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Supporting Material

Modeling effects of human SNPs on protein-protein interactions

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Supplementary materials

Additional data regarding the effect of nsSNPs on binding energy with respect to amino acid characteristics

Four different classes of amino acids were considered based on the amino acids' physico-chemical properties: polar (S, T, H, N, Q, Y), charged (E, D, K, R), hydrophobic (W, I, L, M, F) and small (P, A, G, C, V). Below we illustrate the effects of nsSNP mutations on the $\Delta\Delta\Delta G_{tot}(nsSNP)$, $\Delta\Delta\Delta G_{vdw}(nsSNP)$ and $\Delta\Delta\Delta G_{el}(nsSNP)$ (see main body of the manuscript for definition of these quantities) separately for each class and between classes (Table 1S). The corresponding distributions are shown in Fig. 1S. It can be seen that mutations that replace either charged or polar amino acids result in the largest energy change, while the effect is much smaller in the cases of small or hydrophobic residue replacement.

Particular attention deserve the 108 cases of nsSNP mutations that retain the physico-chemical properties of the amino acid present in the target protein-protein complex (case "SAME", e.g. *polar* \rightarrow *polar*; *charged* \rightarrow *charged*, *small* \rightarrow *small* and *hydrophobic* \rightarrow *hydrophobic*), and another 159 cases in which the nsSNP mutation changes the physico-chemical properties of the original amino acid (case "DIFF") (Table 1S). In terms of the means of the distributions, there is no significant difference between the "SAME" and "DIFF" distributions. In both cases, the mean of the total binding energy and its electrostatic component are negative quantities, which means that in both of these cases, the target complex is more stable than the nsSNP variant. At the same time, the mean of the van der Waals energy distribution is positive. The difference is in the standard deviation. The standard deviation of the distribution in "SAME" cases is about two times smaller than the distribution of "DIFF" cases. This indicates that there are cases within the "DIFF" category that result in drastic changes in the binding energy.

Table.1 Parameters of distribution of total binding energy difference and its components

Group	No	$\Delta\Delta\Delta G_{tot}$		$\Delta\Delta\Delta G_{vdw}$		$\Delta\Delta\Delta G_{el}$	
		mean	std	mean	std	mean	std
All	264	-0.86	4.28	-0.05	3.11	-0.78	4.64
OMIM	45	-1.65	3.80	-1.03	3.32	-2.35	5.51
Non-OMIM	219	-0.70	4.36	0.14	3.03	-0.45	4.39
Polar (P)	62	-0.27	3.77	0.38	3.94	-0.83	4.74
P-C	20	0.05	5.58	1.98	6.35	-3.00	7.59
P-H	7	-1.76	3.16	0.54	0.54	-0.66	1.37
P-P	28	-0.29	2.58	-0.50	1.73	0.35	2.07
P-S	7	0.37	1.46	-0.75	1.79	0.44	0.85
Charge (C)	76	-2.01	6.38	-0.33	2.25	-1.37	6.59
C-C	25	-2.16	3.59	-0.45	1.77	-1.76	3.99
C-P	30	-1.03	7.52	0.24	1.68	-0.38	8.53
C-H	3	-5.84	6.23	1.76	2.01	-1.11	10.86
C-S	18	-2.80	6.80	-1.45	0.74	-2.51	5.26
Small (S)	94	-0.74	2.39	-0.03	2.49	-0.78	2.58
S-C	10	0.56	2.72	2.51	3.58	-4.79	4.39
S-H	31	0.04	1.57	0.27	1.83	0.38	1.23
S-P	20	-0.88	1.53	0.01	1.37	-0.81	2.16
S-S	33	-1.79	2.92	-1.11	2.61	-0.65	1.85
Hydrophobic (H)	32	0.32	2.50	-0.36	4.46	0.74	3.23
H-C	2	-1.40	0.51	-0.90	0.33	-3.14	0.07
H-H	19	0.35	1.72	-0.39	1.70	-0.26	1.13
H-P	5	0.56	3.65	2.10	9.45	5.14	5.93
H-S	6	0.60	4.01	-2.14	5.61	1.55	1.40
SAME	108	-1.09	2.97	-0.66	2.05	-0.57	2.58
DIFF	159	-0.72	4.96	0.34	3.60	-0.91	5.61
Conserved	139	-0.85	4.94	-0.07	3.71	-1.05	5.55
Non-Conserved	88	-0.83	3.51	0.06	2.15	-0.72	3.38
High Conserved	176	-0.93	4.84	-0.10	3.45	-1.11	5.16
Low Conserved	51	-0.53	2.58	0.27	2.11	-0.26	3.38

Conserved (SI 100%), Non-Conserved (SI 10%-99%), High Conserved (SI 80%-100%), Low Conserved (SI 10%-79%).

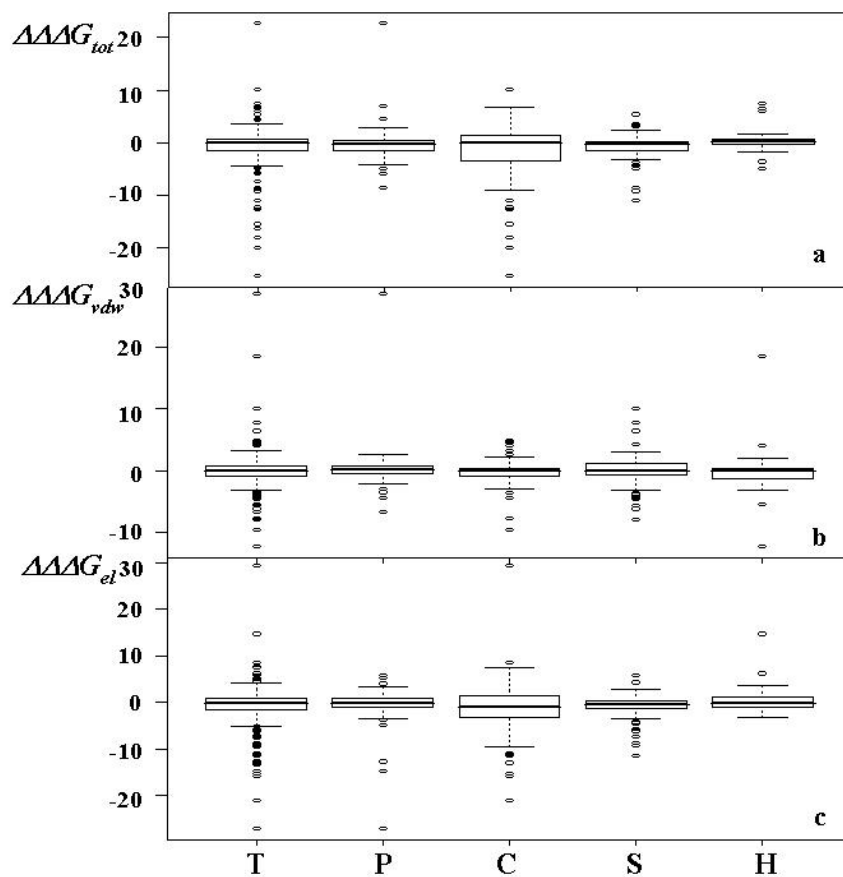


Fig. 1S. Distribution of $\Delta\Delta\Delta G_{tot}(nsSNP)$, $\Delta\Delta\Delta G_{el}(nsSNP)$ and $\Delta\Delta\Delta G_{vdw}(nsSNP)$ in respect with physico-chemical properties of amino acids. T: total, P: polar, C: charged, S: small, H: hydrophobic. The thick black lines show the median, the boxes are drawn between upper and down quartiles and the dotted lines are extended to upper and down whiskers (marked with short horizontal lines).