

(a) Protein complexes

Odd-score cutoff	# Cross-talks	SRCC (p-value)
1.5	228	0.3430 (3e-12)
2	194	0.3358 (1e-11)
3	112	0.2841 (1e-08)
4	60	0.1978 (8e-05)
5	25	0.1046 (4e-02)

(b) Filtered biological processes

Odd-score cutoff	# Cross-talks	SRCC (p-value)
1.5	1955	0.3452 (2e-12)
2	1149	0.3400 (5e-12)
3	199	0.2155 (2e-05)
4	56	0.0885 (0.08*)
5	12	0.0350 (0.5*)

**Table S 6. The significant correlation between cross-talk degree and binary module essentiality persists for a range of odd-scores in the *Direct* network for (a) protein complexes and (b) filtered biological processes. Odd-score cutoff** gives the minimum odd-score for a module pair to be considered a cross-talk. **# Cross-talks** gives the number of cross-talks at each cutoff. **SRCC (p-value)** gives the Spearman’s rho rank correlation coefficient between cross-talk degree and binary module essentiality. For larger odd-score cutoffs, there are fewer cross-talks and this results in somewhat lower SRCC values.