



Integrating genomics and transcriptomics for context-specific modeling of microbial metabolism



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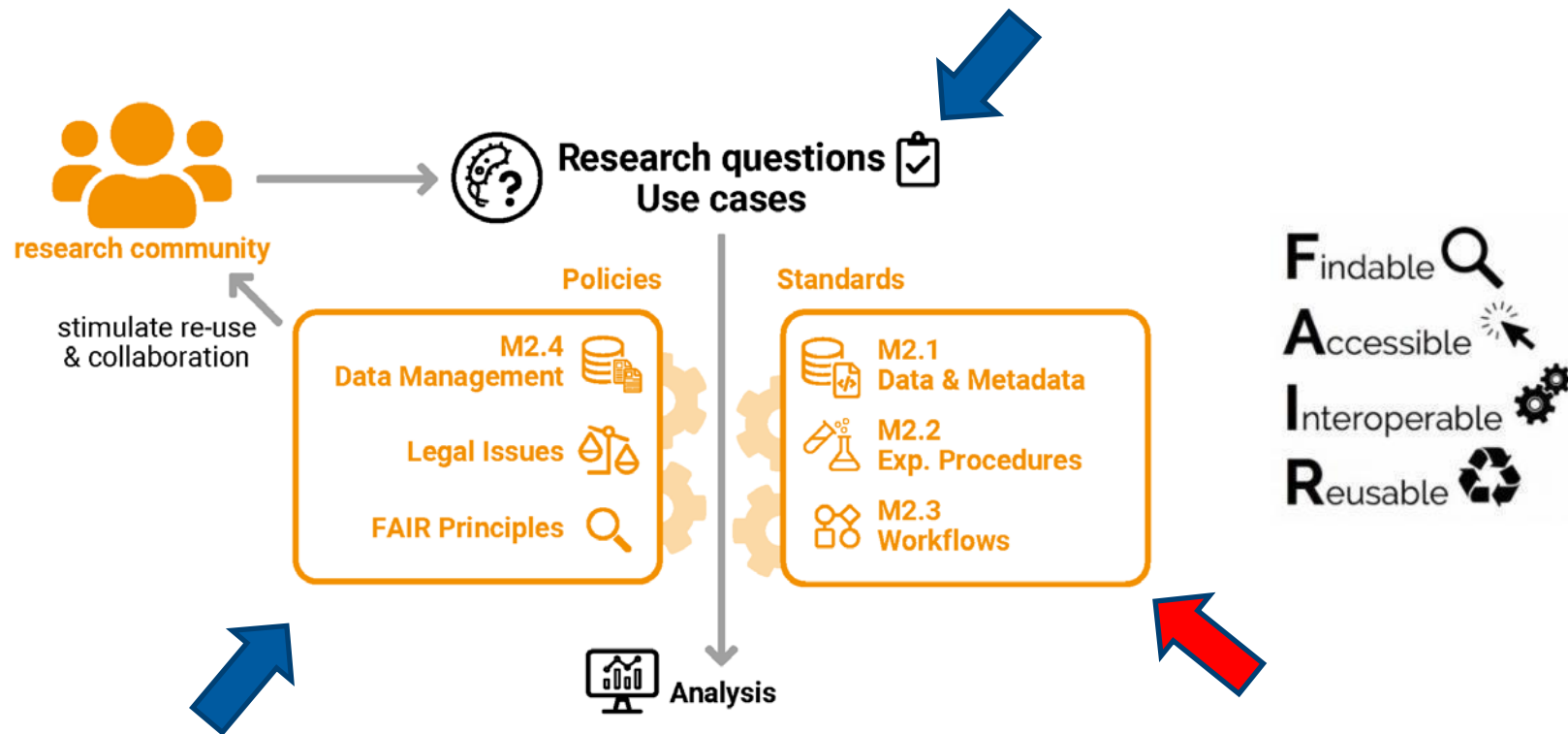
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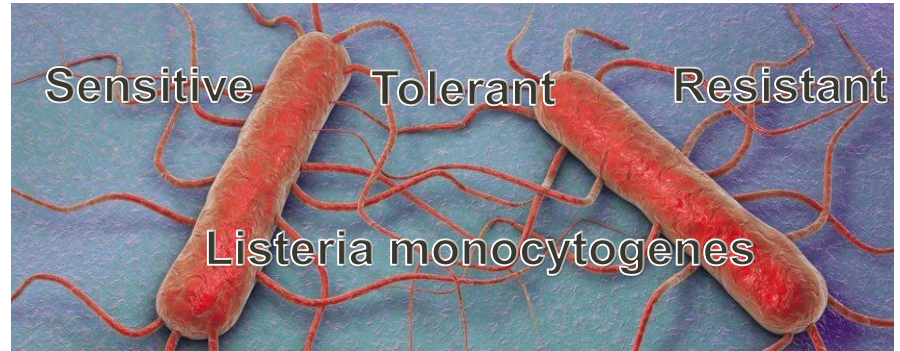
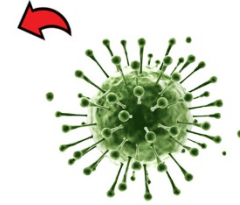
Multi-omics Use Case in the context of the NFDI4Microbiota



Model system



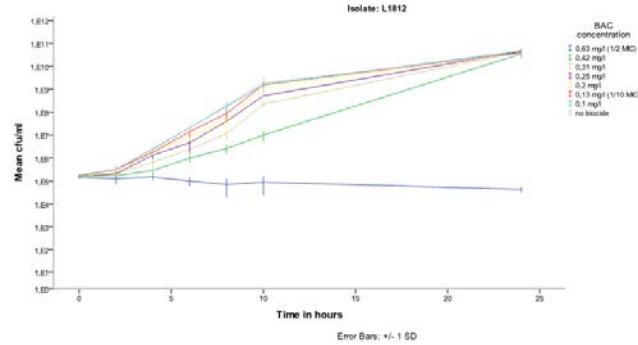
Kills 99.9% of All
Viruses Bacteria & Fungus



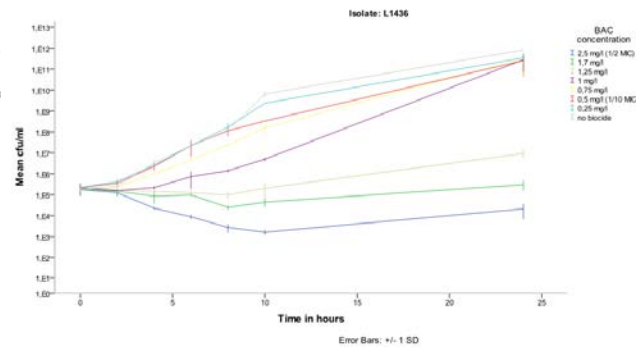
Multi-omics experimental design – effect of concentration

Measure 2.2 SOP Exp. Proc.

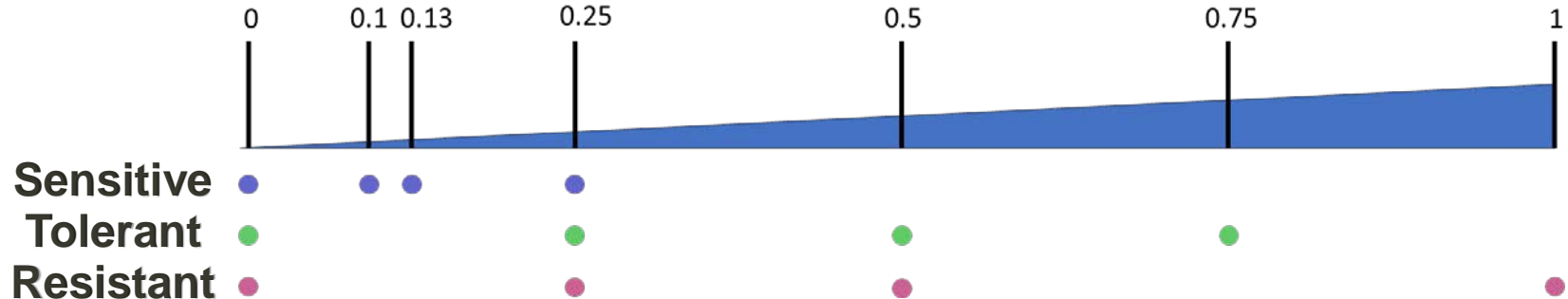
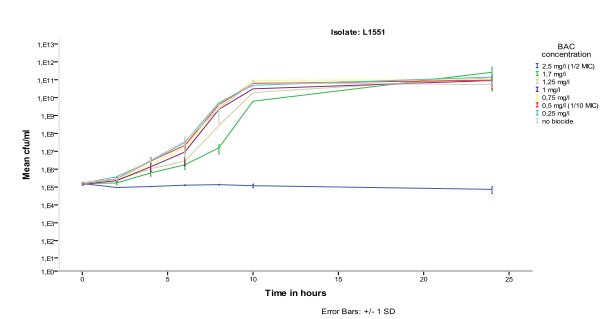
Sensitive



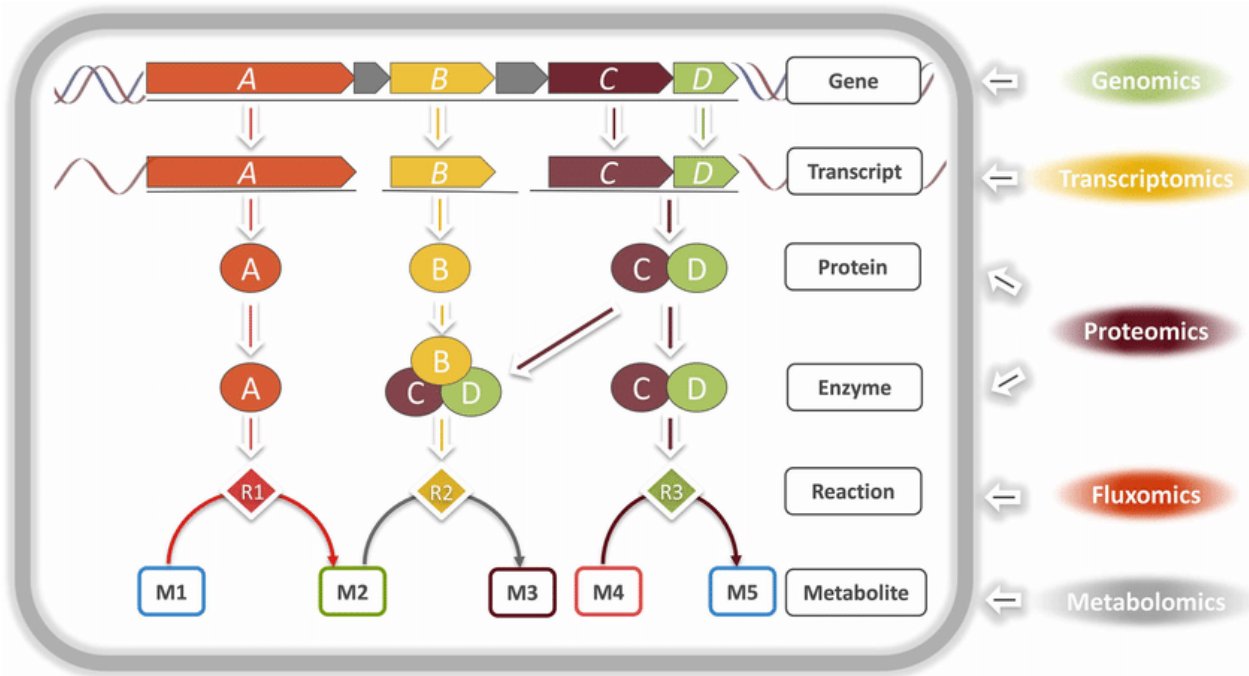
Tolerant



Resistant



Integrating multi-omics data using genome-scale metabolic models



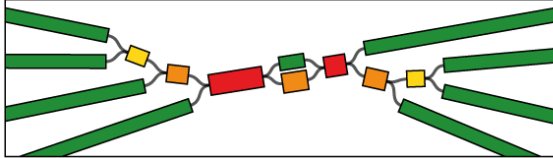
Measure 3.4
Data qual. & prov.

Rau and Zeidan (2018) Biochem. Soc. Trans.

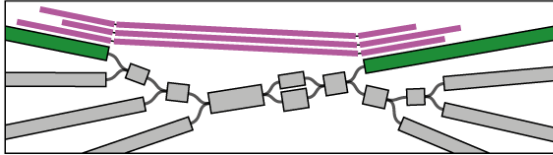
Closing the genomes – hybrid assembly (Illumina + Nanopore DNaseq data)



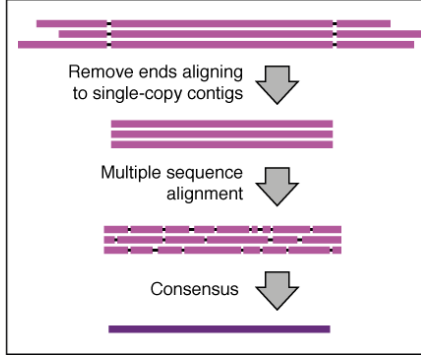
Repeat region in unbridged graph



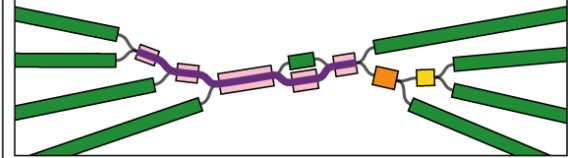
Semi-global long read alignment



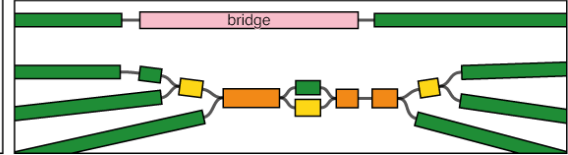
Consensus read sequence



Path finding



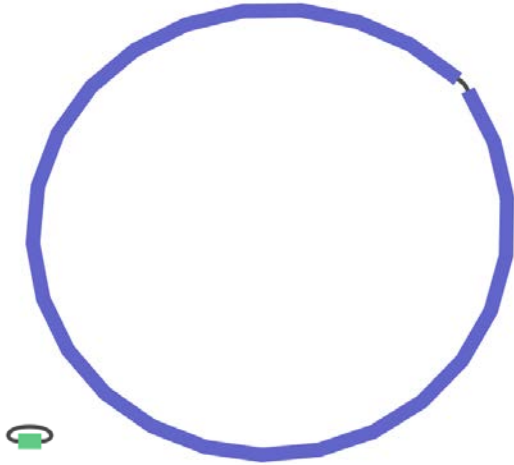
Bridged graph



Measure 2.3
Workflow Std.

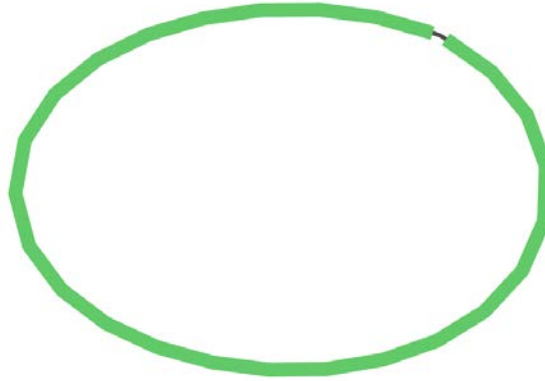
Circularization of genomes

Sensitive



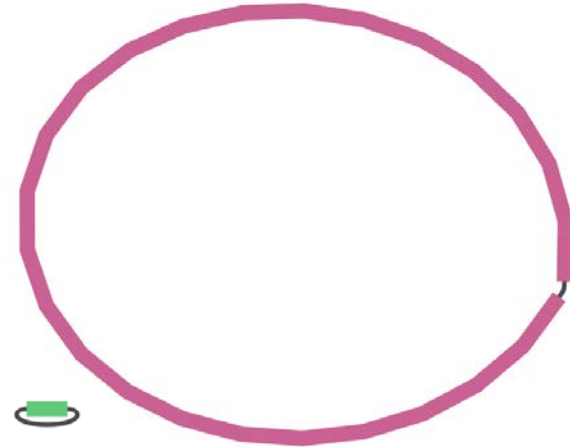
2 contigs
3,076,646 bp
48,878 bp

Tolerant



1 contig
2,978,345 bp

Resistant

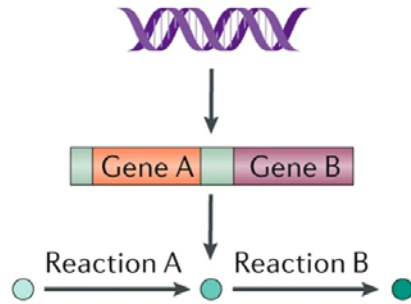


2 contigs
2,972,609 bp
79,345 bp

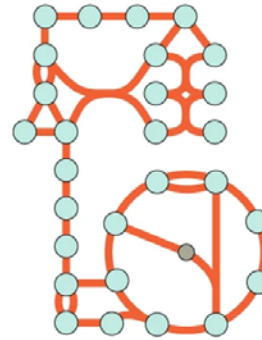
Preparing genome-scale metabolic models

Measure 3.2
Analyt. Serv.

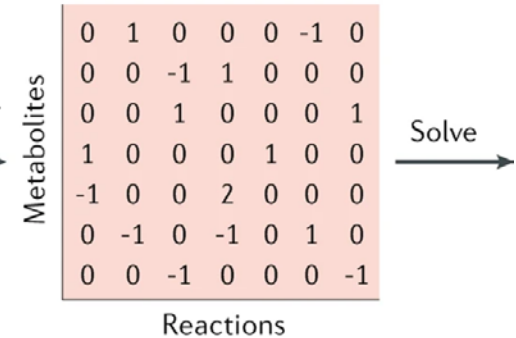
a Annotated genome



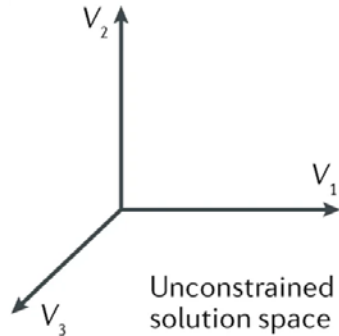
b Metabolic network



c S matrix

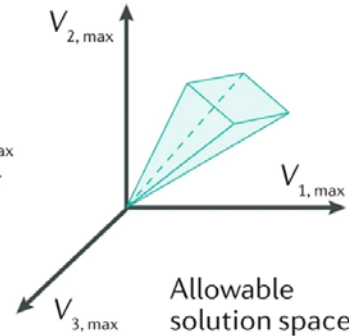


d



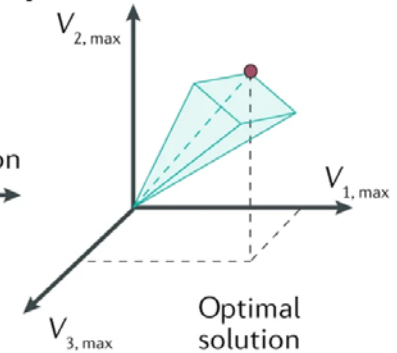
Constraints
1. Mass balance
2. $V_{i, \min} < V_i < V_{i, \max}$

e



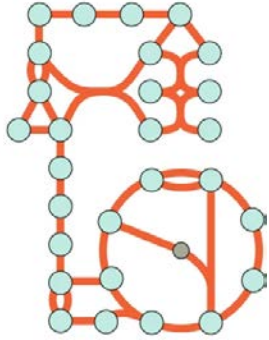
Optimization of
objective function

f

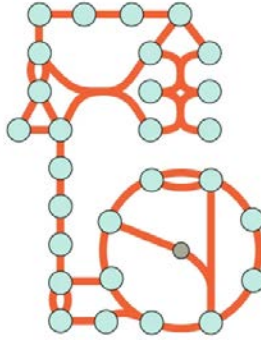


Observed differences in the generated models

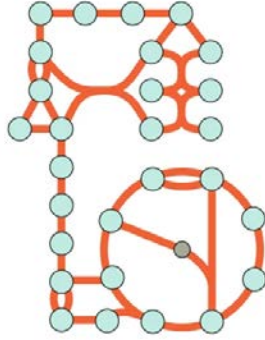
Sensitive



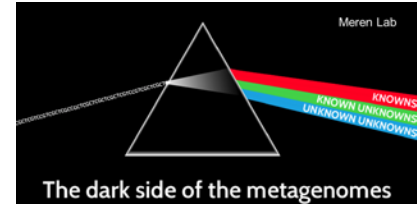
Tolerant



Resistant



Microbial dark matter



Gap filling



Genes linked with biocide metabolism

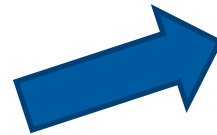
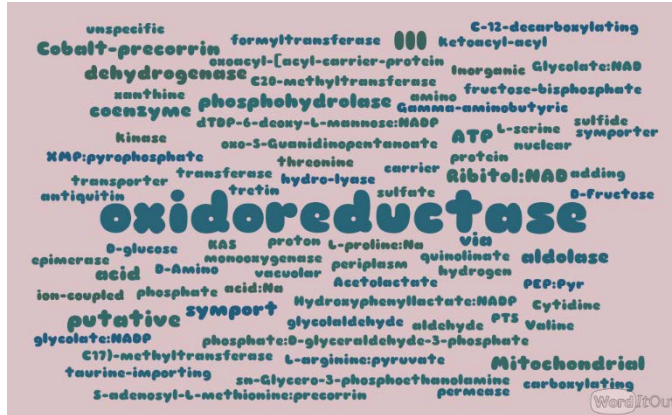


20 genes exclusive in the Resistant

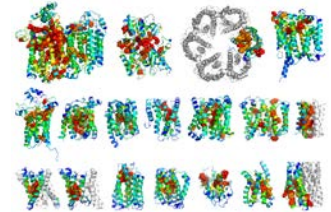
30 genes exclusive in the Sensitive or Tolerant

Testing hypothesis using transcriptomics and proteomics

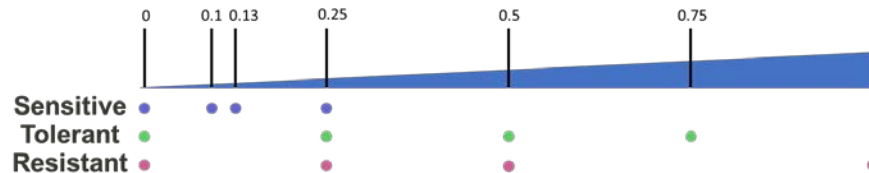
50 genes identified by our modelling approach



Proteomics



Transcriptomics



Why did our first round of proteomic analysis fail?

Measure 2.2 SOP Exp. Proc.

- Use of correct Protein extraction protocol
- Substances in the growth medium interfered with masspec analysis
- Use genomics and transcriptomics data to better predict protein masses to min masspec data



Transcriptomics output analysis

Measure 2.3 Workflow Std.

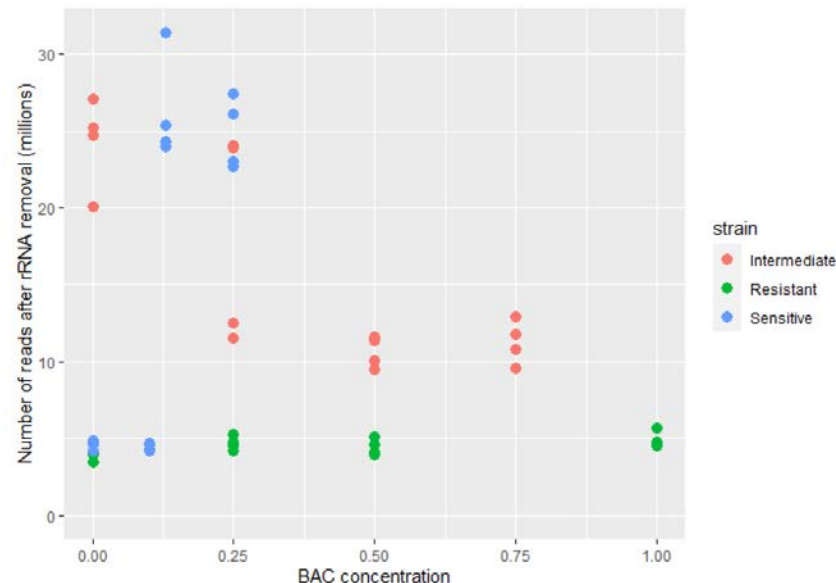
**rRNA depletion is
very important**

Low RNA yields

RNA extraction issues

Good RNA yields – fragmented RNA

RNA yield ok(ish) – RNA quality ok(ish)



Summary

