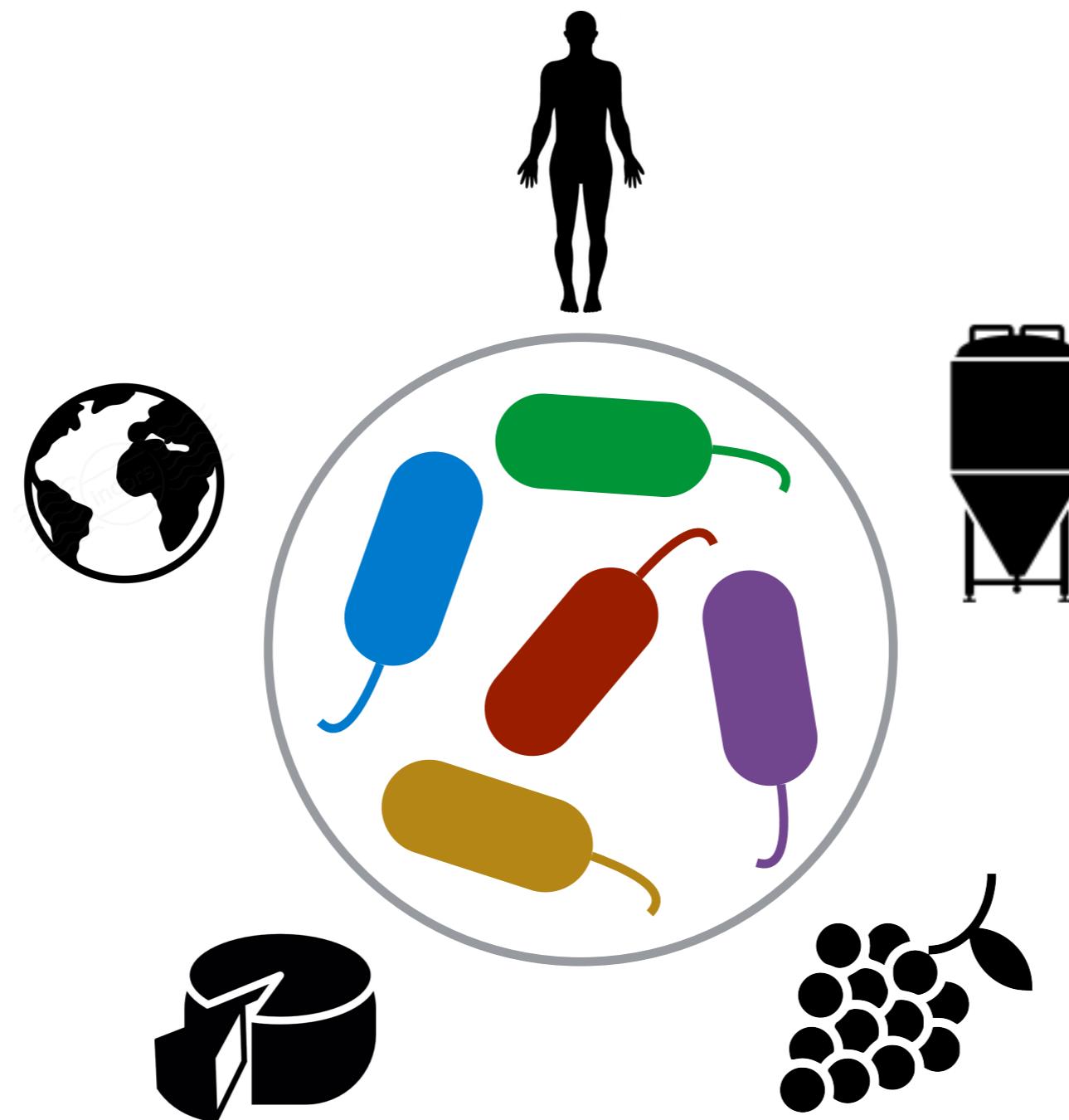
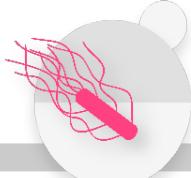


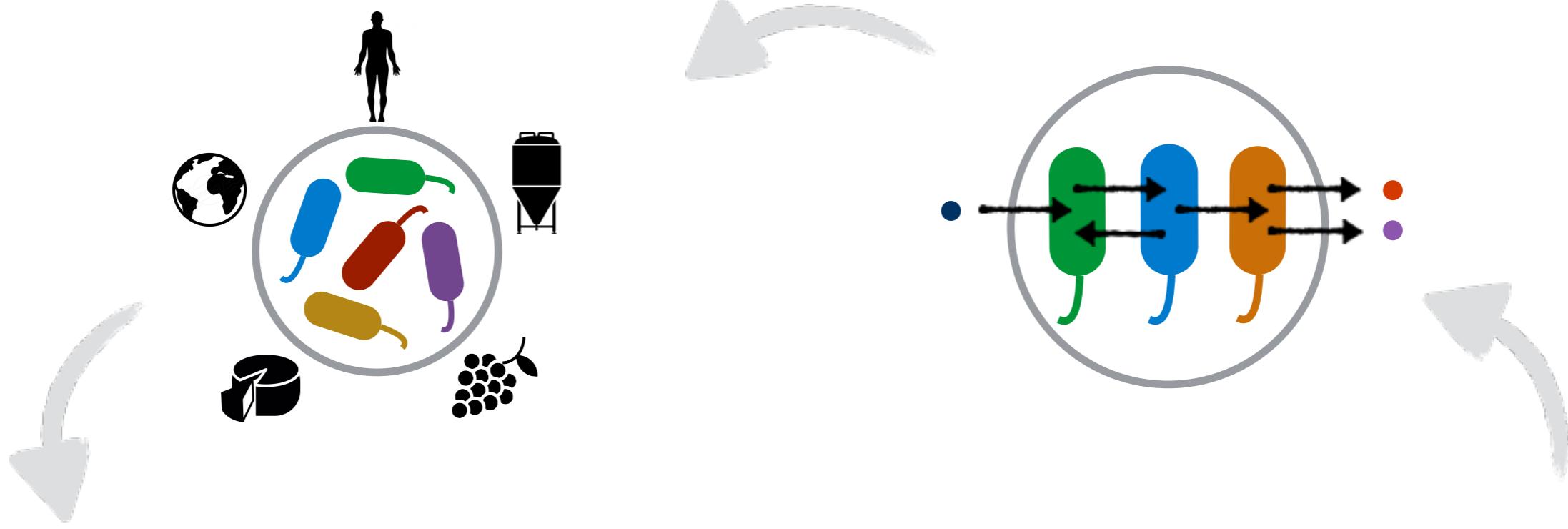
Microbial community modeling

Daniel Machado, Sergej Andrejev
EMBL

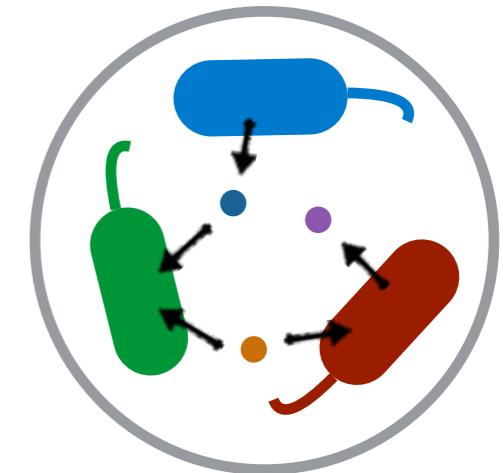
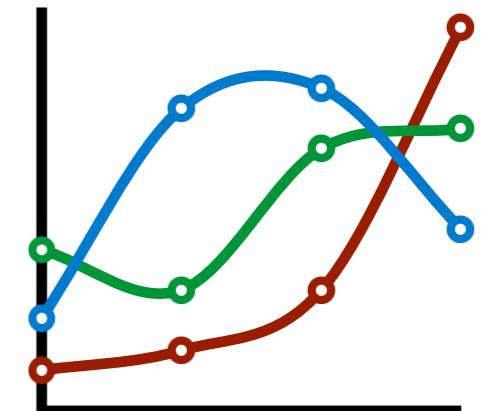
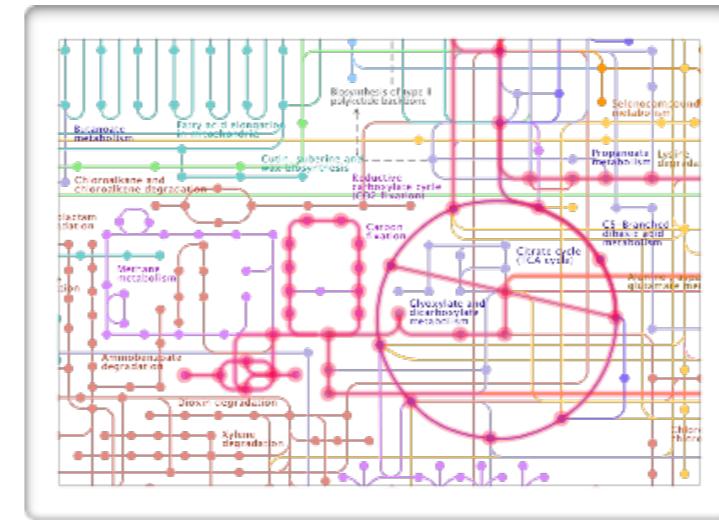
13-SEP-2017

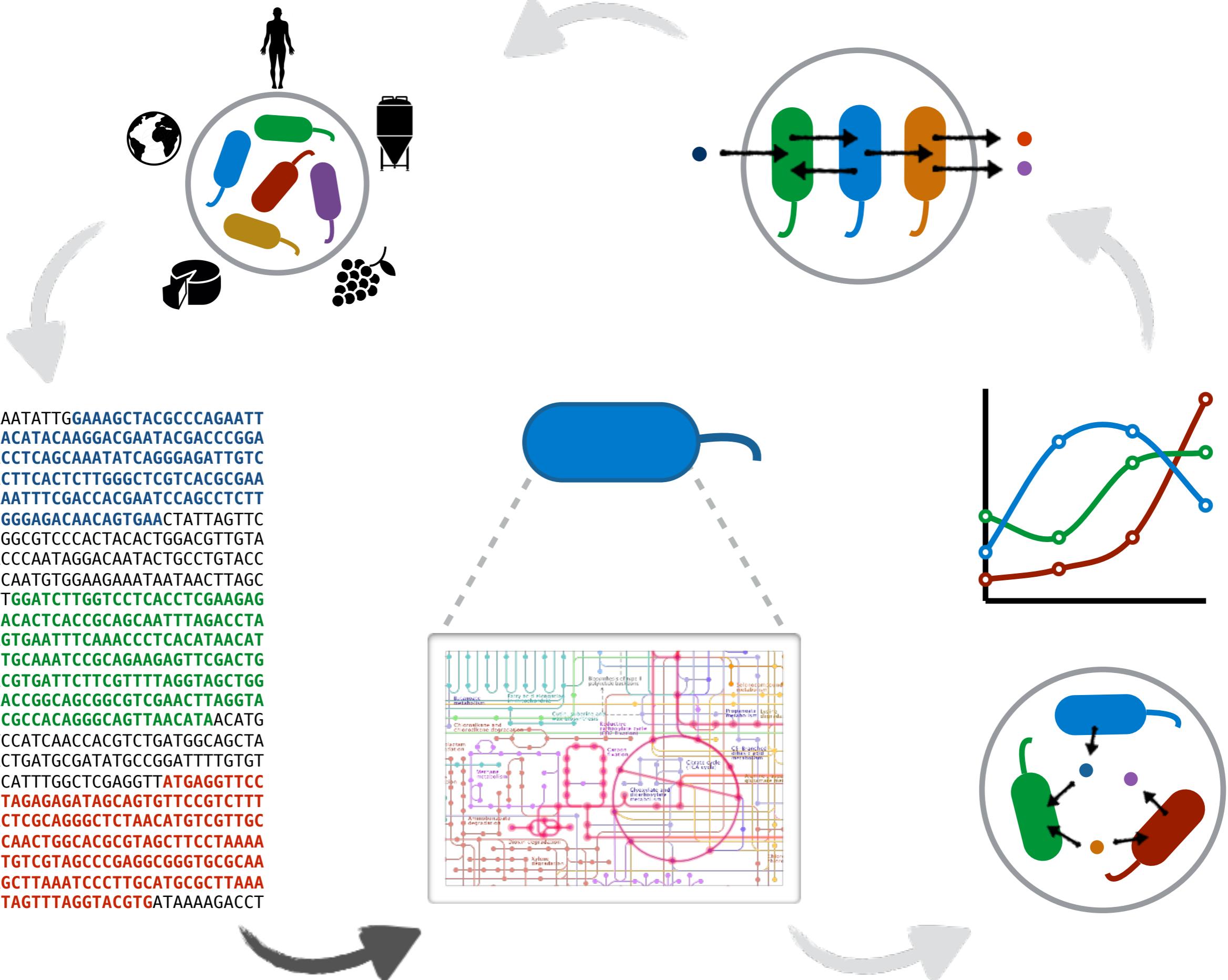
DSM Rosalind Franklin Biotechnology Center
Delft, The Netherlands

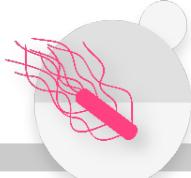




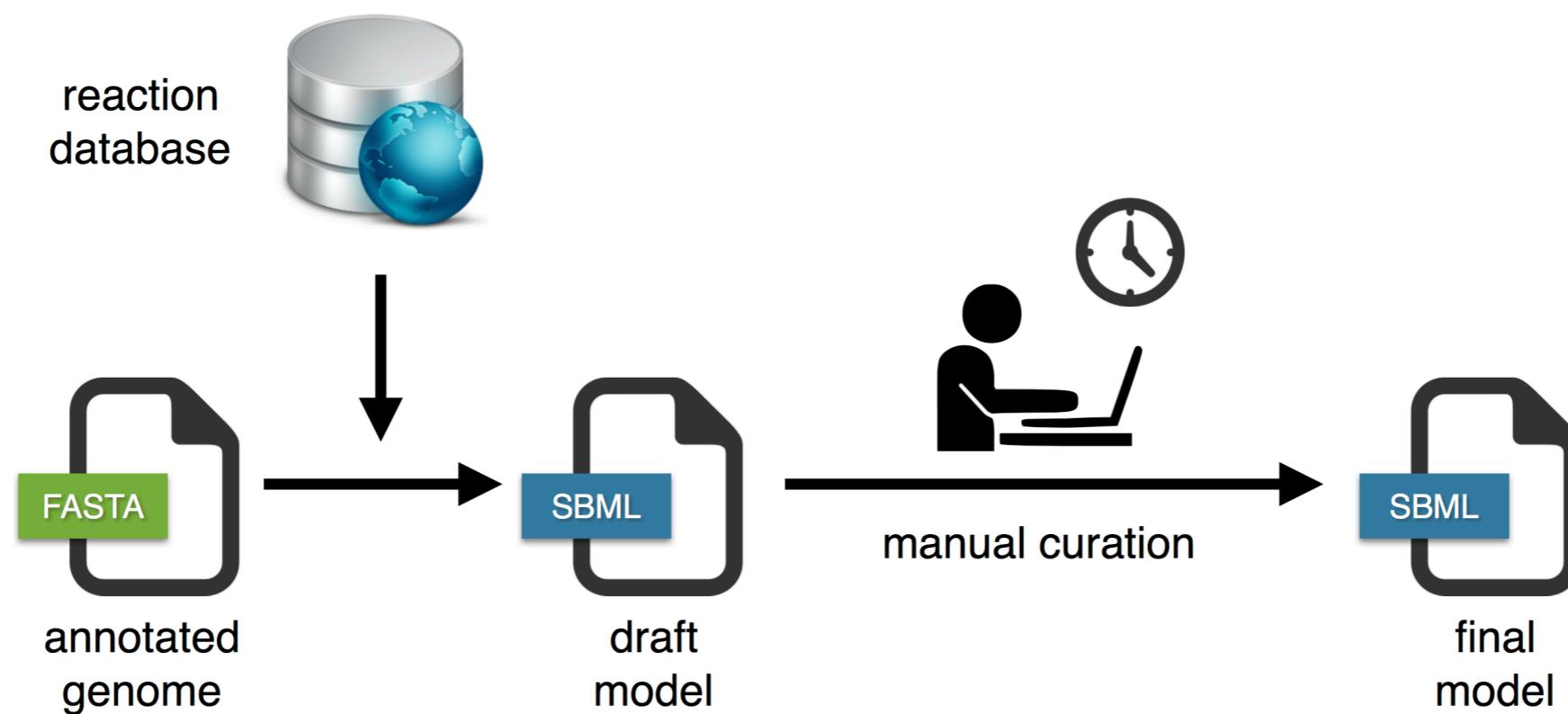
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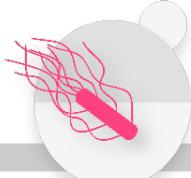




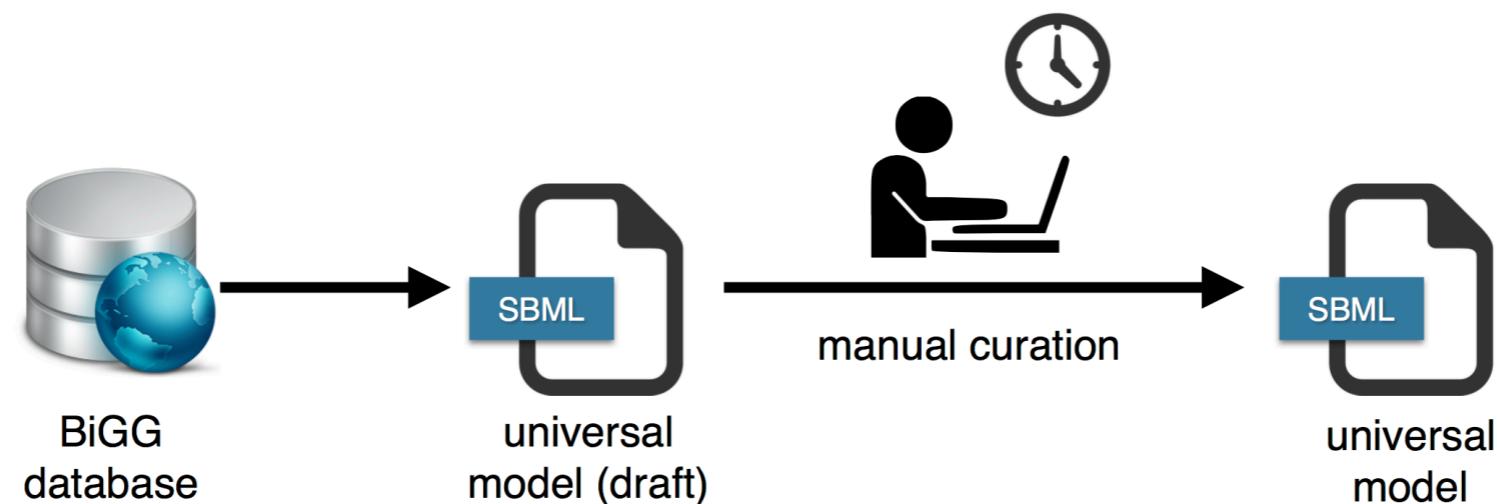


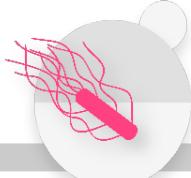
Genome-scale reconstruction (bottom-up)



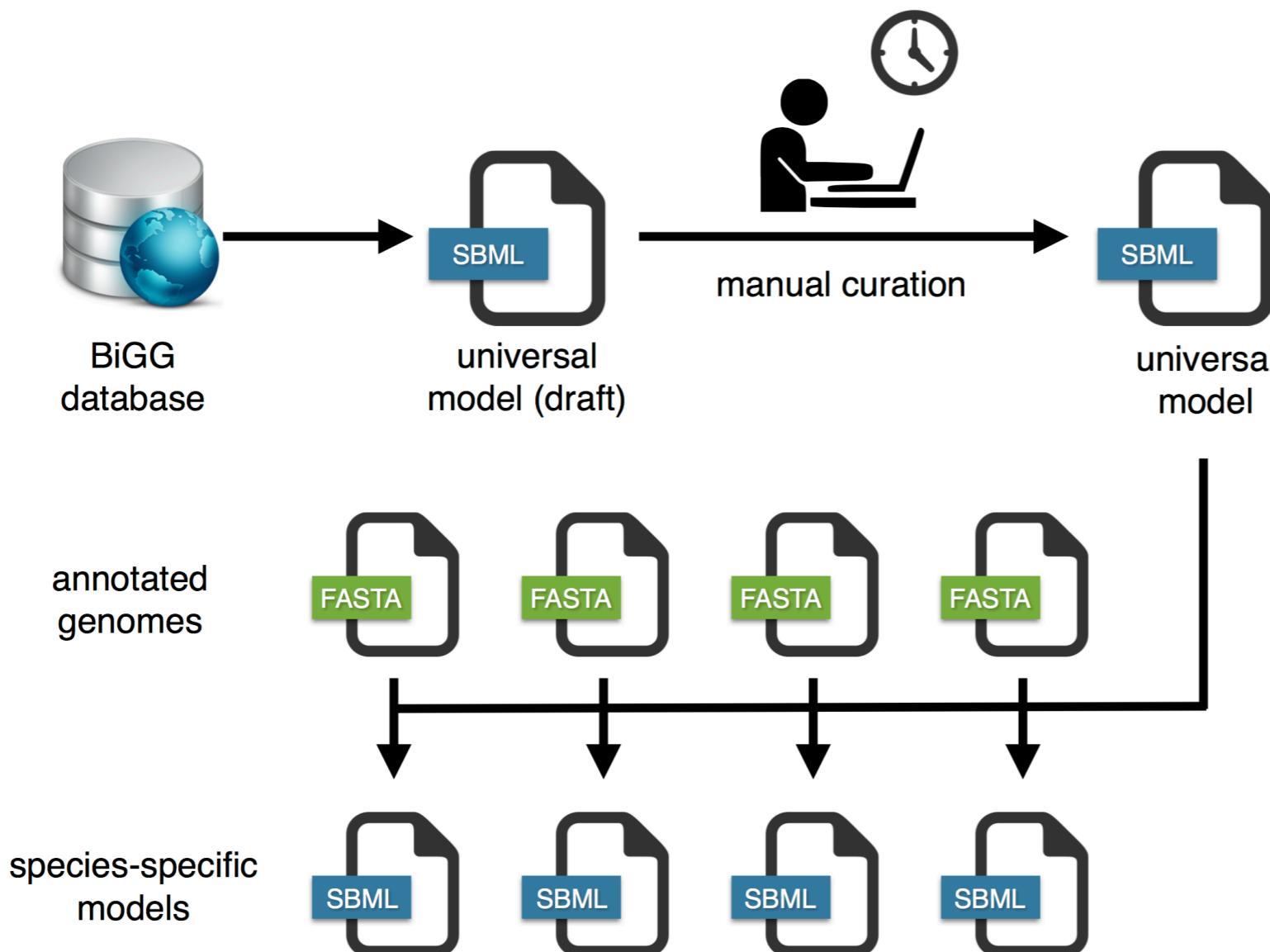


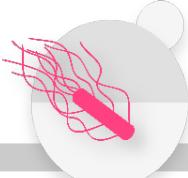
Genome-scale reconstruction (top-down)





Genome-scale reconstruction (top-down)





Universal model

BiGG database:

- Built from curated models
- Human readable identifiers
- Gene-protein-reaction associations
- Reaction compartments

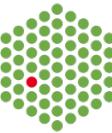
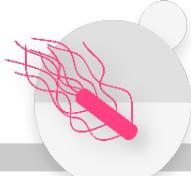


<http://bigg.ucsd.edu>

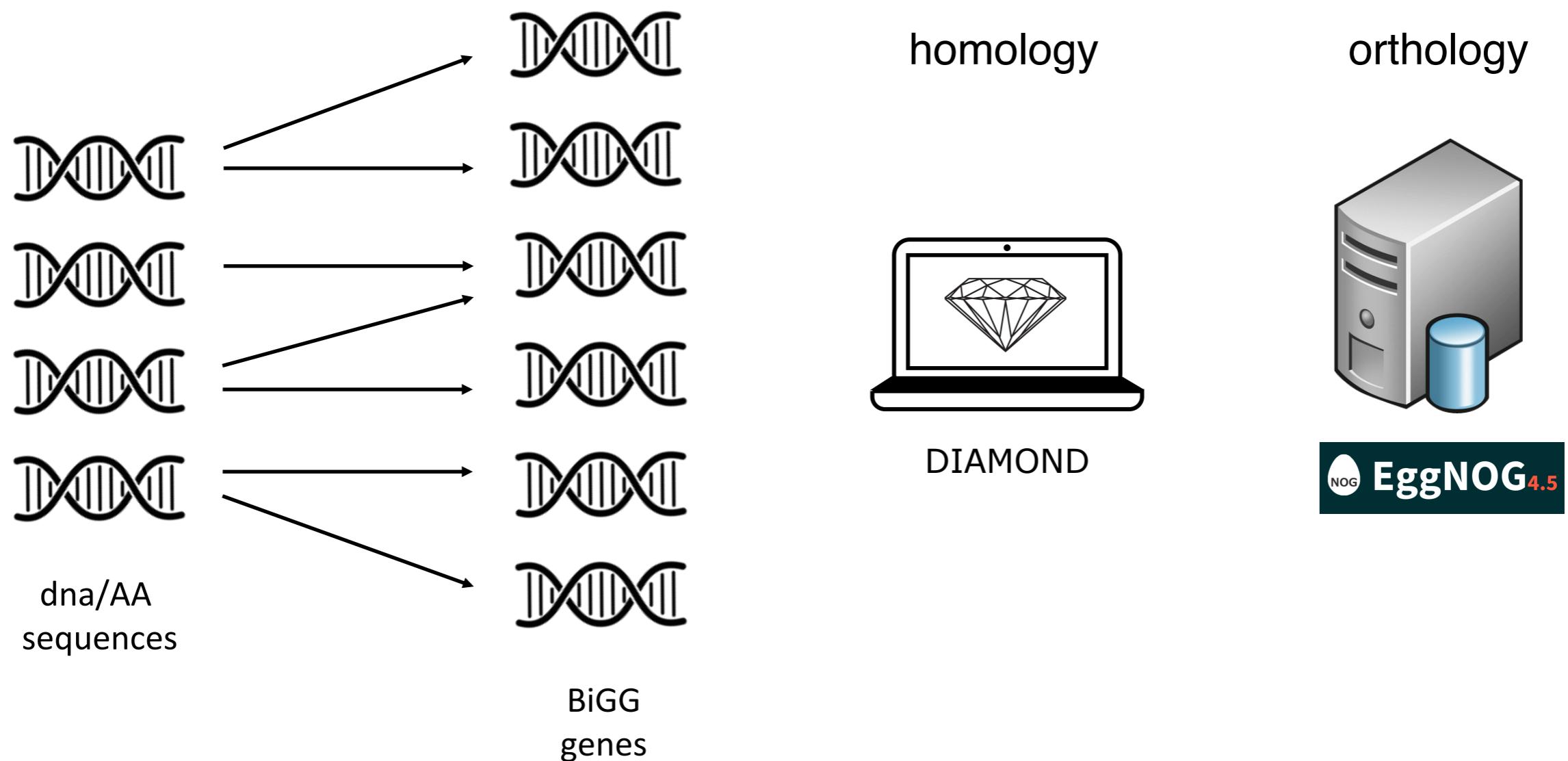
Manual curation:

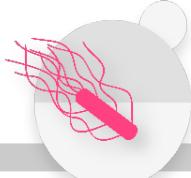
- Reaction balance
- Thermodynamics
- Futile cycles, blocked reactions
- Core biomass composition



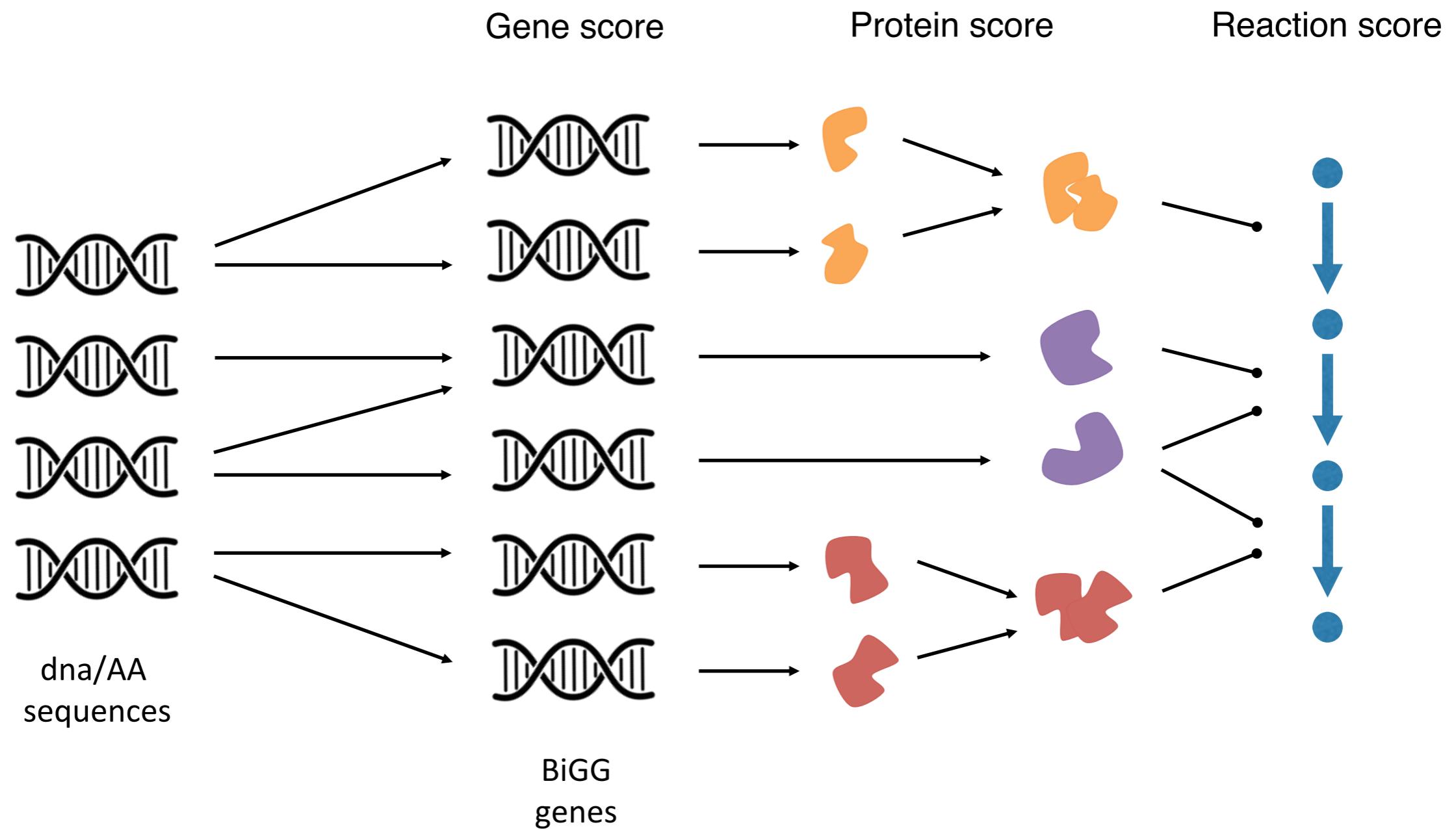


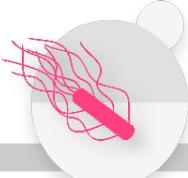
Gene annotation





Reaction scoring





Model carving

$$\max w^T(y^f + y^r)$$

s.t.

$$S \cdot v = 0$$

$$v > -My^r + \varepsilon y^f$$

$$v < -\varepsilon y^r + My^f$$

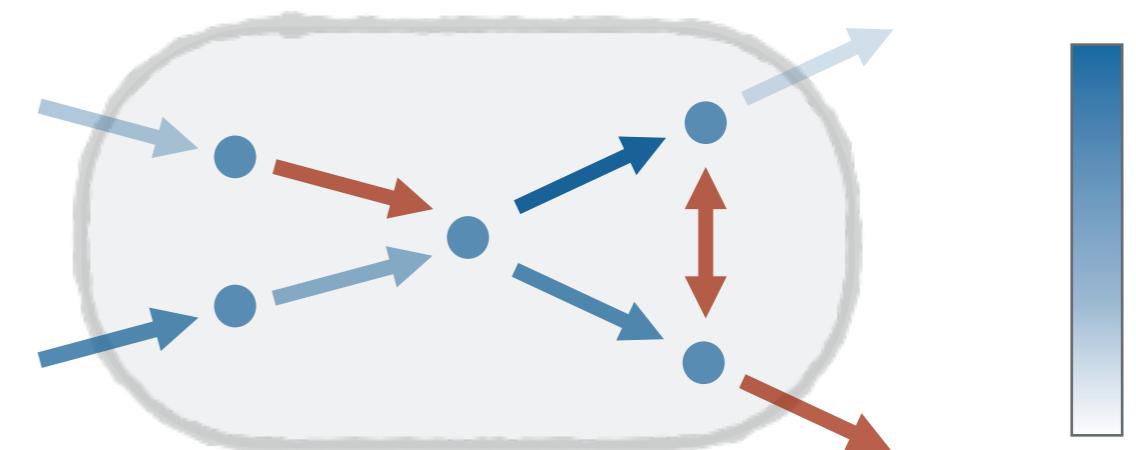
$$v_i > 0 \quad \forall i \in \{\text{forward irrev}\}$$

$$v_i < 0 \quad \forall i \in \{\text{backward irrev}\}$$

$$y^r + y^f \leq 1$$

$$y^r, y^f \in \{0, 1\}^n$$

$$v_{\text{growth}} > v_{\text{growth}}^{\min}$$





Model carving

$$\max w^T(y^f + y^r)$$

s.t.

$$S \cdot v = 0$$

$$v > -My^r + \varepsilon y^f$$

$$v < -\varepsilon y^r + My^f$$

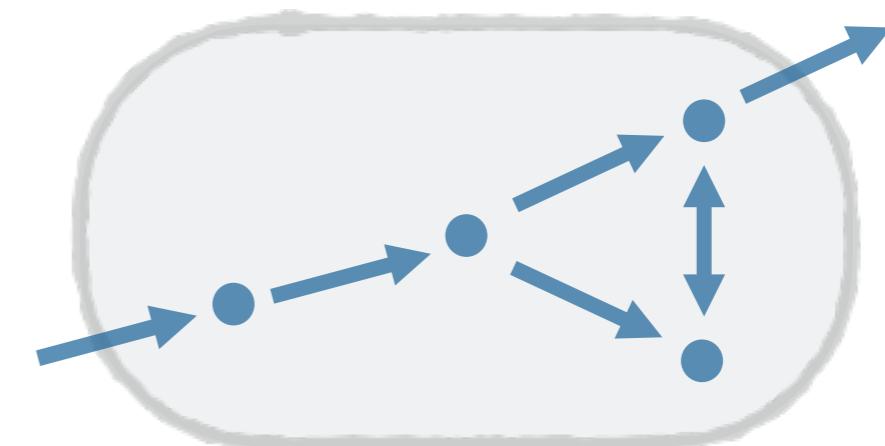
$$v_i > 0 \quad \forall i \in \{\text{forward irrev}\}$$

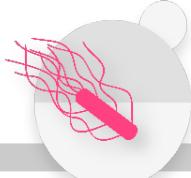
$$v_i < 0 \quad \forall i \in \{\text{backward irrev}\}$$

$$y^r + y^f \leq 1$$

$$y^r, y^f \in \{0, 1\}^n$$

$$v_{\text{growth}} > v_{\text{growth}}^{\min}$$





Installation

As simple as...

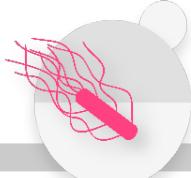
```
> pip install carveme
```

```
> carveme_init
```

Note:

IBM CPLEX Solver (academic license) must be previously installed.





Usage examples

Build from a (protein) fasta file:

```
> carve genome.faa -o model.xml
```

Build from DNA fasta file:

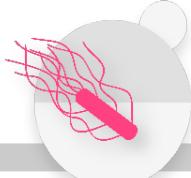
```
> carve --dna genome.fna -o model.xml
```

Build from RefSeq or GenBank accession code:

```
> carve --refseq GCF_000005845.2
```

```
> carve --genbank GCA_000005845.2
```





Usage examples

Build model and gapfill for given media:

```
> carve genome.faa --gapfill M9,LB
```

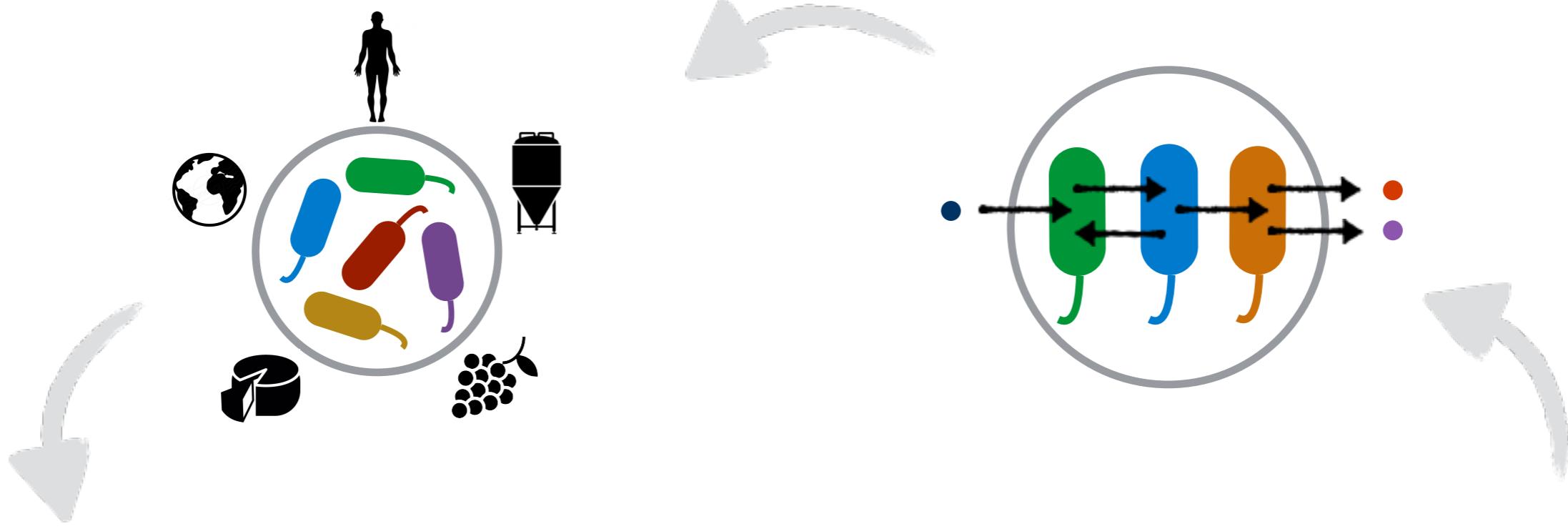
Run in parallel mode:

```
> carve -r folder/*.faa
```

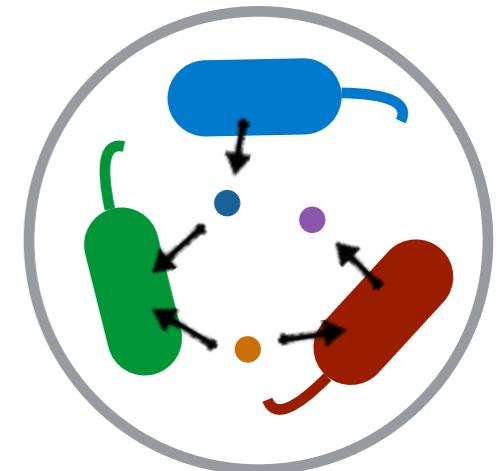
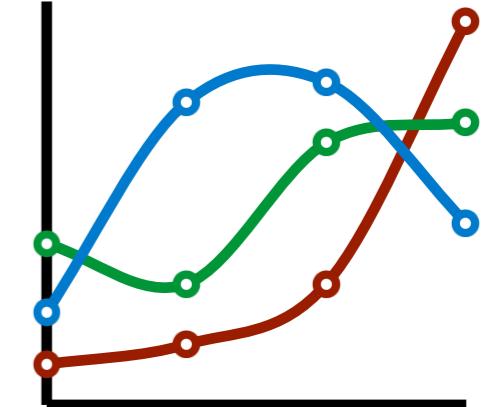
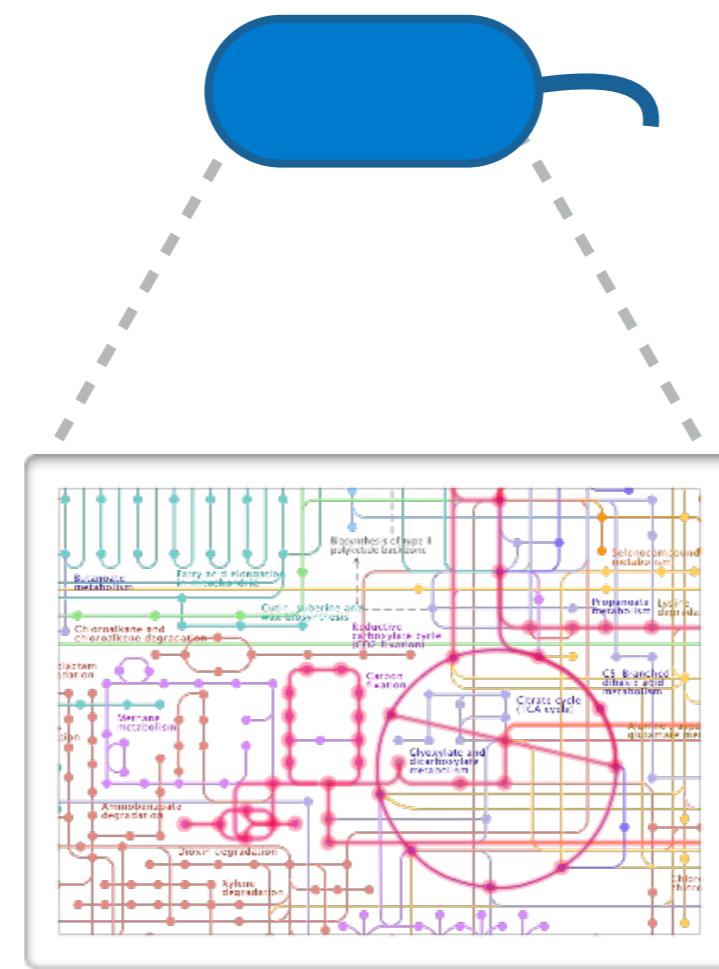
Use a different universe model:

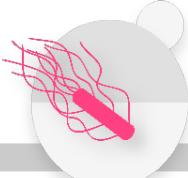
```
> carve genome.faa -u gram_positive.xml
```





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 TGTTCCATCAACCACGTCTGATGGCAGCTA
 CAGACTGATGCGATATGCCGGATTTGTGT
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 CAACTTAGCTTAAATCCCTGCATGCGCTTAAA
TCGGTAGTTAGGTACGTGATAAAAGACCT





Predicting community interactions: SMETANA

Metabolic dependencies drive species co-occurrence in diverse microbial communities

Aleksej Zelezniak¹, Sergej Andrejev¹, Olga Ponomarova¹, Daniel R. Mende, Peer Bork, and Kiran Raosaheb Patil²

Structural and Computational Biology Unit, European Molecular Biology Laboratory, 69117 Heidelberg, Germany

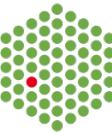
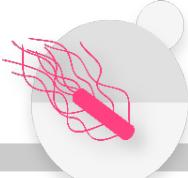
Edited by Philip P. Green, University of Washington School of Medicine, Seattle, WA, and approved April 2, 2015 (received for review November 14, 2014)

Microbial communities populate most environments on earth and play a critical role in ecology and human health. Their composition is thought to be largely shaped by interspecies competition for the available resources, but cooperative interactions, such as metabolite exchanges, have also been implicated in community assembly. The prevalence of metabolic interactions in microbial communities, however, has remained largely unknown. Here, we systematically survey, by using a genome-scale metabolic modeling approach, the extent of resource competition and metabolic exchanges in over 800

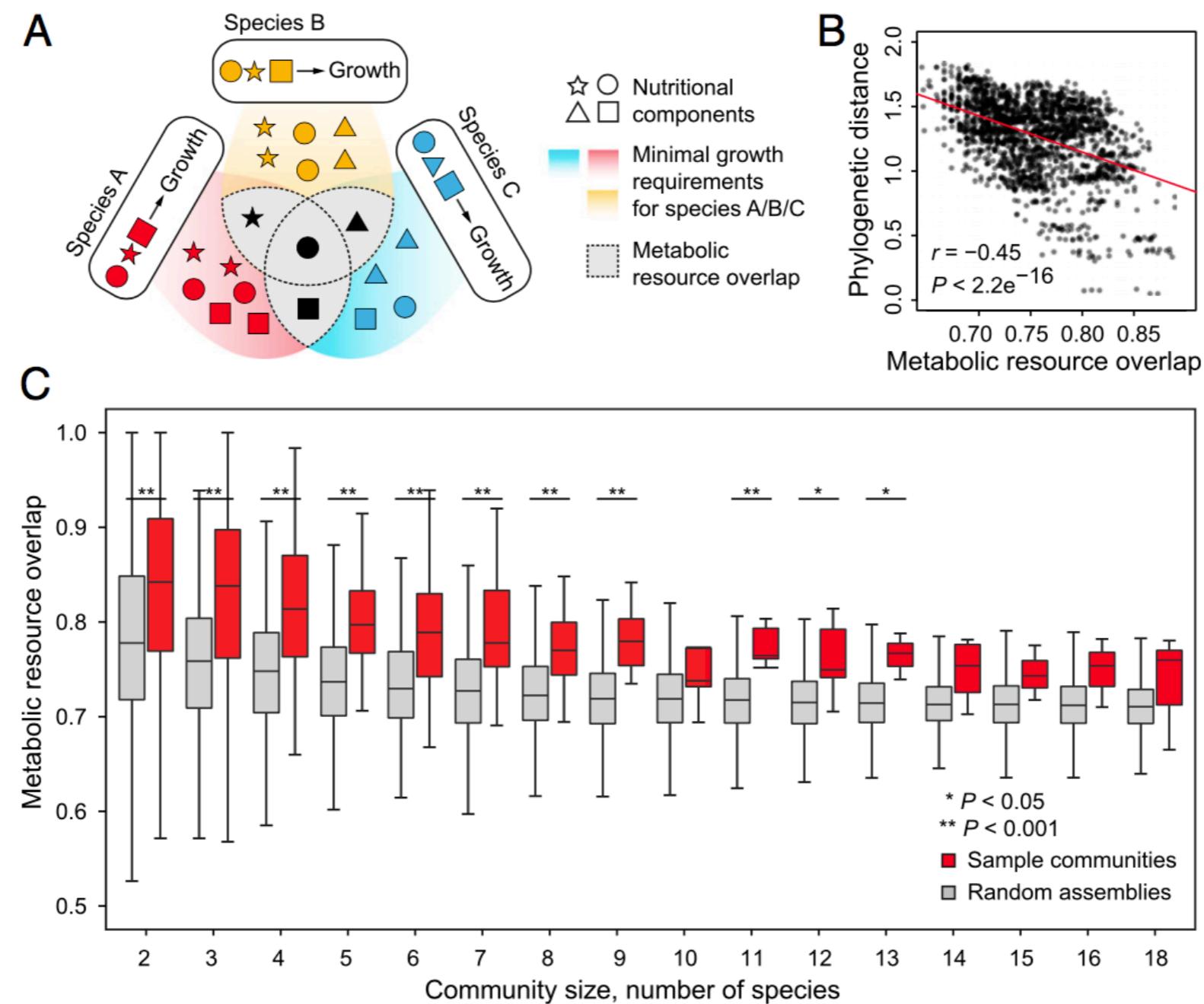
The methodology thus provides an unbiased estimate of the metabolic interaction potential of a community as well as identifies likely exchanged metabolites. We used this approach to interrogate over 800 microbial communities and co-occurring subcommunities therein. To capture interacting species modules beyond pairs, we also considered subcommunities with simultaneous co-occurrence of up to four species. Our results highlight metabolic dependencies as a key biotic force shaping the composition of diverse microbial communities in nature.

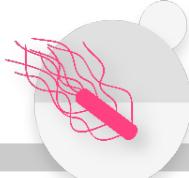
NAS





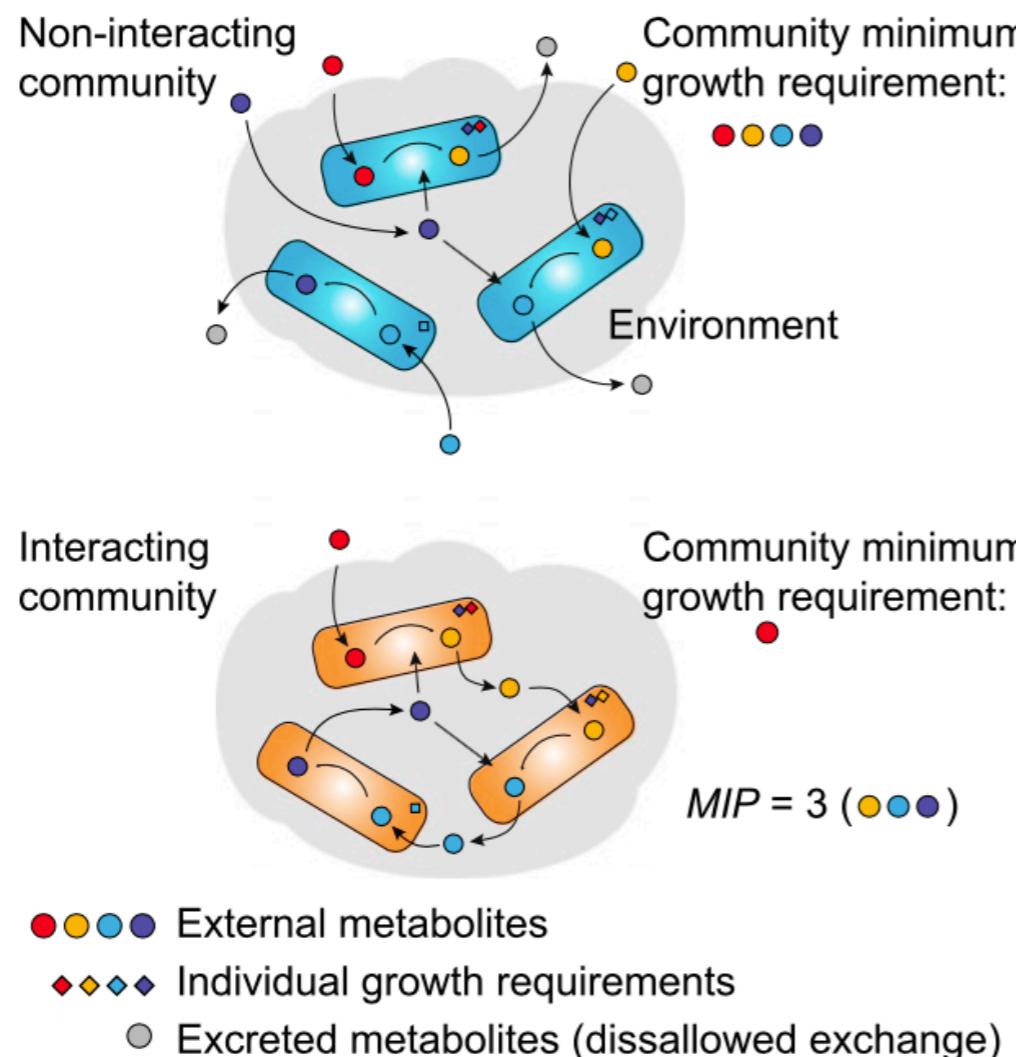
Metabolic Resource Overlap (MRO)



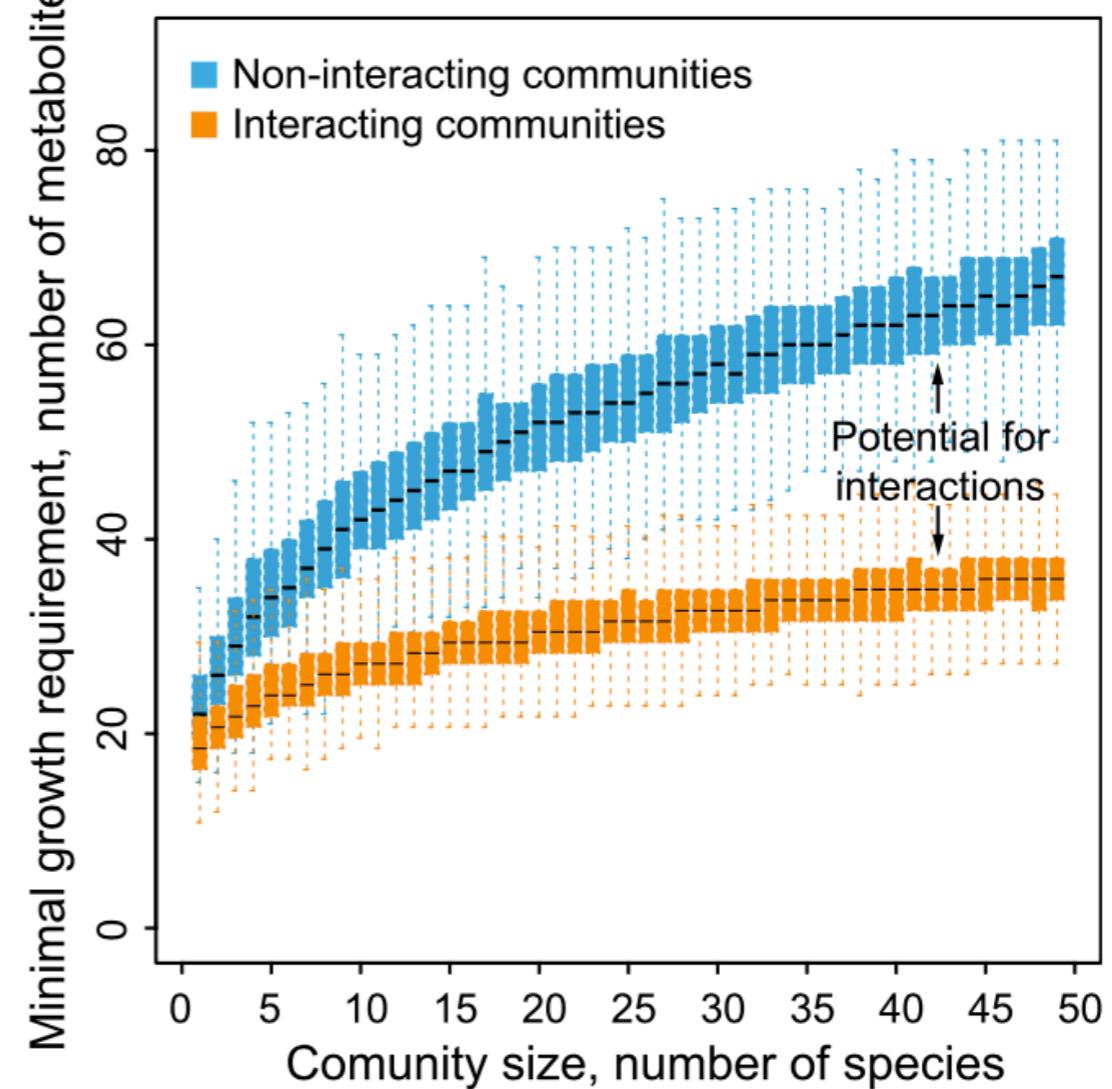


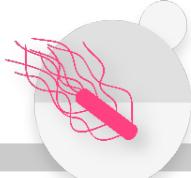
Metabolic Interaction Potential (MIP)

A



B





Installation and usage

Installation as simple as...

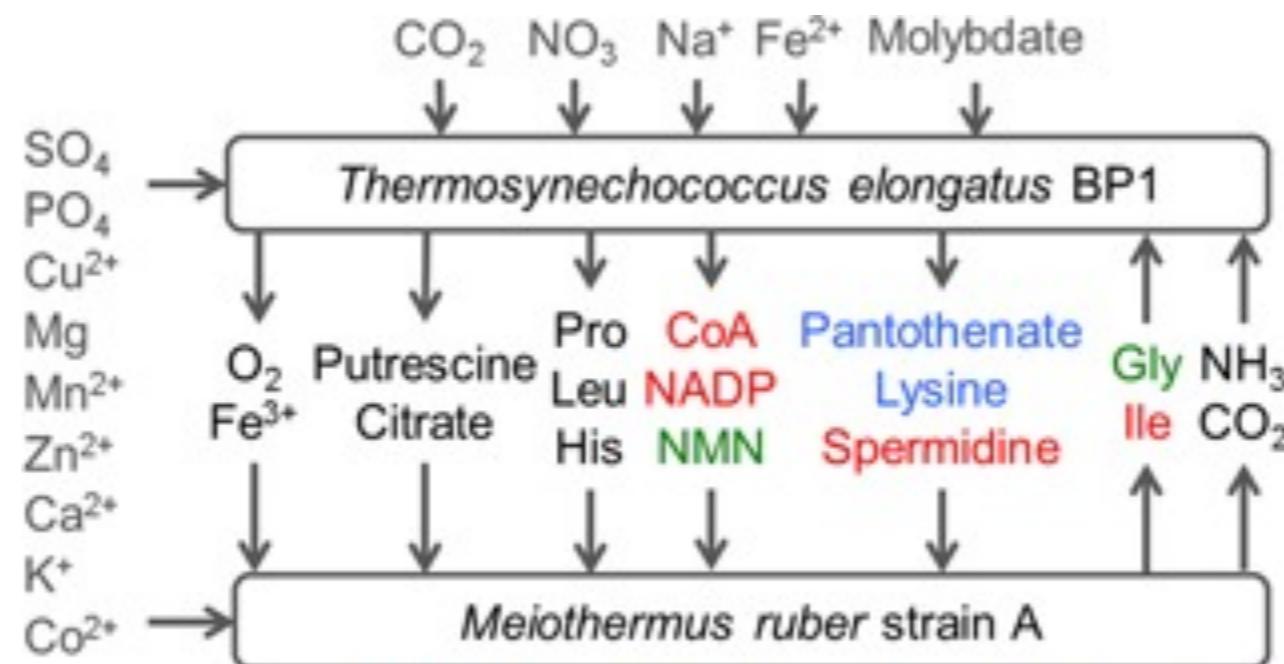
```
> pip install framed
```

Usage example

```
> framed-smetana-pipeline config.cfg output.tsv
```



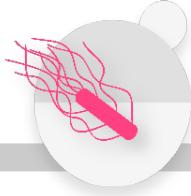
Case study: Photoautotroph–heterotroph



Henry CS. et al, Microbial Community Metabolic Modeling: A Community Data-Driven Network Reconstruction (2016)



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 686070



Thank you for your attention!

