## **Fig S1.** Network distances are similar between the Organic and Cytoscape force-directed layout weighted by E-value.

This page: Statistics (A) describing the comparison of the kinase network from Fig. 3 laid out using the Organic layout (B) or the Cytoscape force-directed layout weighted by edge E-value (C).

Following page: Statistics (D) describing the comparison of the amine GPCR network from Fig. 2B laid out using the Organic layout (E) or the Cytoscape force-directed layout weighted by edge E-value (F).

Α.	A. BLAST E-values		
		А.	
		BLAST E-values	
	B. Organic layout	R: 0.934 ± 0.003	
		Z: 41.2	B.
		P: 0.0	Organic layout
	C. Cytoscape force-	R: 0.895 ± 0.003	R: 0.900 ± 0.003
	directed layout	Z: 35.3	Z: 36.8
	weighted by E-value	P: $7.02 \times 10^{-273}$	P: $2.92 \times 10^{-297}$

Pearson's correlations (R) and associated Z-scores (Z) and P-values (P) describing the similarity between the relative pairwise distances between 419 human kinase domain sequences in common as assessed by (A) all shortest paths between  $-\log_{10}(BLAST E)$ values), (B) the shortest paths between sequences as displayed by the Organic twodimensional graph layout algorithm, and (C) the shortest paths between sequences in the two dimensional Cytoscape force-directed layout, weighted by BLAST E-value. The pairwise BLAST E-values and the graph layout algorithm correspond to a network thresholded at an E-value of  $1 \times 10^{-25}$ 



#### **C.** Force-directed layout weighted by E-value

### Fig S1. Continued

D.	A. BLAST E-values		
		A. BLAST E values	
	B. Organic layout	$R: 0.906 \pm 0.034$	
		Z: 11.87	В.
		$P: 8.04 \times 10^{-55}$	Organic layout
	C. Cytoscape force-	R: $0.850 \pm 0.034$	R: 0.877 ± 0.035
	directed layout	Z: 9.52	Z: 10.16
	weighted by E-value	P: $8.78 \times 10^{-22}$	P: $1.47 \times 10^{-24}$

Pearson's correlations (R) and associated Z-scores (Z) and P-values (P) describing the similarity between the relative pairwise distances between 42 amine GPCR domain sequences in common as assessed by (A) all shortest paths between  $-\log_{10}(BLAST E-values)$ , (B) the shortest paths between sequences as displayed by the Organic two-dimensional graph layout algorithm, and (C) the shortest paths between sequences in the two dimensional Cytoscape force-directed layout, weighted by BLAST E-value. The pairwise BLAST E-values and the graph layout algorithm correspond to a network thresholded at an E-value of  $1 \times 10^{-33}$ .

### E. Organic Layout



# F. Force-directed layout weighted by E-value

