Supporting information

Dynamics of the HAT lysine-rich loop in the catalytic core of CBP

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Supporting Tables

Threshold for unbinding	K1595ac in catalytic core
10 Å	2 ns
12 Å	3 ns
14 Å	4 ns
16 Å	5 ns

Table S1: Characteristic unbinding times of K1595ac from the bromodomain in the catalytic core, obtained from a single-exponential fit. The threshold distances used to define an unbinding event range from 10 to 16 Å. The unbinding times are overall similar, thus the analysis is robust with respect to the chosen threshold.

Threshold for unbinding	AIL endecamer	Histone peptide
10 Å	96 ns	1061 ns
12 Å	107 ns	1083 ns
14 Å	109 ns	1097 ns
16 Å	118 ns	1147 ns

Table S2: Characteristic unbinding times of the acetylated lysine in the bromodomain complexes with AIL endecamer and histone peptide, obtained from a single-exponential fit. The threshold distances used to define an unbinding event range from 10 to 16 Å. Unbinding of the AIL endecamer is always one order of magnitude faster than the histone peptide.

Supporting Figures

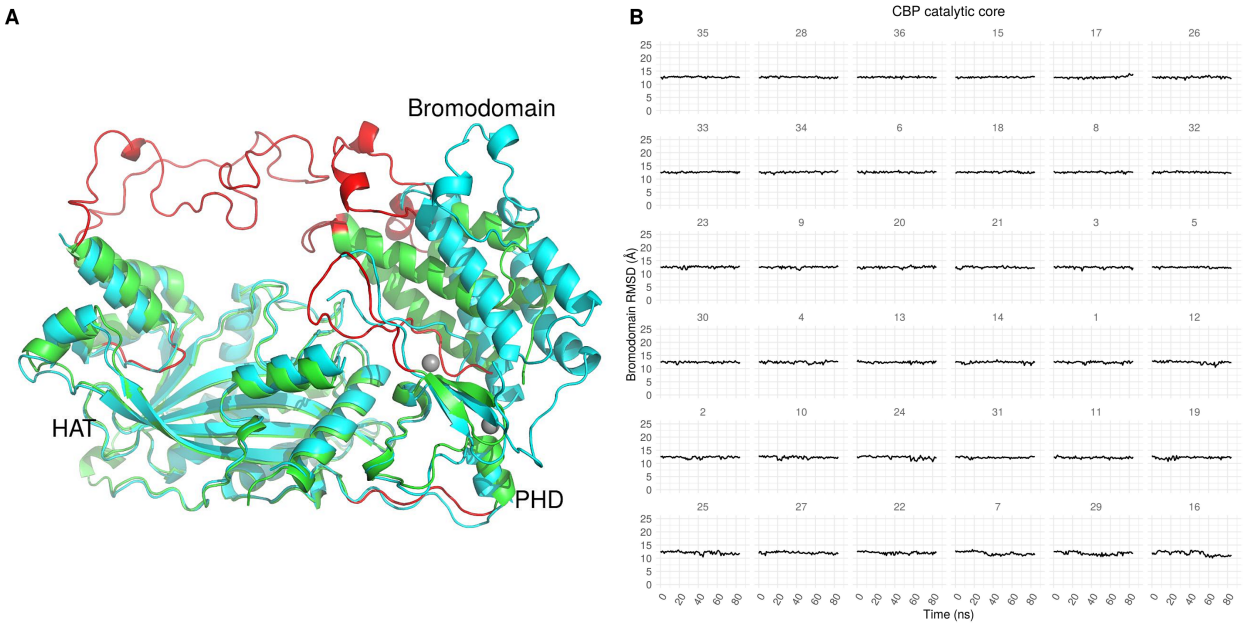

Figure S1: A) Overlap of the CBP crystal structure 5U7G (cyan) and the equilibrated model of the CBP catalytic core (green). All the segments with flexible backbone in the simulations are colored in red. This includes the hinge regions, *i.e.* short loops connecting the structured domains. The bromodomain is the most mobile component as it shifts closer to the HAT domain when inserting K1595ac in the bromodomain pocket. A small shift is observed also for the HAT helix from which the AIL protrudes. The zinc ions (silver spheres) overlap between the two structures. B) Time series of the root-mean-square-deviation (RMSD) of the bromodomain α-helices (Cα atoms) after fitting to the HAT domain (Cα atoms) of the crystal structure. The RMSD does not change between bound and unbound replicas, meaning that the bromodomain does not shift its position relative to the HAT upon AIL unbinding.

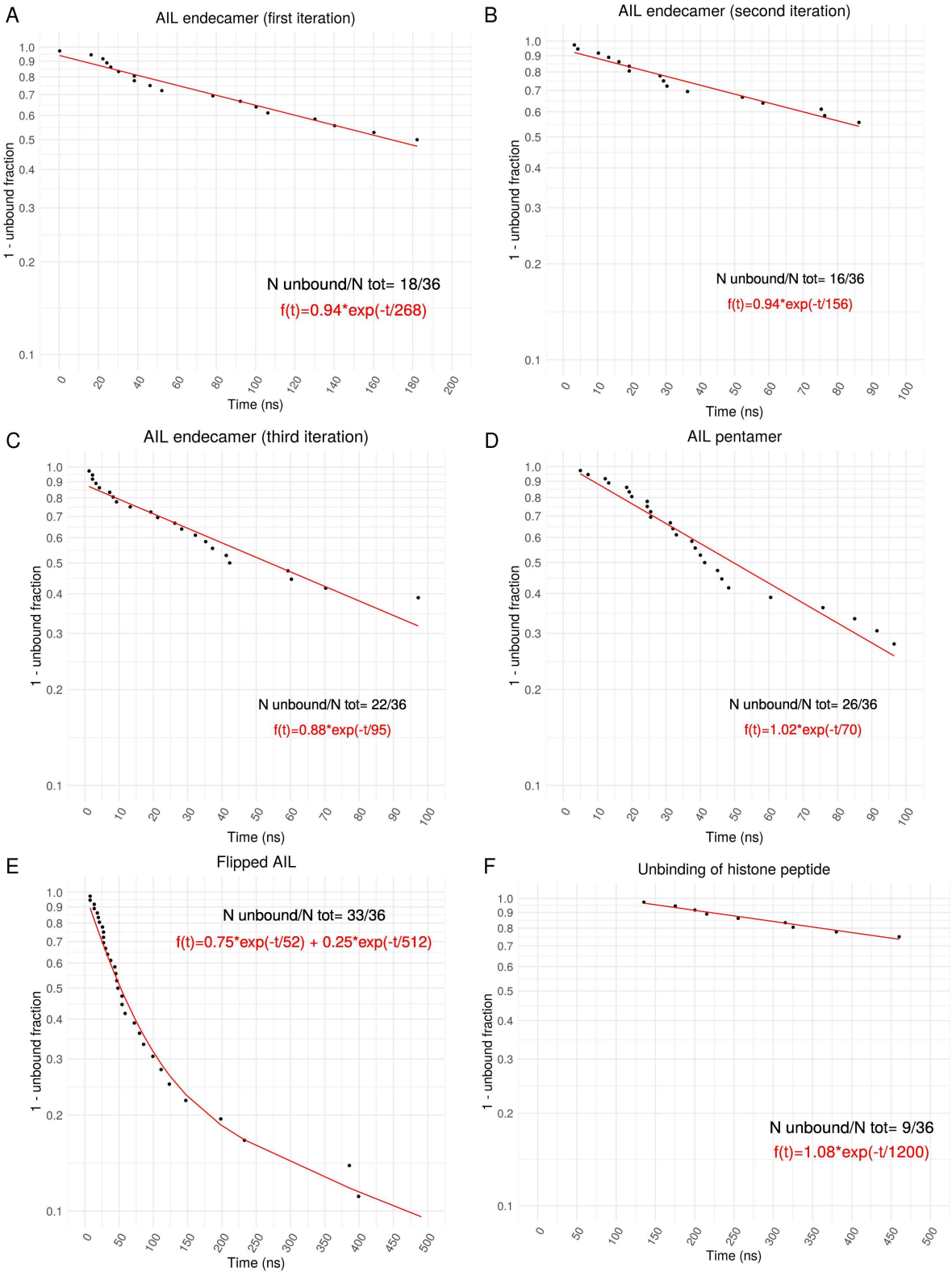

Figure S2: Kinetics of complete peptide unbinding in all the bromodomain-peptide complexes, shown in the individual timescales of sampling. Only the flipped AIL is fit with a double-exponential function, in which the first and second terms represent the fast and slow unbinding phases, respectively. All of the AIL peptides unbind faster than the histone peptide.

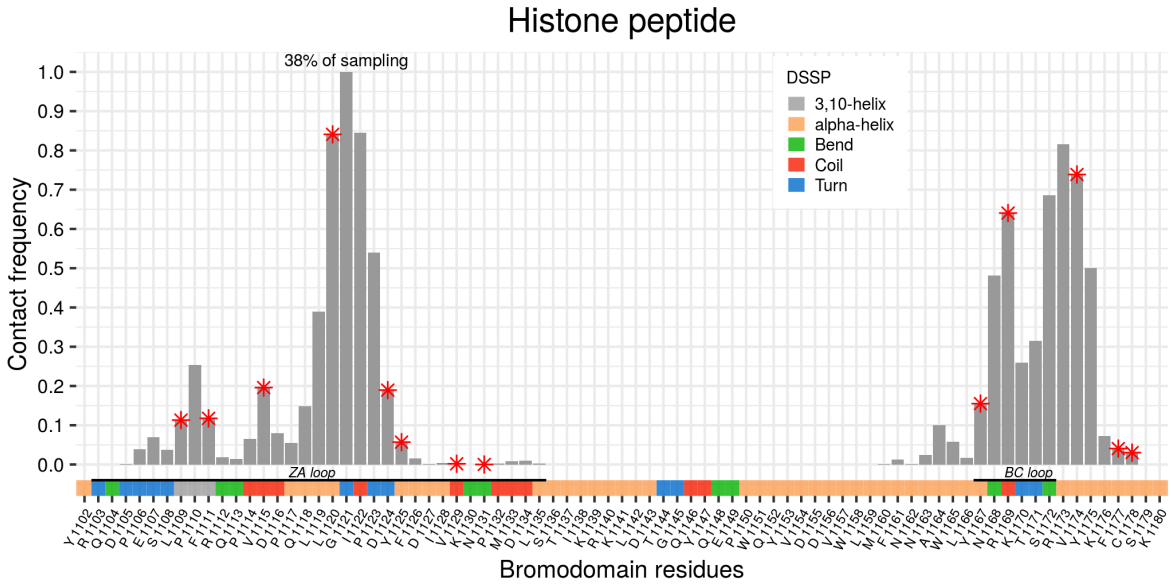

Figure S3: Contact analysis between the bromodomain backbone nitrogen atoms and all heavy atoms of the histone peptide. To define a contact, the same distance threshold of 8 Å as for the AIL endecamer in the main text is used. The percentage of sampling refers to the canonical and intermediate bound states (the K1595ac distance to the structural water is below 20 Å).

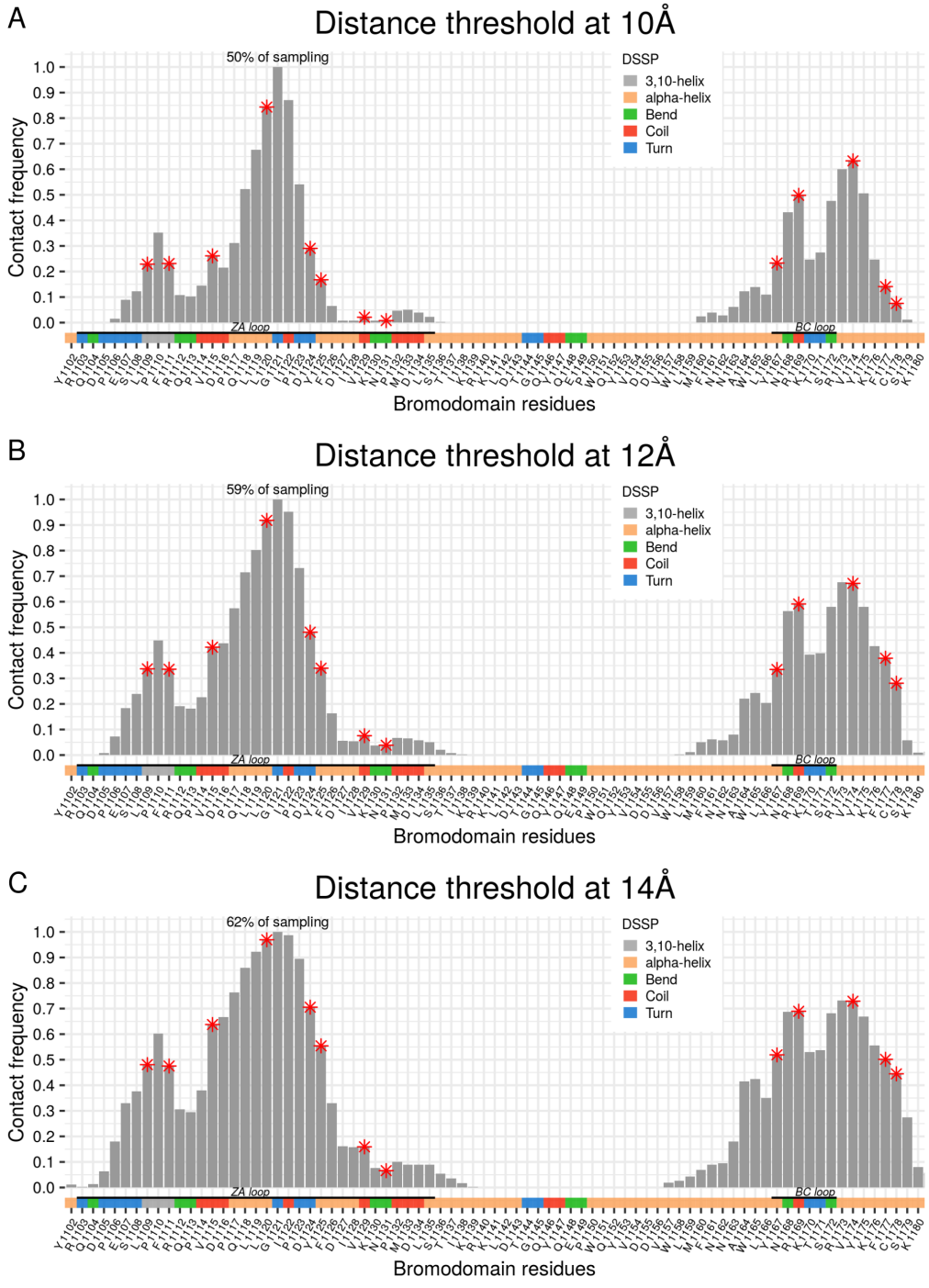

Figure S4: Contact analysis between the bromodomain backbone nitrogen atoms and all heavy atoms of the AIL endecamer, in a range of distance thresholds that define a contact between 10 to 14 Å. The percentage of sampling refers to the canonical and intermediate bound states.

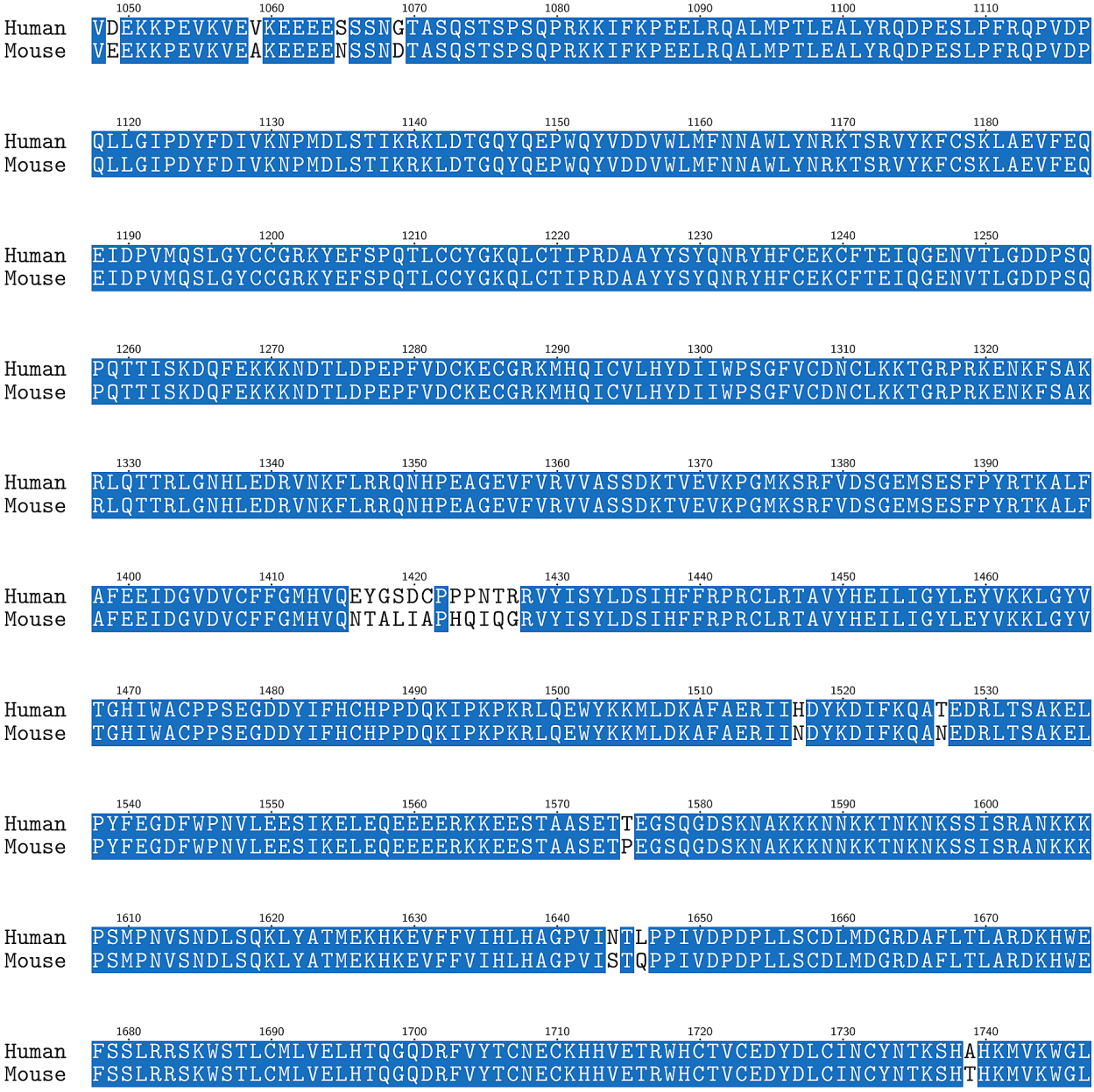

Figure S5: Alignment of the CBP catalytic core sequences from human and mouse organisms. The residue numbering on top refers to the human CBP sequence. The sequence of the catalytic core used in this study starts from residue Lys1082 until residue Asp1701. The residues that differ between the two organisms are indicated in white background. The bromodomain binding site does not have any differing residues. The AIL differs by only one residue (Thr1575 in human CBP is Pro1576 in mouse CBP).