Electronic Supplementary Information for

Preferred microenvironments of halogen bond and hydrogen bond revealed by statistics and QM/MM calculation studies

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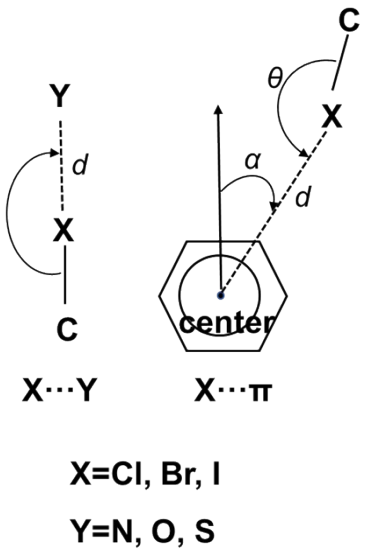

Figure S1. Two types of halogen bonds, *i.e.*, X···Y and X···π in PDB.

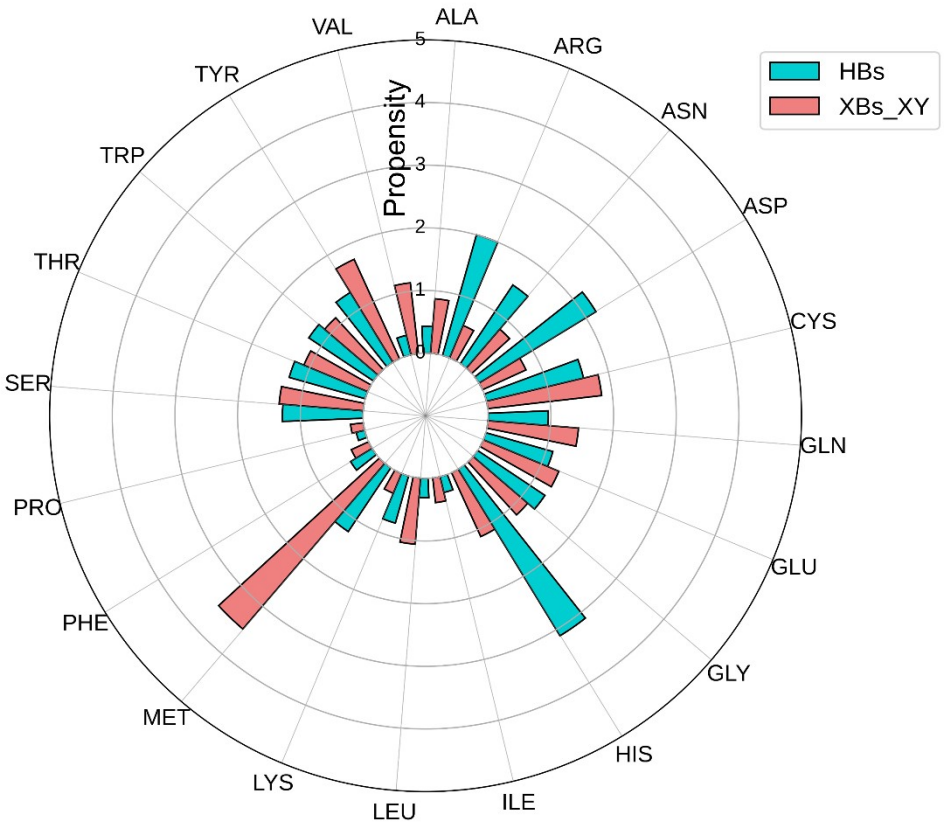

Figure S2. The amino acids distribution of HBs and X···Y XBs. The definition of propensity is that the relative frequency of each residue is divided by its relative background frequency in the whole database.

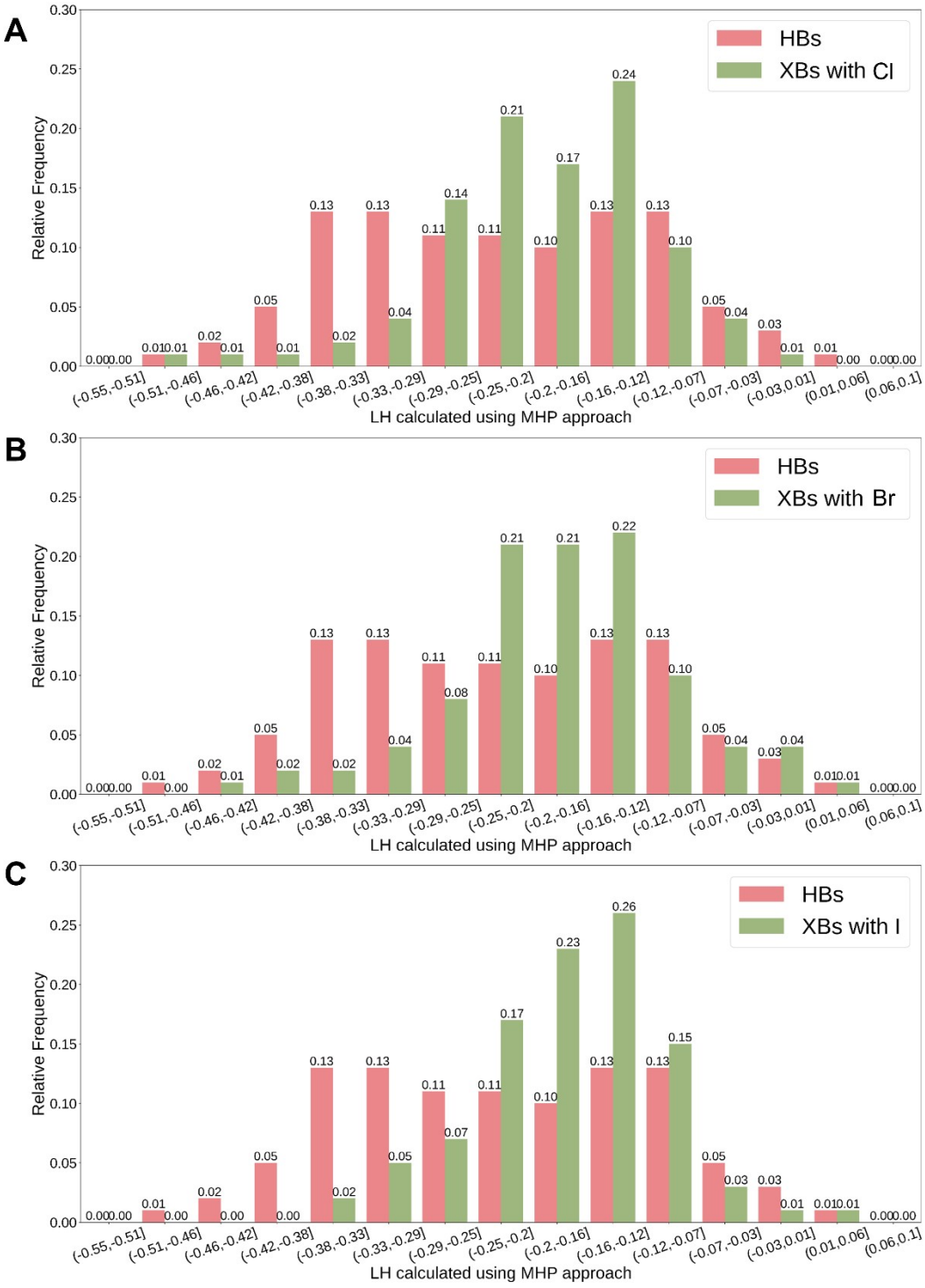

Figure S3. The frequency distribution of LHs for HBs (salmon) and XBs (greyish-green) with Cl (A), Br (B) and I (C). The x-coordinate represents the range of LH, and the y-coordinate represents the relative frequency. The higher the LH value, the greater the hydrophobicity. The unit of LH is log *P* (octanol-water).

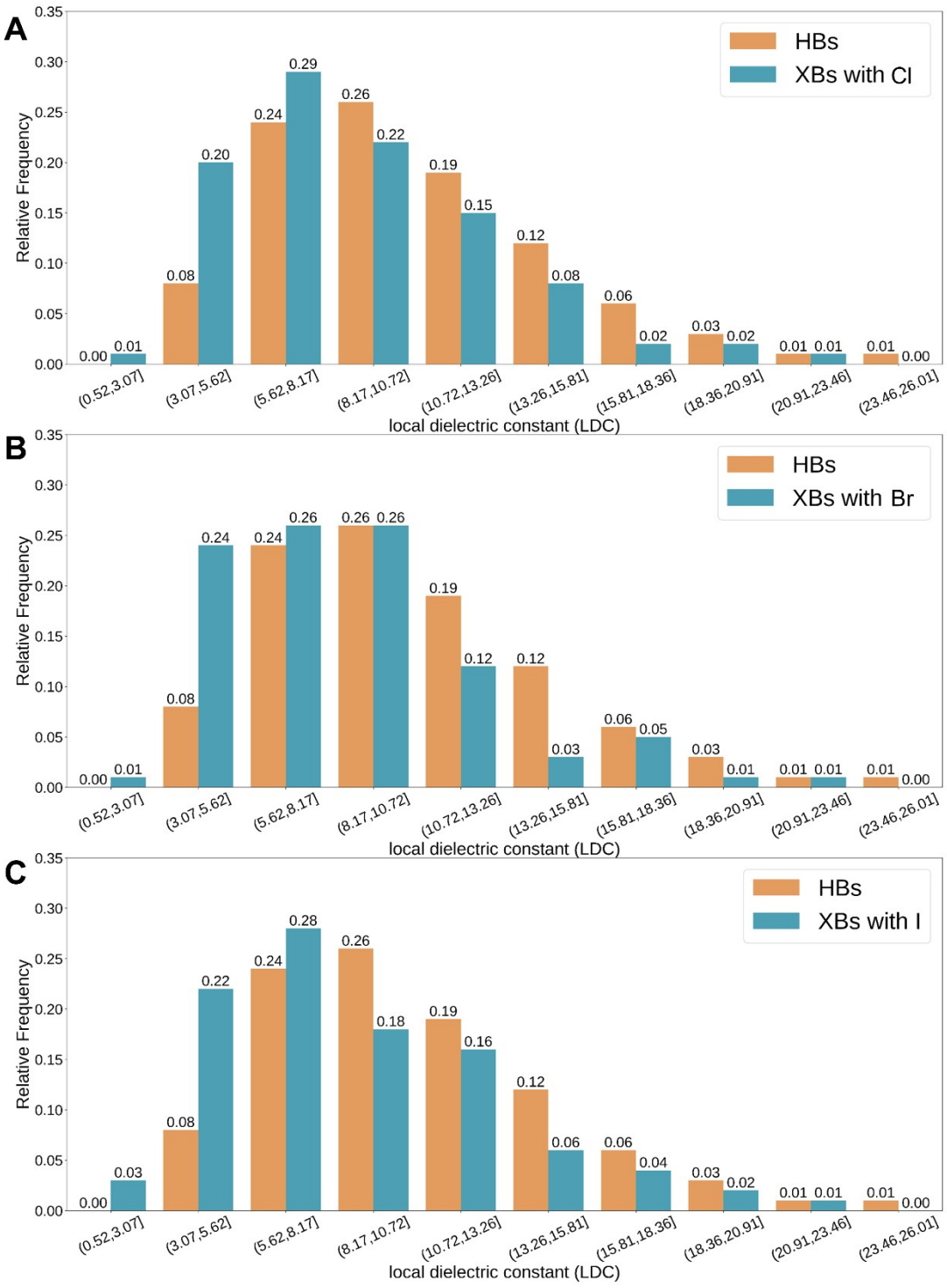

Figure S4. The frequency distribution of LDCs for HBs (darkorange) and XBs (dusty blue) with Cl (A), Br (B) and I (C). The x-coordinate represents the range of LDC, and the y-coordinate represents the relative frequency.

Table S1. The propensity of amino acids involved in HBs and XBs. Propensity is obtained by the relative frequencies divided by the relative background frequency of each residue in the whole database. The amino acids with difference over 0.6 are highlighted with blue and orange.

	HBs	XBs	HBs-XBs
ALA	0.43	0.57	-0.14
ARG	2.00	0.37	1.63
ASN	1.51	0.54	0.97
ASP	2.19	0.50	1.69
CYS	1.59	1.20	0.39
GLN	0.96	0.95	0.01
GLU	1.11	0.86	0.25
GLY	1.29	0.75	0.54
HIS	3.12	1.94	1.18
ILE	0.26	0.26	0.00
LEU	0.31	0.70	-0.39
LYS	0.78	0.22	0.56
MET	1.22	2.29	-1.07
PHE	0.40	3.02	-2.62
PRO	0.14	0.13	0.01
SER	1.28	0.88	0.40
THR	1.26	0.73	0.53
TRP	1.24	1.98	-0.74
TYR	1.31	5.71	-4.40
VAL	0.32	0.75	-0.43

Table S2. The mean and standard deviation of LHs and LDCs for HBs, XBs, XBs with Cl, XBs with Br and XBs with I.

	HBs	XBs	XBs with Cl	XBs with Br	XBs with I
LH (mean±sd)	-0.23±0.13	-0.19±0.10	-0.20±0.10	-0.19±0.10	-0.18±0.07
LDC (mean±sd)	10.69±4.36	8.86±4.00	8.97±3.97	8.53±3.92	8.87±4.26