

Today's Lecture

- Introduction to microbial communities and microbiome studies
- Simple microbial community metabolism design
- (Integer) linear programming
- Set cover (minimal set of species)
- Network flow (provide sufficient metabolic reactions)

Microbial communities influence their environments in a variety of ways

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Nitrification



Microbial communities influence their environments in a variety of ways

Nitrification



Cocoa Fermentation



Microbial communities influence their environments in a variety of ways

Nitrification



Cocoa Fermentation



Sewage Treatment



Microbial communities influence their environments in a variety of ways

Nitrification



Cocoa Fermentation



Sewage Treatment



Gut Metabolism



Microbiome studies often examine two major facets of a community



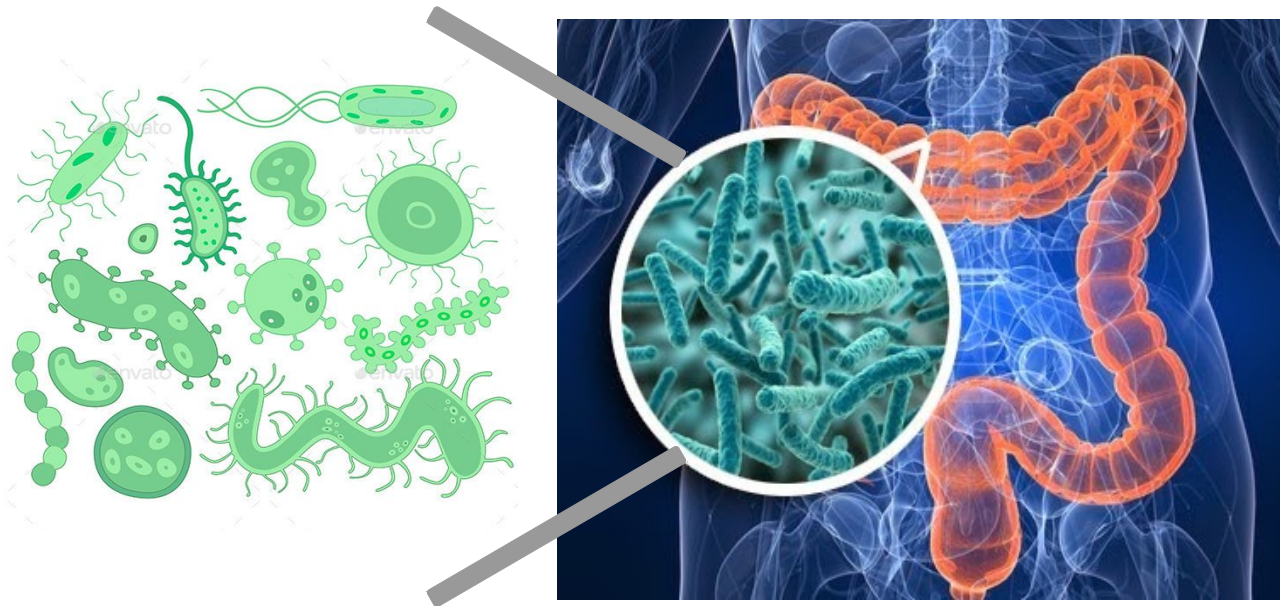
Microbiome studies often examine two major facets of a community

Ecology



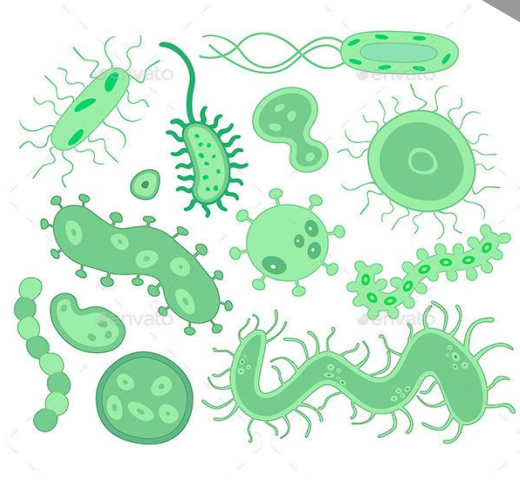
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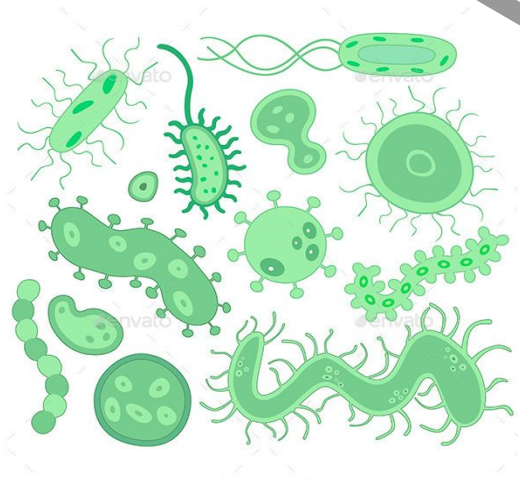


Metagenome

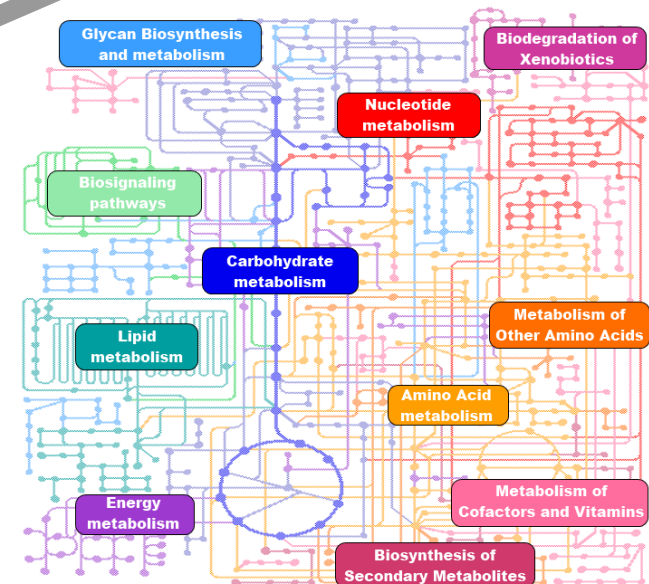


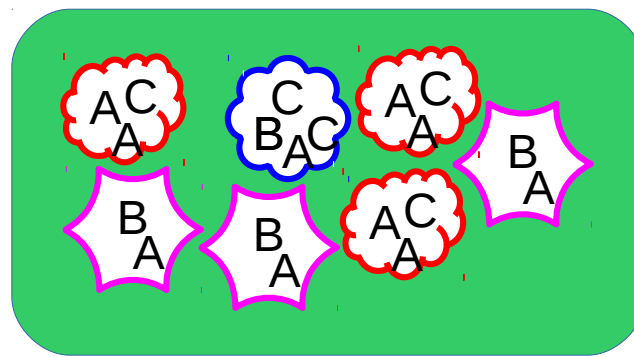
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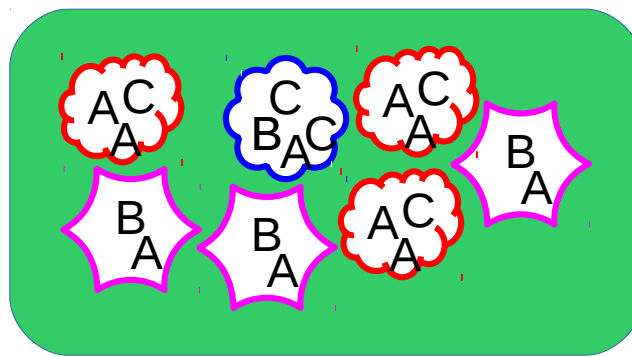


Metagenome

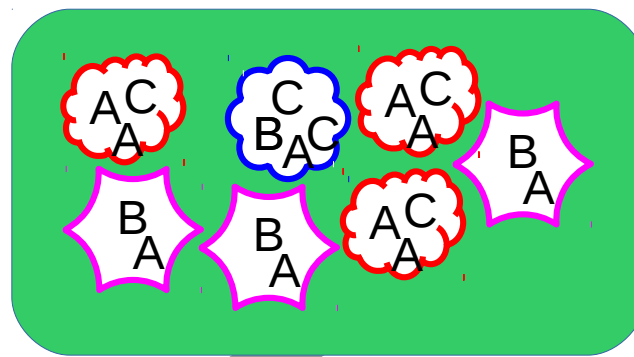




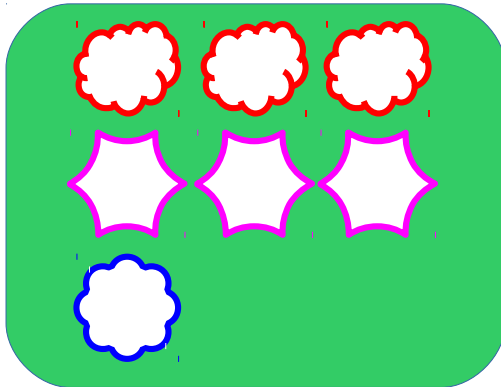
16S rRNA sequencing



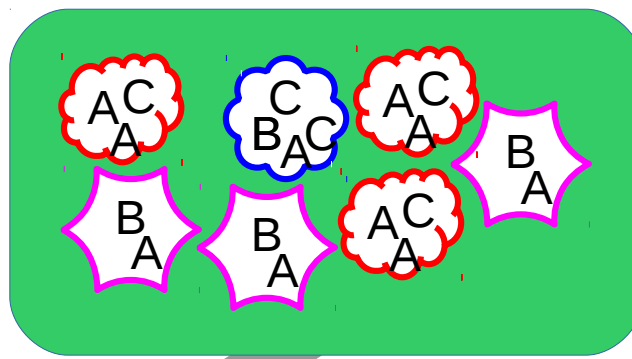
16S rRNA
sequencing



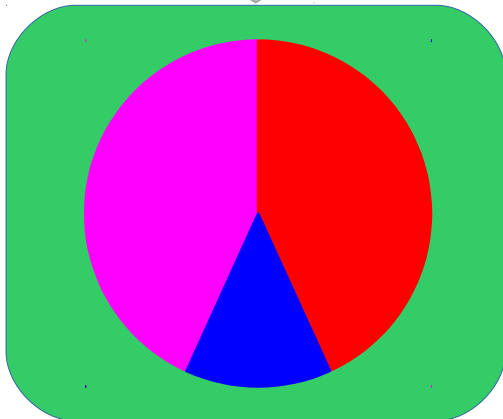
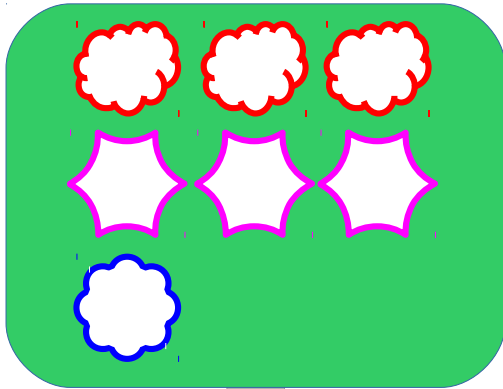
Taxonomic composition



16S rRNA
sequencing



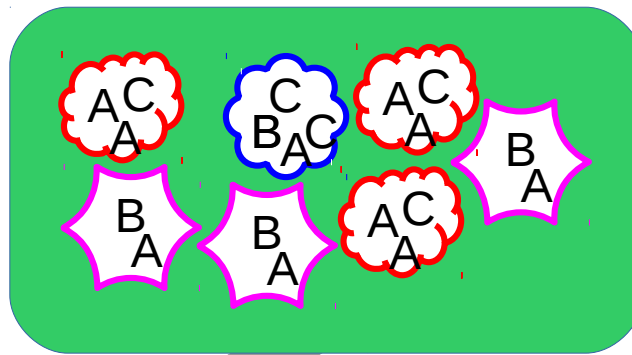
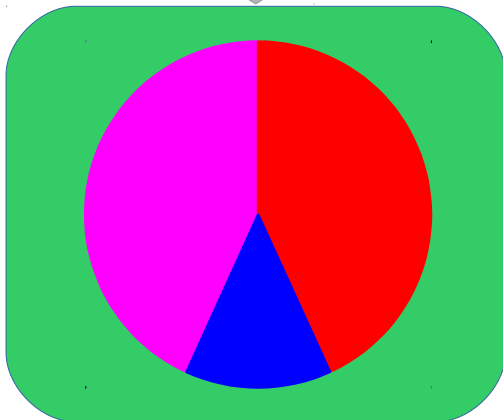
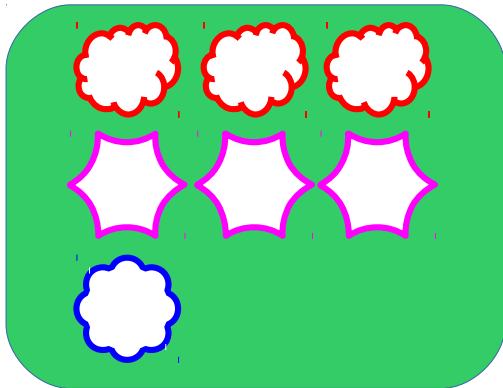
Taxonomic composition



16S rRNA
sequencing

Whole metagenome
shotgun sequencing

Taxonomic composition

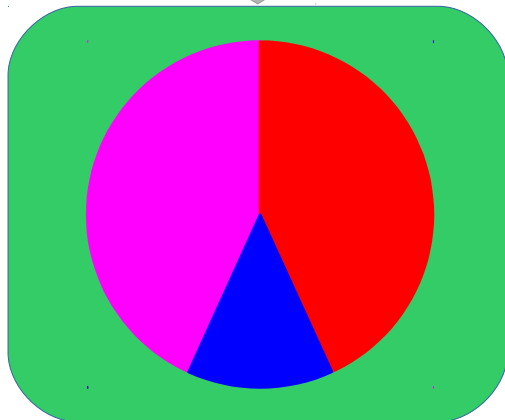
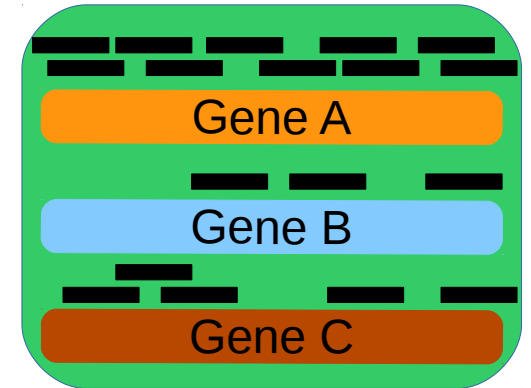
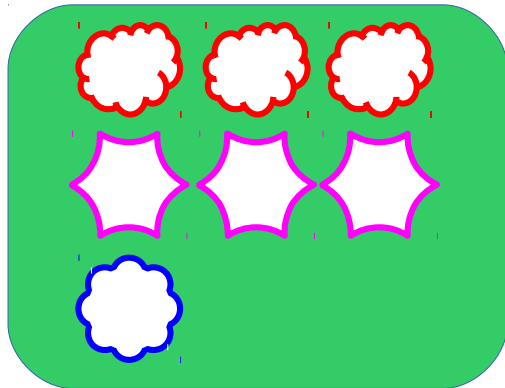
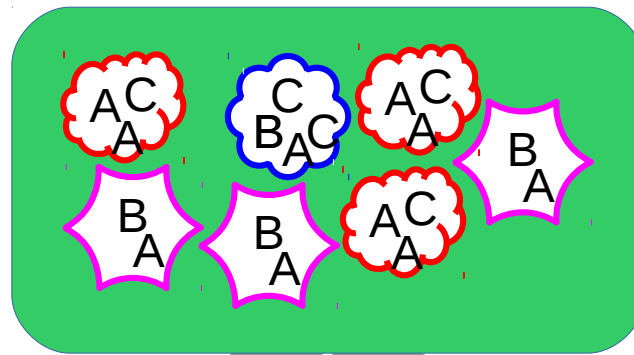


16S rRNA
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Whole metagenome
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Taxonomic composition

Functional profile

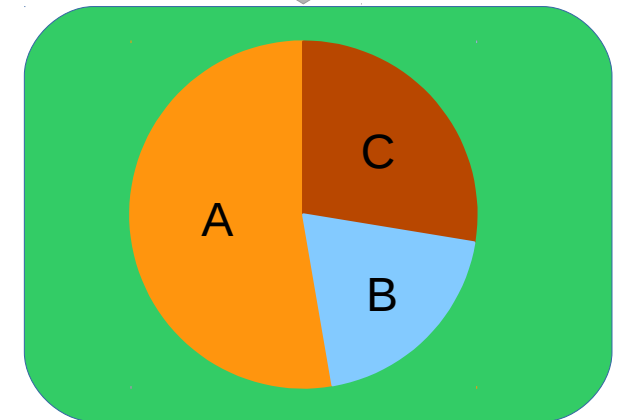
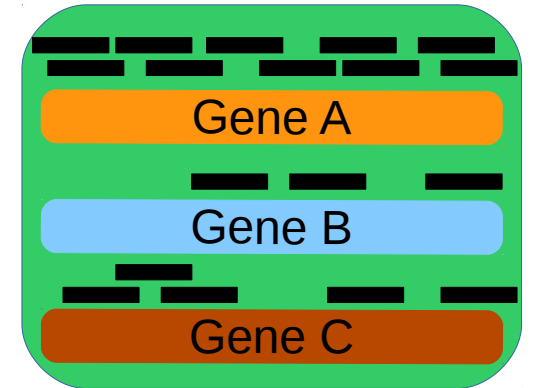
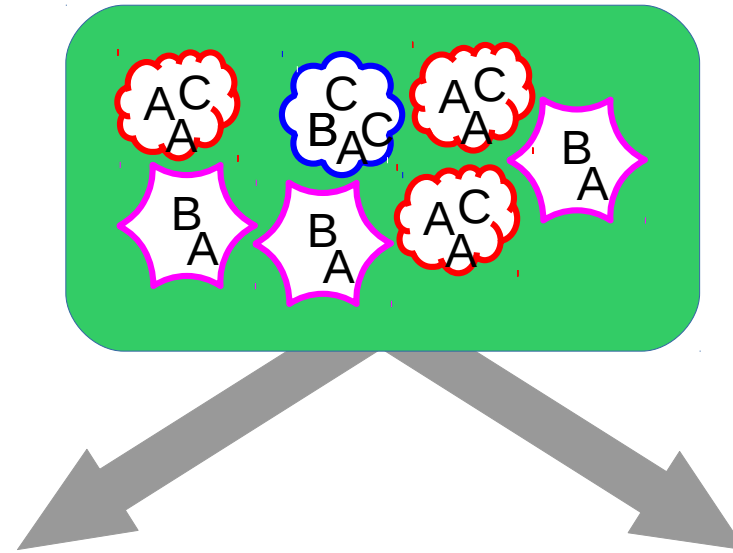
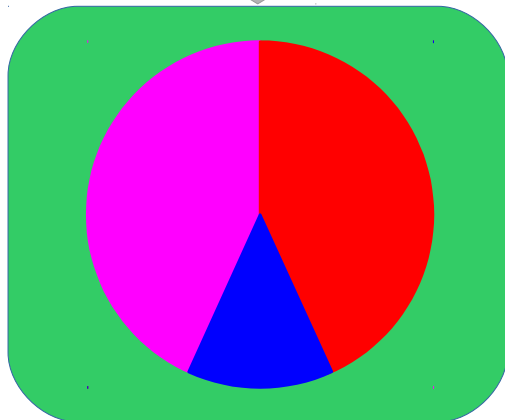
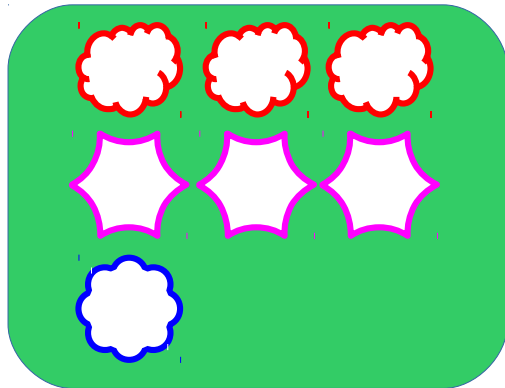


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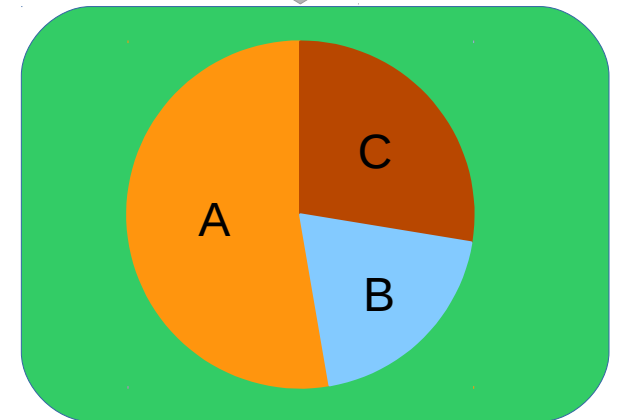
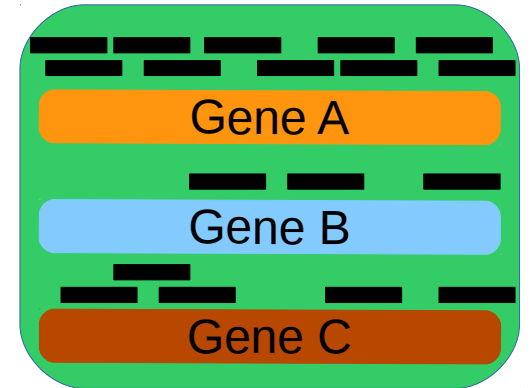
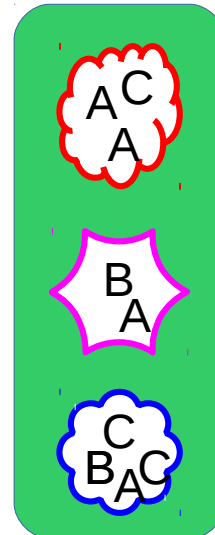
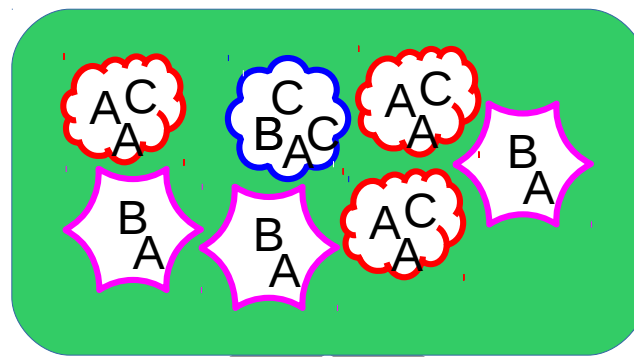
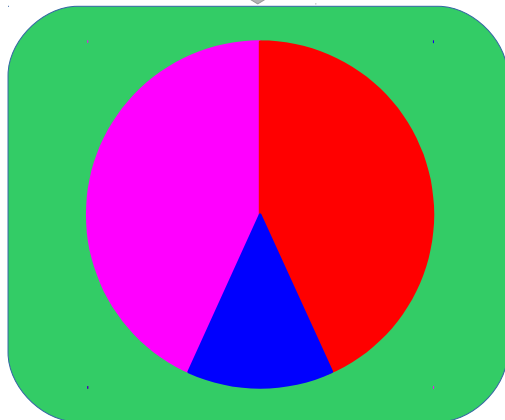
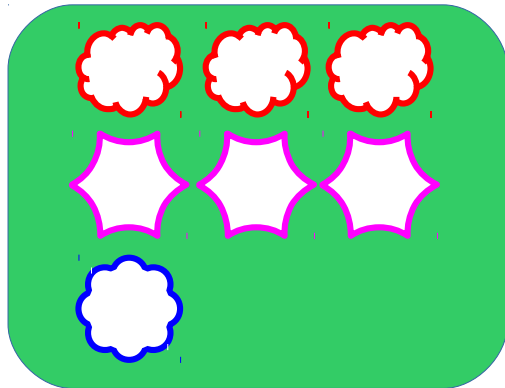
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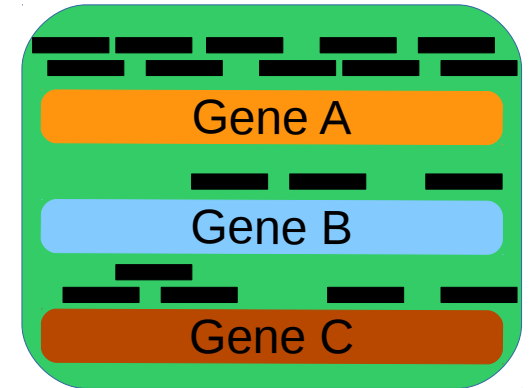
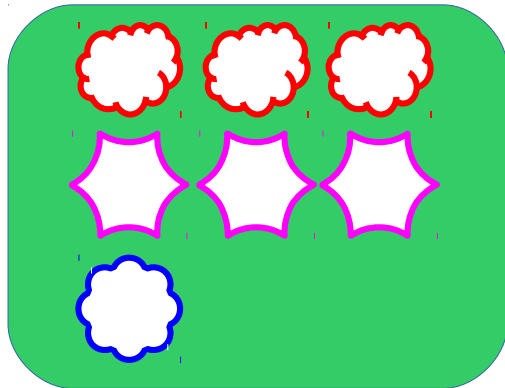


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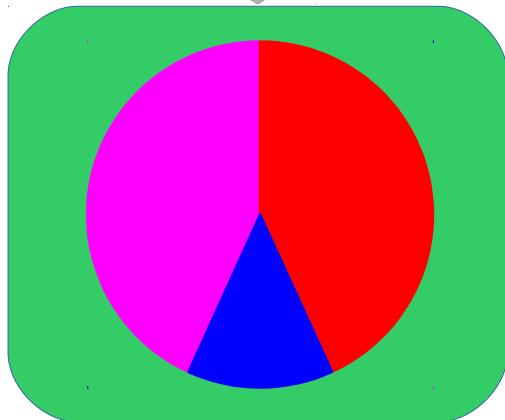
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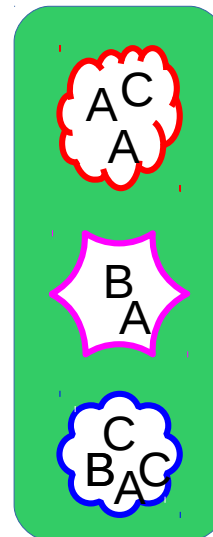
Functional profile



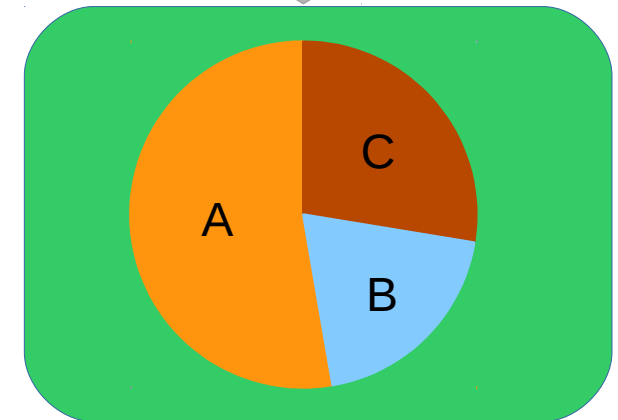
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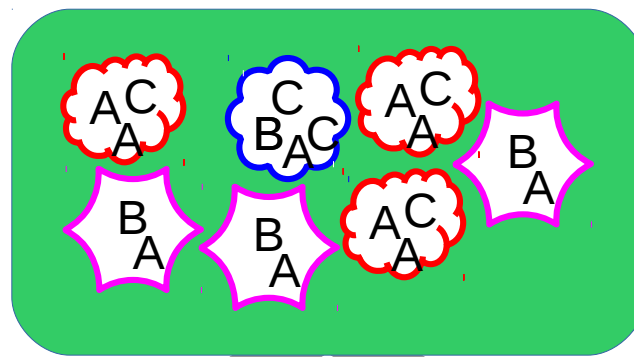


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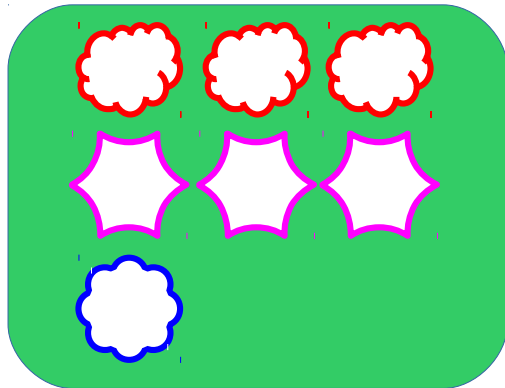


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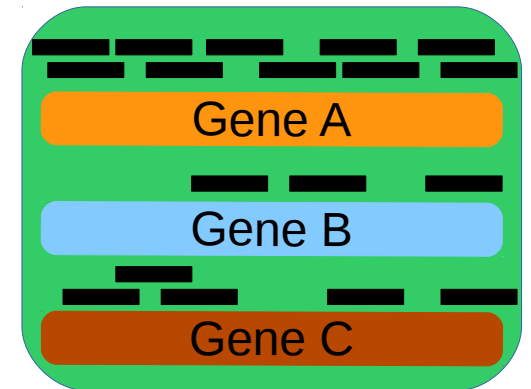
Whole metagenome
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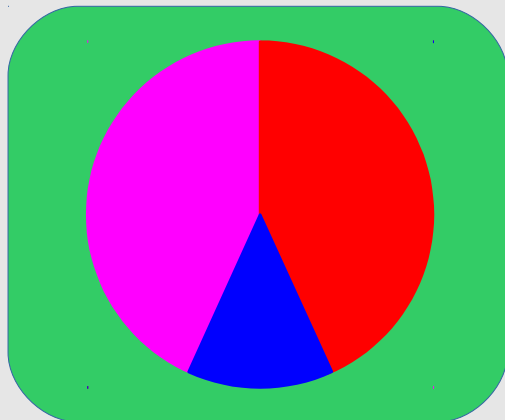
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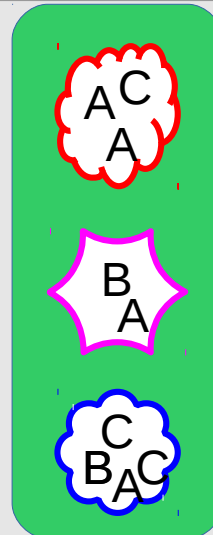
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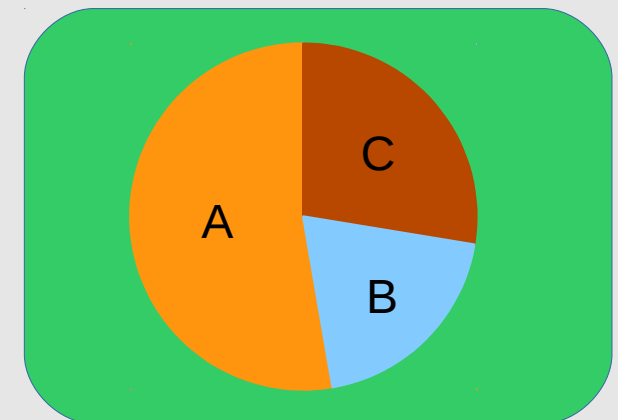
Genomic content



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What can we learn from microbiome data?
Example: Gut communities

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- Determine causal links between microbial communities and health state
 - Communities from obese mice transplanted into germ-free mice lead to obese characteristics
- Develop potential therapeutic communities
 - A synthetic community of 33 common gut species showed positive results in treating *Clostridium difficile* infection

I SEE THE PROBLEM.
YOUR GUT MACROBIOME
IS OUT OF BALANCE.
ONE MOMENT.

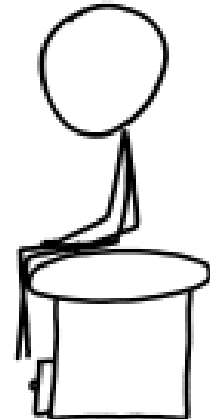
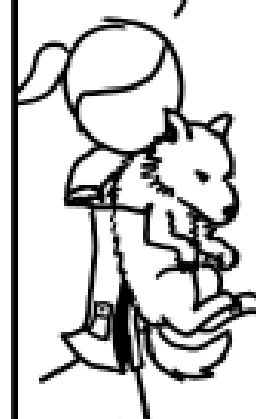


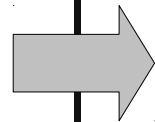
I THINK YOU MEAN
MICROBIOME.

...RIGHT?

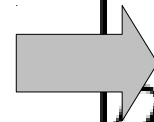


NO. HERE, SWALLOW THIS.
THAT'S A WOLF.
DO YOU NEED A
GLASS OF WATER?





Design
Communities



Designing microbial communities requires
mechanistic information

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- Community dynamics

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 - Is the community detrimental to the host/environment?

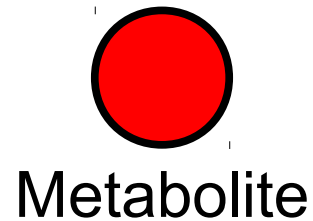
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 - Will the community composition be stable over time?
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Designing microbial communities requires mechanistic information

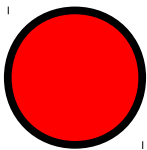
- Community dynamics
 - Will the community composition be stable over time?
 - Can the community adapt properly to perturbations?
- Community function
 - Is the community detrimental to the host/environment?
 - Will the community have a desired metabolic activity?
 - Production/degradation of certain compounds?


Metabolism can be represented as a
directed graph

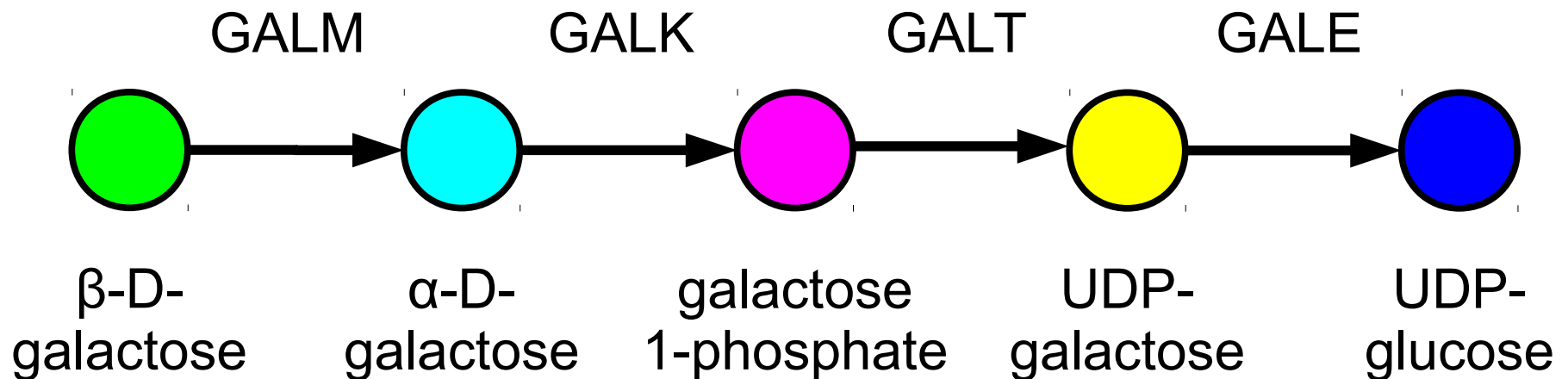


Reaction

Metabolism can be represented as a directed graph


Metabolite


Reaction

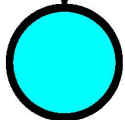
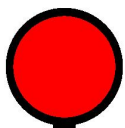


Problem Definition:

Find a minimal set of species which together provide a sufficient set of metabolic reactions to convert a given substrate to a given product.

Desired
Metabolism

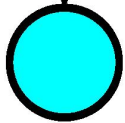
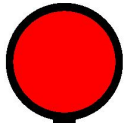
Substrate



Product

Desired Metabolism

Substrate

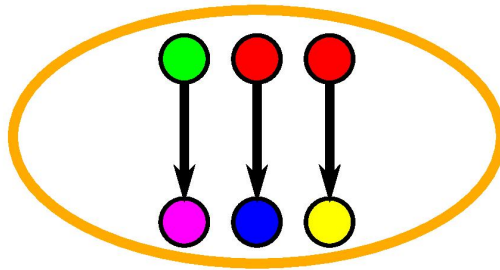


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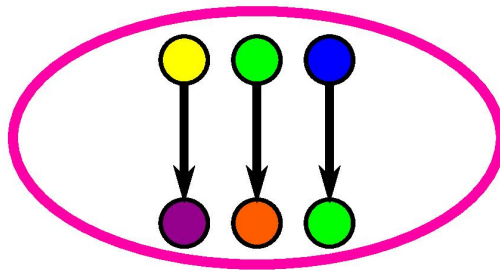


Species and Reactions

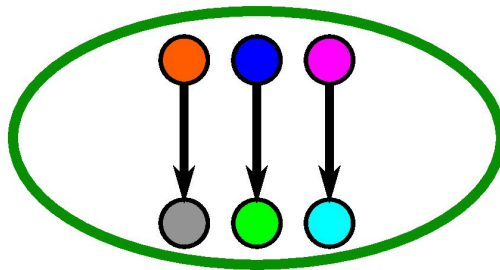
Species 1



Species 2

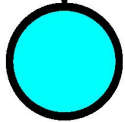
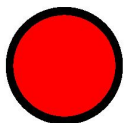


Species 3

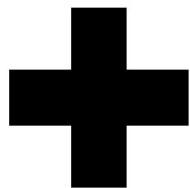


Desired Metabolism

Substrate

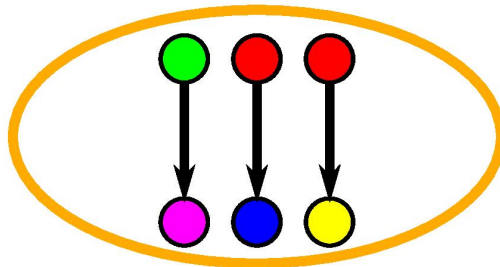


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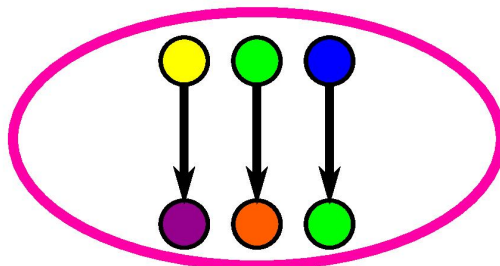


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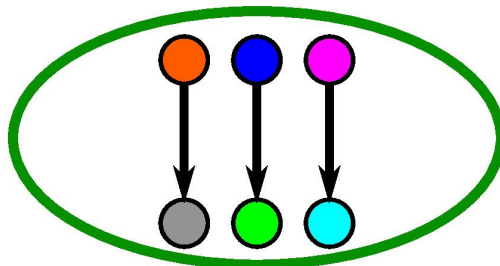
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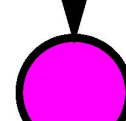
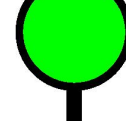
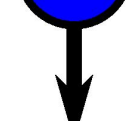
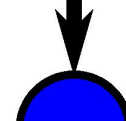
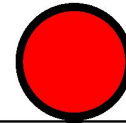


Species 3

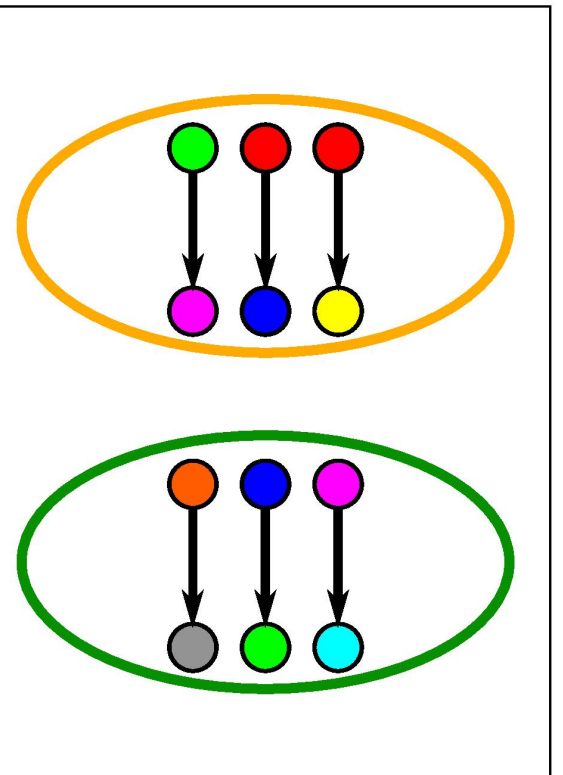


Desired Community

Substrate

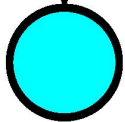
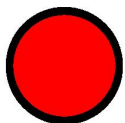


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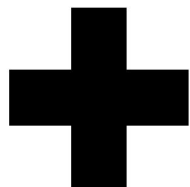


Desired Metabolism

Substrate

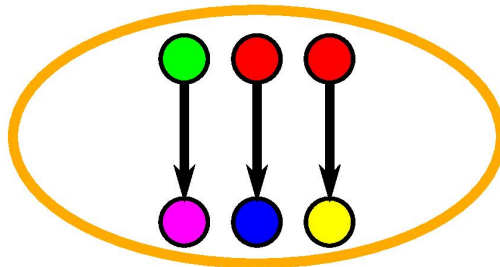


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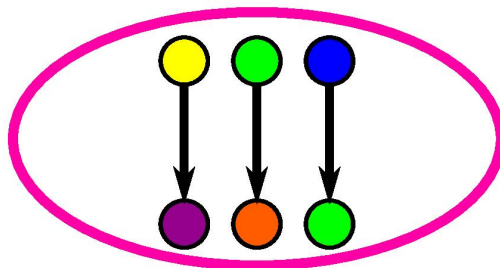


Species and Reactions

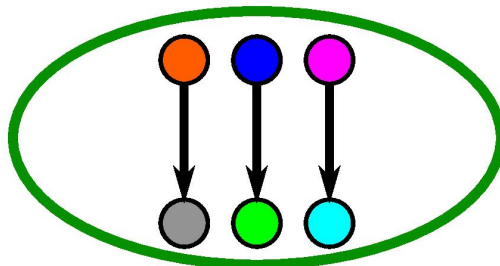
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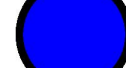
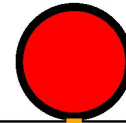


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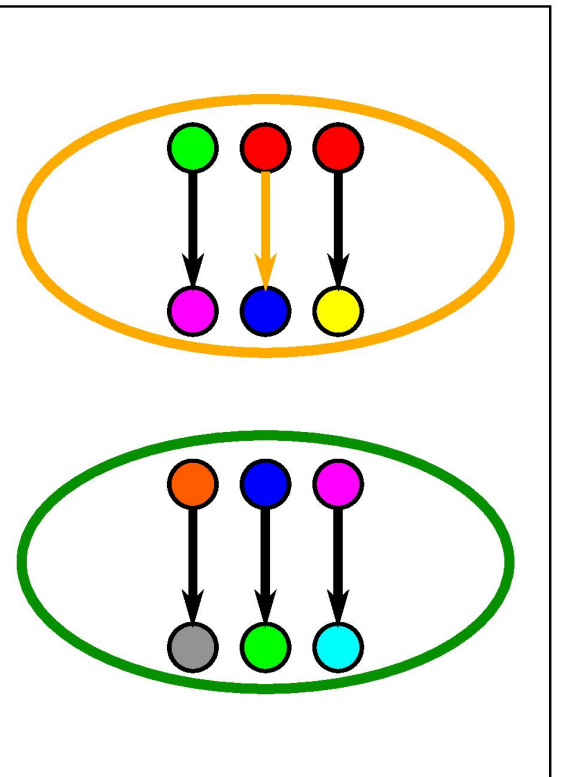


Desired Community

Substrate

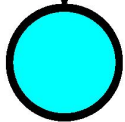
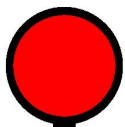


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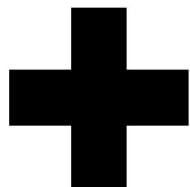


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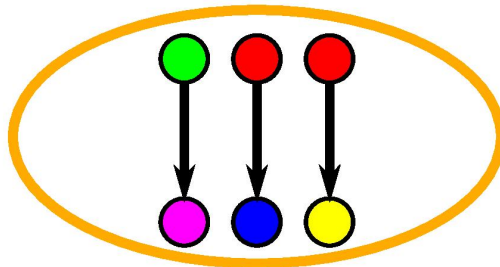


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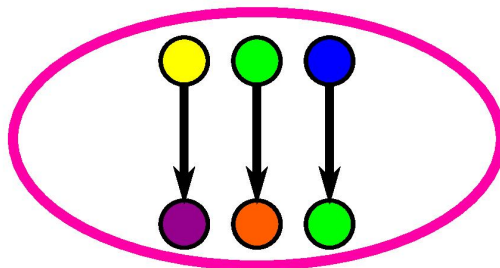


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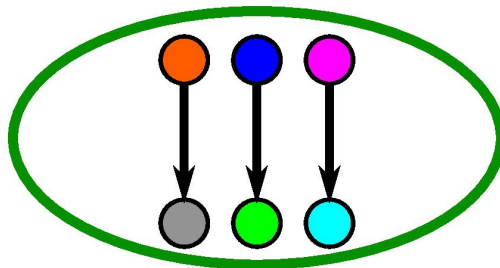
Species 1



Species 2

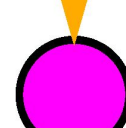
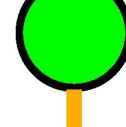
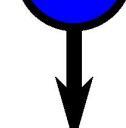
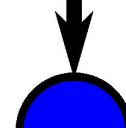
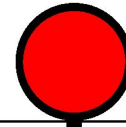


Species 3

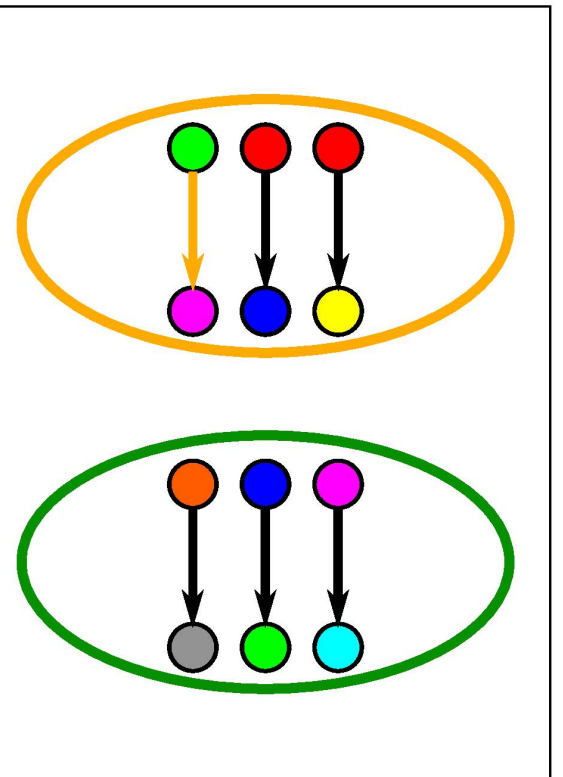


Desired Community

Substrate

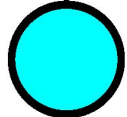
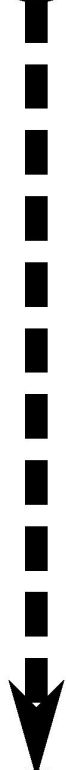
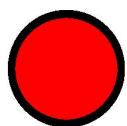


Product



Desired Metabolism

Substrate

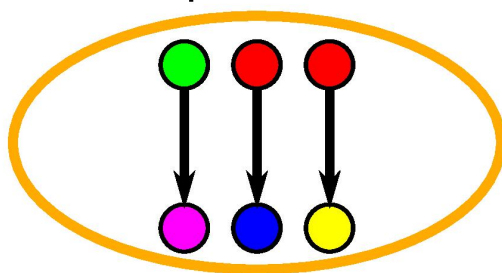


Product

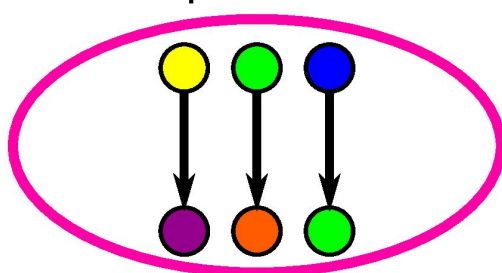


Species and Reactions

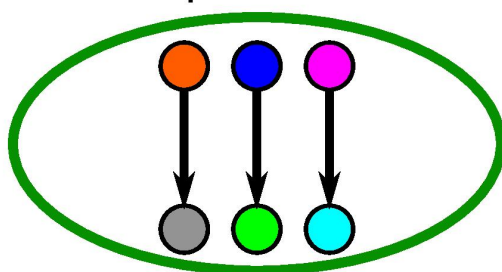
Species 1



Species 2

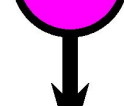
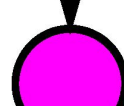
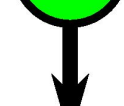
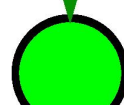
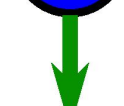
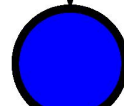
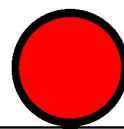


Species 3

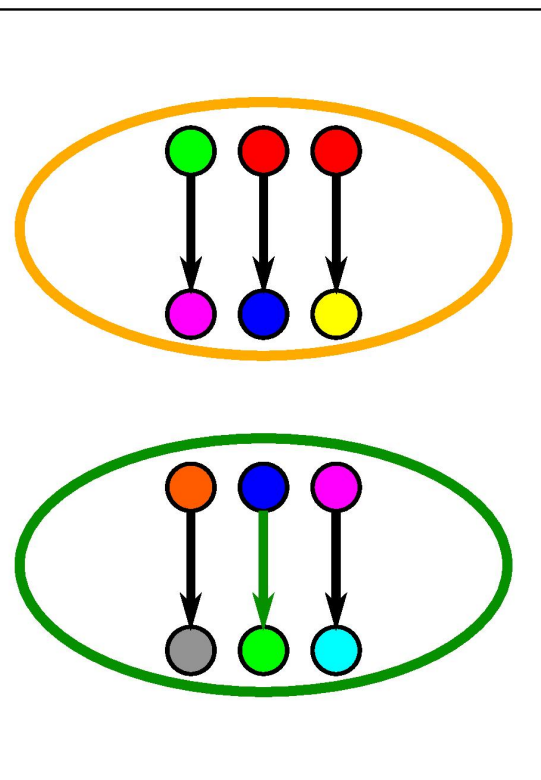


Desired Community

Substrate

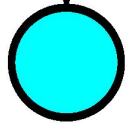
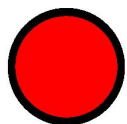


Product

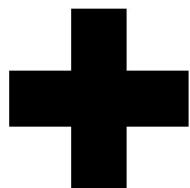


Desired Metabolism

Substrate

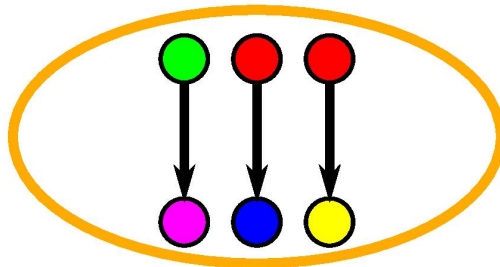


Product

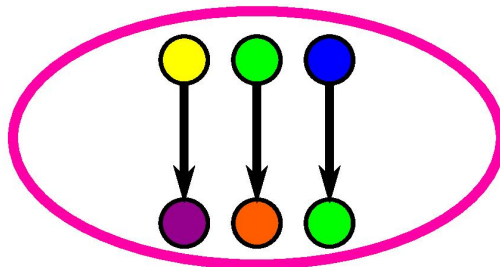


Species and Reactions

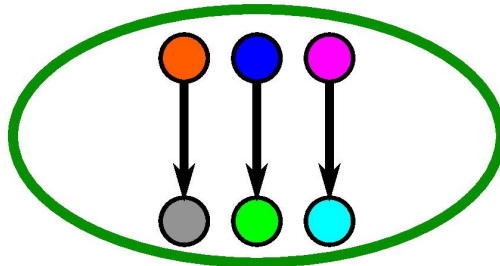
Species 1



Species 2

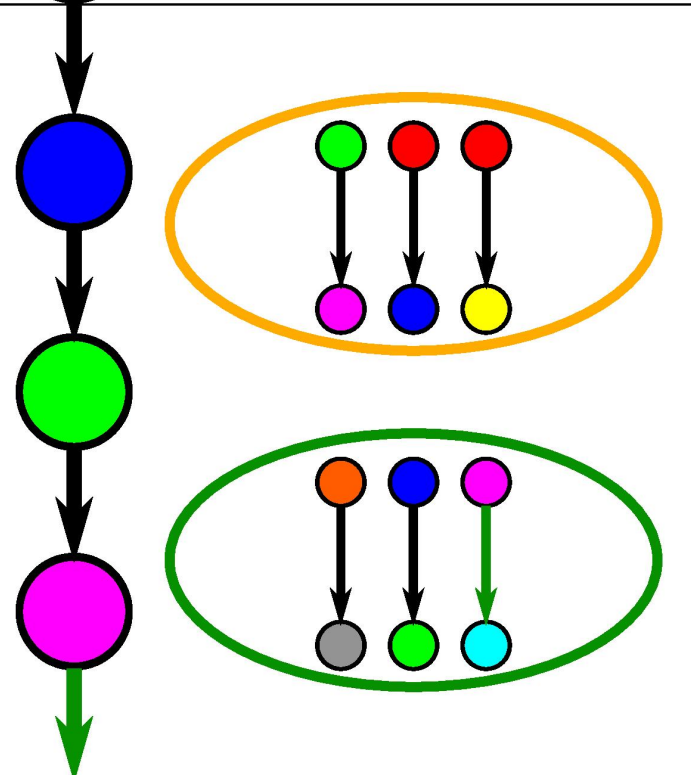
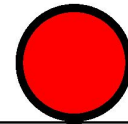


Species 3



Desired Community

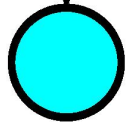
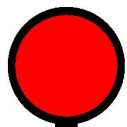
Substrate



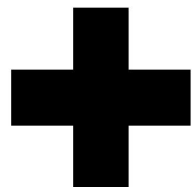
Product

Desired Metabolism

Substrate

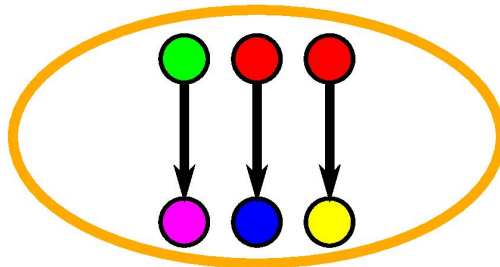


Product

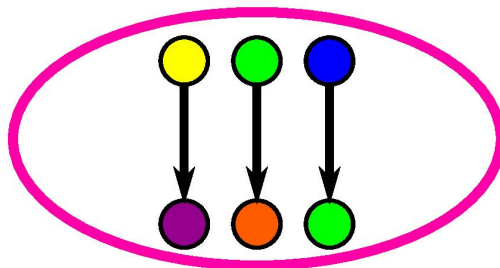


Species and Reactions

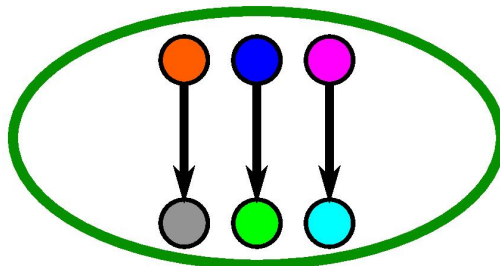
Species 1



Species 2

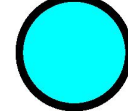
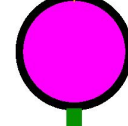
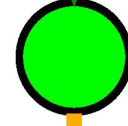
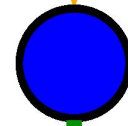
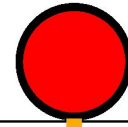


Species 3

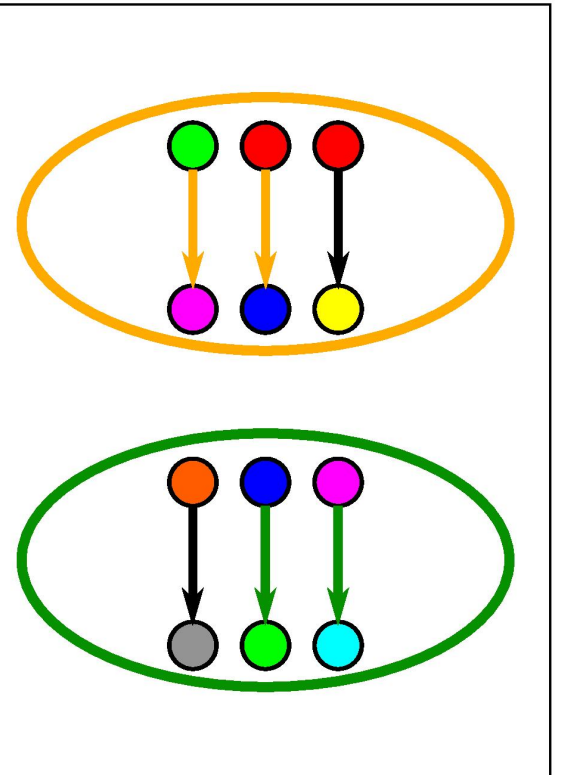


Desired Community

Substrate

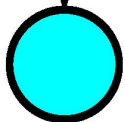
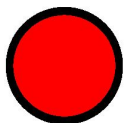


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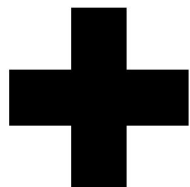


Desired Metabolism

Substrate

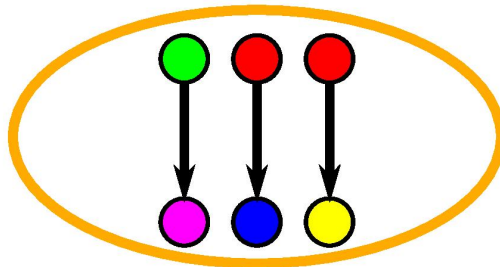


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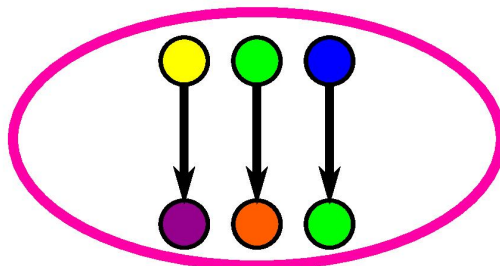


Species and Reactions

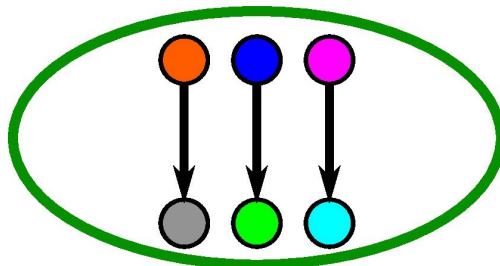
Species 1



Species 2

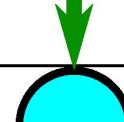
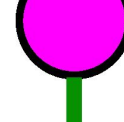
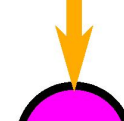
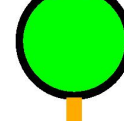
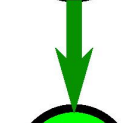
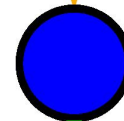
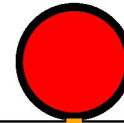


Species 3

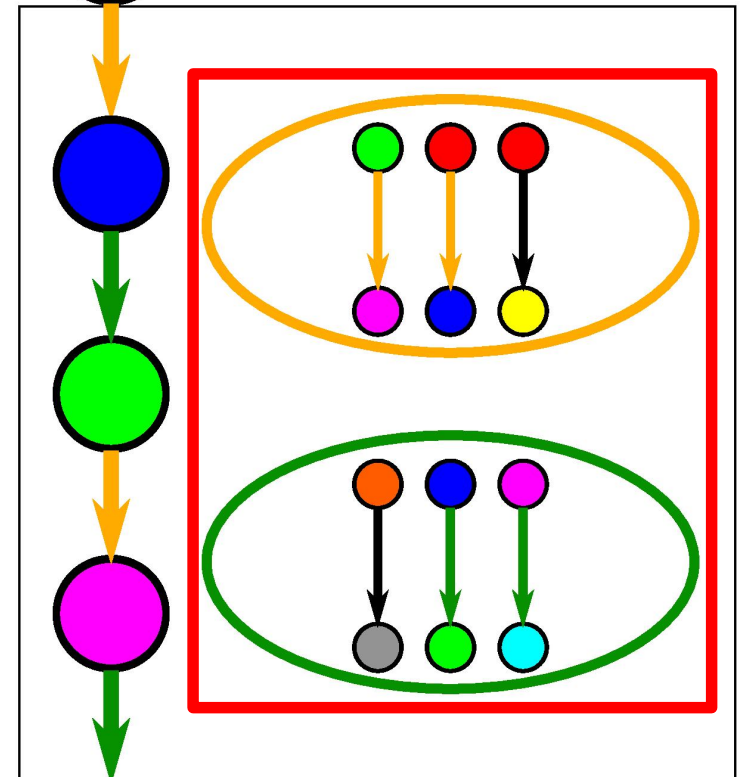


Desired Community

Substrate



Product



We can consider this problem in two pieces

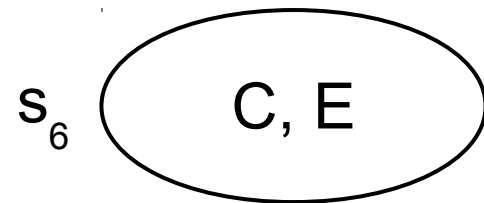
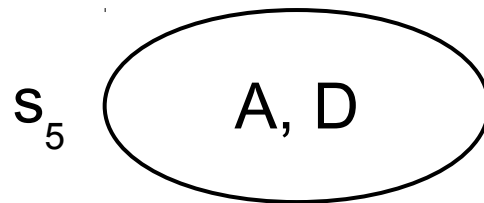
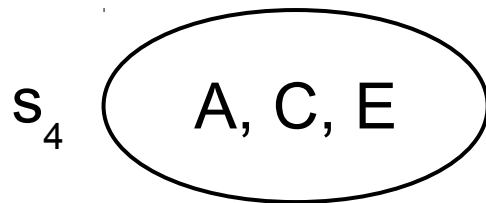
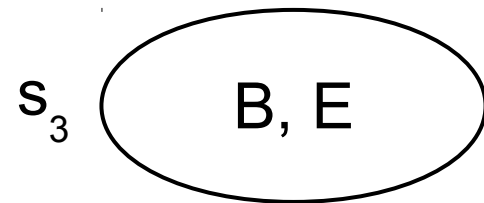
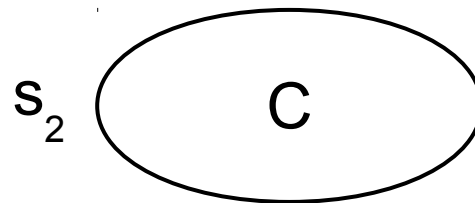
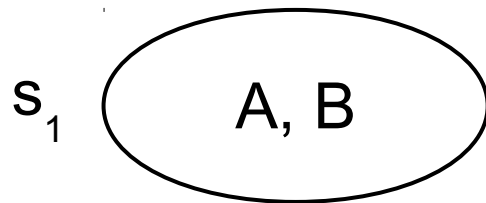
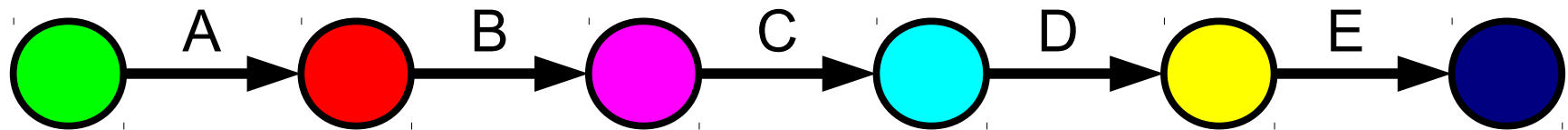
We can consider this problem in two pieces

- First component: Set cover
 - Find a minimal set of species that provide a given set of metabolic reactions

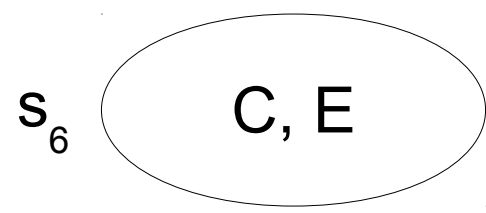
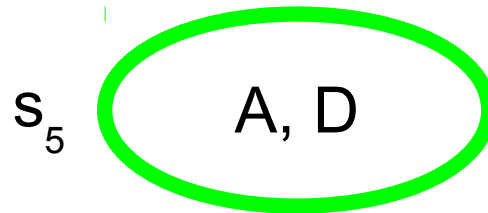
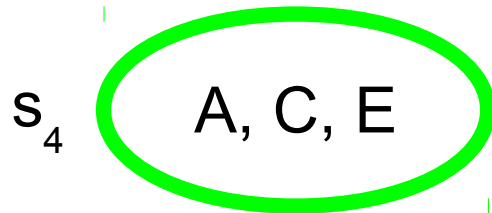
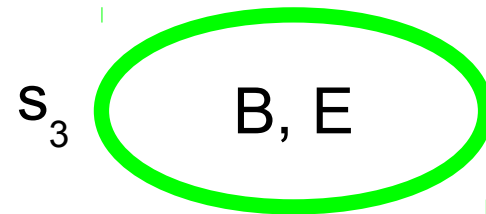
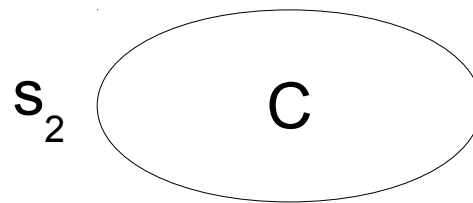
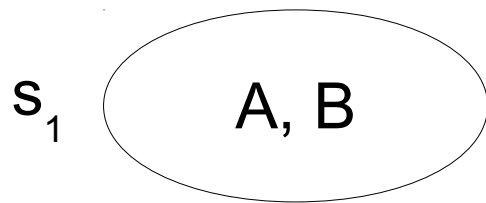
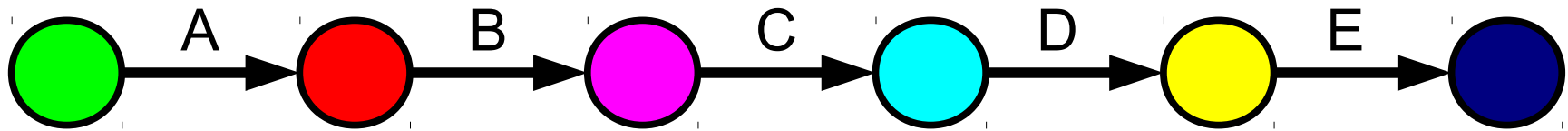
We can consider this problem in two pieces

- First component: Set cover
 - Find a minimal set of species that provide a given set of metabolic reactions
- Second component: Network flow
 - Consider all sets of sufficient metabolic reactions converting substrates to products

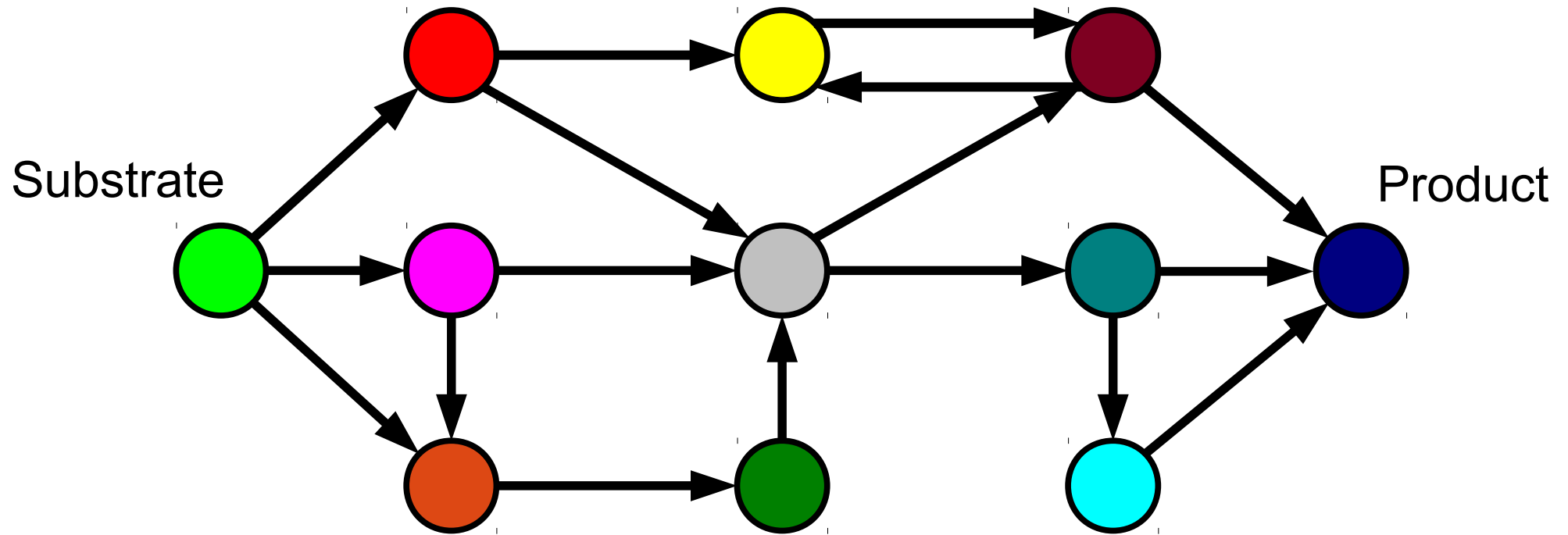
First problem: finding a minimal set of species



First problem: finding a minimal set of species



Second problem: consider all viable paths through the metabolic network



Second problem: consider all viable paths through the metabolic network

