Search strategies for antimicrobial resistance associated genes

Data Science Workshop

Aug 7, 2018

Aram Avila-Herrera

LLNL-PRES-755360

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  - 20 billion per year in costs to US health care system [2]

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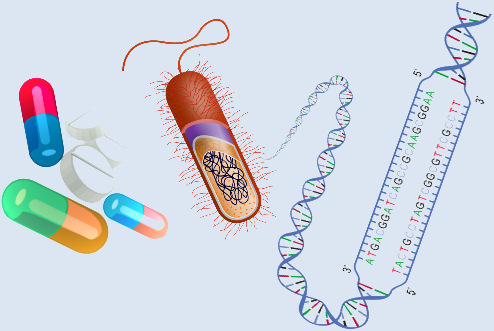

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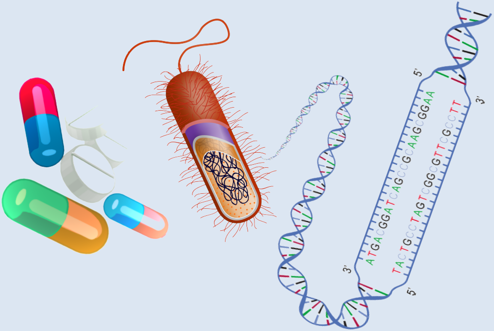

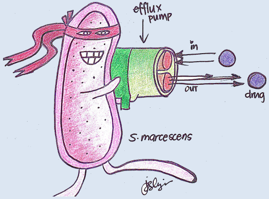

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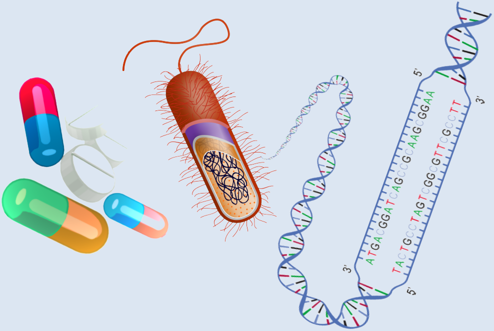

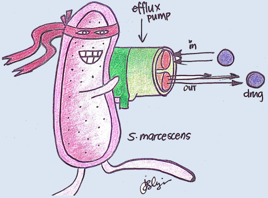

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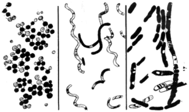
Detect these genes to:

- Prescribe the correct medicine, dosage
- Develop effective new drugs
- Learn about evolution

Gene detection: sequence and search



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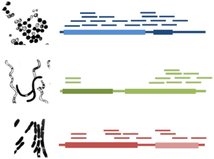

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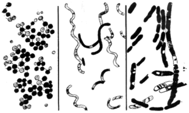

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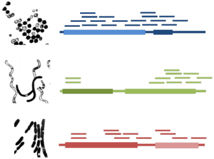

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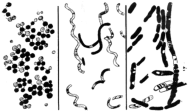

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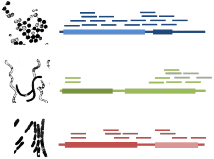

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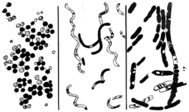

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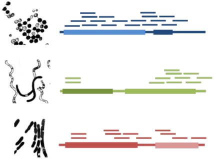

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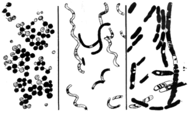

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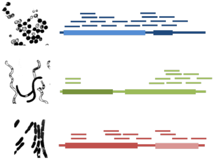

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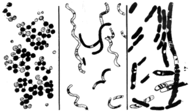

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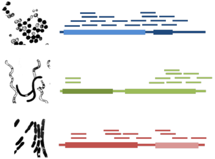

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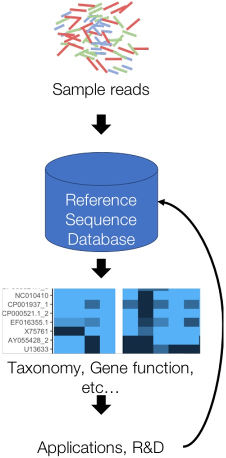

Sample reads

Reference Sequence Database

Taxonomy, Gene function, etc…

Applications, R&D

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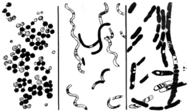

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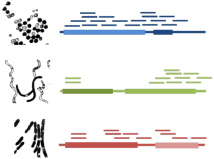

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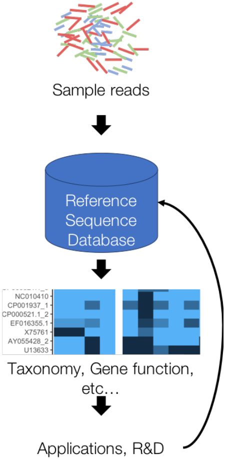

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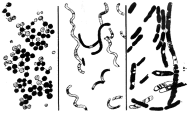

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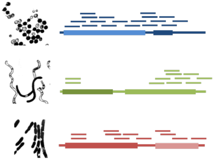

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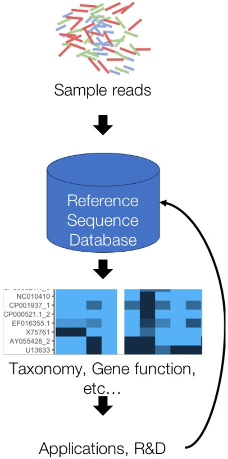

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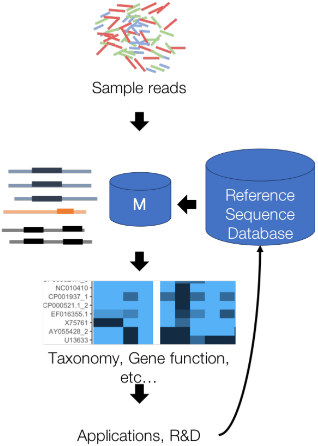
  - Reference DBs can be large, are regularly updated

ShortBRED: addresses reference database size



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Kaminski *et al.*, *PloS Comp Bio* 2015; (Huttenhower lab)

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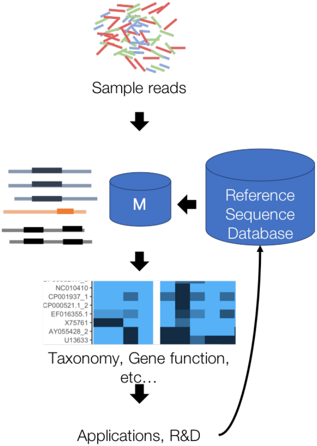

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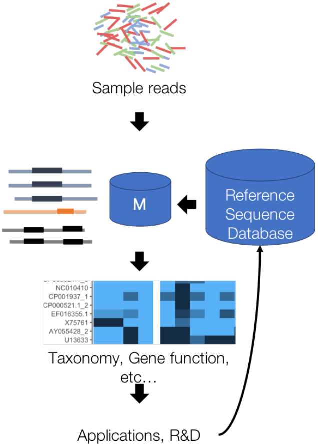

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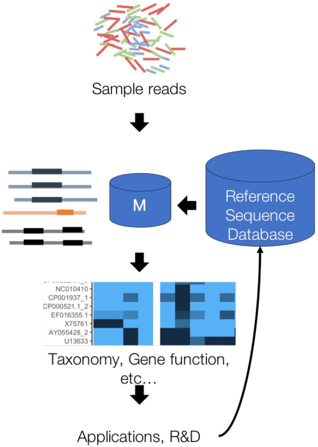

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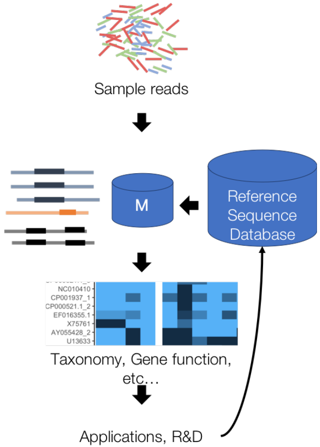

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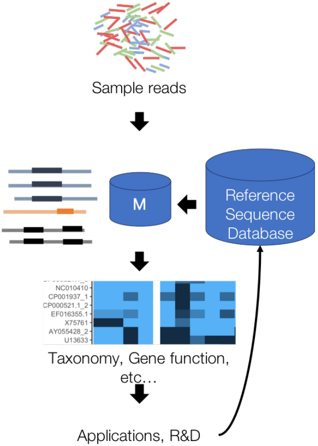

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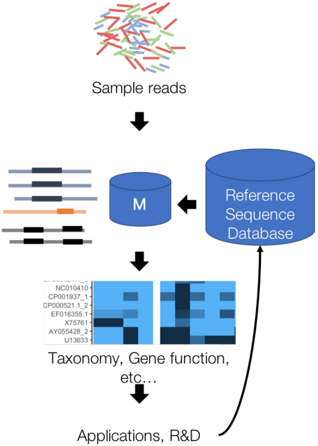

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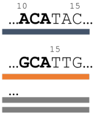
Our approach: De Bruijn graph based data structure

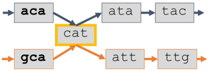
Antibiotic	Gene
Beta-lactam	G1
Erythromycin	G2
…	…

Resistance annotation



Gene sequences

⬌



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Expert curated reference

k-mer index for fast searching

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Pearce, Ames, Zemla, Allen

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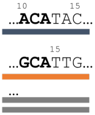

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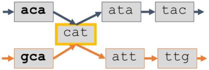

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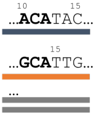

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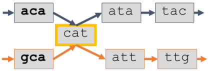

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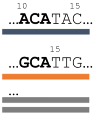

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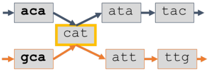

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- Eventually: add ML-based signatures, multiple encodings (ARmo)

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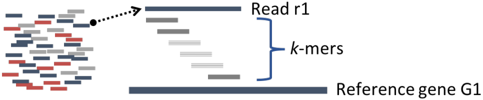
Gene scoring: Maximum exact match lengths as weights



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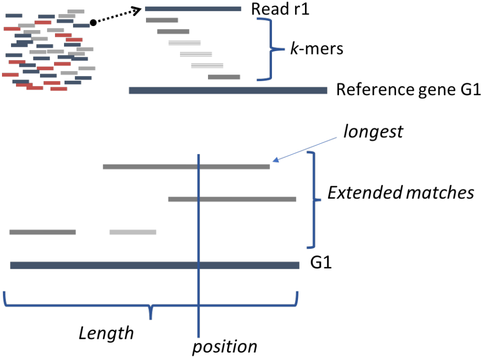

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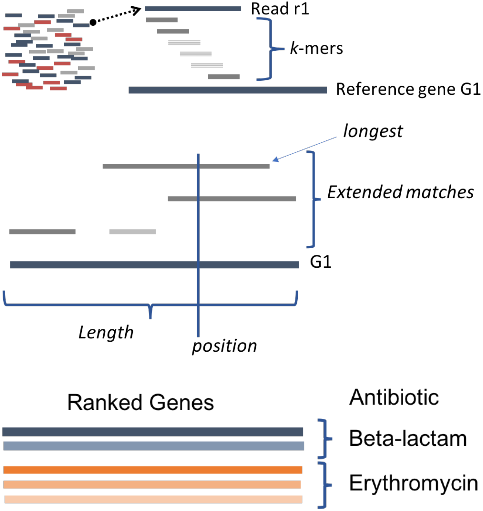

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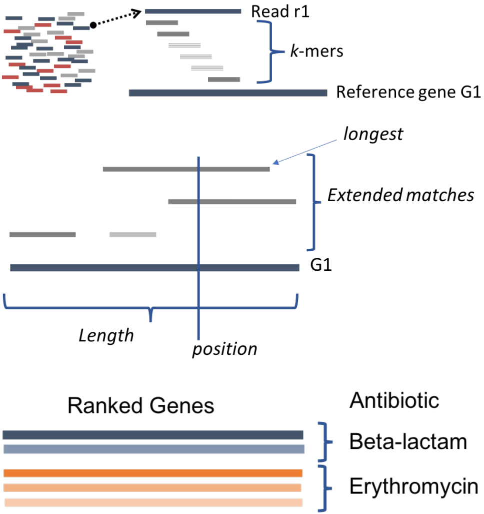

Aggregate gene scores by antibiotic

Antibiotic	Score
Beta-lactam	1.00
Erythromycin	0.88
…	…

Predicting AMR presence and drug class: preliminary results

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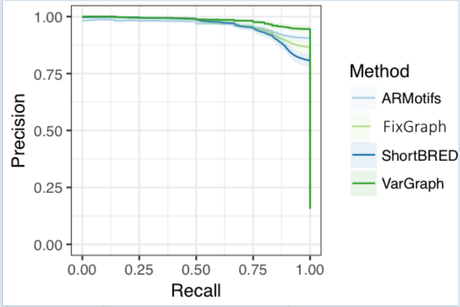

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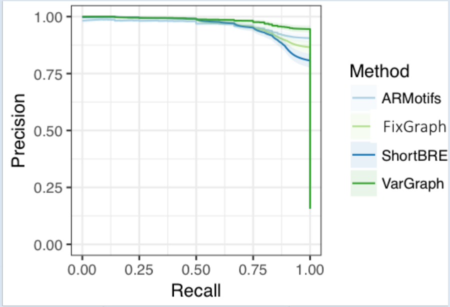
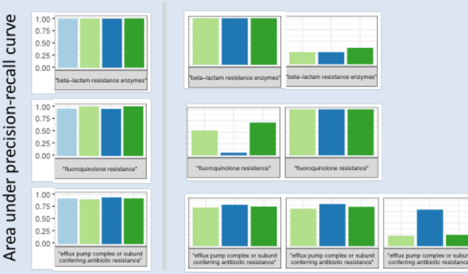


(proportion detected)

AMR drug class



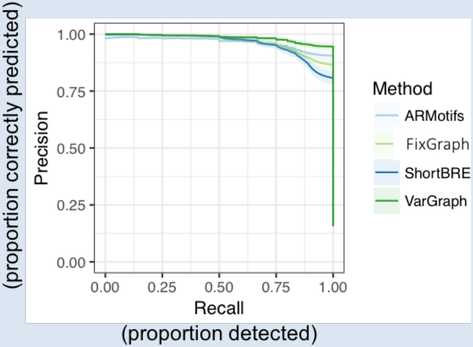
Broadly defined → Narrowly defined

Avila-Herrera, Pearce, Ames, Zemla, Allen, *manuscript in prep*

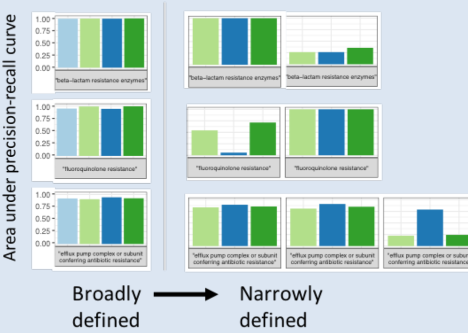
Predicting AMR presence and drug class: preliminary results

- Simulated 500 samples with AMR to multiple drug classes

AMR presence-absence



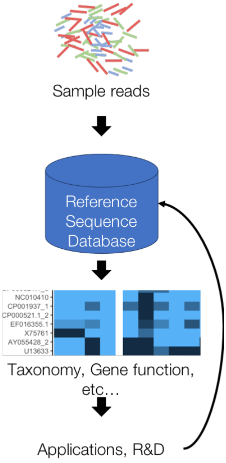
AMR drug class



Avila-Herrera, Pearce, Ames, Zemla, Allen, *manuscript in prep*

- `//TODO: larger standard data set, test scoring functions`

Search tools are critical in modern molecular biology



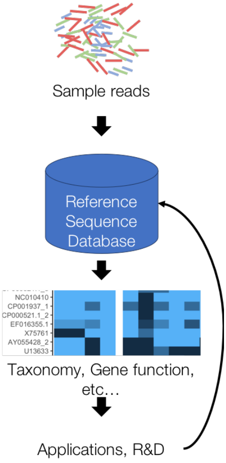
Sample reads

Reference Sequence Database

Taxonomy, Gene function, etc…

Applications, R&D

Search tools are critical in modern molecular biology



Sample reads

Reference Sequence Database

Taxonomy, Gene function, etc…

Applications, R&D

Goal: release tool to compbio community

- Accelerate basic research
- Enable continuous biosurveillance of AMR crisis
- Work towards timely precision medical diagnostics

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Related AMR projects

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- Crystal Jaing
- Tom Slezak

Fin

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