinates for the order parameters in Ala4

For Ala4, two sets of reference coordinates were used on each dimension. In the first dimension, the set of $N = 5$ torsions $\{\phi_2, \psi_2, \phi_3, \psi_3, \phi_4\}$ were measured and a dihedral distance $D = \sqrt{\frac{1}{N}\sum_i d_i^2}\ \epsilon\ [0, 180]$ is used with respect to the reference values $\{-83.9, 166.8, -48.7, -43.7, -54.0\}$, where d_i is the circular distance between the current value of the i-th angle and our reference, i.e., the smaller of the two arclengths along the circumference. Those reference values were chosen in order to have a good separation of states (see Fig. 3 in the main document).

In the second dimension, a regular RMSD, using only heavy atoms, is measured with respect to the following structure given in PDB format.

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REMARK   1                    PDB file used as reference in 2nd dimension
ATOM      1  N   ALA     1       1.705  -0.670   6.305  0.00  0.00
ATOM      2  H1  ALA     1       1.470  -0.554   5.330  0.00  0.00
ATOM      3  H2  ALA     1       0.936  -0.333   6.867  0.00  0.00
ATOM      4  H3  ALA     1       2.060  -1.605   6.444  0.00  0.00
ATOM      5  CA  ALA     1       2.848   0.235   6.617  0.00  0.00
ATOM      6  HA  ALA     1       2.592   0.962   7.388  0.00  0.00
ATOM      7  CB  ALA     1       4.035  -0.597   7.105  0.00  0.00
ATOM      8  HB1 ALA     1       4.309  -1.323   6.340  0.00  0.00
ATOM      9  HB2 ALA     1       4.883   0.059   7.303  0.00  0.00
ATOM     10  HB3 ALA     1       3.760  -1.121   8.021  0.00  0.00
ATOM     11  C   ALA     1       3.236   1.010   5.363  0.00  0.00
ATOM     12  O   ALA     1       2.963   0.576   4.243  0.00  0.00
ATOM     13  N   ALA     2       3.877   2.159   5.556  0.00  0.00
ATOM     14  H   ALA     2       4.068   2.489   6.491  0.00  0.00
ATOM     15  CA  ALA     2       4.300   2.985   4.432  0.00  0.00
ATOM     16  HA  ALA     2       3.459   3.174   3.764  0.00  0.00
ATOM     17  CB  ALA     2       4.830   4.326   4.942  0.00  0.00
ATOM     18  HB1 ALA     2       5.678   4.154   5.605  0.00  0.00
ATOM     19  HB2 ALA     2       5.148   4.937   4.097  0.00  0.00
ATOM     20  HB3 ALA     2       4.042   4.845   5.488  0.00  0.00
ATOM     21  C   ALA     2       5.385   2.280   3.627  0.00  0.00
ATOM     22  O   ALA     2       5.377   2.312   2.395  0.00  0.00
ATOM     23  N   ALA     3       6.317   1.642   4.328  0.00  0.00
ATOM     24  H   ALA     3       6.297   1.654   5.338  0.00  0.00
ATOM     25  CA  ALA     3       7.404   0.930   3.666  0.00  0.00
ATOM     26  HA  ALA     3       7.981   1.614   3.043  0.00  0.00
ATOM     27  CB  ALA     3       8.337   0.316   4.711  0.00  0.00
ATOM     28  HB1 ALA     3       7.776  -0.378   5.337  0.00  0.00
ATOM     29  HB2 ALA     3       9.144  -0.219   4.209  0.00  0.00
ATOM     30  HB3 ALA     3       8.757   1.106   5.333  0.00  0.00
ATOM     31  C   ALA     3       6.852  -0.170   2.764  0.00  0.00
ATOM     32  O   ALA     3       7.249  -0.294   1.606  0.00  0.00
ATOM     33  N   ALA     4       5.934  -0.966   3.304  0.00  0.00
ATOM     34  H   ALA     4       5.647  -0.841   4.264  0.00  0.00
ATOM     35  CA  ALA     4       5.335  -2.053   2.539  0.00  0.00
ATOM     36  HA  ALA     4       6.104  -2.751   2.209  0.00  0.00
ATOM     37  CB  ALA     4       4.328  -2.809   3.406  0.00  0.00
ATOM     38  HB1 ALA     4       3.546  -2.125   3.736  0.00  0.00
ATOM     39  HB2 ALA     4       3.882  -3.616   2.825  0.00  0.00
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ATOM     40  HB3 ALA     4       4.837  -3.226   4.275  0.00  0.00
ATOM     41  C   ALA     4       4.634  -1.510   1.297  0.00  0.00
ATOM     42  O   ALA     4       4.769  -2.062   0.205  0.00  0.00
ATOM     43  OXT ALA     4       3.885  -0.426   1.473  0.00  0.00
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S2. Visualization of the states used in Ala4 (A1, A2, B1 and B2)

In the main document, we showed the definition of the states used in the system Ala4. Here we show representative structures of them.

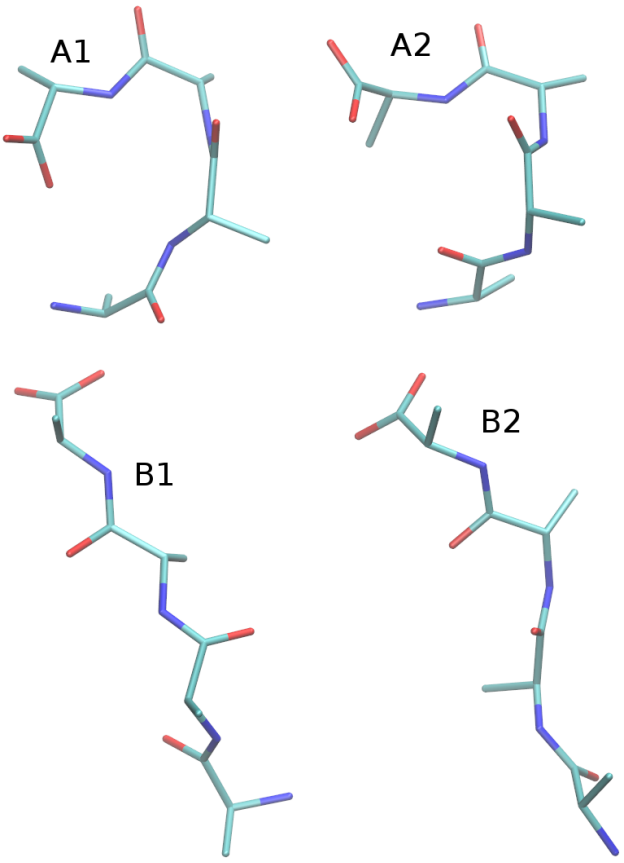

Figure 1: Representative structures for the states A1, A2, B1 and B2.

S3. Maximum likelihood estimation reversible Markov State Models)

The next figure shows that the regular Markovian approach, in our methane system, even if it is improved by a more realistic model where the flux matrix is symmetric [J. Chem. Theory Comput. 2011, 7, 3412], is still biased. This is not surprising, since the our WE simulation was long enough to overcome any low sampling issue that may be improved by a better estimation.

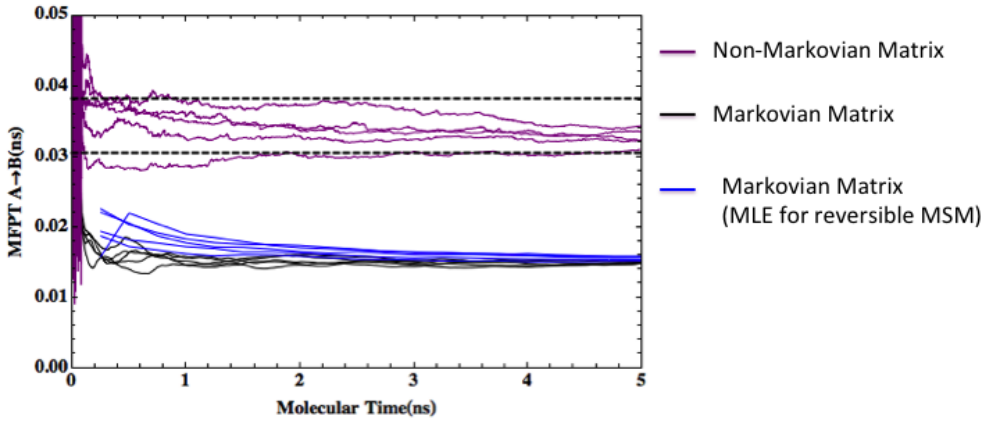

Figure 2: Markovian, non-Markovian and Maximum Likelihood for reversible Markov State Models estimates for mean first passage times (MFPTs) from A($r < 5$Å) to B($r > 11$Å) are plotted vs. molecular time. Five independent WE runs are shown, each based on 0.4 s of total simulation time. Dashed lines indicate roughly a 95% confidence interval based on 0.4 s of brute force simulation. Each ns of molecular time corresponds to approximately 80 ns of WE simulation accounting for all trajectories in a single run.