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
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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.
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Ecology
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- Ecology
- Metagenome
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- **Ecology**
- **Metagenome**
16S rRNA sequencing
16S rRNA sequencing

Taxonomic composition
16S rRNA sequencing

Taxonomic composition
16S rRNA sequencing

Whole metagenome shotgun sequencing

Taxonomic composition
**Taxonomic composition**

- Gen A
- Gen B
- Gen C

**Functional profile**

- Gene A
- Gene B
- Gene C

**16S rRNA sequencing**

**Whole metagenome shotgun sequencing**
**Taxonomic composition**

**Functional profile**

**Genomic content**

16S rRNA sequencing

Whole metagenome shotgun sequencing
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Genomic content
What can we learn from microbiome data?
Example: Gut communities
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- Identify species/strains associations
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  - e.g. Increased Firmicutes abundance in the gut is associated with obesity in mice and humans
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- Determine causal links between microbial communities and health state
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  – Communities from obese mice transplanted into germ-free mice lead to obese characteristics
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- Develop potential therapeutic communities
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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 \textit{Clostridium difficile} infection
I see the problem. Your gut microbiome 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?
I see the problem. Your gut microbiome is out of balance.

One moment.

No. Here, swallow this. That's a wolf. Do you need a glass of water?
Designing microbial communities requires mechanistic information
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- Community dynamics
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• Community dynamics
  – Will the community composition be stable over time?
Designing microbial communities requires mechanistic information

- Community dynamics
  - Will the community composition be stable over time?
  - Can the community adapt properly to perturbations?
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- **Community function**
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- **Community function**
  - Is the community detrimental to the host/environment?
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- **Community function**
  - Is the community detrimental to the host/environment?
  - Will the community have a desired metabolic activity?
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.
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β-D-galactose \rightarrow α-D-galactose \rightarrow galactose 1-phosphate \rightarrow UDP-galactose \rightarrow UDP-glucose
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

Species and Reactions

Desired Community

Substrate

Species 1

Species 2

Species 3

Product

Substrate

Product
We can consider this problem in two pieces
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• 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