Reviewers’ comments

Vince, a quick question.

Recalling an earlier exchange we had about MSM (see bottom of this email for your contribution), could you edit (if necessary) the following response to reviewer #1's comments about Markov modeling?

Reviewer #1 says:

While I appreciate the amount of effort put into these calculations, I am not sure if the authors have a clear take-home message. As such I am afraid I cannot recommend publication in its current form.  
  
Is it that kinetic coarse-graining will fail for any complex system, with inter-particle interactions? That is too bold of a claim, given that the system here is simple and the analyses numerical at best. How about the numerous kinetics papers coming from the Markov model community - are the authors implying they are all incorrect?

Our response:

In our revised manuscript we have strived to make the main message more clear, which is:   even with an optimal choice of reaction coordinate in a simple two-state kinetic Ising system, microcanonical coarse-graining leads to systematic error that can be attributed to memory efforts.

This is not to say that kinetic coarse-graining will fail for any complex system with inter-particle interactions, nor that Markov models are incorrect.   We have built Markov models of the kinetic Ising model (not published or described in the current manuscript), which do lead to the correct rate constants for long simulation times.  The amount of simulation time needed for good statistics, however, is comparable to the with the brute-force method – such Markov models are essentially phenomenological and require long lag times to make memory effects negligible.