

Table S1: **Summary of protein and small molecule binding sites in families of protein structures.**

<i>Number of families</i>	Total	bind small molecules	≥ 5 bi-functional positions
Total	3,463	1,131	
Domain-peptide	469	232	150
Domain-domain, inter-chain	2,120	900	570
Domain-domain, intra-chain	1,189	562	356
Total protein-binding	2,619	1,028	736

The number of protein families with at least 5 bi-functional positions are shown for each kind of protein interface. Bi-functional positions refer to alignment positions that bind both small molecules (250-1000 Da) and proteins.