Part 2: Reanalysis

**Paper**: Identification of critical connectors in the directed reaction-centric graphs of microbial metabolic networks

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We intend to recreate Figure 3 from the paper which describes the proportion of total reactions relative to essential reactions captured by each centrality metric for the *E. Coli* metabolite network. Figure 3 uses the adjacency matrix presented in the supplementary materials to generate a directed graph where nodes represent genes and edges represent metabolic reactions. Node-wise measures including bridging centrality, betweenness centrality, clustering coefficient, and total degree are computed, which are then plotted on a bar graph showing the distribution of essential reactions captured relative to all reactions. We intend to generate the same distribution bar graph for *E. Coli* and then for the other four microbes as those were not included in the original manuscript.

We will use NetworkX to first plot the adjacency matrix as a directed graph - the directionality is specified in the methods section of the paper. We intend to use the centrality measures specified in the methods for *E. Coli* and the remaining four microbes; this will give us the node distributions for each centrality measure per microbe. Next, we will compute the essentiality of reactions using [flux balance analysis](https://www.nature.com/articles/nbt.1614) (FBA). This process describes the flow of metabolites in a large network and helps predict reactions that may be essential to organism growth and function. The paper notes that the tool [COBRA](https://opencobra.github.io/cobratoolbox/stable/modules/analysis/FBA/index.html) through MATLAB was used to identify essential reactions; we aim to replicate their results by using the same models used in the paper for *E. coli* and then repeat for *S. Cerevisiae*. We downloaded the models from [BiGG](https://doi.org/10.1093/nar/gkv1049) and intend to run FBA simulations by using [COBRApy](https://bmcsystbiol.biomedcentral.com/articles/10.1186/1752-0509-7-74), estimating the growth rate with the same metabolite parameters as in the paper, and iterating over the absence of a reaction. In the case where replicating or identifying essential reactions is difficult, we also intend to test various other centrality metrics with the *E. Coli* data, including but not limited to eigenvector centrality, harmonic centrality, and closeness centrality. This will allow us to test how generalizable the metrics are across different microbial species (gauges the sensitivity of the methods used).