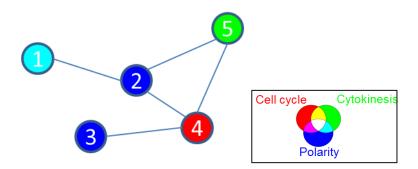
## Text S2: Analysis of the neighbors of high linkerity proteins

We tested the relationship between the linkerity of a node in the network and the functional annotation of its neighbors. To do this, for every node with a given functional annotation, we calculated the ratio of its interactions with neighbors sharing a functional annotation versus neighbors with different functional annotations. For neighbors with multiple functional annotations, we counted each functional annotation individually.

For example, looking at a simplified network:



Given node 2 with a polarity functional annotation (in blue), and four neighbours (1, 3, 4, 5) we obtain:

## Self annotations:

2-1 (Polarity to Polarity)

## Non-self annotations:

2-1 (Polarity to Cytokinesis)

2-5 (Polarity to Cytokinesis)

2-4 (Polarity to Regulation of Cell Cycle)

Giving a ratio of 1/3.

We then calculated the Spearman correlation between the other/self interaction ratio and the linkerity measure for the proteins in every functional category.

	Budding Yeast		Fission Yeast	
	Spearman Corr:	p-value	Spearman Corr:	p-value
Polarity:	0.49	<10 <sup>-9</sup>	0.60	<10 <sup>-9</sup>
Cell Cycle:	0.42	<10 <sup>-8</sup>	0.30	<10 <sup>-7</sup>
Cytokinesis:	0.42	<10 <sup>-4</sup>	0.36	<10 <sup>-4</sup>