Microbial Network Evolution

via critical connectors in directed reaction-centric graphs metabolic networks

Tara Pande

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Background

Models and methods from the graph theory have been developed to characterize structural properties in various kinds of complex networks in social, technological, and biological areas [1, 2]. In the analysis of biological networks, graph theory has been successful in detecting global topological features of biological networks such as short path lengths, scale-freeness with the appearance of hubs [3], hierarchical modular structures [4], and network motifs [5].

"While the **topological analysis as a whole can give insight on network evolution** and cellular robustness, investigation of influences of individual nodes in a biological network has potential for practical applicability..."

analyses have been mostly performed using undirected bionetworks. Recent studies extended several global measures, such as in/out-degree distribution, betweenness, closeness, clustering coefficient, and modularity for application into directed networks [1, 12, 13]. These measures are strongly correlated with high degrees, focusing on densely connected sub-structures. Although they discovered global topological properties and global roles of individual nodes, they are insufficient to explain connections between modules and local connectivity, typically within a few of steps of neighbors surrounding the node, in networks with directed flows. For example, nodes of high degree have global topological importance in a network, however, the fact that they have so many interactions means that they are poor channels for conveying

Sections Figures References

Fig. 1

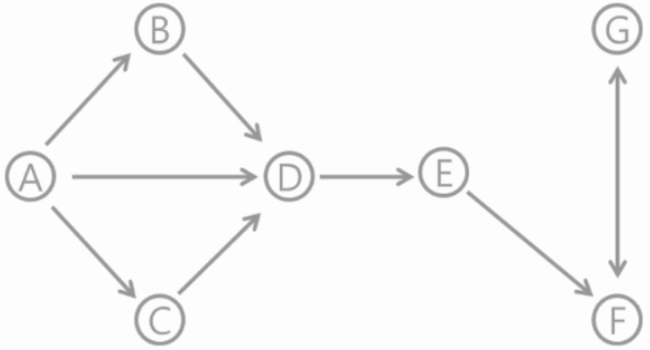

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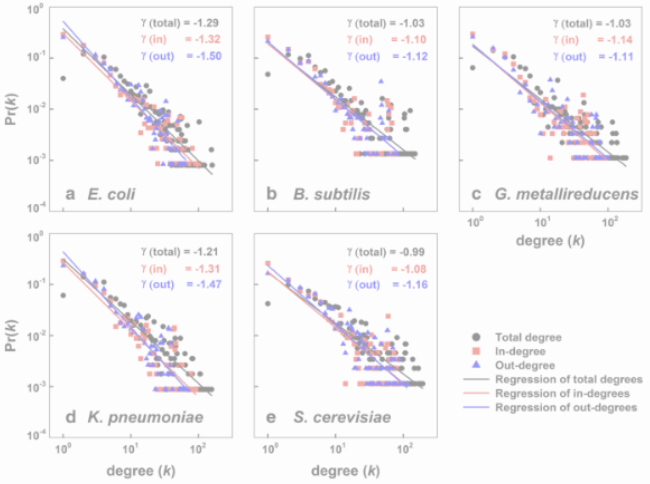
Fig. 2



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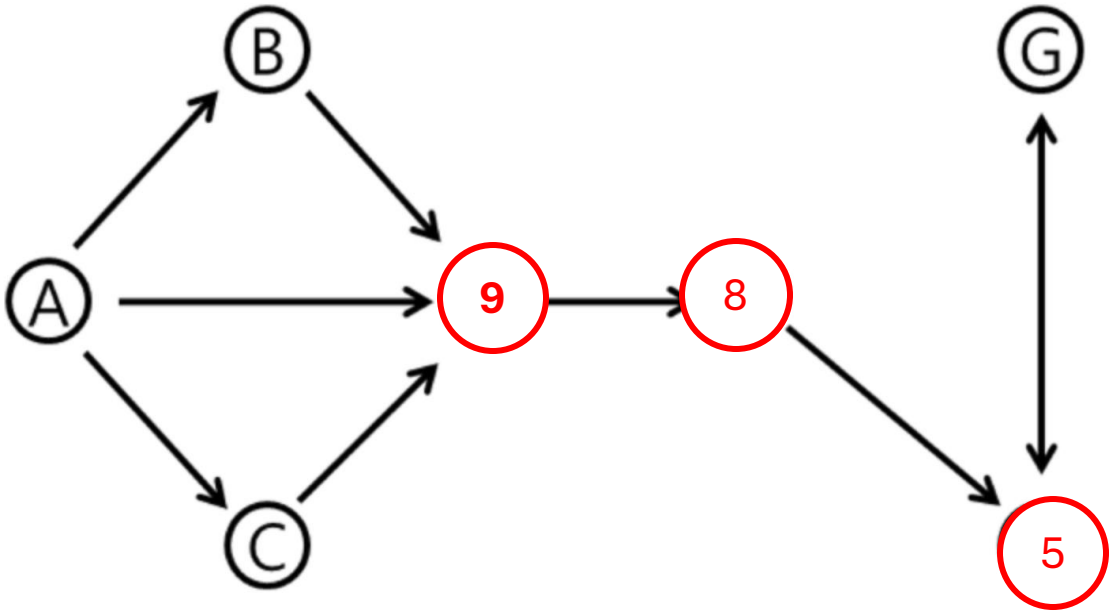
Topology Metrics

Betweenness Centrality (B)

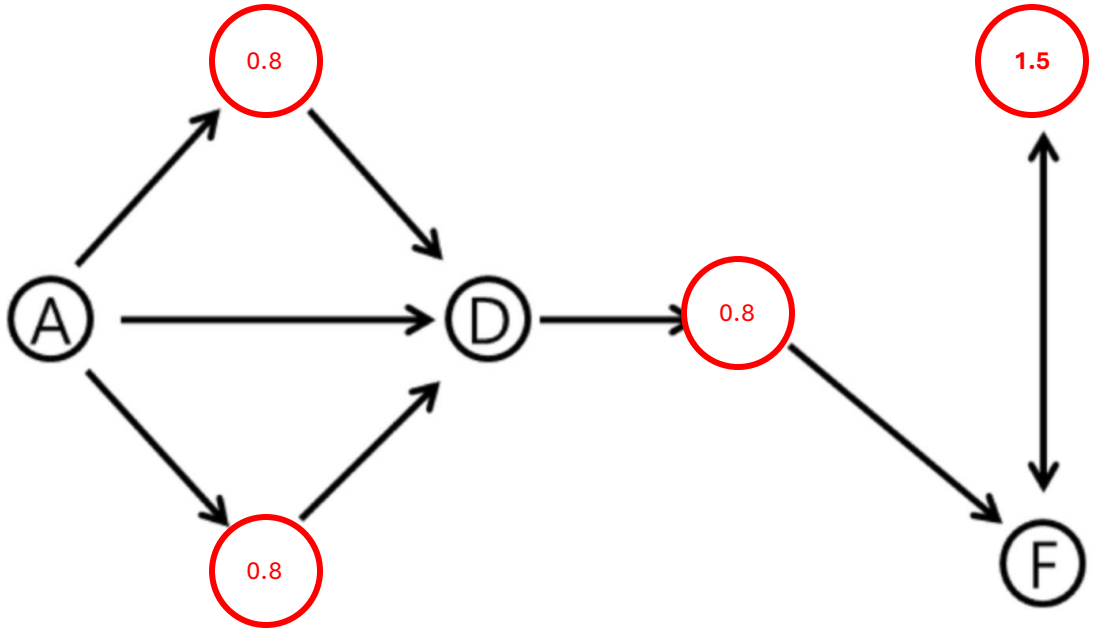


Node	B	BC	BrC	CN
A	0	0.2667	0	4
B	0	0.8571	0	0
C	0	0.8571	0	0
D	9	0.1364	1.2273	1
E	8	0.8571	6.8571	0
F	5	0.3333	1.6667	1
G	0	1.5000	0	0

$$B(i) = \sum_{j \neq i \neq k} \frac{\sigma_{jk}(i)}{\sigma_{jk}}$$

Bridging Coefficient (BC)

Undirected calculation!



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D	9	0.1364	1.2273	1
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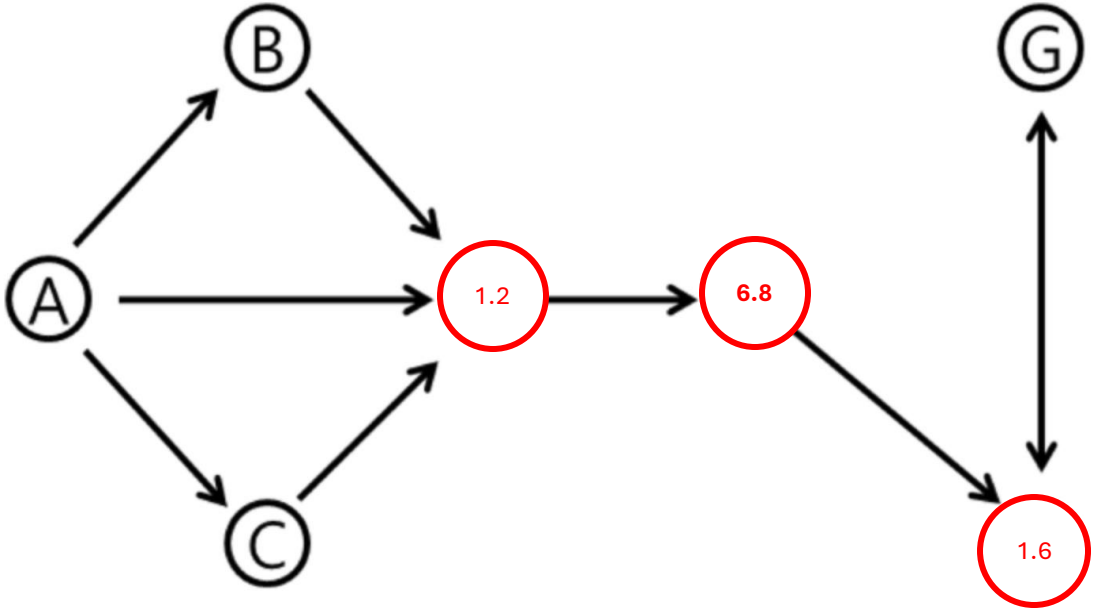
G	0	1.5000	0	0

$$BC(i) = \begin{cases} \dfrac{(degree_{total}(i))^{-1}}{\sum_{j\ in\ \Lambda(i)} (degree_{total}(j))^{-1}} & if\ degree_{in}(i) \neq 0\ and\ degree_{out}(i) \neq 0 \\ 0 & otherwise \end{cases}$$

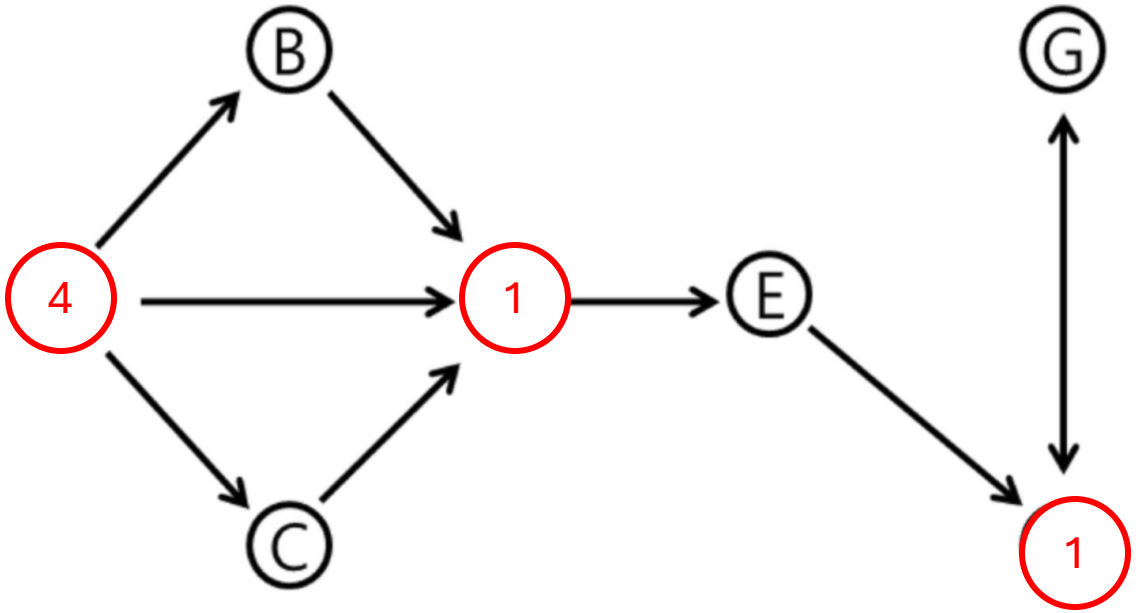
Bridging Centrality (BrC)



Node	B	BC	BrC	CN
A	0	0.2667	0	4
B	0	0.8571	0	0
C	0	0.8571	0	0
D	9	0.1364	1.2273	1
E	8	0.8571	**6.8571**	0
F	5	0.3333	1.6667	1
G	0	1.5000	0	0

$$BrC(i) = B(i) \times BC(i)$$

Cascade Number (CN)



Node	B	BC	BrC	CN
A	0	0.2667	0	4
B	0	0.8571	0	0
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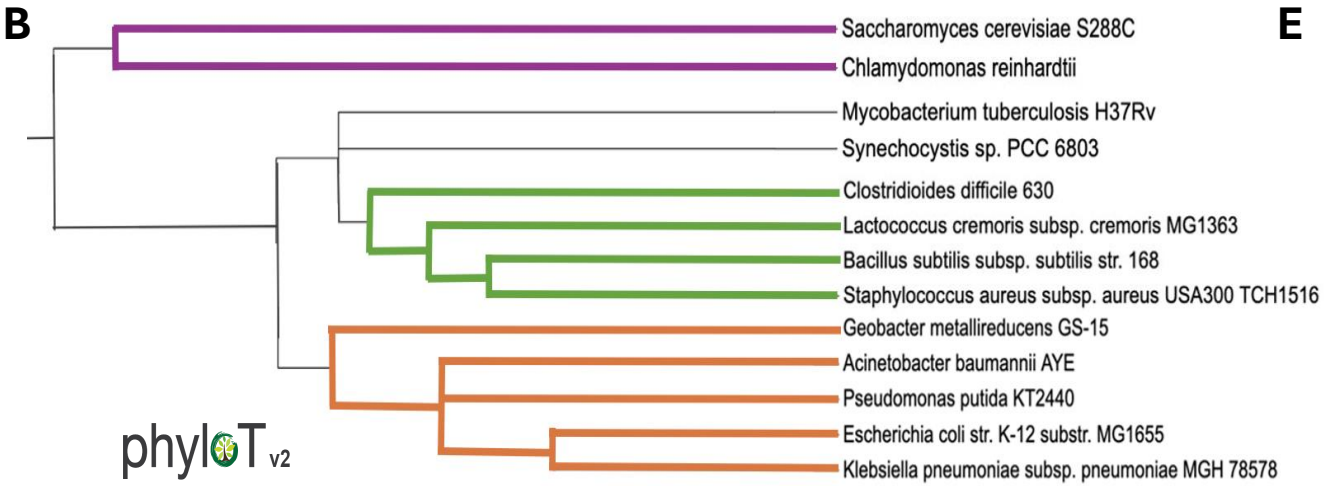
E	8	0.8571	6.8571	0
F	5	0.3333	1.6667	1
G	0	1.5000	0	0

Methods & Results

A

Model	Organism	Phylum
iAF987	Geobacter metallireducens GS-15	Pseudomonadota
iCN718	Acinetobacter baumannii AYE	Pseudomonadota
iCN900	Clostridioides difficile 630	Bacillota
iEK1008	Mycobacterium tuberculosis H37Rv	Actinomycetota
iJN678	Synechocystis sp. PCC 6803	Cyanobacteriota
iJN1463	Pseudomonas putida KT2440	Pseudomonadota
iJO1366	Escherichia coli str. K-12 substr. MG1655	Pseudomonadota
iMM904	Saccharomyces cerevisiae S288C	Ascomycota (E)
iNF517	Lactococcus lactis subsp. cremoris MG1363	Bacillota
iRC1080	Chlamydomonas reinhardtii	Chlorophyta (E)
iYL1228	Klebsiella pneumoniae subsp. pneumoniae MGH 78578	Pseudomonadota
iYO884	Bacillus subtilis subsp. subtilis str. 168	Bacillota
iYS854	Staphylococcus aureus subsp. aureus USA300_TCH1516	Bacillota

B



E

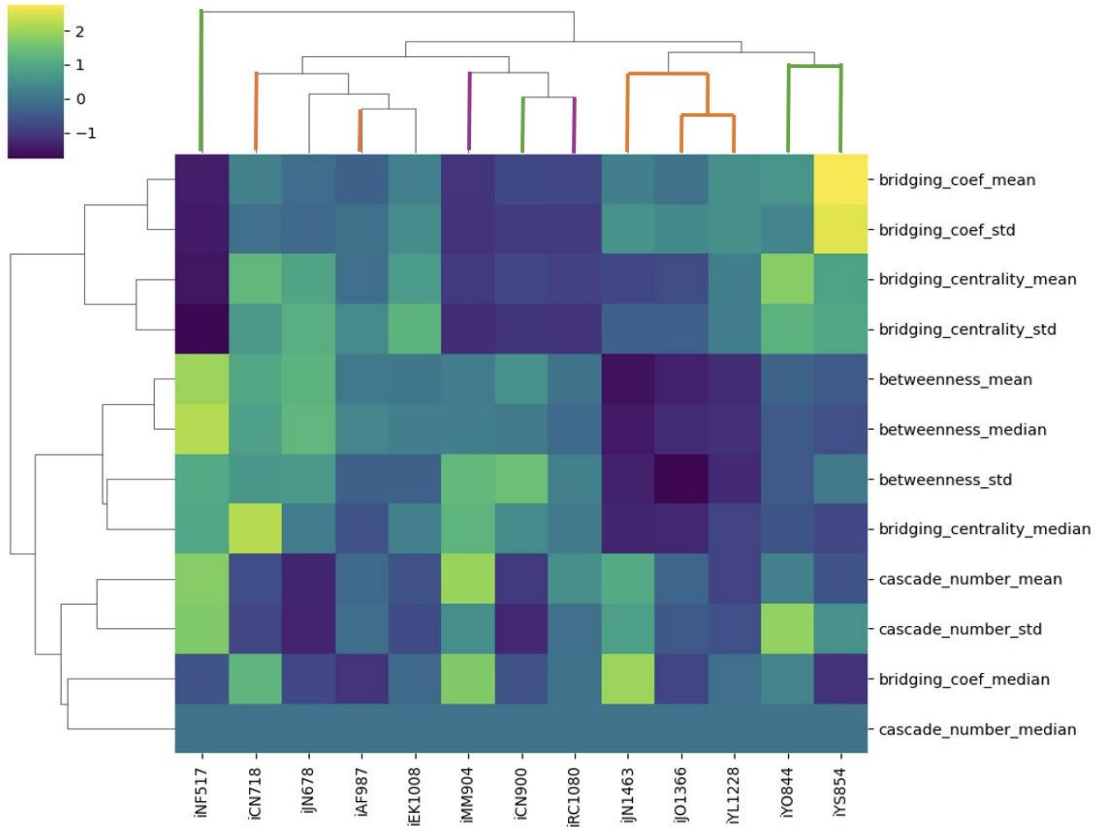
Robinson–Foulds (RF) Distance Ratio

	NT	FE
GT	14/18 (0.778)	14/18 (0.778)
NT		18/20 (0.900)

Triplets Distance (Local)

	NT	FE
GT	14	14
NT		18

C



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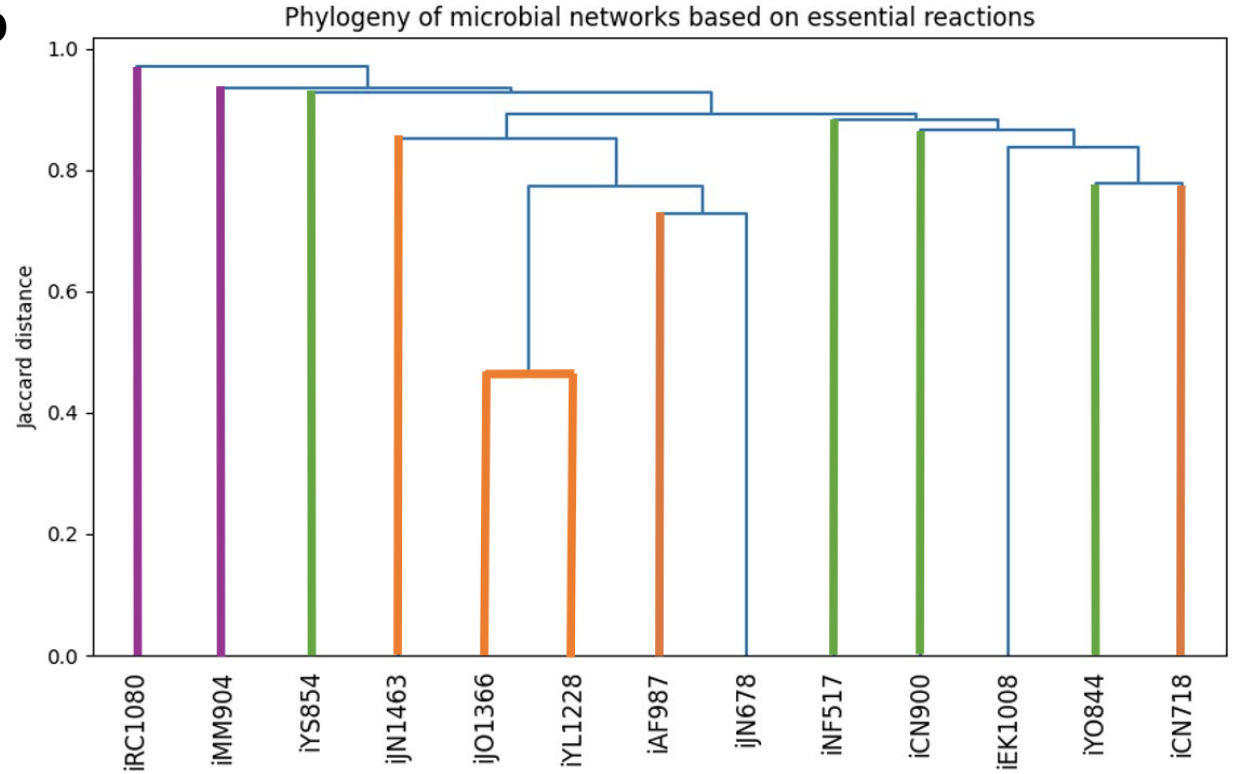


Figure A

Model Organisms Dataset

Model	Organism	Phylum	EssR
iAF987	Geobacter metallireducens GS-15	Pseudomonadota	8.79%
iCN718	Acinetobacter baumannii AYE	Pseudomonadota	7.39%
iCN900	Clostridioides difficile 630	Bacillota	8.14%
iEK1008	Mycobacterium tuberculosis H37Rv	Actinomycetota	8.08%
iJN678	Synechocystis sp. PCC 6803	Cyanobacteriota	8.57%
iJN1463	Pseudomonas putida KT2440	Pseudomonadota	7.69%
iJO1366	Escherichia coli str. K-12 substr. MG1655	Pseudomonadota	7.55%
iMM904	Saccharomyces cerevisiae S288C	Ascomycota (E)	10.0%
iNF517	Lactococcus lactis subsp. cremoris MG1363	Bacillota	9.68%
iRC1080	Chlamydomonas reinhardtii	Chlorophyta (E)	7.49%
iYL1228	Klebsiella pneumoniae subsp. pneumoniae MGH 78578	Pseudomonadota	6.76%
iYO884	Bacillus subtilis subsp. subtilis str. 168	Bacillota	6.32%
iYS854	Staphylococcus aureus subsp. aureus USA300_TCH1516	Bacillota	7.70%

Figure B

Expected Microbial Evolution

phyloT v2

A phylogenetic tree generator based on NCBI taxonomy

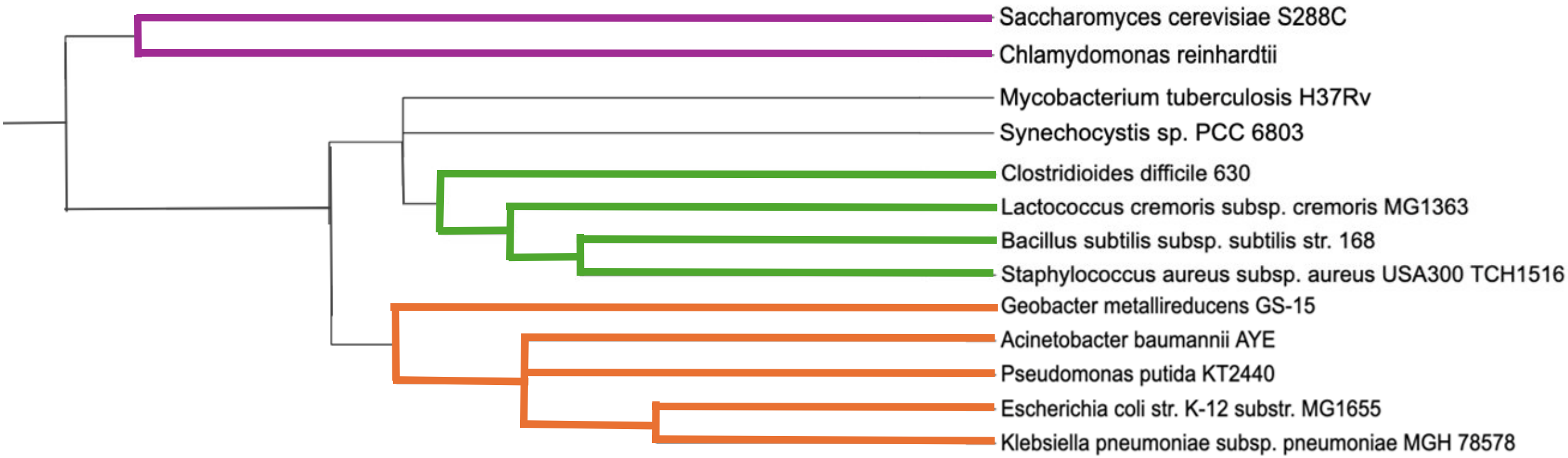
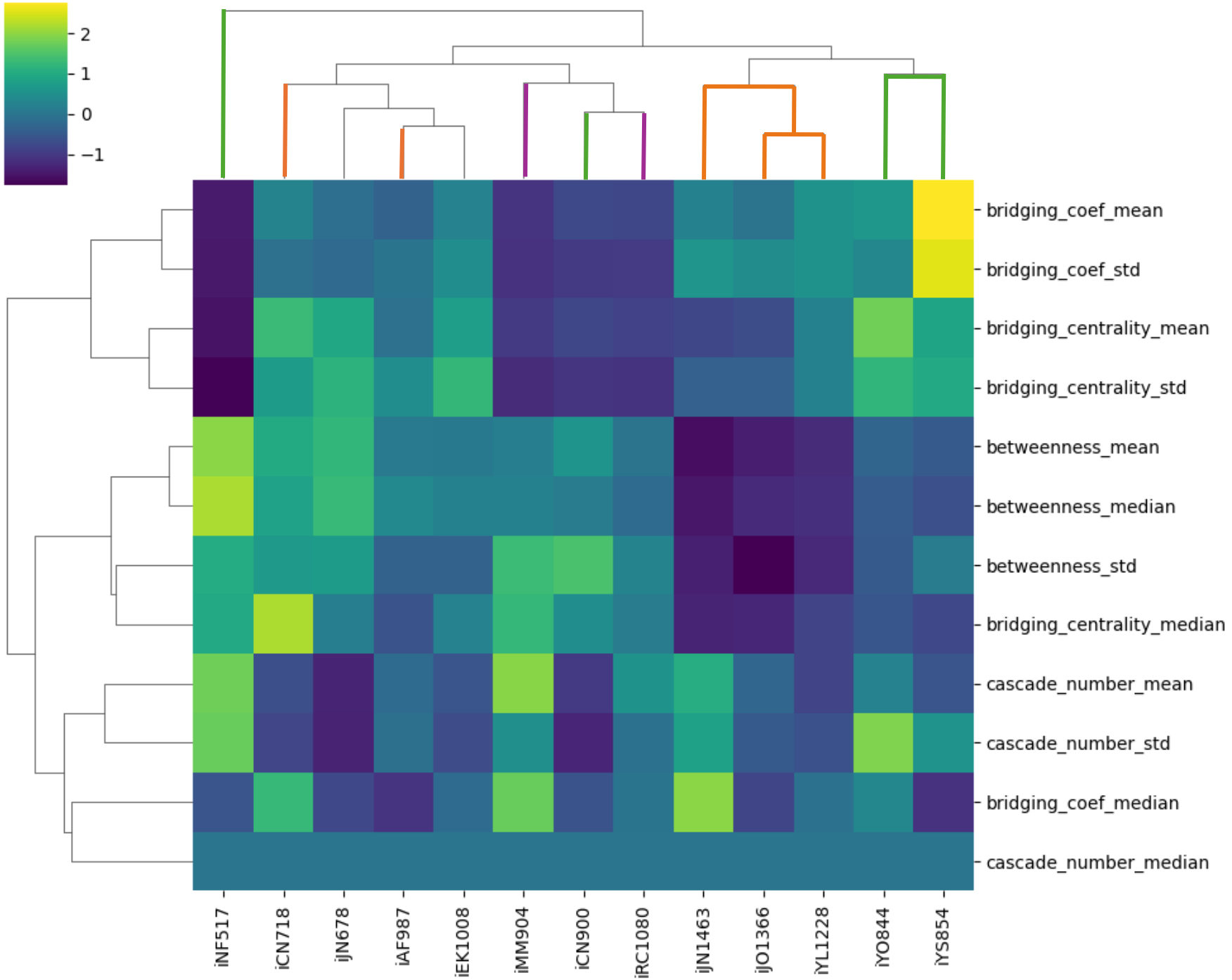
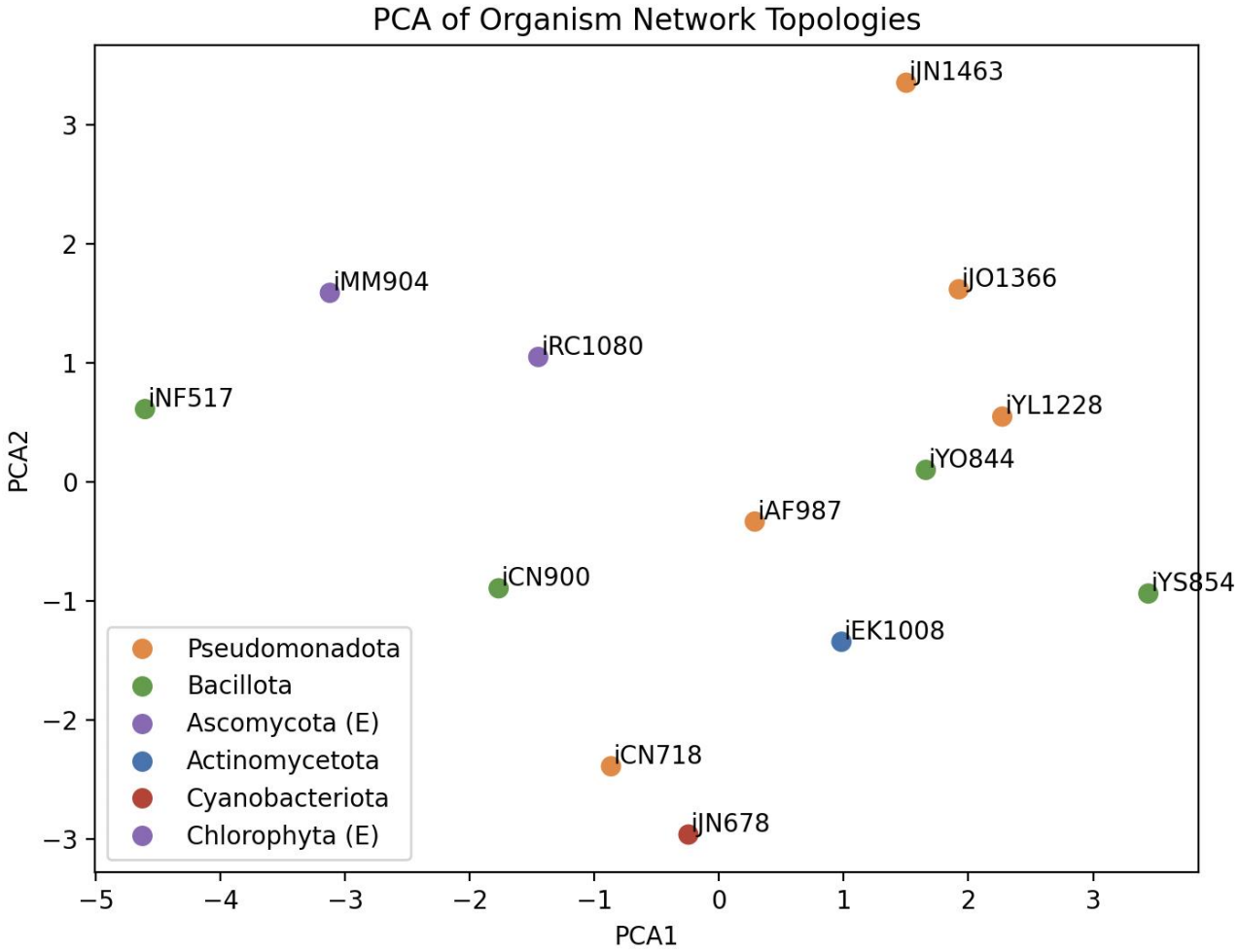


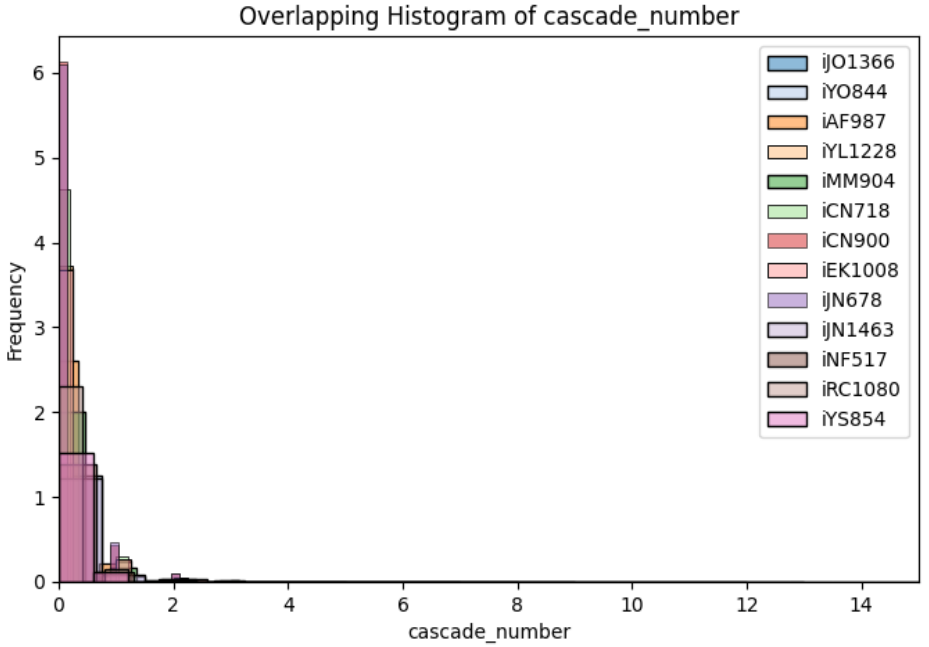
Figure C

Network Topology Dendrogram



Topology Weaknesses





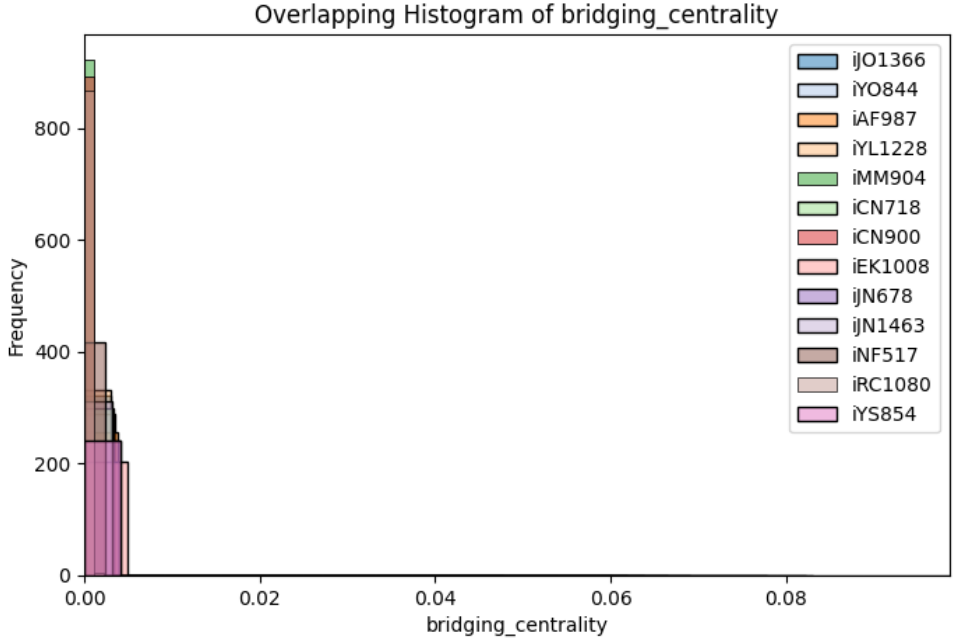


Figure D

Functional Essentiality Phylogram

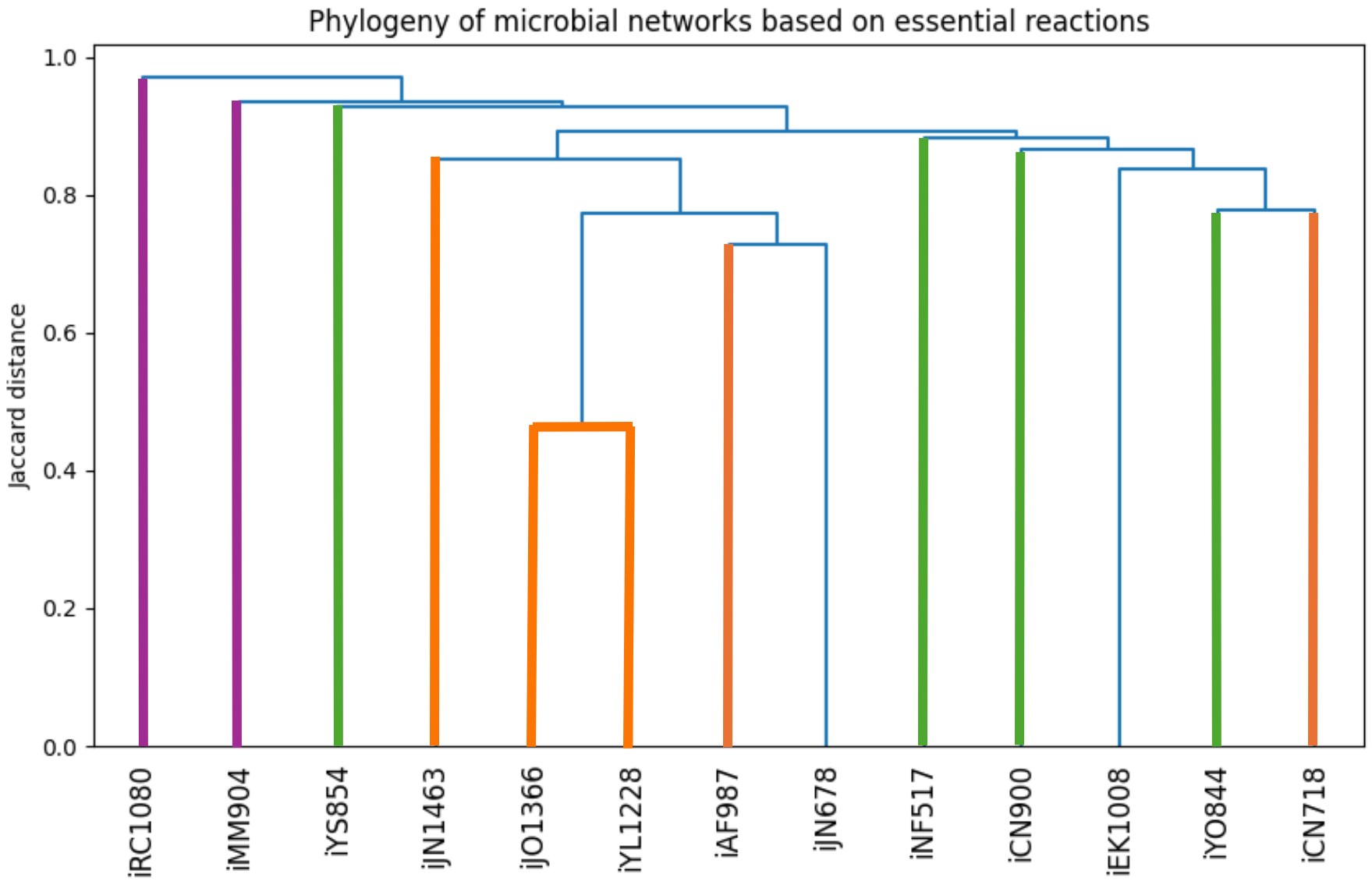


Figure E Phylogeny Metrics

Robinson–Foulds (RF) Distance Ratio

	NT	FE
GT	14/18 (0.778)	14/18 (0.778)
NT		18/20 (0.900)

Triplets Distance (Local)

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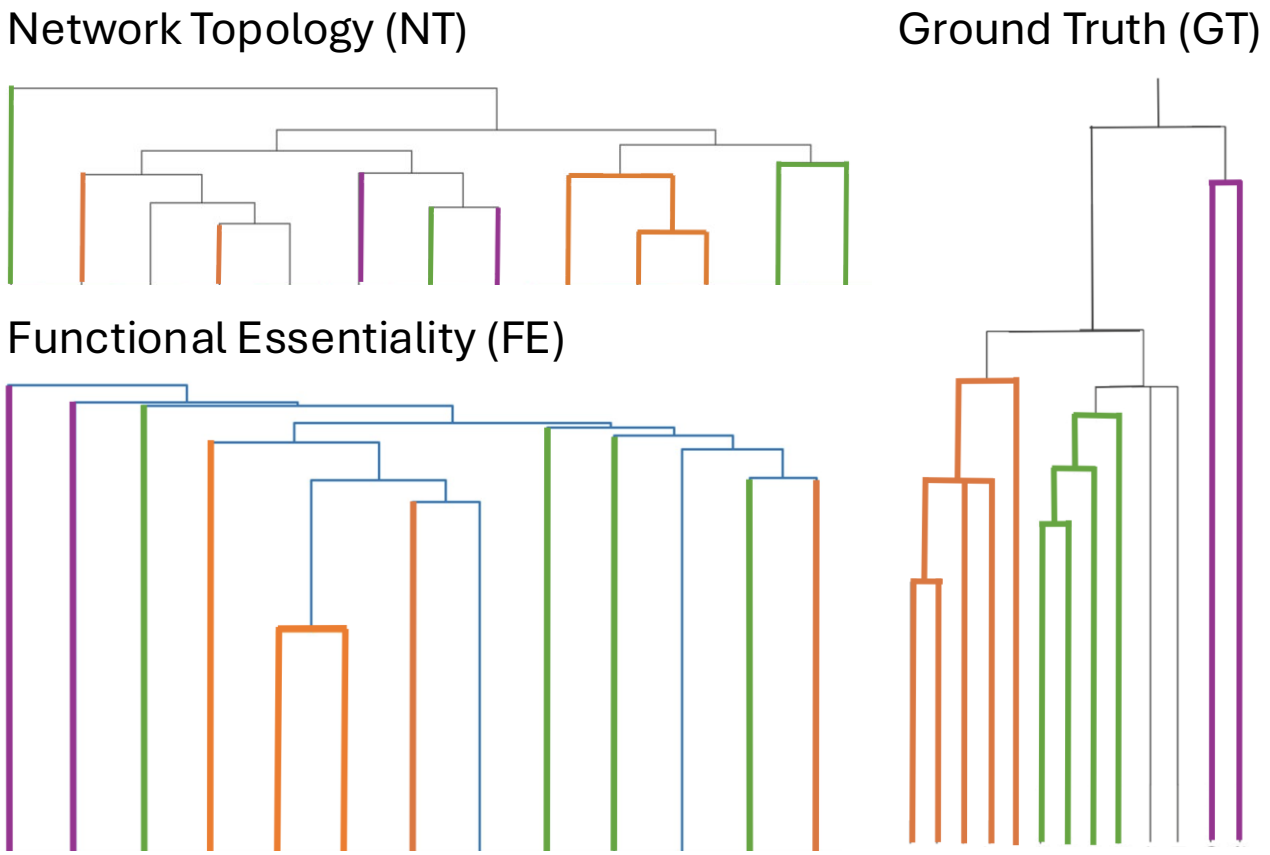
NT		18



Conclusions

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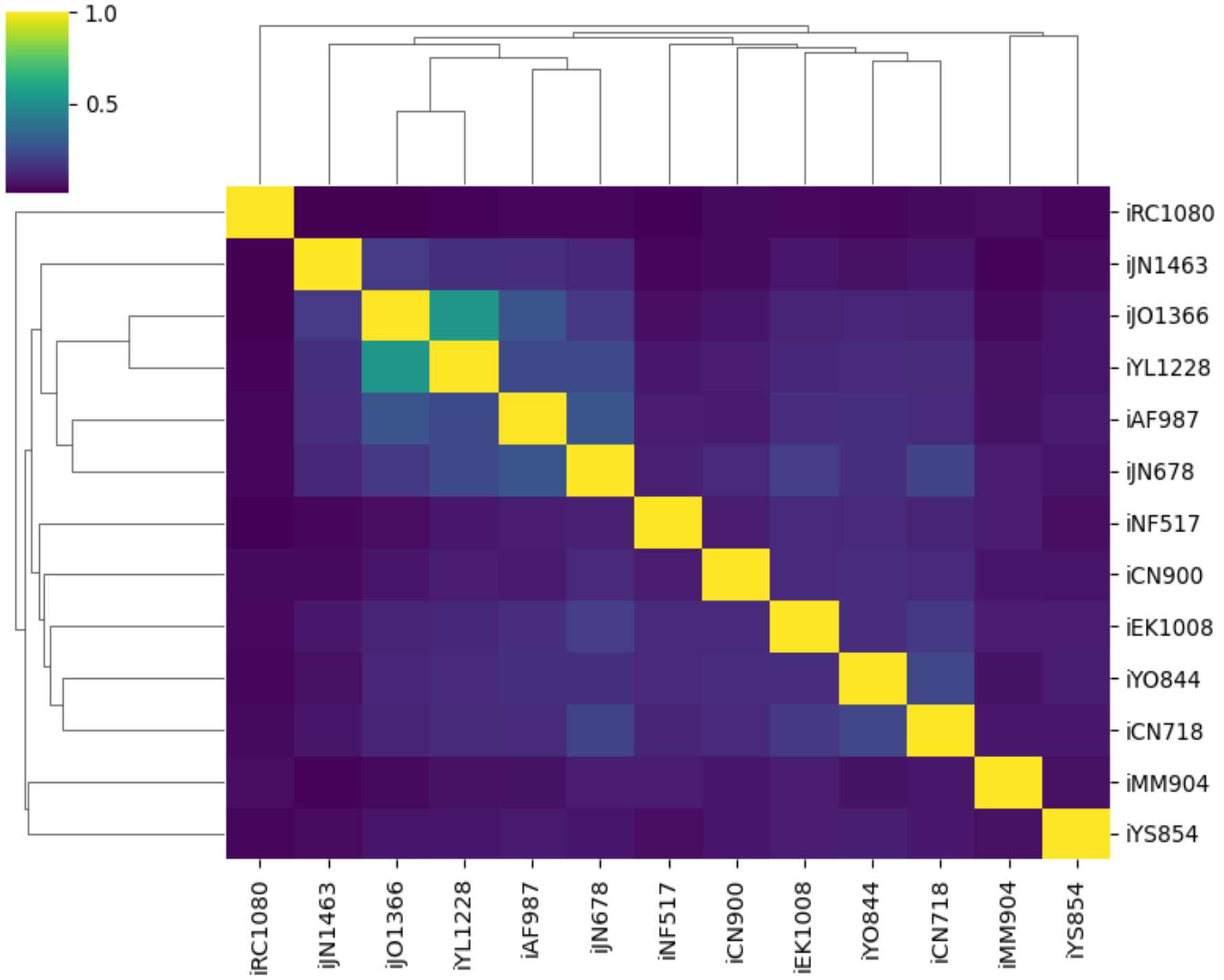
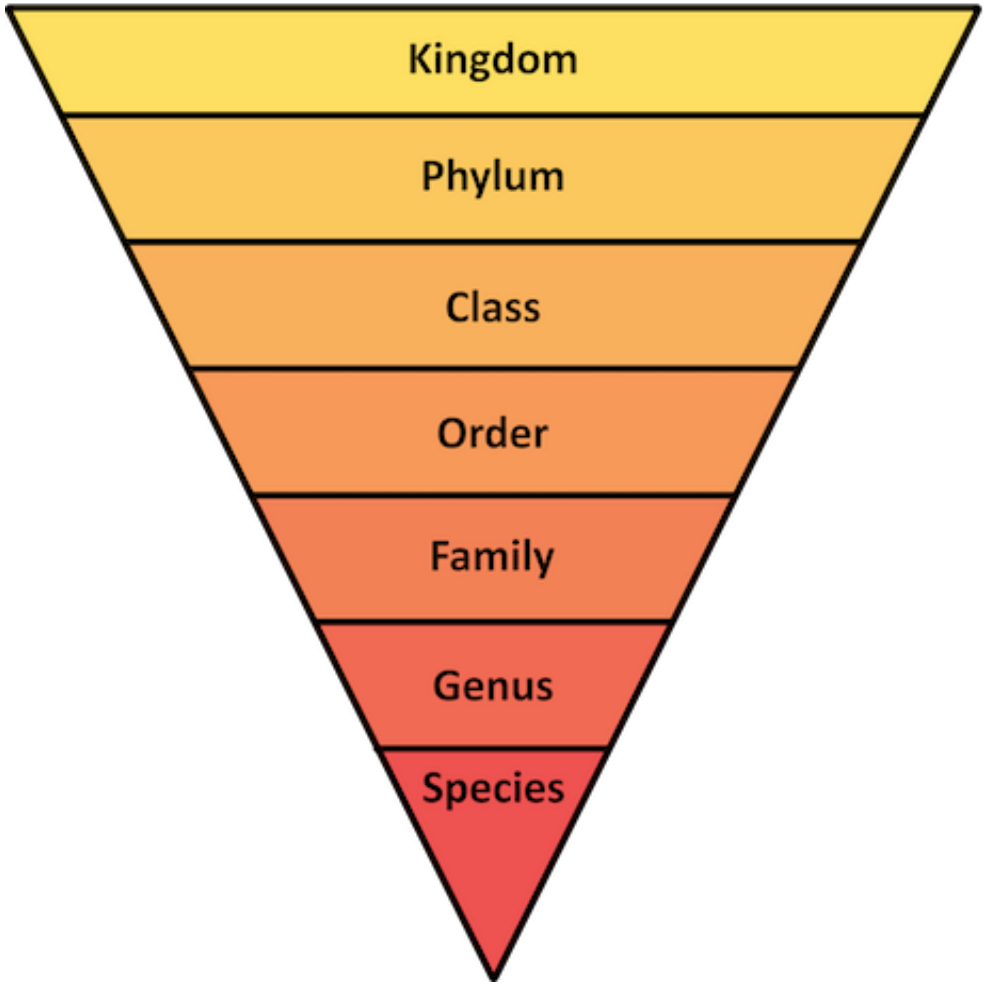
Functional Essentiality Dendrogram



Conclusions

NCBI Taxonomical Hierarchy

Bacteria		
Pseudomonadota		
Gammaproteobacteria		
Pseudomonadales	Enterobacterales	
Pseudomonadaceae	Enterobacteriaceae	
Pseudomonas	Escherichia	Klebsiella
Pseudomonas putida	Escherichia coli	Klebsiella pneumoniae



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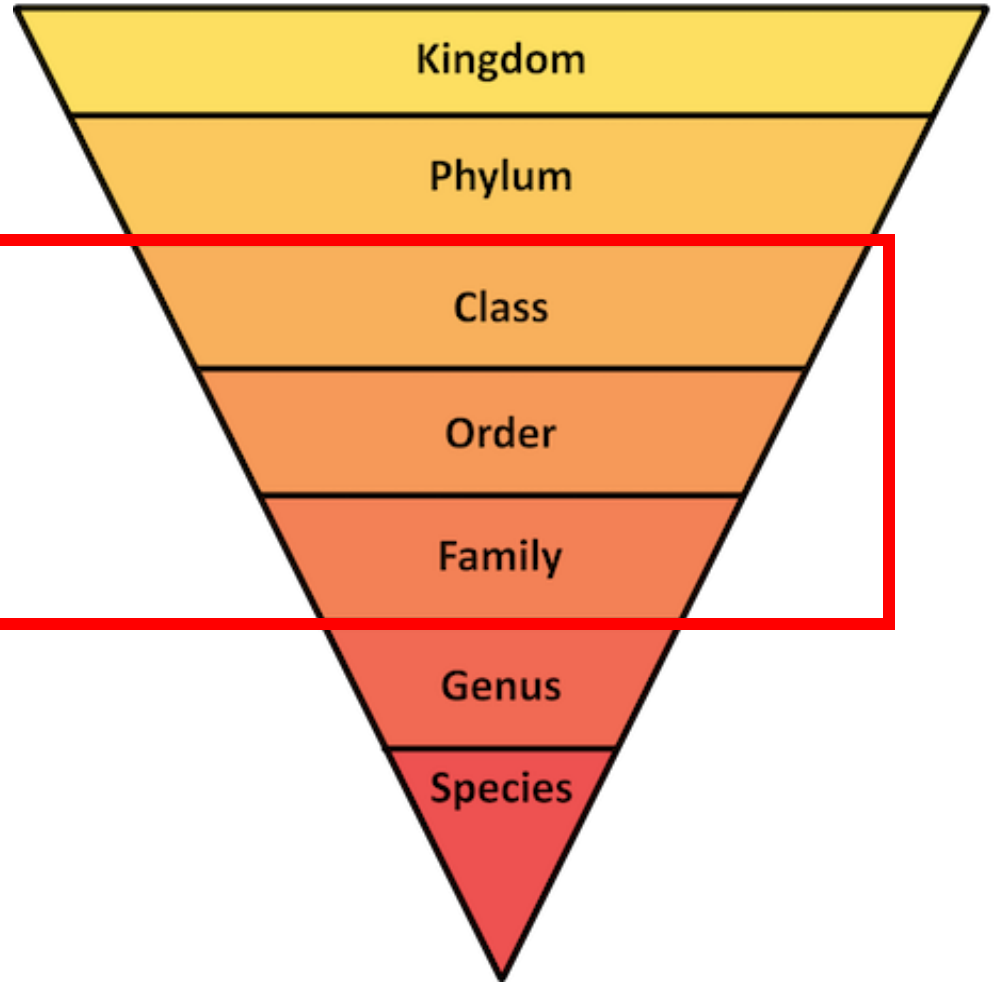

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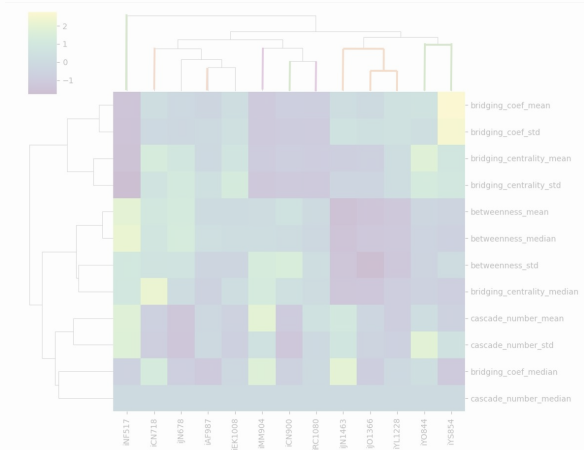
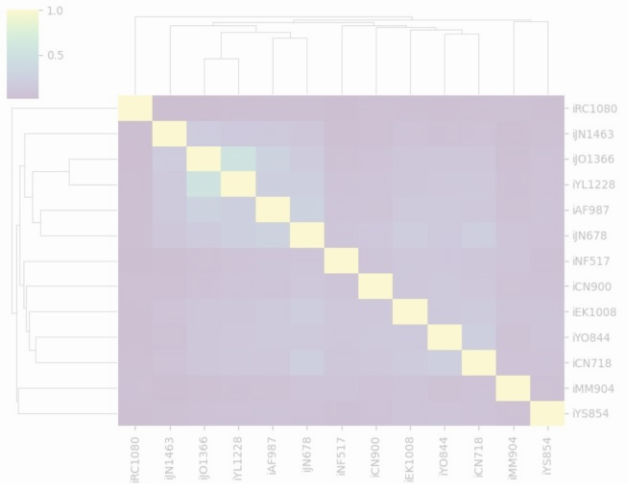
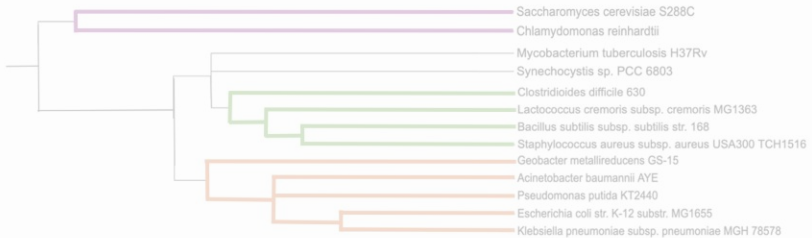
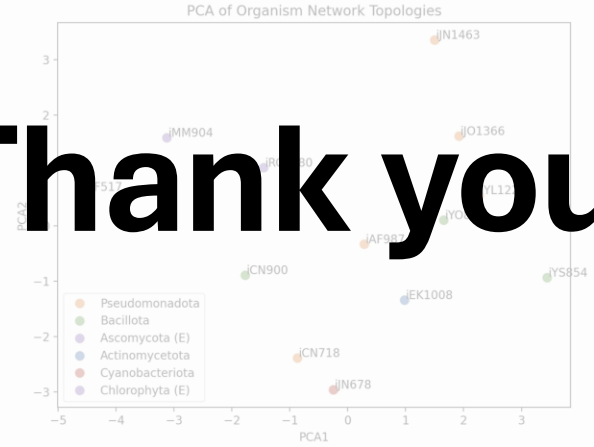
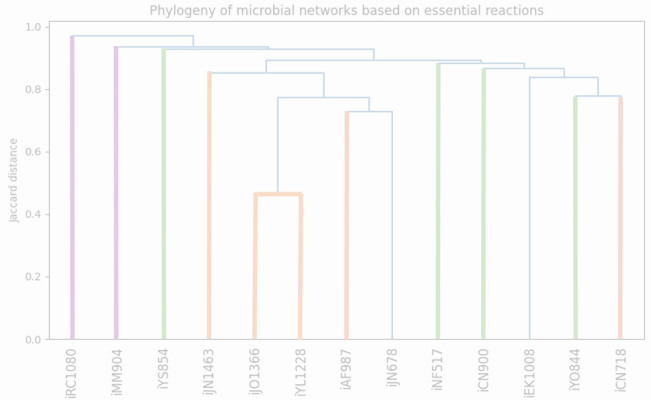


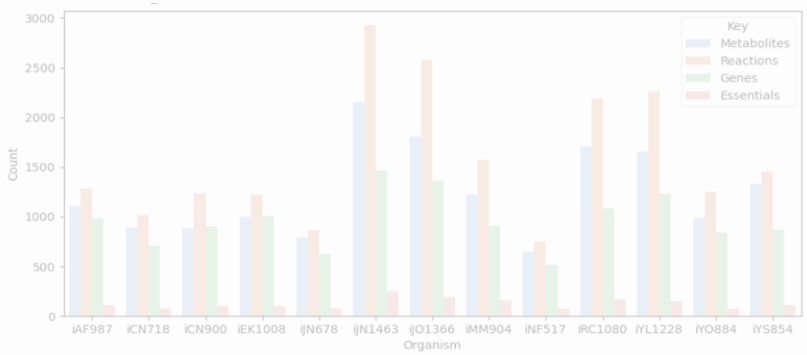


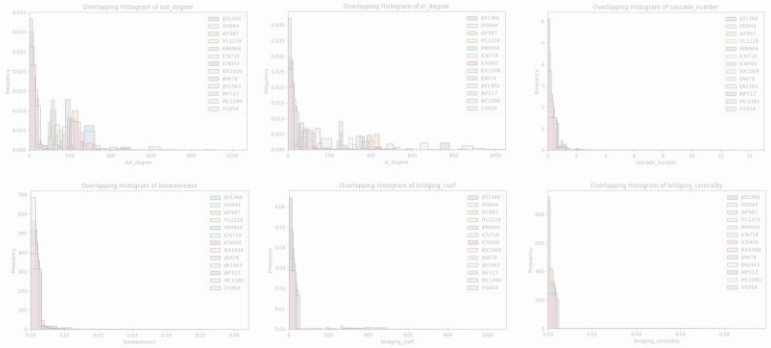


Thank you!









Robinson–Foulds (RF) Distance Ratio

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Triplets Distance (Local)

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GT	14	14
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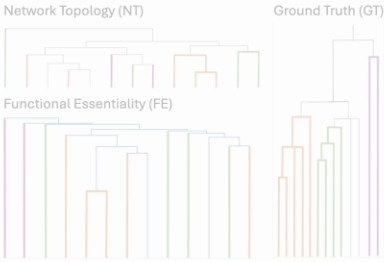


Supplemental Figures

Figure S1 Model Organism Network Counts

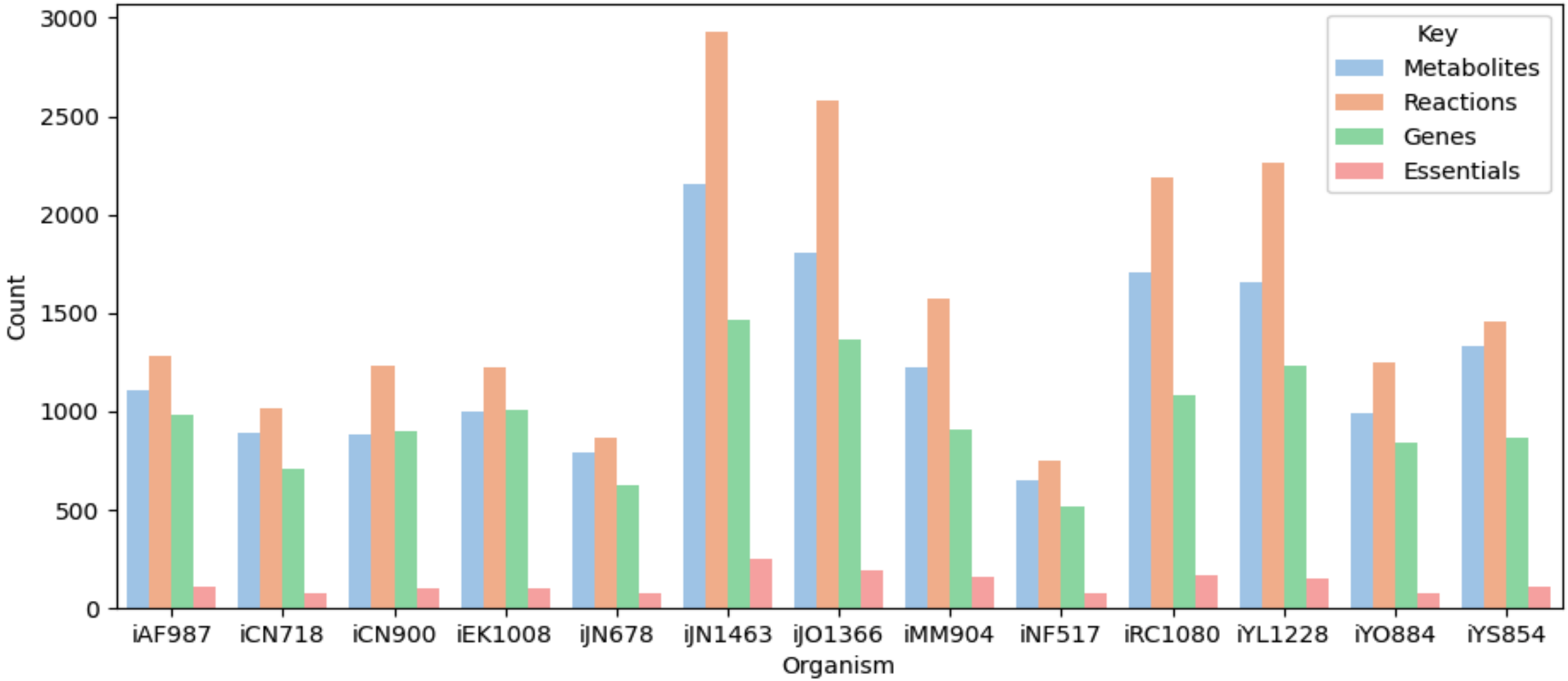


Figure S2

Network Topology PCA

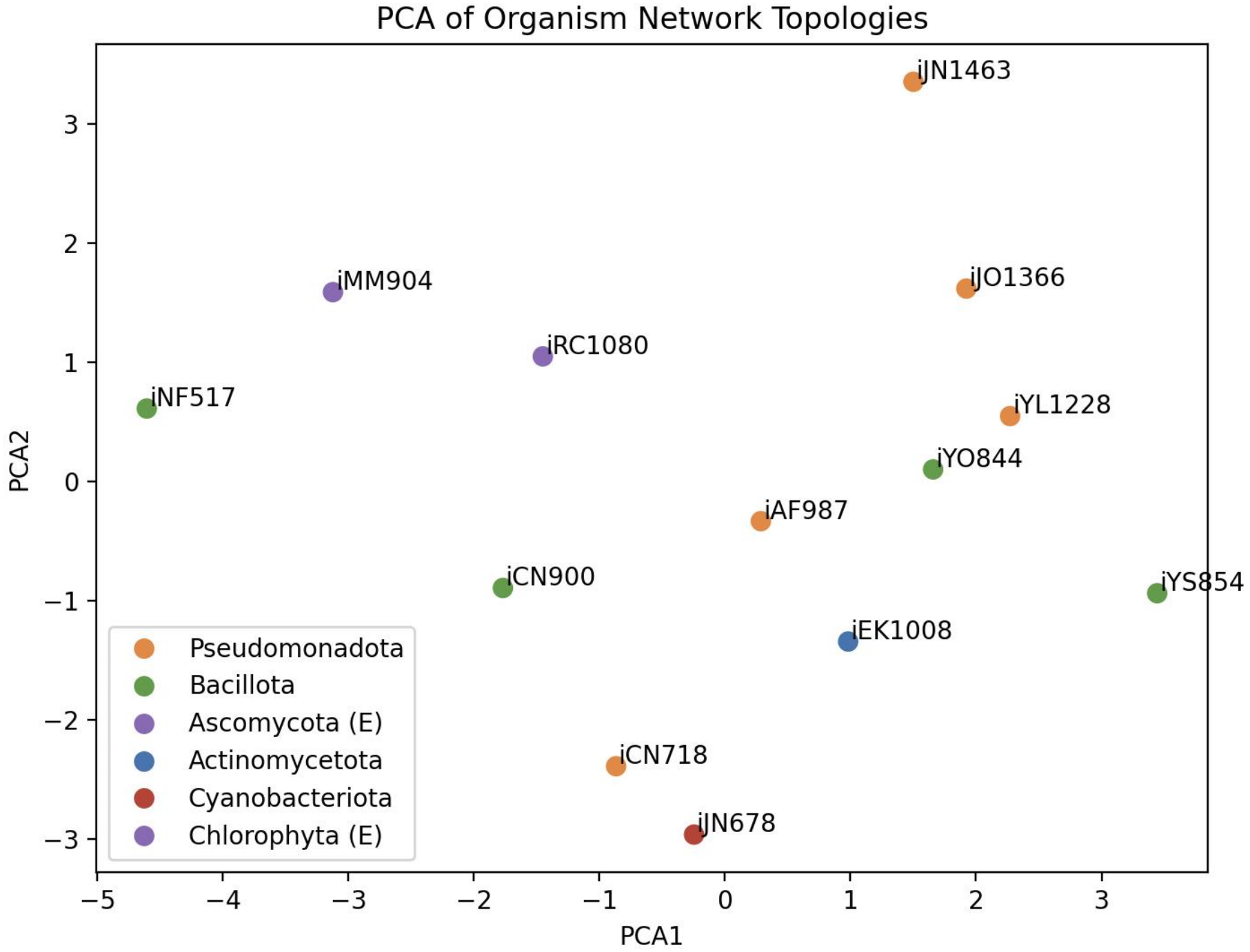
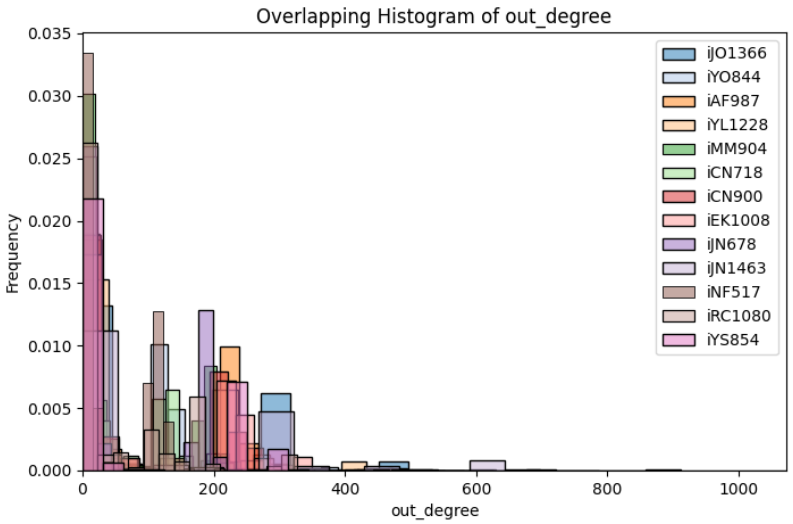
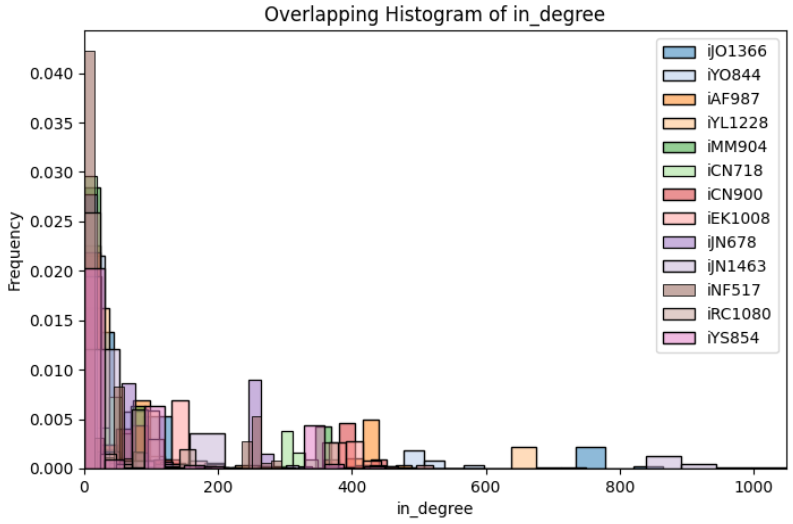
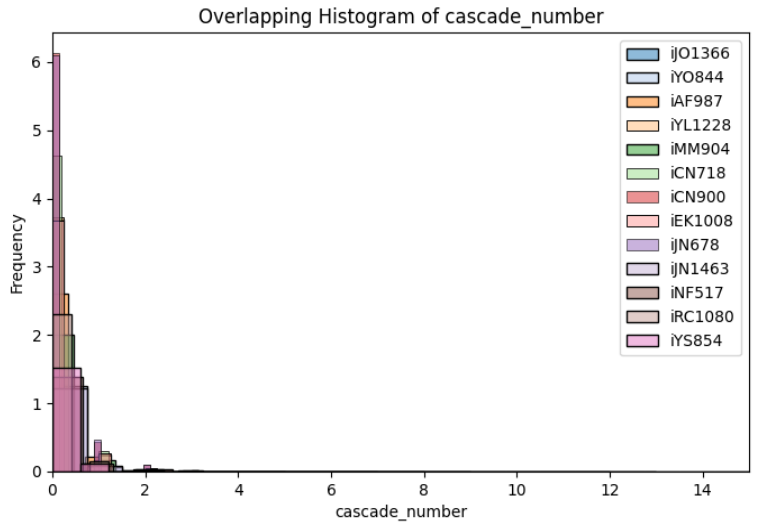
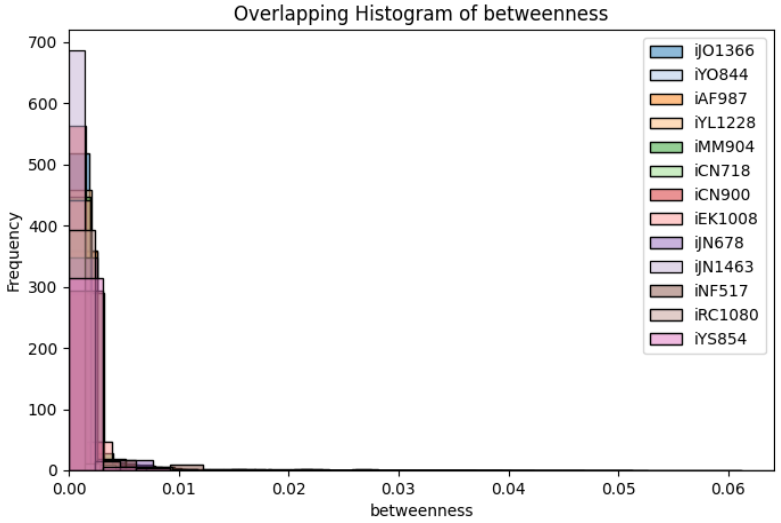


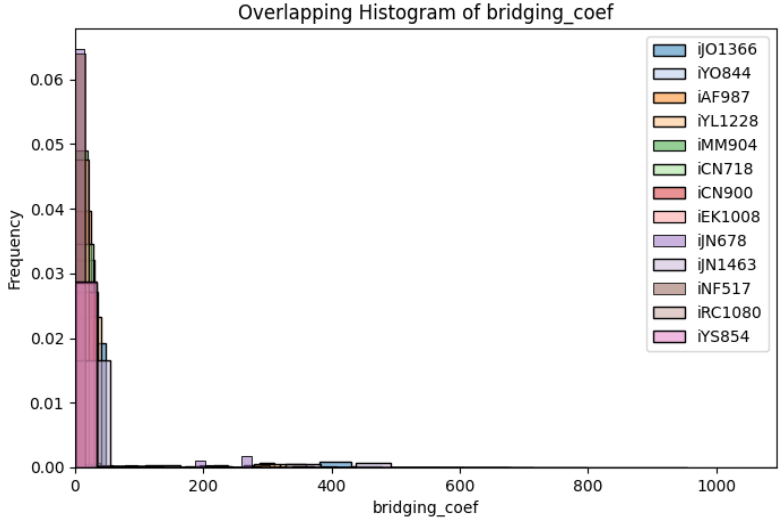
Figure S3 Network Topology Distributions











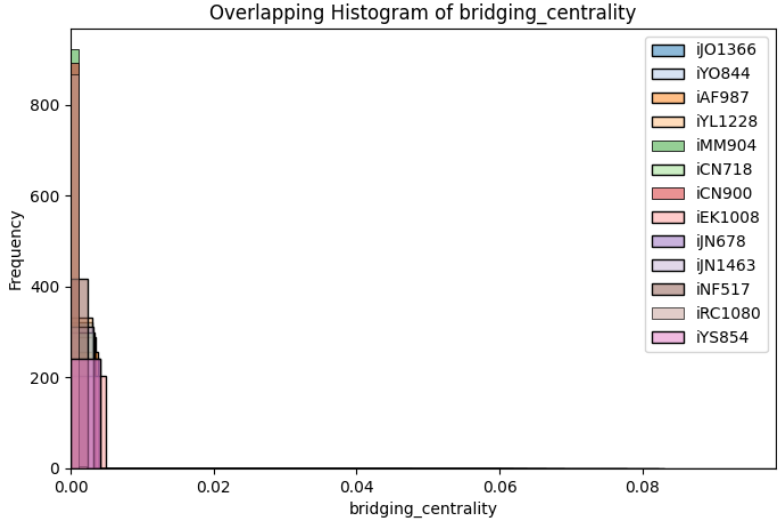
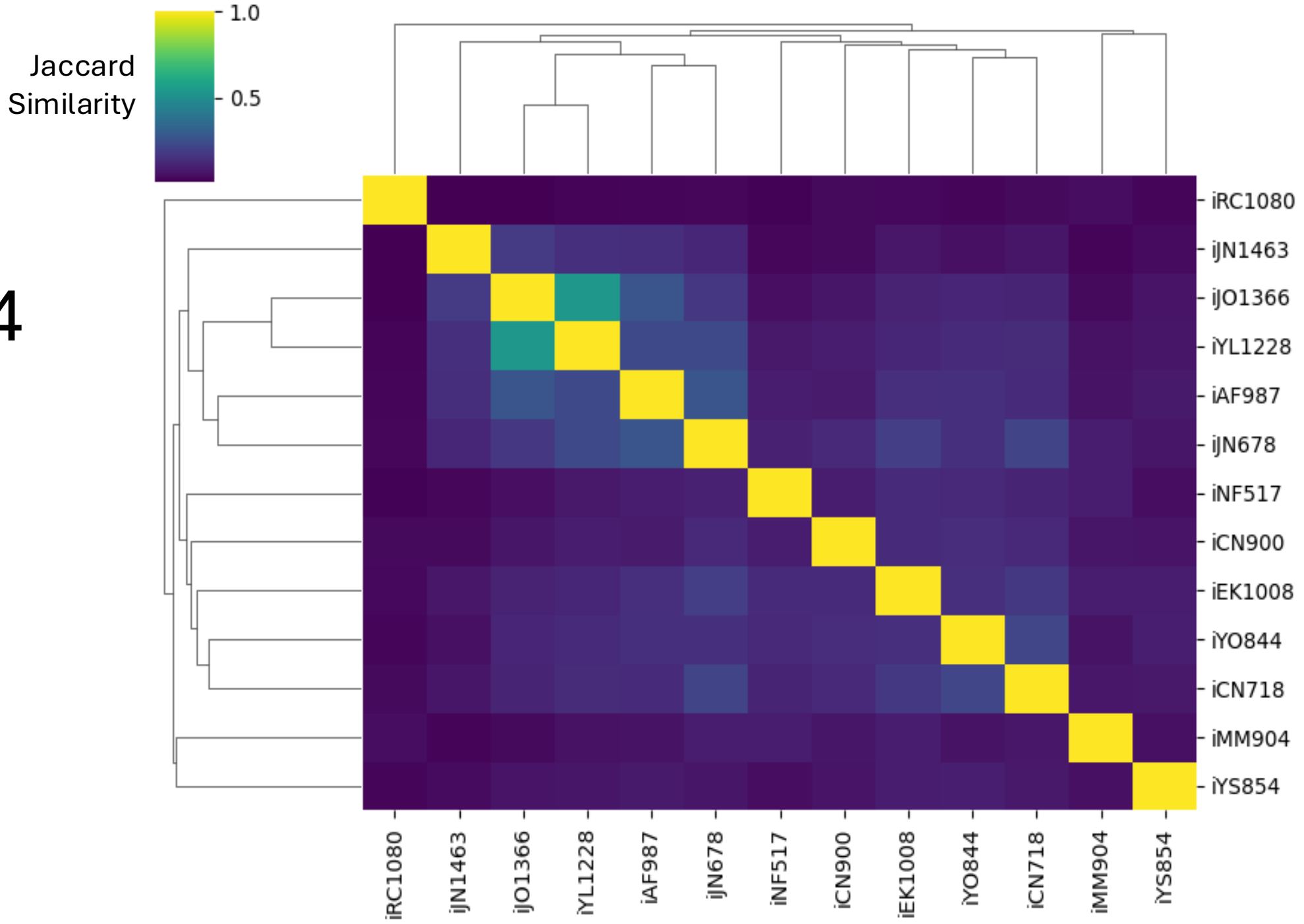


Figure S4

Functional Essentiality Heatmap & Dendrogram