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Supplementary Information For Mechanistic insights into thrombin's switch between "slow" and "fast" forms

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Table S1 Thrombin catalytic sub-pocket residues. The full list of catalytic sub-pocket residues under our residue ID numbering scheme was followed the definition in [1].

Pocket	Residues
S1	resid 79 235 to 241 261 to 264 266 267 268 274 275
S2	resid 79 83 86 132 238 262 263
S3	resid 86 263 264 265 266
S4	resid 213 215 263 264 265
S5	resid 215 265
S6	resid 214 215

Table S2 p-values in Welch's t-tests on SASA measurements. The values less than machine epsilon ($\sim$2.2E-16) are written as '< 2.2E-16'. As indicated by the asterisk symbols, rejection decisions for the null hypothesis on the SASA distributions in the Welch's t-tests were made at the 1% significance level.

	NaOn vs. NaOff	NaOn vs. KOn	NaOff vs. KOff	KOn vs. KOff
S1	1.4E-02	1.1E-20*	< 2.2E-16*	< 2.6E-5*
S2	5.7E-12*	1.4E-01	< 2.2E-16*	< 2.2E-16*
S3	8.5E-01	< 2.2E-16*	< 2.2E-16*	1.8E-02
S4	< 2.2E-16*	< 2.2E-16*	< 2.2E-16*	< 2.2E-16*
S5	< 2.2E-16*	2.0E-07*	< 2.2E-16*	8.9E-03
S6	2.4E-07*	< 2.2E-16*	< 2.2E-16*	< 2.2E-16*
CatalyticTriad	< 2.2E-16*	< 2.2E-16*	< 2.2E-16*	8.7E-09*
WholeProtein	< 2.2E-16*	< 2.2E-16*	< 2.2E-16*	< 2.2E-16*

Table S3 Mean values of SASA measurements with 99% confidence intervals

	S1	S2	S3	S4	S5	S6	CatalyticTriad	WholeProtein
Na (on)	54.43(7)	43.04(9)	39.00(6)	33.60(7)	17.52(5)	26.93(5)	4.91(3)	1627.4(5)
Na (off)	54.7(2)	43.2(2)	38.9(1)	35.4(2)	18.36(8)	26.61(9)	4.66(4)	1636.1(7)
K (on)	54.6(2)	43.0(2)	37.34(9)	32.7(1)	17.62(6)	26.93(7)	5.36(4)	1658.1(6)
K (off)	53.7(2)	42.3(2)	37.14(8)	34.09(9)	17.56(6)	25.58(6)	5.24(5)	1666.3(5)

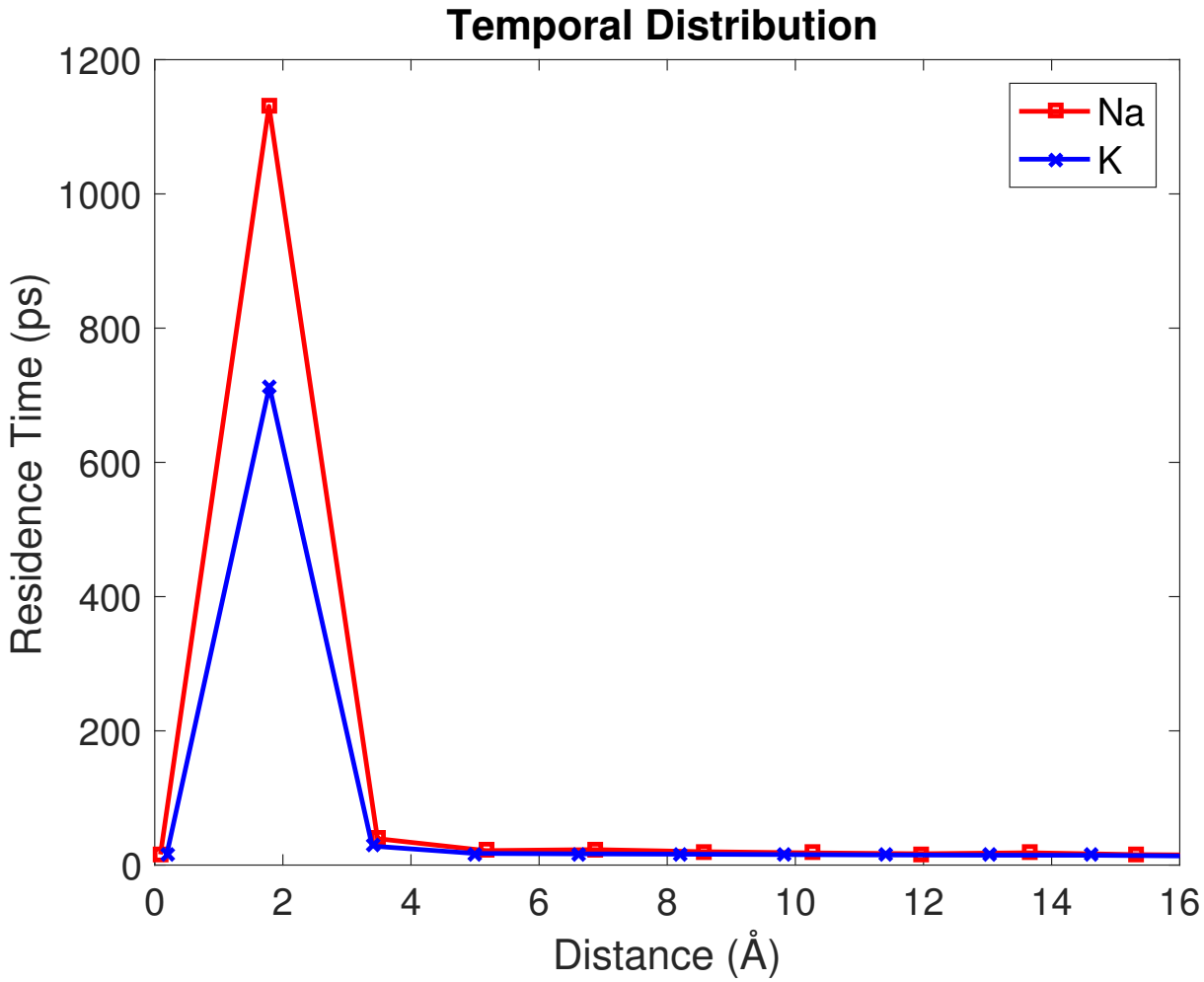

Fig. S1 Temporal distribution of nearest Na^+/K^+ distance to 220s loop under the bin width of 1.6 Å.

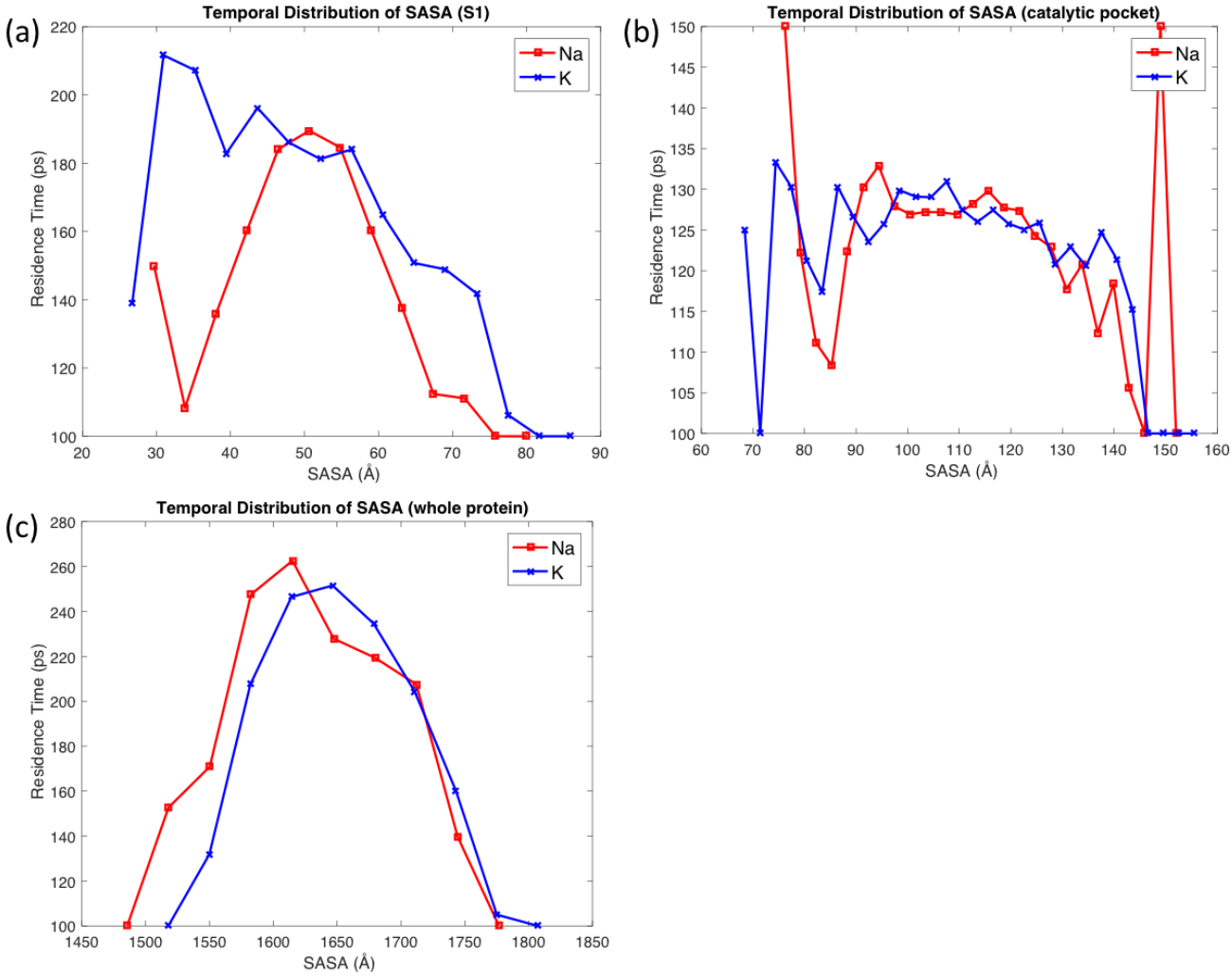

Fig. S2 Temporal distribution of SASA.

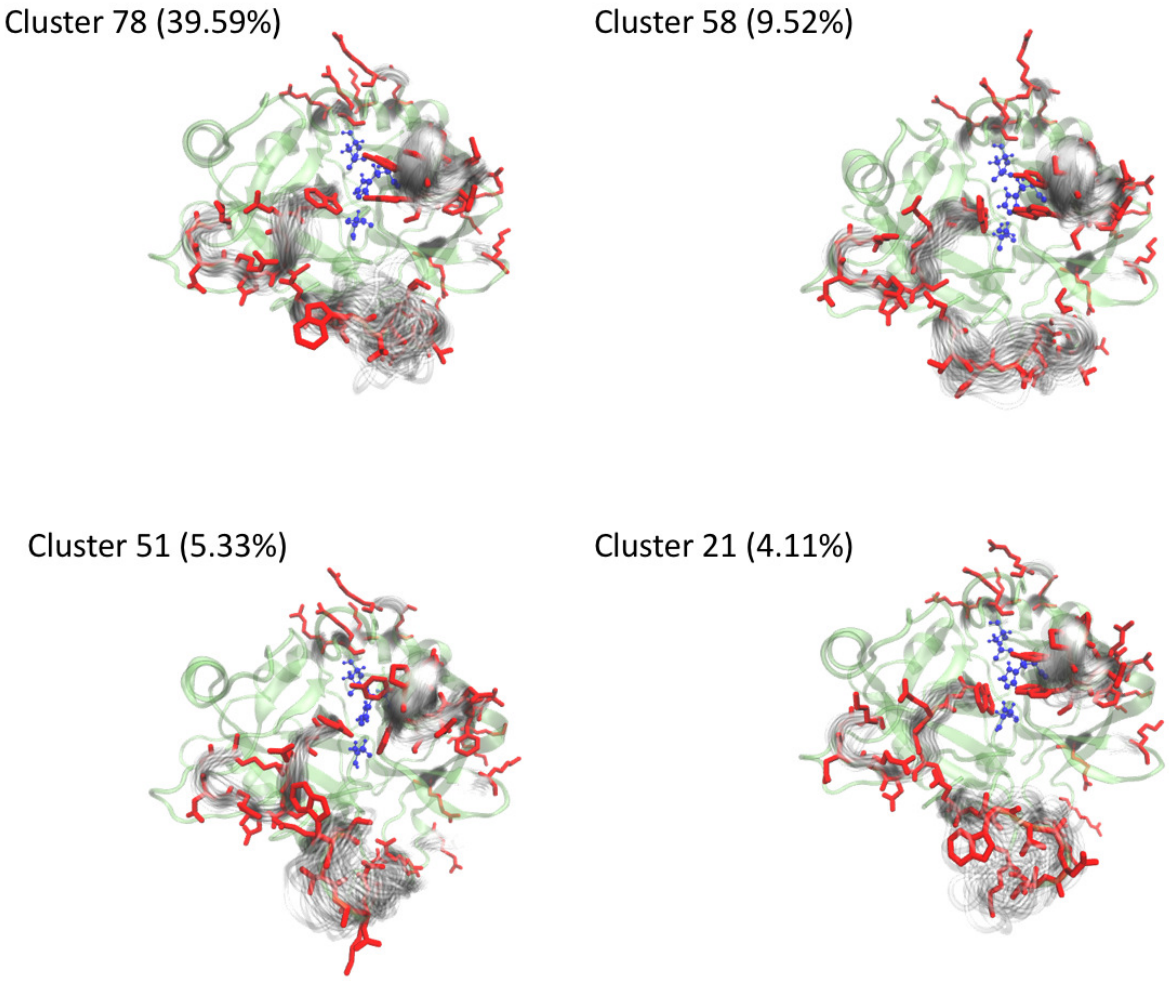

Fig. S3 Visualization of structures of the top four non-noise clusters

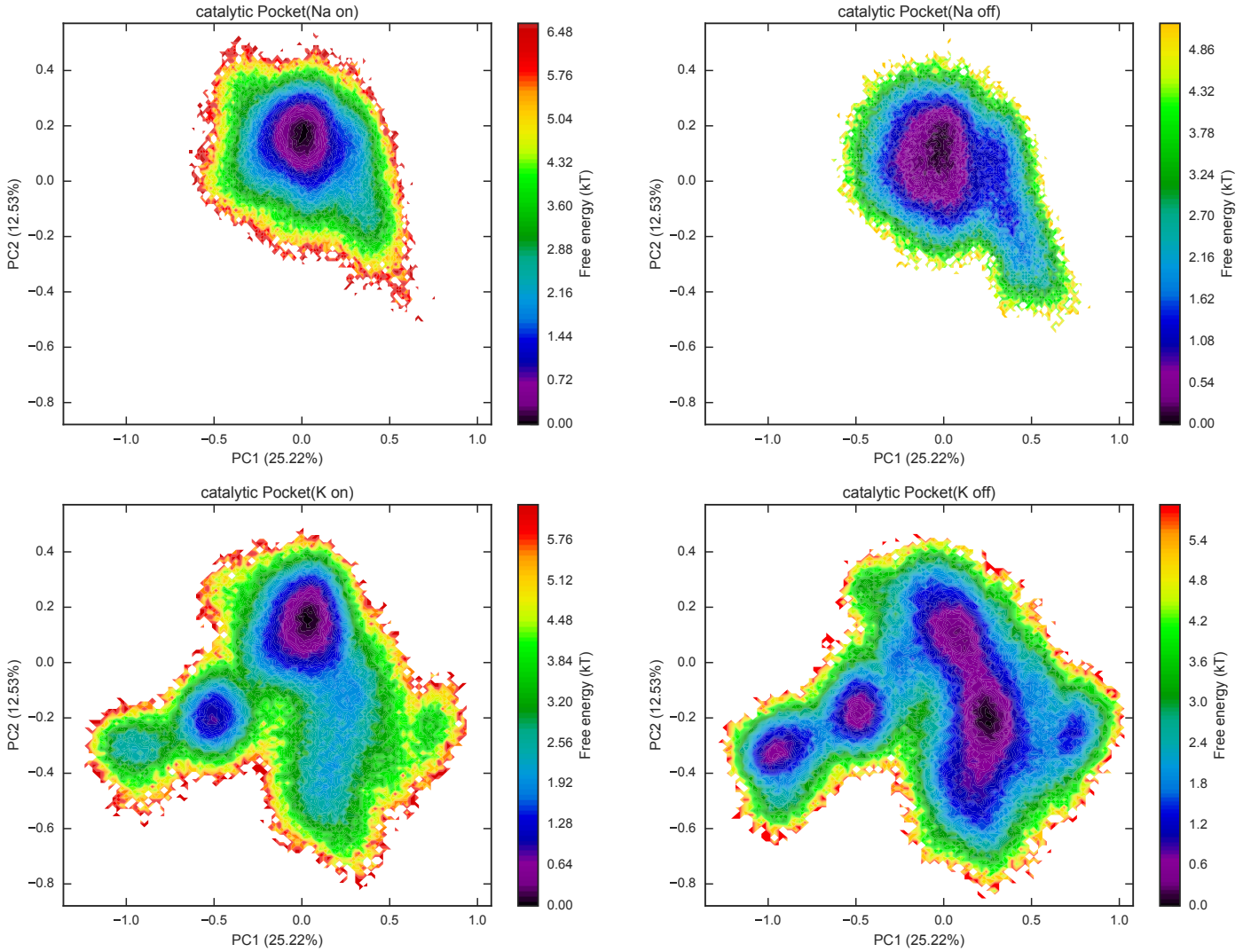

Fig. S4 Conformational free energy surfaces of the alpha carbons in the catalytic pocket regarding conformations with a Na^+-binding/unbinding and K^+-binding/unbinding.