

Supporting information for:

**Conformational Heterogeneity in the Michaelis
Complex of Lactate Dehydrogenase: An Analysis of
Vibrational Spectroscopy Using Markov and Hidden
Markov Models**

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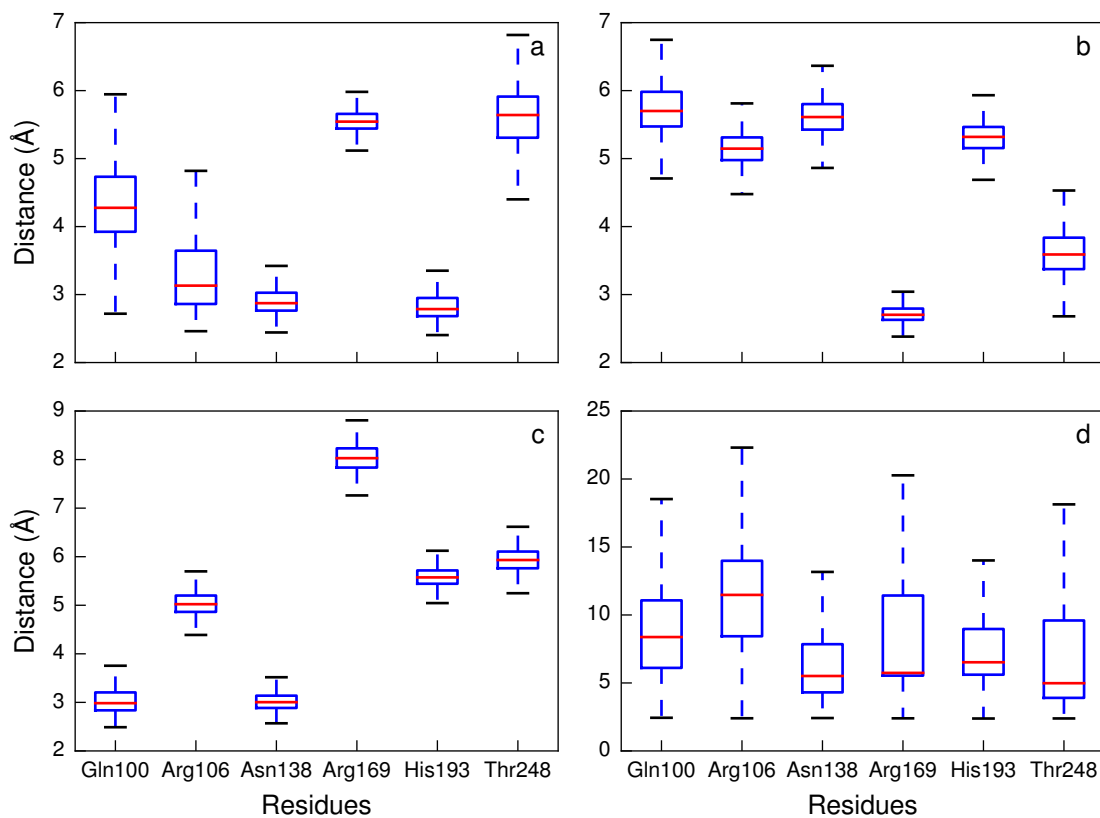


Figure S1: Box plot of the distributions of the minimum distances between carbonyl oxygen of pyruvate and active site residues in (a) the X-ray structure state S_{xray} , (b) the flipped state S_{flip} , (c) the rotated state S_{rotate} , and (d) the associated/unbound state $S_{\text{a/u}}$.

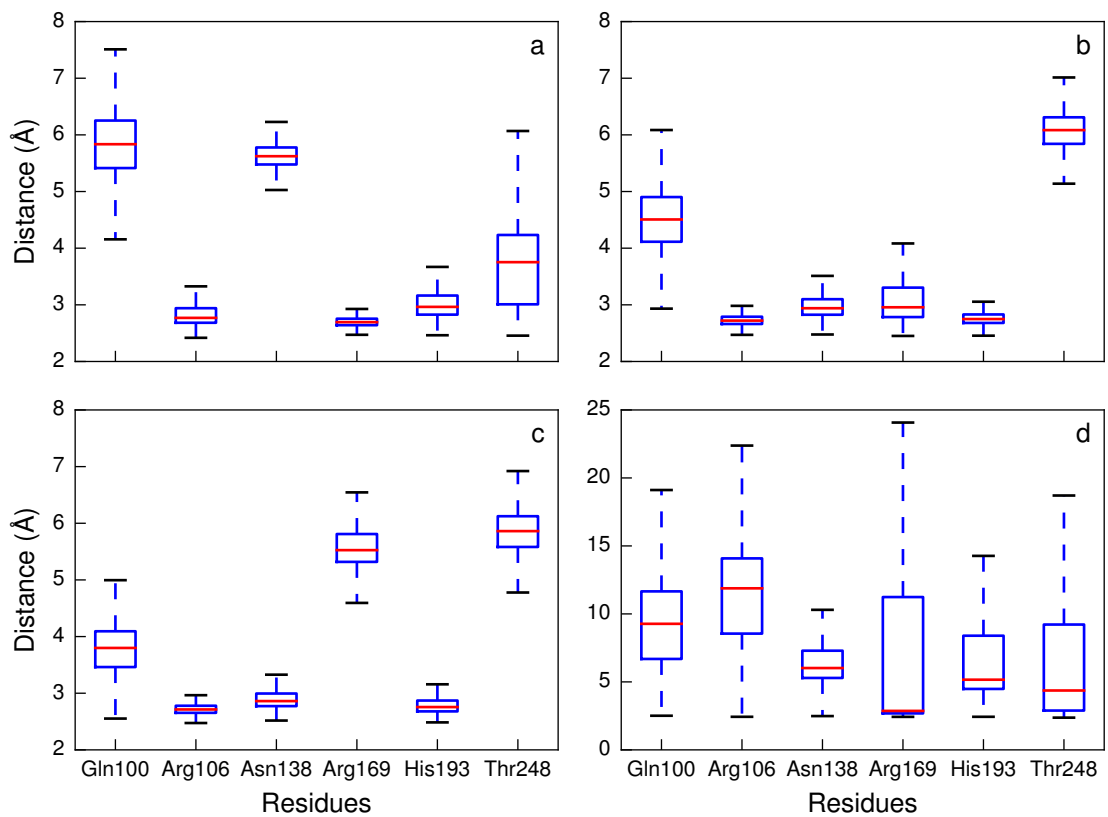


Figure S2: Box plot of the distributions of the minimum distances between carboxyl oxygens of pyruvate and active site residues in (a) the X-ray structure state S_{xray} , (b) the flipped state S_{flip} , (c) the rotated state S_{rotate} , and (d) the associated/unbound state $S_{\text{a/u}}$.

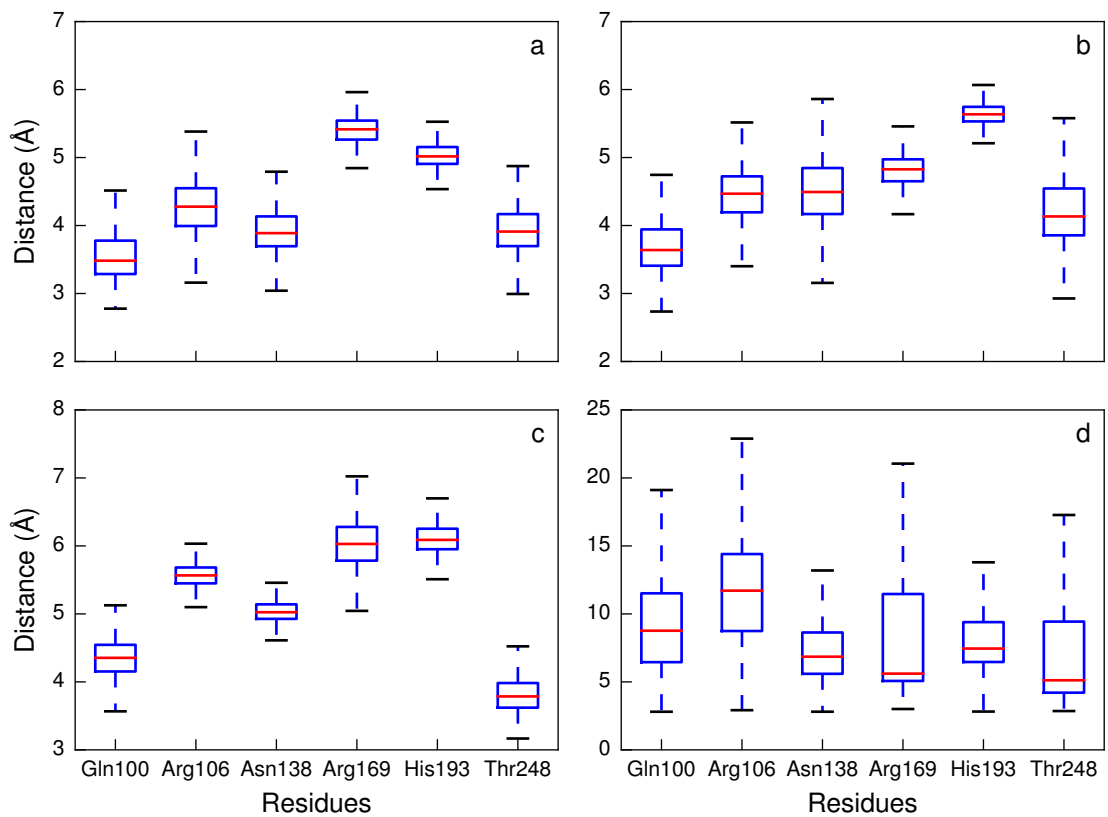


Figure S3: Box plot of the distributions of the minimum distances between methyl carbon of pyruvate and active site residues in (a) the X-ray structure state S_{xray} , (b) the flipped state S_{flip} , (c) the rotated state S_{rotate} , and (d) the associated/unbound state $S_{\text{a/u}}$.

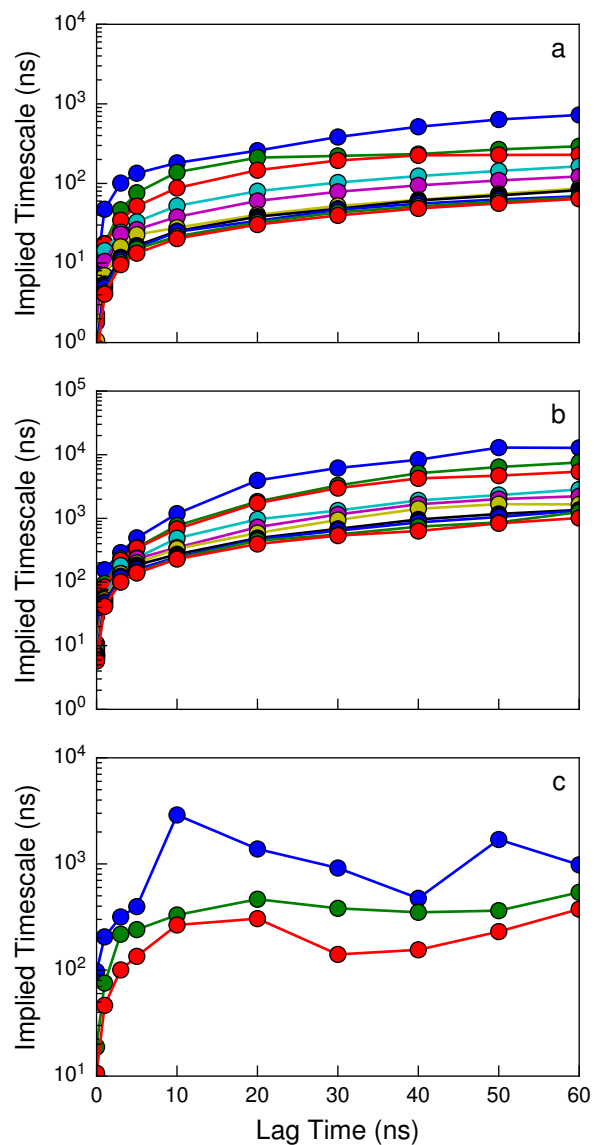


Figure S4: Implied relaxation timescales as a function of lag time for (a) the MSM estimated from the microstates on the basis of the substrate binding only, (b) the MSM estimated from the microstates on the basis of the protein conformations as well as the substrate binding, and (c) the coarse-grained kinetic model (hidden Markov model) estimated from the same microstates as in (b).

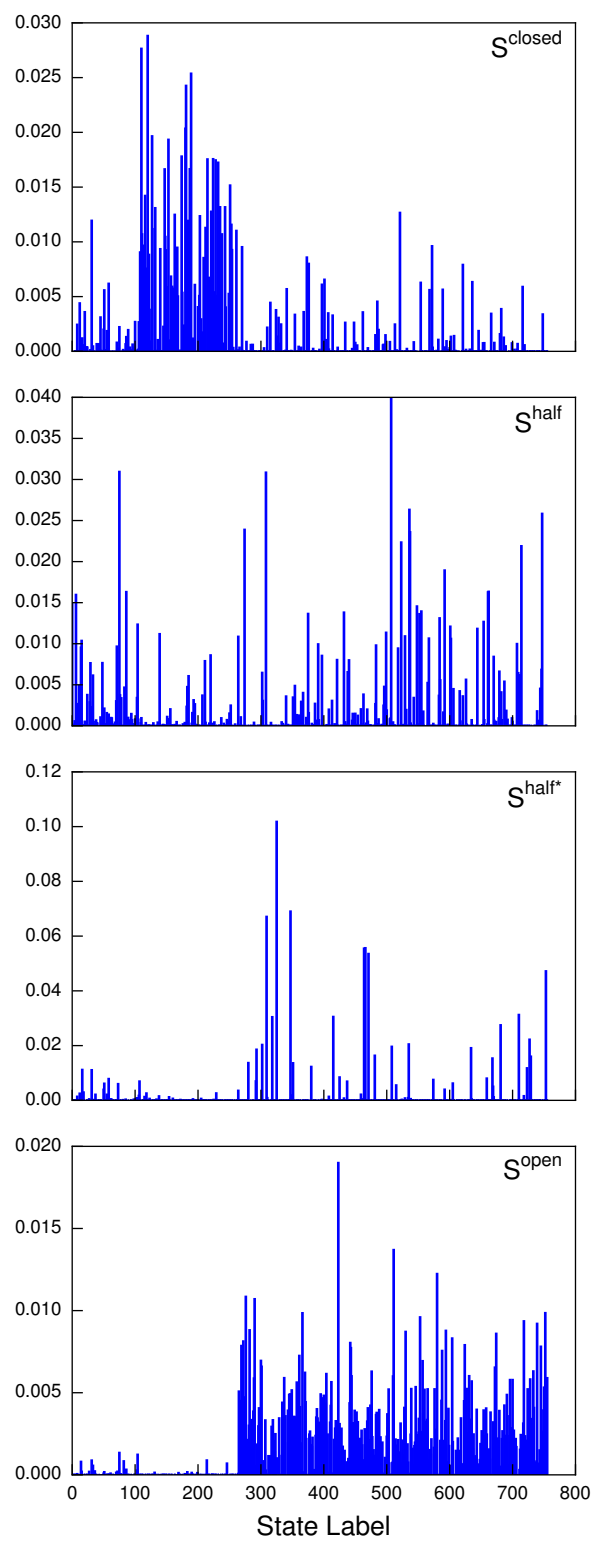


Figure S5: Output probabilities from hidden to observable discrete states.