

Learning from minimal natural cells

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ECSB II: Design, programming and
optimisation of biological systems

29 March – 03 April 2009

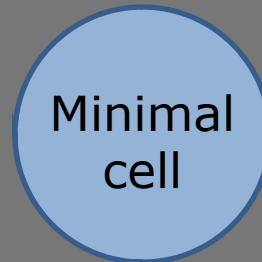
Sant Feliu de Guixols

“Top-down” approach

In vitro genome synthesis

Comparative Genomics

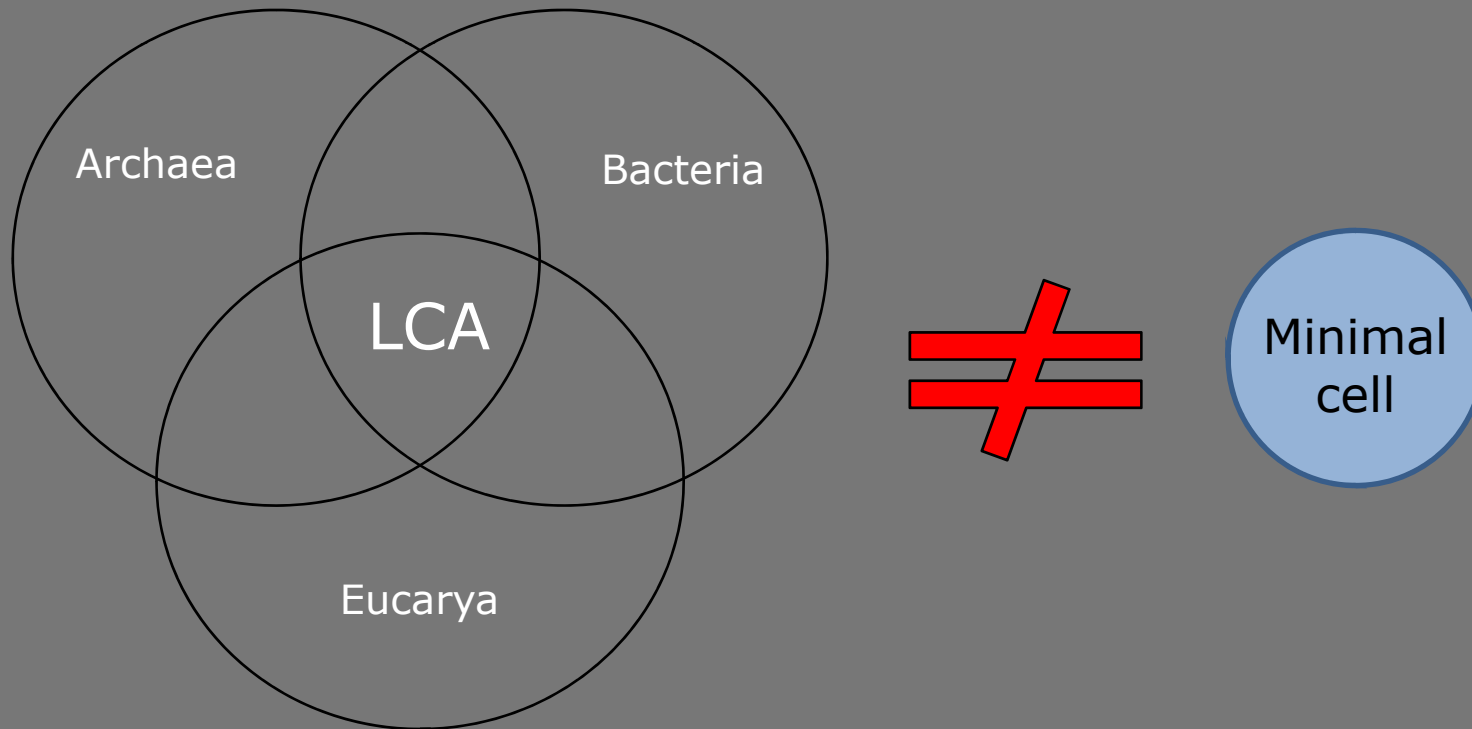
Gene deletion experiments



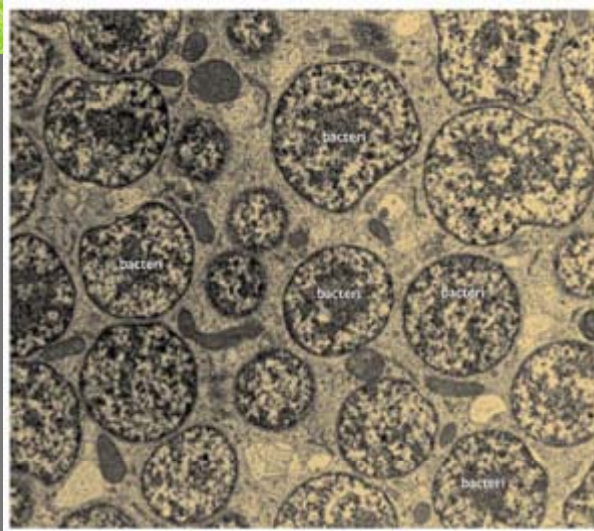
Synthesis of a proto-cell from scratch

“Bottom-up” approach

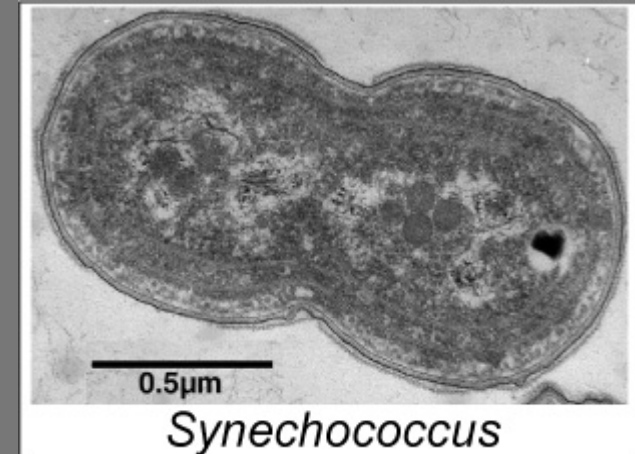
The LCA is not the same as the minimal cell



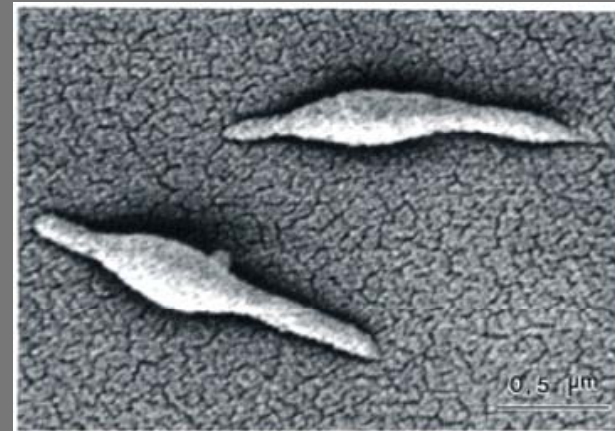
However, natural evolved reduced genomes are, *par excellence*, examples of minimal cells ...



Buchnera aphidicola

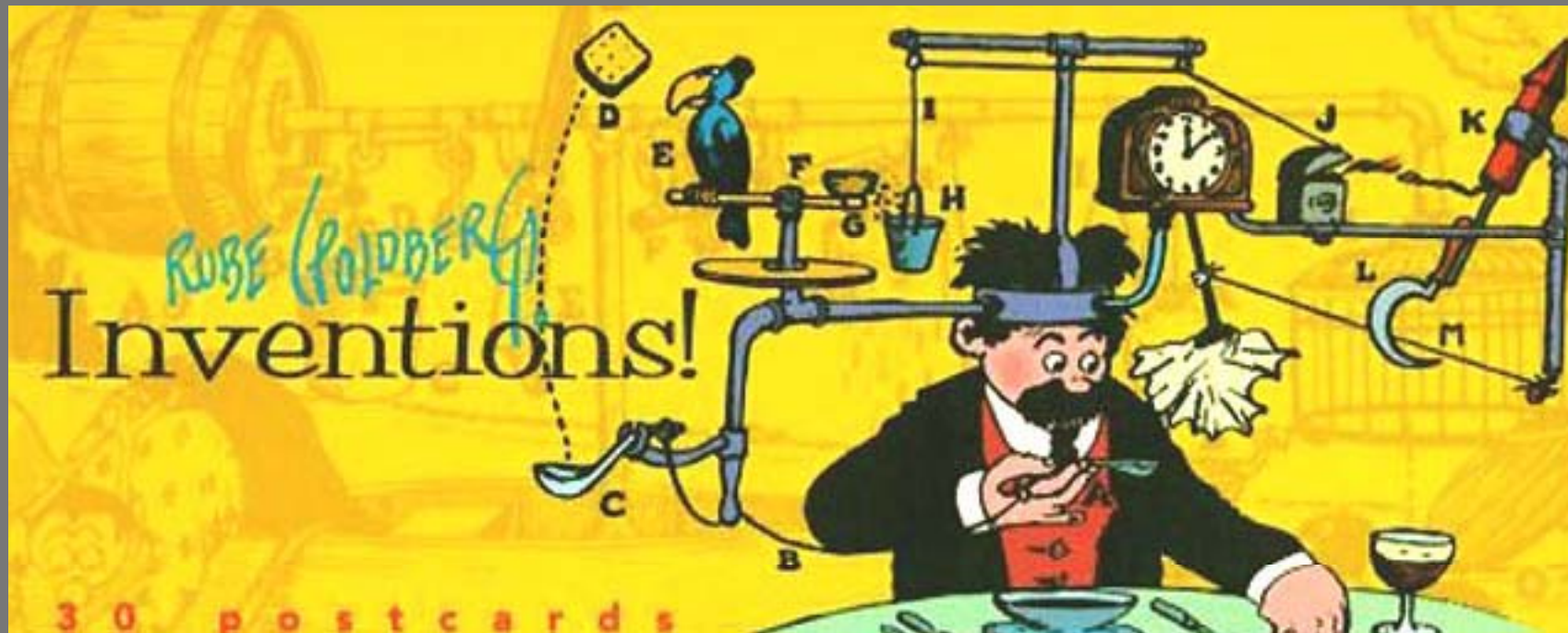


Synechococcus

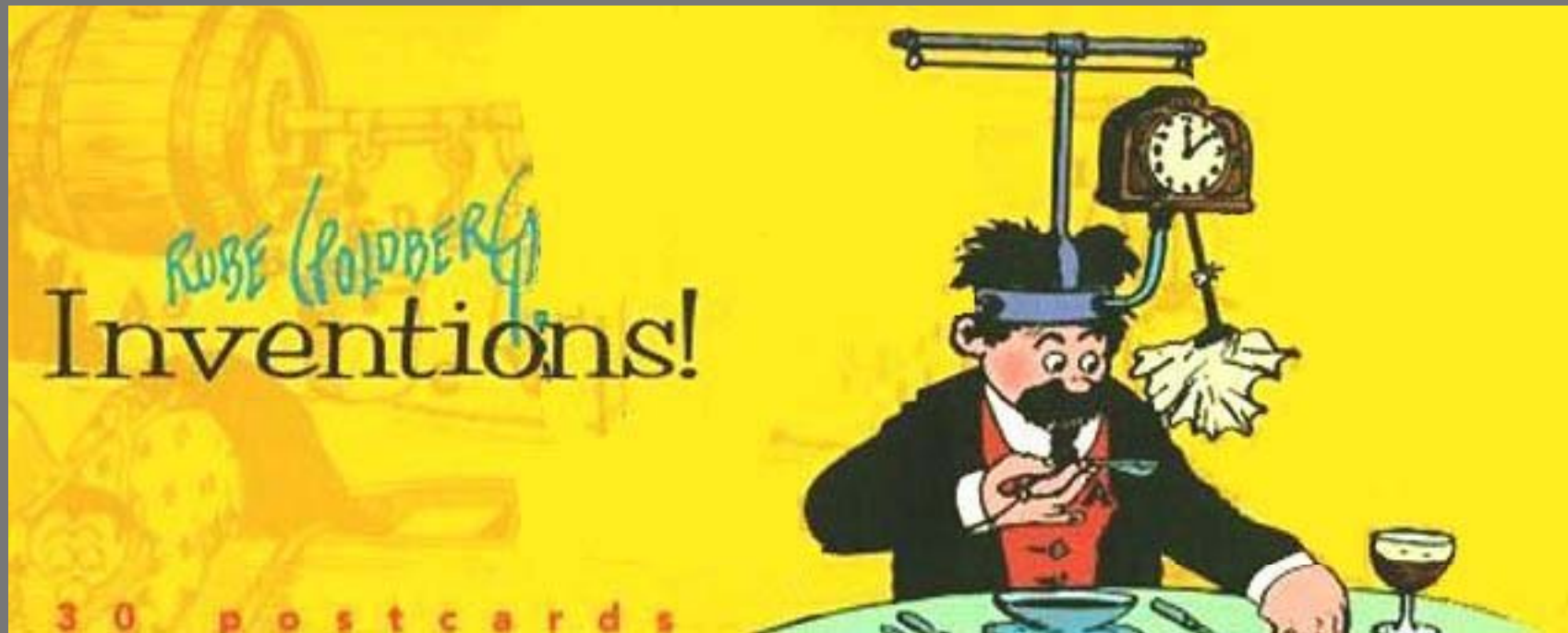


Mycoplasma pneumoniae

Because they are products of extensive natural genome reductions....



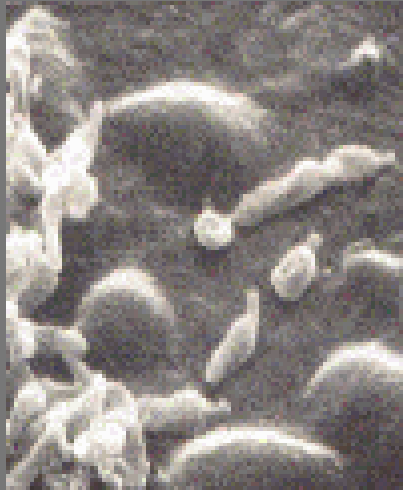
Because they are product of intensive genome reductions...



... they can give us clues as to what must be retained

Definition of a minimal gene set in relation to the environment

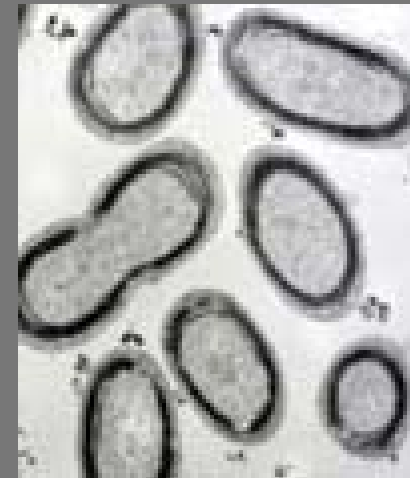
Chemically complex
environment
(host associated)



Mycoplasma genitalium

525 genes

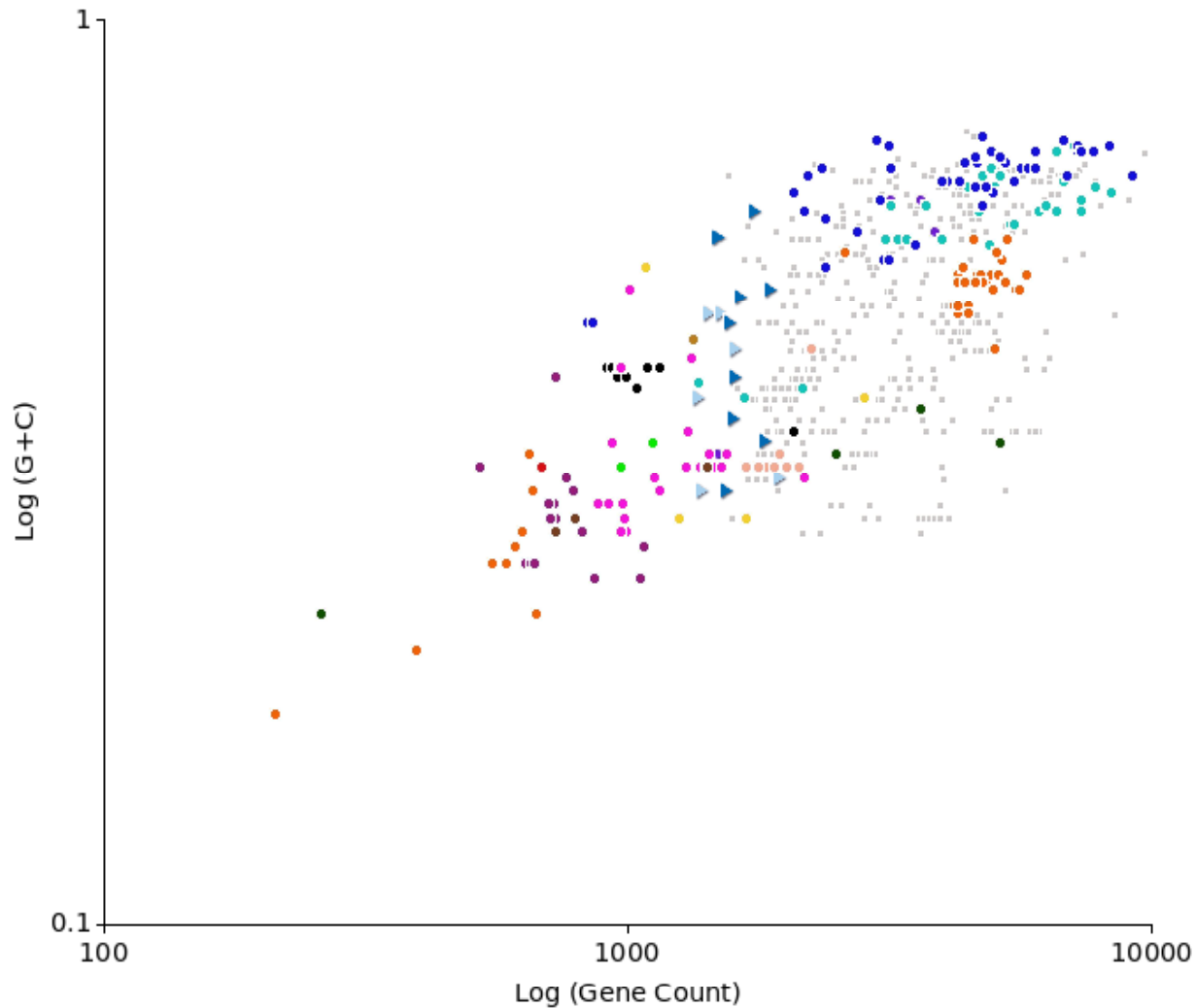
Chemically simple
environment (free-living)



Prochlorococcus marinus

1765 genes

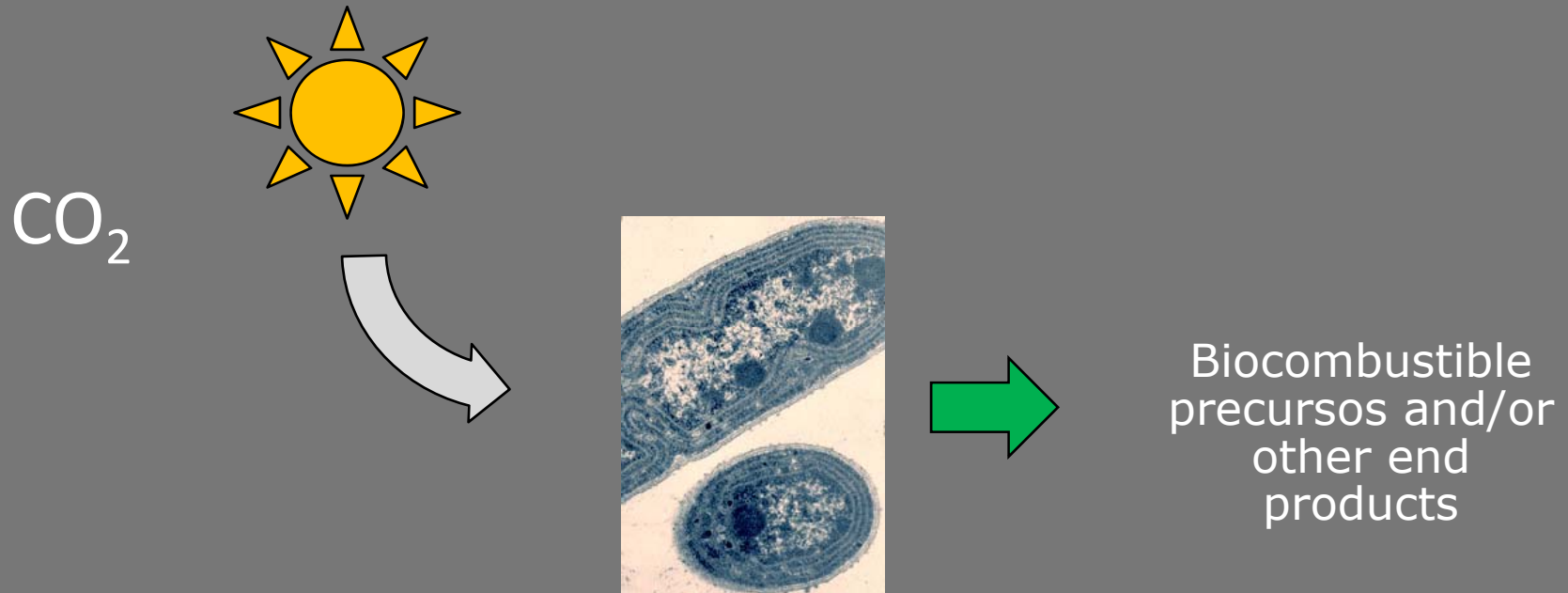
Several orders of prokaryotes have independently evolved reduced genomes



- | | | | |
|-------------------|--------------------|----------------|-------------------|
| Enterobacteriales | Flavobacteriales | Nanoarchaeales | Mycoplasmatales |
| Acholeplasmatales | Entomoplasmatales | Rickettsiales | Actinomycetales |
| Spirochaetales | sulfur-oxidizing | Chlamydiales | Cardiobacteriales |
| Rhizobiales | Desulfovibrionales | Thiotrichales | Others |

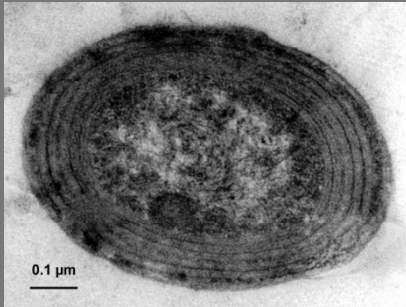
Objective

Design and Engineer a reduced/optimized genome/metabolism for *Synechococcus elongatus* PCC7942 that maintains its free living condition and its genetic transformation



Synechococcus elongatus PCC7942

Comparative genome analysis



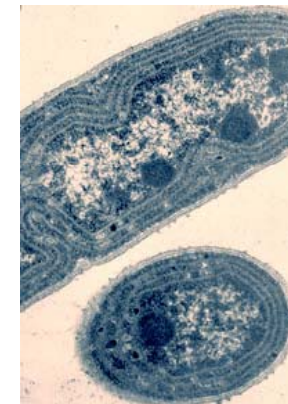
Prochlorococcus marinus
CORE



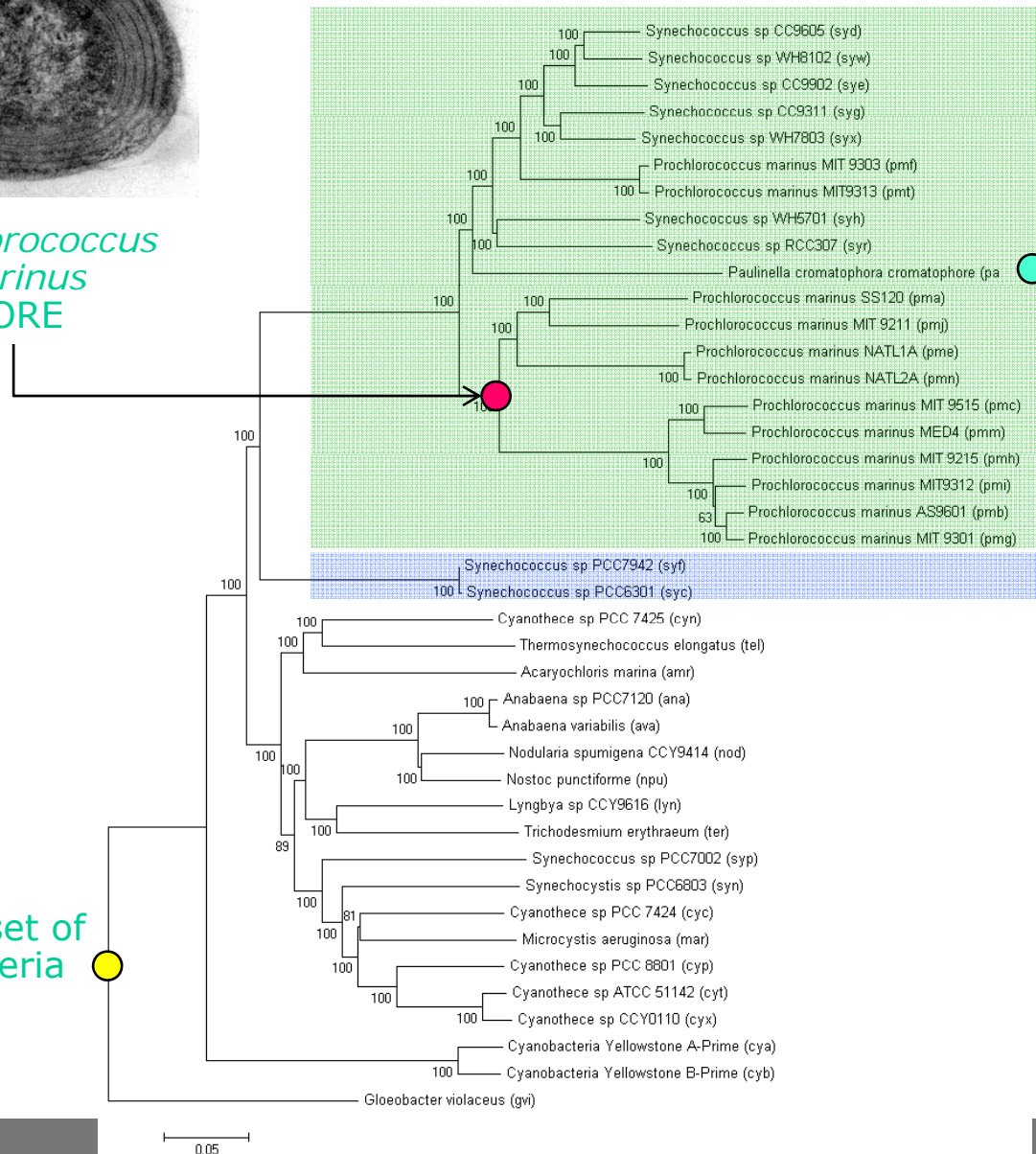
Paulinella chromatophora
(cromatophore)

Marine

Fresh-water



S. elongatus



Universal set of cyanobacteria

Step 1

In silico analysis

Synechococcus elongatus
PCC7942

2665 genes

Metabolic model

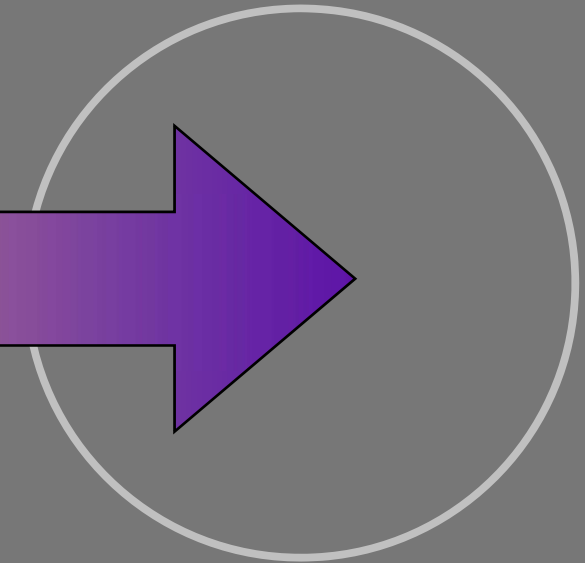


A + B -> C

Optimized
metabolismo/genome

< 2665 genes

Identify dispensable genes through
comparative genomics

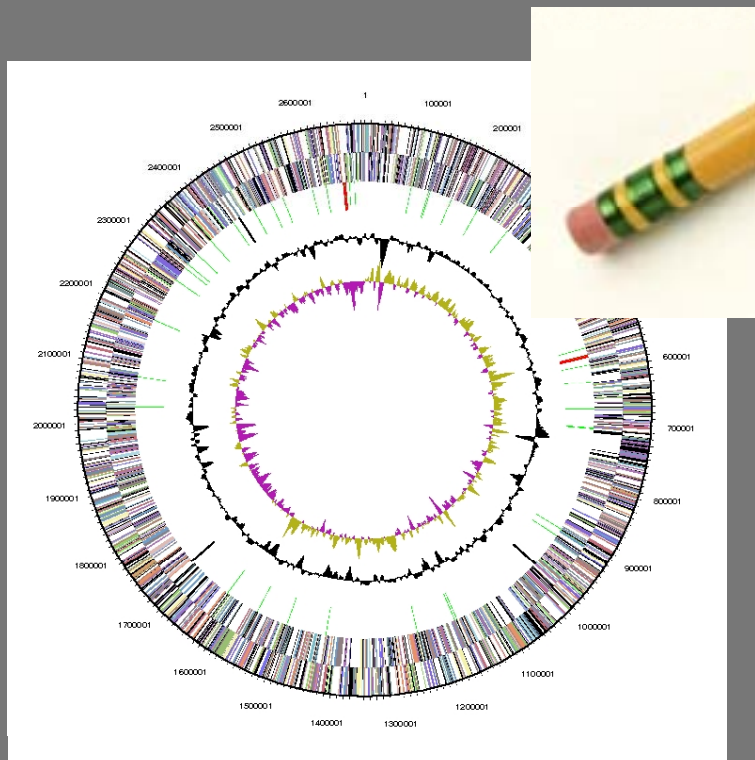


Step 2

In vitro analysis

To identify deletable genes

To test the predictions by deleting genes from the genome



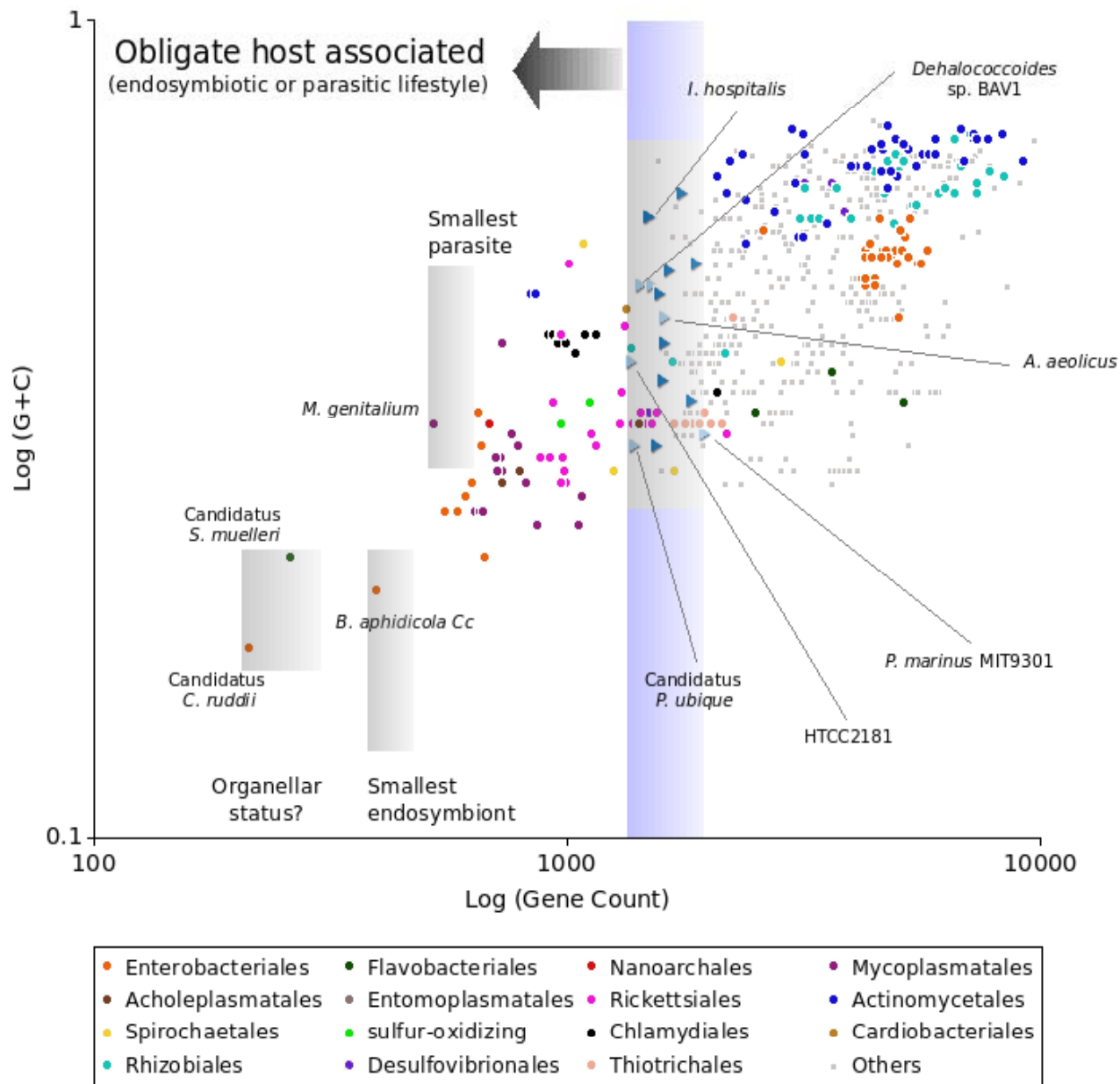
Synechococcus elongatus PCC7942



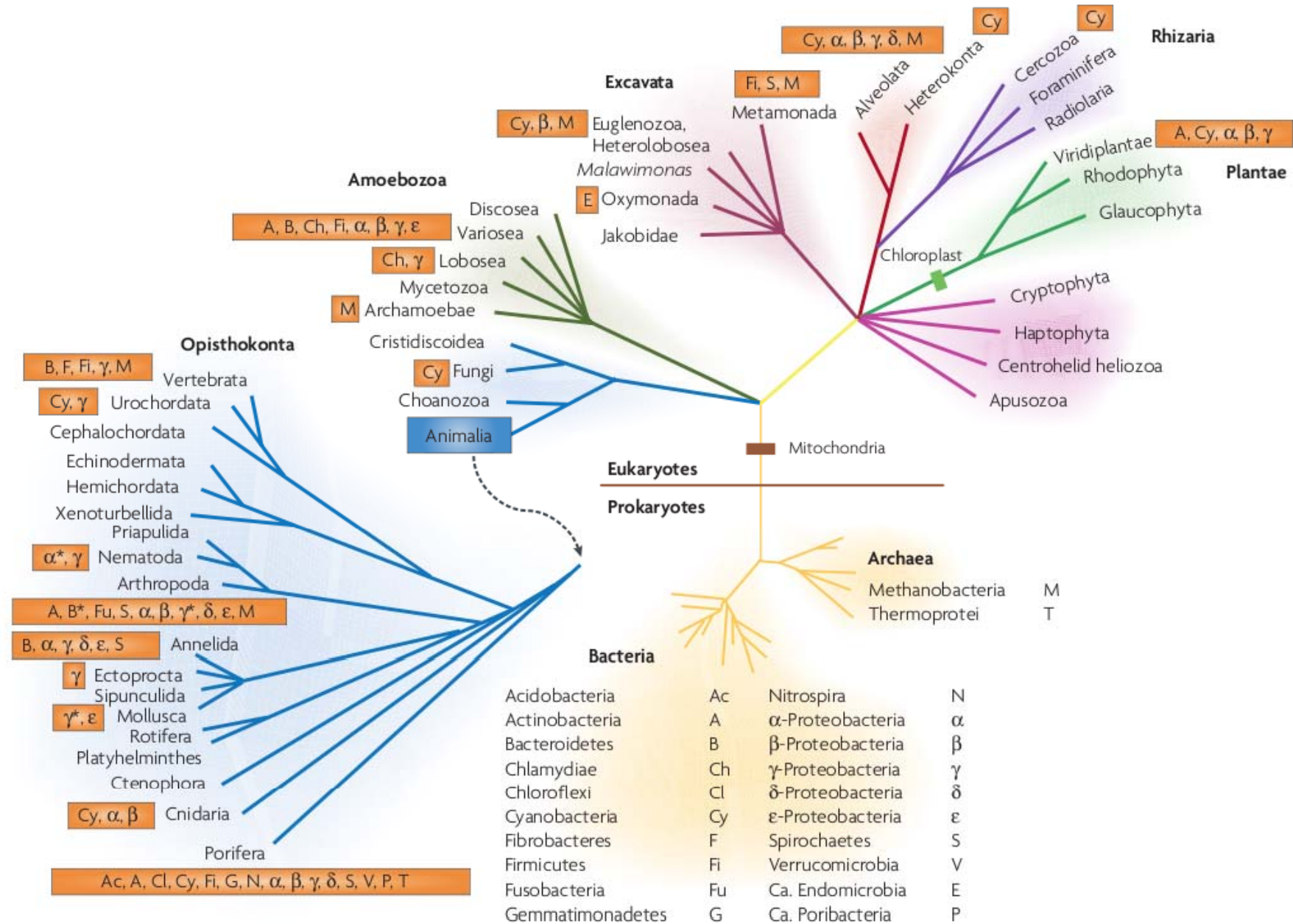
Prof. Fernando de la Cruz



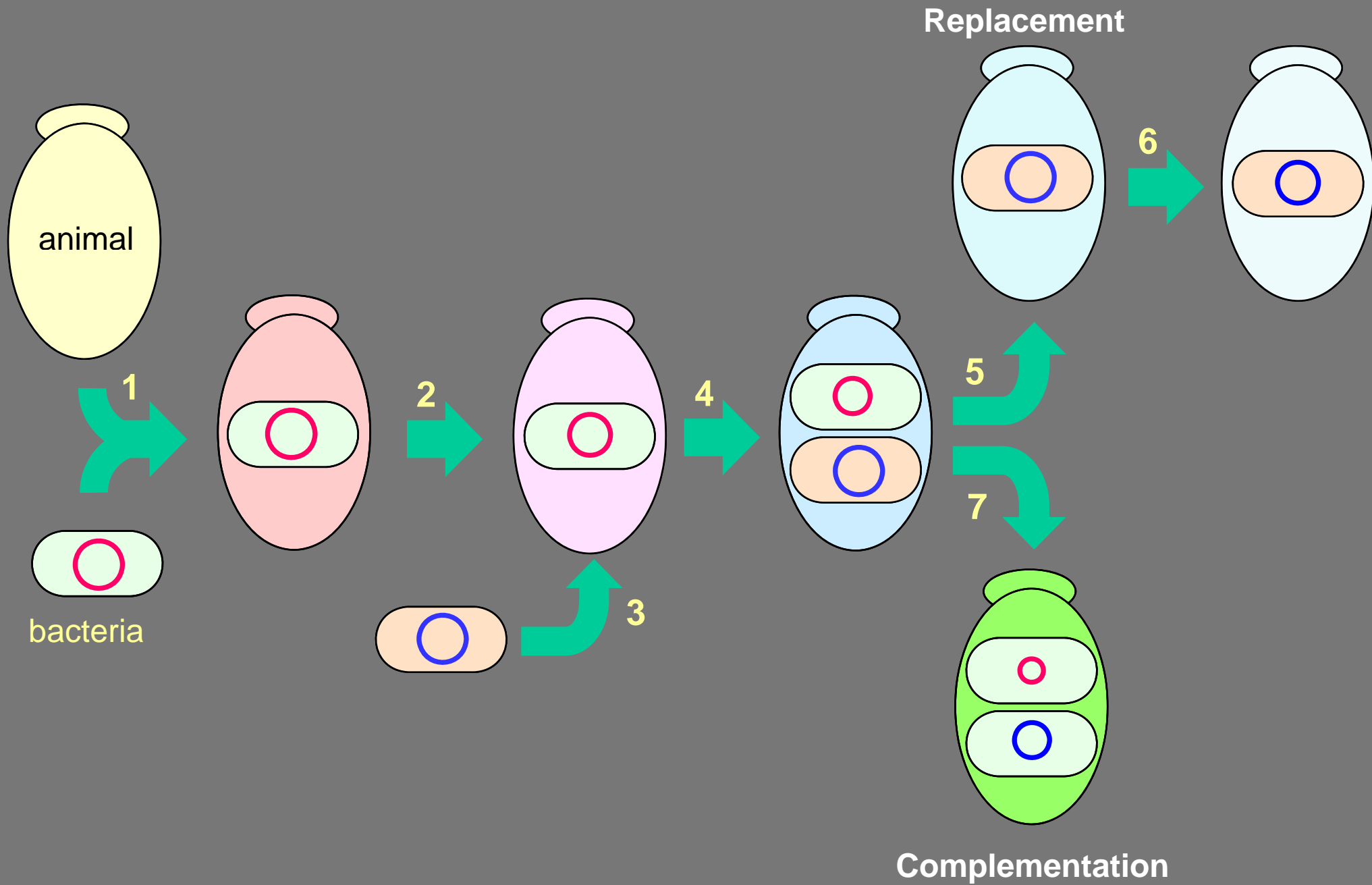
Endosymbiosis produces the smallest genomes



Symbiosis is a clearly widespread phenomena in the biosphere



Stablishment, maintenance and evolution of symbiosis

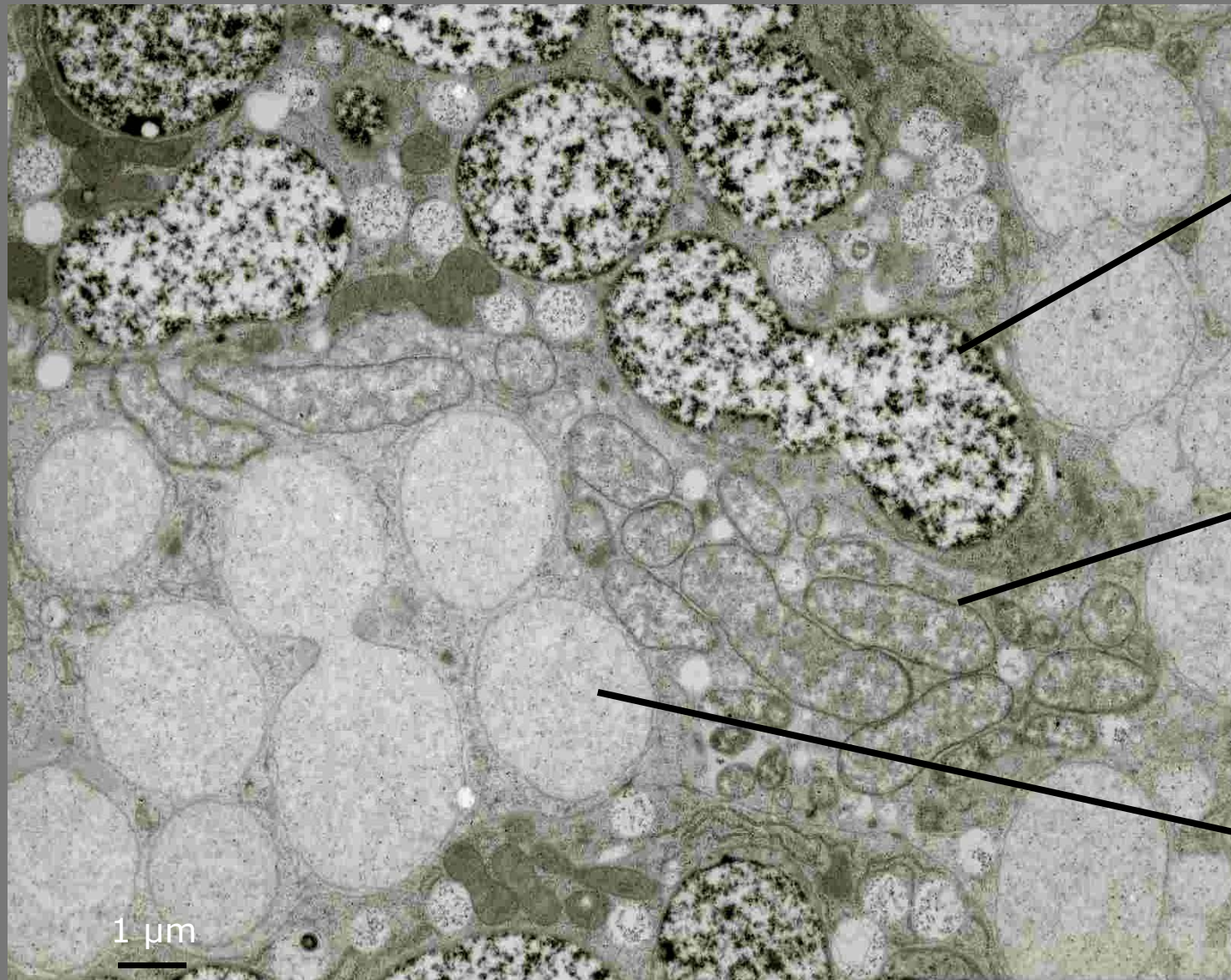


Cinara cedri



Buchnera aphidicola: 416 kb

Symbionts of *C. cedri*



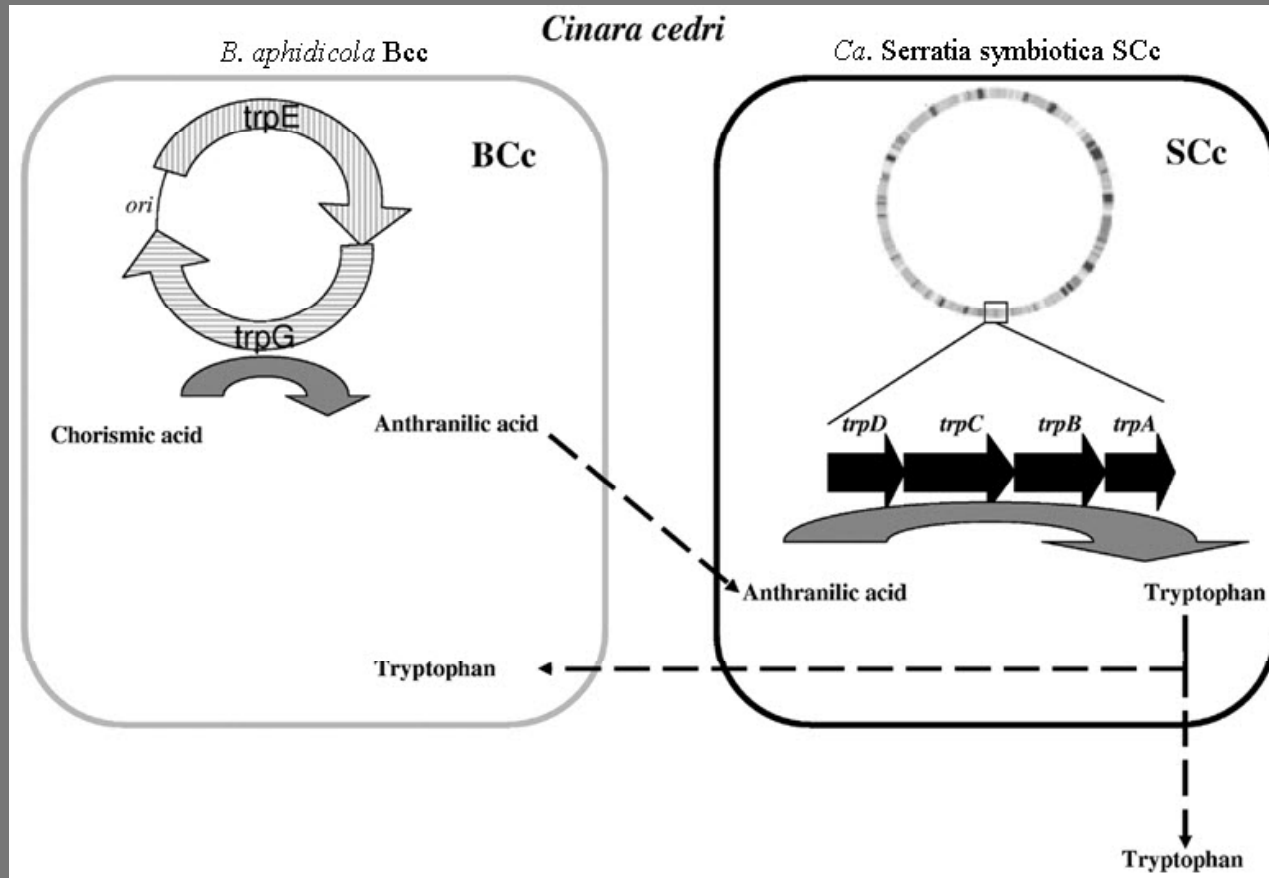
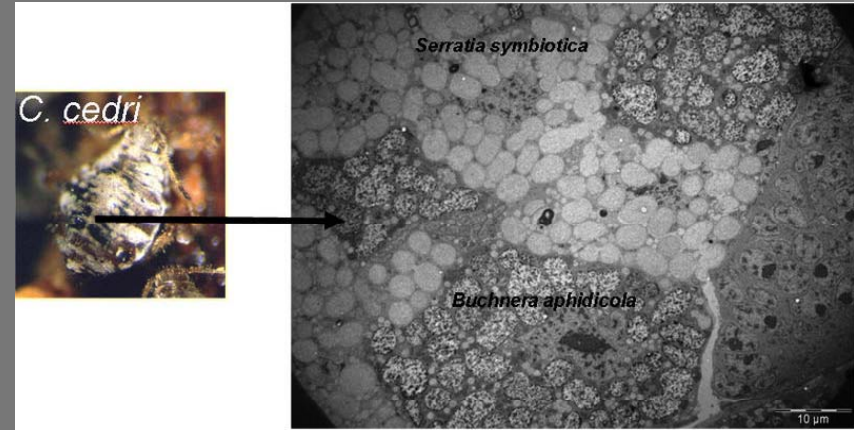
B. aphidicola

Wolbachia

*Serratia
symbiotica*

1 μm

Metabolic complementarity allows for small genome size among endosymbionts



Thanks!!

