

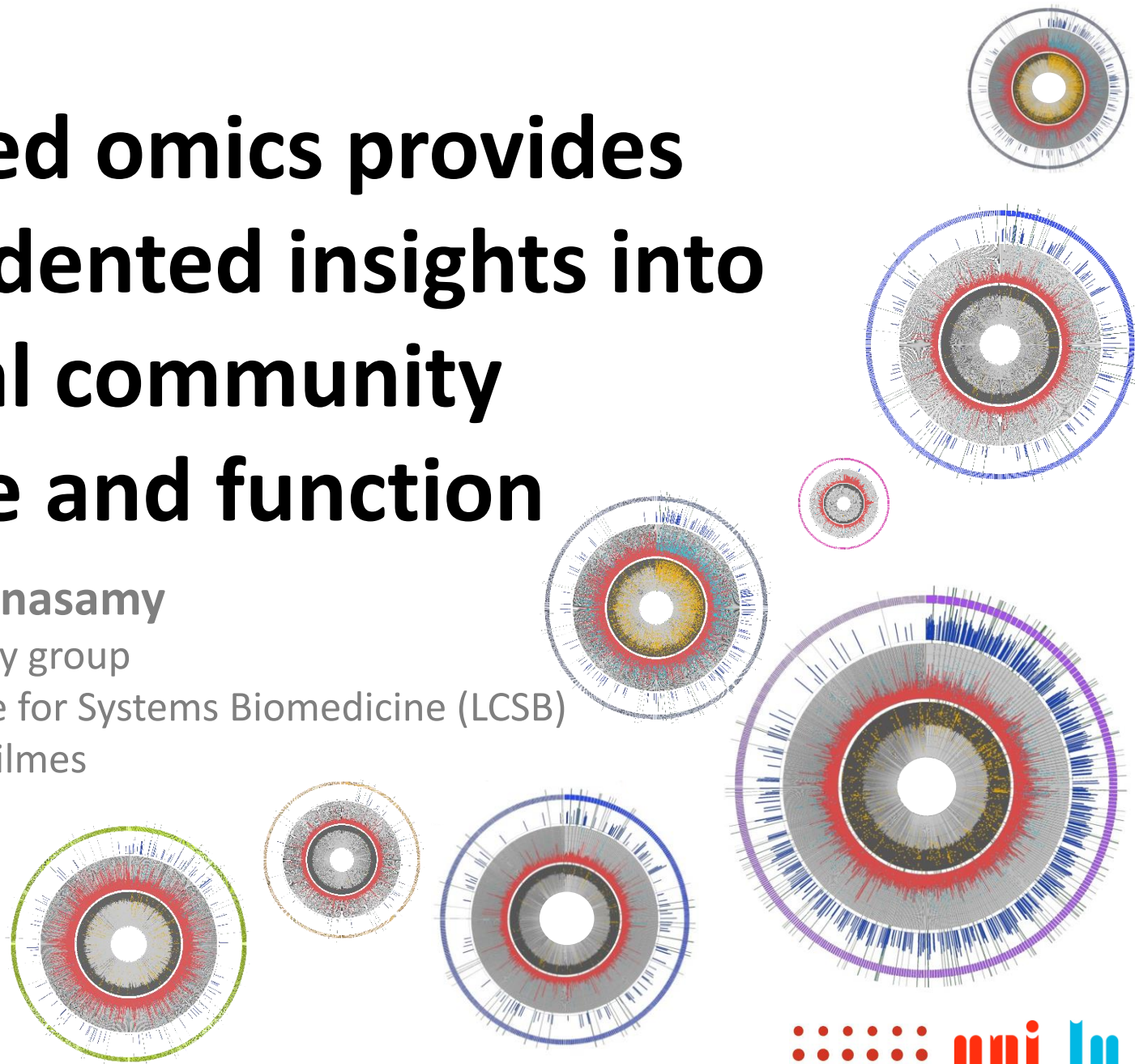
# Integrated omics provides unprecedented insights into microbial community structure and function

Shaman Narayanasamy

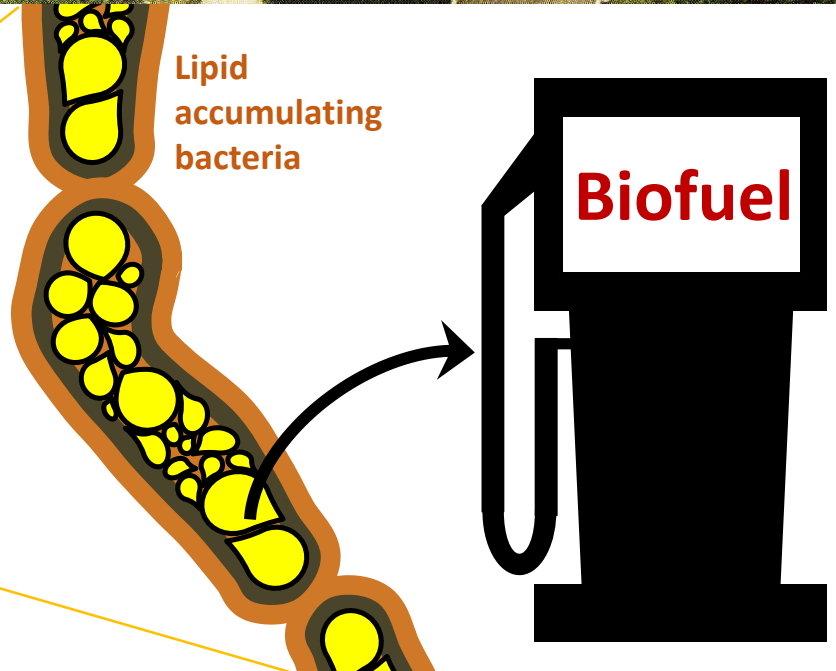
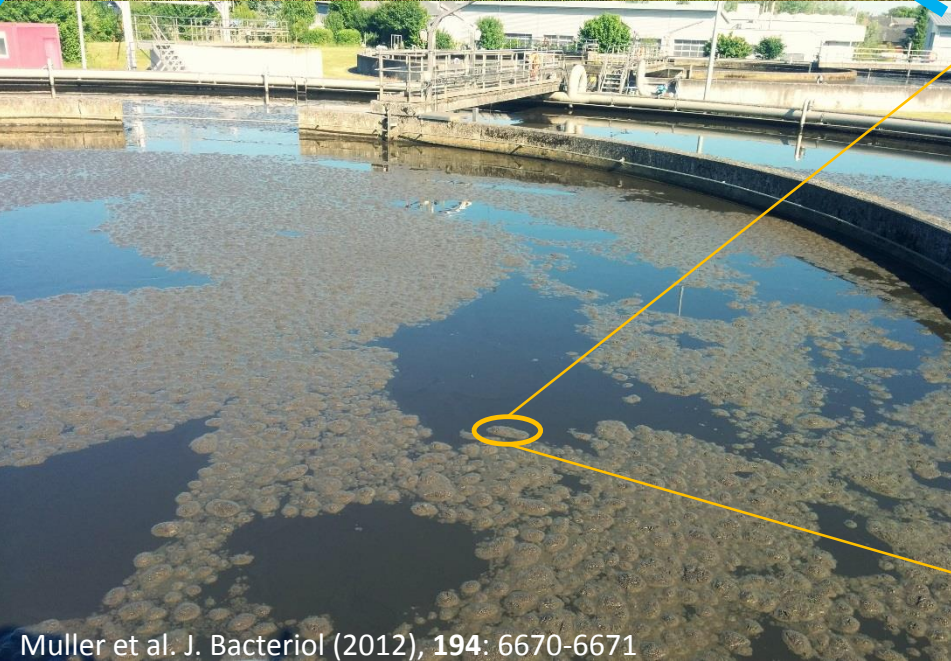
Eco-Systems Biology group

Luxembourg Centre for Systems Biomedicine (LCSB)

Supervisor: Paul Wilmes



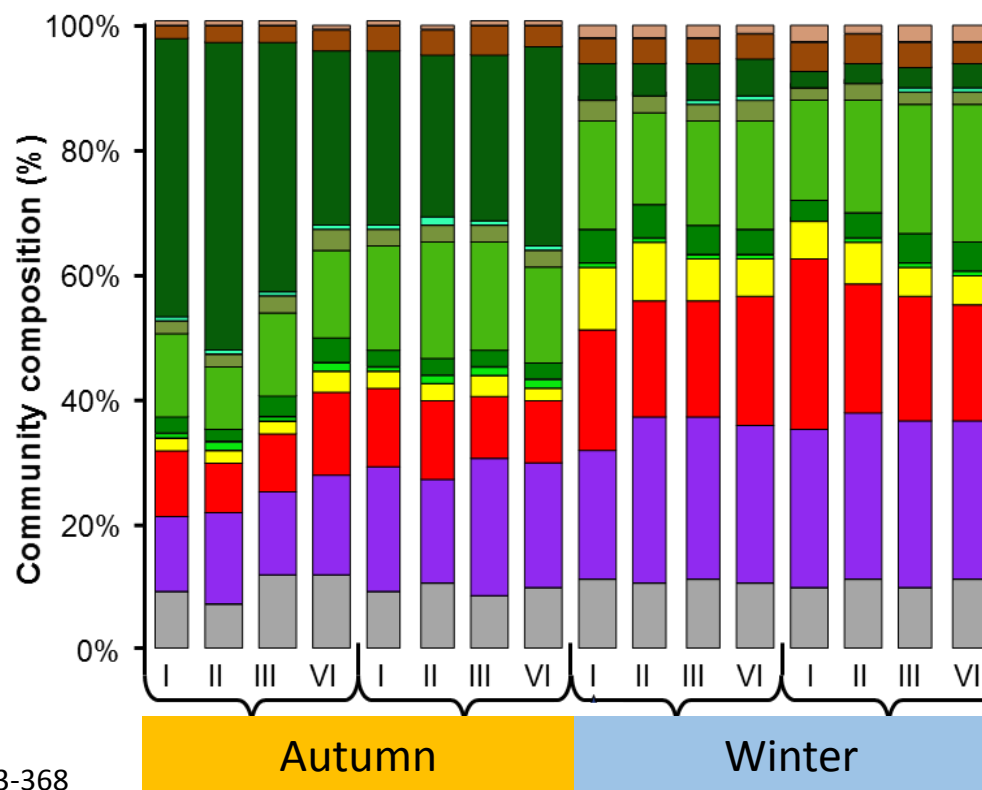
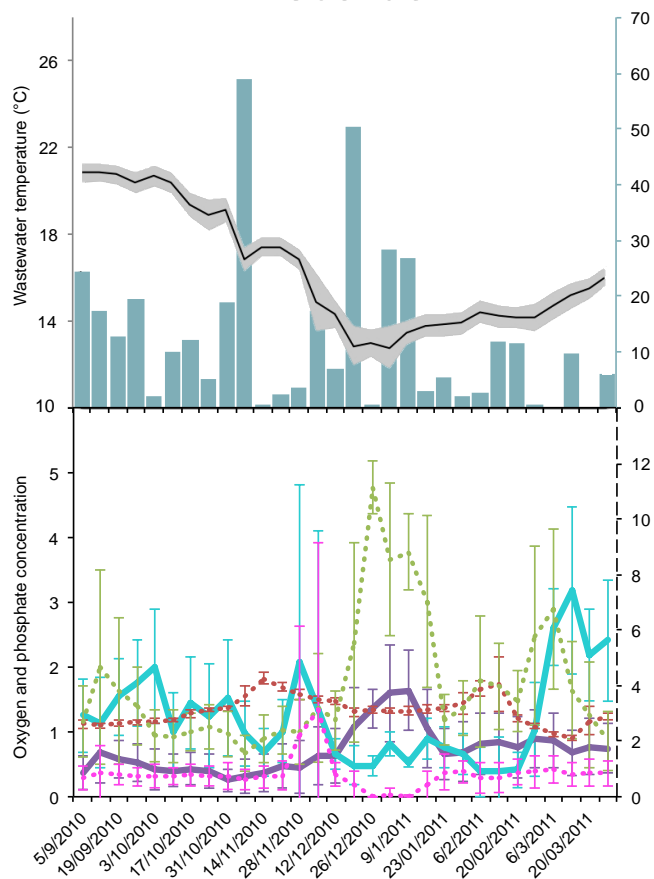
# Model system: Biotechnological relevance



Muller et al. *J. Bacteriol* (2012), **194**: 6670-6671  
Muller *et al.* *Curr Opp in Biotech* (2013), **30**: 9-16  
Sheik et al. *Frontiers in Microbiol* (2014), **10**: 3389

# Model system: Fundamental importance

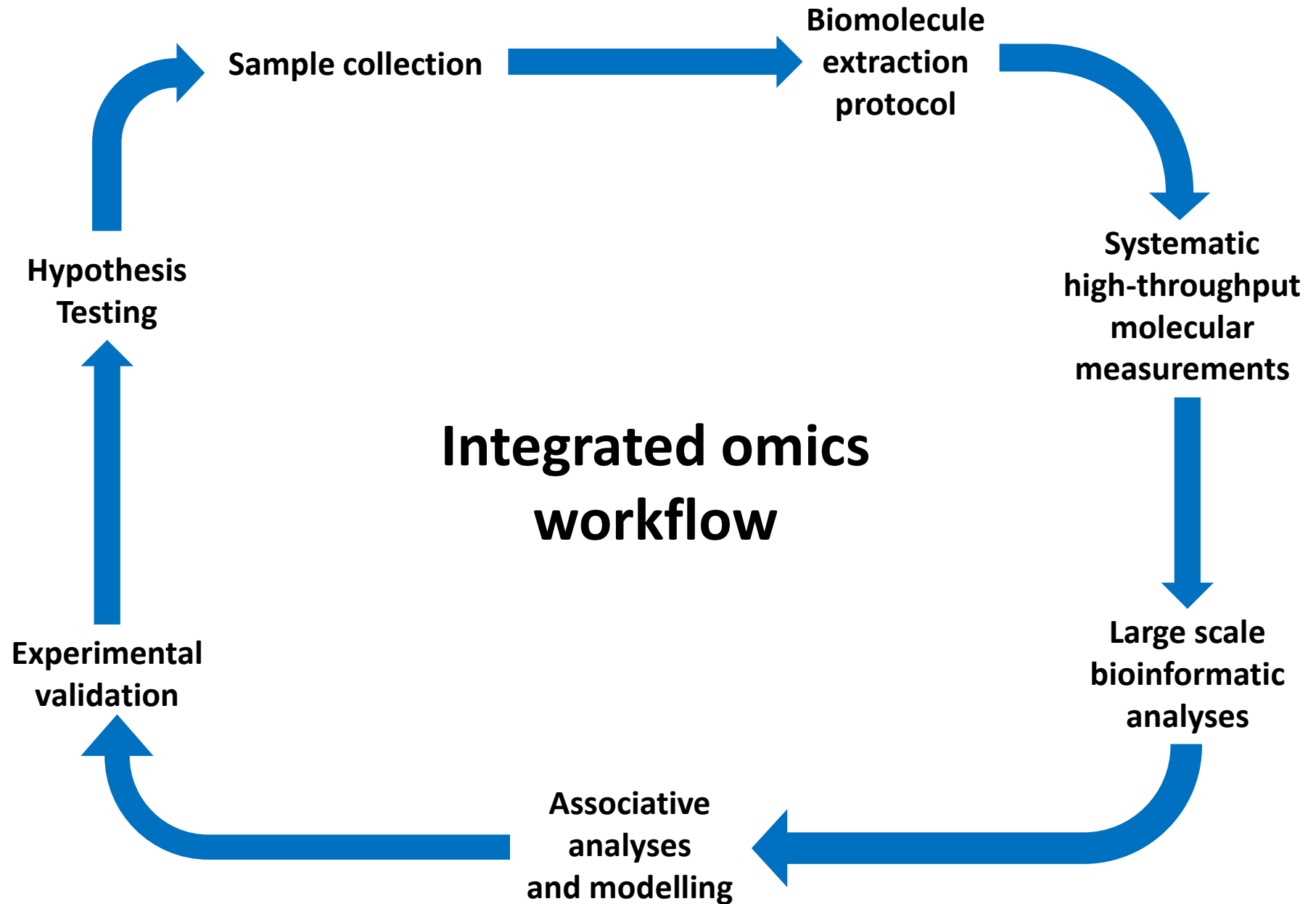
## Physico-chemical records

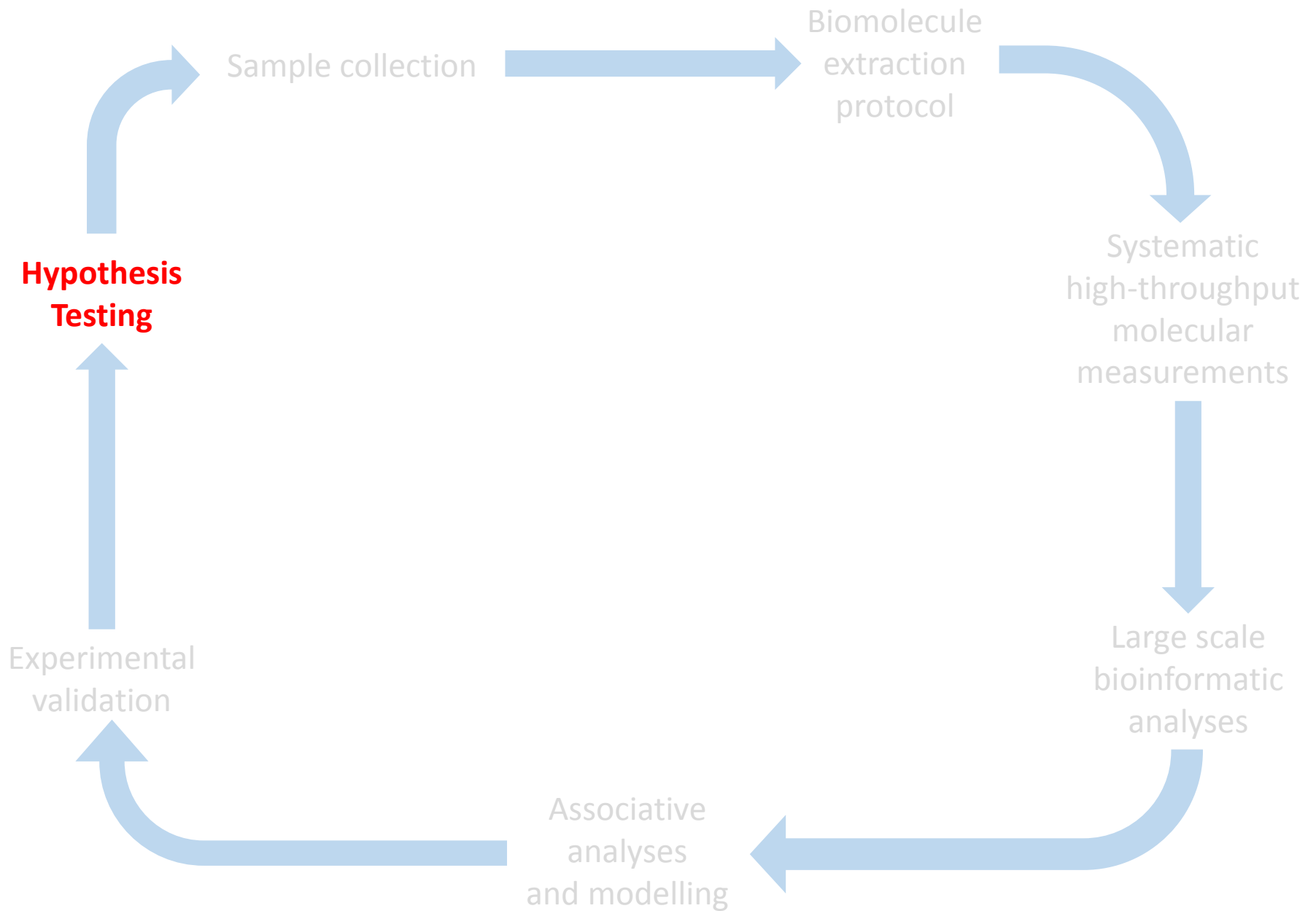


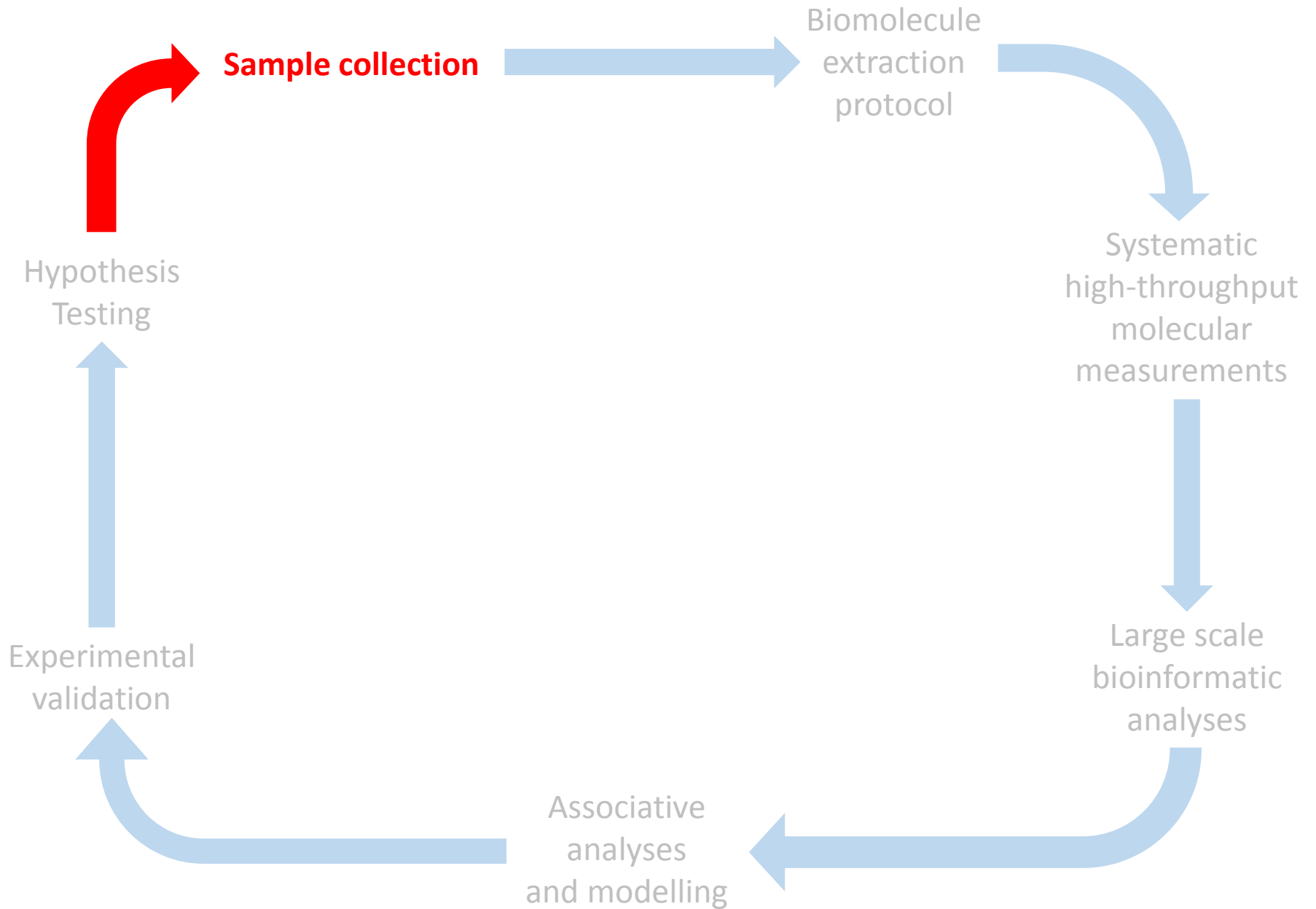
Muller *et al.* Trends in Microbiol (2014), **21**: 325-33

Muller, Pinel *et al.* Nat Comm (2014), **5**: 5603

Narayanasamy *et al.* Microbial Biotech (2015), **8**: 363-368



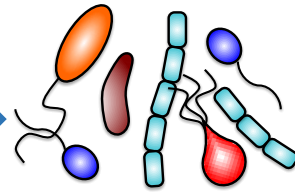




# Sample collection



Wastewater  
sludge



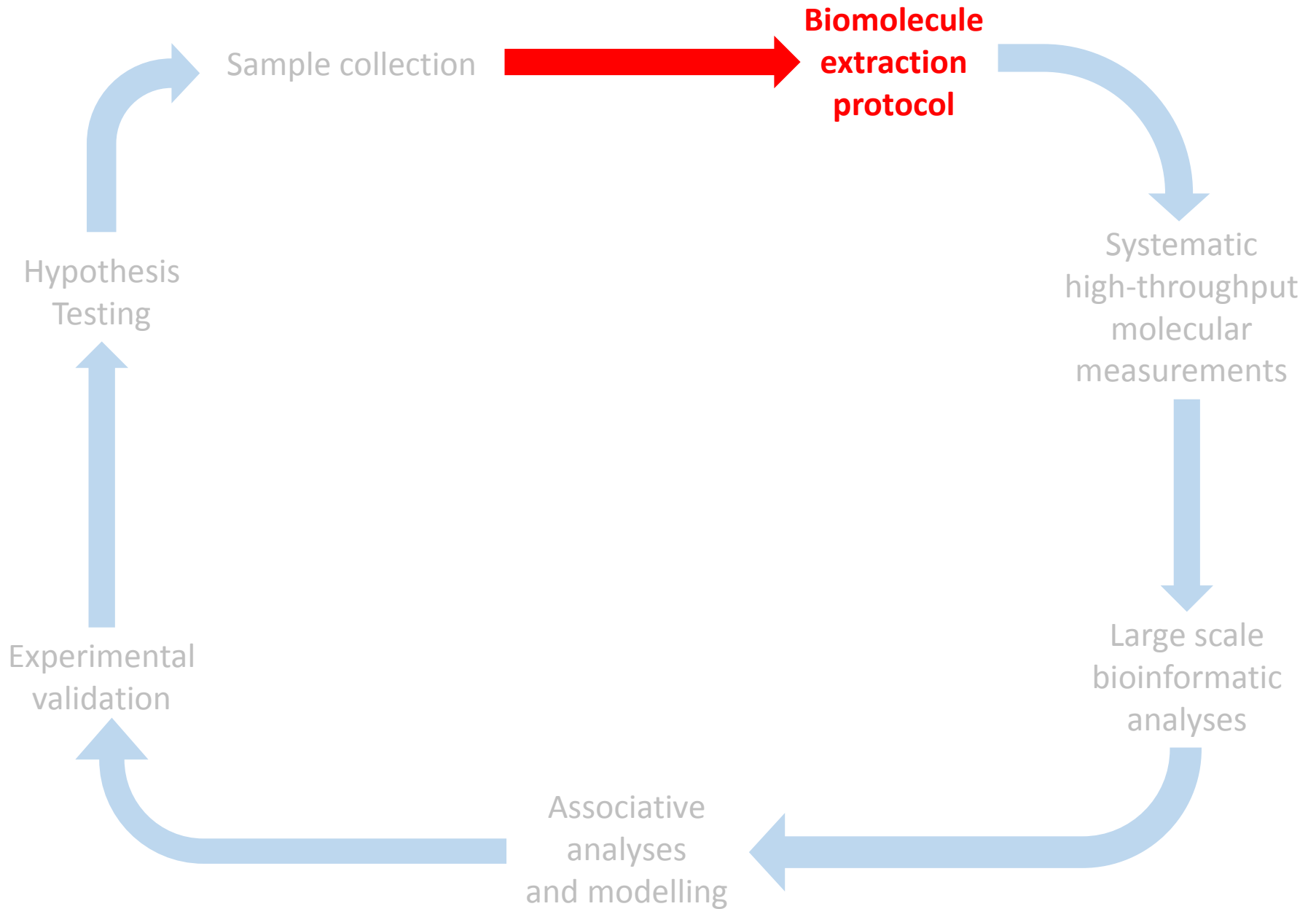
Snap freeze



Biomedical

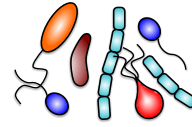


Preservation and tracking

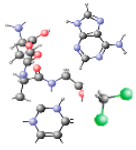
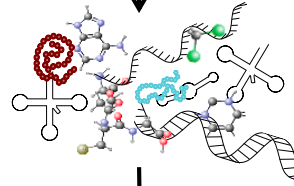




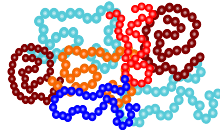
# Laboratory protocol



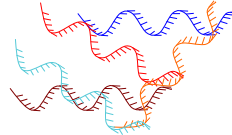
Comprehensive cell lysis



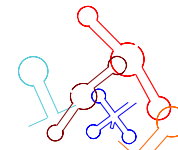
metabolites



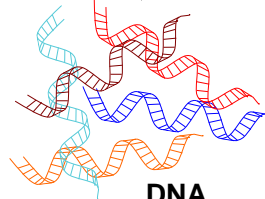
proteins



RNA



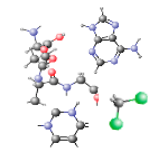
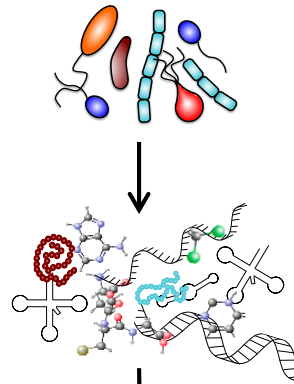
Small RNA



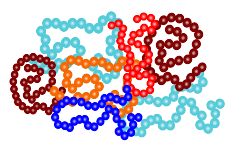
DNA

High-quality biomolecules

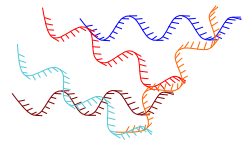
# Laboratory protocol



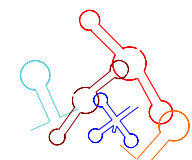
metabolites



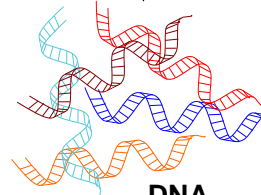
proteins



RNA



Small RNA



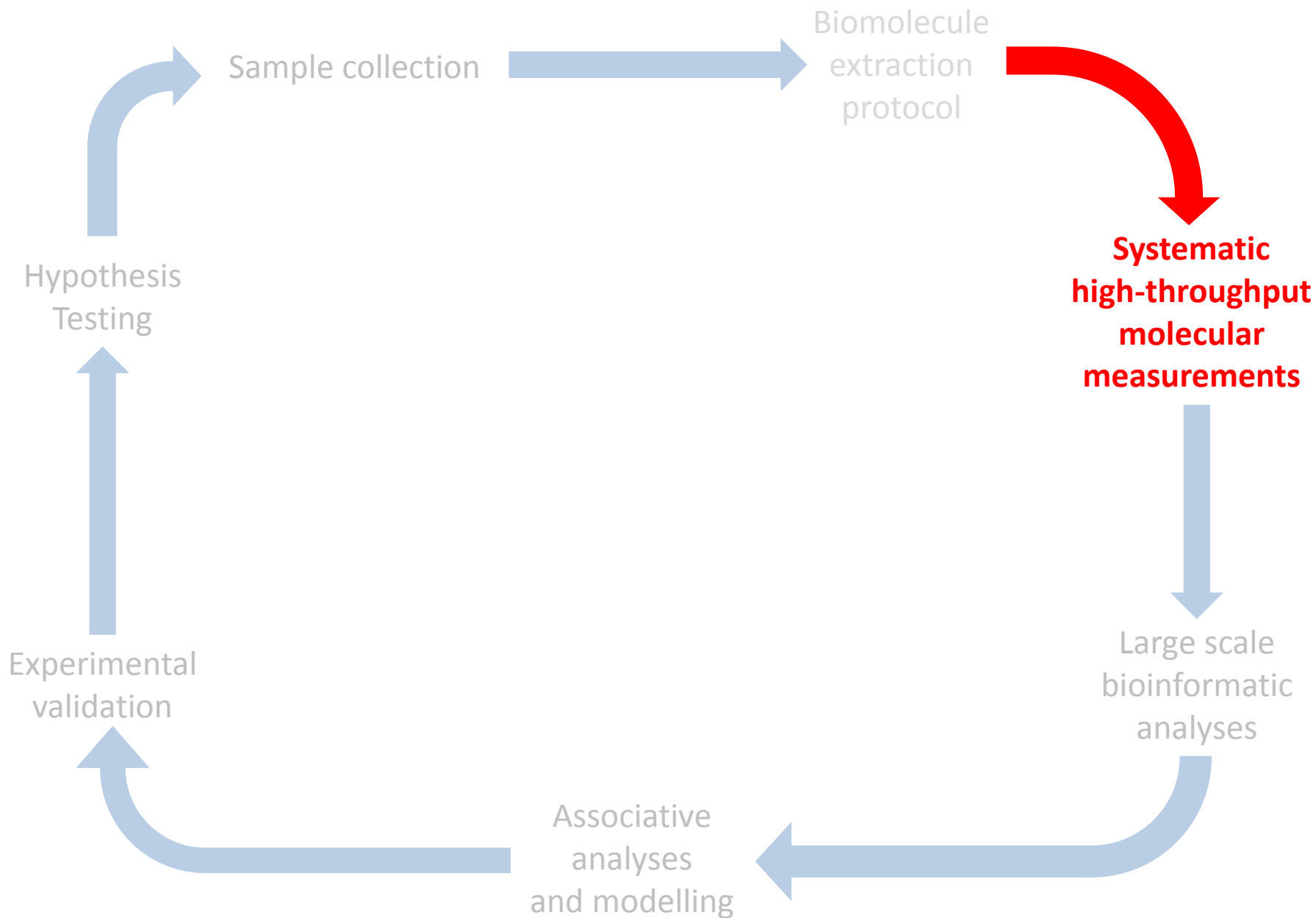
DNA

**Labor-intensive and operator-dependent**

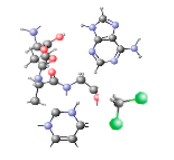
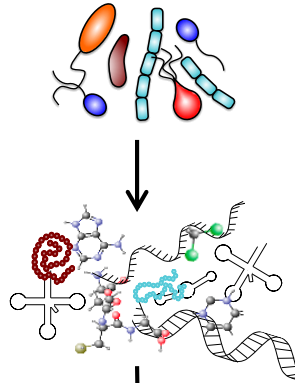
# High-throughput biomolecular isolations



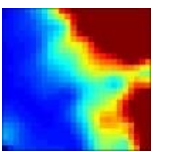
in collaboration with  **TECAN**.



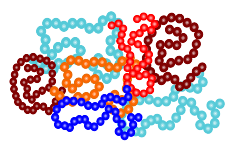
# Systematic measurements



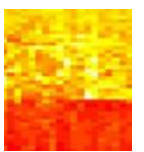
metabolites



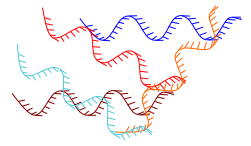
metabolomics



proteins



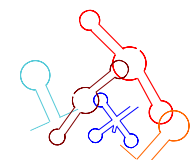
meta-proteomics



RNA



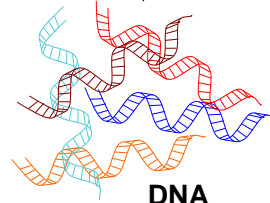
meta-transcriptomics



Small RNA



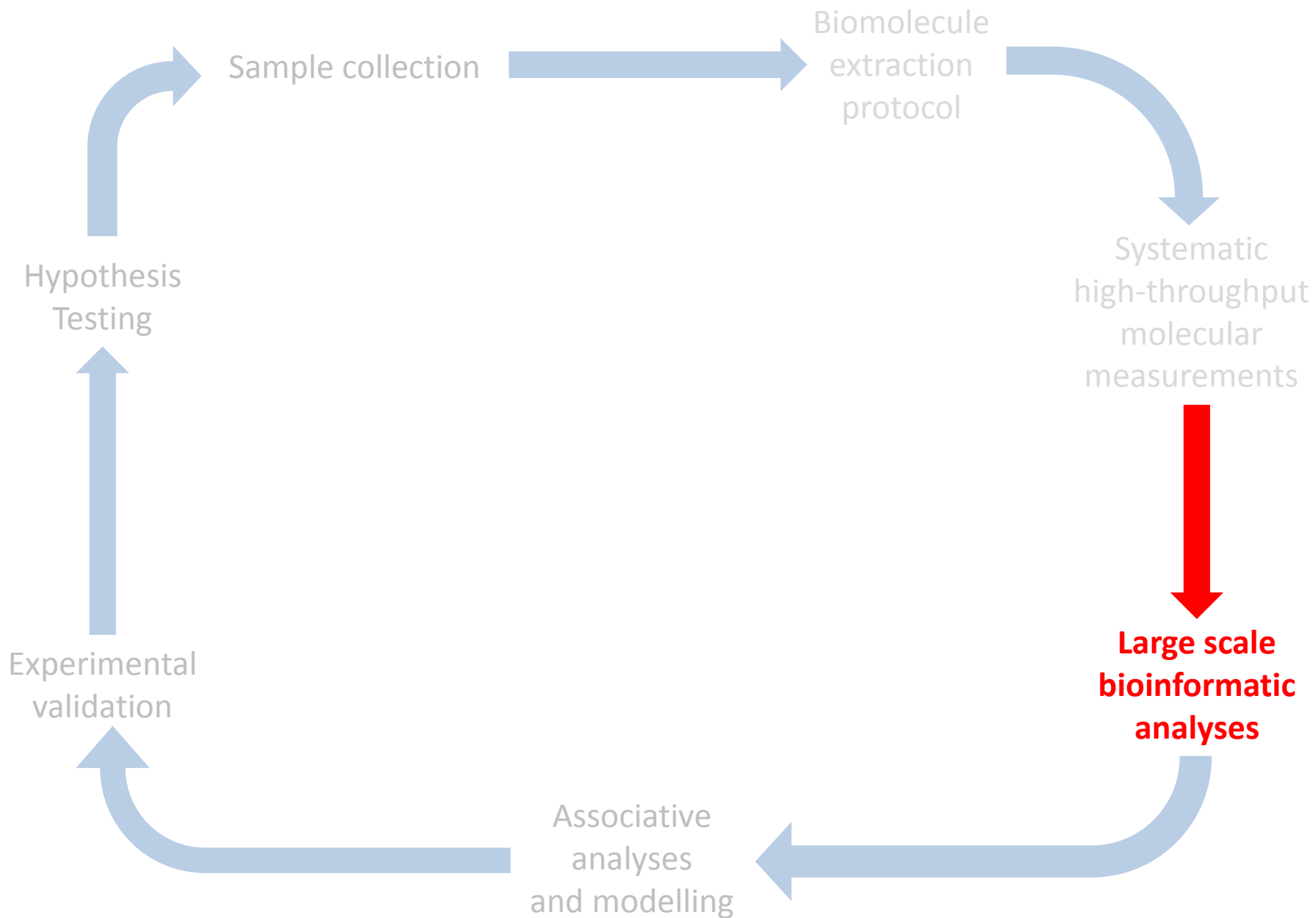
meta-transcriptomics



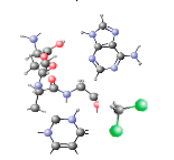
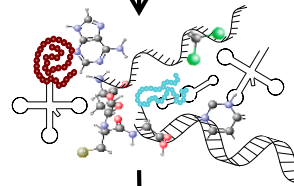
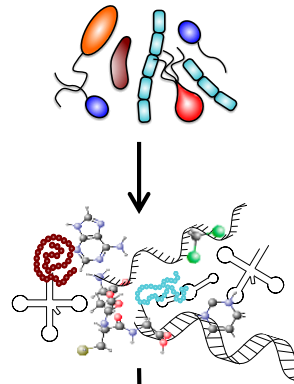
DNA



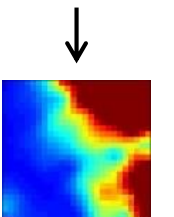
meta-genomics



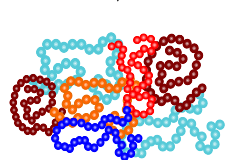
# Integrated analysis



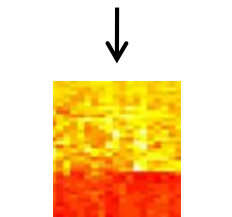
metabolites



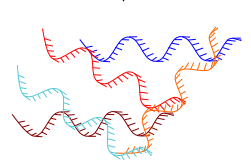
metabolomics



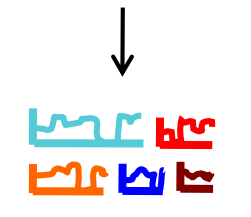
proteins



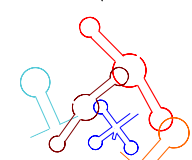
meta-proteomics



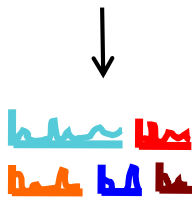
RNA



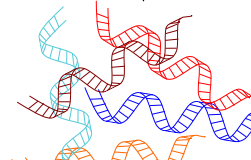
meta-transcriptomics



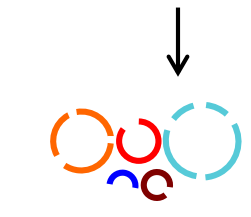
Small RNA



meta-transcriptomics



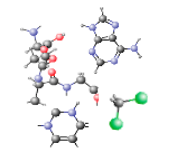
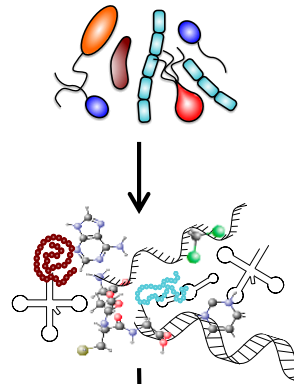
DNA



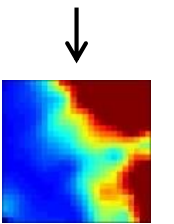
meta-genomics

Integrative analyses??

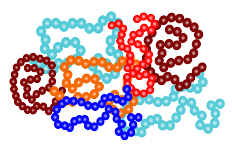
# Integrated analysis



metabolites



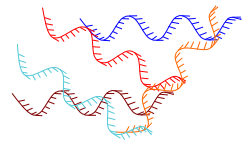
metabolomics



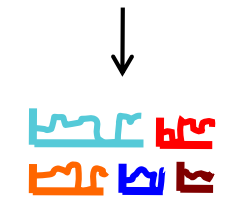
proteins



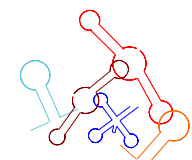
meta-proteomics



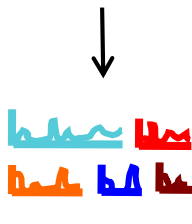
RNA



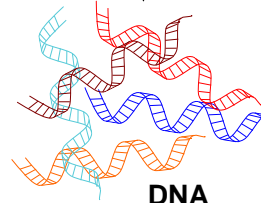
meta-transcriptomics



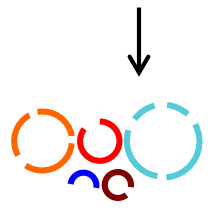
Small RNA



meta-transcriptomics

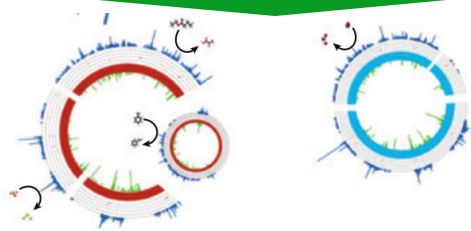


DNA



meta-genomics

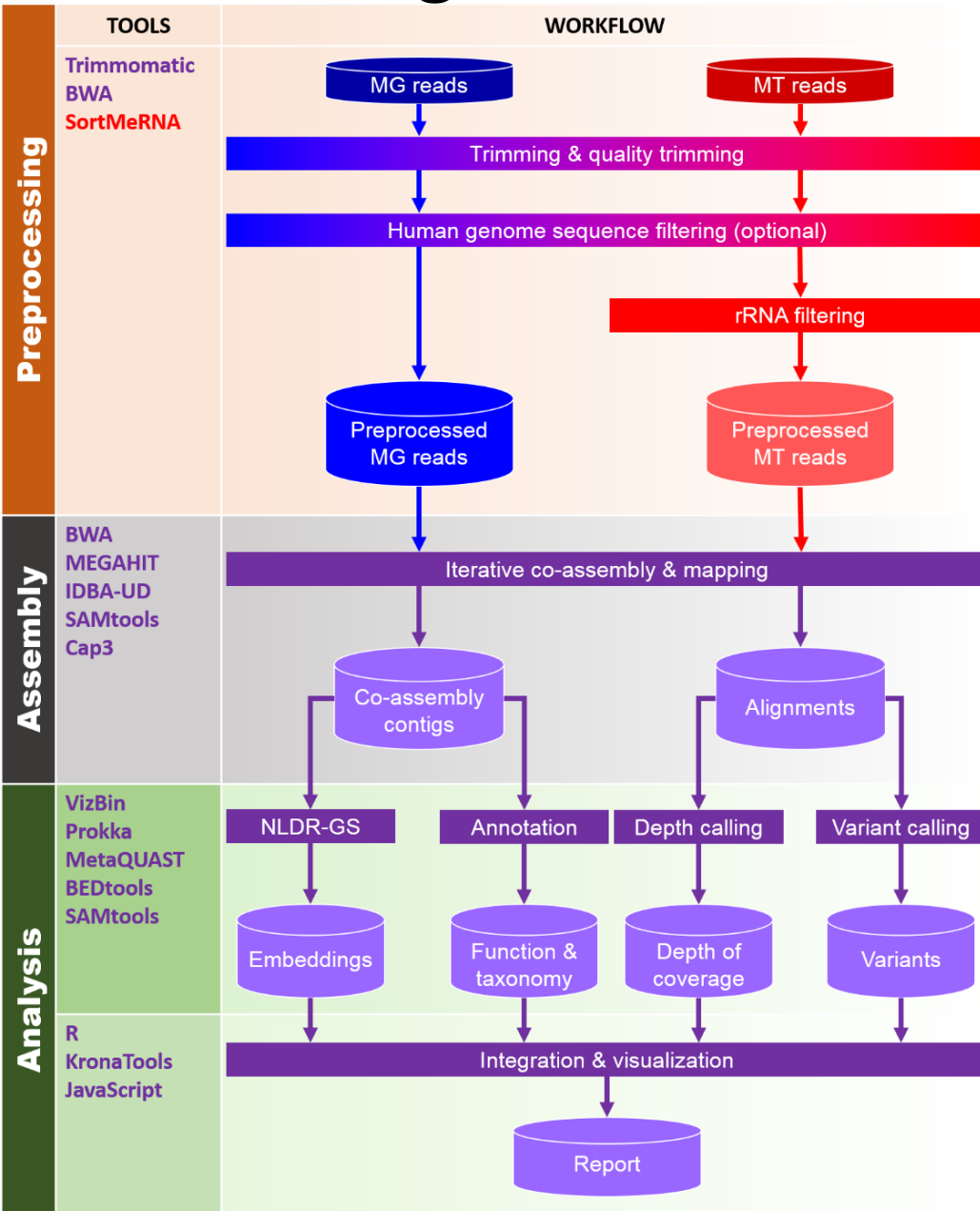
## VizBin & Integrated Meta-omic Pipeline (IMP)



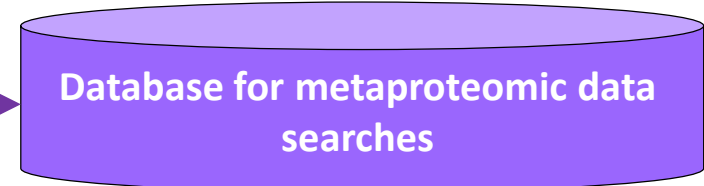
Muller *et al.* Trends in Microbiol (2013) **21**:325-33  
Muller, Pinel *et al.* Nat Comm (2014) **5**:5603  
Narayanasamy *et al.* Microbial Biotech (2015), **8**: 363-368

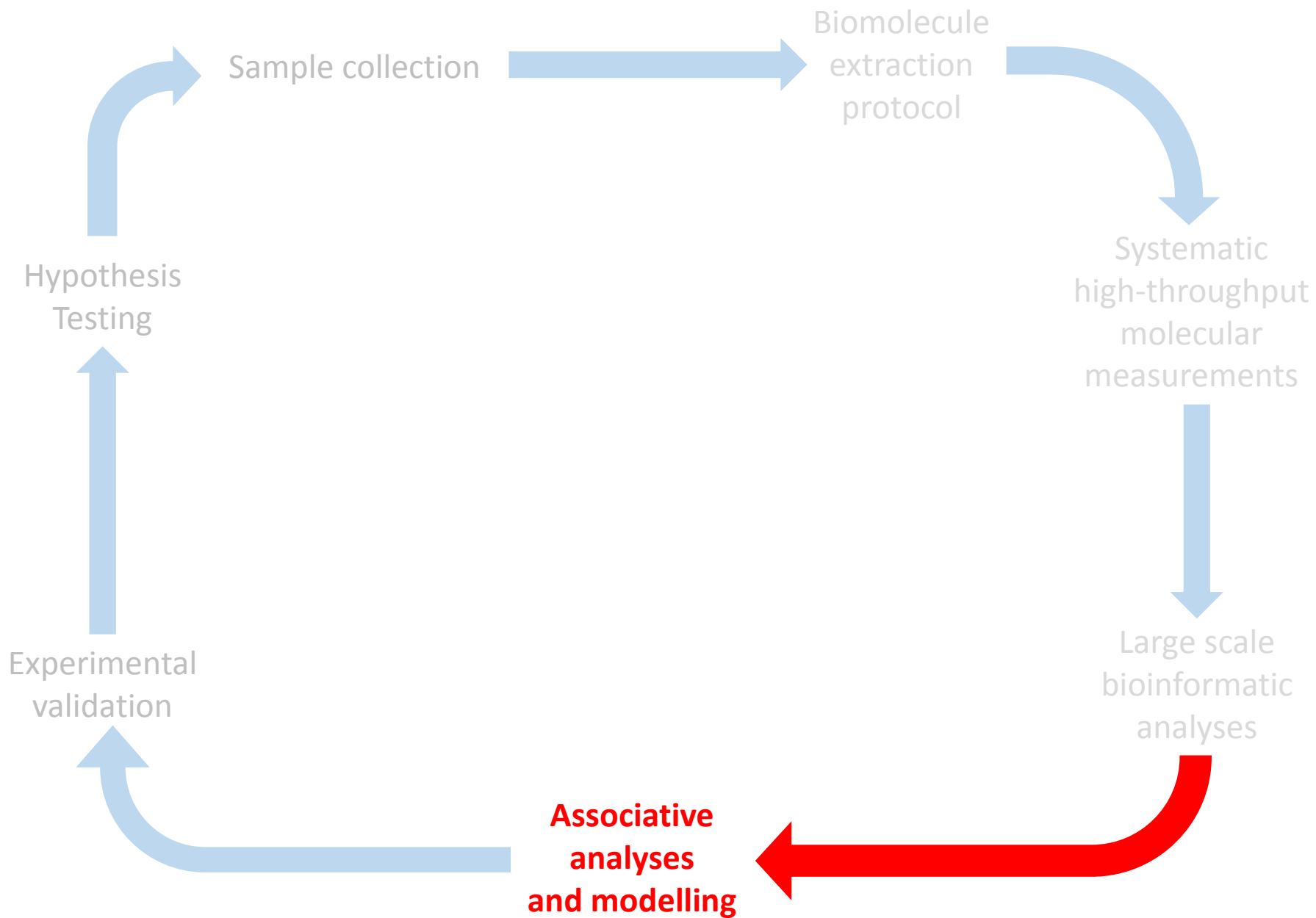


# Integrated meta-omics pipeline (IMP)

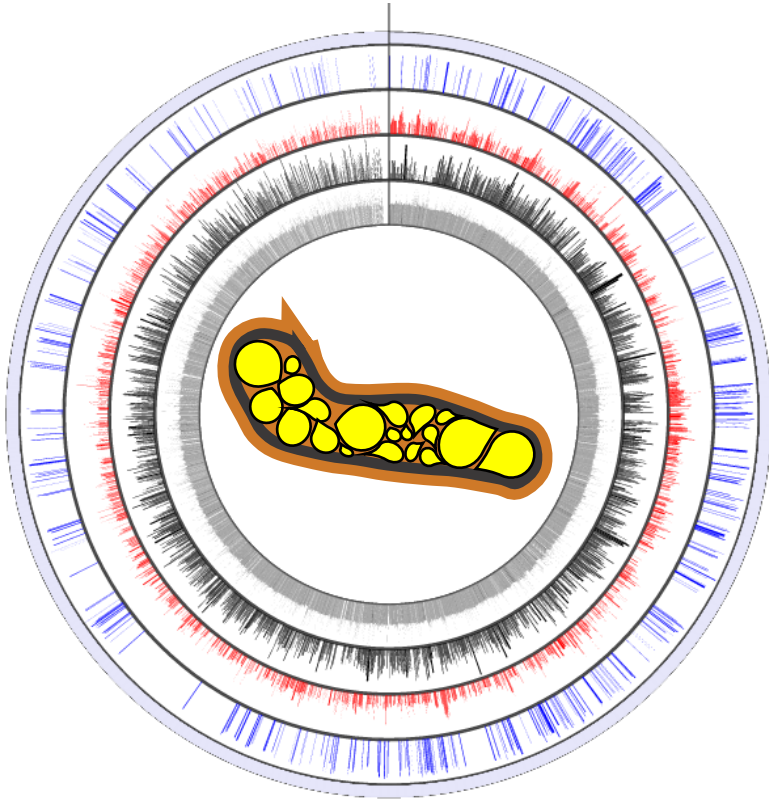


**IMP** available at:  
<http://r3lab.uni.lu/web/imp>

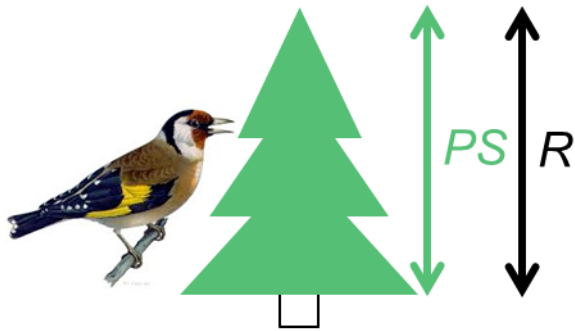
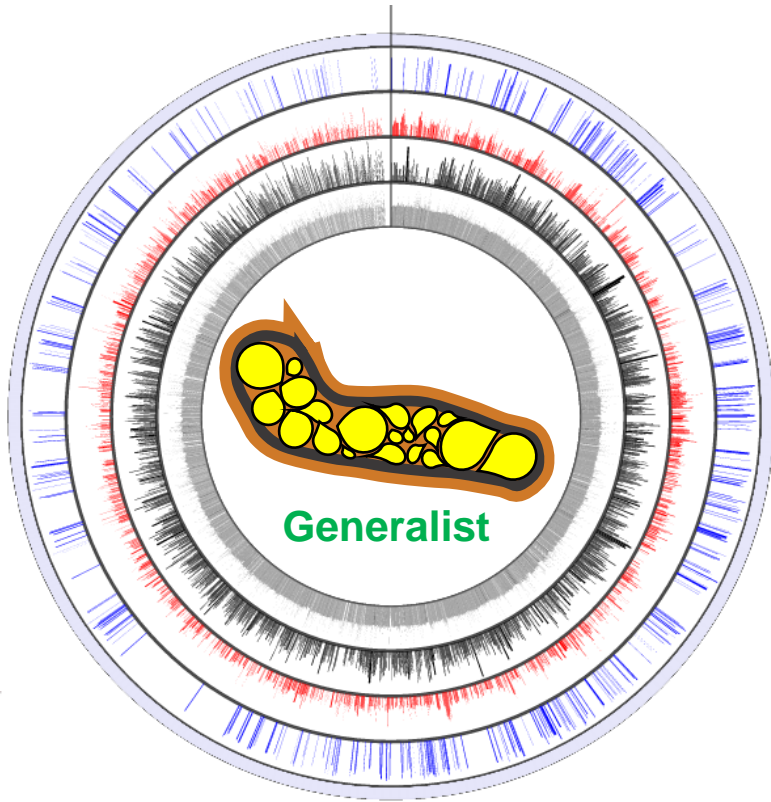




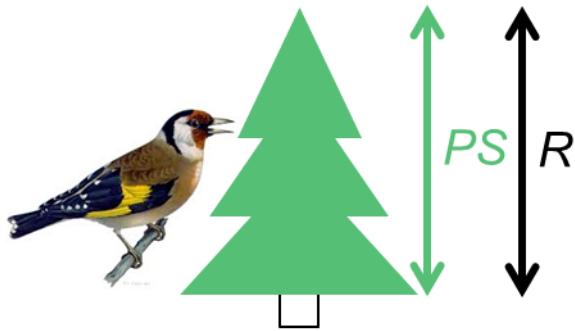
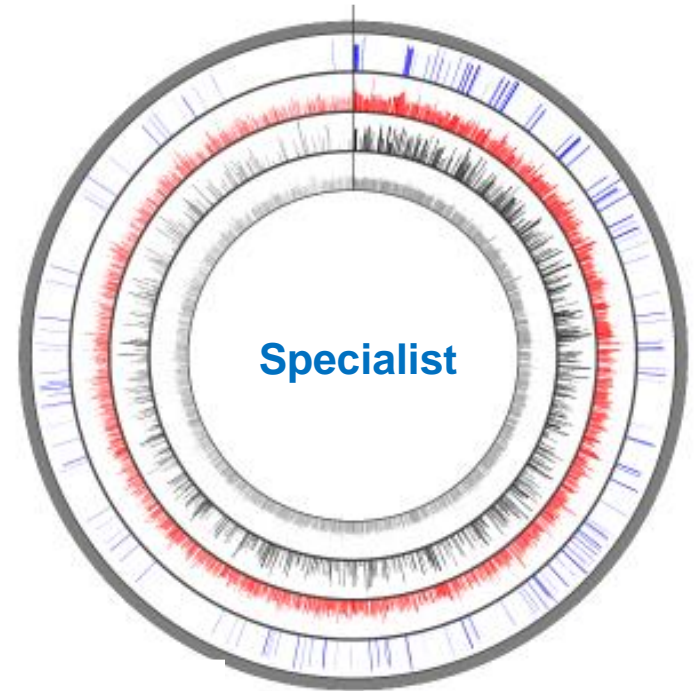
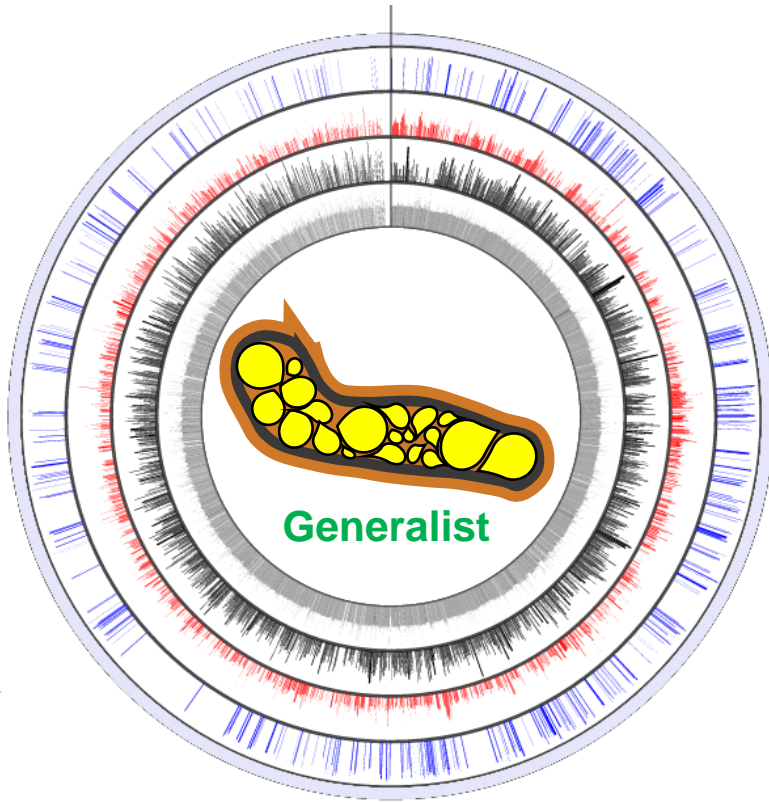
# Population lifestyle strategies



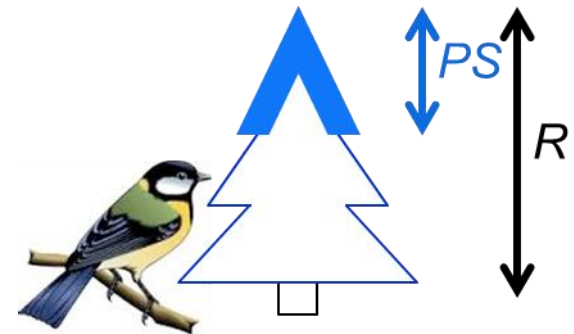
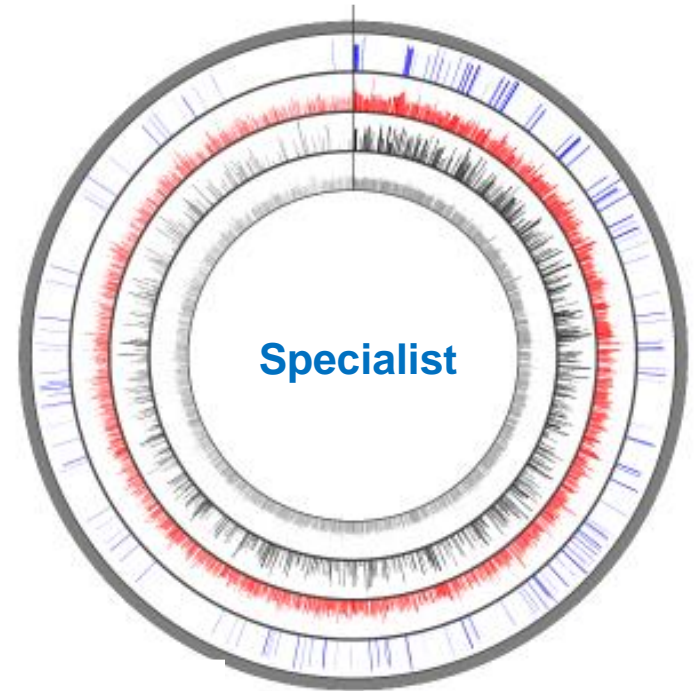
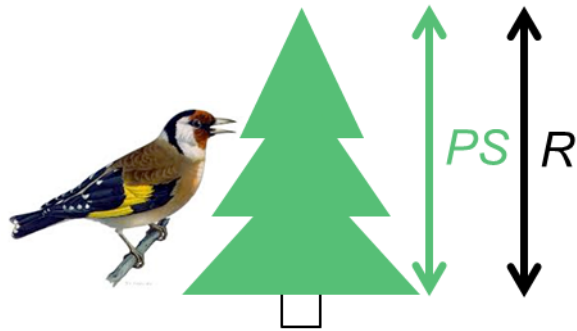
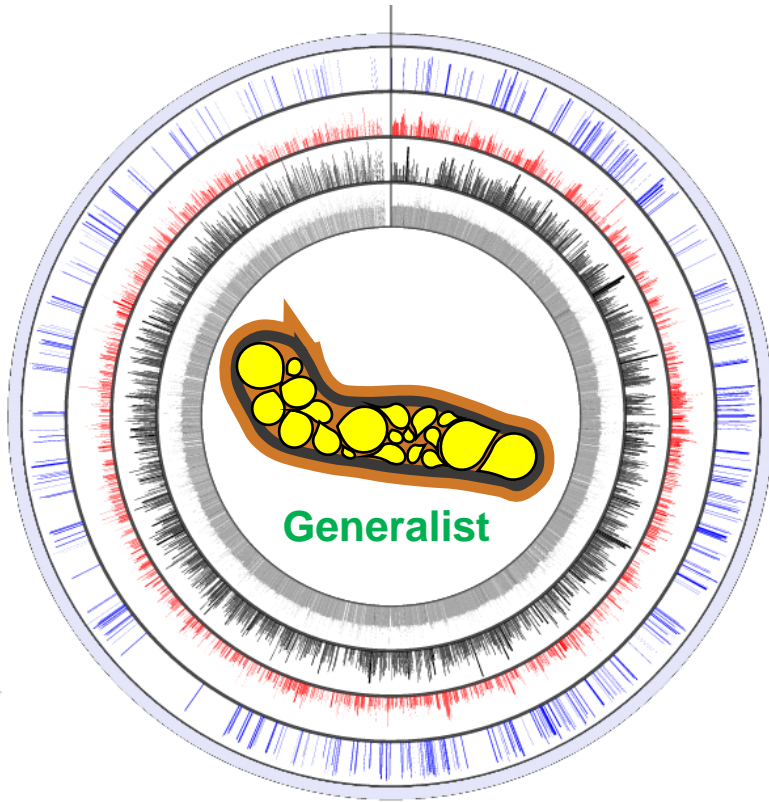
# Population lifestyle strategies

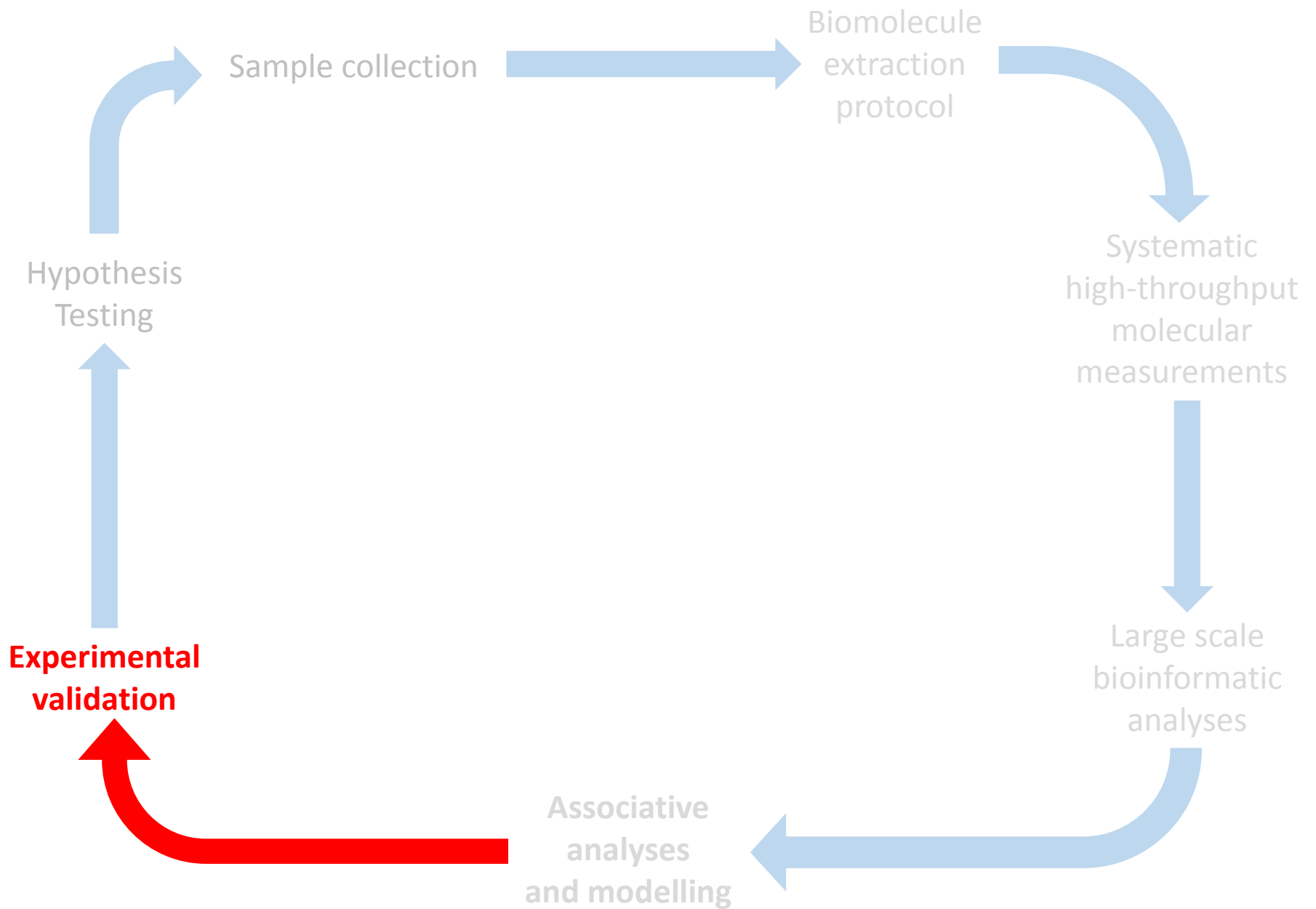


# Population lifestyle strategies



# Population lifestyle strategies

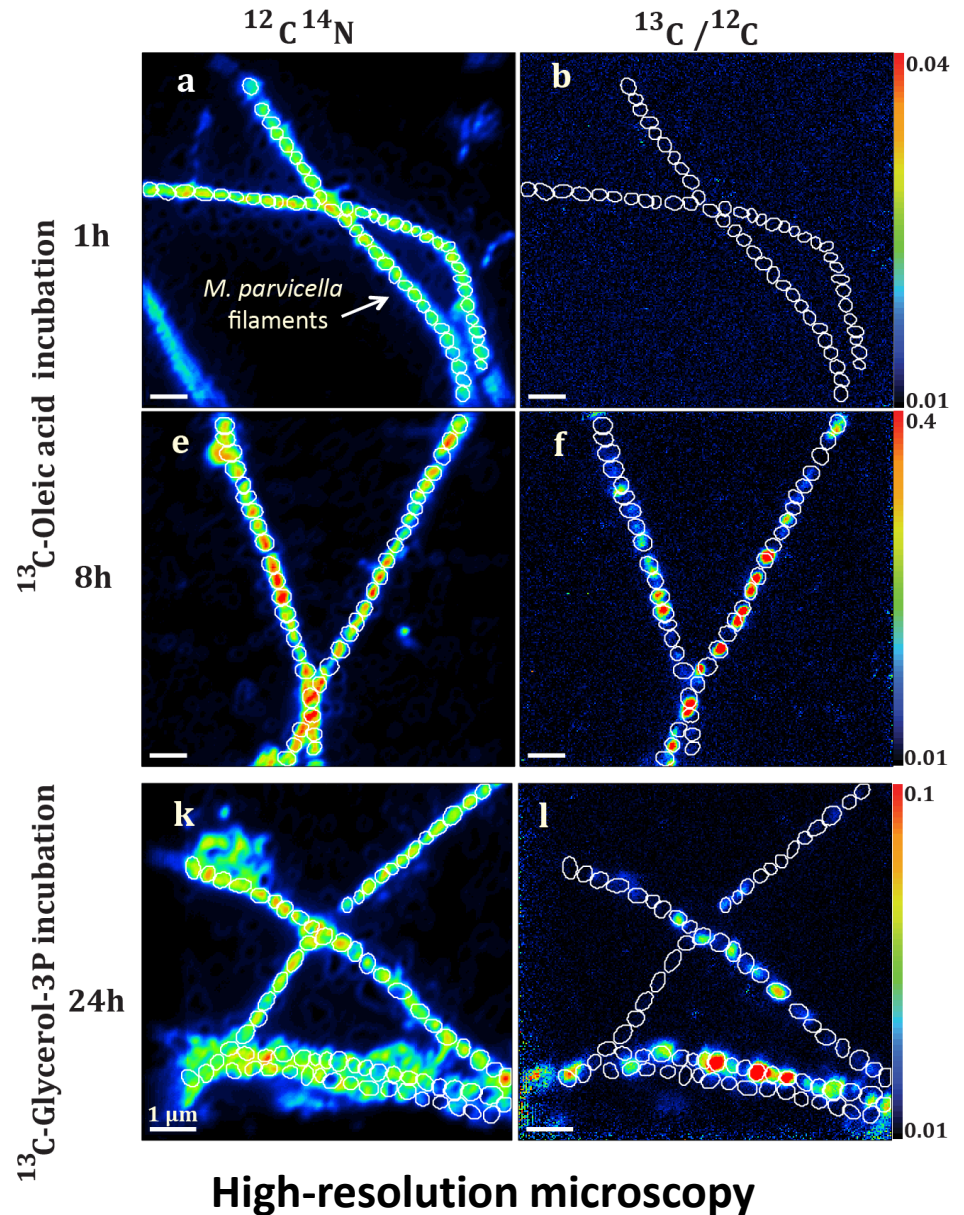




# Single-cell level resource usage



Sludge bioreactor

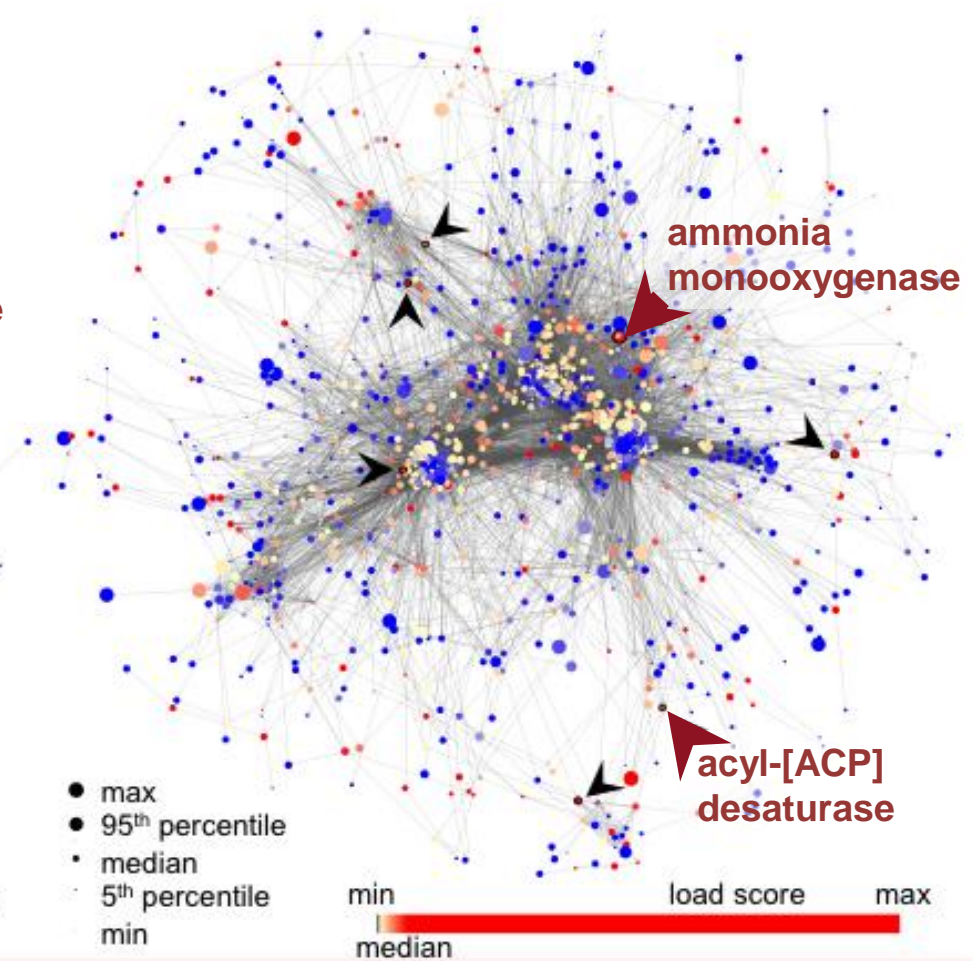
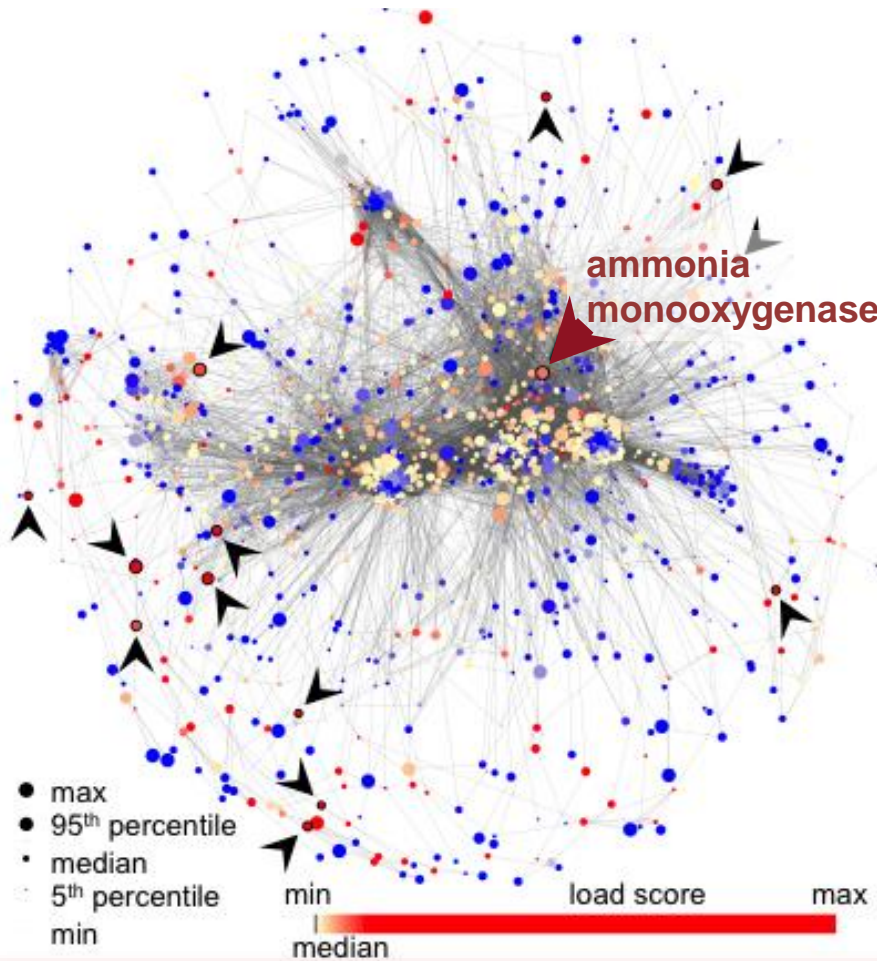




# Keystone-genes and -species

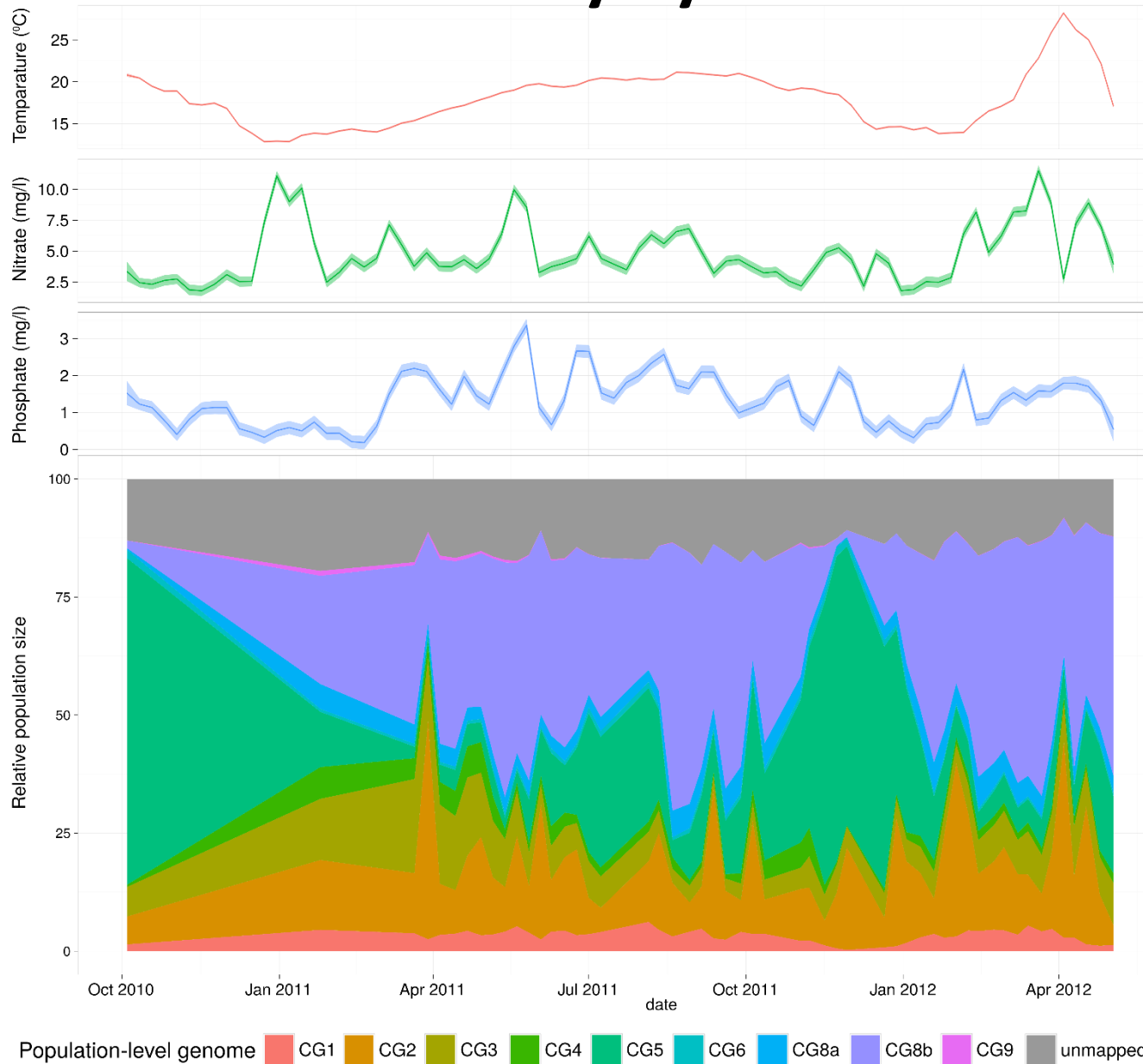
Autumn

Winter



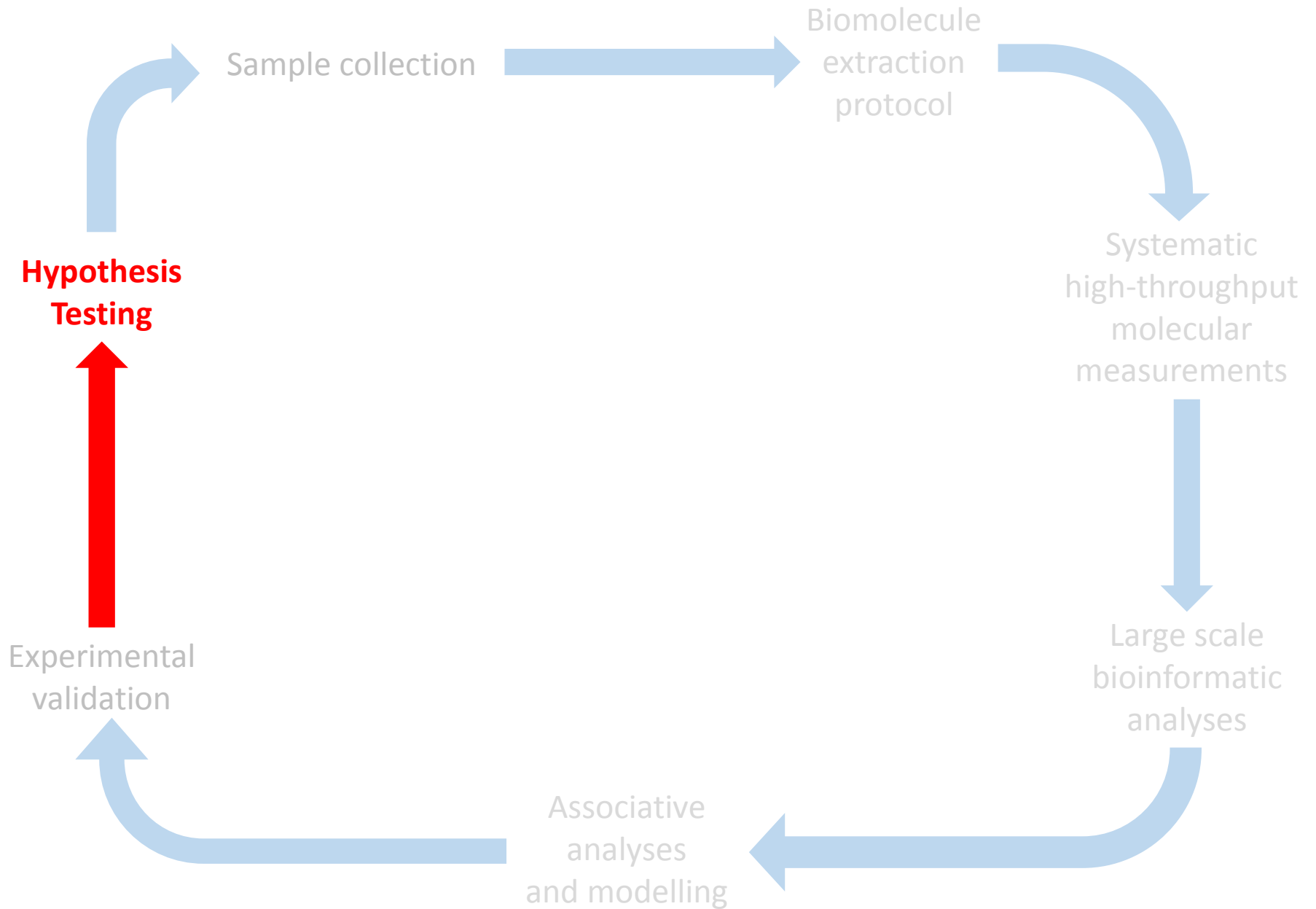
**Key functionalities** should be encoded by keystone community members, i.e. **keystone species**

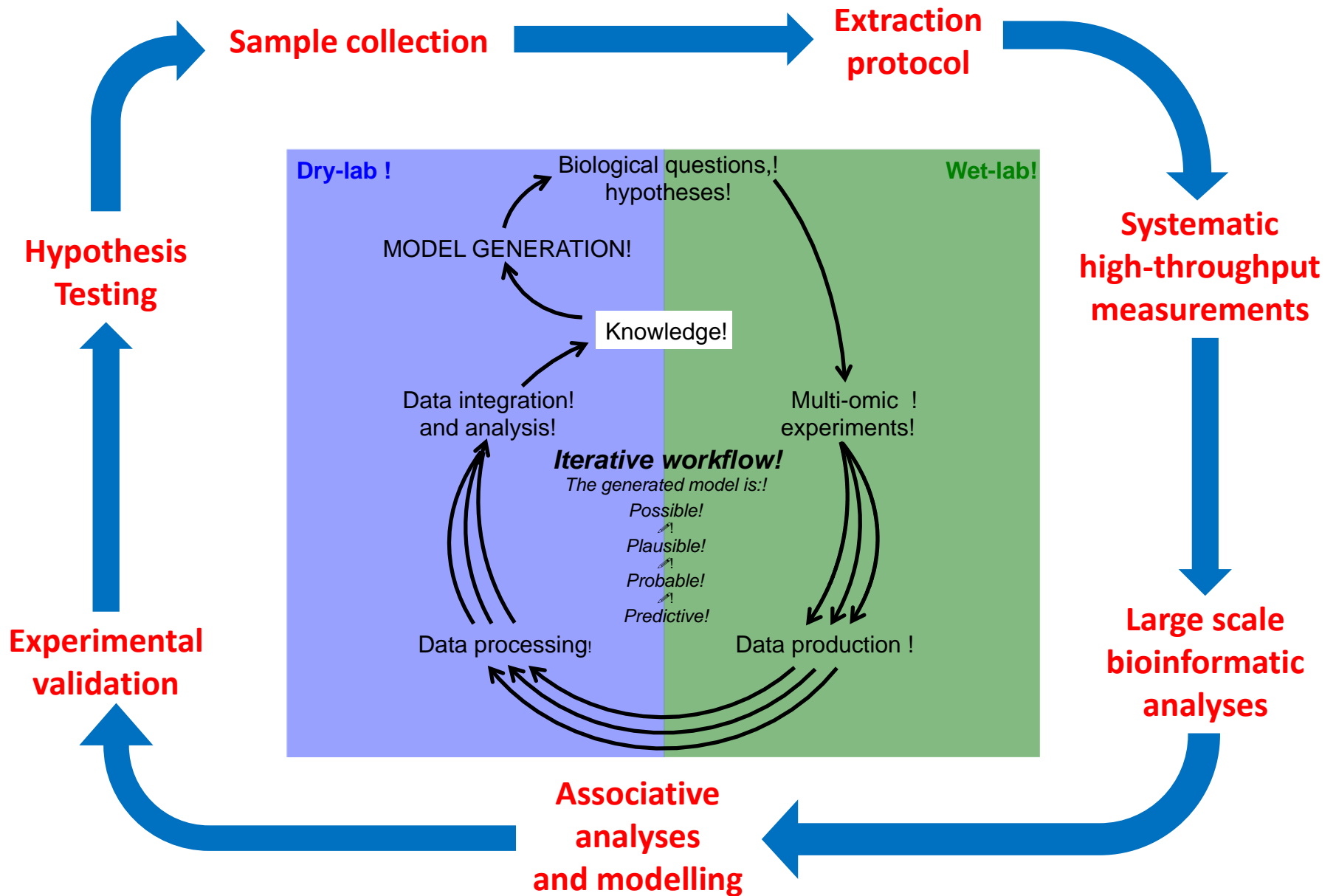
# Community dynamics



Muller, Pinel *et al.* Nat Comm (2014) 5:5603

Roume, Buschart *et al.* Microbiome and Biofilms (2015), 1:15007



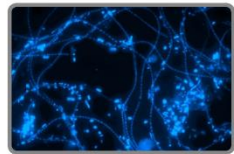


# Outlook: From discovery to mechanism

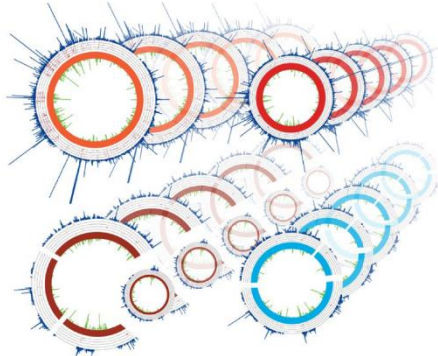
## Hypothesis Generation



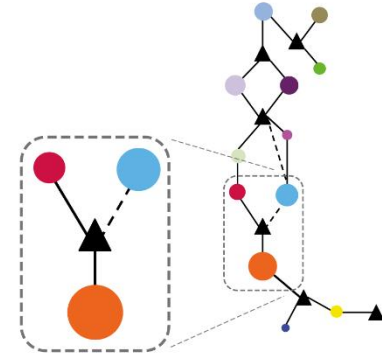
human microbiota



LAOs



systematic measurements

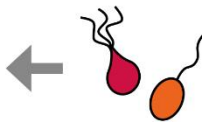


associations

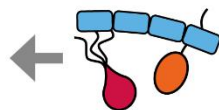
## Validation



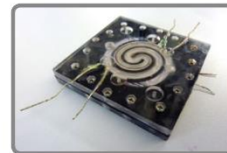
*in vivo*



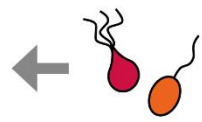
*in situ*



## *In vitro* Hypothesis Testing



*in vitro*



*in vitro*



# Acknowledgements

## Eco-Systems Biology group:

Emilie Muller  
Abdul Sheik  
Cedric Laczny  
Laura Lebrun  
Malte Herold  
Anne Kaysen  
Anna Buschart  
*et al.*

## Former ESB:

Hugo Roume  
Nicolas Pinel  
Myriam Zeimes

## BioCore:

Patrick May

## R3 initiative:

Yohan Jarosz  
Venkata Satagopam  
Christophe Trefois  
Wei Gu  
Sergio Coronado  
Reinhard Schneider  
Sarah Diehl

## Supervisors:

Paul Wilmes (ESB group)  
Jorge Goncalves (System Control group)



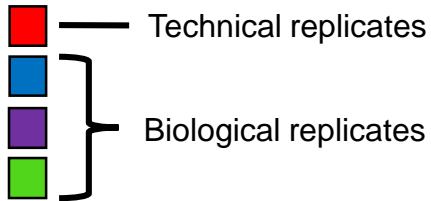
PHD-2014-1/7934898



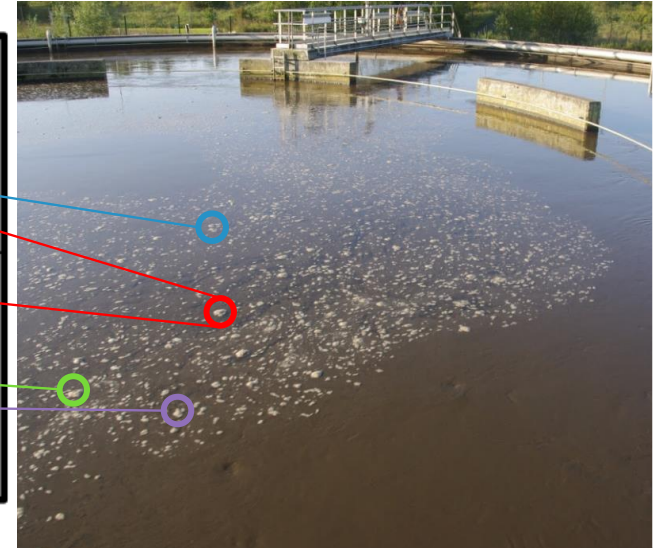
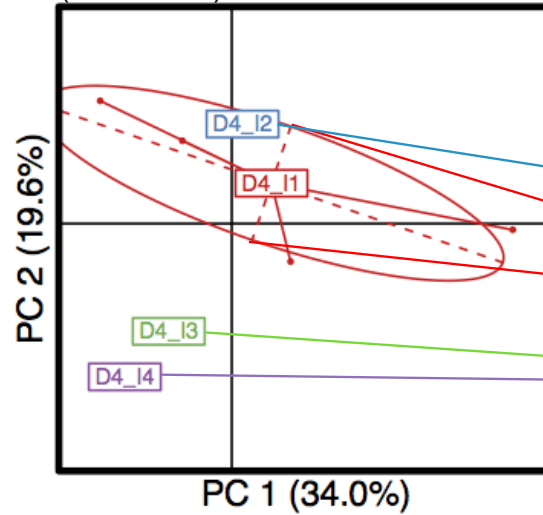
Fonds National de la  
Recherche Luxembourg



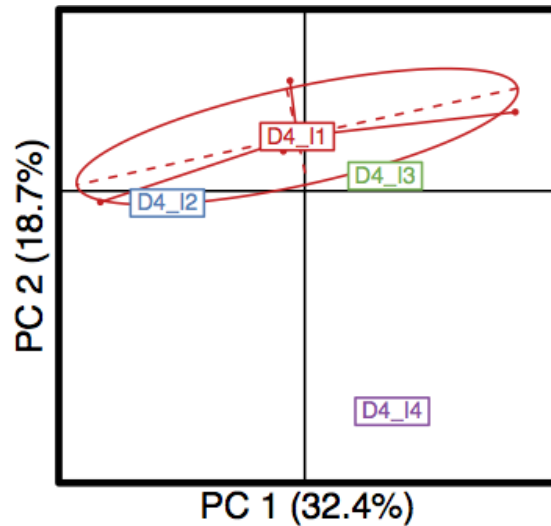
# Heterogeneity



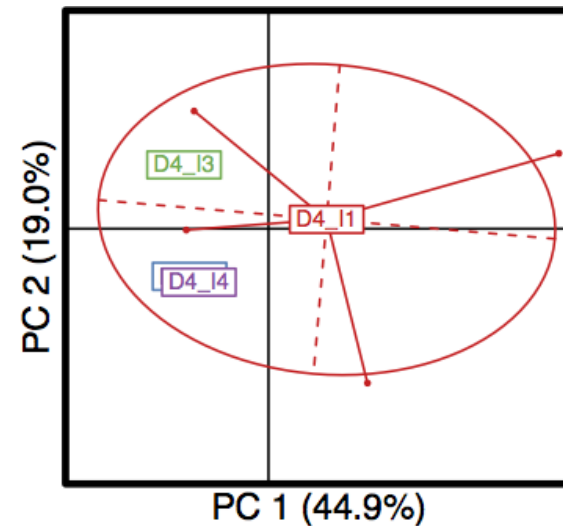
Phylum-level variation  
(16S rRNA)



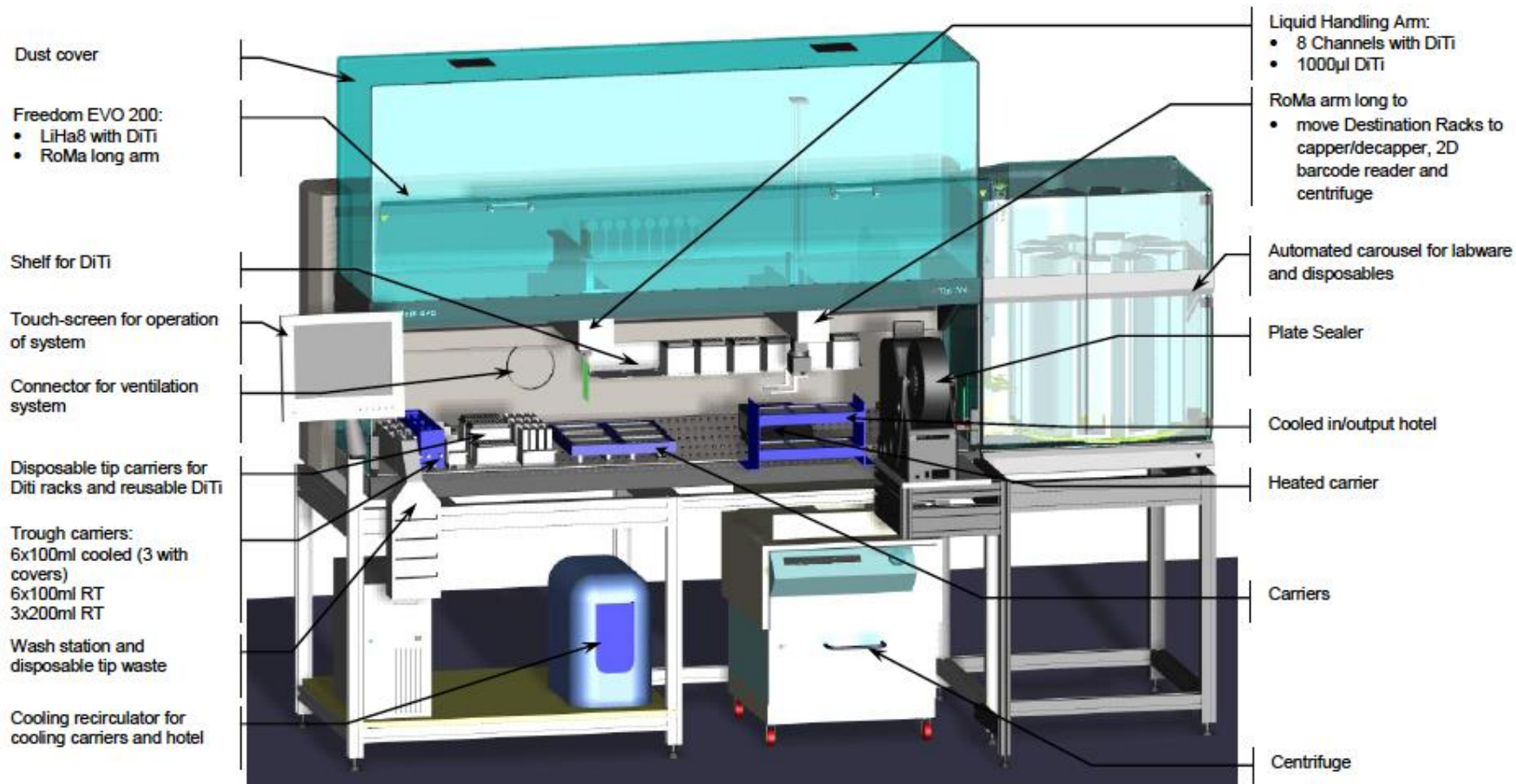
Metagenomes  
(functional annotation)



Metabolomes  
(polar metabolites)



# Supplementary: TECAN robot for high-throughput platform





# Shotgun sequencing

*Biological*

*In silico*

# Shotgun sequencing

DNA / cDNA

*Biological*

*In silico*

# Shotgun sequencing

DNA / cDNA

Fragment and  
sequence

*Biological*

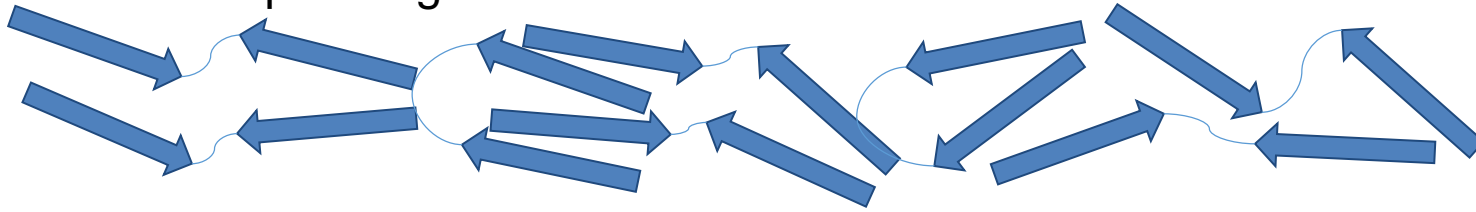
*In silico*

# Shotgun sequencing

DNA / cDNA

Fragment and  
sequence

Sequencing reads



*Biological*

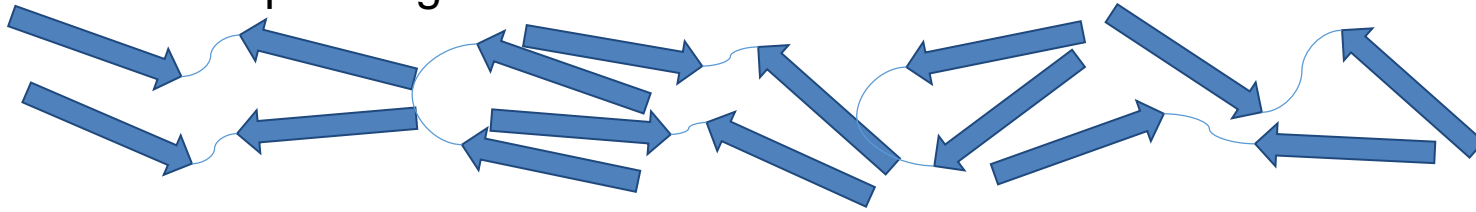
*In silico*

# Shotgun sequencing

DNA / cDNA

Fragment and  
sequence

Sequencing reads



Assembly

*Biological*

*In silico*

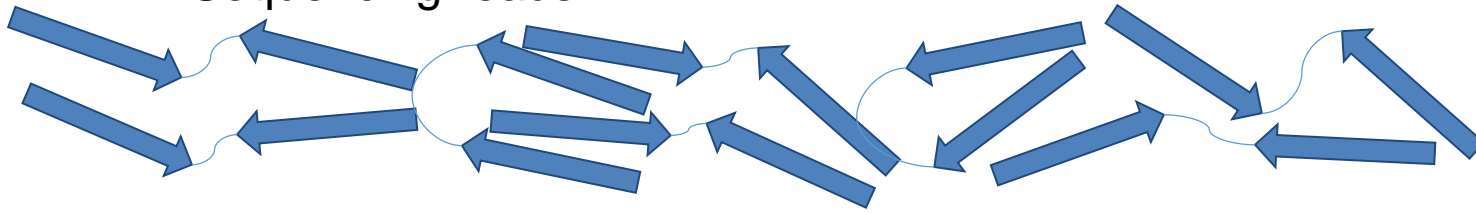
# Shotgun sequencing

DNA / cDNA

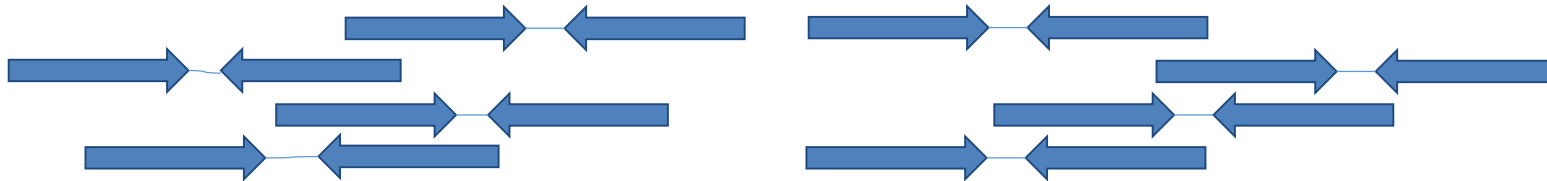
*Biological*

Fragment and  
sequence

Sequencing reads



Assembly



*In silico*

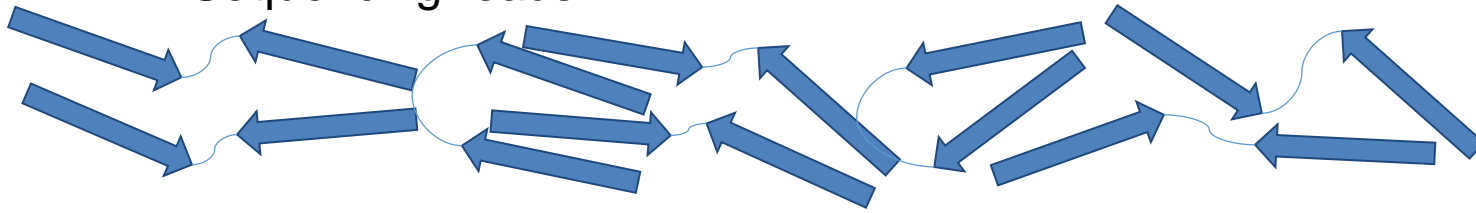
# Shotgun sequencing

DNA / cDNA

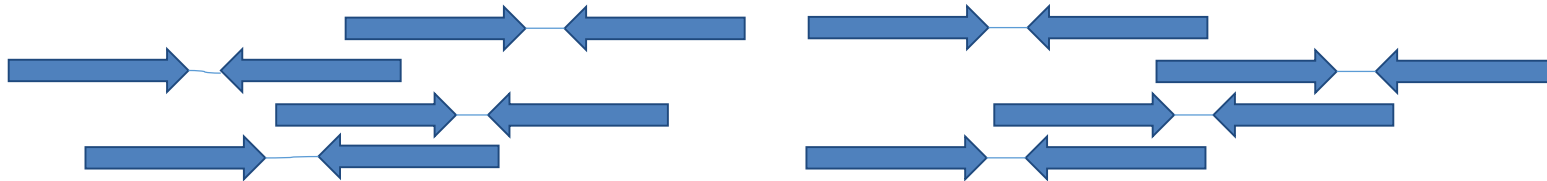
*Biological*

Fragment and  
sequence

Sequencing reads



Assembly

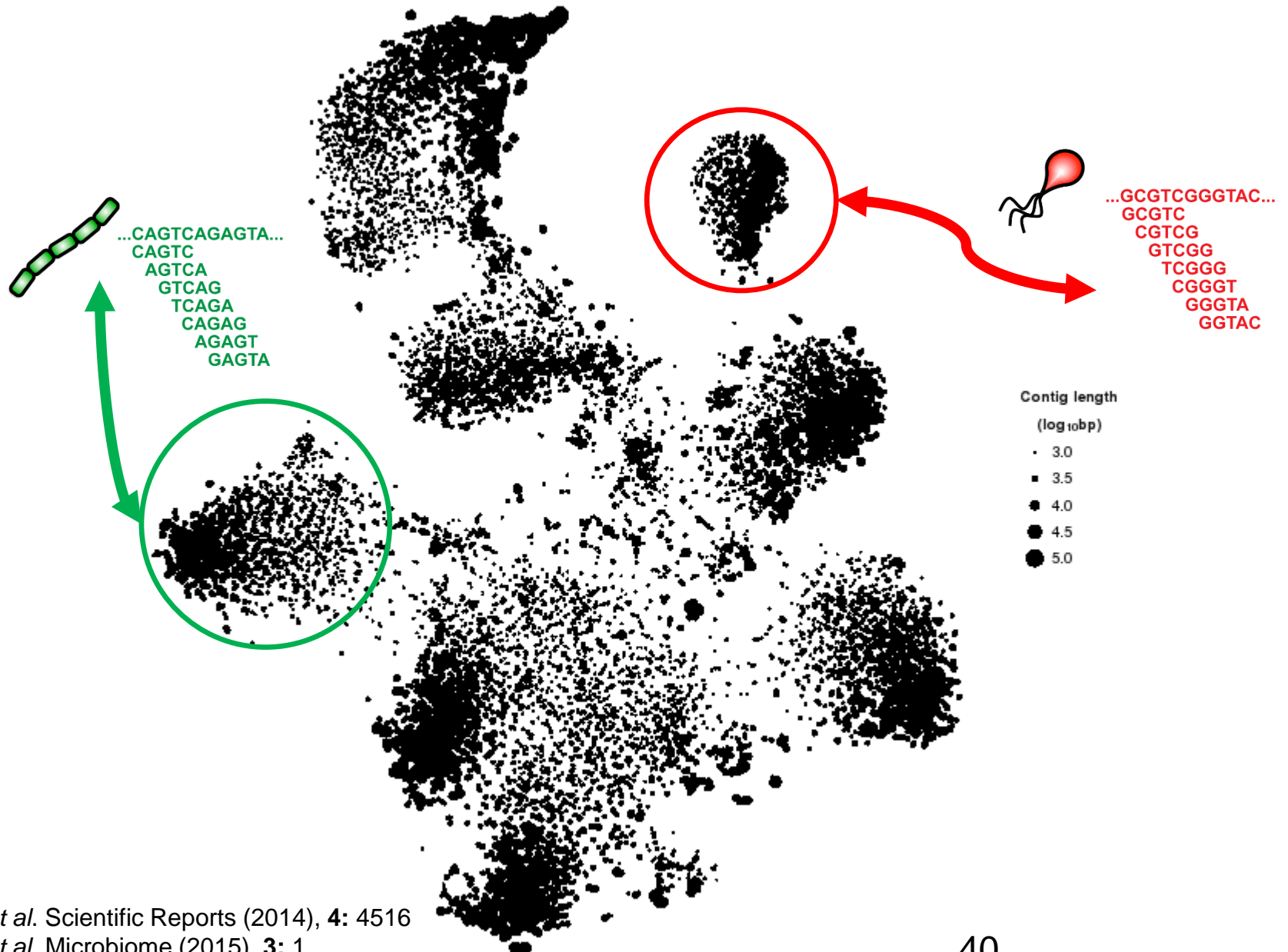


**Contig 1 (contiguous sequence)**

**Contig 2**

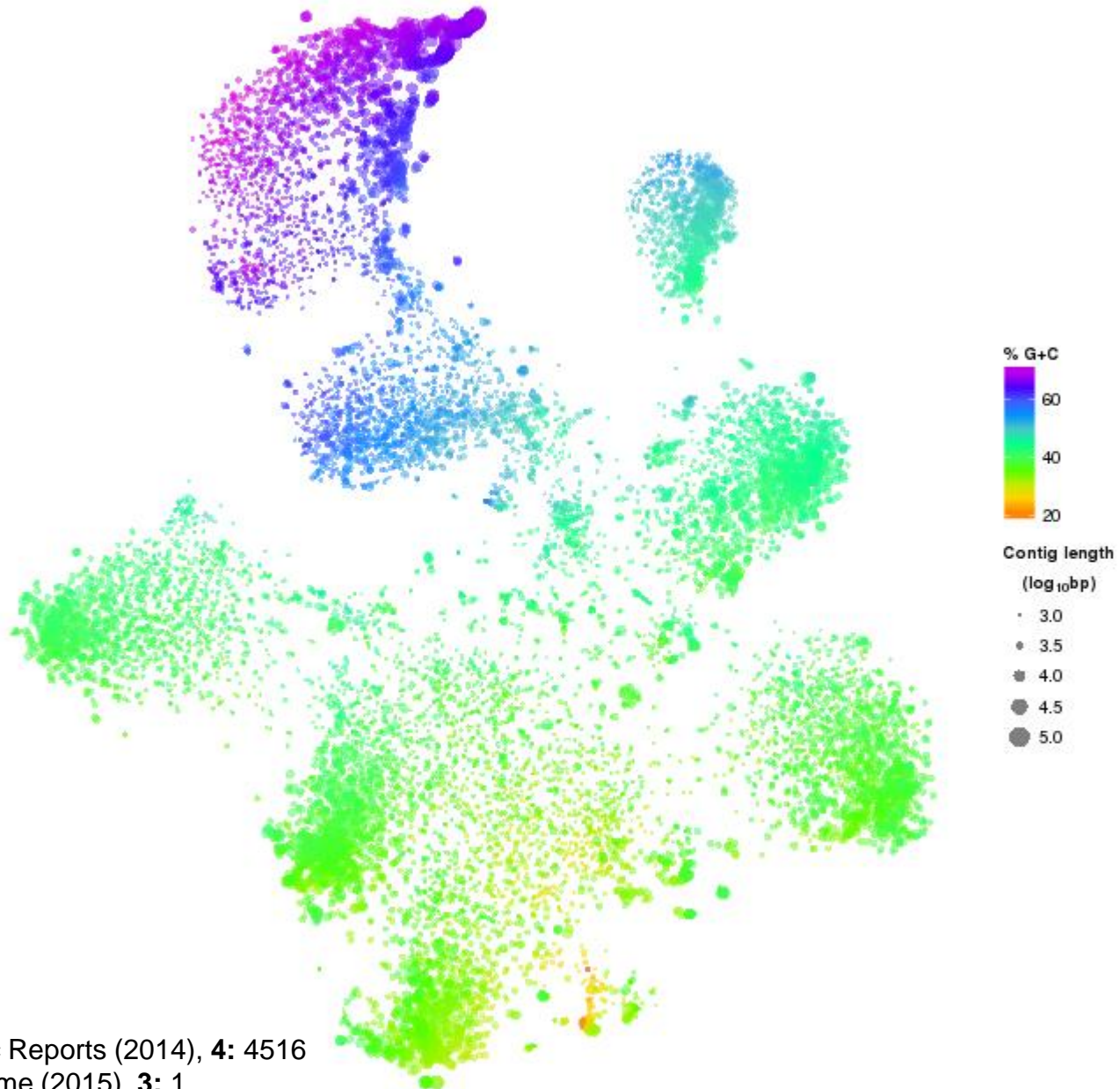
*In silico*

# IMP summary report





# IMP-VizBin: % G + C

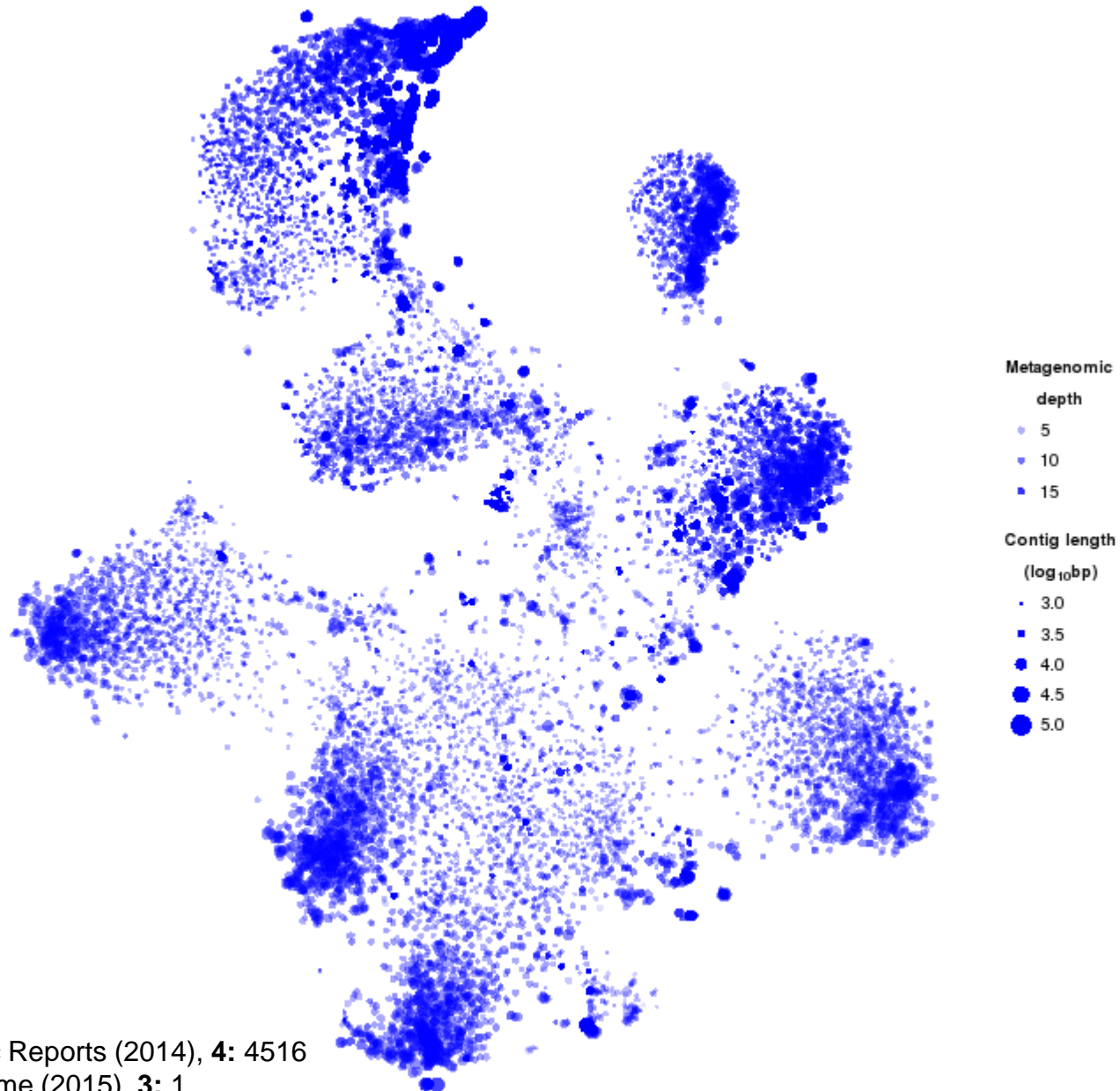


Laczny *et al.* Scientific Reports (2014), **4**: 4516

Laczny *et al.* Microbiome (2015), **3**: 1

Narayanasamy & Jarosz *et al.*, in prep; Supp. Figure

# IMP-VizBin: Length, MG-depth

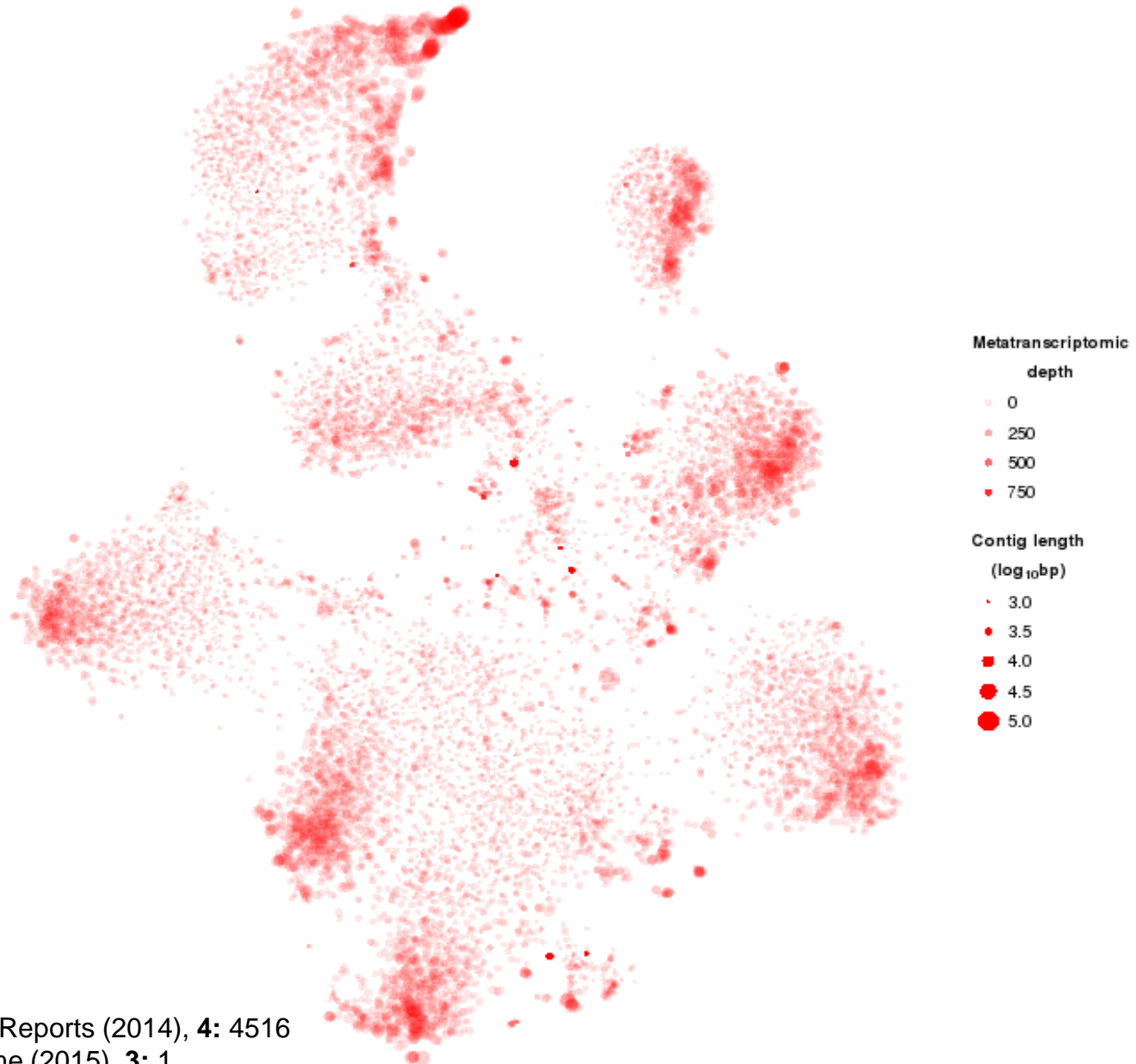


Laczny *et al.* Scientific Reports (2014), **4**: 4516

Laczny *et al.* Microbiome (2015), **3**: 1

Narayanasamy & Jarosz *et al.*, in prep; Supp. Figure

# IMP-VizBin: Length, MT-depth

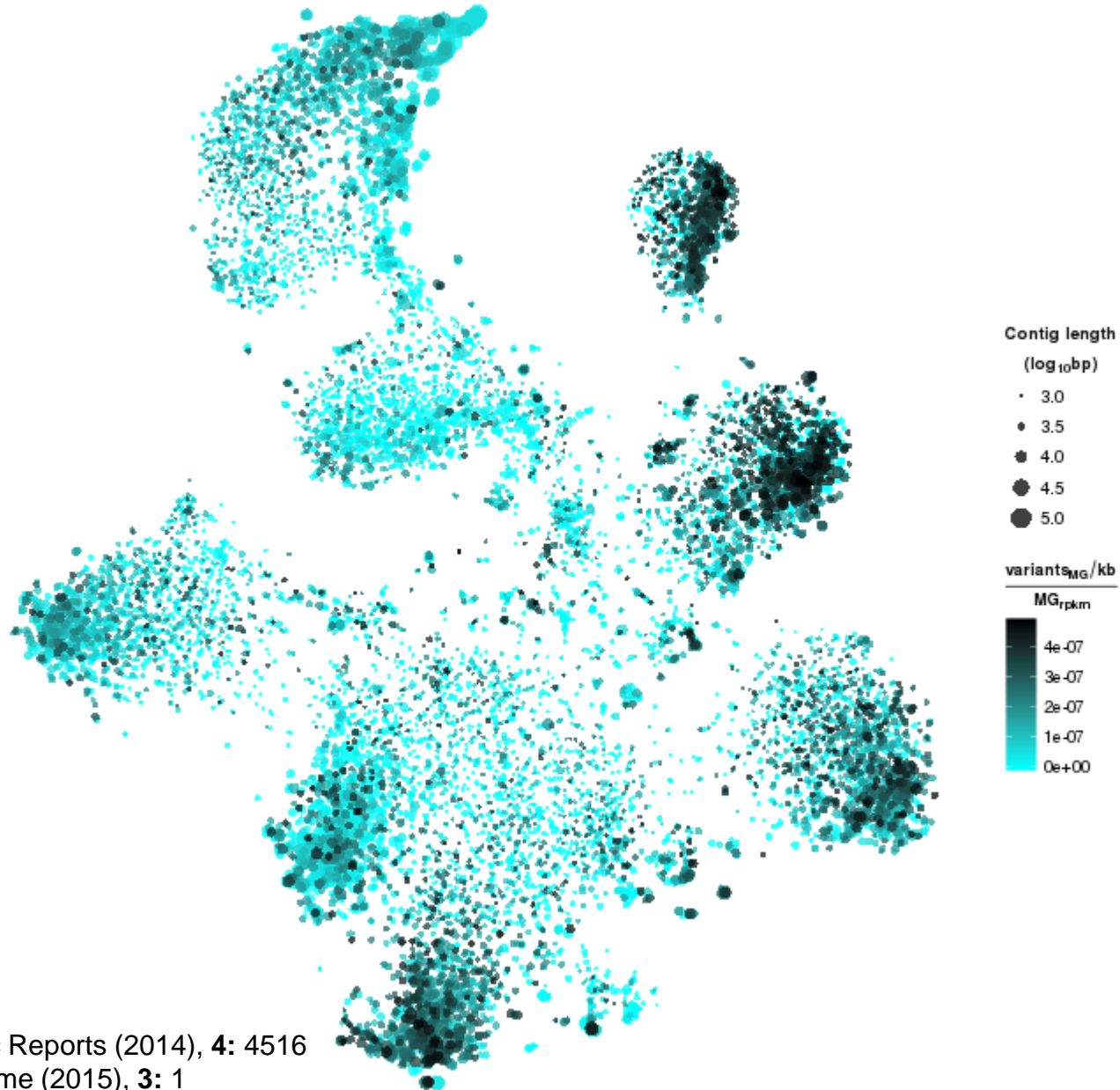


Laczny *et al.* Scientific Reports (2014), **4**: 4516

Laczny *et al.* Microbiome (2015), **3**: 1

Narayanasamy & Jarosz *et al.*, in prep; Supp. Figure

# IMP-VizBin: MG variant density

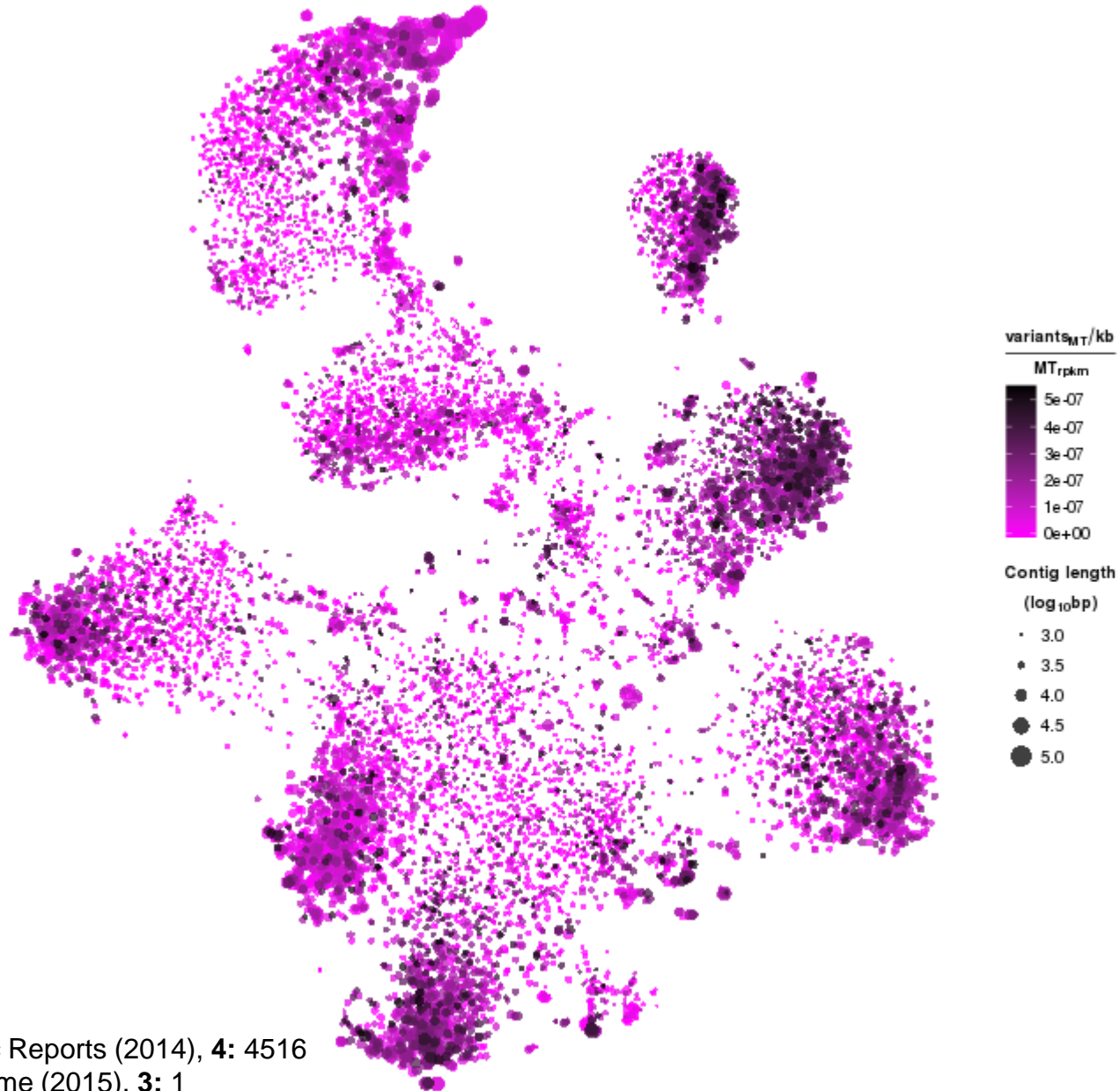


Laczny *et al.* Scientific Reports (2014), **4**: 4516

Laczny *et al.* Microbiome (2015), **3**: 1

Narayanasamy & Jarosz *et al.*, in prep; Supp. Figure

# IMP-VizBin: MT variant density

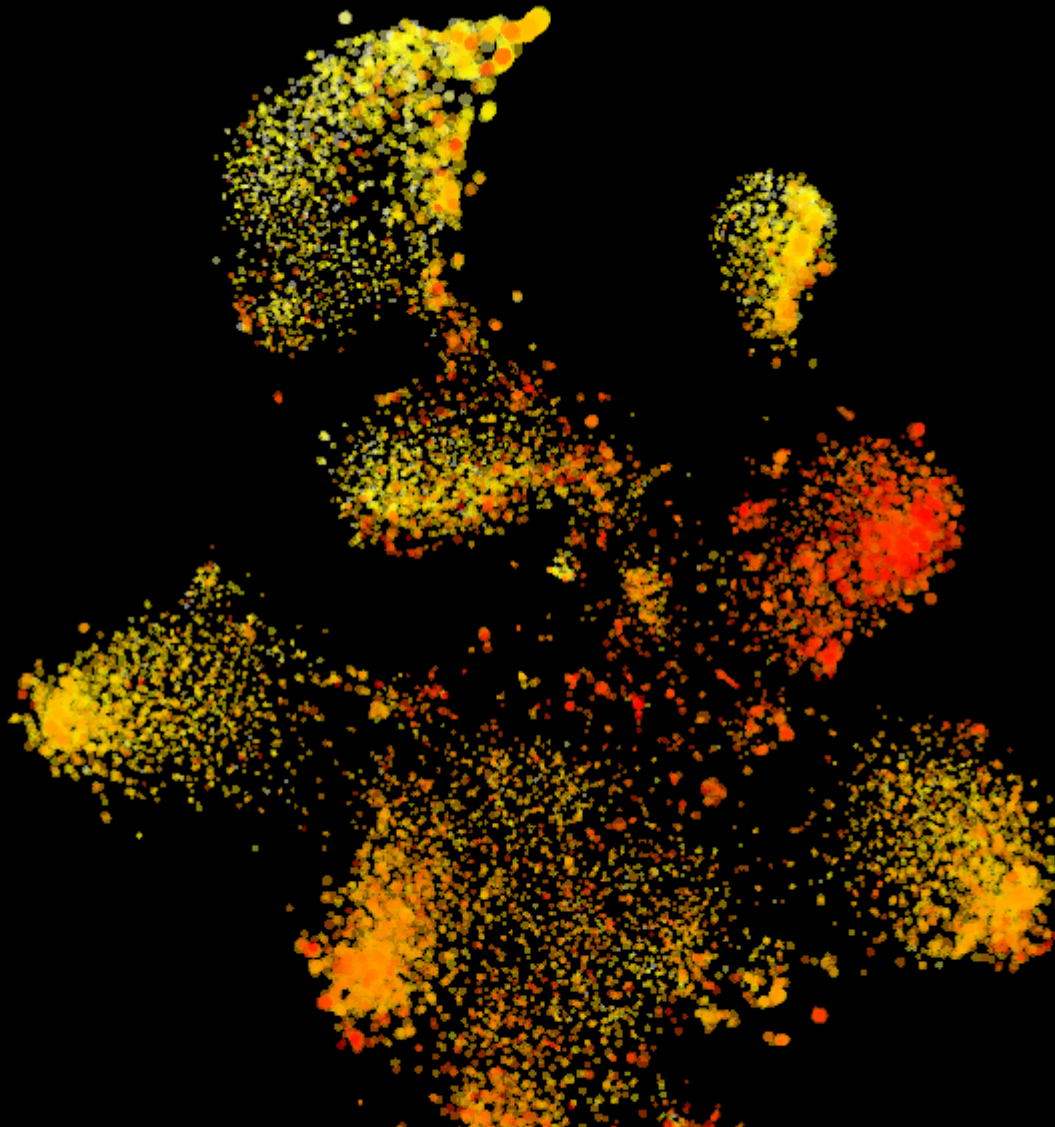


Laczny *et al.* Scientific Reports (2014), **4**: 4516

Laczny *et al.* Microbiome (2015), **3**: 1

Narayanasamy & Jarosz *et al.*, in prep; Supp. Figure

# IMP-VizBin: MT/MG depth



Laczny *et al.* Scientific Reports (2014), 4: 4516

Laczny *et al.* Microbiome (2015), 3: 1

Narayanasamy & Jarosz *et al.*, in prep; Supp. Figure