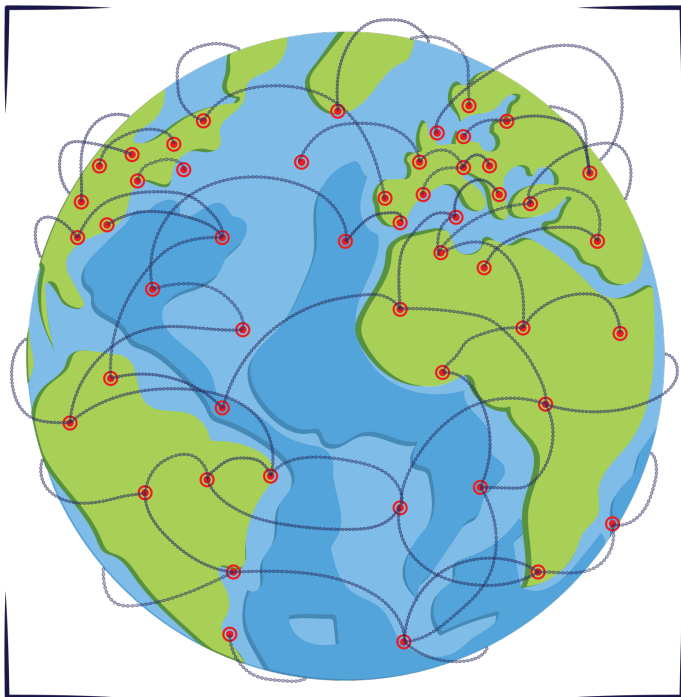


Hannah-Marie Martiny

# Unravelling the co-occurrence patterns of antimicrobial resistance within 214K metagenomes

# Global distribution of antimicrobial resistance in 214K metagenomic samples

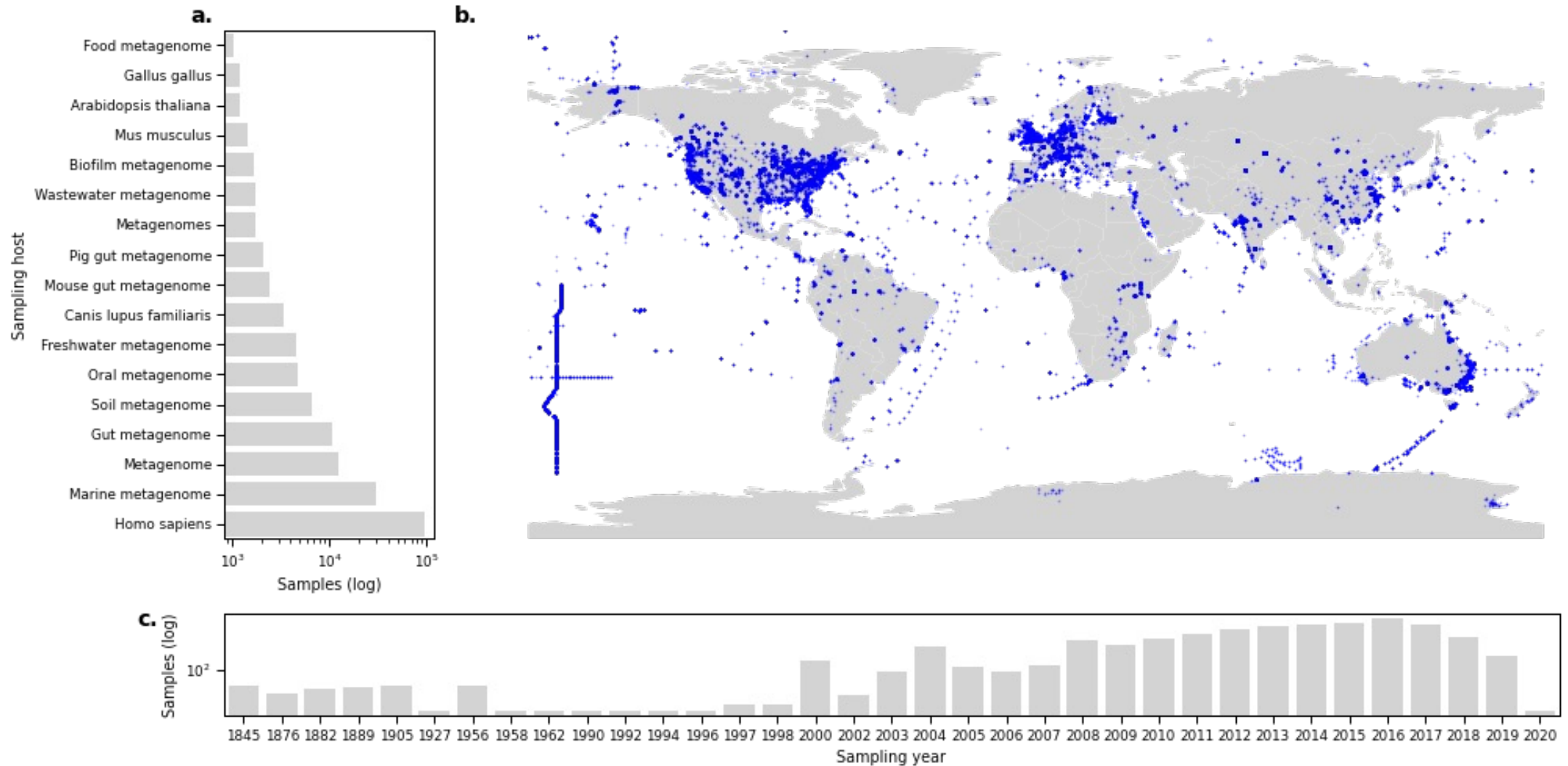


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Downloaded **214K host and environmental metagenomes** from the European Nucleotide Archive to analyze the global resistome.

↓  
Map sequencing reads with KMA<sup>1</sup> against databases ResFinder and Silva

↓  
Analyze ARG abundances with methods from **compositional data analysis**

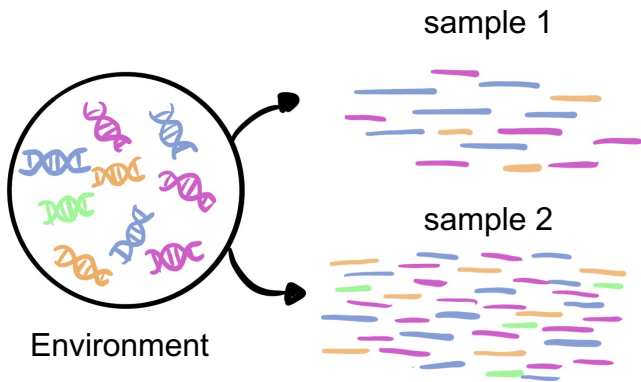


Martiny, H. M., Munk, P., Brinch, C., Aarestrup, F. M., & Petersen, T. N. (2022). A curated data resource of 214K metagenomes for characterization of the global resistome. *bioRxiv*. <https://www.biorxiv.org/content/10.1101/2022.05.06.490940v1>

# Co-occurrence of ARGs

Does the abundance of ARGs of different resistance classes correlate with each other?

## Inferring the truth from random samples

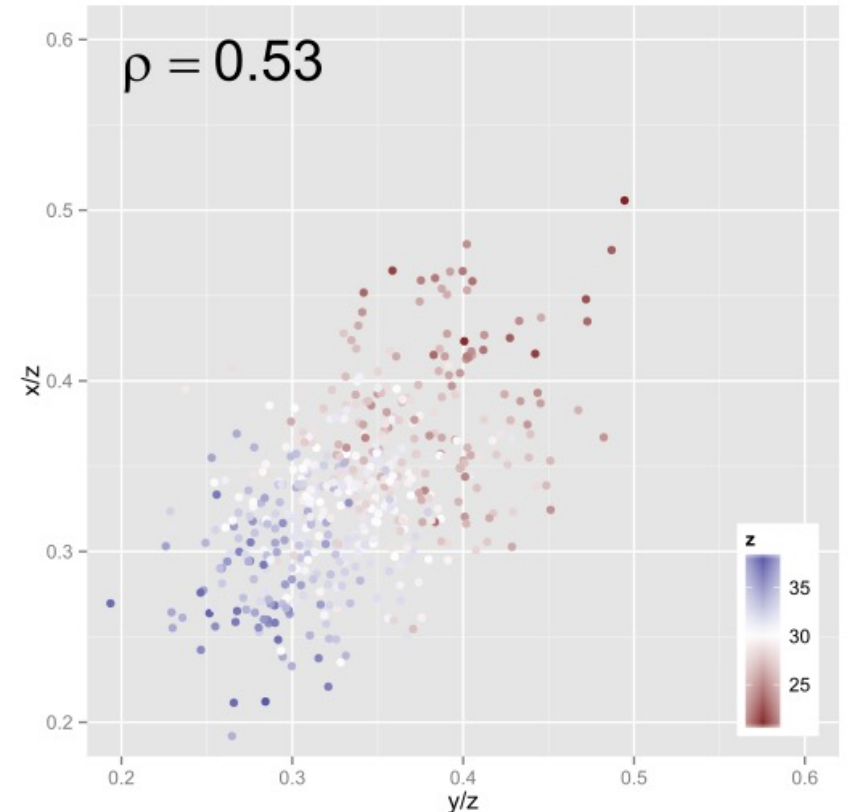


Observed counts are relative.

$x$ : count of gene 1  
 $y$ : count of gene 2  
 $z$ : total number of reads

Sample 500 times:  
 $x, y \sim N(10,1)$   
 $z \sim N(30,3)$

Pearson, Karl (1897): Mathematical contributions to the theory of evolution.— On a form of spurious correlation which may arise when indices are used in the measurement of organs.  
 Proc. R. Soc. Lond.60489 [doi.org/10.1098/rspl.1896.0076](https://doi.org/10.1098/rspl.1896.0076)

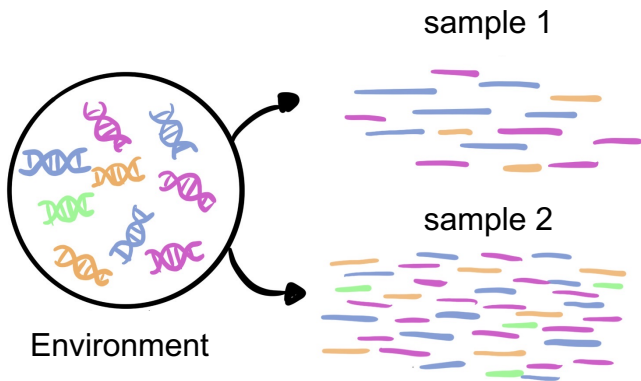


[https://en.wikipedia.org/wiki/Spurious\\_correlation\\_of\\_ratios](https://en.wikipedia.org/wiki/Spurious_correlation_of_ratios)

# Co-occurrence of ARGs

Does the abundance of ARGs of different resistance classes correlate with each other?

## Inferring the truth from random samples



Observed counts are relative.

Friedman, Jonathan, and Eric J. Alm. (2012)  
 Inferring Correlation Networks from Genomic Survey Data.  
 PLOS Computational Biology 8(9): e1002687.

### SparCC: Sparse Correlations for Compositional Data

Estimates linear Pearson correlations between log-transformed components by two assumptions:

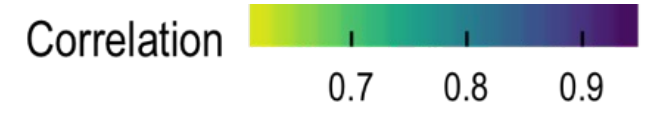
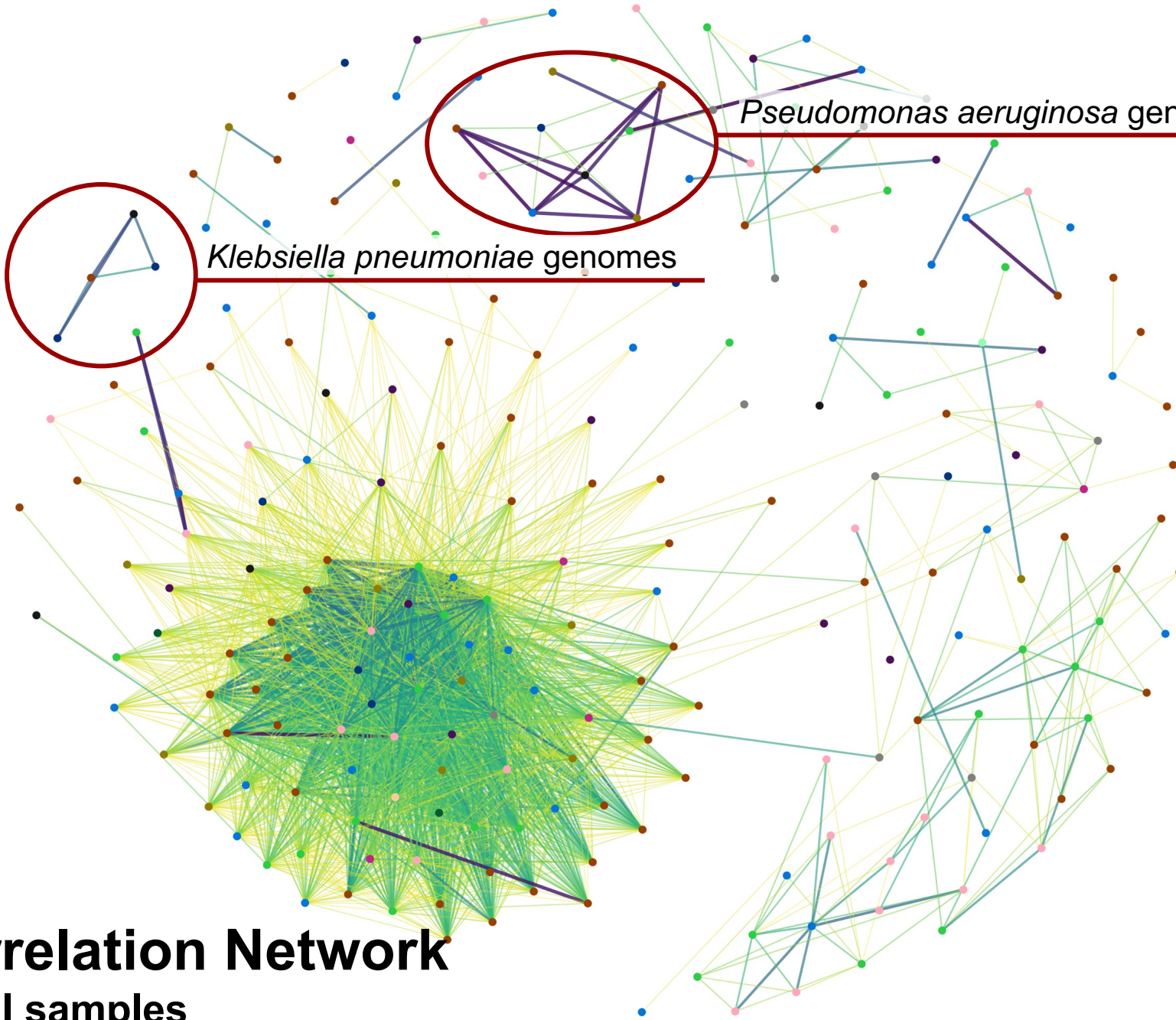
- 1) Number of different genes are large
- 2) The true correlation network is sparse

### Inferring pairwise correlations with SparCC

3085 ARGs → 716 homology-grouped ARGs

#### Selection criteria:

1. Pairs must be ARGs of different classes
2. Correlation  $\geq 0.6$  and p-value  $\leq 0.01$



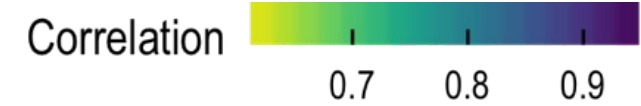
- ResFinder class
- Aminoglycoside/Fluoroquinolone/Macrolide/Phenicol/Rifampicin/Tetracycline
  - Aminoglycoside/Fluoroquinolone/Quinolone
  - Beta\_lactam
  - Folate\_pathway\_antagonist
  - Fosfomycin
  - Glycopeptide
  - Lincosamide/Macrolide/Oxazolidinone/Phenicol/Pleuromutilin/Streptogramin
  - Macrolide/Tetracycline
  - Missing
  - Oxazolidinone/Phenicol/Tetracycline
  - Phenicol
  - Polymyxin
  - Quinolone
  - Tetracycline

**Correlation Network**  
for all samples

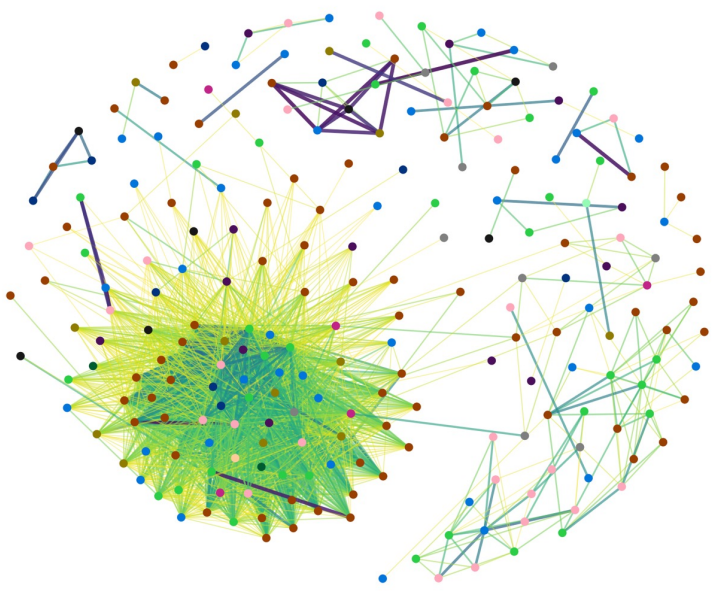
**225 ARG nodes**  
**2,344 correlation edges**

# Co-occurrence of ARGs: Source-specific networks

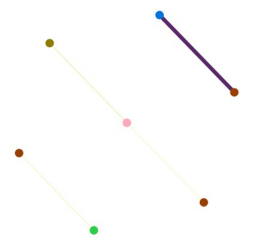
Are the correlations magnified in specific sampling sources?



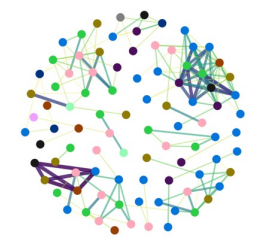
All



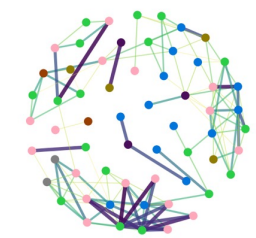
Air



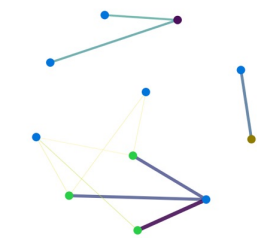
Chicken



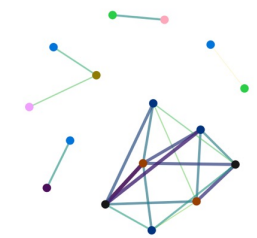
Cow



Dog



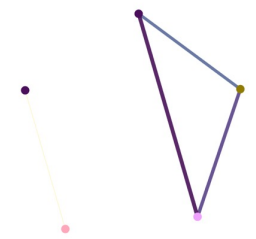
Freshwater



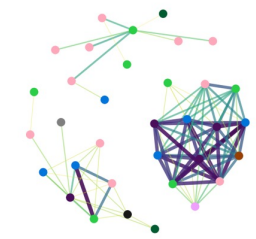
Human



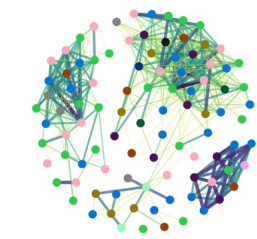
Marine



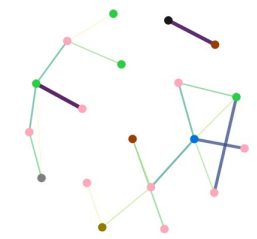
Mouse



Pig



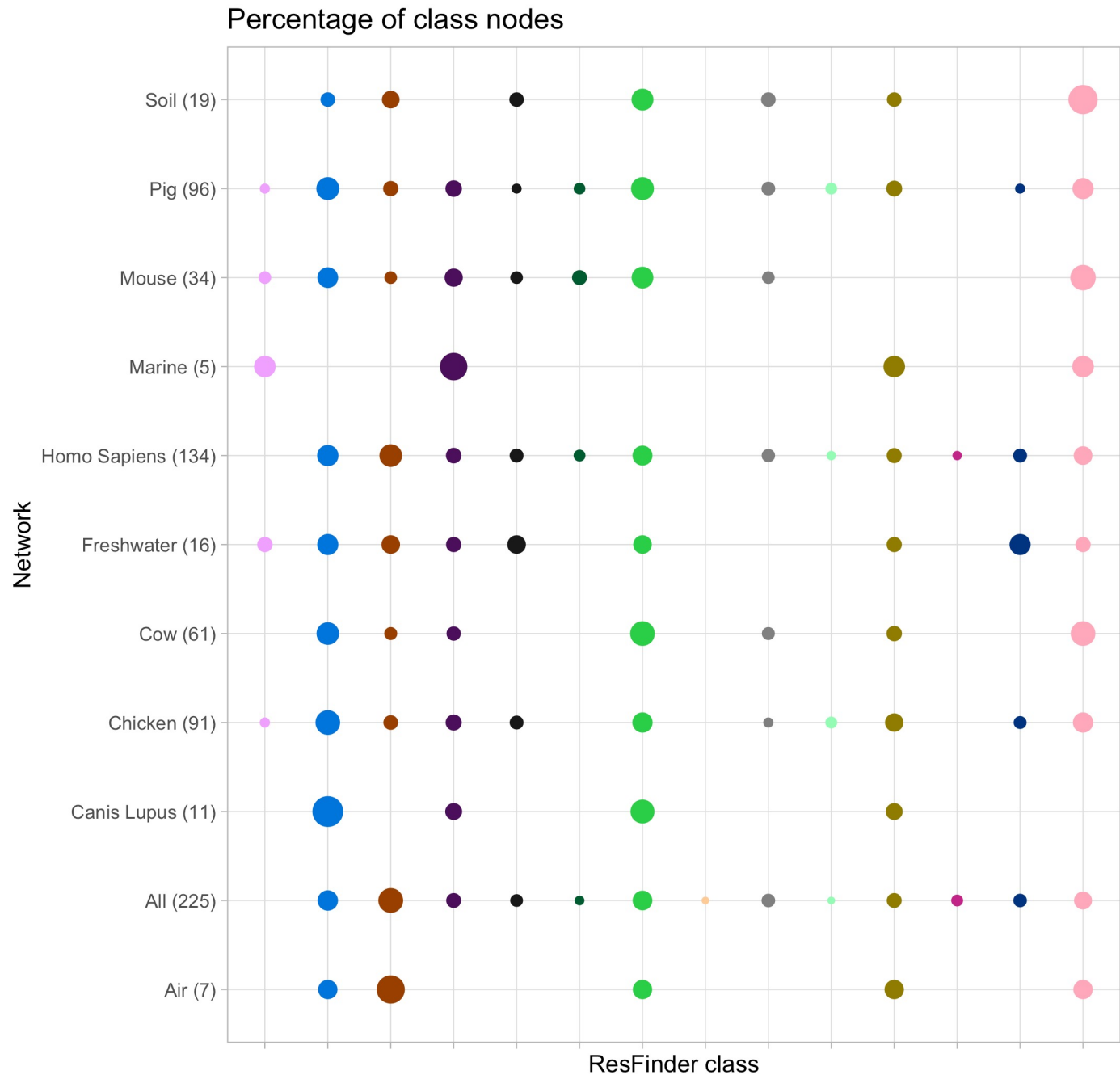
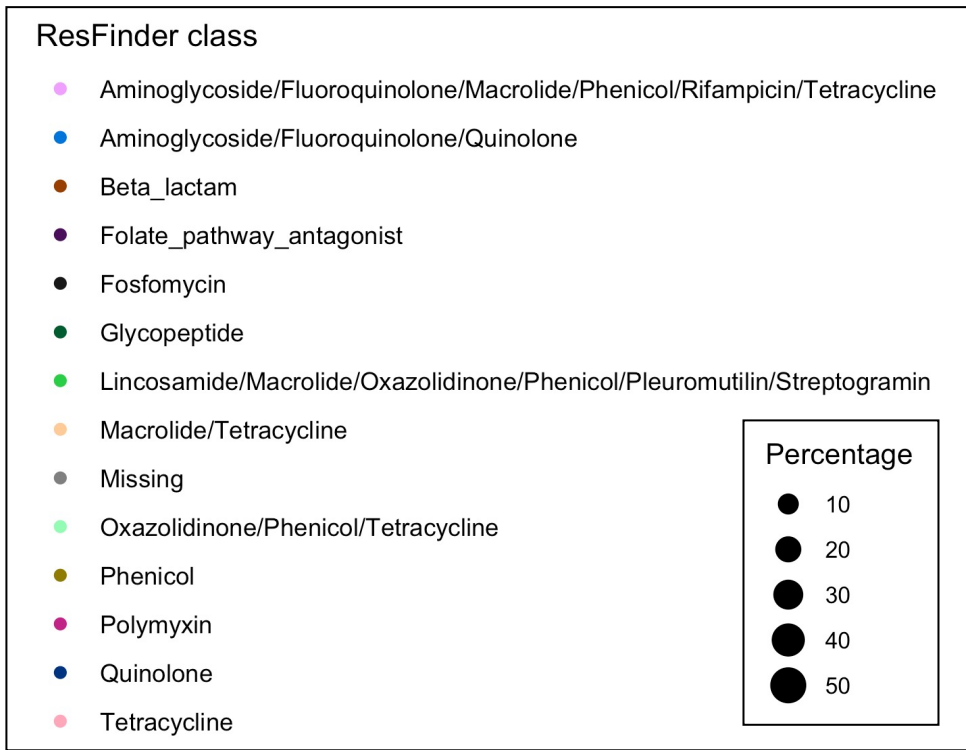
Soil



- Aminoglycoside/Fluoroquinolone/Macrolide/Phenicol/Rifampicin/Tetracycline
- Fosfomycin
- Missing
- Polymyxin
- Aminoglycoside/Fluoroquinolone/Quinolone
- Glycopeptide
- Oxazolidinone/Phenicol/Tetracycline
- Quinolone
- Beta\_lactam
- Lincosamide/Macrolide/Oxazolidinone/Phenicol/Pleuromutilin/Streptogramin
- Phenicol
- Steroid\_antibacterial
- Folate\_pathway\_antagonist
- Macrolide/Tetracycline
- Pleuromutilin
- Tetracycline

# Co-occurrence of ARGs: Node classes

Some classes are more prevalent in specific environments



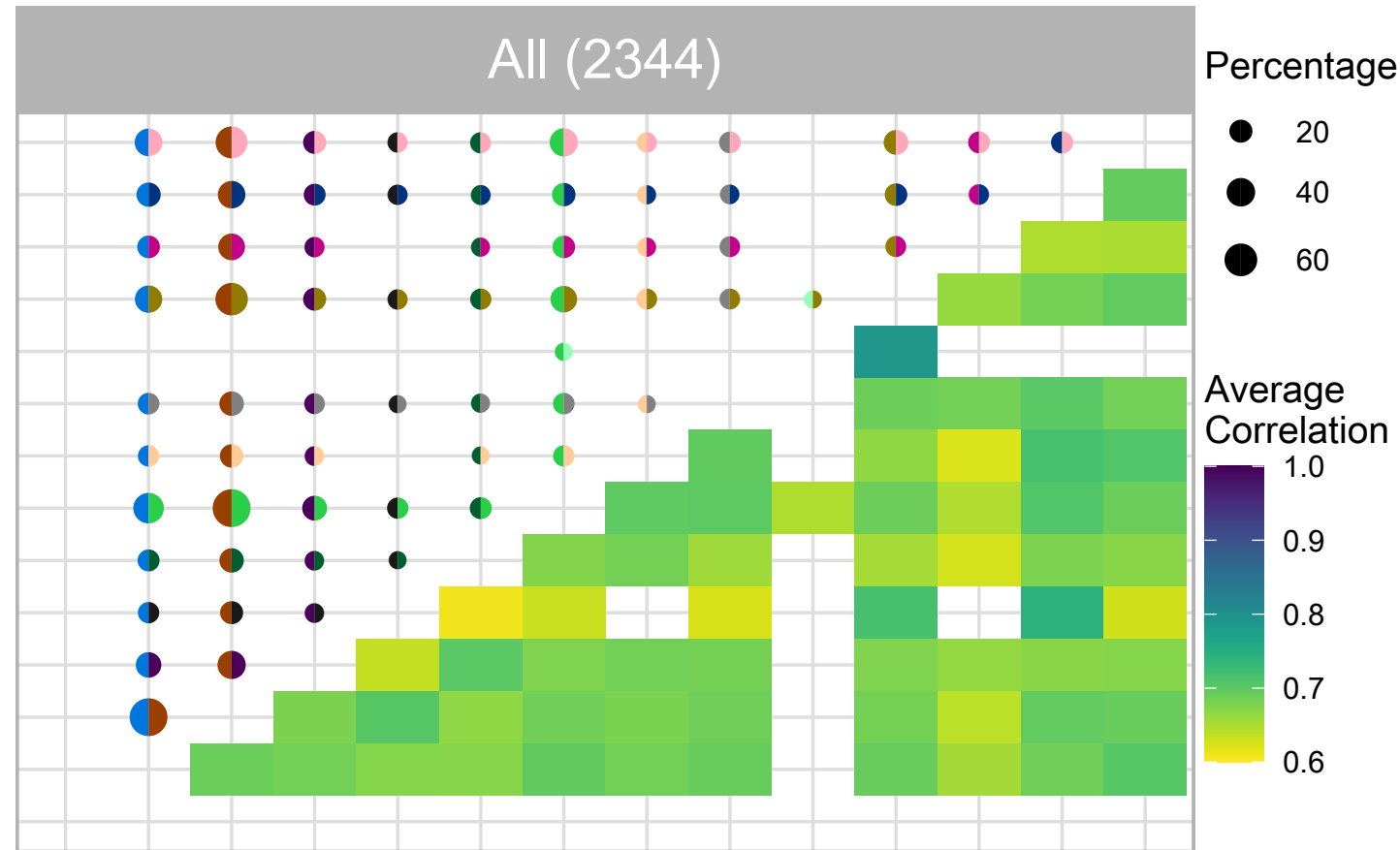


# Co-occurrence of ARGs: Edge classes

Many correlations between  
**Aminoglycoside/Fluoroquinolone/Quinolone**  
and **Beta lactams**

### ResFinder class

- Aminoglycoside/Fluoroquinolone/Macrolide/Phenicol/Rifampicin/Tetracycline
- Aminoglycoside/Fluoroquinolone/Quinolone
- Beta\_lactam
- Folate\_pathway\_antagonist
- Fosfomycin
- Glycopeptide
- Lincosamide/Macrolide/Oxazolidinone/Phenicol/Pleuromutilin/Streptogramin
- Macrolide/Tetracycline
- Missing
- Oxazolidinone/Phenicol/Tetracycline
- Phenicol
- Polymyxin
- Quinolone
- Tetracycline

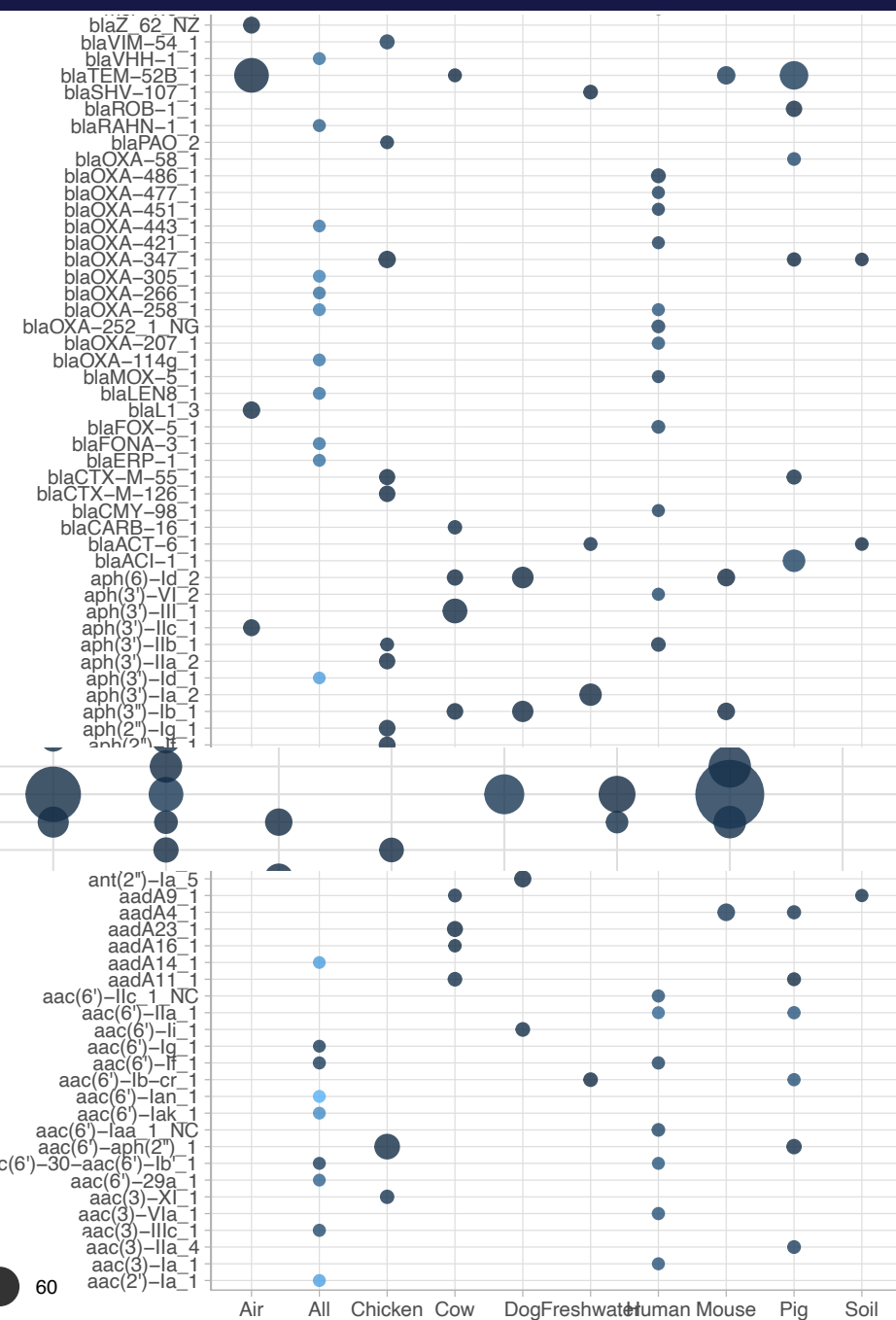
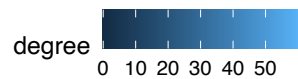


# Co-occurrence of ARGs: Edge classes

Many correlations between  
Aminoglycoside/Fluoroquinolone/Quinolone  
and Beta lactams

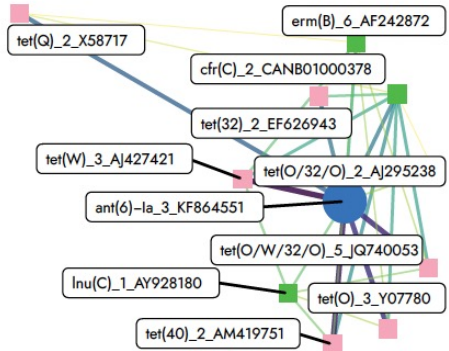
So which genes are we  
talking about in these  
two classes?

ant(6)-la\_5  
**ant(6)-la\_3**  
ant(6)-la\_2  
ant(3'')-la\_1

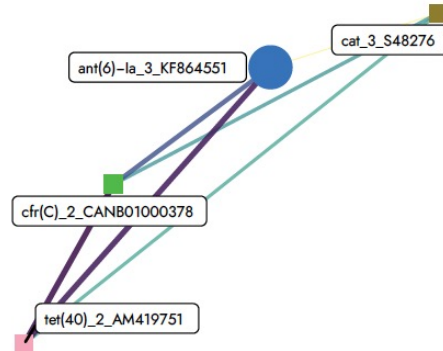


# Co-occurrence of ARGs: Edge classes

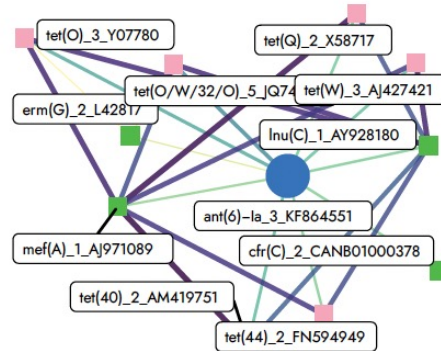
All



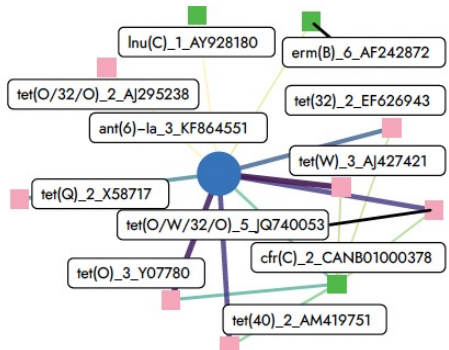
Chicken



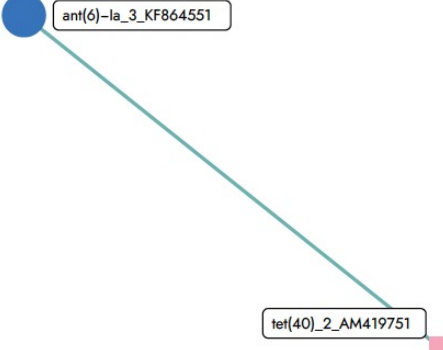
Cow



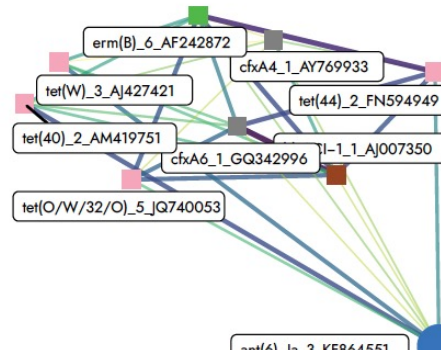
Human



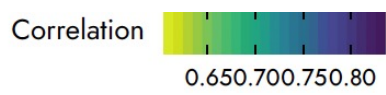
Mouse



Pig



- Aminoglycoside/Fluoroquinolone/Quinolone
- Lincosamide/Macrolide/Oxazolidinone/Phenicol/Pleuromutilin/Streptogramin
- Tetracycline
- Beta-lactam
- Phenicol



Highlighted ● Yes ■ No

DTU

