**Author corrections**

A1. Line 14: remove “the so-called”.

A2. Line 43: remove “the” from “the so-called”

A3. change “*u*(*x*)” to math-typeset “V(x)”

A4. Line 498. Put space in between 5.2 and $\mu$s.

**Response to proof editors’ queries**

Q1. Please check that the author names are in the proper order and spelled correctly. Also, please ensure that each author’s given and surnames have been correctly identified (given names are highlighted in red and surnames appear in blue).

Response to Q1: YES, given names and surnames are correct

Q2. Figure 2 was not cited in the text. We have inserted a citation in the sentence beginning “Diffusion on the 1-D . . .” Please check and reposition if necessary.

Response to Q2: The citation is fine. Thanks.

Q3. Figures 5 and 6 were not cited in the text. We have inserted a citation in the sentence beginning “The K12M mutant of . . .” Please check and reposition if necessary.

Response to Q3: These citations are fine. Thanks.

Q4. Please reword the sentence beginning with “We have illustrated these problems . . .” so that your meaning will be clear to the reader.

Response to Q4: Please remove the last words “generated these scenarios” so that the sentence is changed to: “We have illustrated these problems in simple 1D diffusion models and in large-scale all-atom simulations of protein folding by testing the performance of various MSM estimators on adaptive seeding data.”

Q5. References (2 and 41), (18 and 23), (20 and 46), (21 and 28), and (42 and 48) contain identical information. Please check and provide the correct reference or delete the duplicate reference. If the duplicate is deleted, renumber the reference list as needed and update all citations in the text.

Response to Q5: All five references were duplication errors. PDF Annotations have been added denoting the correct numbers in the text and in the References section.

Q6. Please provide publisher’s name in Ref. 5.

Response to Q6: Springer

Q7. Please confirm the change in journal title in Ref. 8.

Response to Q7. That is correct.

Q8. If preprint Ref. 12 has subsequently been published elsewhere, please provide updated reference information (journal title, volume number, and page number).

Response to Q8. This article has indeed since been published: J. Phys. Chem. B **122**, 8386 (2018)

Q9. Please confirm the volume number and page number in Ref. 16, as we have inserted the required information.

Response to Q9. That is correct.

Q10. We were unable to locate a digital object identifier (doi) for Ref. 17. Please verify and correct author names and journal details (journal title, volume number, page number, and year) as needed and provide the doi. If a doi is not available, no other information is needed from you. For additional information on doi’s, please select this link: http//www.doi.org/.

Response to Q10. The correct citation (and DOI) for this article is: Dixon, T., Lotz, S.D. & Dickson, A. Predicting ligand binding affinity using on- and off-rates for the SAMPL6 SAMPLing challenge. *J Comput Aided Mol Des* **32,**1001–1012 (2018) doi:10.1007/s10822-018-0149-3

Q11. Please confirm the change in page number in Ref. 36.

Response to Q11. That is correct.