Electronic Supplementary Information

A QM/MM MD Study of the pH-dependent Ring-Opening Catalysis and Lid Motif Flexibility in Glucosamine 6-Phosphate Deaminase

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Table S1 The glucosamine 6-phosphate deaminases (NagBs) from *Escherichia coli*, *Homo sapiens*, *Bacillus subtilis*, and *Streptococcus mutans*.

	State	PDB
Escherichia coli	NagB-2Pi	1DEA[a]
	NagB-Inhibitor-Pi	1HOR[a]
	NagB-GlcNAc-Pi	1HOT[a]
	NagB	1FS6,1FSF[b]
	NagB-F6P	1FQO[b]
	NagB-GlcNAc	1FRZ,1FS5[b]
Homo sapiens	NagB-GlcNAc	1NE7[c]
Bacillus subtilis	NagB-Pi	2BKV[d]
	NagB-F6P	2BKX[d]
Streptococcus mutans	NagB	2RI0[e]
	NagB-GlcN6P	2RI1[e]

[a] Ref (3). [b] Ref (4). [c] Ref (5). [d] Ref (6). [e] Ref (7).

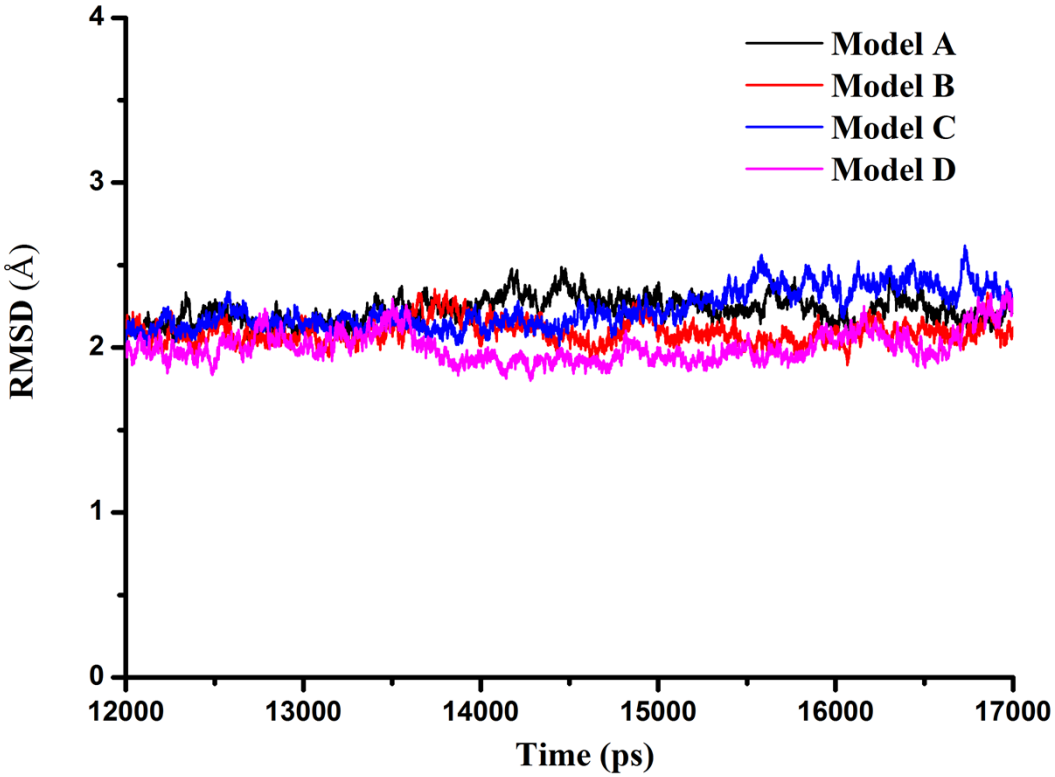
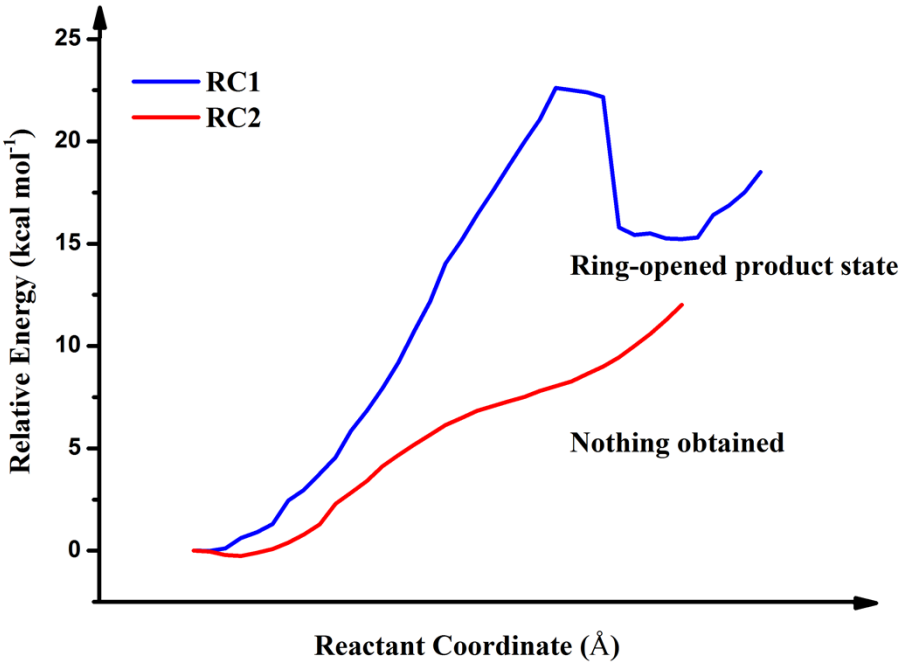


Fig. S1 The RMSD values of all the backbone atoms as function of time for the apo-state *Smu*NagB and the *Smu*NagB-GlcN6P complex in acid (Models A and B) and alkaline solution (Models C and D) after 12ns.

(a)



(b)

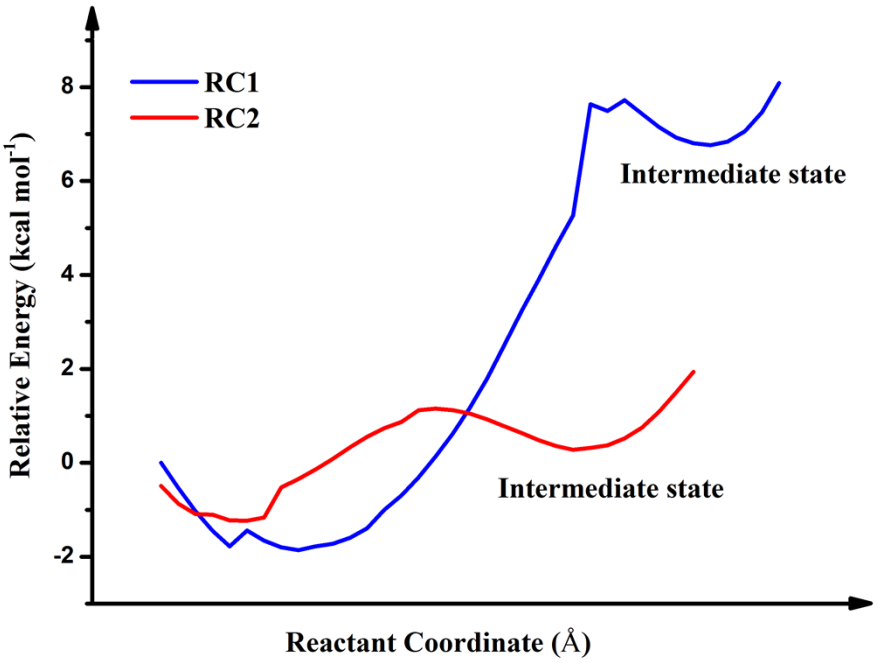


Fig. S2 Relative energy profiles along the defined reaction coordinates RC1 and RC2 for Models E **(a)** and F **(b)**.

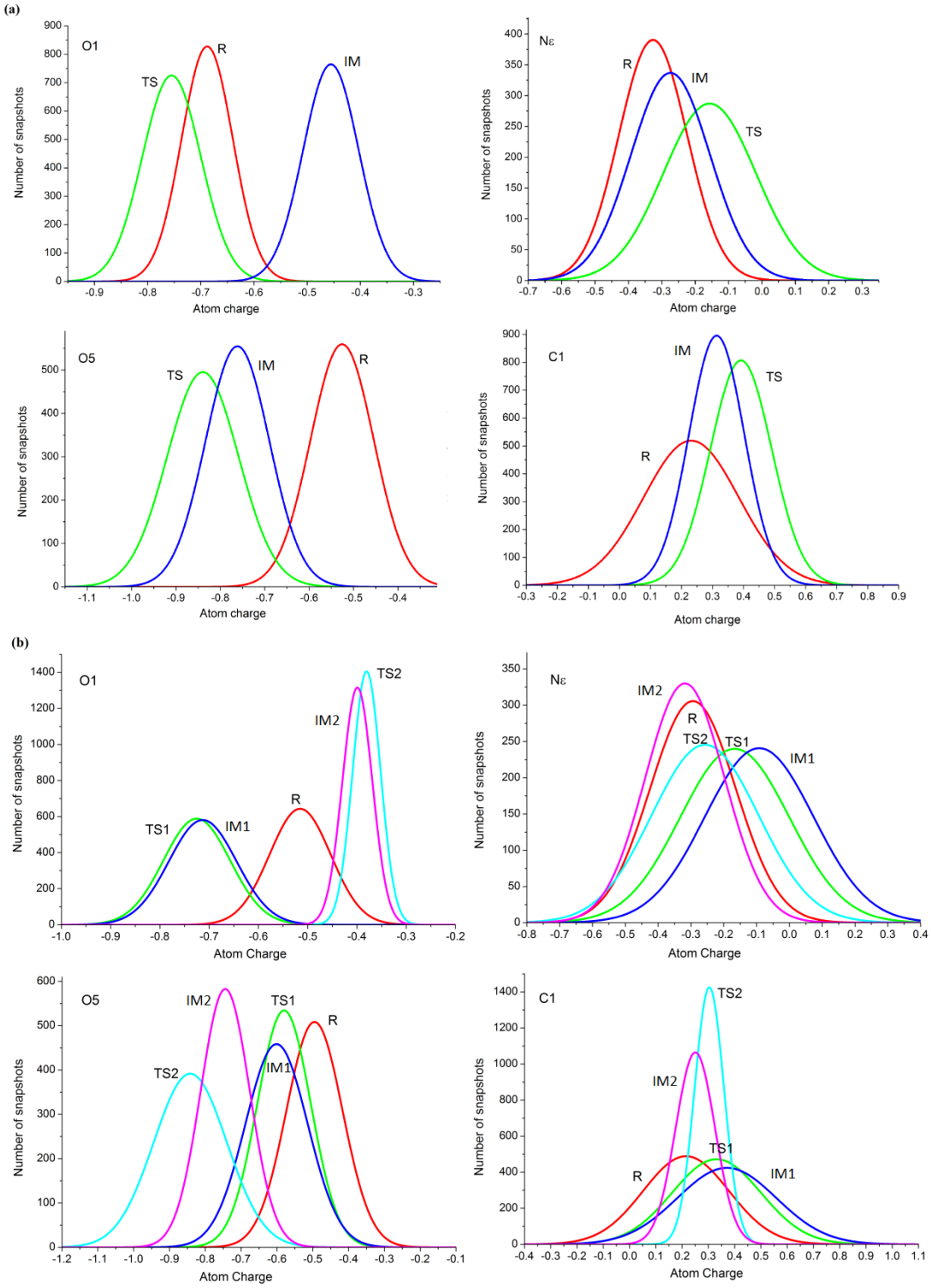


Fig. S3 The statistical Mulliken charges of main atoms in the active site of reactant, transition state, and intermediate for Model E **(a)** and Model F **(b).**

(a)

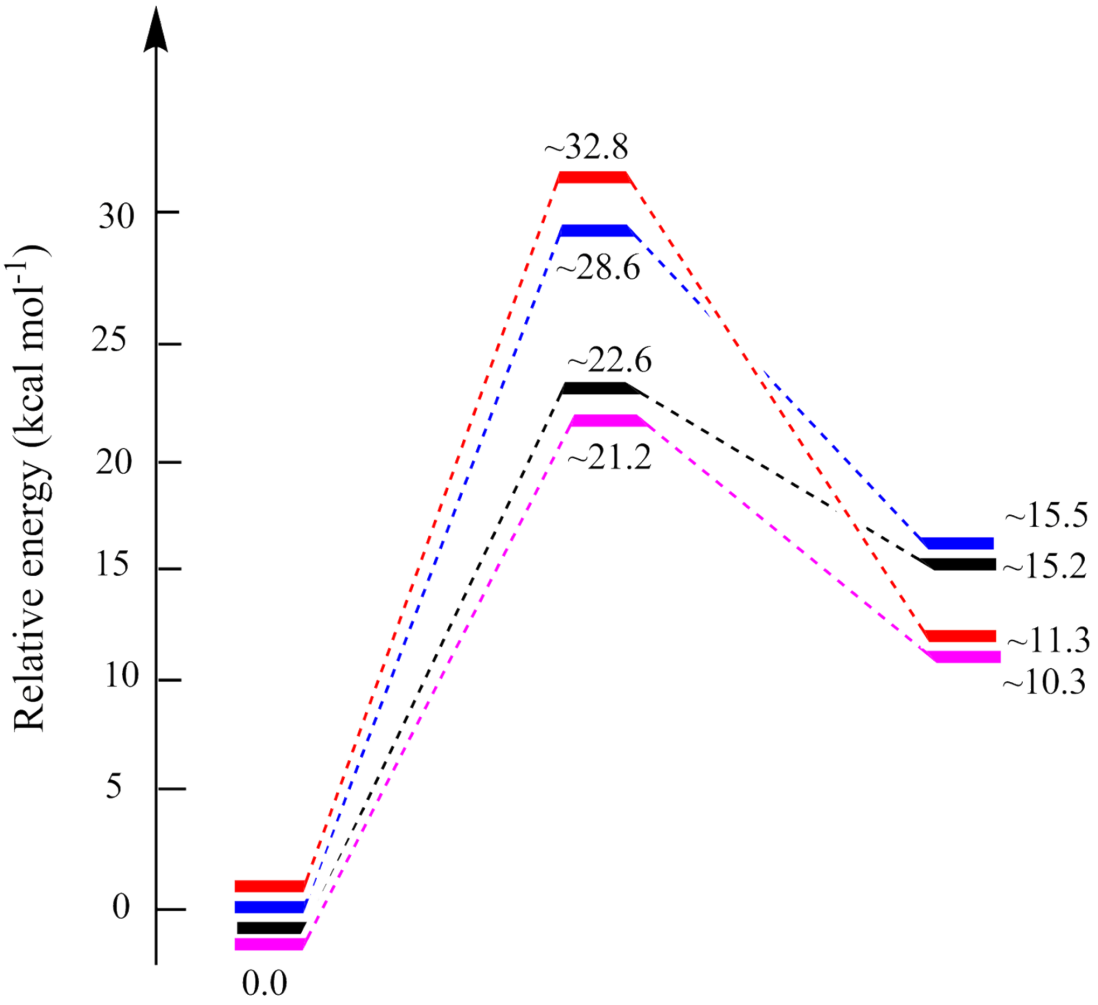


Fig. S4 (a) The relative energies for the rate-limiting step in Model E by the QM/MM energy scanning. The black, red, blue, and magenta lines are denoted for wild, double mutant, Asn128Ala, and Glu135Ala single mutant systems, respectively.

(b)

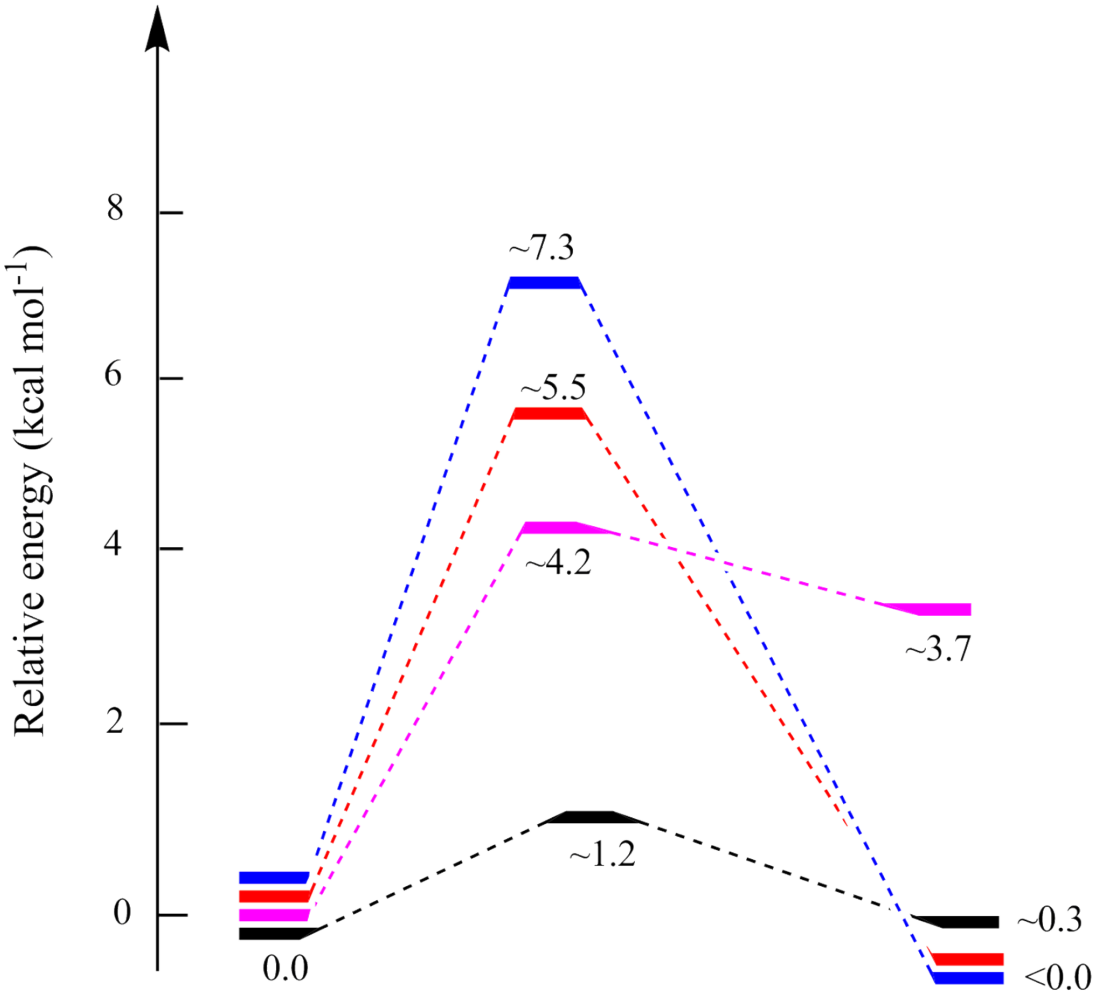


Fig. S4 (b) The relative energies for the hydrogen-transfer step in Model F by the QM/MM energy scanning. The black, red, blue, and magenta lines are denoted for wild, double mutant, Asn128Ala, and Glu135Ala single mutant systems, respectively.

(c)

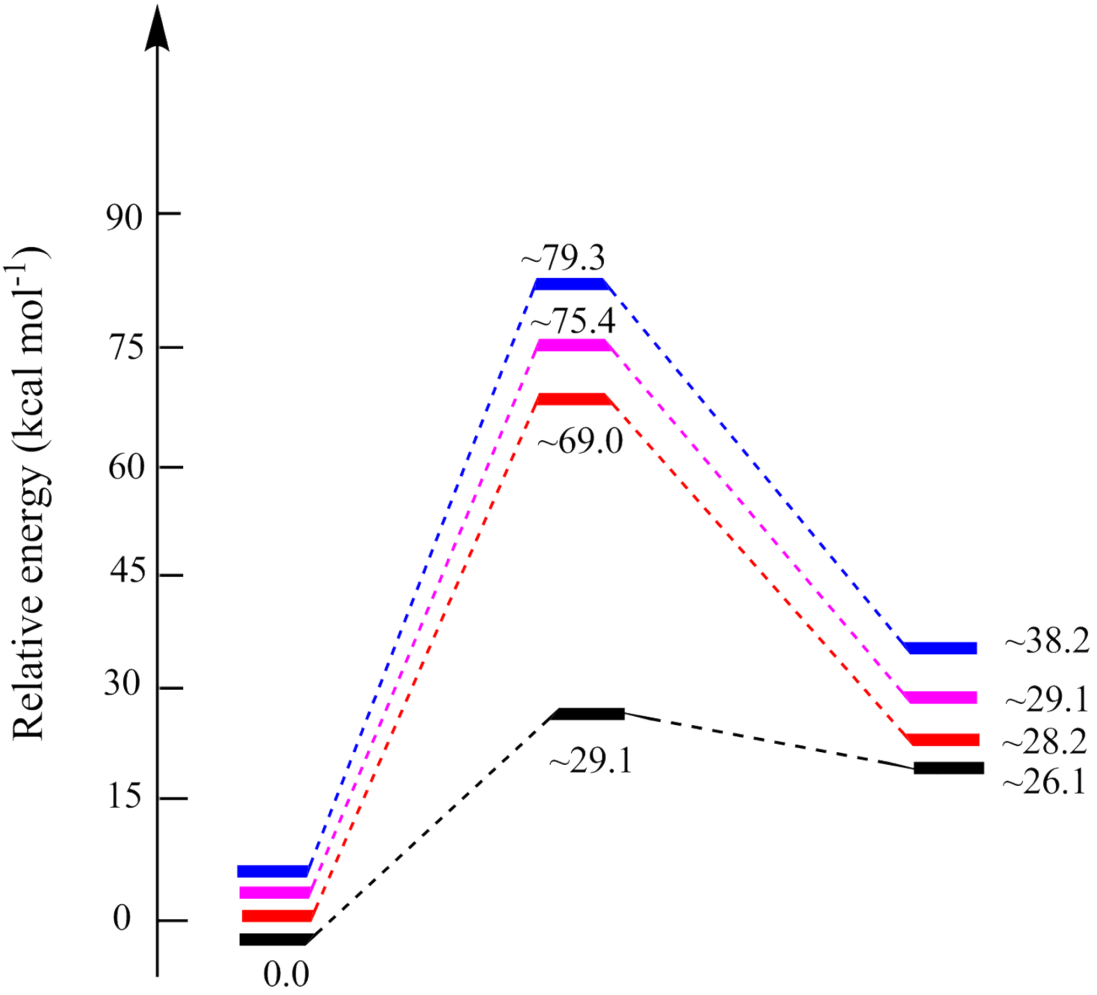


Fig. S4 (c) The relative energies for the rate-limiting step in Model F by the QM/MM energy scanning. The black, red, blue, and magenta lines are denoted for wild, double mutant, Asn128Ala, and Glu135Ala single mutant systems, respectively.