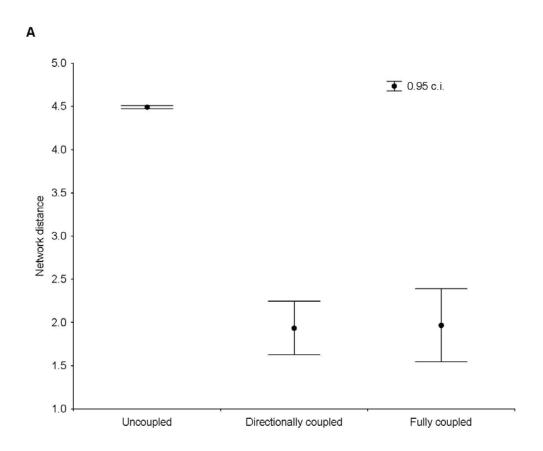
## **Supporting figures**

**Figure S1A** Uncoupled gene pairs have higher network distances than flux coupled pairs (i.e. fully and directionally) in the metabolic network of *E. coli* (Wilcox robust one-way ANOVA,  $p \approx 0$ ), but fully and directionally coupled gene pairs do not differ in terms of overall network distance (Wilcox robust one-way ANOVA, p = 0.9).



**Figure S1B** mRNA-level co-expression correlates with the type of flux coupling in the metabolic network of *E. coli* (Wilcox robust one-way ANOVA,  $p < 10^{-14}$ ).

