

(a) Protein complexes

Network	$\text{SRCC}_{\text{degree}}$	$\text{SRCC}_{\text{degree/size}}$	$\text{SRCC}_{\text{degree}\cdot\text{size}}$
Direct	0.3358 (1e-11)	0.2735 (4e-08)	0.2233 (9e-06)
Pull-down	0.3917 (1e-15)	0.2923 (4e-09)	0.2729 (5e-08)
Full	0.4081 (0e+00)	0.2824 (1e-08)	0.2924 (4e-09)

(b) Filtered biological processes

Network	$\text{SRCC}_{\text{degree}}$	$\text{SRCC}_{\text{degree/size}}$	$\text{SRCC}_{\text{degree}\cdot\text{size}}$
Direct	0.3400 (5e-12)	0.2262 (6e-06)	0.2326 (3e-06)
Pull-down	0.3866 (2e-15)	0.2656 (1e-07)	0.2838 (1e-08)
Full	0.3606 (2e-13)	0.1253 (1e-02)	0.2533 (4e-07)

**Table S 3. Correlation between cross-talk (CT) degree and binary module essentiality for (a) protein complexes and (b) filtered biological processes.**  $\text{SRCC}_{\text{degree}}$  gives the SRCC between cross-talk degree and essentiality.  $\text{SRCC}_{\text{degree/size}}$  gives the SRCC between the normalized cross-talk degree (i.e., cross-talk degree of the module divided by the module size) and essentiality.  $\text{SRCC}_{\text{degree}\cdot\text{size}}$  gives the partial SRCC between cross-talk degree and essentiality when controlling for the module size.  $P$ -values for the SRCCs are shown within parentheses. A module is considered essential if has at least one essential protein, and not essential otherwise.