



HAL
open science

Absence of a core metabolic network common to symbiotic bacteria

Cecilia Coimbra Klein, Ludovic Cottret, Hubert Charles, Christian Gautier,
Ana Tereza Ribeiro de Vasconcelos, Vincent Lacroix, Marie-France Sagot

► **To cite this version:**

Cecilia Coimbra Klein, Ludovic Cottret, Hubert Charles, Christian Gautier, Ana Tereza Ribeiro de Vasconcelos, et al.. Absence of a core metabolic network common to symbiotic bacteria. 6. Meeting GDRE-RA Comparative genomics, Nov 2011, Lyon, France. 33 diapositives. hal-02806316

HAL Id: hal-02806316

<https://hal.inrae.fr/hal-02806316>

Submitted on 6 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Absence of a core metabolic network common to symbiotic bacteria

Cecilia C. Klein^{1,2,5}, Ludovic Cottret³, Hubert Charles^{1,4},
Christian Gautier^{1,2}, Ana Tereza Ribeiro de Vasconcelos^{2,4,5},
Vincent Lacroix^{1,2}, Marie-France Sagot^{1,2}

¹ BAMBOO Team, INRIA Grenoble-Rhône-Alpes, France

² CNRS, UMR5558, Laboratoire de Biométrie et Biologie Évolutive, UCBL, France

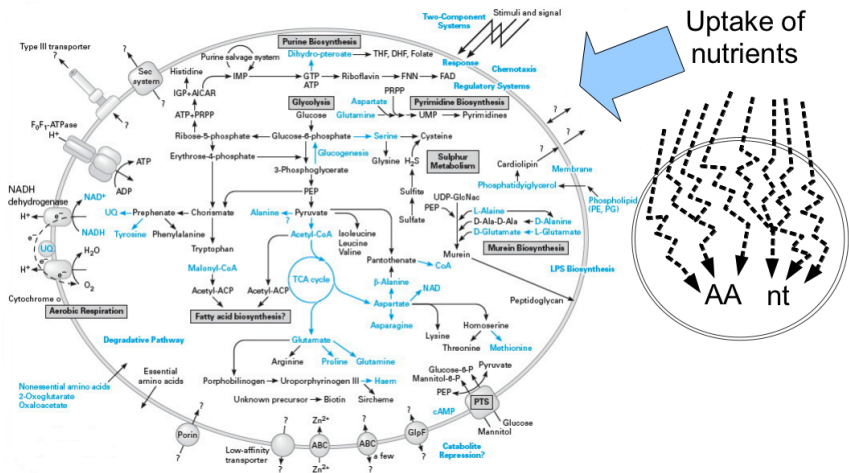
³ UMR1089 Xénobiotiques INRA-ENVT, Toulouse, France

⁴ UMR203 Biologie Fonctionnelle Insectes et Interactions, INRA, INSA-Lyon, France

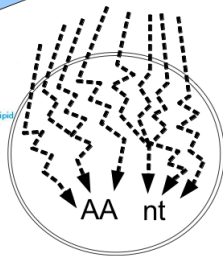
⁵ Laboratório Nacional de Computação Científica (LNCC), Brazil

GDRE Comparative Genomics
November 2011

Metabolism - basic building blocks

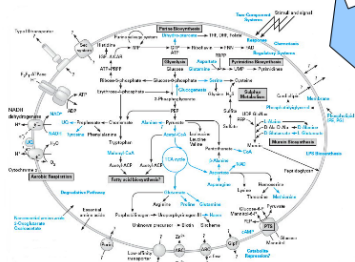


Uptake of nutrients



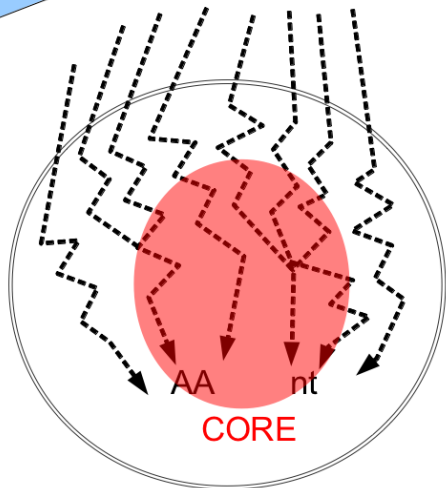
Modified from <http://www.foodmate.net/4images/3/5/21525.html>

A core of metabolic reactions ??

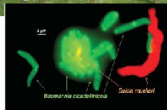
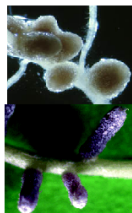
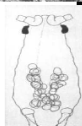
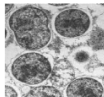


Small Molecule
Metabolism
of bacteria

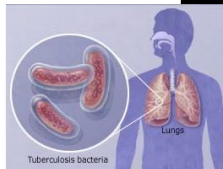
Uptake of
nutrients



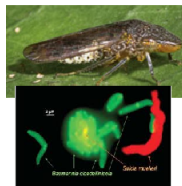
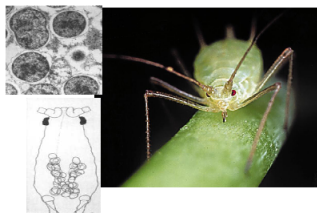
A core of metabolic reactions ??



Lifestyle



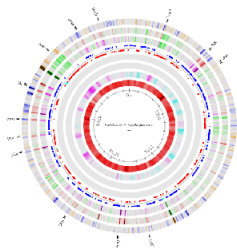
A core of metabolic reactions ??



Environment is
the host cell

Type of interaction
Reproductive manipulators
Nutritional mutualism
Host defense

...



Genome reduction
Reduced metabolism

How to do it?

- By comparing several metabolic networks of bacteria with different lifestyles
- By comparing the reaction and compound content

Dataset

Intracellular

Intracellular mutualists vertically transmitted (MIV)

Candidatus Hodgkinia cicadicola Dsem (HODCCD)
Candidatus Carsonella ruddii PV (CARRP)
Candidatus Sulcia muelleri GWSS (SULMW)
Buchnera aphidicola Cc (BUCCC)
Buchnera aphidicola APS (BUCAI)
Blattabacterium sp., Bge (BLASB)
Baumannia cicadellinicola str. Hc (BAUCH)
Candidatus Blochmannia floridanus (BLOFL)
Wigglesworthia glossinidia (WIGBR)
Candidatus Blochmannia pennsylvanicus (BLOPB)
Wolbachia pipentis wBm (WOLTR)

Intracellular parasites vertically transmitted (PIV)

Rickettsia typhi Wilmington (RICTY)
Wolbachia pipentis wMeI (WOLPM)
Orientia tsutsugamushi Boryong (ORITB)

Intracellular parasites horizontally transmitted (PIH)

Chlamydia trachomatis D/UW-3/CX (CHLTR)
Lawsonia intracellularis PHE/MN1-00 (LAWIP)

Cell associated (CA)

Cell associated mutualists vertically transmitted (MCAV)

Candidatus Hamiltonella defensa T5A (HAMD5)
Sodalis glossinidius morsitans (SODGM)

Cell associated parasites horizontally transmitted (PCAH)

Mycoplasma genitalium G37 (MYCGE)
Mycoplasma hyopneumoniae J (MYCHJ)
Bartonella quintana Toulouse (BARQU)
Helicobacter pylori 26695 (HELPHY)
Neisseria gonorrhoeae NCCP11945 (NEIG2)
Listeria monocytogenes EGD-e (LISMO)
Brucella melitensis bv 1 16M (BRUME)
Yersinia pestis CO92 (YERPE)
Yersinia pseudotuberculosis YPIII (YERPY)
Mycobacterium tuberculosis H37Rv (MYCTU)
Salmonella enterica serovar Typhi (SALTY)
Shigella flexneri 2a str. 301 (SHIFL)
Photobacterium luminescens TTO1 (PHOLL)
Burkholderia mallei ATCC 23344 (BURMA)
Bacillus anthracis Ames Ancestor (BACAN)

Extracellular

Extracellular mutualists horizontally transmitted (MEH)

Cupriavidus taiwanensis LMG19424 (CUPTR)
Frankia alni ACN14a (FRAAA)
Sinorhizobium meliloti 1021 (RHIME)

Extracellular commensals horizontally transmitted (CEH)

Streptococcus thermophilus LMD-9 (STRTD)
Wolfinella succinogenes DSM 1740 (WOLSU)
Lactobacillus casei ATCC 334 (LACC3)
Bacillus amyloliquefaciens FZB42 (BACA2)
Escherichia coli K-12 (ECOLI)
Pseudomonas fluorescens SBW25 (PSEFS)
Mycobacterium smegmatis MC2 155 (MYCS2)

Extracellular parasites horizontally transmitted (PEH)

Streptococcus agalactiae 2803V/R (STRA5)
Xylella fastidiosa 9a5c (XYLFA)
Vibrio cholerae O1 biovar El Tor str. N16961 (VIBCH)
Erwinia carotovora subsp. atroseptica SCRI1043 (ERWCT)
Pseudomonas entomophila L48 (PSEE4)
Escherichia coli O157:H7 (ECO57)
Bacillus thuringiensis serovar konkukian str. 97-27 (BACHK)
Agrobacterium tumefaciens C58 (AGRT5)
Pseudomonas aeruginosa UCBPP-PA14 (PSEAB)

Free-living (FL)

Thiomicrospira crunogena XCL-2 (THICR)
Desulfotalea psychrophila Lsv54 (DESPS)
Pseudoalteromonas haloplanktis TAC125 (PSEHT)
Bacillus subtilis 168 (BACSU)
Rhodobacter sphaeroides 2.4.1 (RHOSA)
Ralstonia eutropha H16 (RALEH)

Data acquisition & methods

- MicroCyc/MicroScope¹:
 - ▶ genomic data and metabolic network reconstructions
 - ▶ to avoid as much as possible introducing biases related to different annotation techniques

- HAMAP classification²:
 - ▶ guide the grouping of the organisms

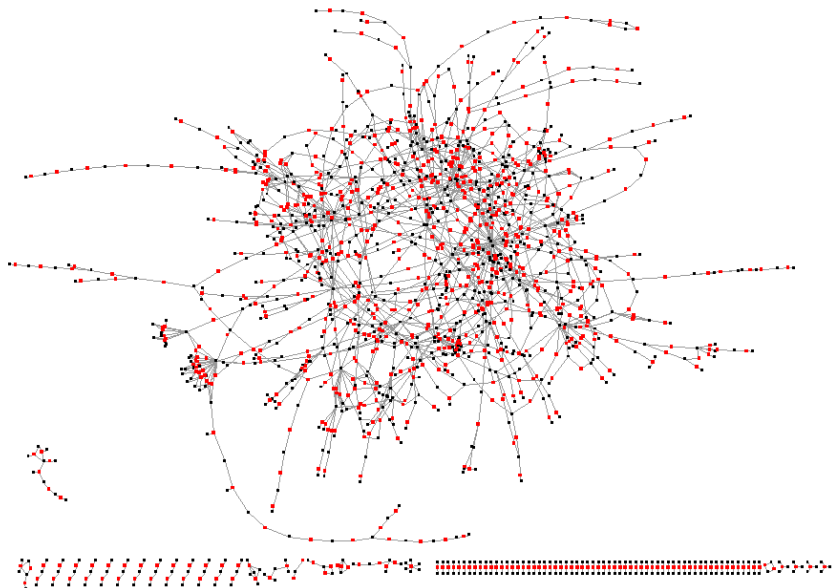
¹Vallenet *et al.* 2009 Database (Oxford).

²Lima *et al.* 2009 Nucleic Acids Res.

How to do it?

- Comparison of several metabolic networks of bacteria with different lifestyles
- By comparing the reaction and compound content

Metabolic network



Data acquisition & methods

- MetExplore: network modelling and filtering¹
 - ▶ Small molecule metabolism filtering
- Cytoscape: visualisation of the networks²
- Analyses were performed using R³:
 - ▶ *ade4* package for statistics⁴
 - ▶ *Igraph* package for graph manipulation⁵

¹Cottret *et al.* 2010 Nucleic Acids Res.

²Shannon *et al.* 2003 Genome Res.

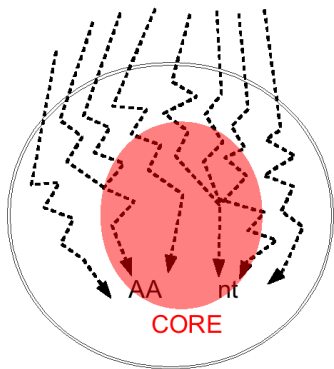
³<http://cran.r-project.org/>

⁴Dray & Dufour *et al.* 2007 Journal of Statistical Software

⁵Csardi *et al.* 2006 InterJournal Complex Systems

Metabolic core

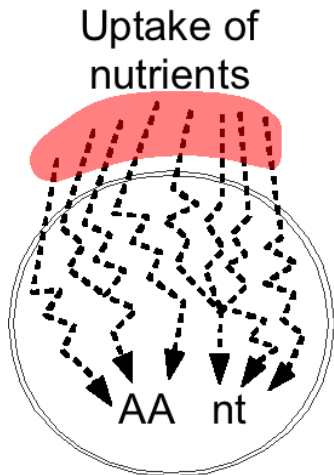
- Metabolic core: a conserved set of elements in these bacteria
- It was obtained by computing the intersection of the sets of reactions (resp. compounds) for each species



Environment: inputs to the network

Identification of potential inputs to the networks using the Borenstein method¹

- ▶ metabolites each bacterium potentially acquires from its environment

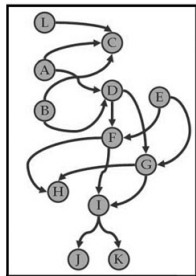


¹Borenstein *et al.* 2008 Proc Natl Acad Sci U S A

Environment: inputs to the network

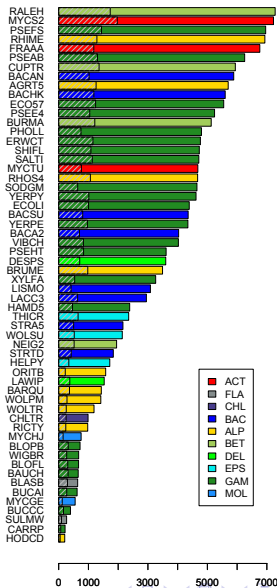
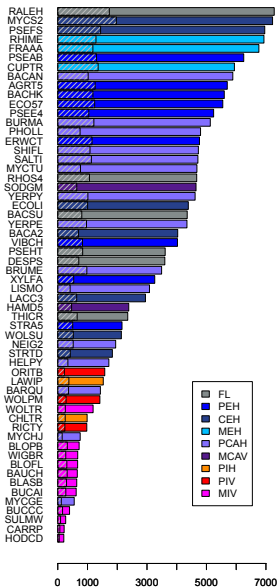
Identification of potential inputs to the networks using the Borenstein method¹

- ▶ metabolites each bacterium potentially acquires from its environment
- ▶ directed compound graph
- ▶ cofactors and current compounds filtered
- ▶ based on the detection of the strongly connected components (SCC) in the compound graph
- ▶ a version of the Borenstein method using the Igraph package in R

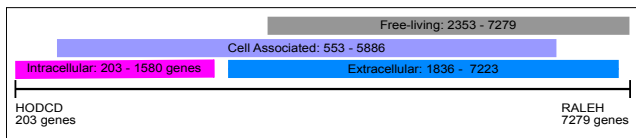


¹Borenstein *et al.* 2008 Proc Natl Acad Sci U S A

Data overview: number of genes

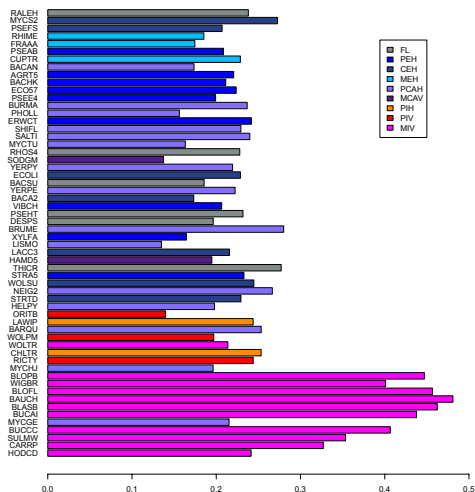


Data overview: number of genes

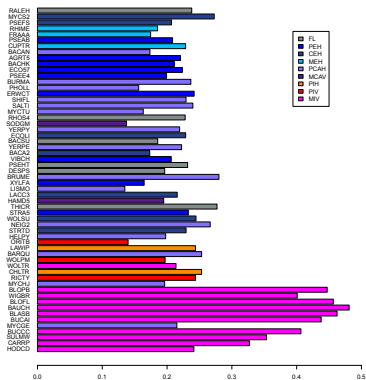


The intracellular life is paired with an extreme reduction of the genome and of the metabolism

Ratio metabolic genes over the total number of genes

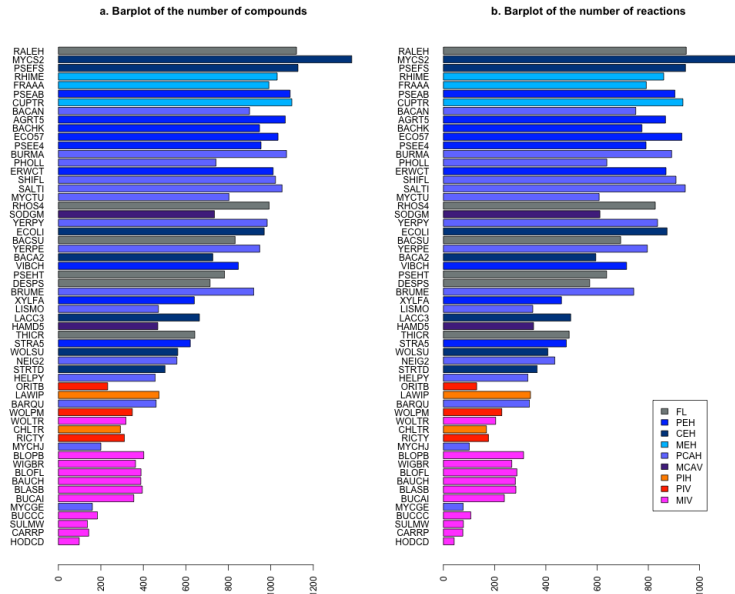


Ratio metabolic genes over the total number of genes



The portion dedicated to metabolism is greater in the genomes of the mutualistic endosymbionts

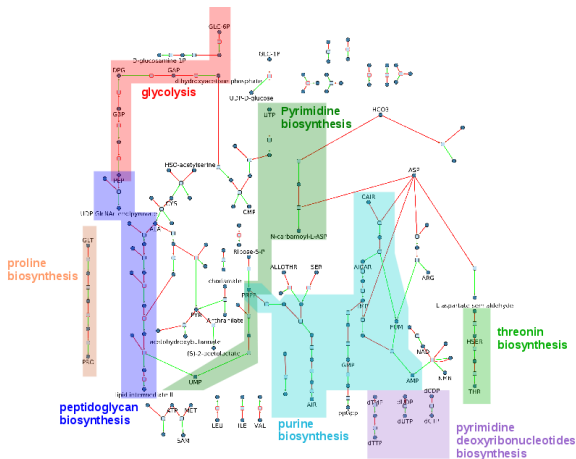
Number of compounds and reactions



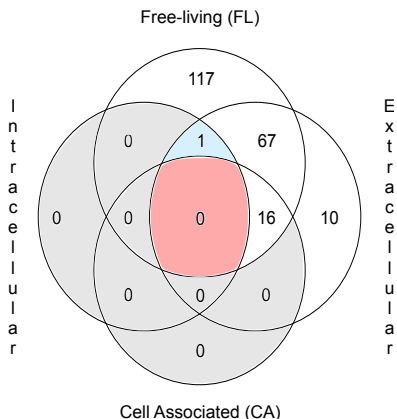
Core metabolism - extracellular bacteria

94 reactions:

- ▶ most of them (88%) are classified in biosynthetic processes according to BioCyc metabolic processes
- ▶ they participate in glycolysis, nucleotide and amino acid biosynthesis and degradation pathways, and peptidoglycan biosynthesis



Core metabolism - reactions

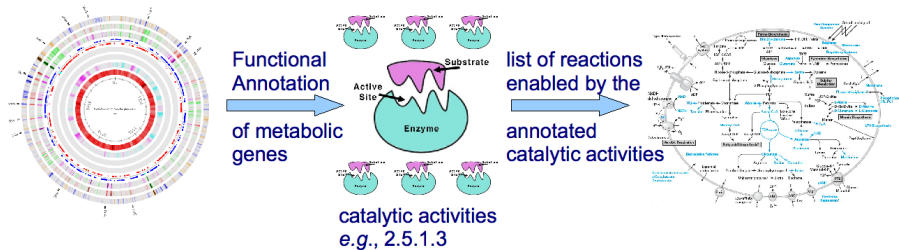


- ▶ There is not a single enzymatic reaction common to all 58 bacteria
- ▶ No metabolic core is preserved among the endosymbionts
- ▶ The reduction of the metabolism affects different parts of the network among the endosymbionts

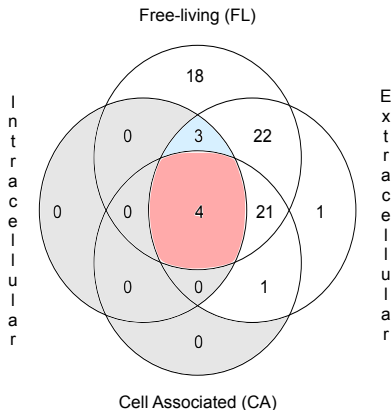
EC number sets

- The analysis of partial EC number sets, e.g. 2.5.1.-, may allow some flexibility, possibly increasing the size of the common sets.

Metabolic network reconstruction from genomic data



EC number sets



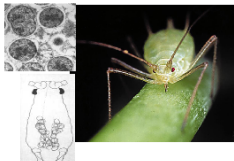
EC number	Classification
2	Transferases
2.3	Acytransferases
2.3.1	Transferring groups other than aminoacyl groups
2.5	Transferring alkyl or aryl groups, other than methyl groups
2.5.1	Transferring alkyl or aryl groups, other than methyl groups (only subclass identified to date)
3	Hydrolases
3.5	Acting on carbon-nitrogen bonds, other than peptide bonds
3.5.1	In linear amides
4	Lyases
4.2	Carbon-oxygen lyases
4.2.1	Hydro-lyases

EC number sets - simulation

The small intersection could be explained by differential random loss of enzymes during genome reduction of intracellular symbionts?



For each MIV
 γ -proteobacteria (7)

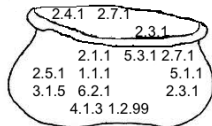
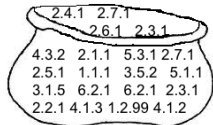


Randomly picked
one extracellular
 γ -proteobacteria

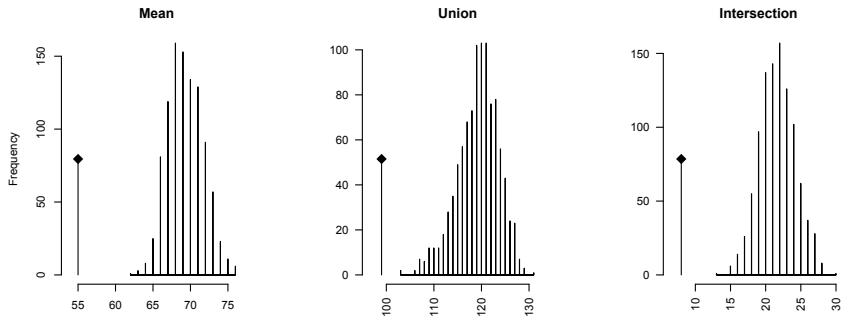
Randomly removed
elements, until we reached
the size of the MIV
metabolic network

Buchnera: 246 partial EC numbers

246 partial EC numbers

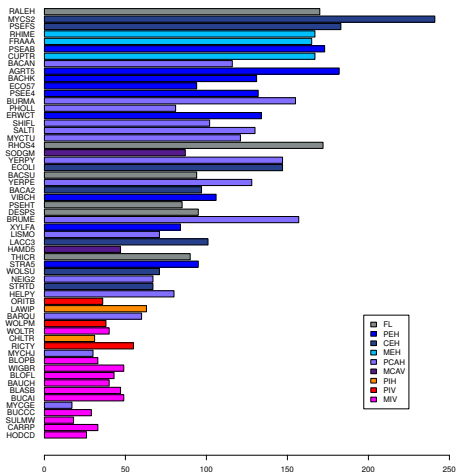


EC number sets - simulation



	Mean	Union	Intersection
MIV	55	99	8
Simulation	69 ± 4.7	119 ± 8.5	22 ± 5.0
Estimated p - value	≤ 0.001	≤ 0.001	≤ 0.001

Environment - inputs in the network



Is the absence of a metabolic core in the obligate intracellular bacteria linked to the differences in their environment?

Conclusions

- Comparison of the small molecule metabolism of 58 bacteria representing a wide range of lifestyles
- No enzymatic reaction common to all of them
- It is essentially due to intracellular symbionts

Conclusions

- Extracellular symbionts:
 - ▶ a core restricted to 94 reactions
 - ▶ this core is however non connected

 - ▶ it involves mainly biosynthetic reactions (88%)
 - ▶ Vieira *et al.* 2011¹ found that the core-metabolism of *Escherichia coli* is enriched in biosynthetic pathways

 - ▶ they have similar needs in terms of the building blocks of their cells
 - ▶ each one of them has to adapt to a distinct environment

¹Vieira *et al.* 2011 J Bacteriol.

Conclusions

- Obligate intracellular symbionts:
 - ▶ the host provides an interface between the external and the internal environments
 - ▶ most degradation pathways have disappeared and have been outsourced to the host
 - ▶ synthetic routes have not all disappeared but they have been selected for, depending on the nature of the symbiosis

- The fact that there is no reaction common to all symbionts implies that virtually any reaction can be outsourced to the host

Thanks

- Funding:
 - ▶ French project ANR MIRI BLAN08-1335497
 - ▶ ERC Advanced Grant SISYPHE
 - ▶ FAPERJ/INRIA

