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

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-02806316v1

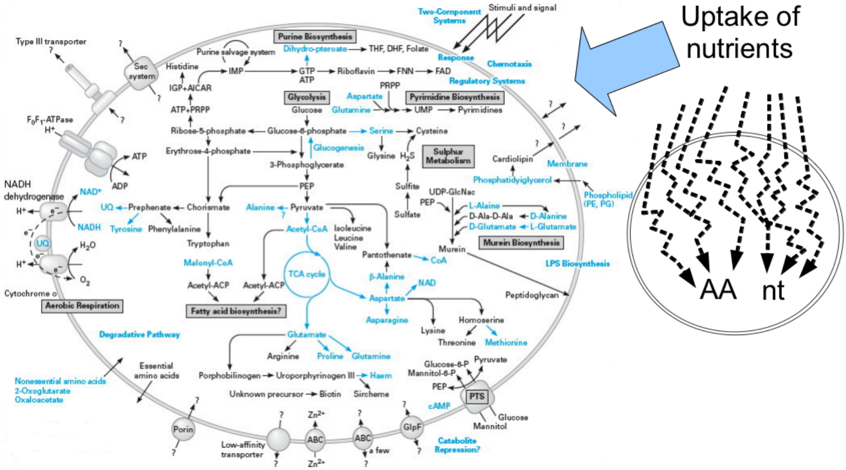
Absence of a core metabolic network common to symbiotic bacteria

Cecilia C. Klein[1,2,5], Ludovic Cottret[3], 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

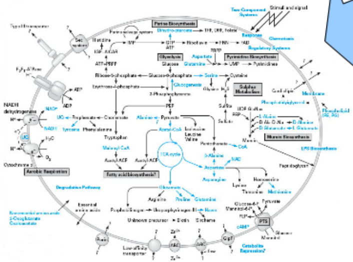
GDRE Comparative Genomics
November 2011

Metabolism - basic building blocks

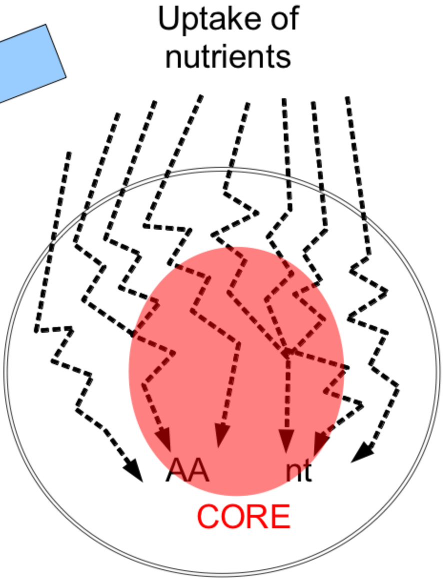


Modified from http://www.foodmate.net/4images/3/5/21525.html

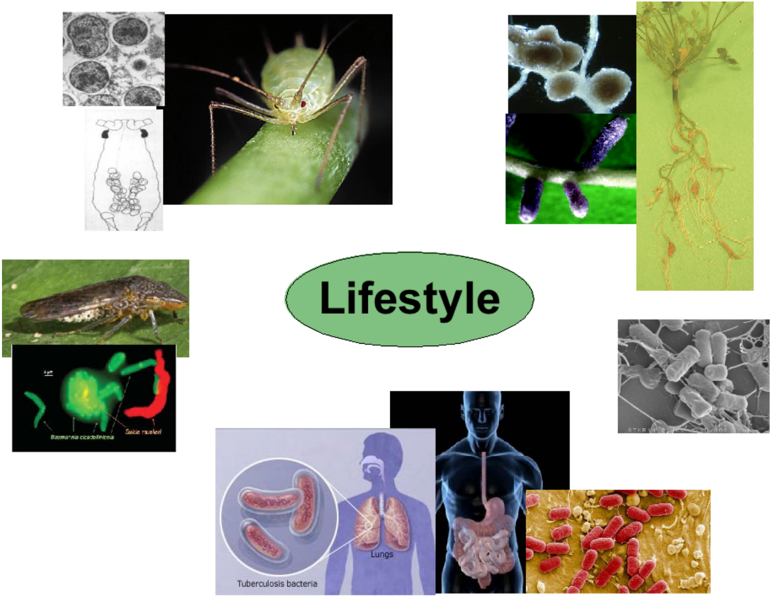
A core of metabolic reactions ??



Small Molecule
Metabolism
of bacteria

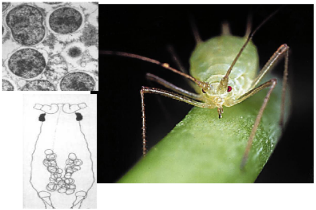


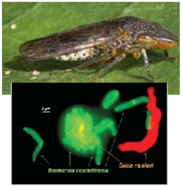
A core of metabolic reactions ??



Lifestyle

A core of metabolic reactions ??





Environment is
the host cell

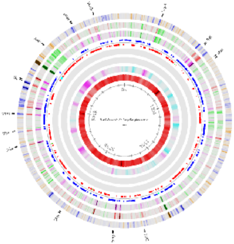
Type of interaction

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 (HODCD)
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 pipientis wMel (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 (HELPY)
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 (SALTI)
Shigella flexneri 2a str. 301 (SHIFL)
Photorhabdus 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)
Wolinella 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 2603V/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 (RHOS4)
Ralstonia eutropha H16 (RALEH)

Data acquisition & methods

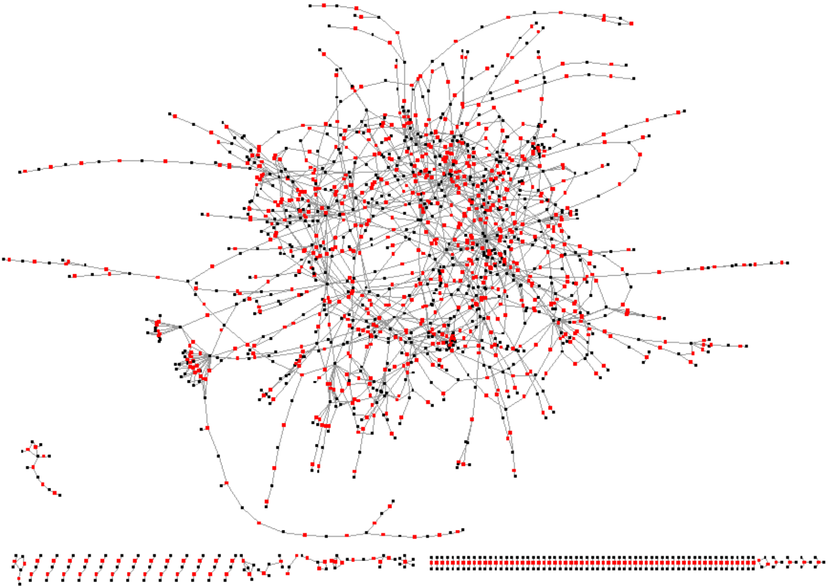
- MicroCyc/MicroScope[1]:
    - genomic data and metabolic network reconstructions
    - to avoid as much as possible introducing biases related to different annotation techniques
- HAMAP classification[2]:
    - guide the grouping of the organisms

[1] Vallenet *et al*. 2009 Database (Oxford).
[2] Lima *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



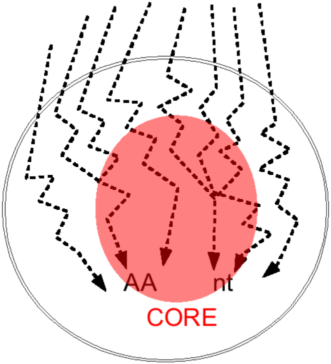
Data acquisition & methods

- MetExplore: network modelling and filtering[1]
    - Small molecule metabolism filtering
- Cytoscape: visualisation of the networks[2]
- Analyses were performed using R[3]:
    - *ade*4 package for statistics[4]
    - *Igraph* package for graph manipulation[5]

[1] Cottret *et al*. 2010 Nucleic Acids Res.
[2] Shannon *et al*. 2003 Genome Res.
[3] http://cran.r-project.org/
[4] Dray & Dufour *et al*. 2007 Journal of Statistical Software
[5] Csardi *et al*. 2006 InterJournal Complex Systems

Metabolic core

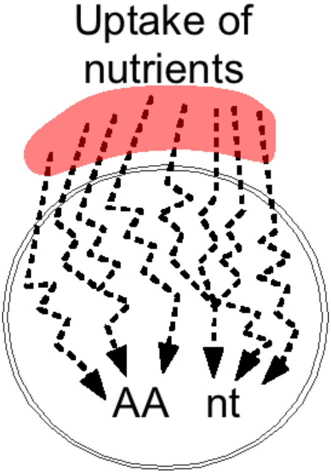
- Metabolic core: a conserved set of elements in these bacteria
- It was obtained by computing the intersection of the sets of reactions (resp. compounds) for each species



Environment: inputs to the network

Identification of potential inputs to the networks using the Borenstein method[1]

- metabolites each bacterium potentially acquires from its environment



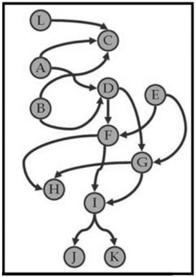
---

[1] Borenstein *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 method[1]

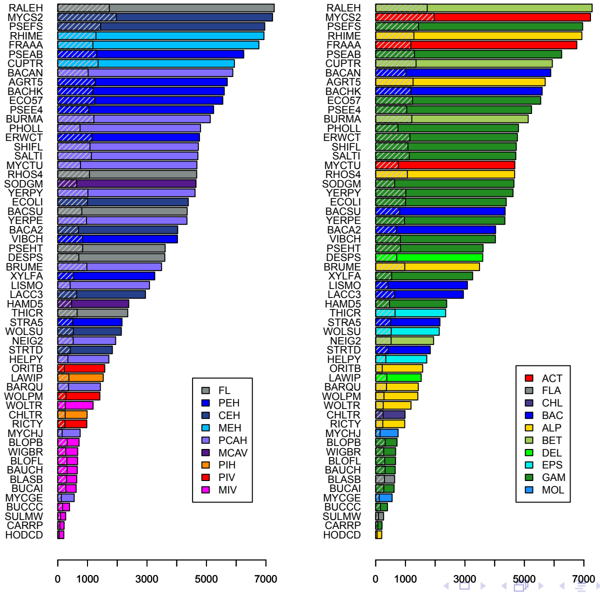
- metabolites each bacterium potentially acquires from its environment
- directed compound graph
- cofactors and current compounds filtered
- based on the detection of the strongly connected components (SCC) in the compound graph
- a version of the Borenstein method using the Igraph package in R



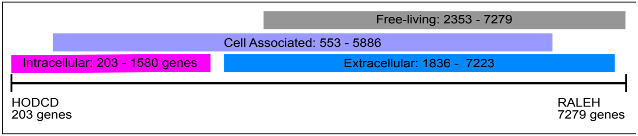
---

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

Data overview: number of genes

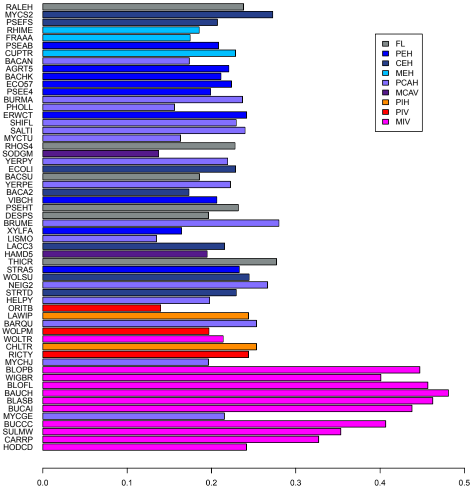


Data overview: number of genes

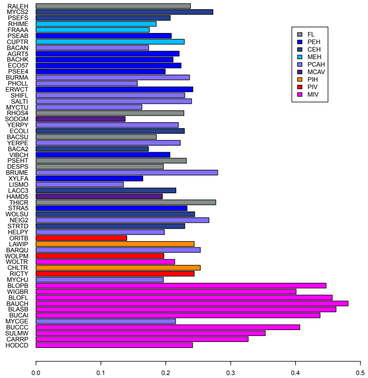


The intracellular life is paired with an extreme reduction of the genome and of the metabolism

Ratio metabolic genes over the total number of genes

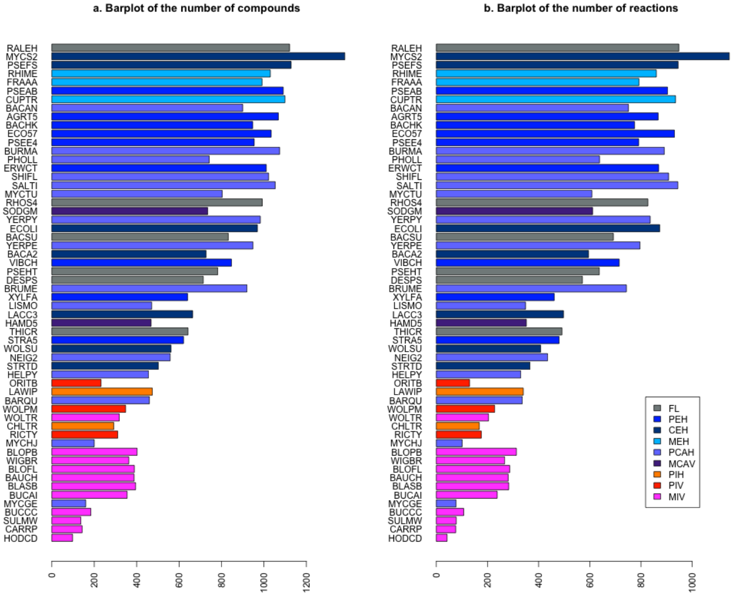


Ratio metabolic genes over the total number of genes



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

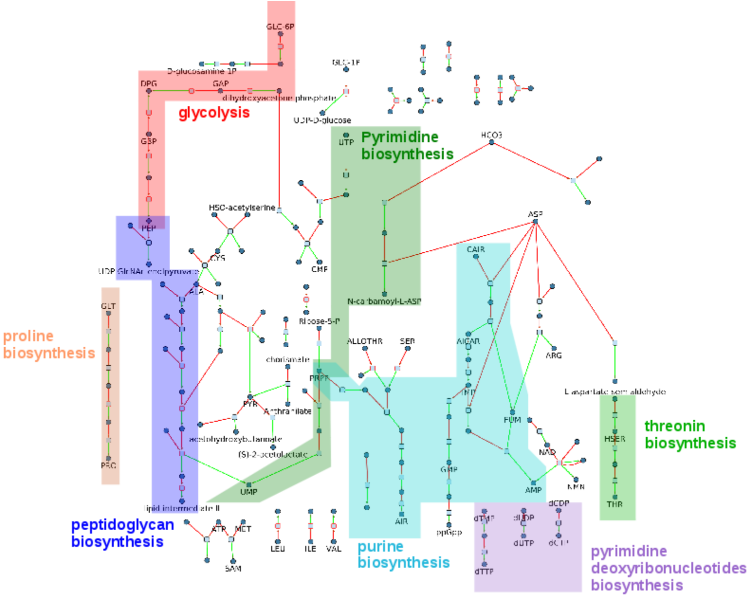
Number of compounds and reactions



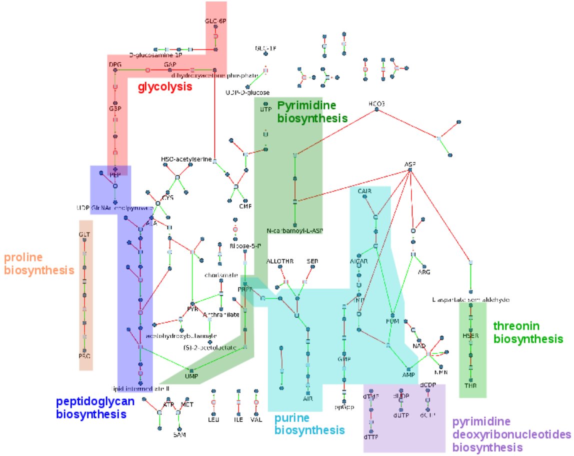
a. Barplot of the number of compounds

b. Barplot of the number of reactions

Core metabolism - extracellular bacteria



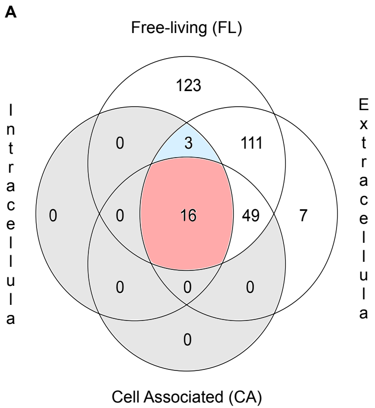
Core metabolism - extracellular bacteria



94 reactions:

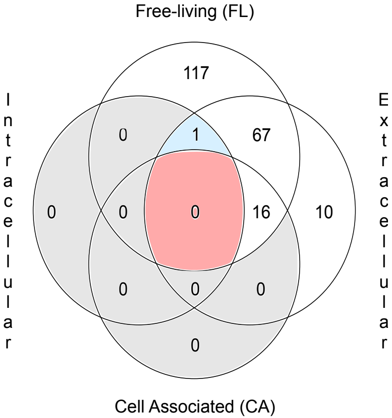
- most of them (88%) are classified in biosynthetic processes according to BioCyc metabolic processes
- they participate in glycolysis, nucleotide and amino acid biosynthesis and degradation pathways, and peptidoglycan biosynthesis

Core metabolism - compounds



Compounds	Classification
pyruvate	Acids
L-alanine	Amino Acids
L-cysteine	Amino Acids
L-glutamate	Amino Acids
L-glutamine	Amino Acids
L-serine	Amino Acids
D-ribose-5-phosphate	Carbohydrates
coenzyme A	Cofactors
diphosphate	Ions
phosphate	Ions
H+ (PROTON)	Ions
AMP	Nucleosides
ADP	Nucleosides
ATP	Nucleosides
formate	Unclassified
H2O (WATER)	Unclassified

Core metabolism - reactions

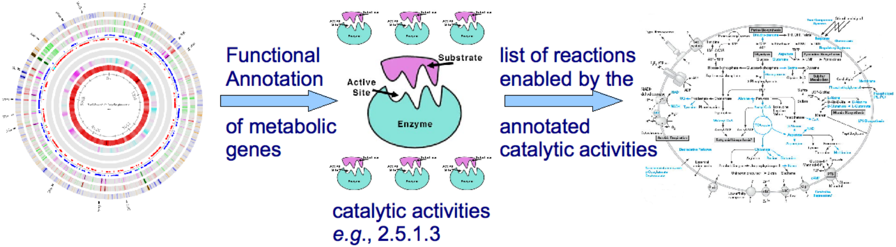


- There is not a single enzymatic reaction common to all 58 bacteria
- No metabolic core is preserved among the endosymbionts
- The reduction of the metabolism affects different parts of the network among the endosymbionts

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



Functional Annotation

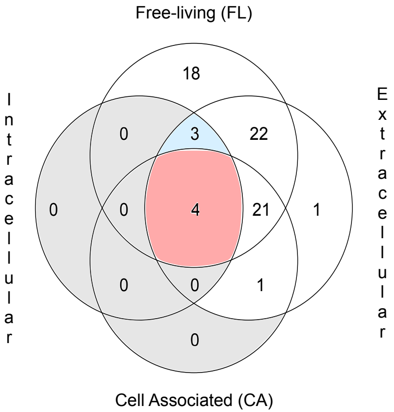
of metabolic genes

list of reactions enabled by the

annotated catalytic activities

catalytic activities
e.g., 2.5.1.3

EC number sets



EC number	Classification
2	**Transferases**
2.3	Acyltransferases
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

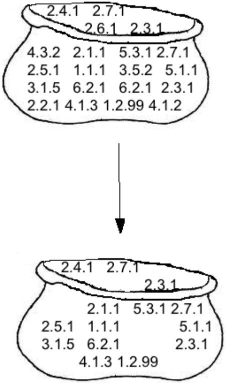
EC number sets - simulation

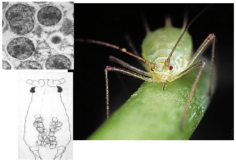
The small intersection could be explained by differential random loss of enzymes during genome reduction of intracellular symbionts?

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

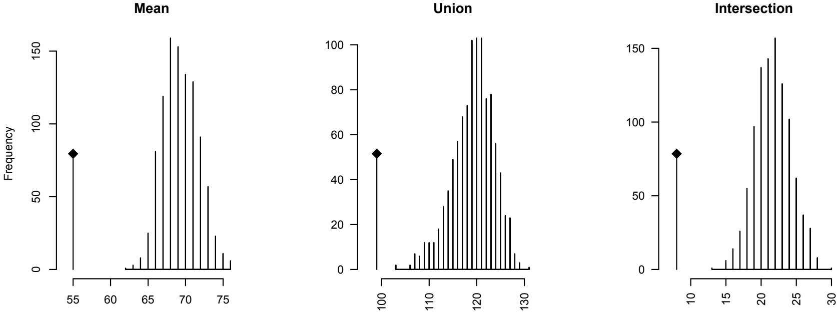




Buchnera: 246 partial EC numbers

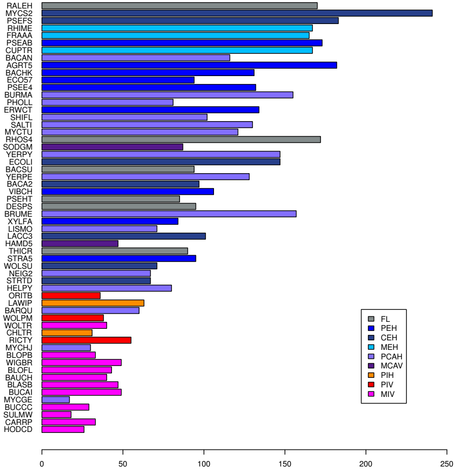
246 partial EC numbers

EC number sets - simulation



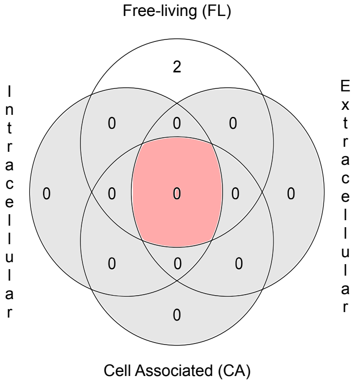
	Mean	Union	Intersection
MIV	55	99	8
Simulation	69 ± 4.7	119 ± 8.5	22 ± 5.0
Estimated $p - value$	≤ 0.001	≤ 0.001	≤ 0.001

Environment - inputs in the network



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

Environment - inputs in the network



The absence of common potential inputs to the bacteria

It indicates that the diversity of the environment alone does not explain the loss of a metabolic core

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*. 2011[1] 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

[1] Vieira *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

Inria INVENTEURS DU MONDE NUMÉRIQUE

LBBE

UCB

cnrs

Laboratório de Bioinformática

Laboratório Nacional de Computação Científica

CAPES