Final project report

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Abstract

The project aimed to study the interaction of metabolic network between multiple species.
The steps to fulfill my goal:

1. Simplify the individual network based on the method in reference paper (Borenstein, Kupiec et al. 2008).
2. Produce a whole network of metabolism including all species (directed)
3. map the network of each species into the whole metabolic network
4. if two species have a lot of edges; for example, if one point to another a lot, one may be benefit to another, so there is an edge pointed to another from one. If one shares a lot of nodes point to them, they may compete for the resource of nodes, there should be a negative edge between them
5. we can get a metabolic relation network of species.
6. build a microbial interaction network using abundance correlation
7. test if metabolic network has some prediction of the structure of microbial interaction network.

Metabolic network

Network has been developed as a common method in microbial ecology nowadays. Metabolic network, which describes how metabolites are utilized and transformed inside or around cells, is the key to interpreting the unique functions and traits of each species.

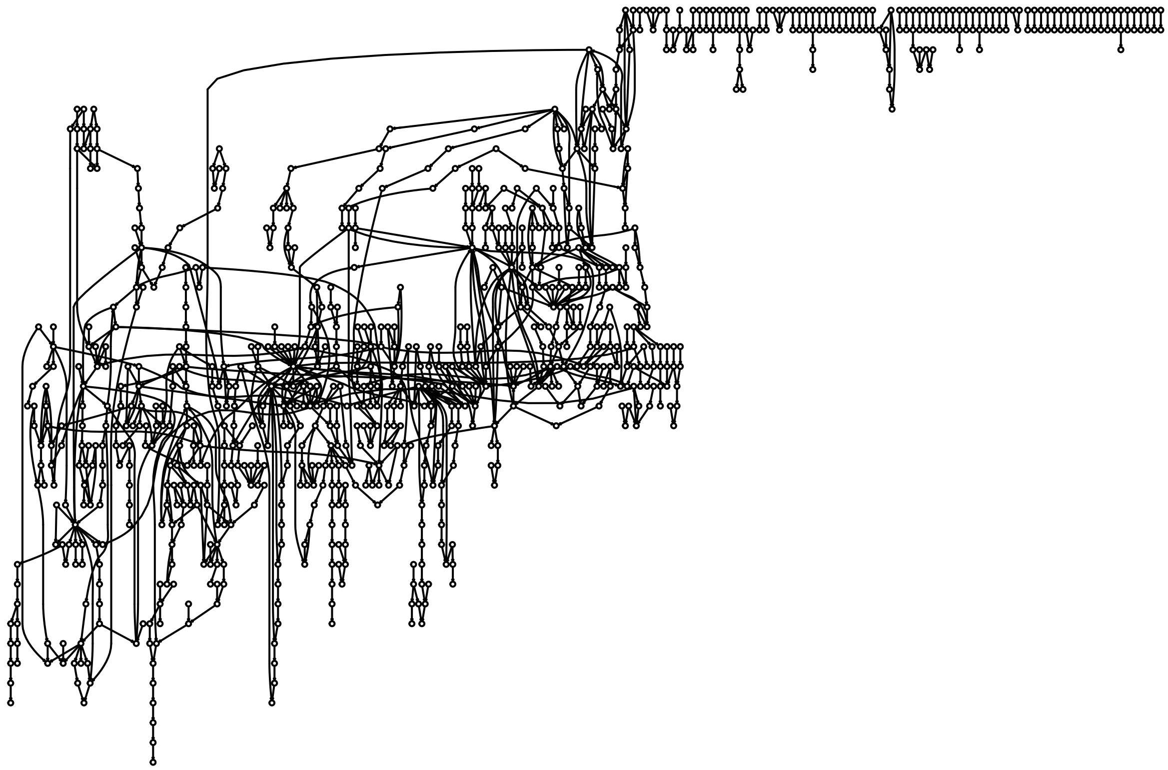


Fig. 1 The whole reaction network of E.coli. Each node is one metabolite. Each edge is a reaction. The graph is directed because reaction has substrates and products.

Get strongly connected components of thw whole network

To simplify the metabolic network, we need find the strongly connected components in metabolic network

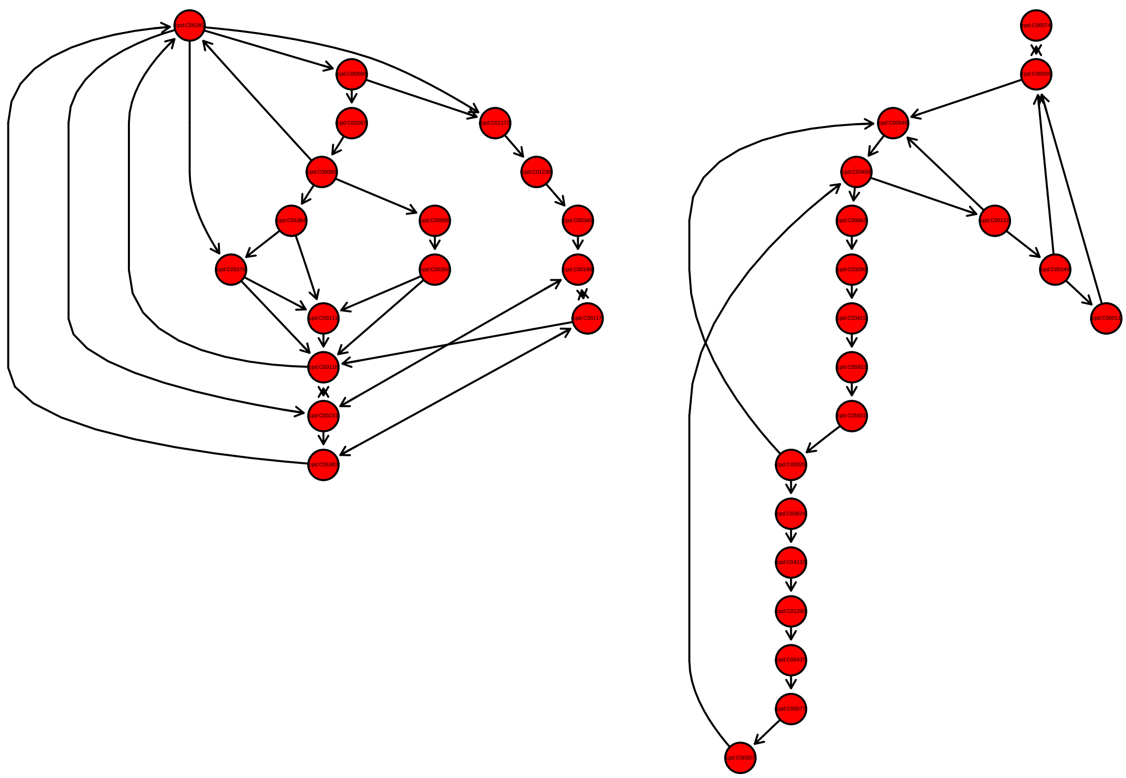
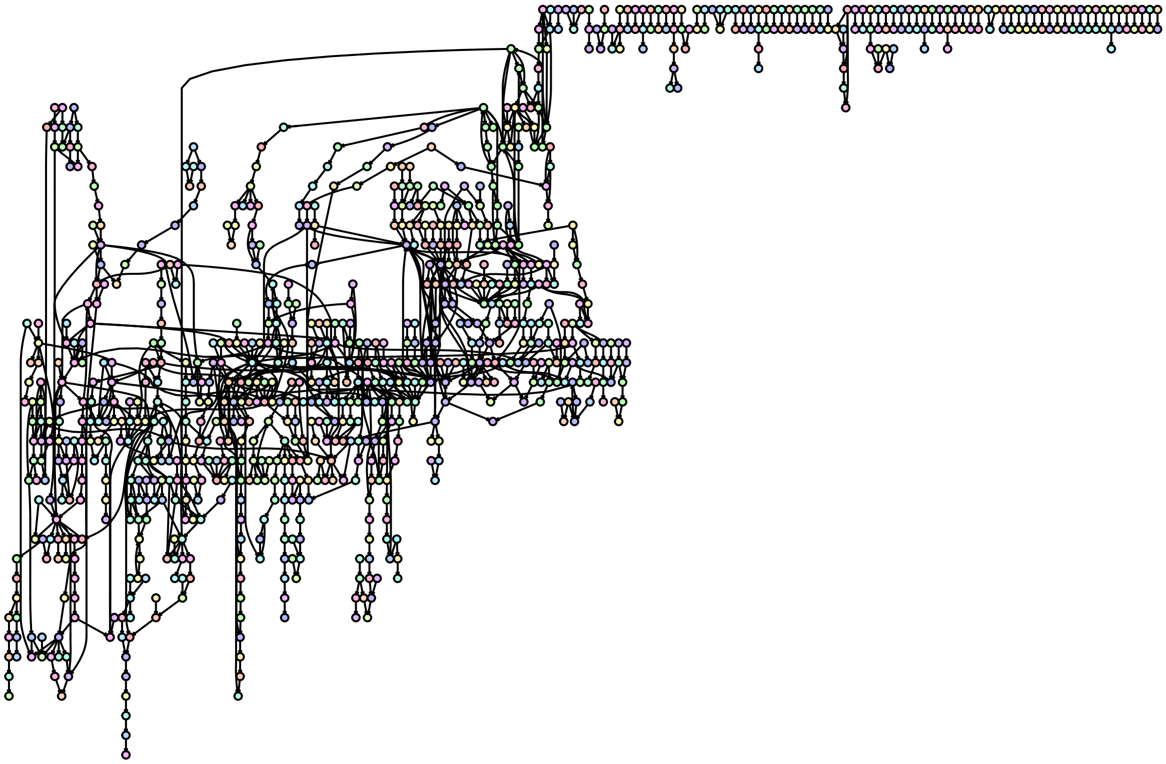


Fig. 2 The first two largest strongly connected components of the reaction network. Each node is one metabolite. Each edge is a reaction. The graph is directed because reaction has substrates and products.

Annotate the strongly connected components in graph

Below showed that the nodes are annotated with different colors for different strongly connected components they belong to.



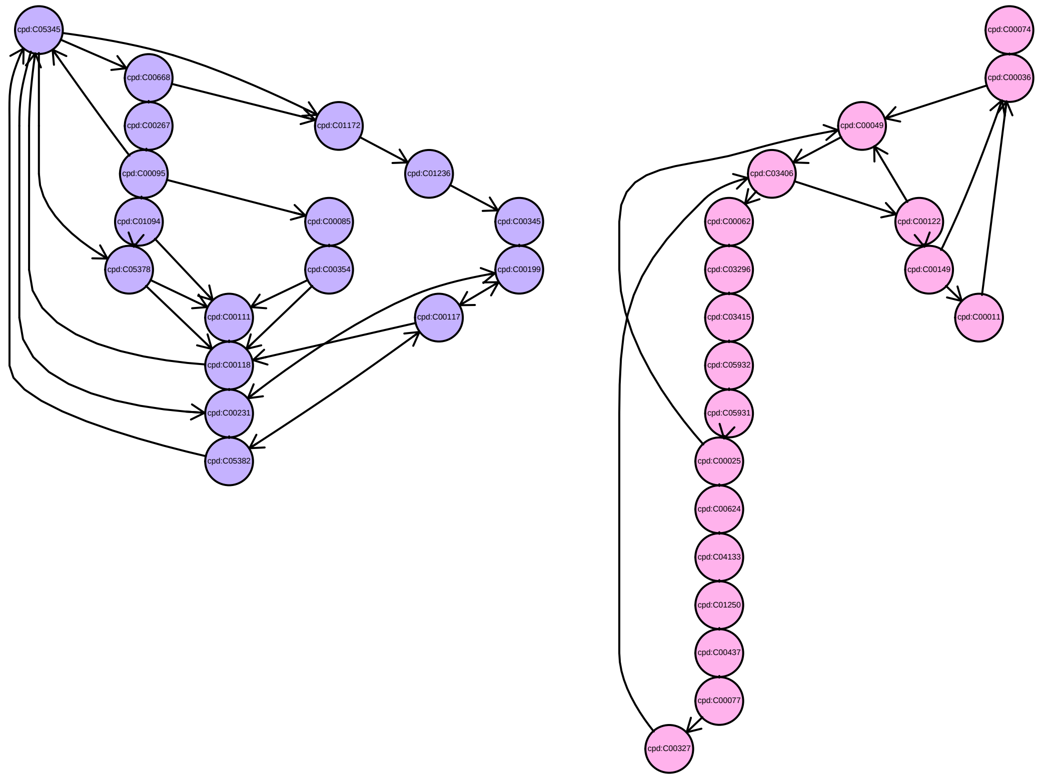


Fig. 3 Nodes of different strongly connected components are attributed with different colors.

Contract several vertices of the same components into a single one

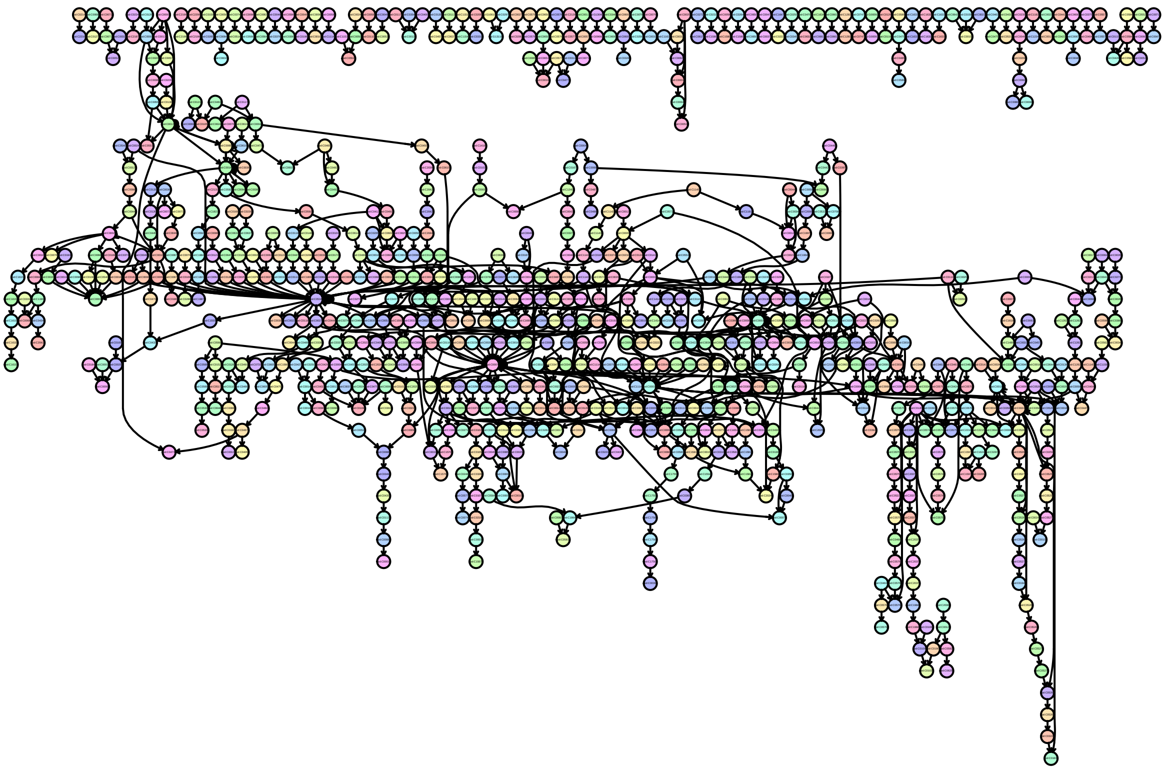


Fig. 4 The contracted reaction network.

We can see the number of nodes is reduced from 924 to 841

Seed set and product set of a metabolic network

Next, I want to determine what nutrients should be obtained by microbes to produce other compounds. In the network, they are the nodes which only have outdegree, which means these compounds can only be taken up from environment.These nodes are defined as seed set here. While the remaining nodes with indegree are the compounds which can be produced by the seed set.These nodes are defined as product sets.

seed set of metabolic network of E.Coli

```
##   [1] "cpd:C02147" "cpd:C00685" "cpd:C06714" "cpd:C02247" "cpd:C03319"
##   [6] "cpd:C05847" "cpd:C21994" "cpd:C22068" "cpd:C00173" "cpd:C00423"
##  [11] "cpd:C00127" "cpd:C01594" "cpd:C00561" "cpd:C03742" "cpd:C20396"
##  [16] "cpd:C00986" "cpd:C00296" "cpd:C00632" "cpd:C11457" "cpd:C05629"
##  [21] "cpd:C12621" "cpd:C05607" "cpd:C02265" "cpd:C00582" "cpd:C05332"
##  [26] "cpd:C00483" "cpd:C03964" "cpd:C05998" "cpd:C00793" "cpd:C00491"
##  [31] "cpd:C01888" "cpd:C00740" "cpd:C00940" "cpd:C02362" "cpd:C02376"
##  [36] "cpd:C02354" "cpd:C02355" "cpd:C02067" "cpd:C20254" "cpd:C00881"
##  [41] "cpd:C02353" "cpd:C06194" "cpd:C01260" "cpd:C00700" "cpd:C00081"
##  [46] "cpd:C00301" "cpd:C00580" "cpd:C11142" "cpd:C00288" "cpd:C01417"
##  [51] "cpd:C11537" "cpd:C00565" "cpd:C14180" "cpd:C00672" "cpd:C00121"
##  [56] "cpd:C00620" "cpd:C00490" "cpd:C00497" "cpd:C01412" "cpd:C00583"
```

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##  [61] "cpd:C04593" "cpd:C02225" "cpd:C01127" "cpd:C00898" "cpd:C01380"
##  [66] "cpd:C03451" "cpd:C00937" "cpd:C01177" "cpd:C01204" "cpd:C00270"
##  [71] "cpd:C00963" "cpd:C00879" "cpd:C01132" "cpd:C02262" "cpd:C05402"
##  [76] "cpd:C05404" "cpd:C00492" "cpd:C00618" "cpd:C11516" "cpd:C00794"
##  [81] "cpd:C01487" "cpd:C00392" "cpd:C01019" "cpd:C00507" "cpd:C01934"
##  [86] "cpd:C00502" "cpd:C00312" "cpd:C04053" "cpd:C02059" "cpd:C00828"
##  [91] "cpd:C15930" "gl:G10610"  "cpd:C02970" "cpd:C00272" "cpd:C01007"
##  [96] "cpd:C05791" "cpd:C00853" "cpd:C05766" "cpd:C21284" "cpd:C01935"
## [101] "cpd:C01898" "cpd:C16241" "cpd:C05980" "cpd:C02356" "cpd:C00461"
## [106] "cpd:C15532" "cpd:C00800" "cpd:C05841" "cpd:C03150" "cpd:C15811"
## [111] "cpd:C15810" "cpd:C20247" "cpd:C04294" "cpd:C01279" "cpd:C00378"
## [116] "cpd:C00068" "cpd:C00189" "cpd:C00989" "cpd:C16675" "cpd:C20386"
## [121] "cpd:C00072" "cpd:C00114" "cpd:C00880" "cpd:C01697" "cpd:C01013"
## [126] "cpd:C02612" "cpd:C01847" "cpd:C00053" "cpd:C00818" "cpd:C00243"
## [131] "gl:G13040"  "cpd:C03460" "cpd:C06001" "cpd:C00184" "cpd:C00791"
## [136] "cpd:C00198" "cpd:C06473" "cpd:C00469" "cpd:C02282" "cpd:C00798"
## [141] "cpd:C03089" "cpd:C03546" "cpd:C05730" "cpd:C21028" "cpd:C11638"
## [146] "cpd:C07335" "cpd:C02723" "cpd:C02325" "cpd:C00590" "cpd:C02646"
## [151] "cpd:C02730" "cpd:C03114" "cpd:C05775" "cpd:C06508" "cpd:C06505"
## [156] "cpd:C00430" "cpd:C00473" "cpd:C03479" "cpd:C00568" "cpd:C01063"
## [161] "cpd:C00250" "cpd:C00016" "cpd:C16476" "cpd:C02501" "cpd:C04706"
## [166] "cpd:C16348" "cpd:C06613" "cpd:C12835" "cpd:C07478" "gl:G00092"
## [171] "cpd:C01290" "cpd:C05892" "cpd:C01212" "cpd:C06397" "cpd:C06251"
## [176] "cpd:C04121" "cpd:C04652" "cpd:C00448" "cpd:C16339" "cpd:C16335"
## [181] "cpd:C16331" "cpd:C06427" "cpd:C01595" "cpd:C00219" "cpd:C04635"
## [186] "cpd:C04317" "cpd:C00641" "cpd:C00350" "cpd:C00093" "cpd:C00245"
## [191] "cpd:C05688" "cpd:C00295" "cpd:C02350" "cpd:C11821" "cpd:C00002"
## [196] "cpd:C03090" "cpd:C00059" "cpd:C11453" "cpd:C00249" "cpd:C03939"
## [201] "cpd:C04618" "cpd:C04620" "cpd:C04619" "cpd:C01209" "cpd:C04633"
## [206] "cpd:C05261" "cpd:C04405" "cpd:C00233" "cpd:C04411" "cpd:C02504"
## [211] "cpd:C04272" "cpd:C06010" "cpd:C06007" "cpd:C01165" "cpd:C03758"
## [216] "cpd:C05577" "cpd:C00082" "cpd:C01267" "cpd:C01157" "cpd:C05946"
## [221] "cpd:C00322" "cpd:C04462" "cpd:C00047" "cpd:C05527" "cpd:C00979"
## [226] "cpd:C00021" "cpd:C01077" "cpd:C05519" "cpd:C01242" "cpd:C01005"
## [231] "cpd:C00152" "cpd:C00246" "cpd:C01213" "cpd:C00163" "cpd:C05668"
## [236] "cpd:C00988" "cpd:C00168" "cpd:C04006" "cpd:C00096" "cpd:C00159"
## [241] "cpd:C04631" "cpd:C01170" "cpd:C02352" "cpd:C00369" "cpd:C00714"
## [246] "cpd:C00333" "cpd:C03033" "cpd:C00259" "cpd:C01101"
```

There are 249 strongly connected components as the seed set.The ID are the KEGG accession numbers. The compounds in the strongly connected components are named by one of the nodes.

Product set

Then the remained (841-249)=591 components belong to product set

Plot the seed set and product set in graph

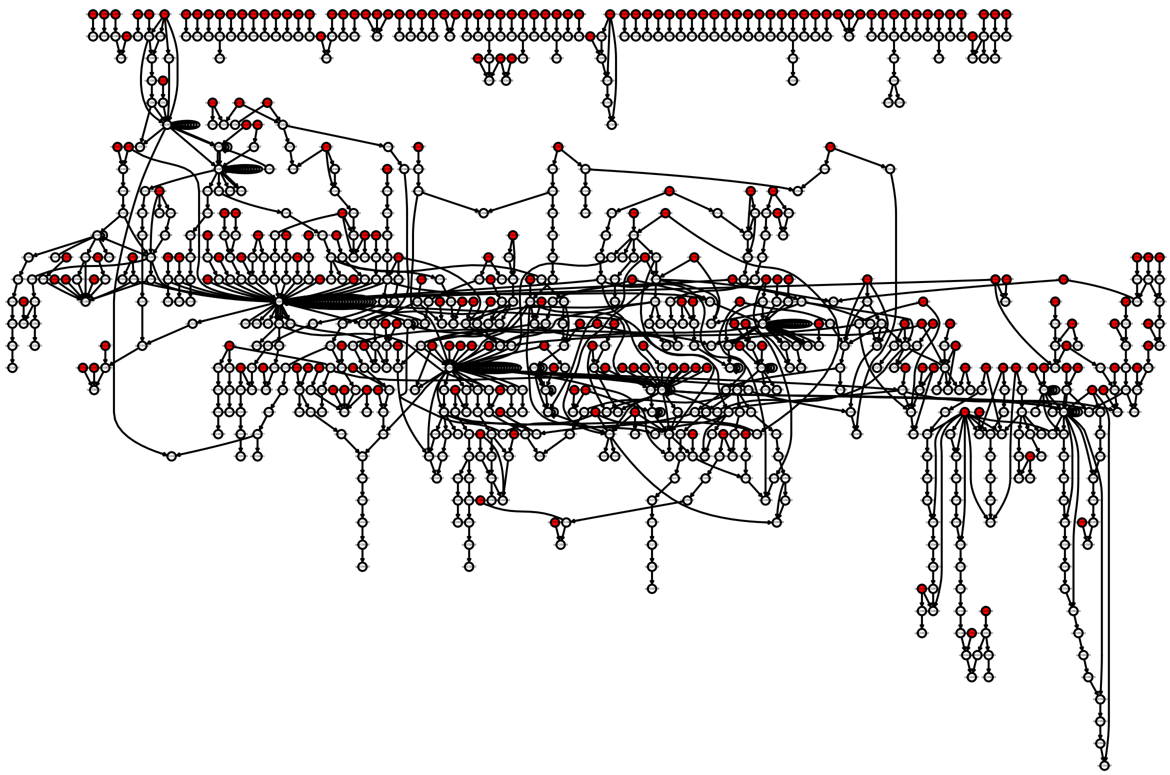


Fig. 5 The network colored by seed set (red) and product set(white).

Metabolic competition and complementarity

Using the seed set and product set, we can define metabolic competition and complementarity indexes. The metabolic competition index represents the similarity in two species' nutritional profiles. It is calculated as the fraction of compounds of query species X's seed set that are also present in the seed set of a target Y. The metabolic complementarity index is calculated as the fraction of seed compounds of a query species X that are producible by the metabolic network of a target Y but are not a part of Y's seed set.

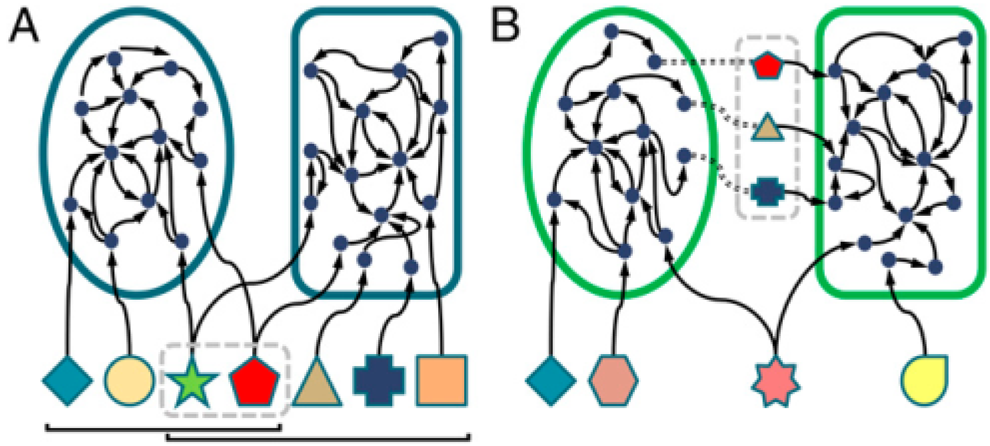


Fig. 6 The big circle and rectangle represents metabolic network while small icons represent metabolites which are also the nodes in network. The edges represent the pathway. The A graph shows the competition for food (the green and red icons), while B graph shows complementarity because the left cell provides some metabolites to right cell.

- It should be noted that this interaction is not symmetric. For example, A may compete with B because 90% of seed set of A is shared by B. However, B may only share 50% of seed set with A, so B would not competed with A.

Here, I will use two microbial species: E.Coli and Streptomyces coelicolor as a example and calculate the two indexes for their metabolic network.

I have shown the network for E.Coli. So I will show the graph of Streptomyces coelicolor.

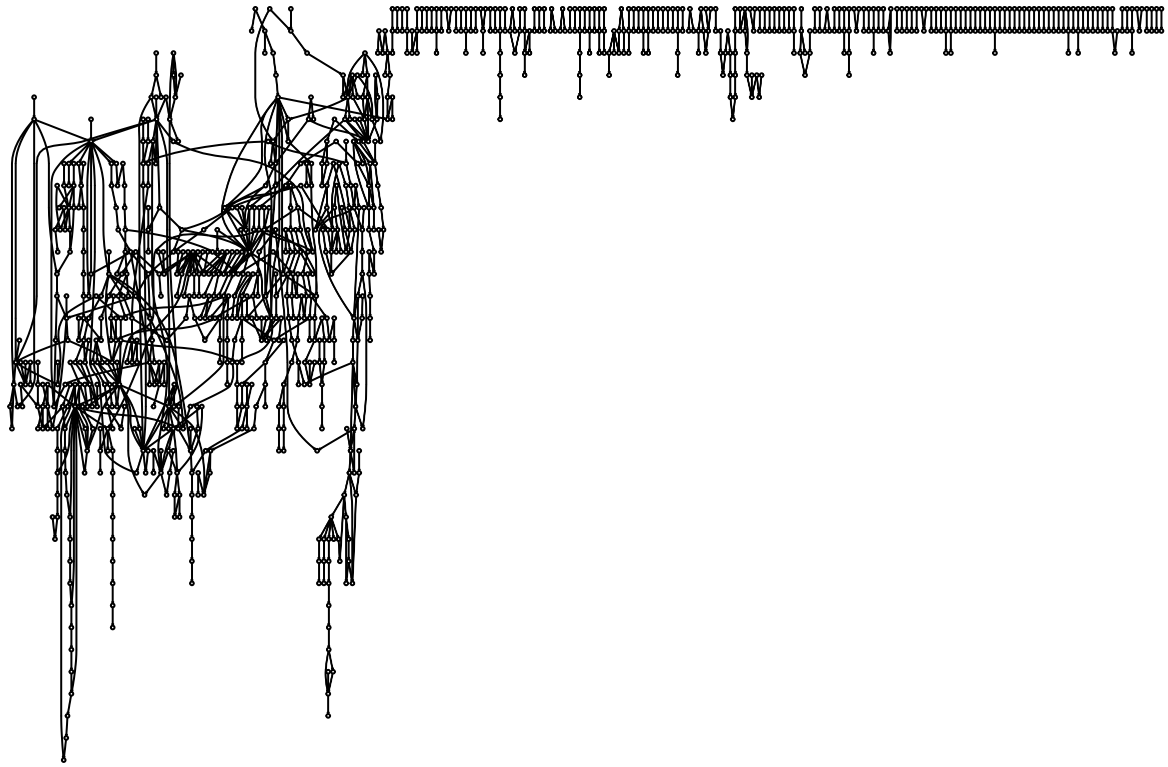


Fig. 7 The metabolic network of Streptomyces coelicolor.

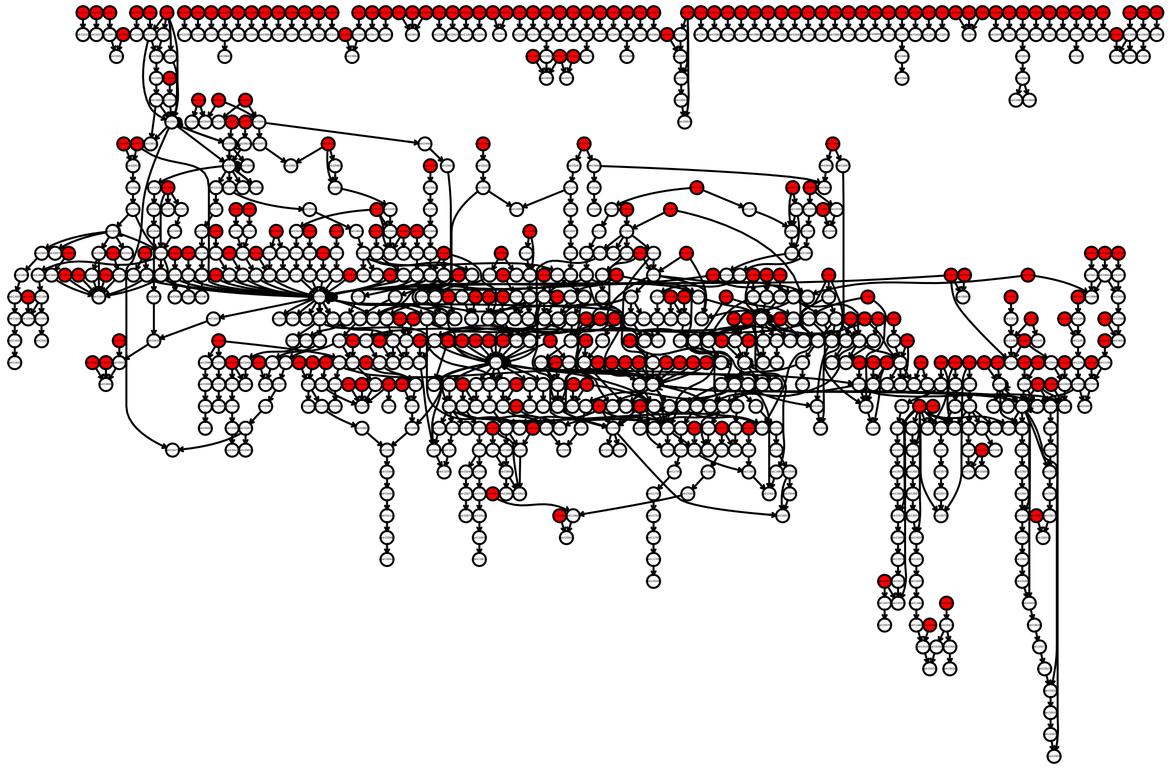
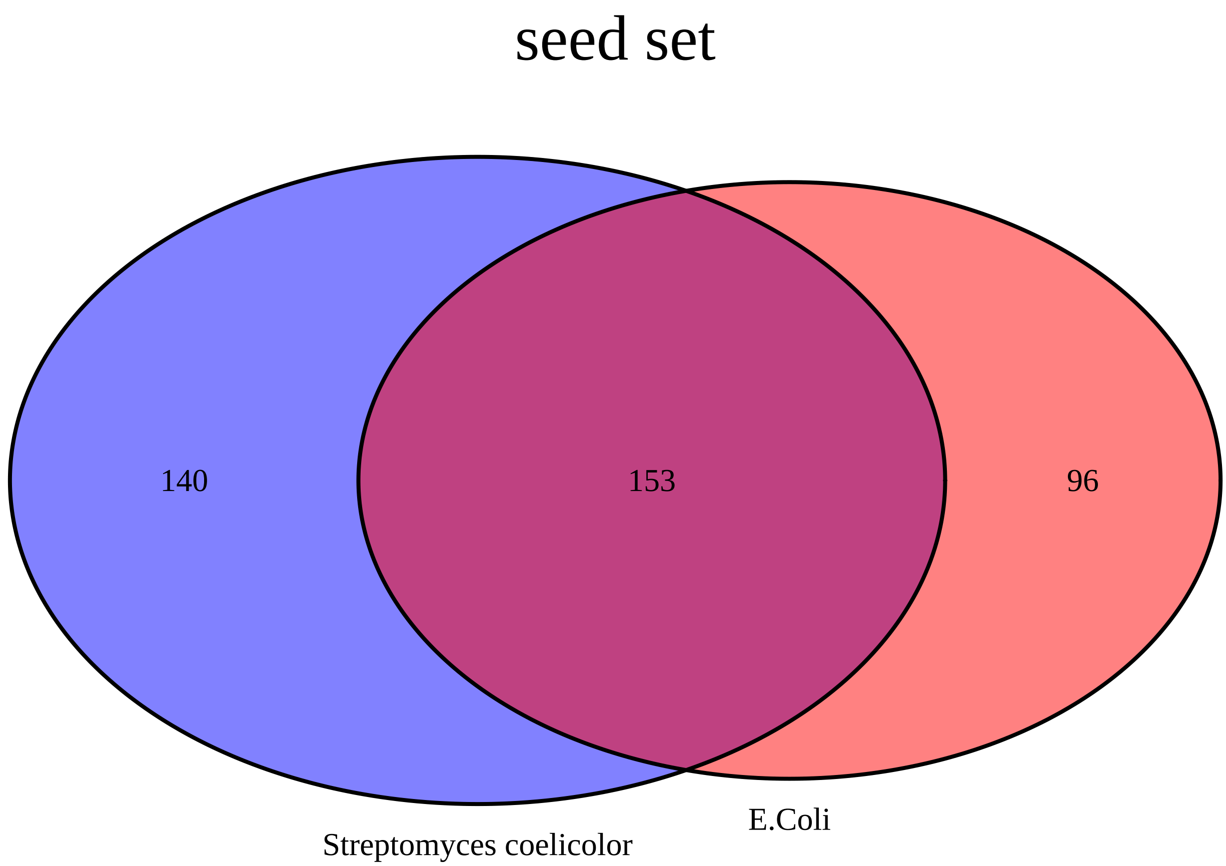


Fig. 8 The network colored by seed set (red) and product set(white) of Streptomyces coelicolor.

The competition index

So we need to see the shared red nodes (i.e. seed set) of two species.

The shared seed set

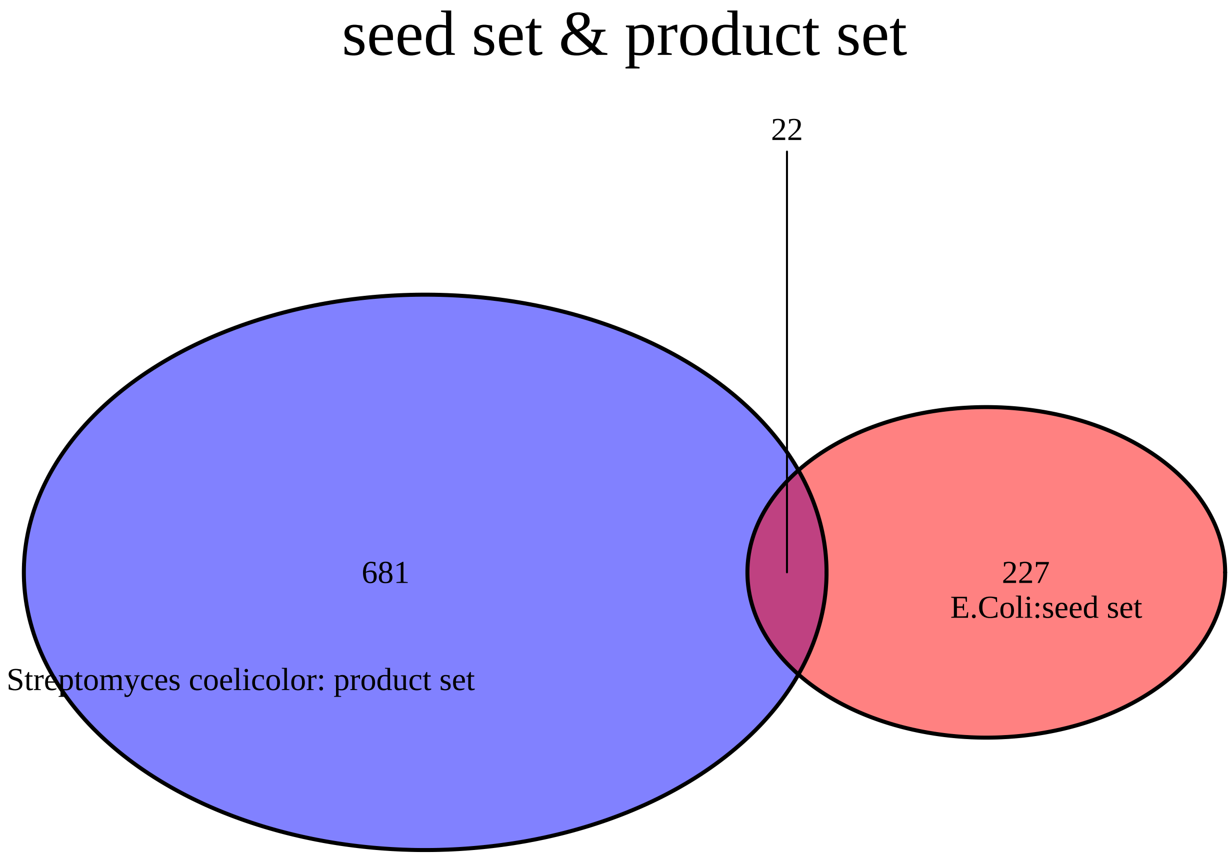


So the competition index for E. coli -> Streptomyces is $153/(96 + 153) = 0.6144578$ while the index for Streptomyces -> E.Coli is $140/(140 + 153) = 0.4778157$. There values represent how many types of nutrition they may need in common.

The complementarity index

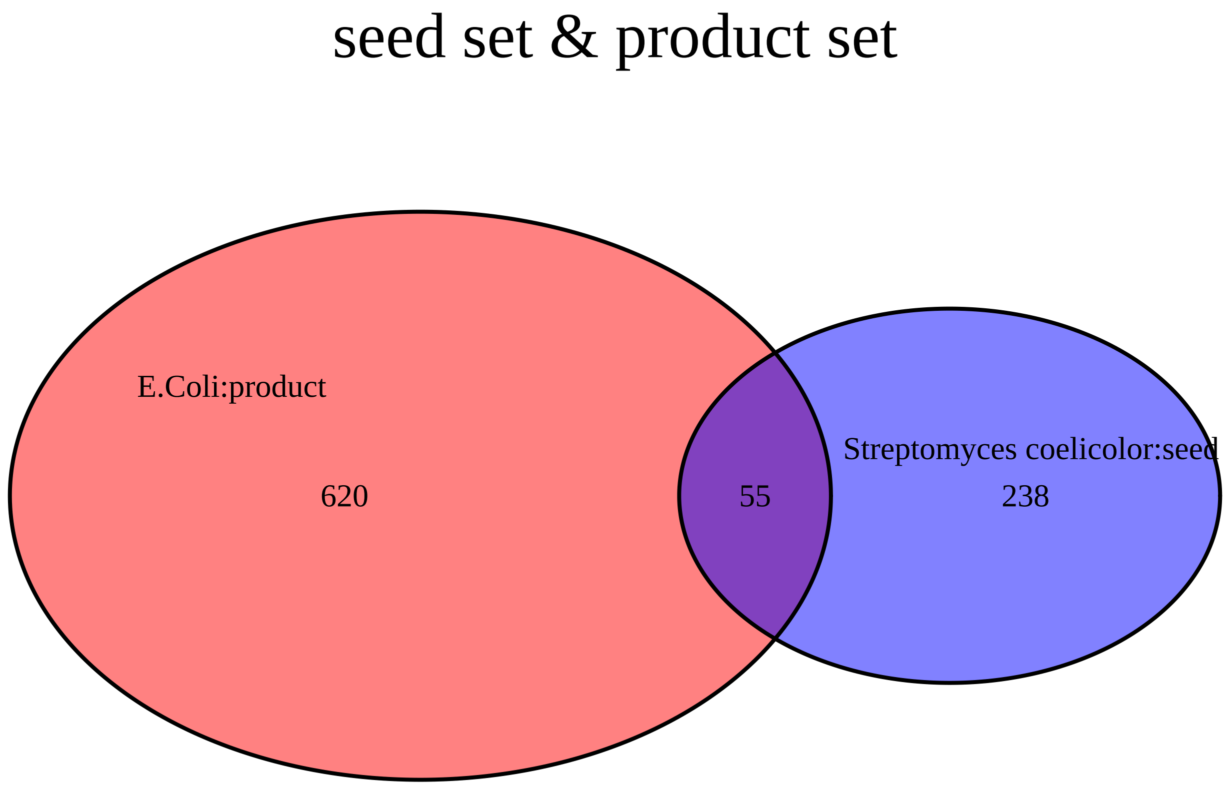
There are two directions, too. 1. The product of streptomyces could be used as seed set of E.Coli; 2.The product of E.Coli could be used as seed set of Streptomyces.

shared seed set of E.Coli and product set of Streptomyces



So the complementarity index for Streptomyces -> E.Coli is $22/(22 + 227) = 0.0883534$,, which means 0.0883534 of nutrition requirement of E.Coli could be provided by products of Streptomyces.

shared seed set of Streptomyces and product set of E.Coli



So the complementarity index for E.Coli -> Streptomyces is $55/(55+238) = 0.1877133$, which means 0.1877133 of nutrition requirement of Streptomyces could be provided by products of E.Coli.

So the next step, I will include more species to build a competion network and a complementary network based on the two indexes.