A Metabolic Tree of Life

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- General approach: what context does studying emergence of metabolism provide to discussions on emergence of life?

Relevant efforts to the emergence of metabolism (by no means a complete list!)

- Geochemistry: Chemical, kinetic & energetic boundary conditions
- Microbiology/enzymology: Context from extant biochemistry

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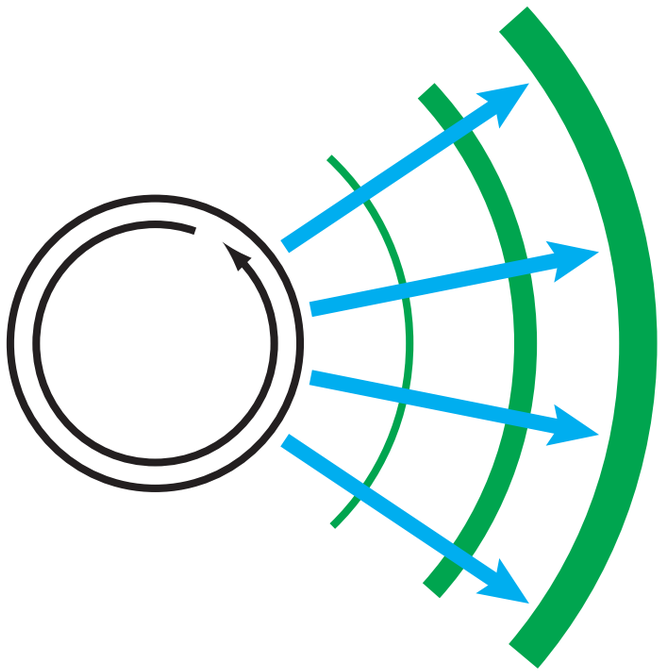
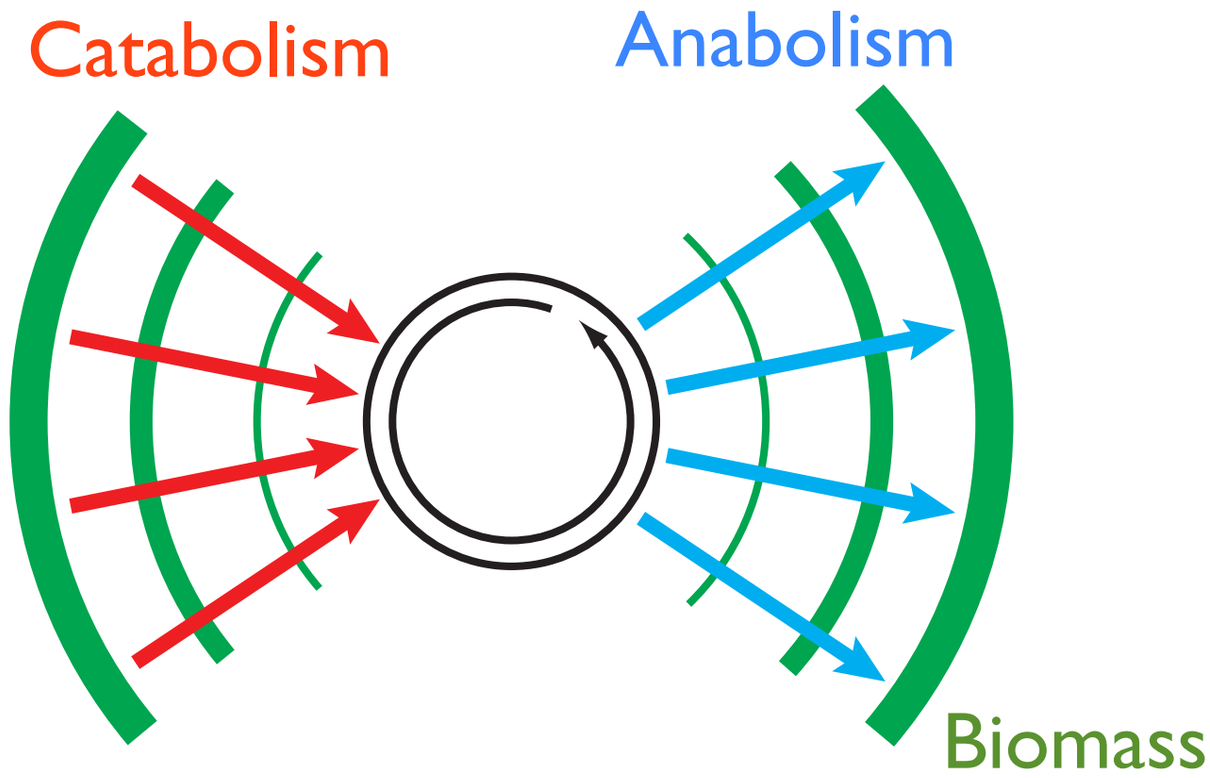
- Geochemistry: Chemical, kinetic & energetic boundary conditions
- Microbiology/enzymology: Context from extant biochemistry
- Phylogenomics: Statistics on metabolic content of LUCA
- Computer science/systems biology/chemistry : Network/system-level properties of (organic) chemistry

There are two main classes of pathways and whole-metabolisms

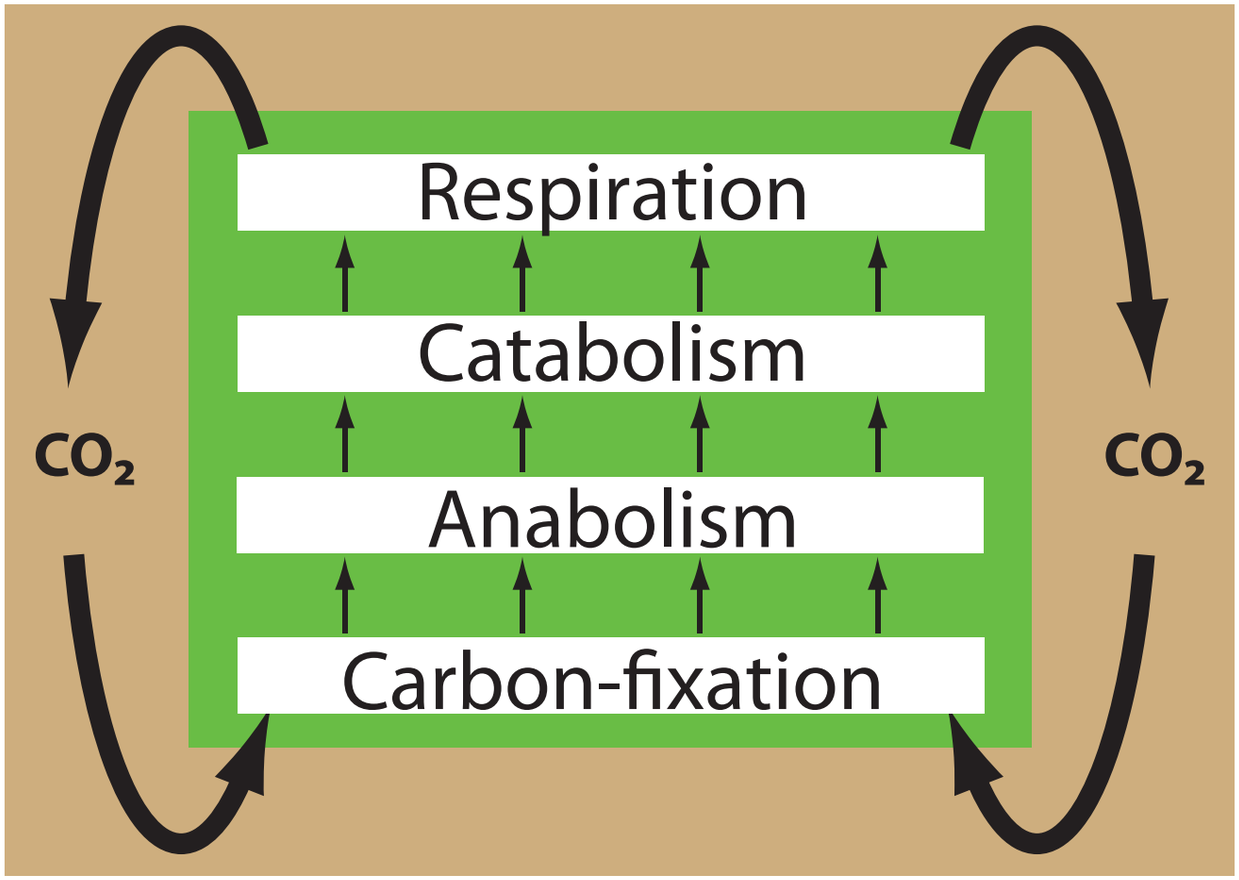




Autotroph
Input = Inorganics
Anabolism only

Heterotroph
Input = Organics
Catabolism + Anabolism

The biosphere is globally autotrophic



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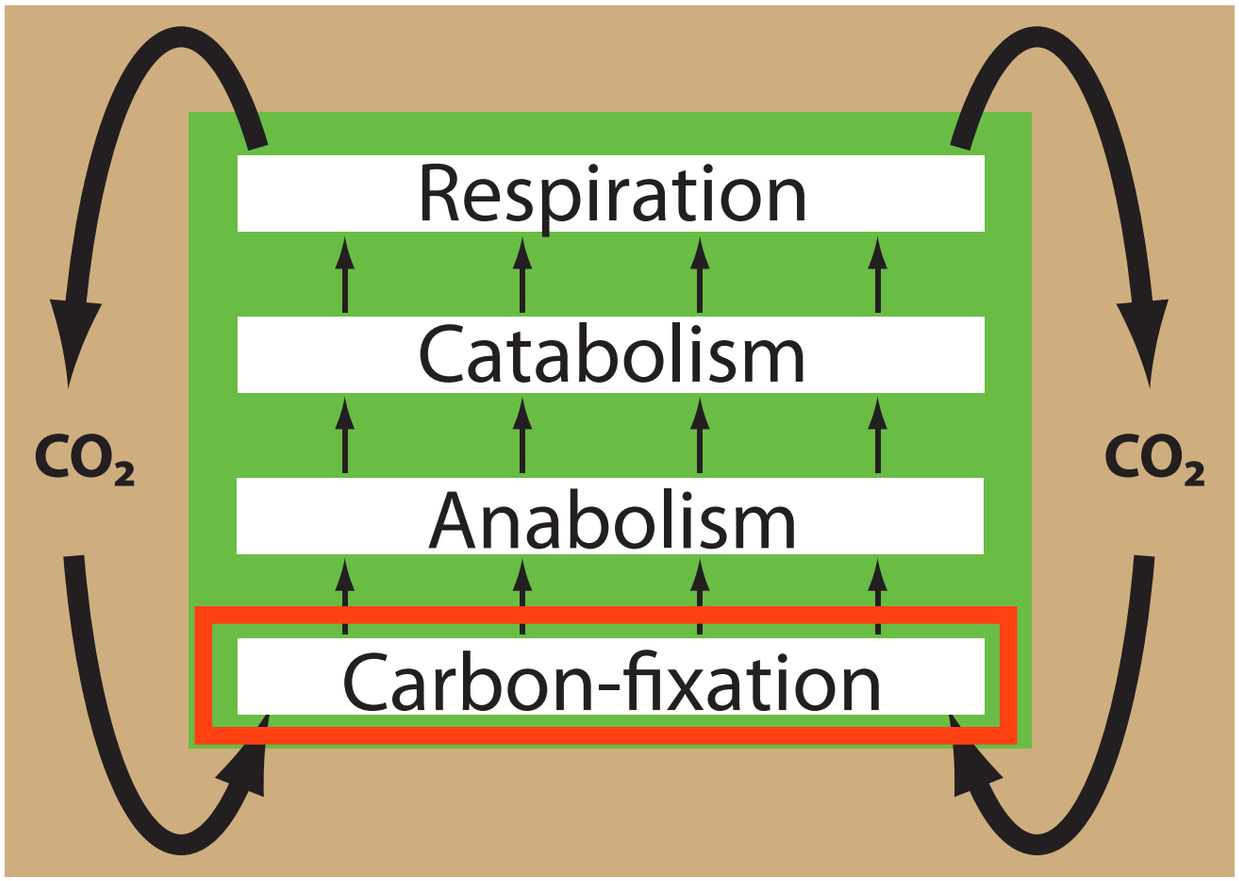


Carbon-fixation is the metabolic foundation of the biosphere, and the base of a metabolic tree of life

Work with:

Eric Smith (Santa Fe Institute)

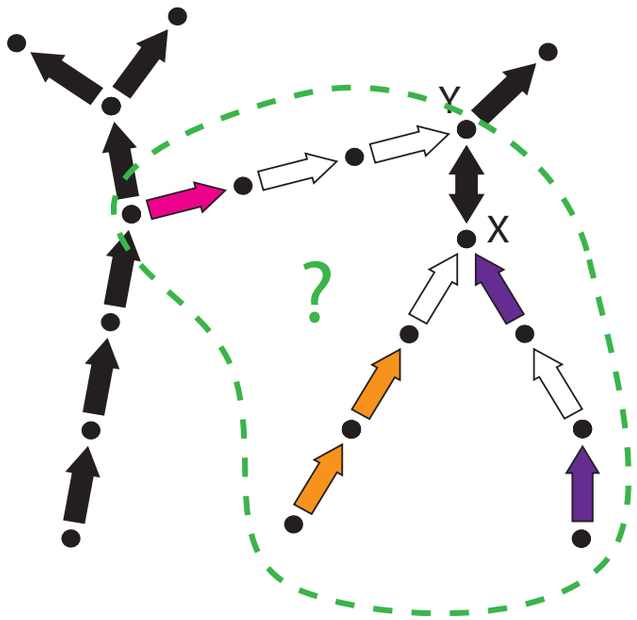
References:

Braakman & Smith (2012), "The emergence and early evolution of biological carbon-fixation", PLoS Comp Bio 8, e1002455

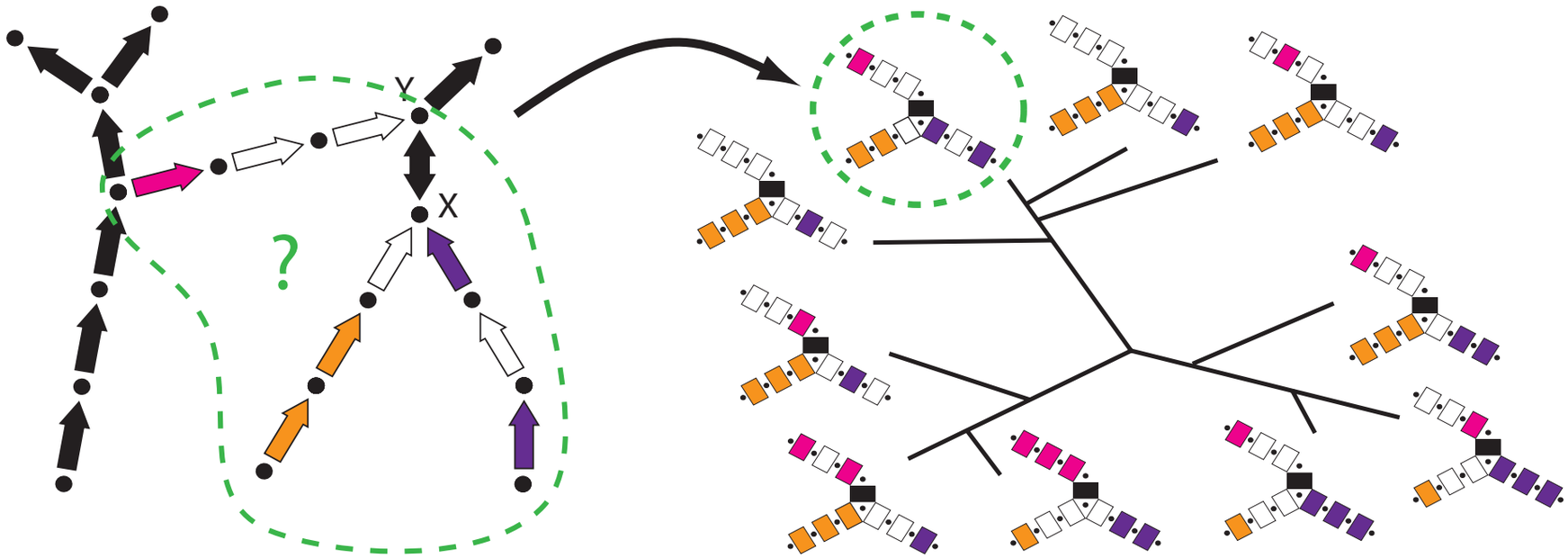
Braakman & Smith (2013), "The compositional and evolutionary logic of metabolism", Physical Biology 10, 011001

Building metabolic trees: integrating phylogenetic and metabolic reconstructions

“Phylometabolic” analysis: phylogenetics provides context for metabolic reconstructions



“Phylometabolic” analysis: phylogenetics provides context for metabolic reconstructions



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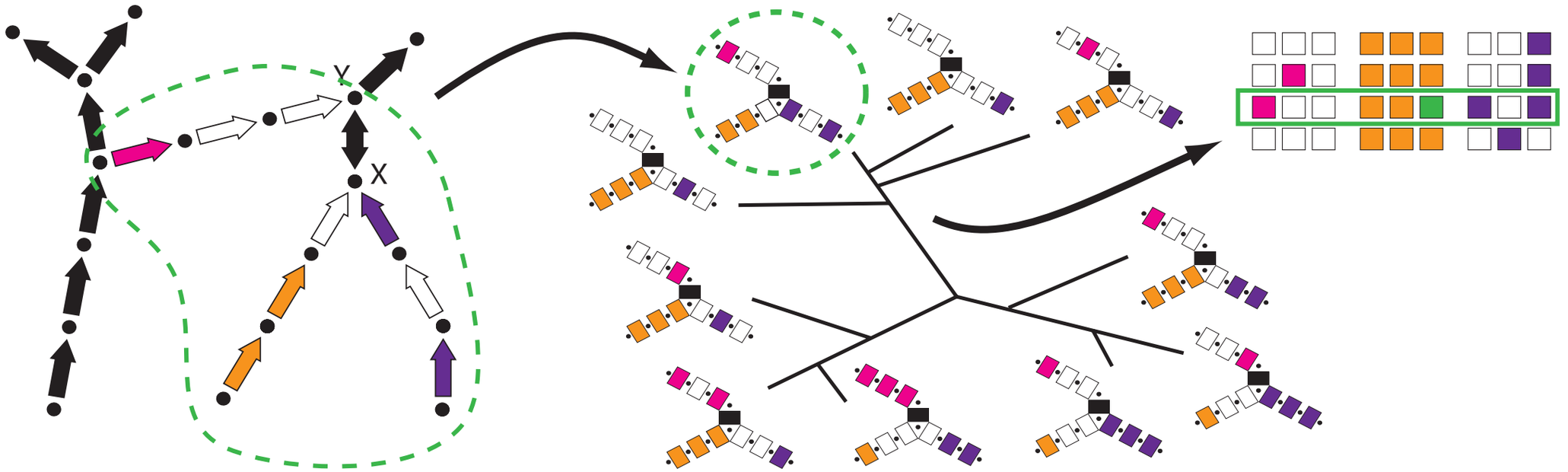

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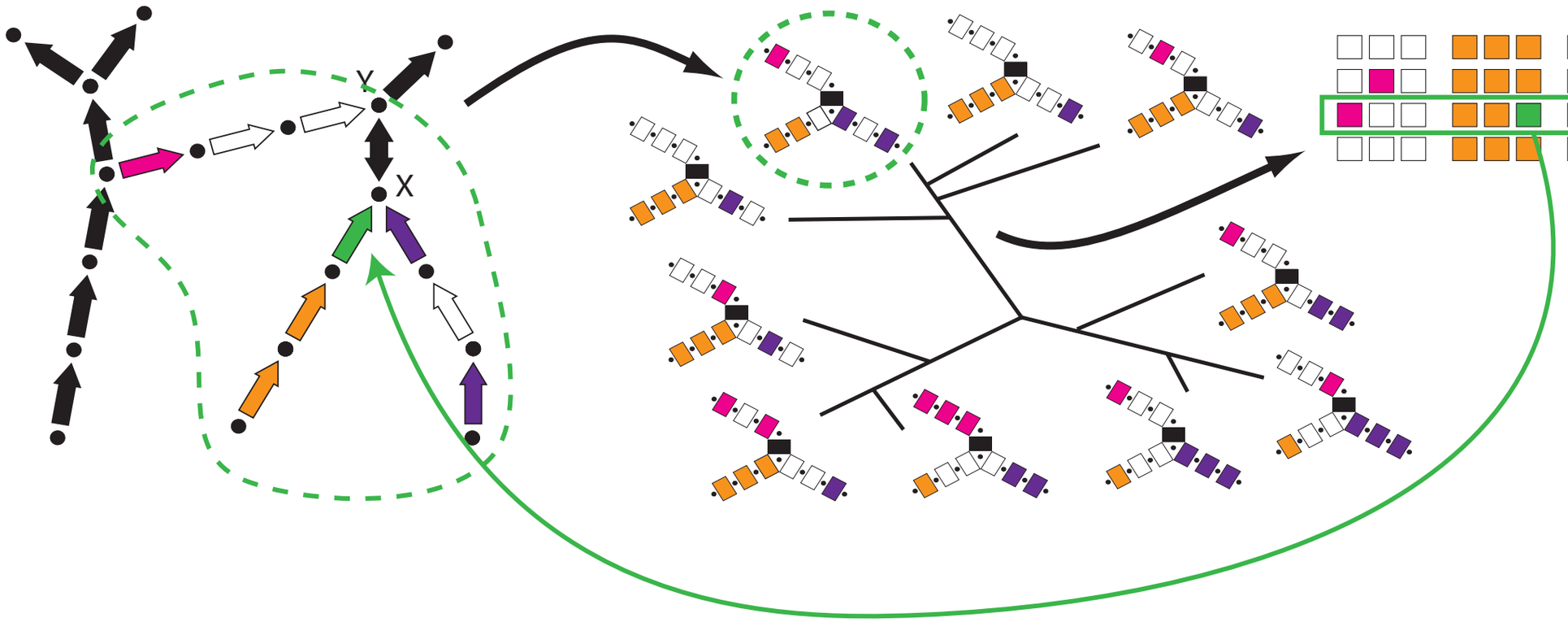
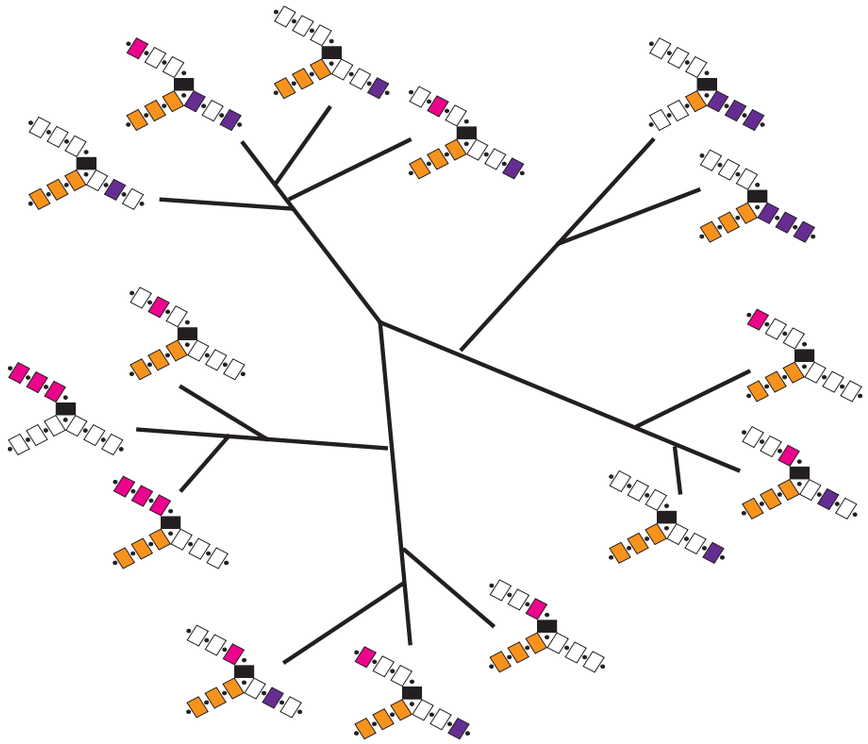


Phylometabolic analysis: phylogenetic distributions of pathways contains signal on their evolution



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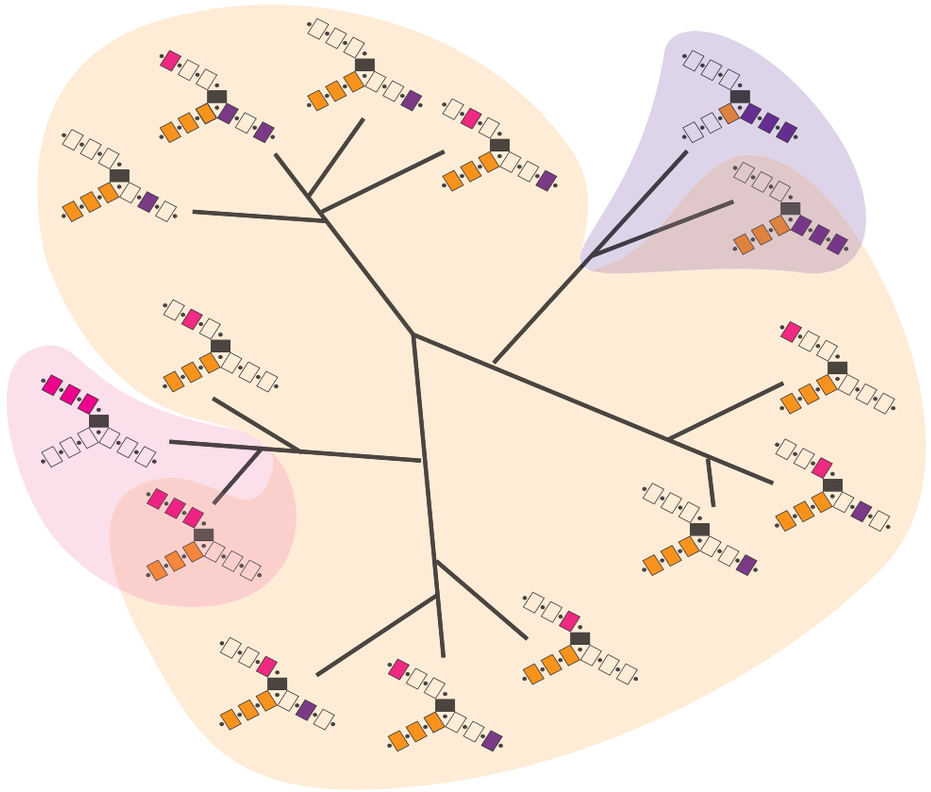

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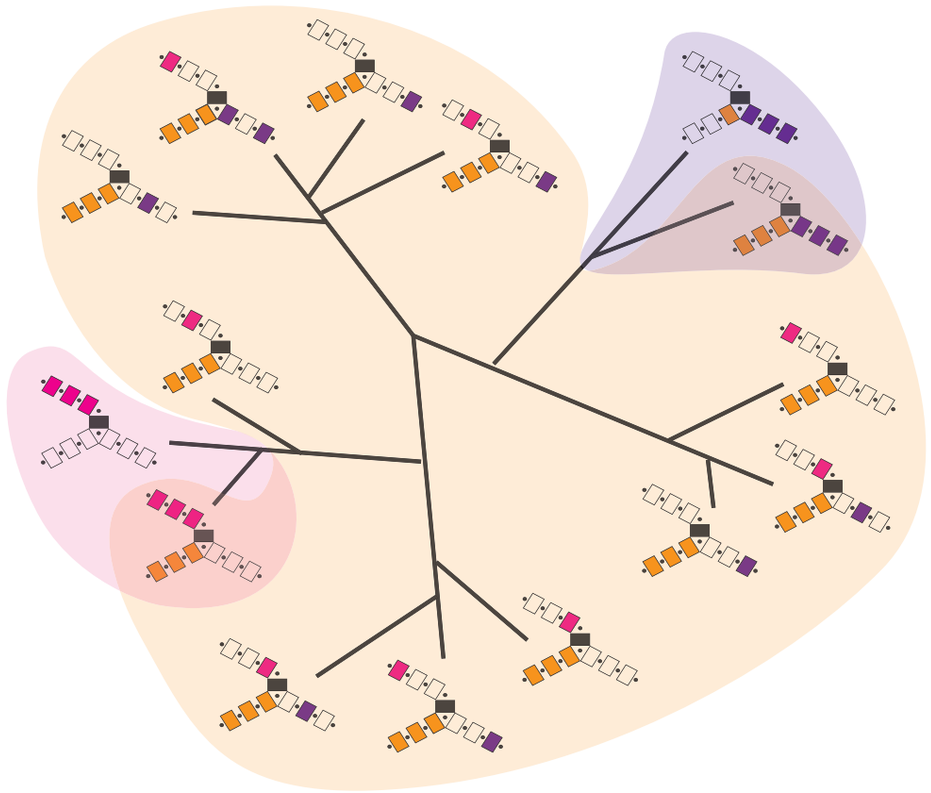
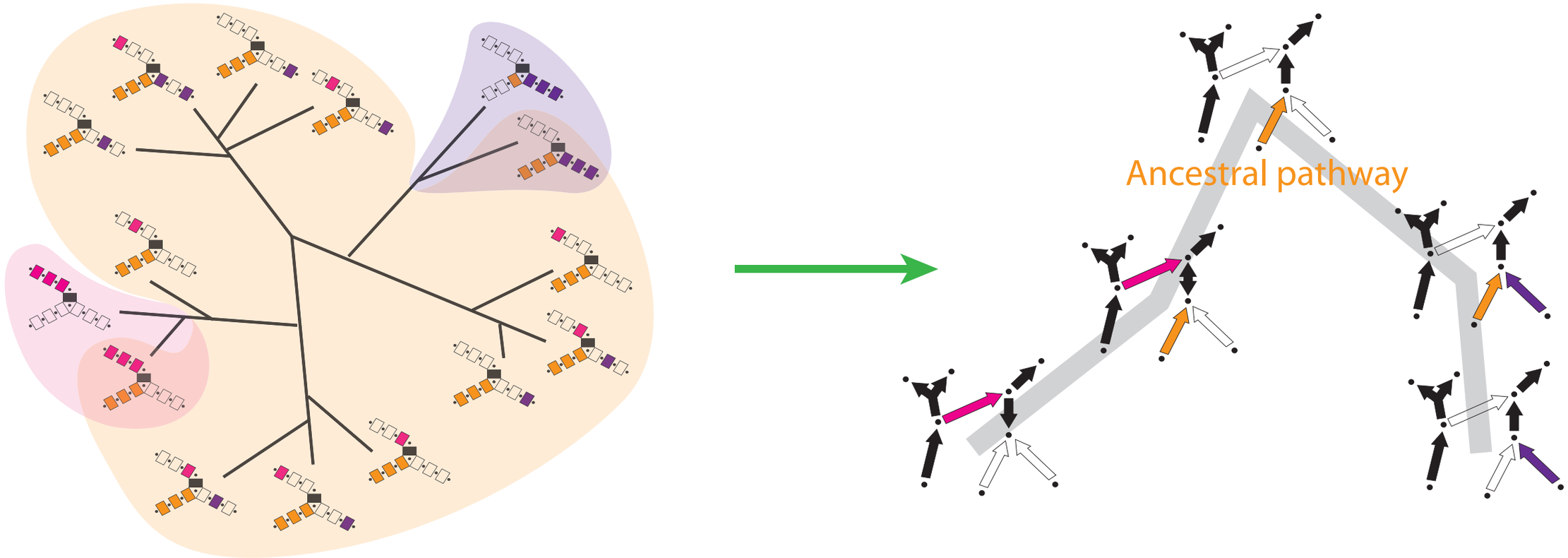


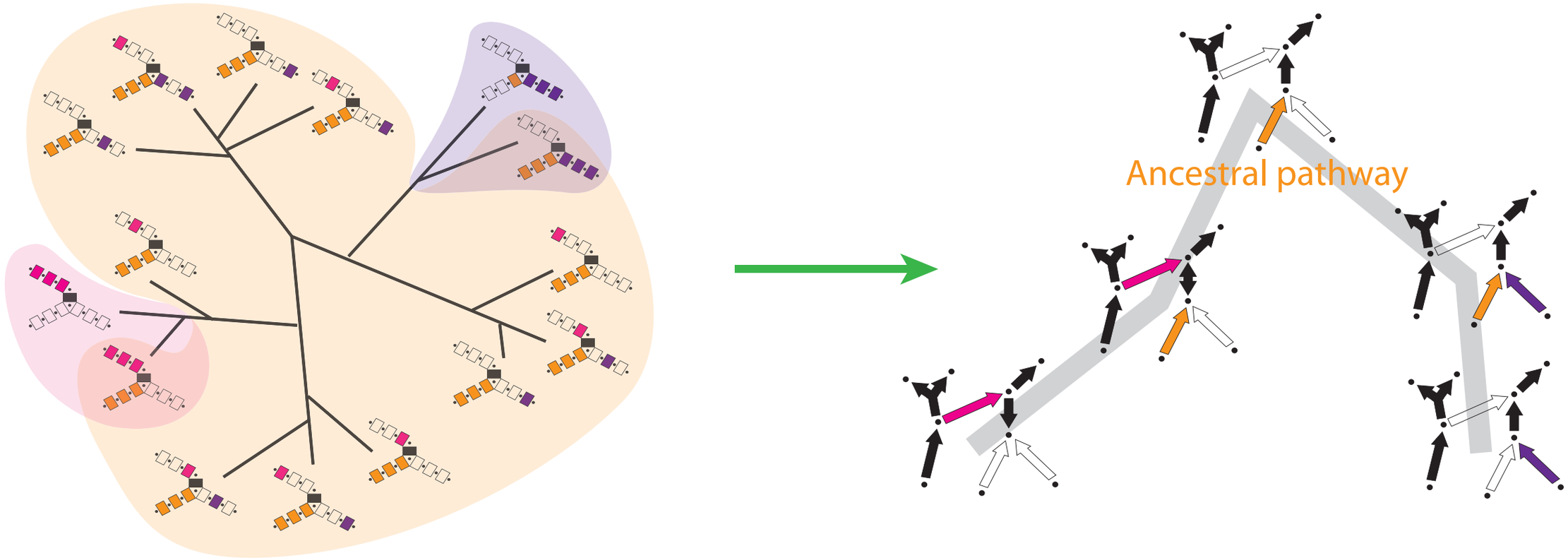
Orange pathway is the ancestral form, others are derived

Phylometabolic Trees: Lineages of functional metabolic networks



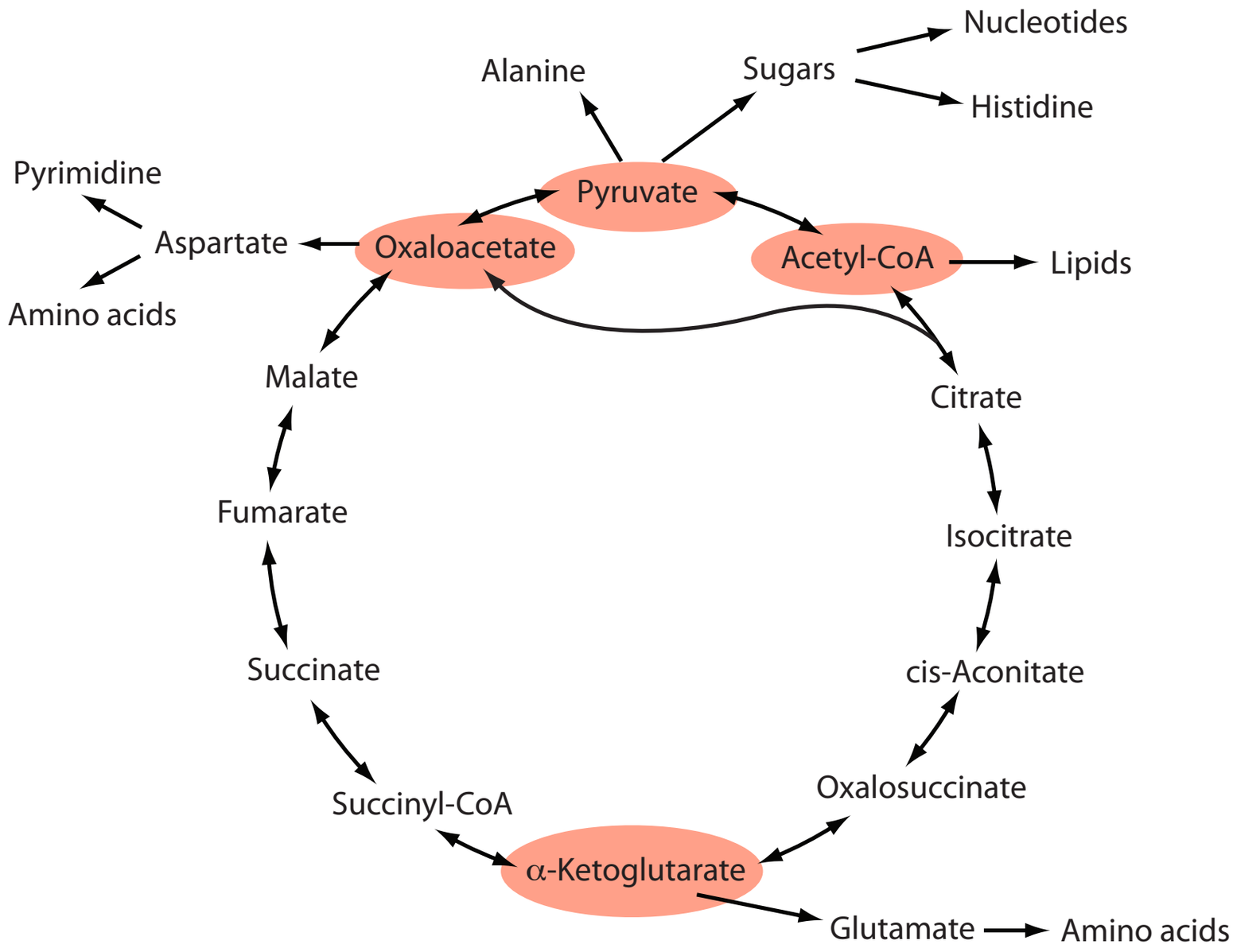
Continuity in metabolite production provides functional constraint to reconstruct tree of phenotypes

Phylometabolic Trees: Lineages of functional metabolic networks



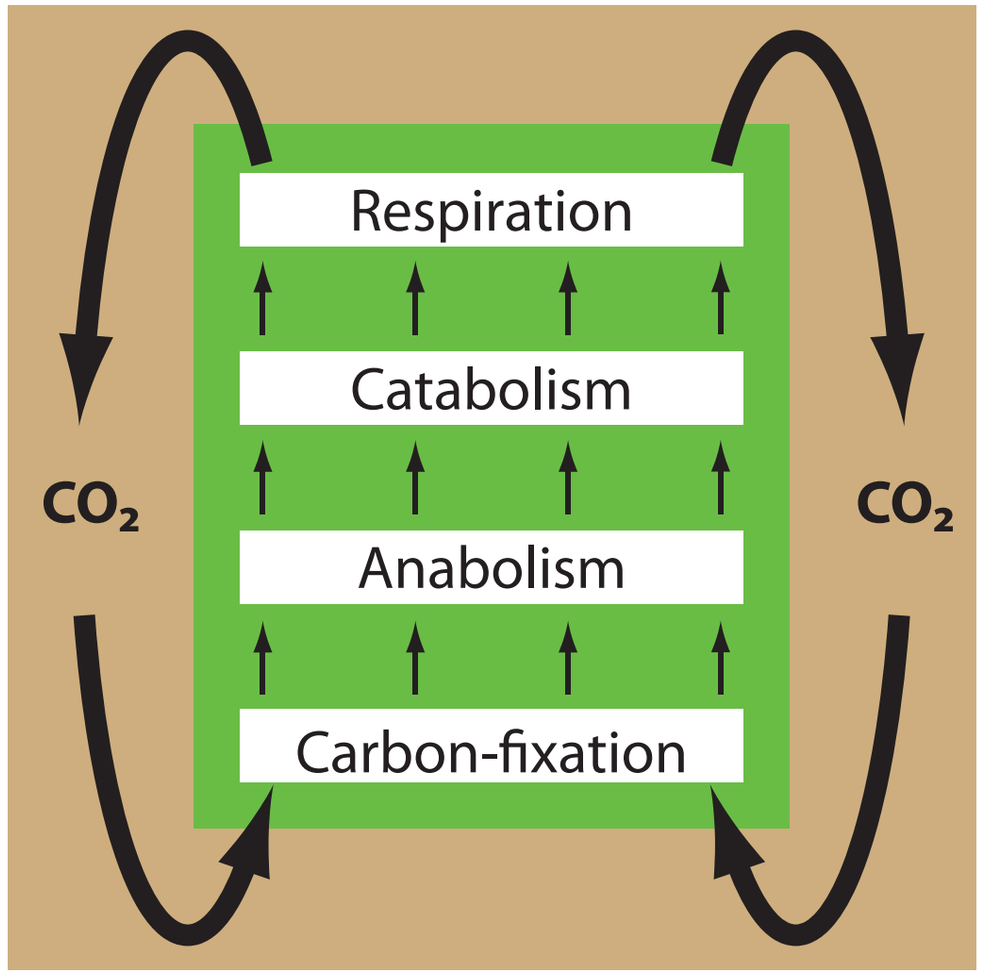
Use topological bottlenecks to delineate evolution of metabolic sub-systems

Citric acid cycle: bottleneck between carbon-fixation and anabolism



Nearly all anabolic pathways start from TCA intermediates, which must thus be reached during carbon-fixation!

Bottlenecks allow us to focus on the evolution of individual layers within the biosphere



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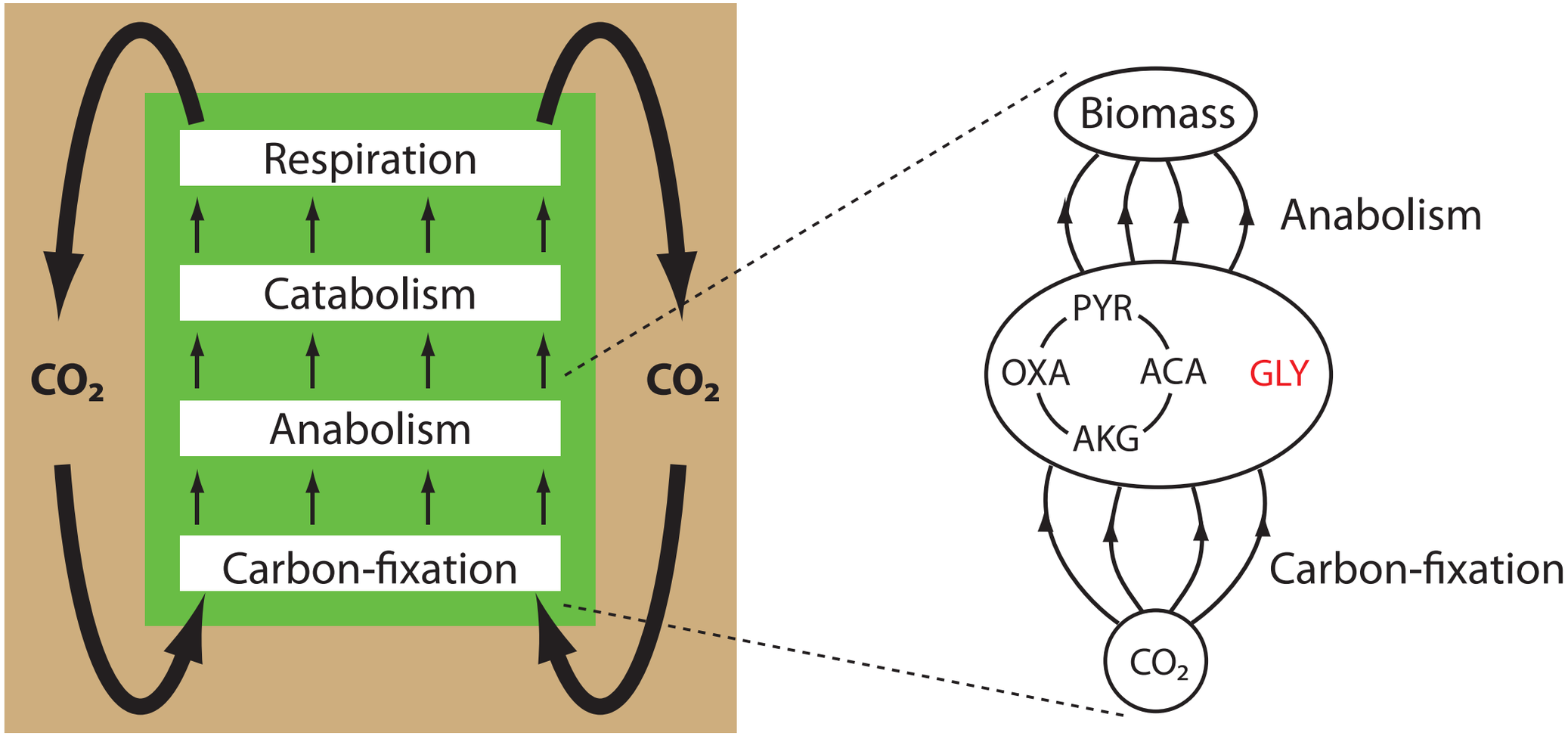
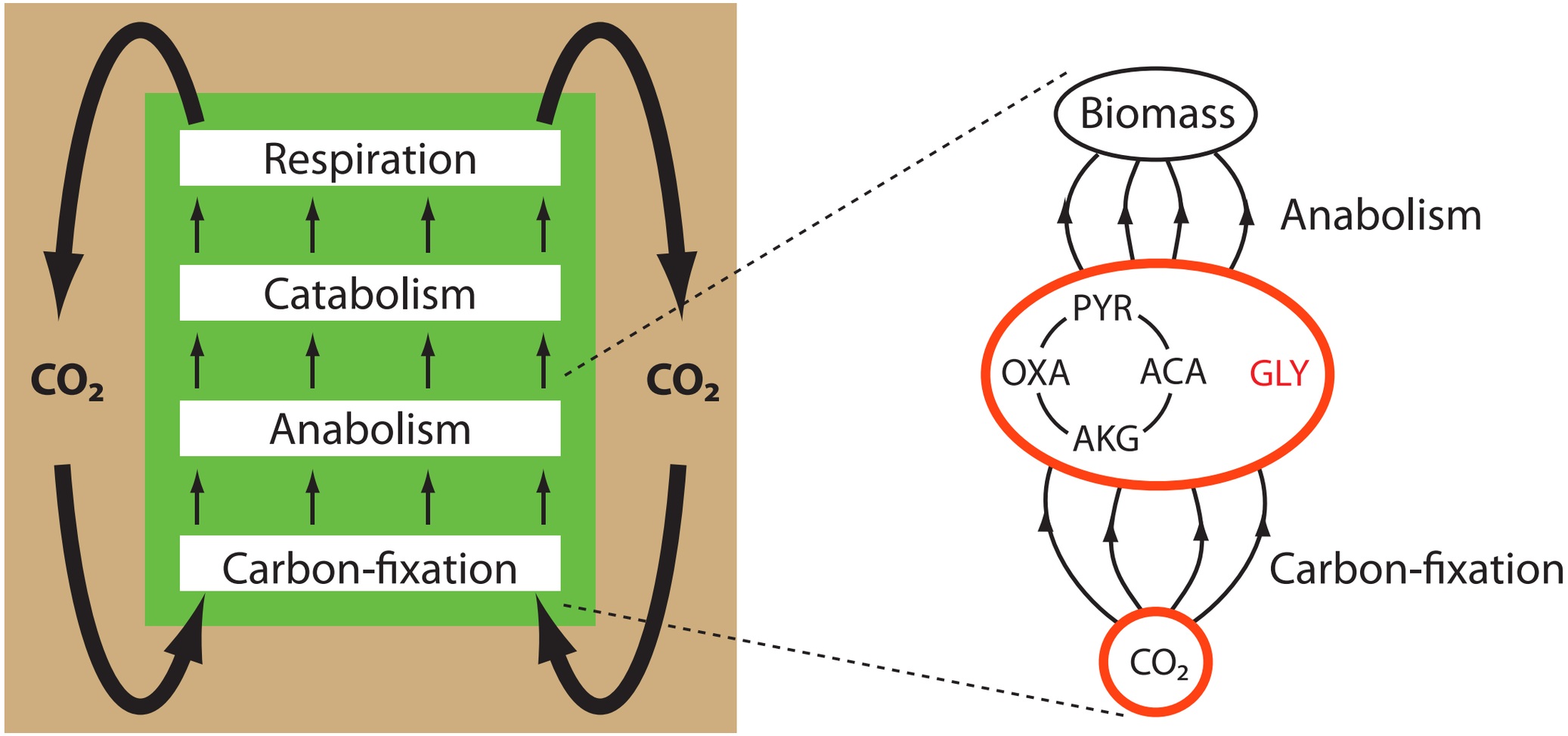


Continuity in connection between CO2 and bottlenecks to anabolism delineates evolution of carbon-fixation

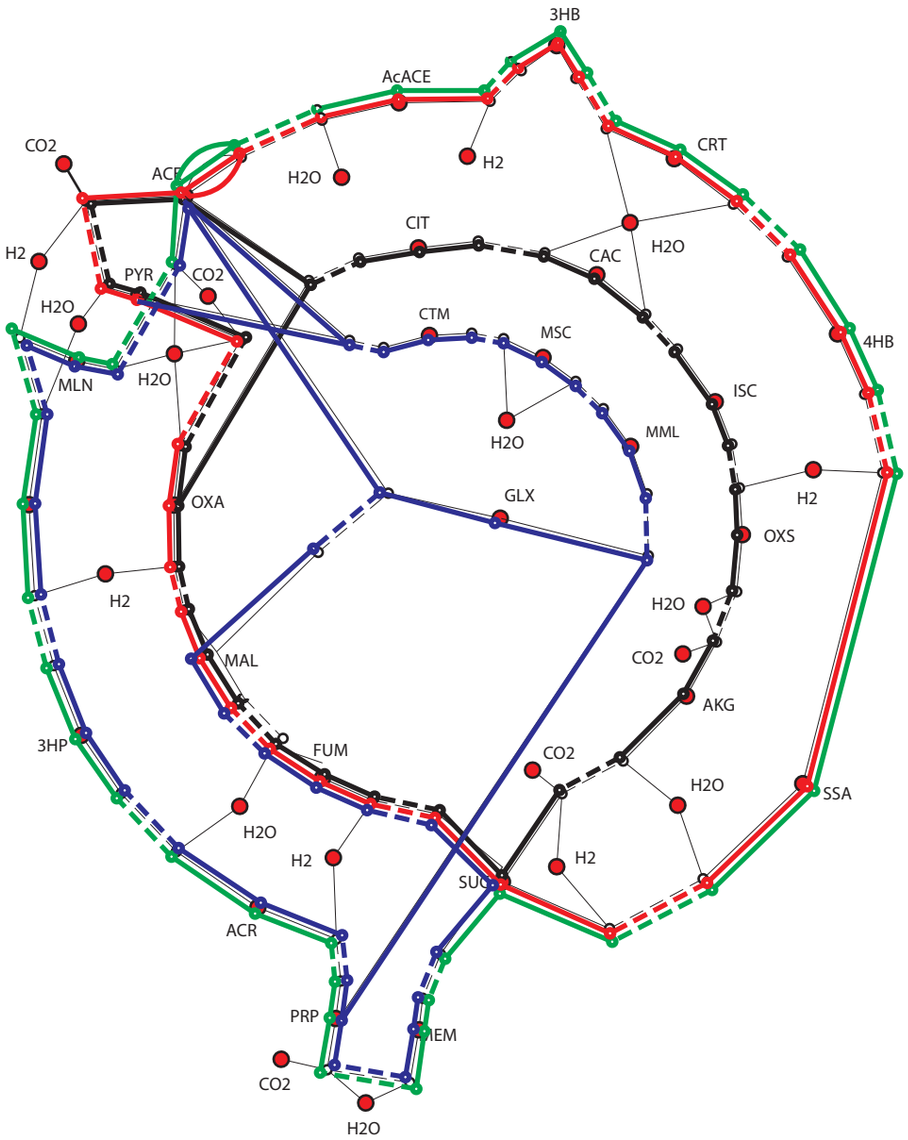


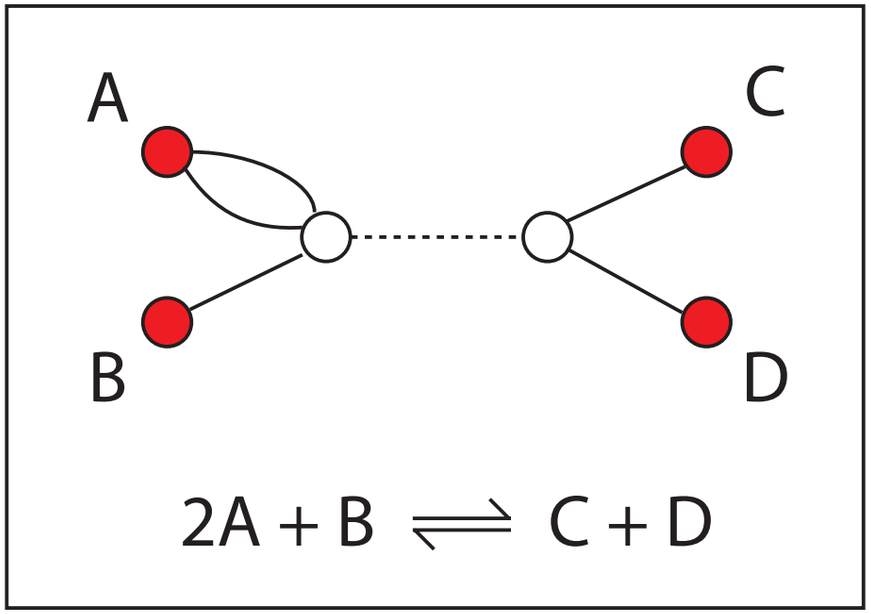
There are 6 known carbon-fixation pathways across the tree of life: 5 cyclic, 1 linear

- Calvin-Benson-Bassham cycle: dominant fixation pathway, but late in evolution, and distinct in (phosphate-sugar) chemistry

- Five remaining (deep-branching) pathways: 4 cycles, 1 linear

4 Deep-branching cycles share arcs, swapping out others, but connection points are preserved





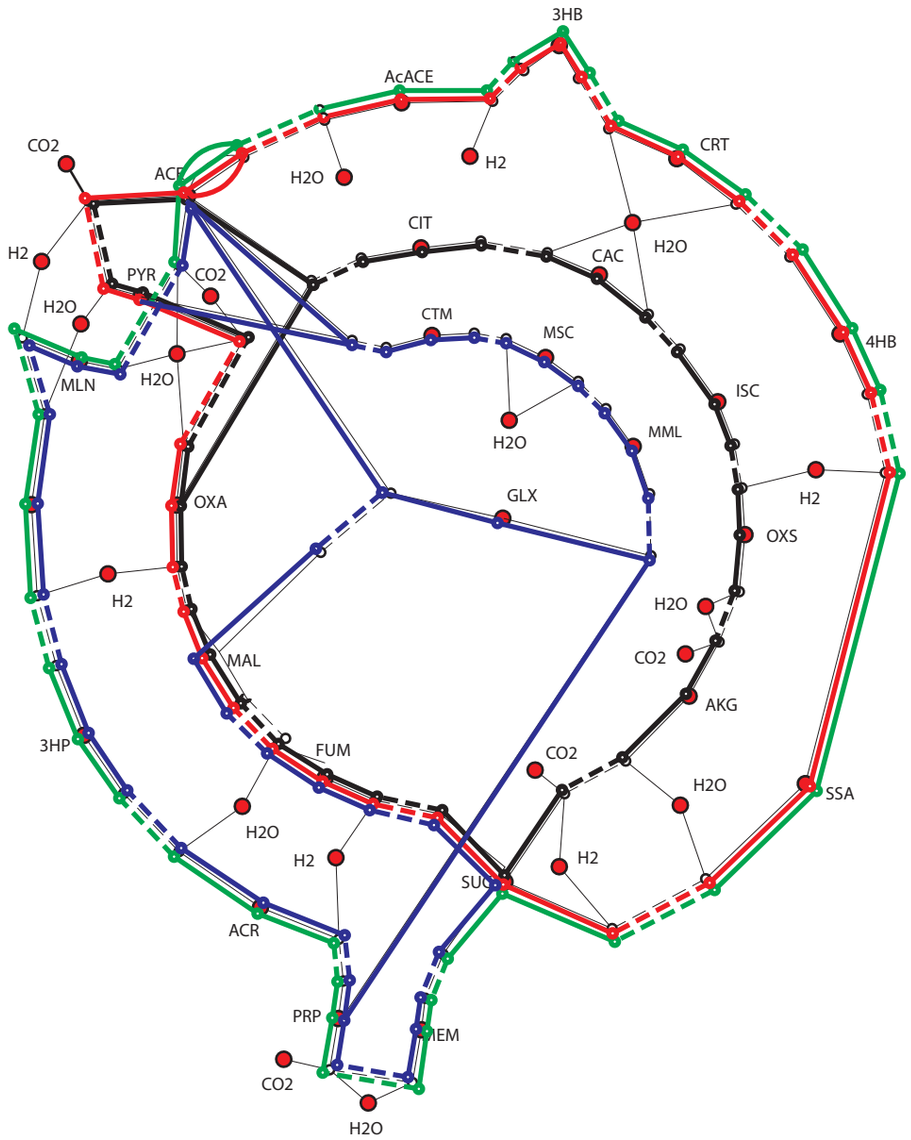
rTCA

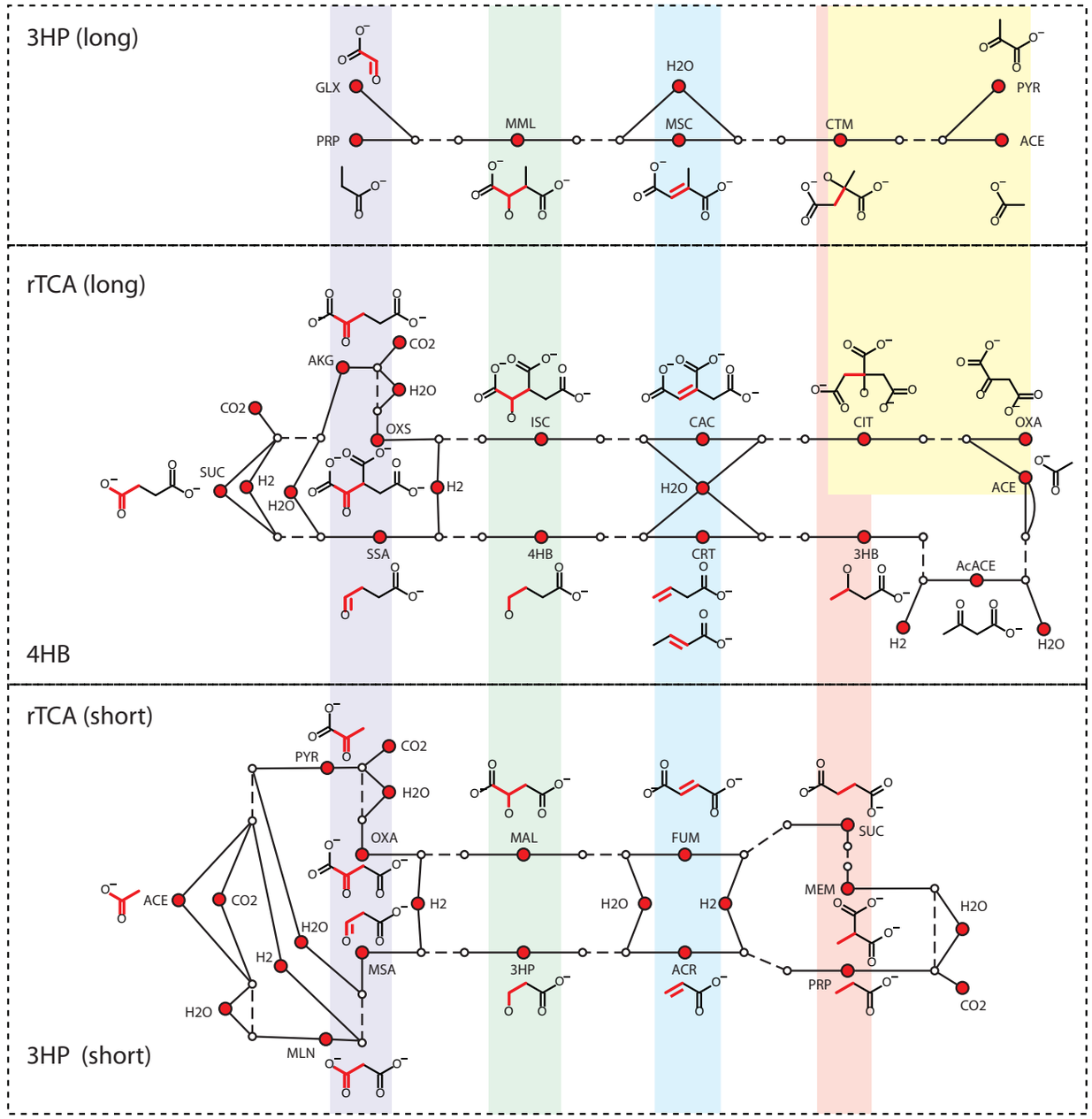
DC-4HB cycle

3HP bicycle

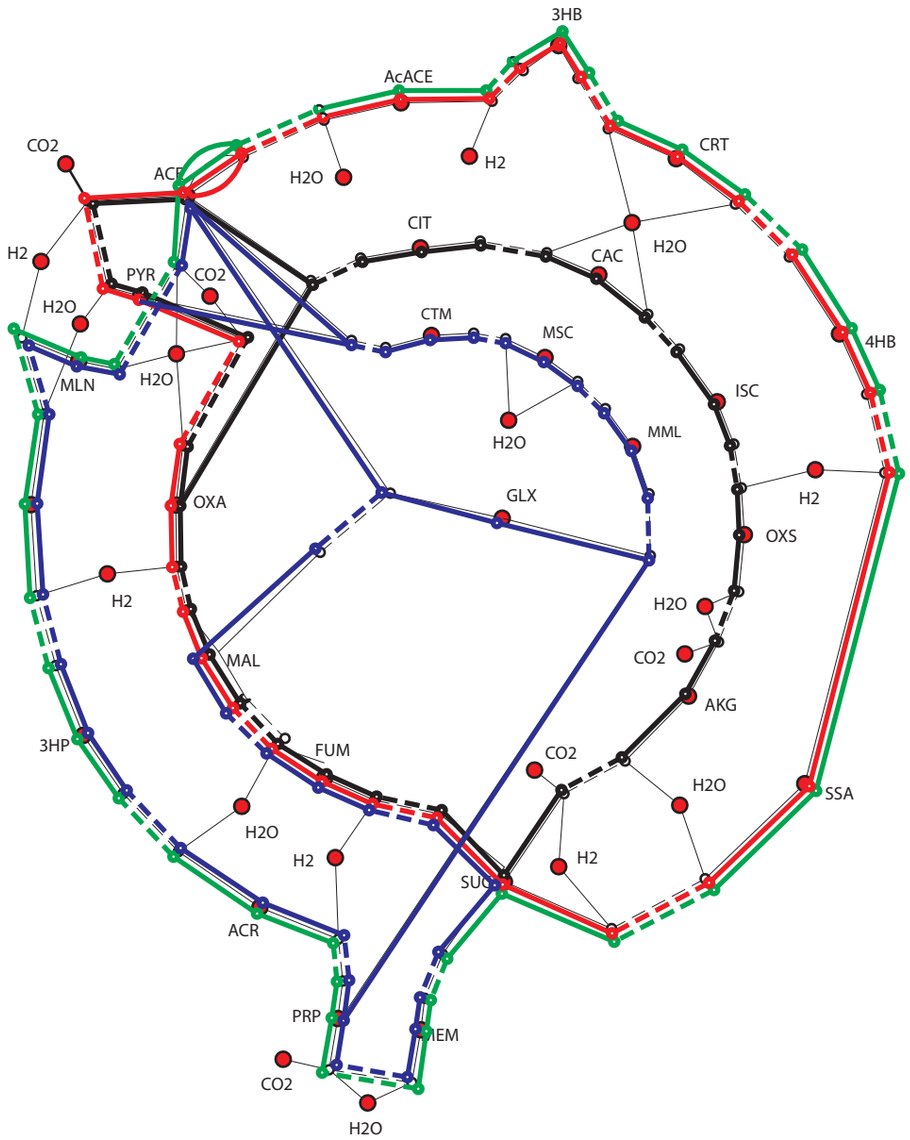
3HP-4HB cycle

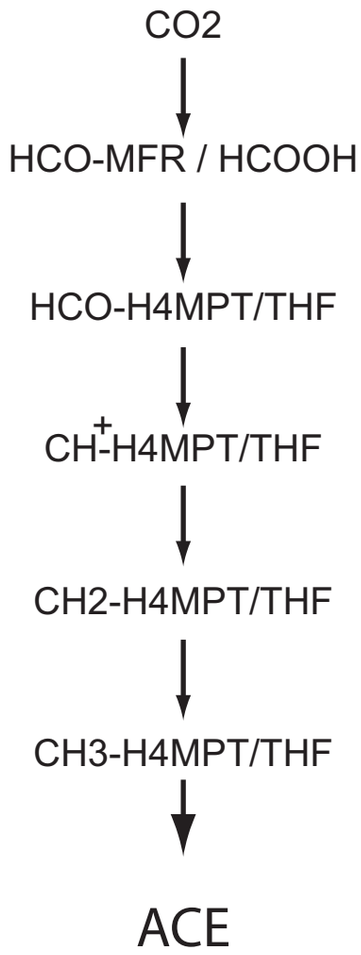
Arcs repeat the same simple local functional group chemistry, while "crux moves" are complex and highly conserved





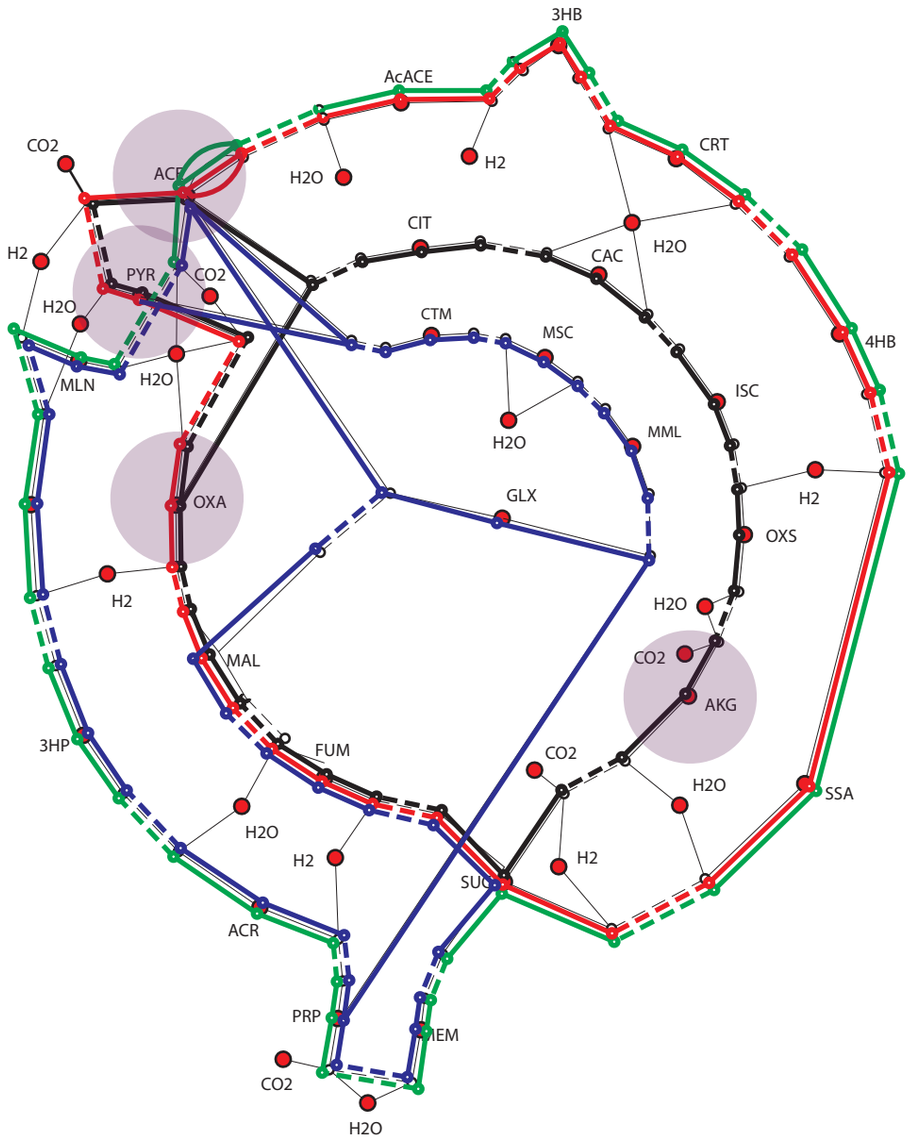
Linear (WL) pathway is unique for being universal as well as for how it uses cofactors

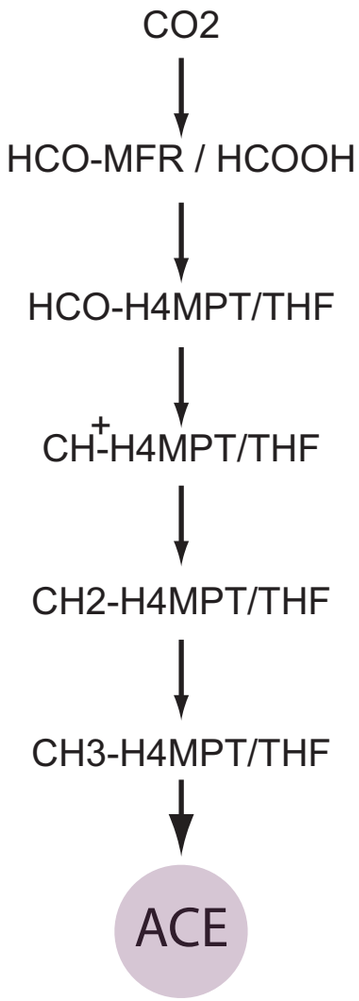




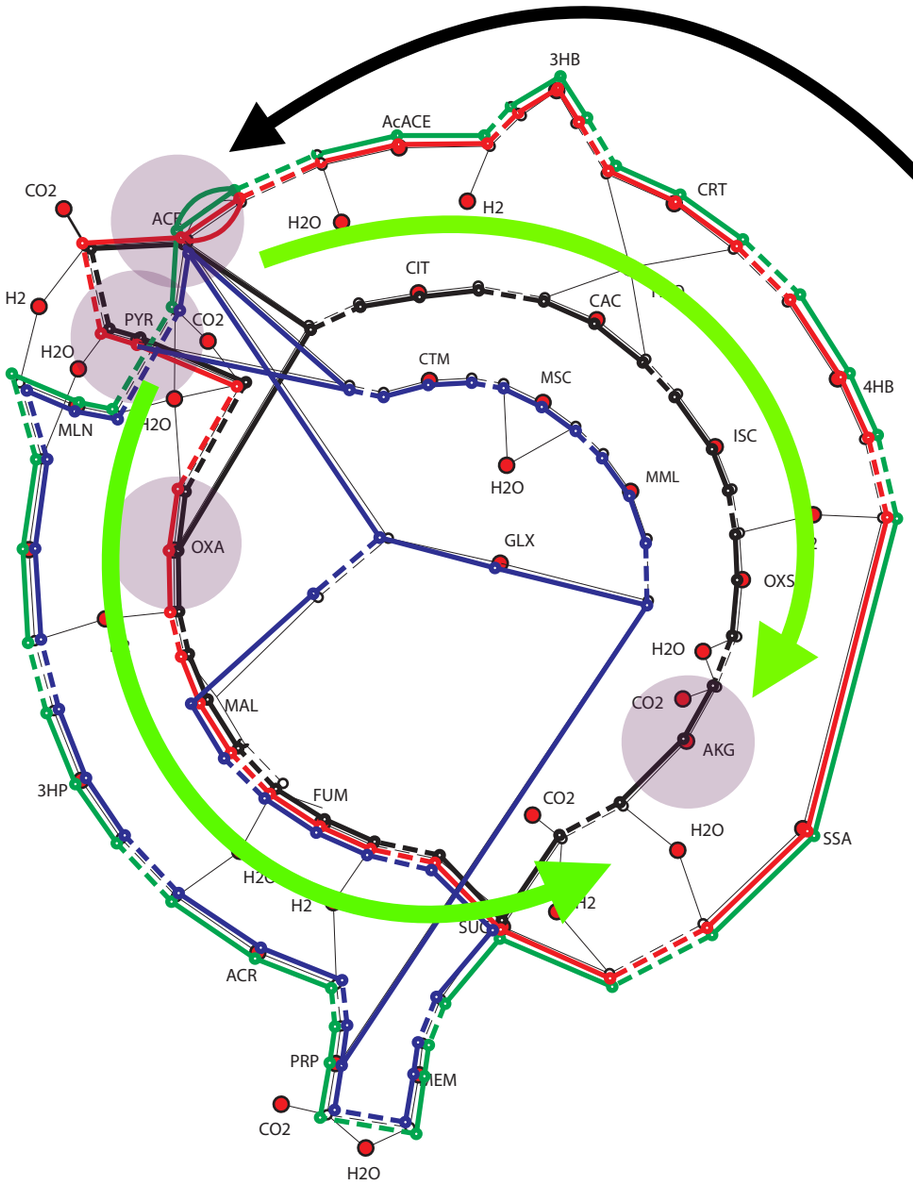
Wood-Ljungdahl

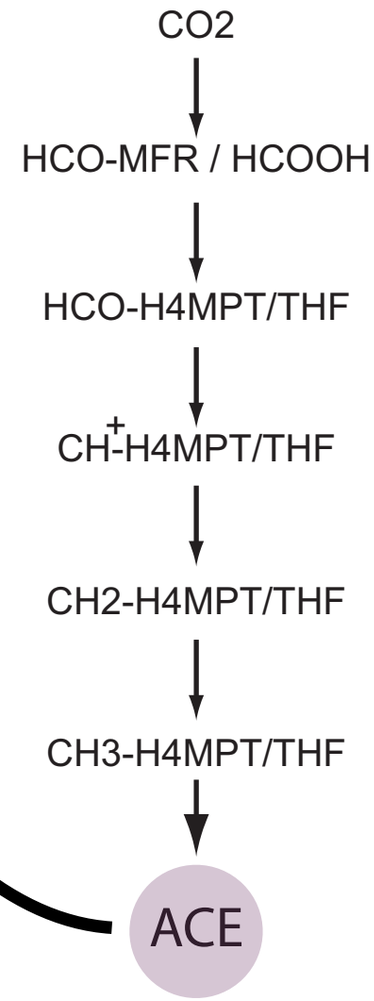
Fixation pathways generally do not reach all bottlenecks to anabolism within TCA directly





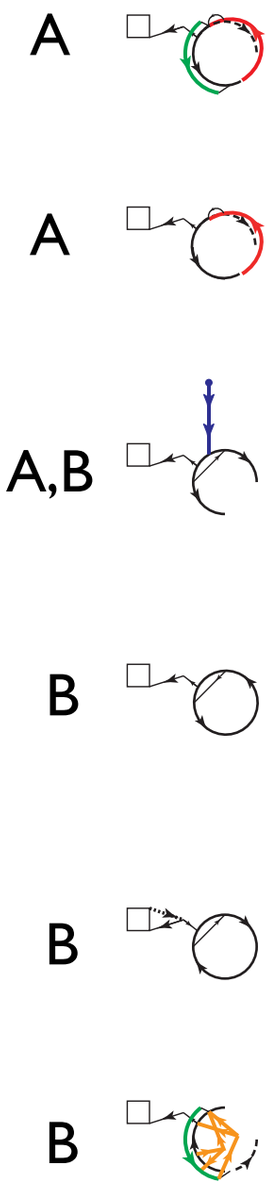
Pathways always complete the set by reusing TCA arcs





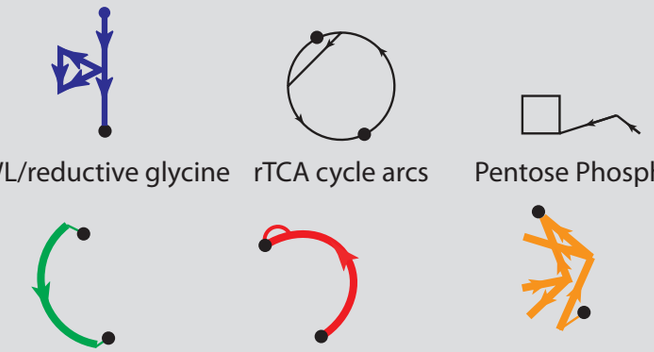
Re-use of reaction sequences and sharing of pathway arcs allows us to “coarse-grain” carbon-fixation

“Coarse-grained” carbon-fixation: reaching all TCA intermediates



A - Archaea
B - Bacteria

Modules:



“Coarse-grained” carbon-fixation: reaching all TCA intermediates

A

A

A,B WL

B rTCA

B

B

A - Archaea
B - Bacteria

Modules:


WL/reductive glycine


rTCA cycle arcs

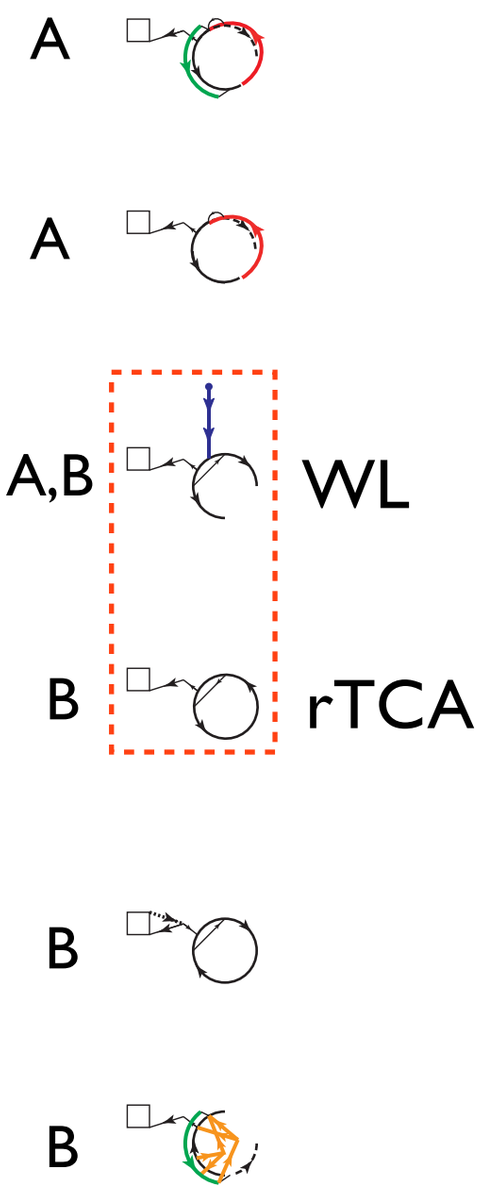

Pentose Phosphate


3HP pathway


4HB pathway

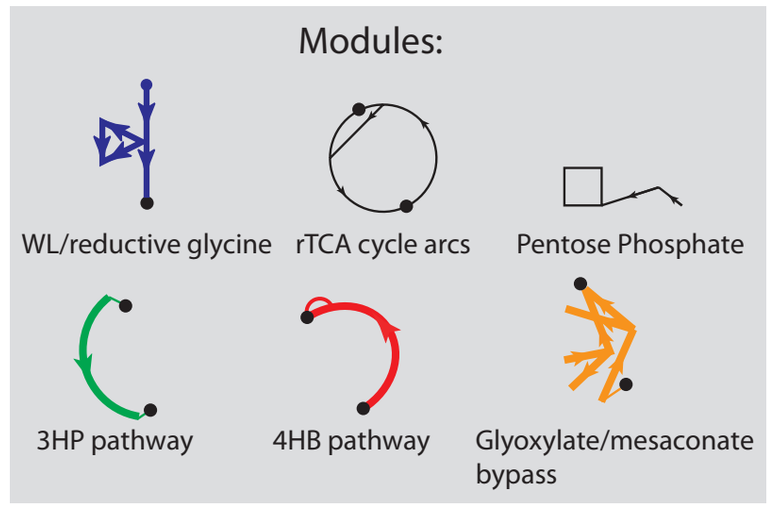

Glyoxylate/mesaconate bypass

“Coarse-grained” carbon-fixation: reaching all TCA intermediates

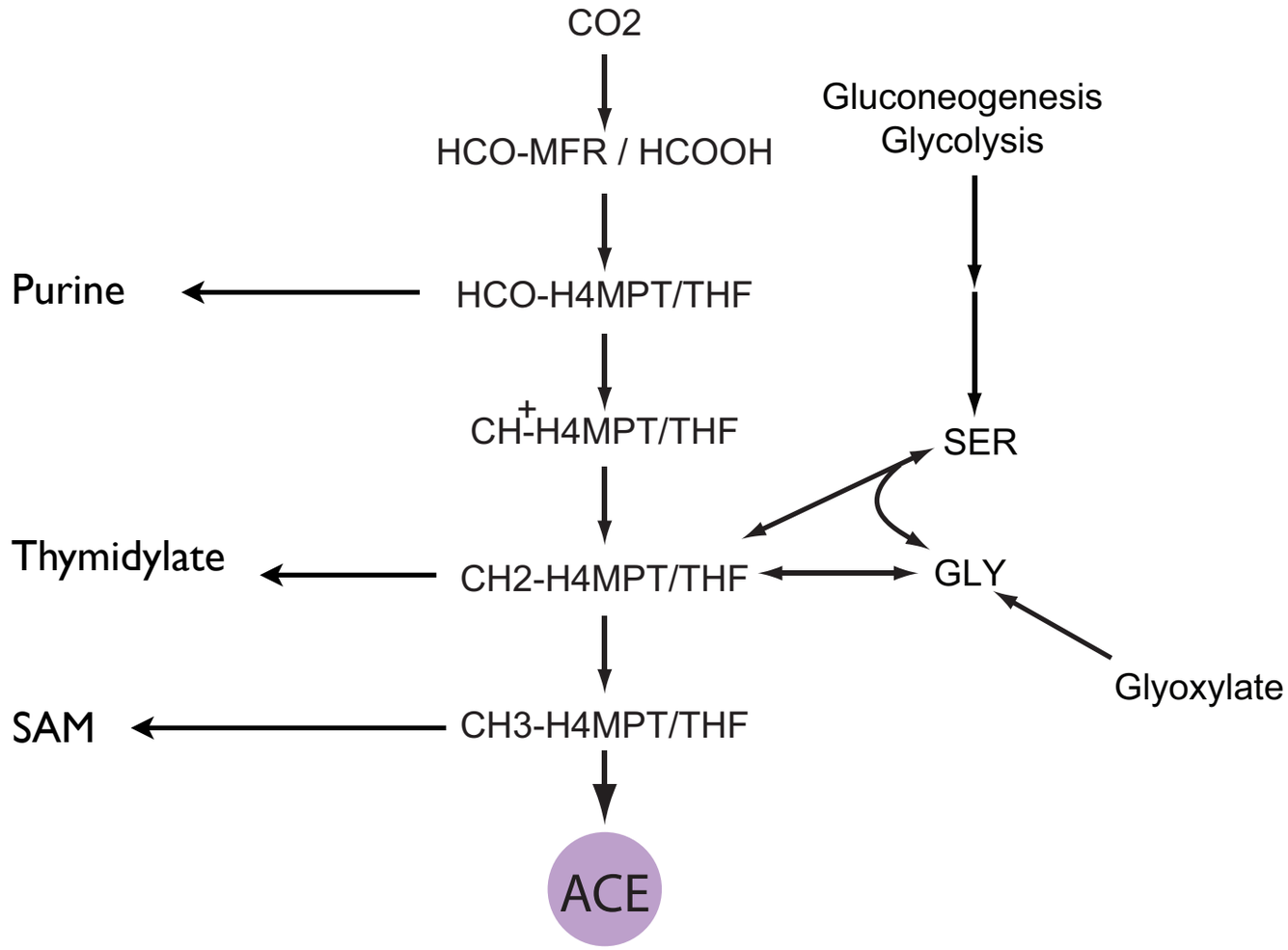


A - Archaea
B - Bacteria

Glycine synthesis helps clear things up



Additional carbon-fixation bottlenecks that can be made directly from CO2: Glycine and Serine



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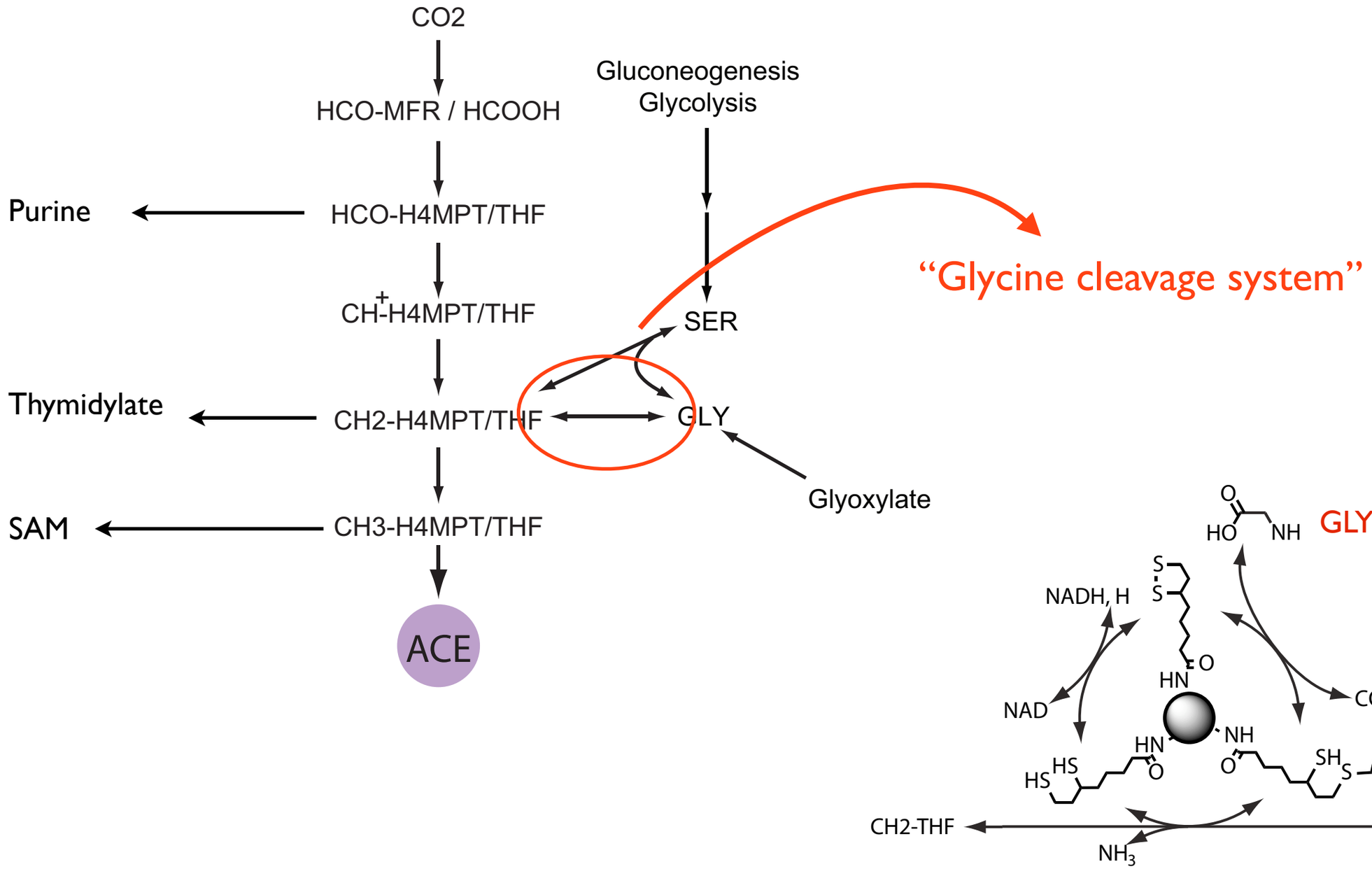

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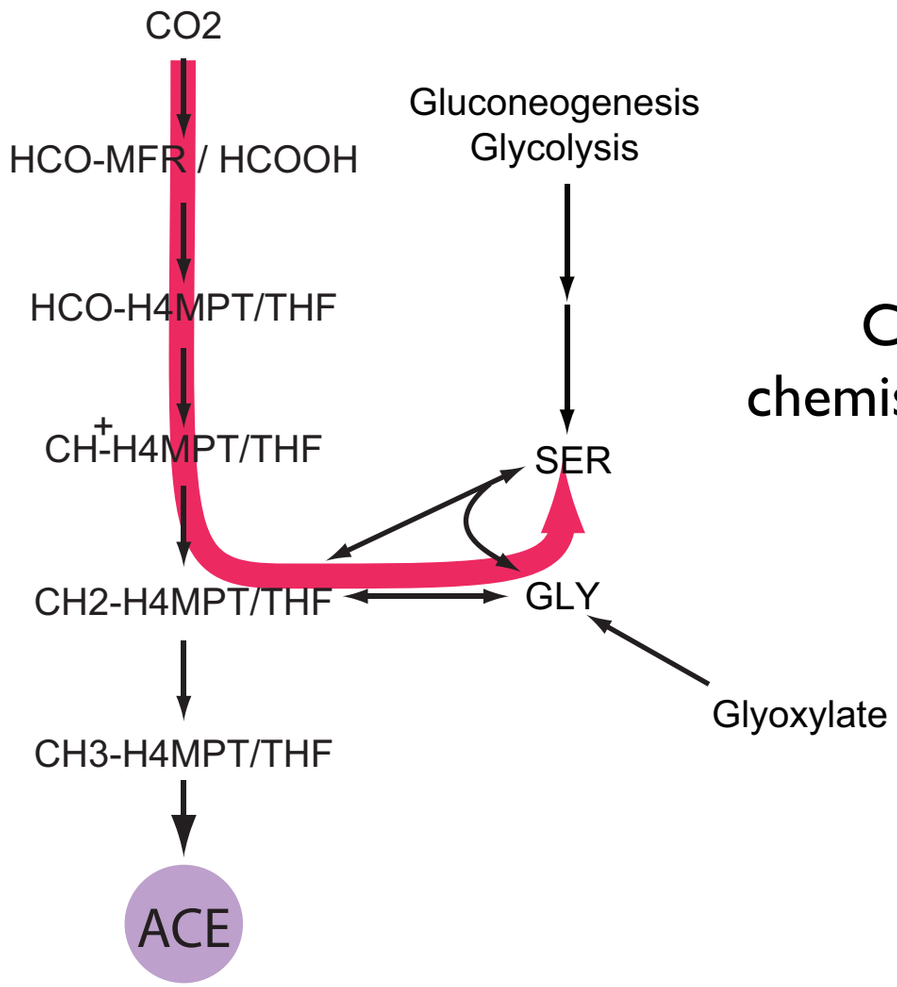
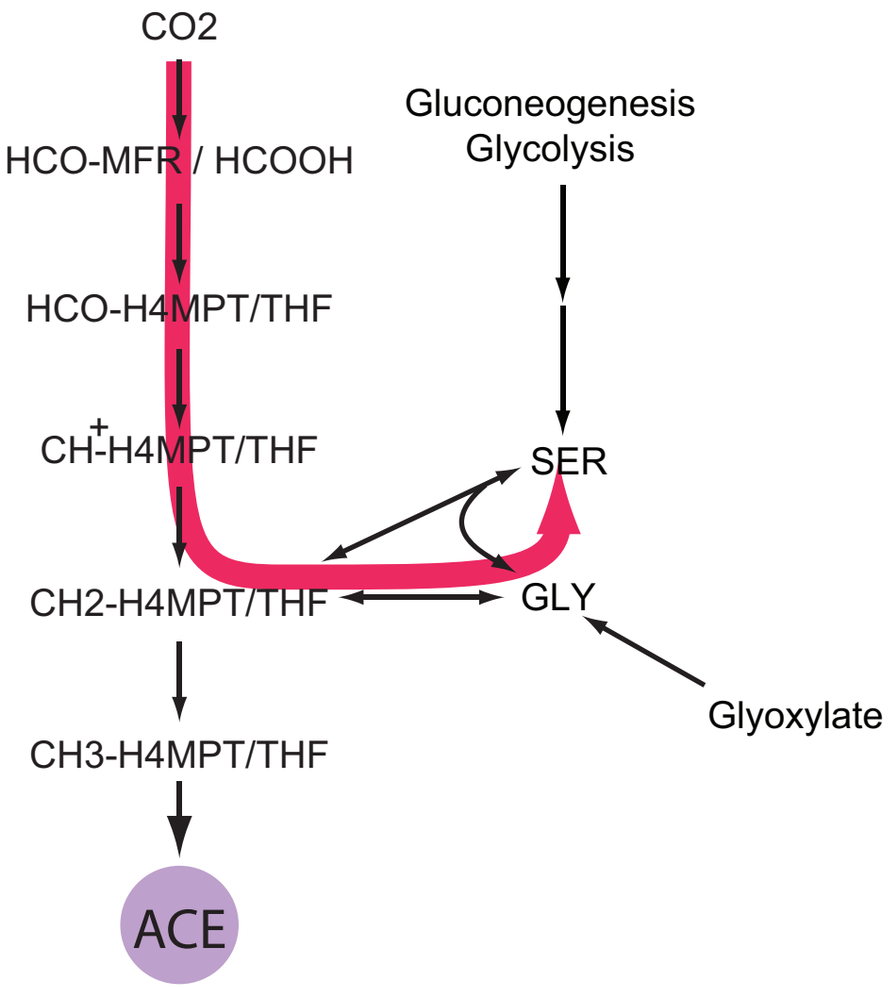
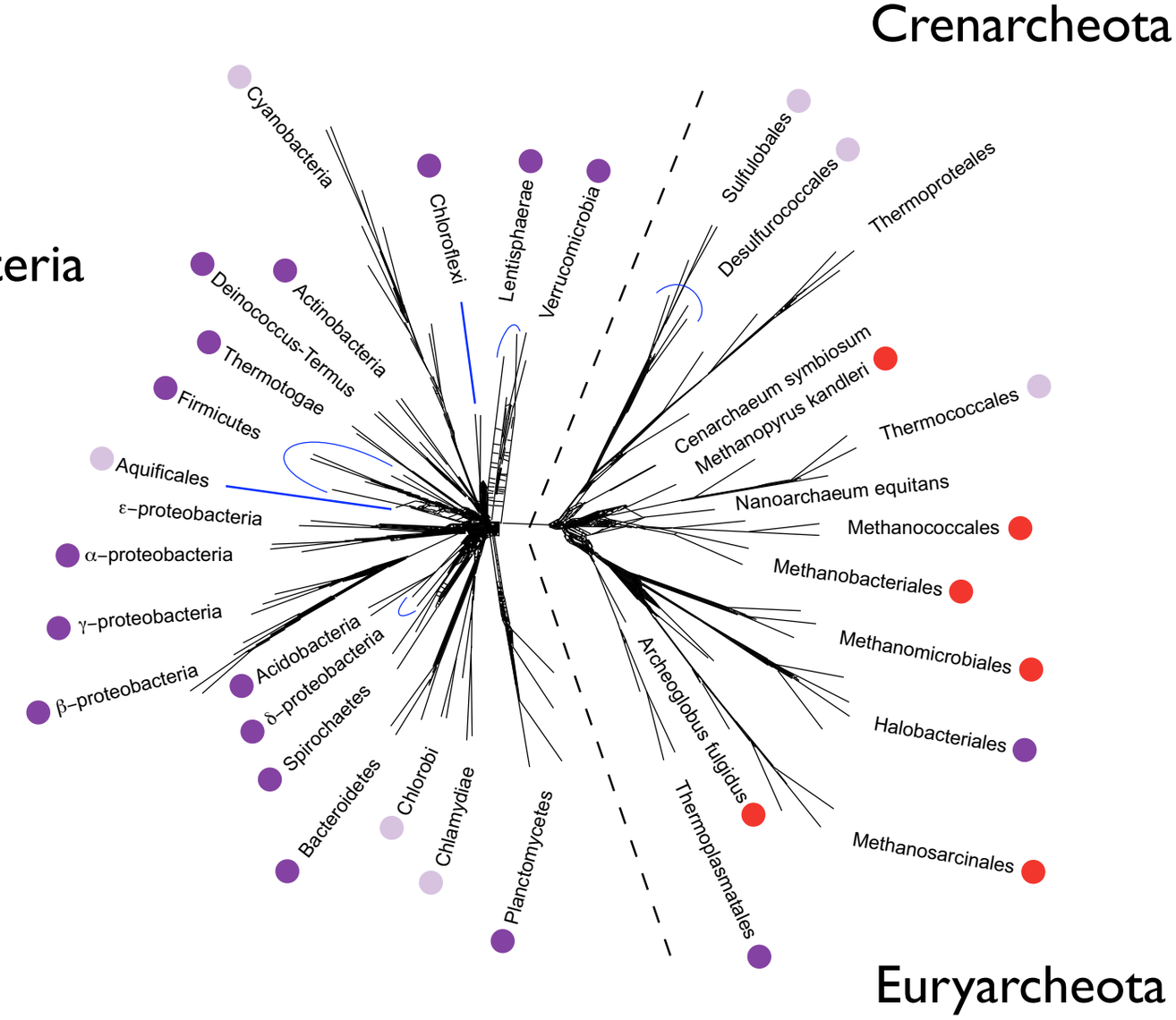


Completely reductive folate chemistry only recognized in WL, but all parts are reversible

Folate pathway to glycine and serine is widespread, represents ancestral route to these molecules





Tree adapted from Puigbo et al (2009)

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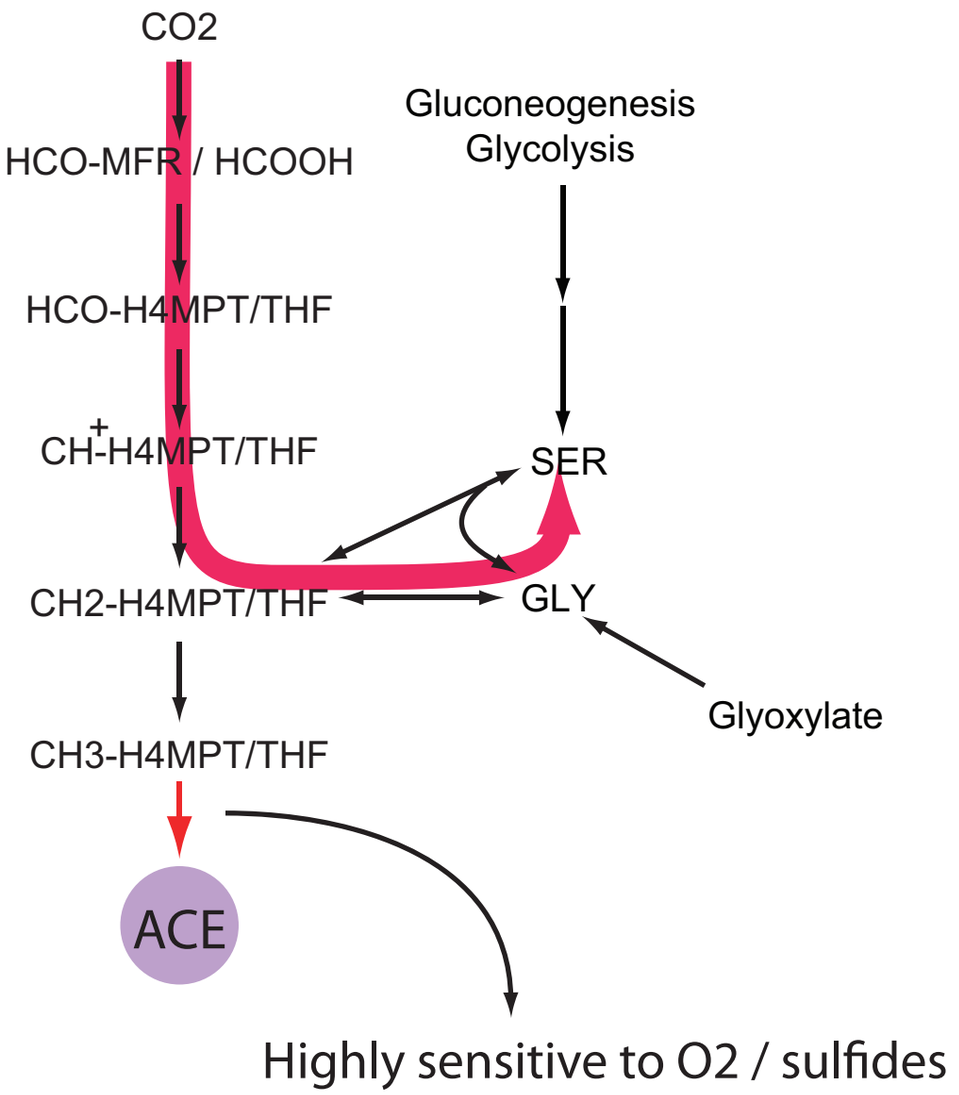

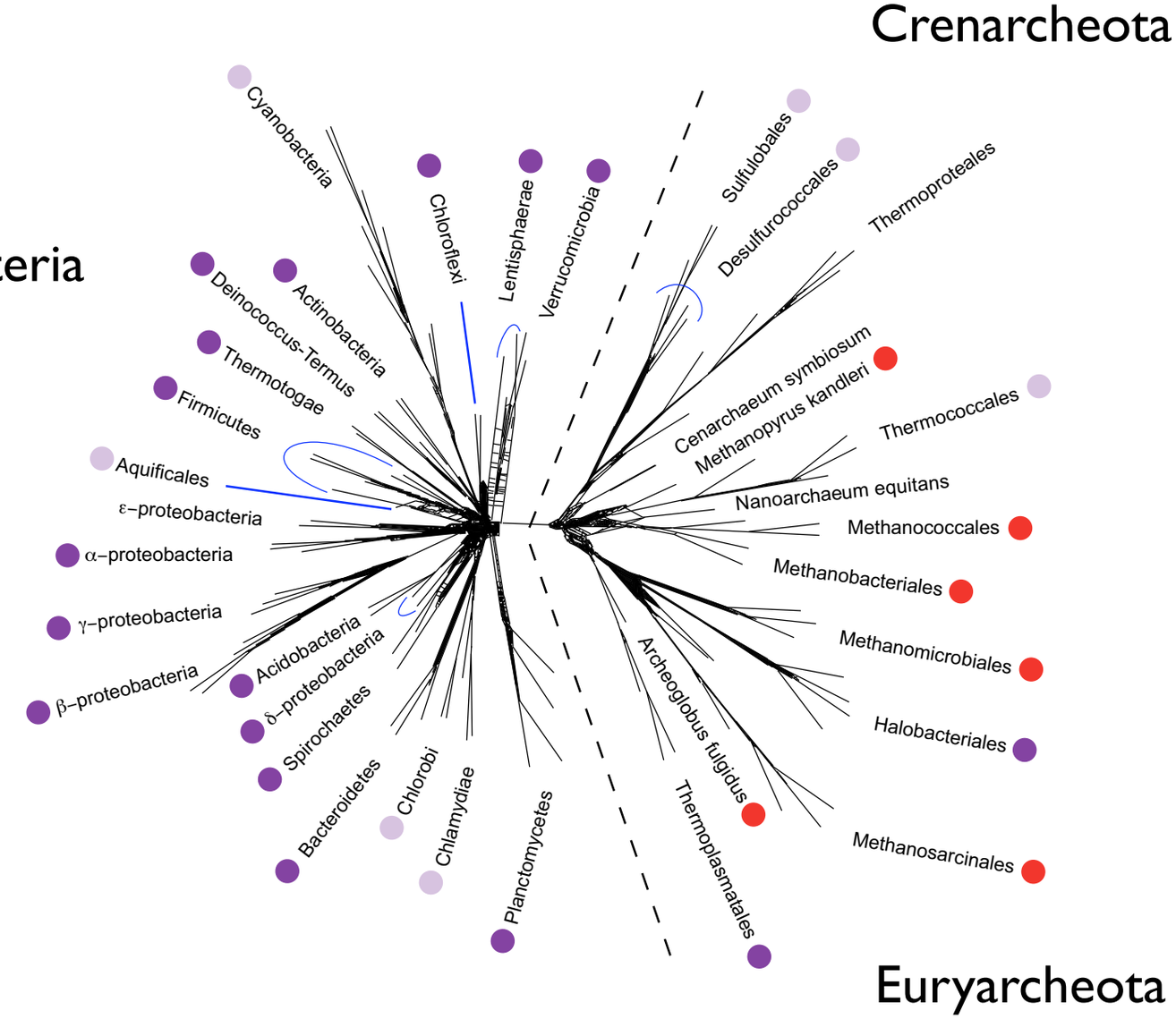

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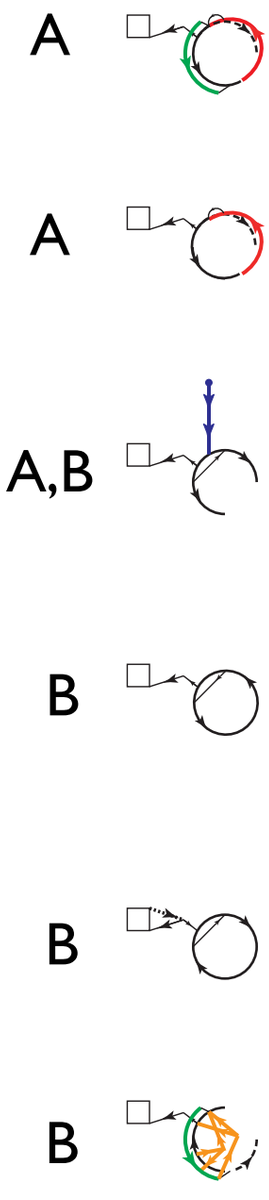
“Coarse-grained” carbon-fixation: reaching all TCA intermediates



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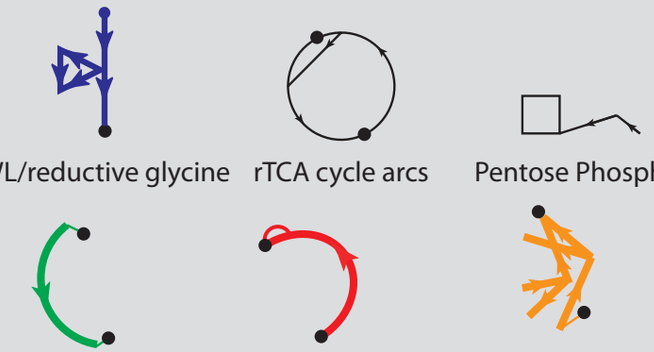
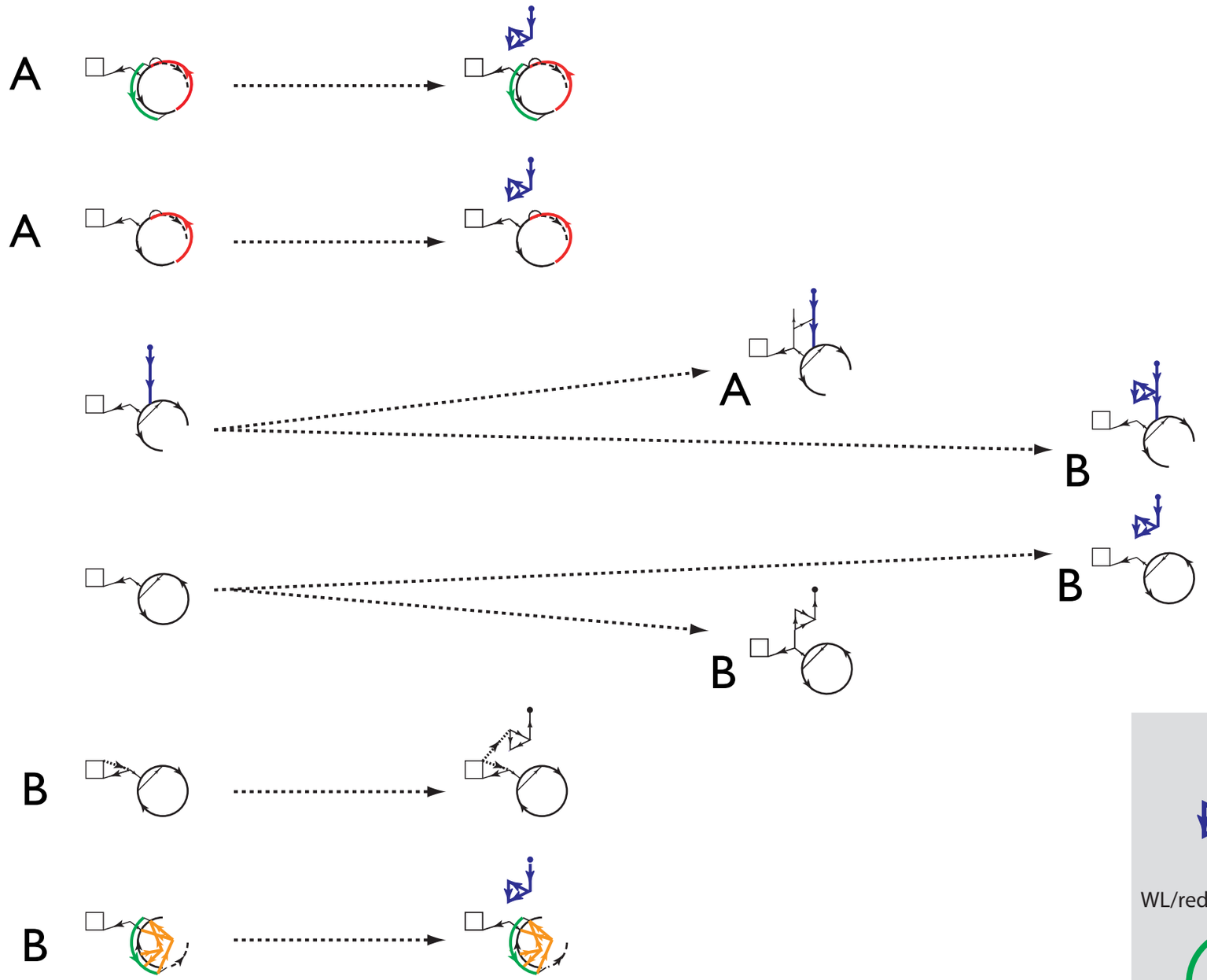
B - Bacteria

Modules:



“Coarse-grained” carbon-fixation: reaching all TCA intermediates plus glycine



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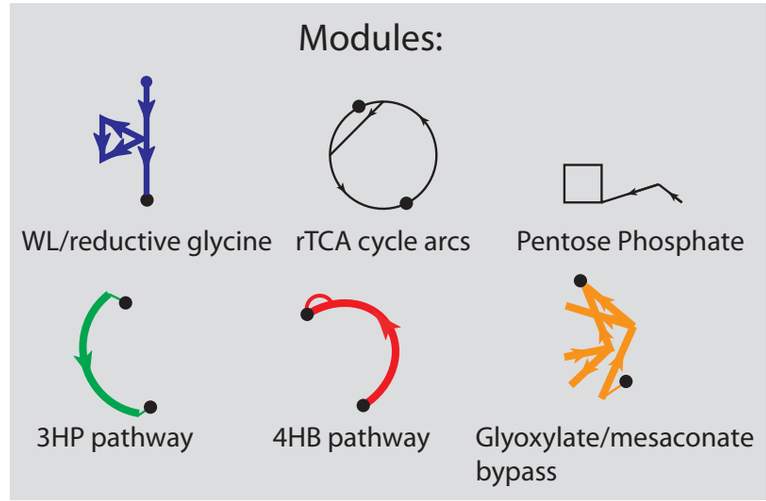
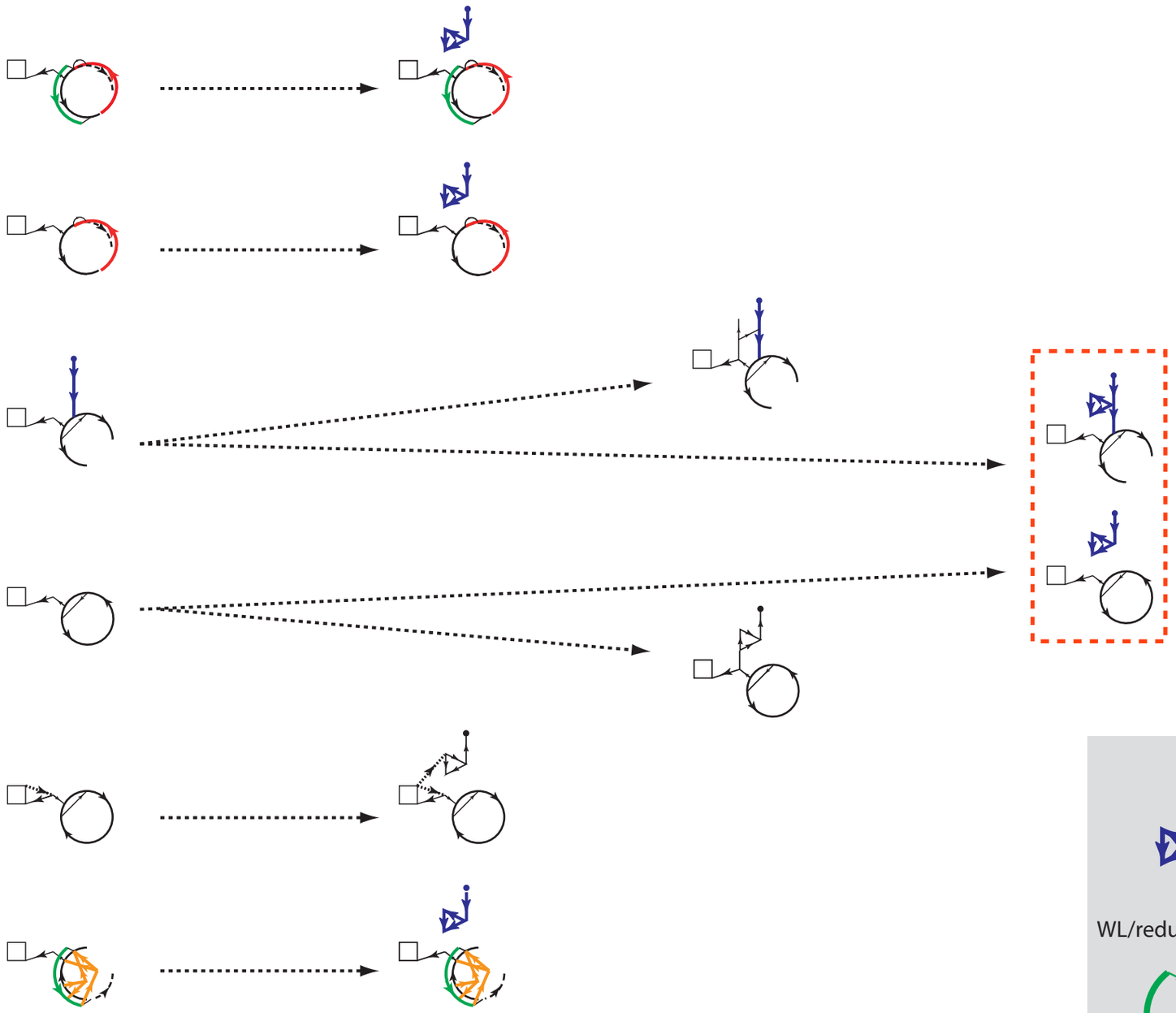
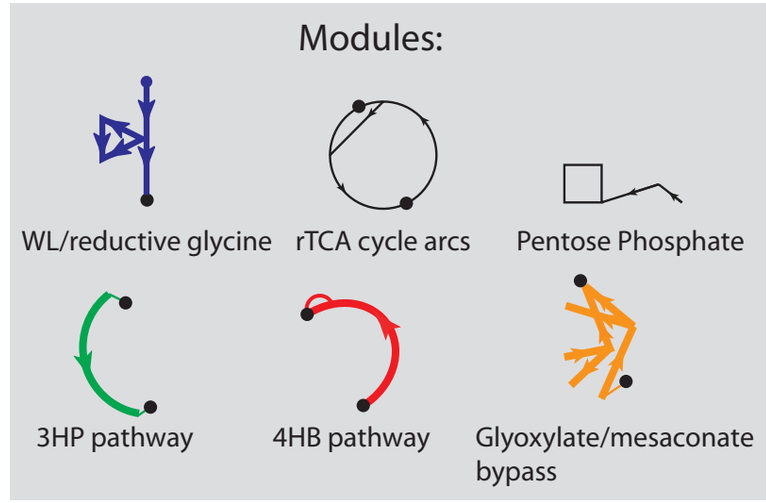


Increased similarity between deep-branching rTCA and WL suggest underlying template





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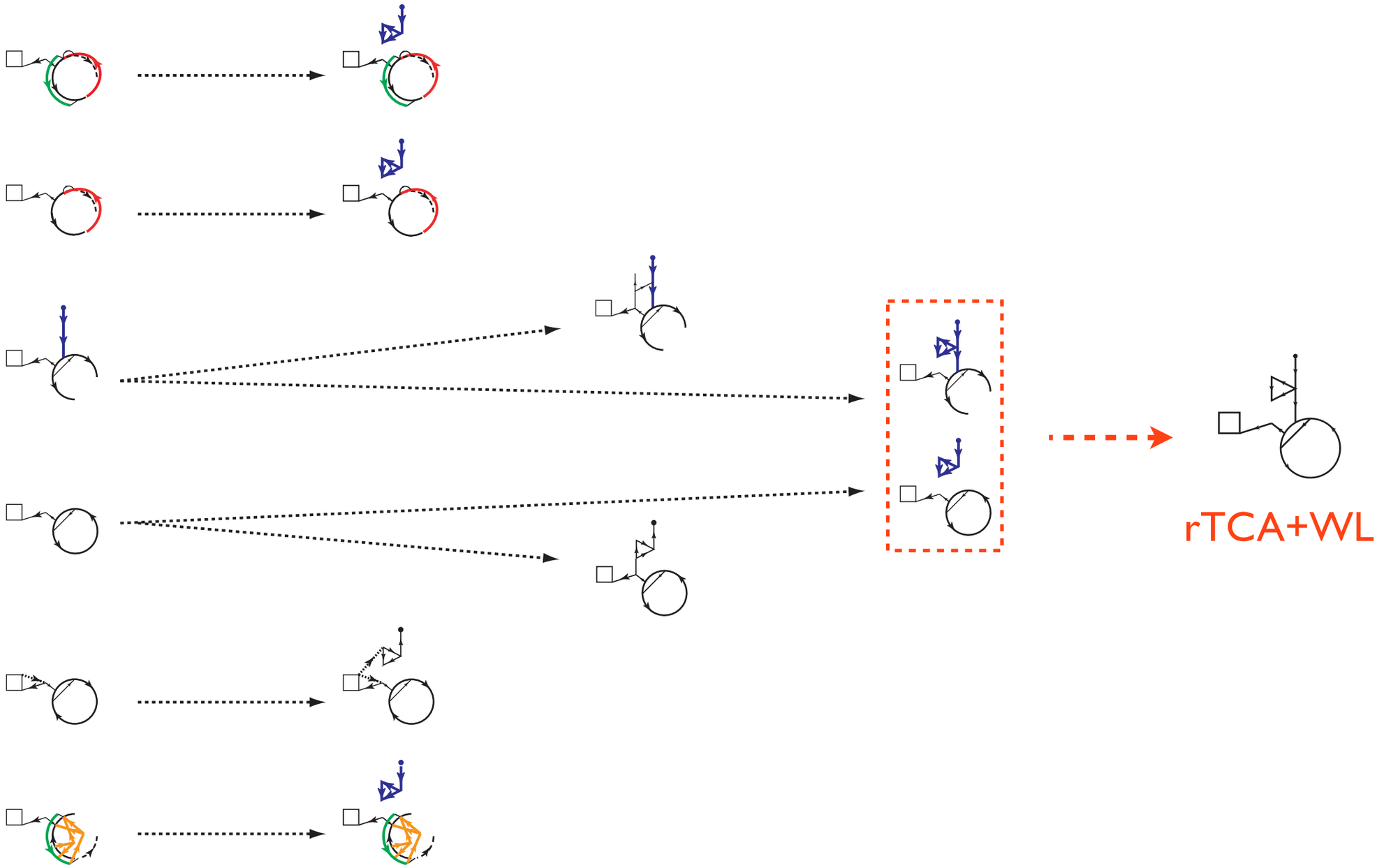
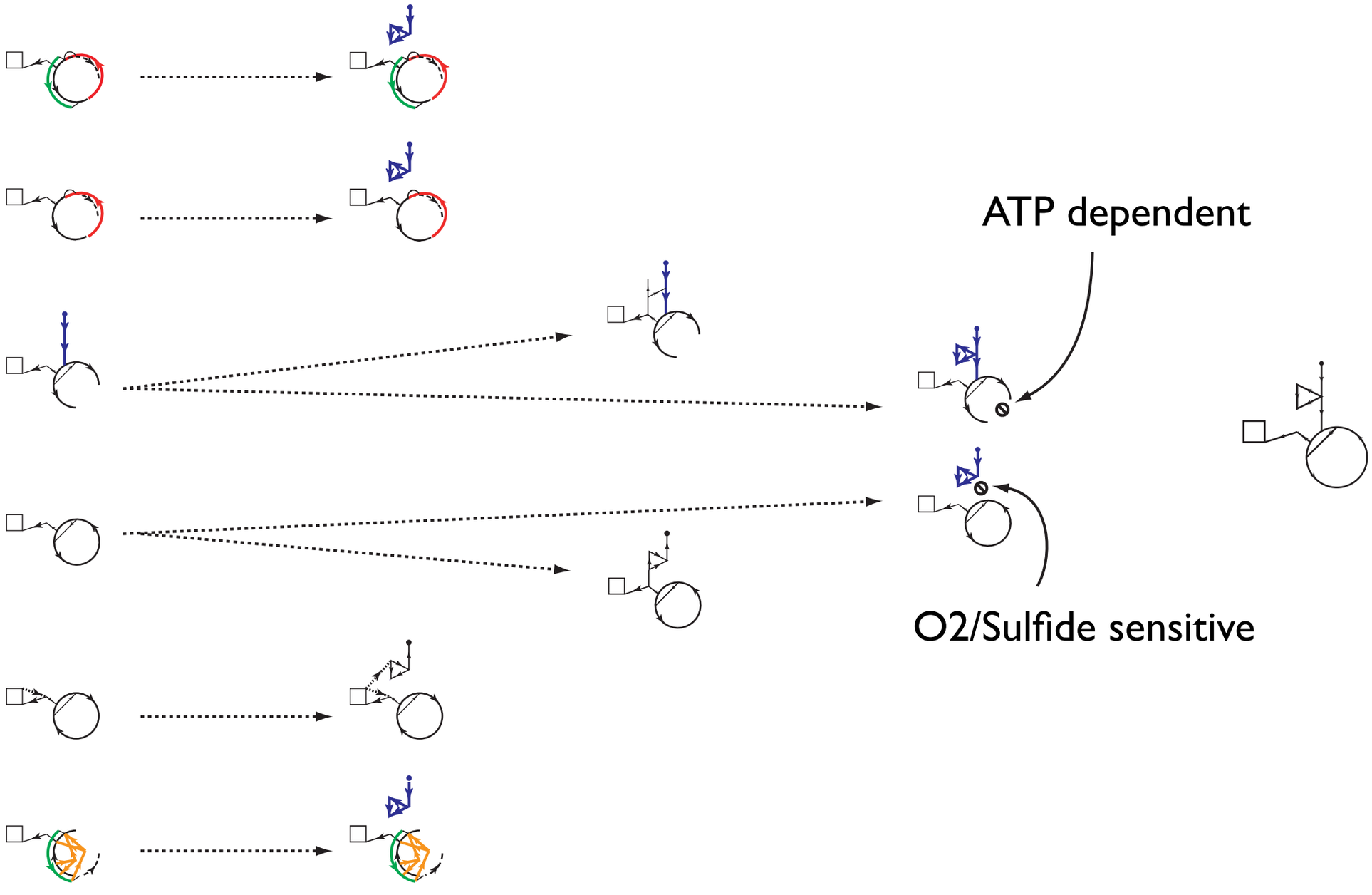
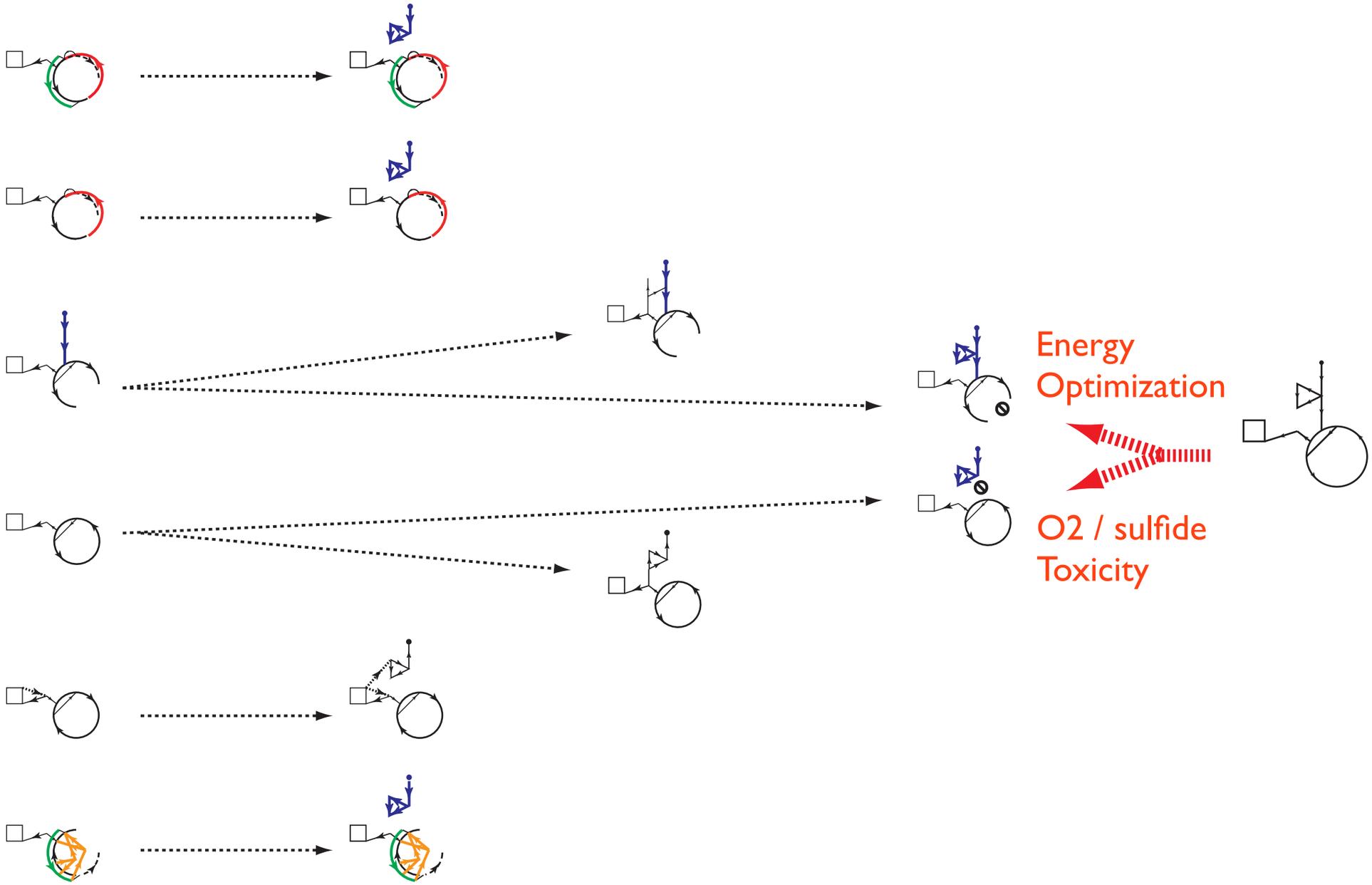


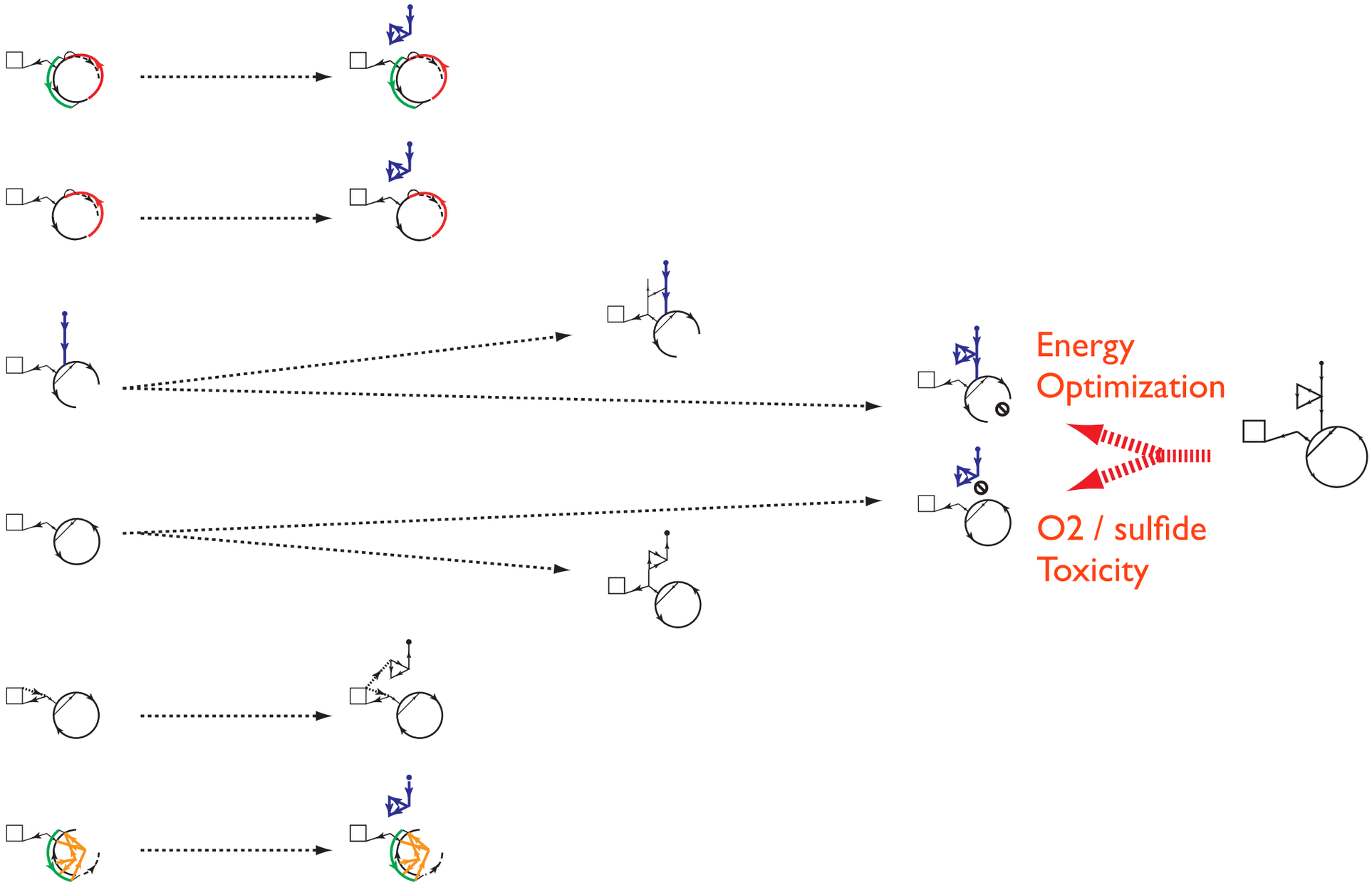
rTCA and WL lack distinctive components relative to linked rTCA+WL, suggesting evolutionary connection



A proto-tree of carbon-fixation begins to emerge



Chemical distinction between WL forms suggests additional energetic divergence



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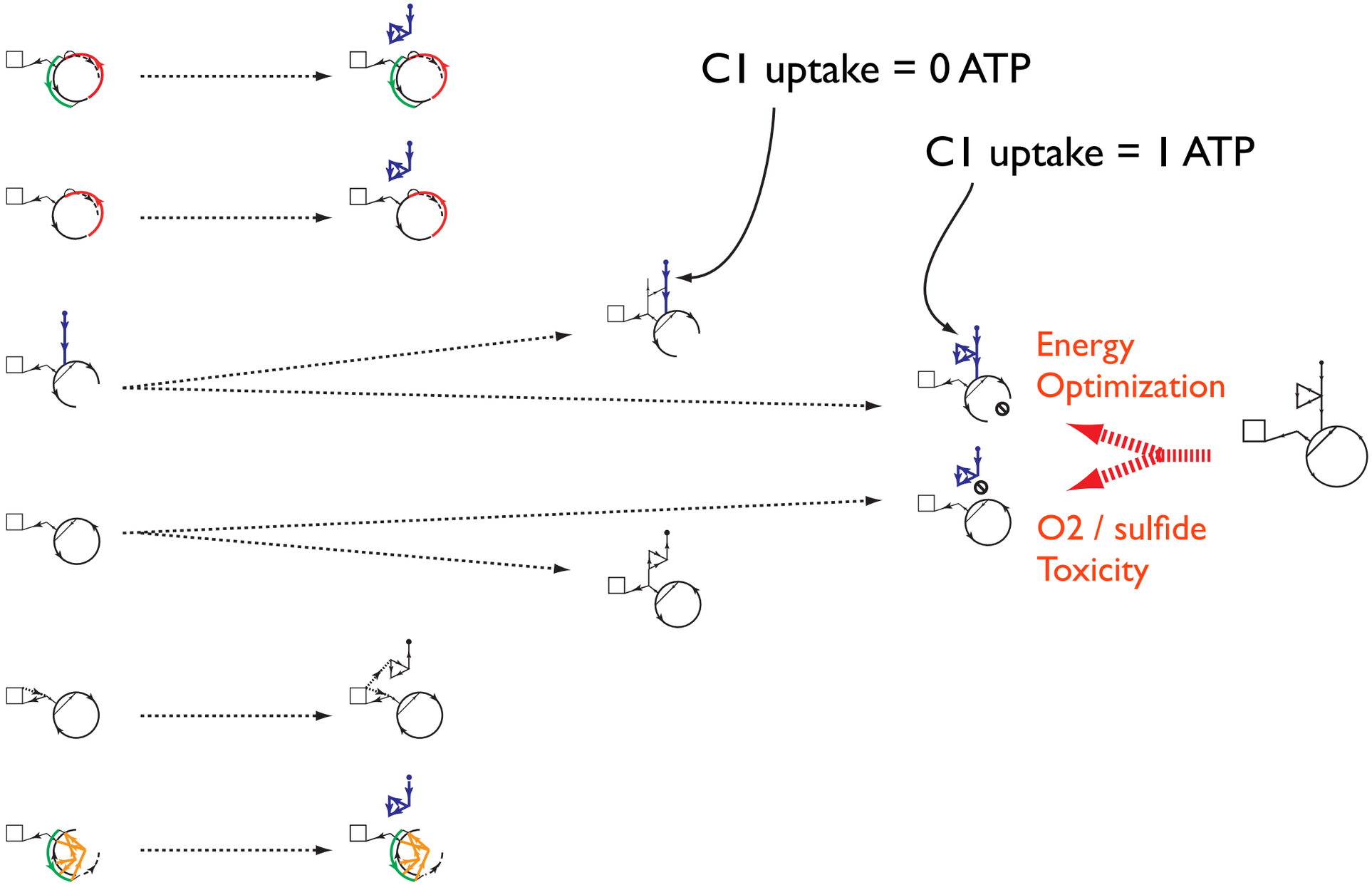
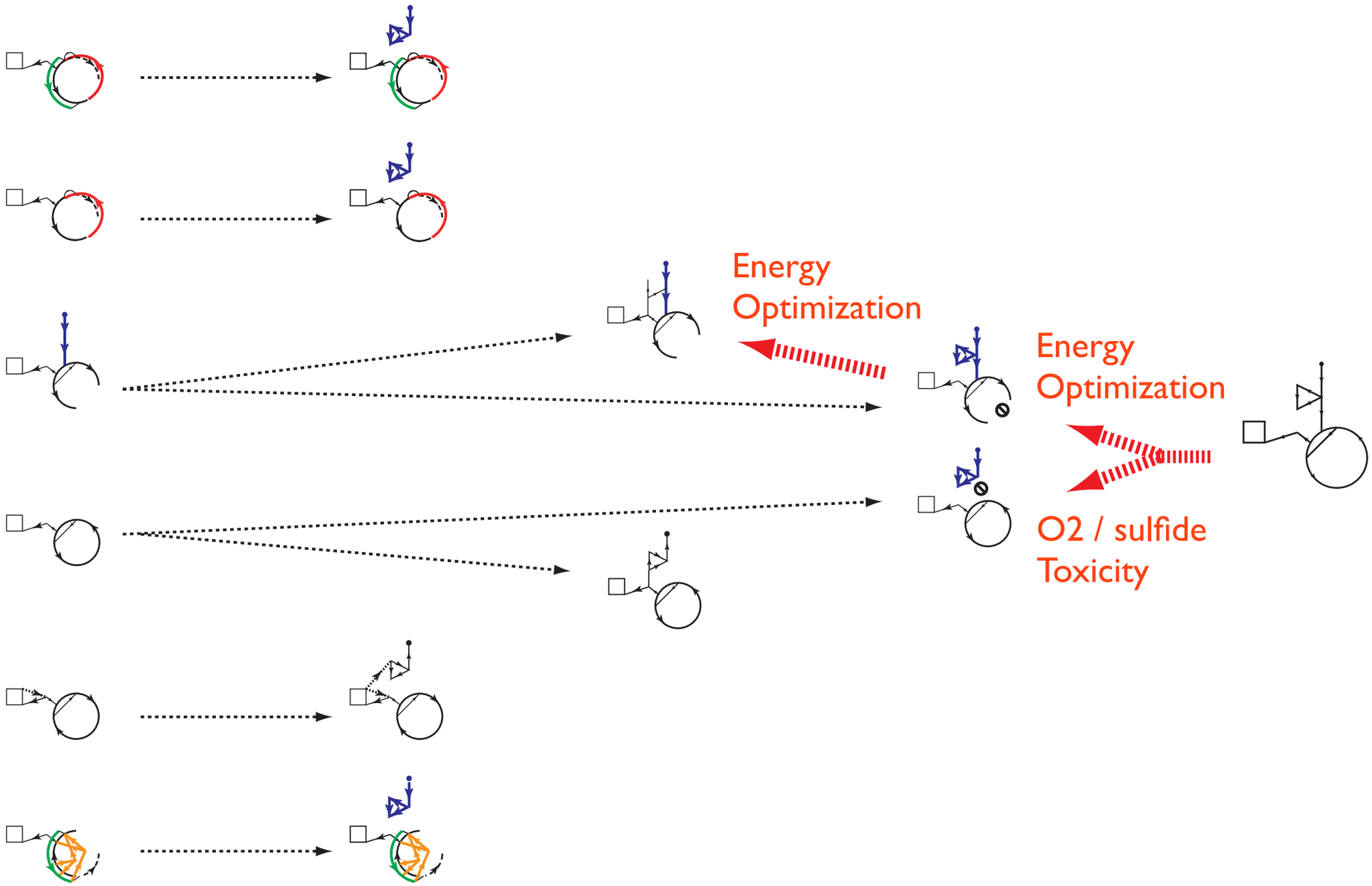
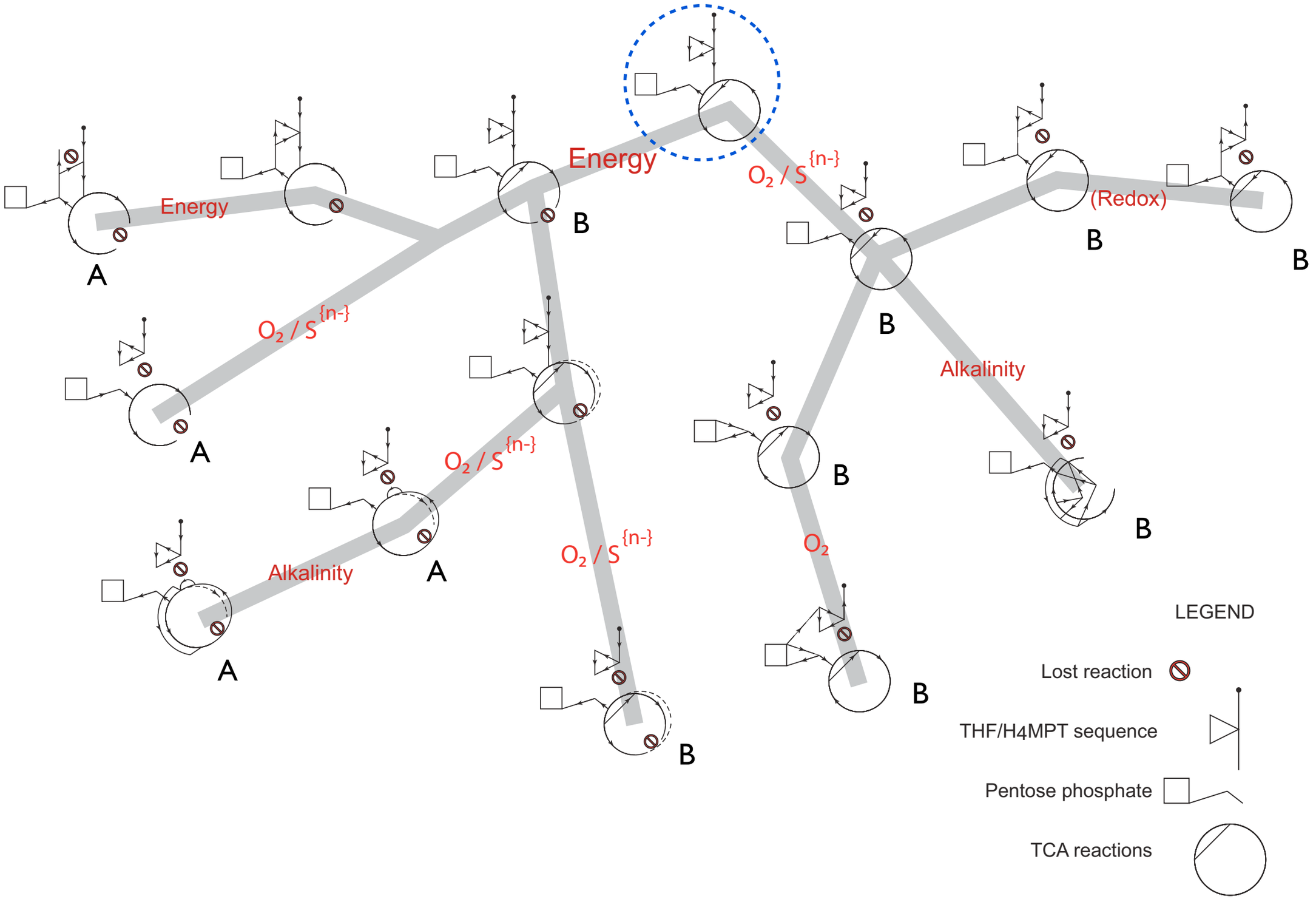


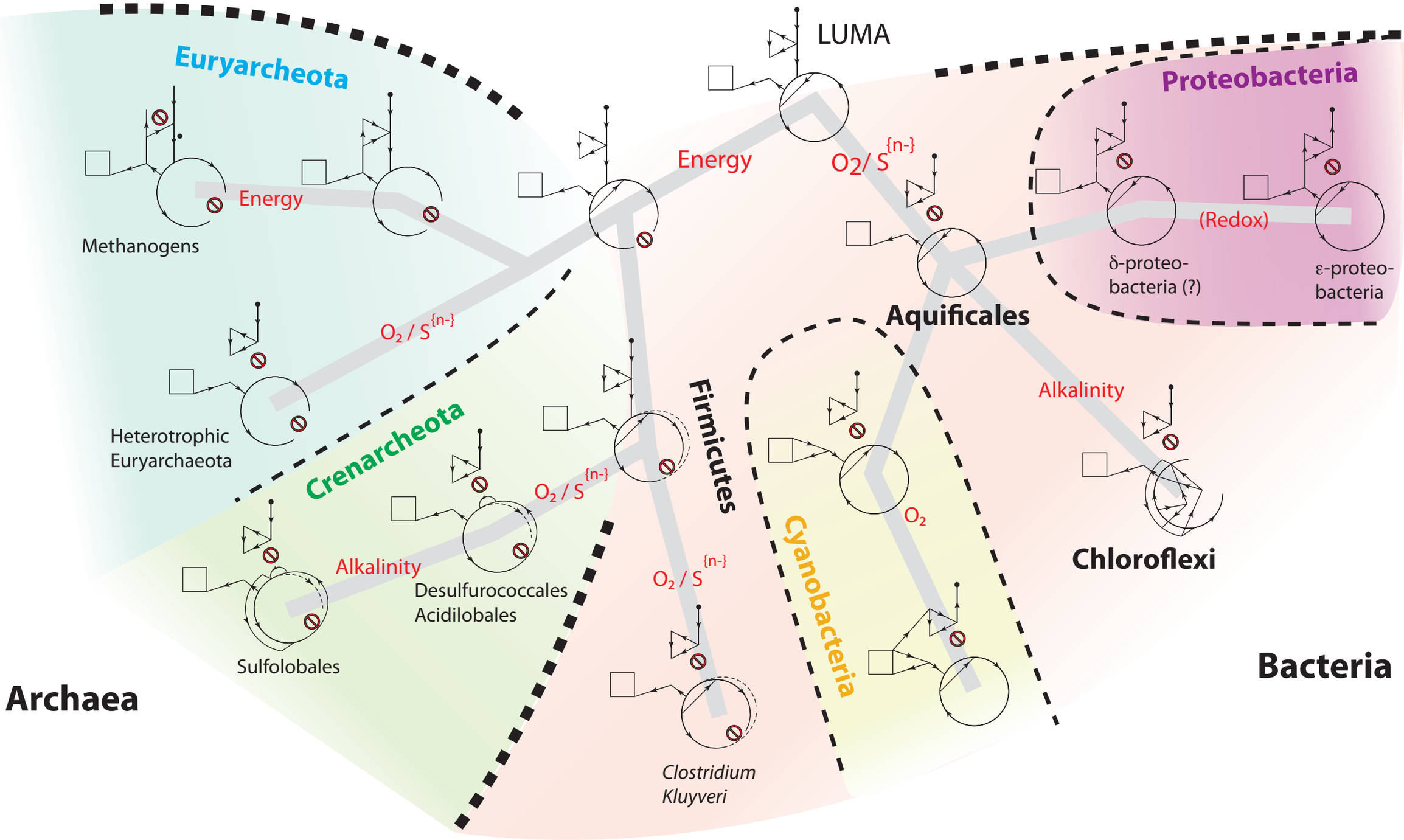
Proto-tree of carbon-fixation takes further shape



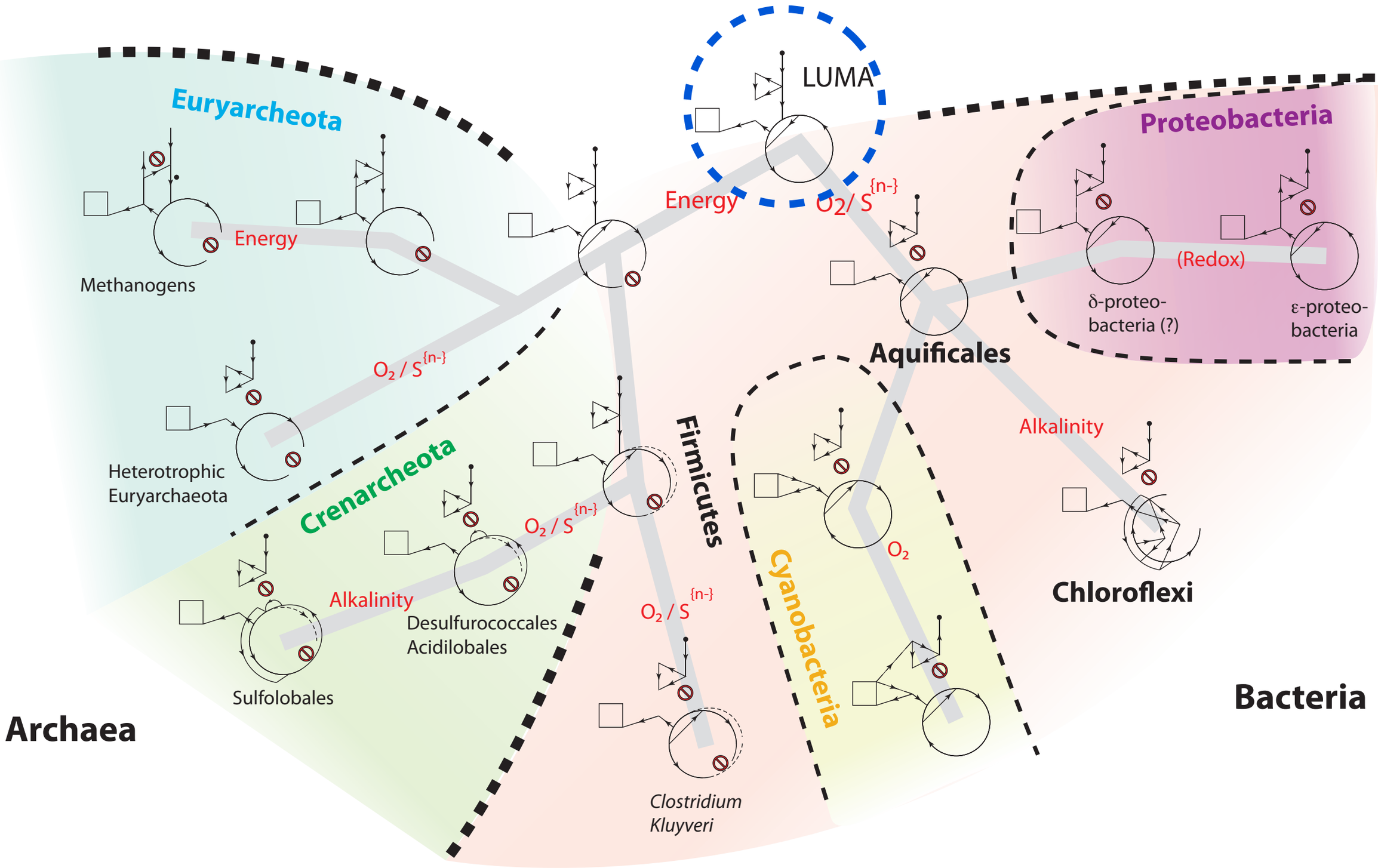
All forms connected: phylometabolic tree of carbon-fixation



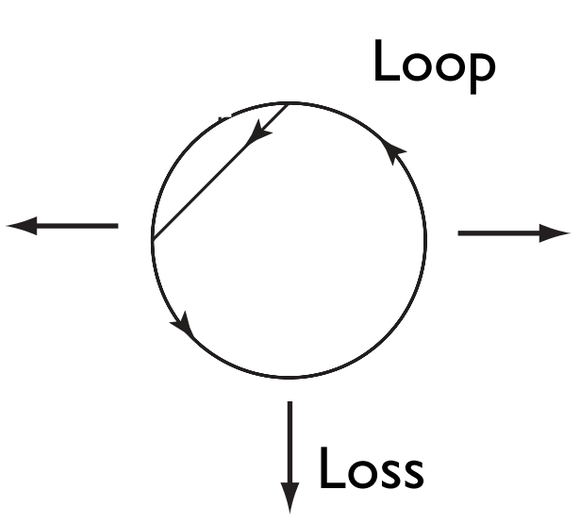
Innovations in carbon-fixation appear to underlie many of the deepest branches in the tree of life

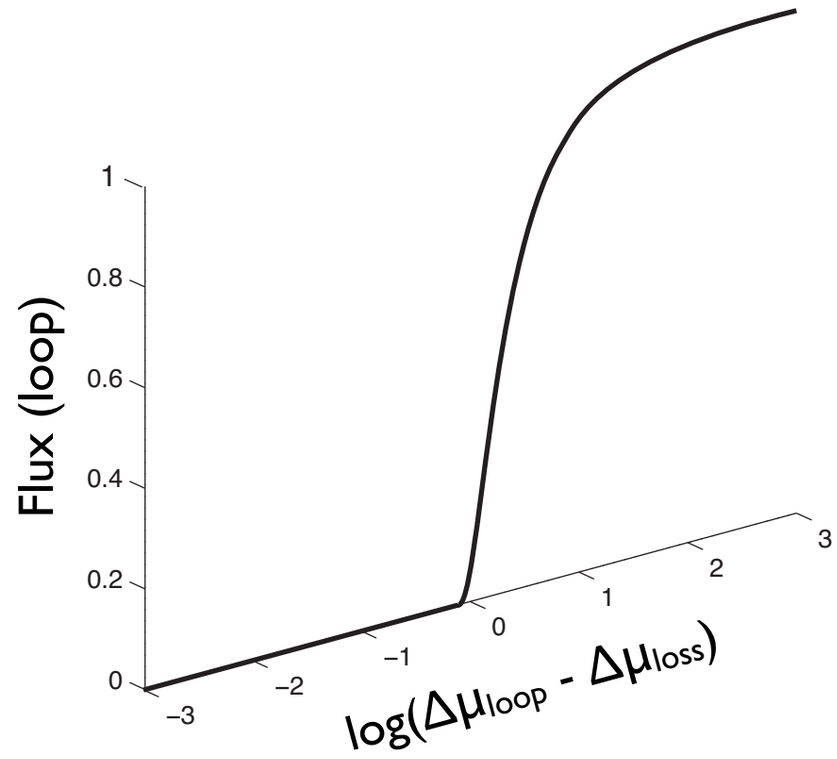


What does tree teach us about ancestral carbon-fixation (and its emergence)?



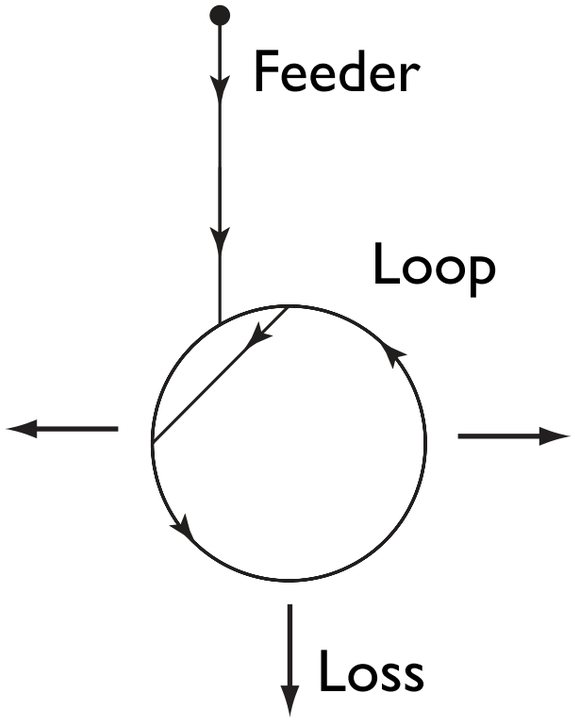
Topological analysis: rTCA+WL would be kinetically favored under abiotic conditions!

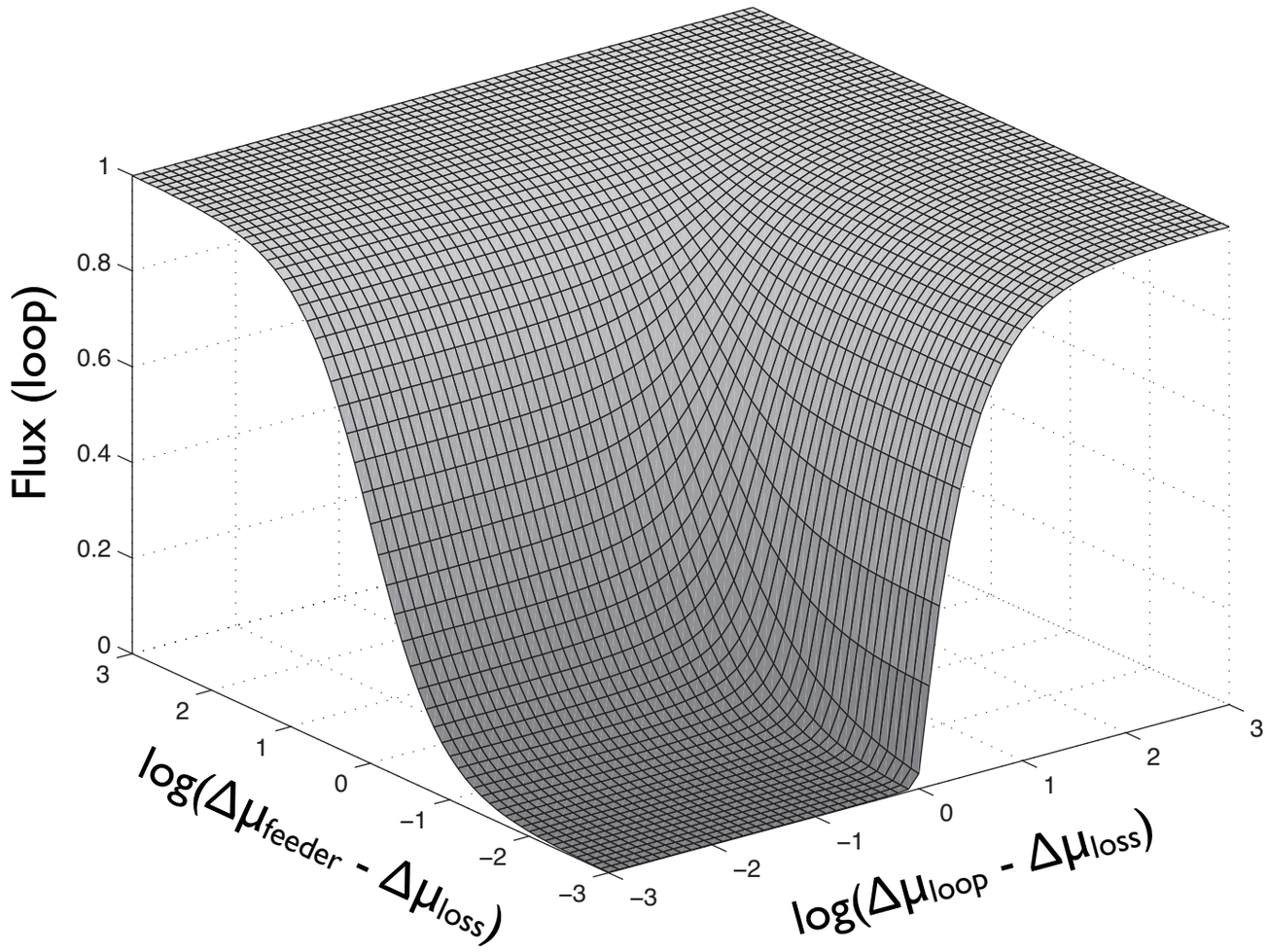




Topology of rTCA allows exponential growth,
but has threshold fragility

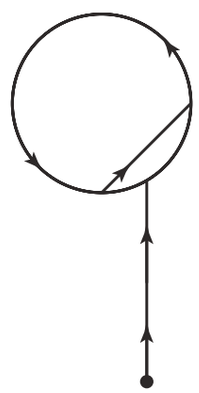
Topological analysis: rTCA+WL would be kinetically favored under abiotic conditions!





Adding WL to rTCA removes threshold behavior, leading to more robust form of exponential growth

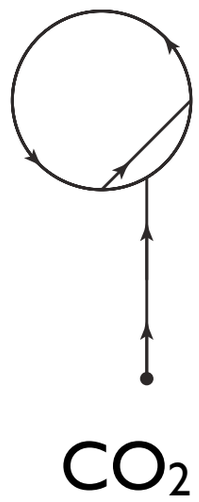
rTCA-WL allows an ordered flow of organic chemistry, increasing probability of additional feedback



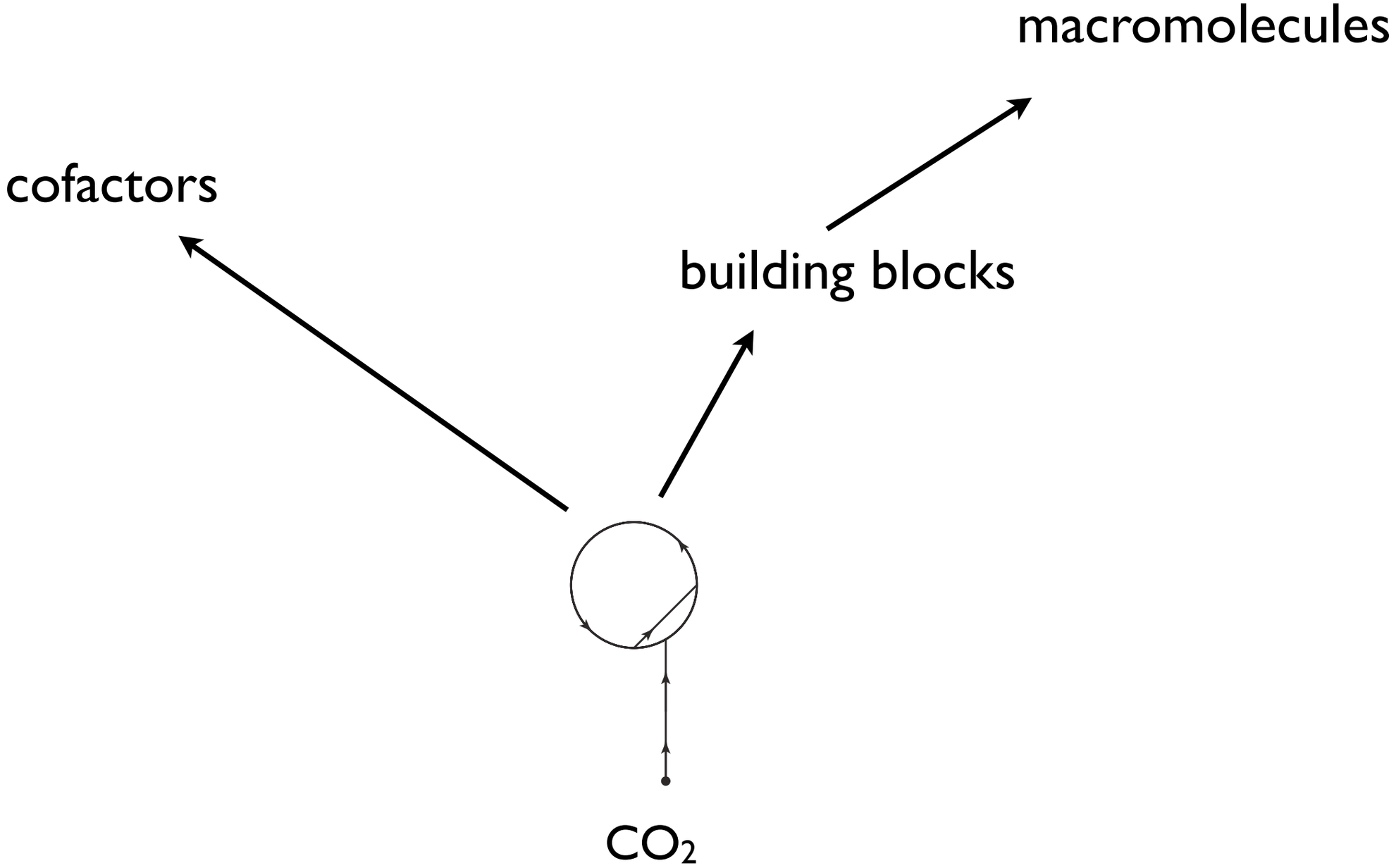
CO_2

rTCA-WL allows an ordered flow of organic chemistry, increasing probability of additional feedback

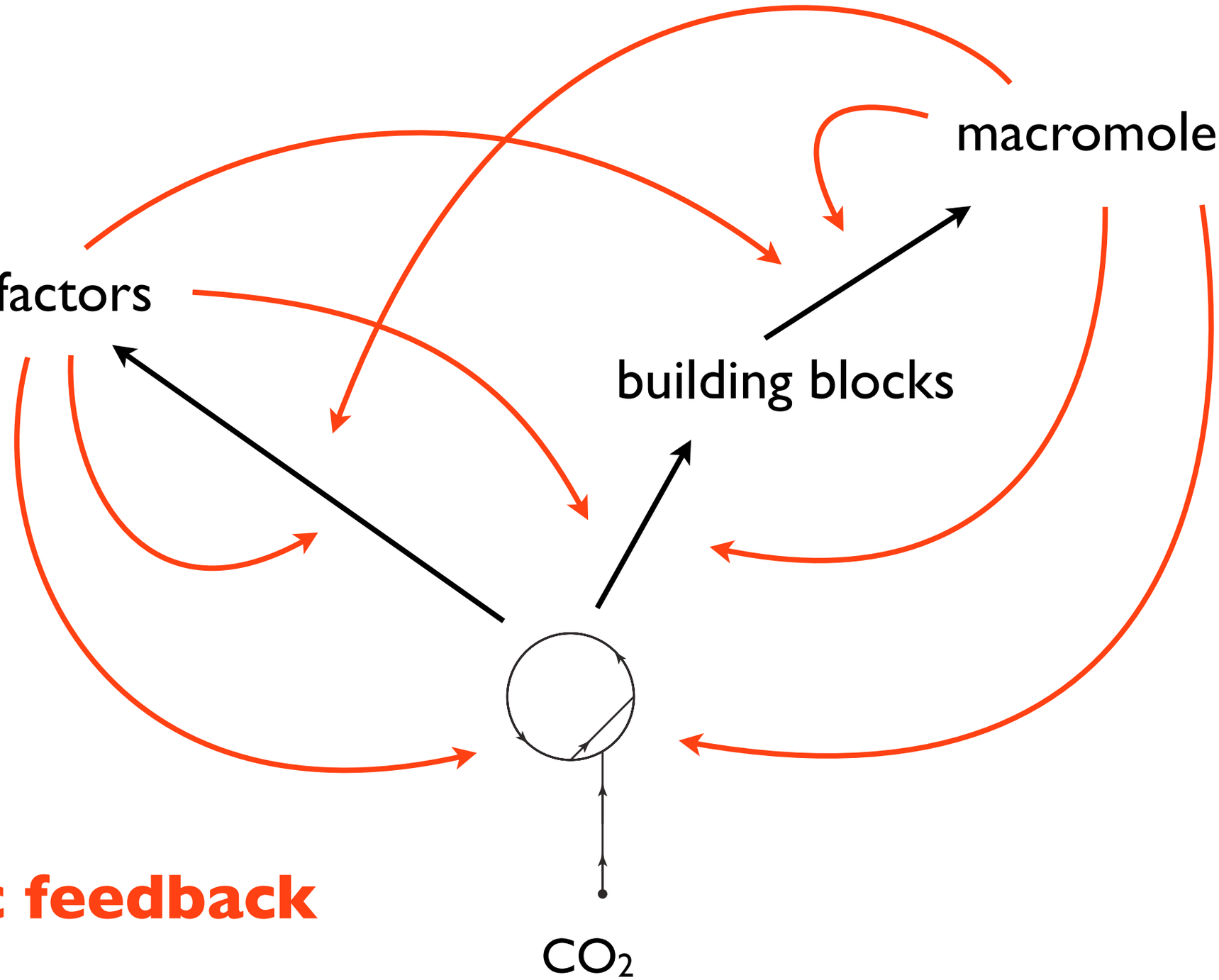
How is it embedded within the rest of metabolism?



Metabolism is an “onion” with a heart of carbon-fixation - peeling back its layers tells a story of emergence

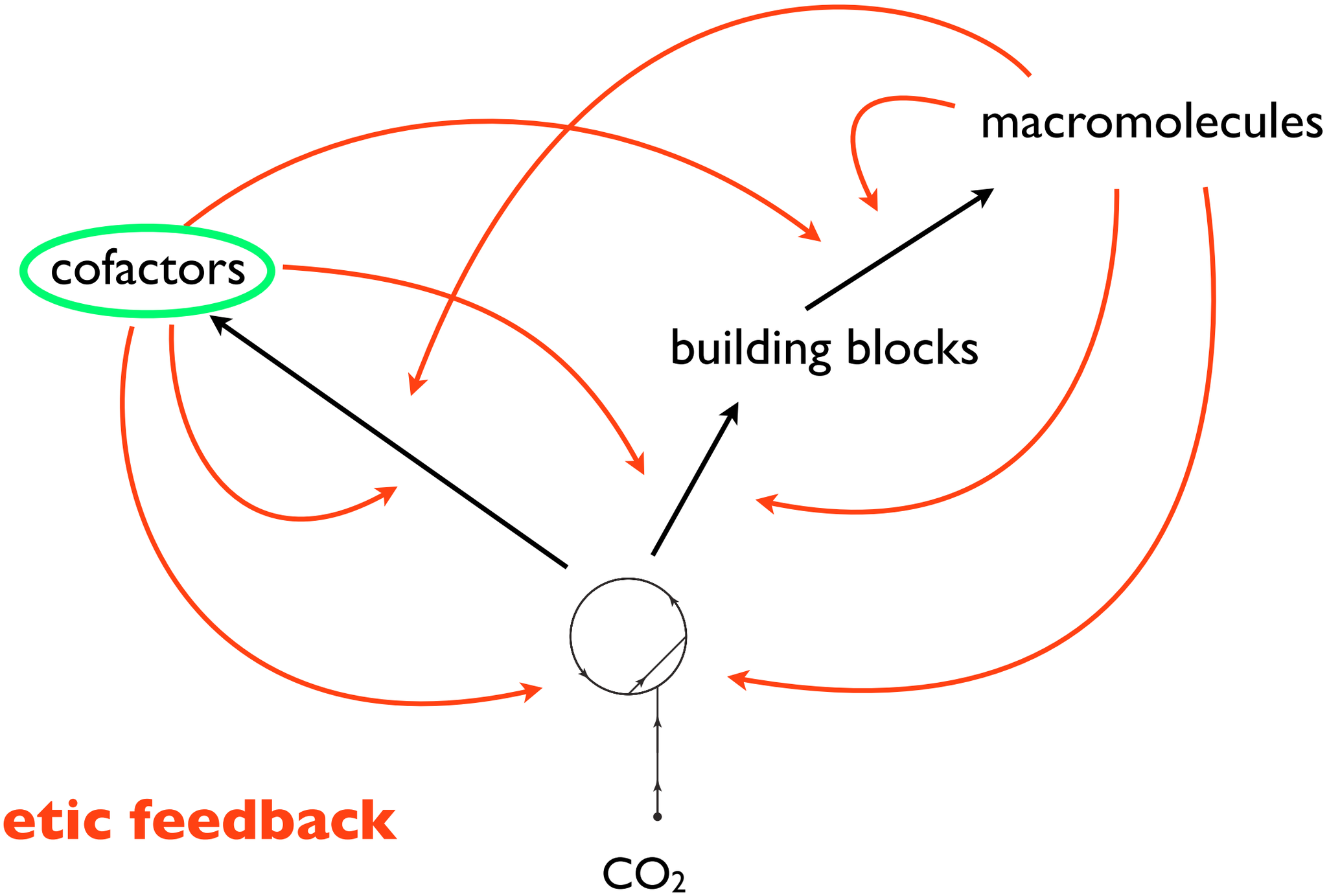


Metabolism is an "onion" with a heart of carbon-fixation - peeling back its layers tells a story of emergence



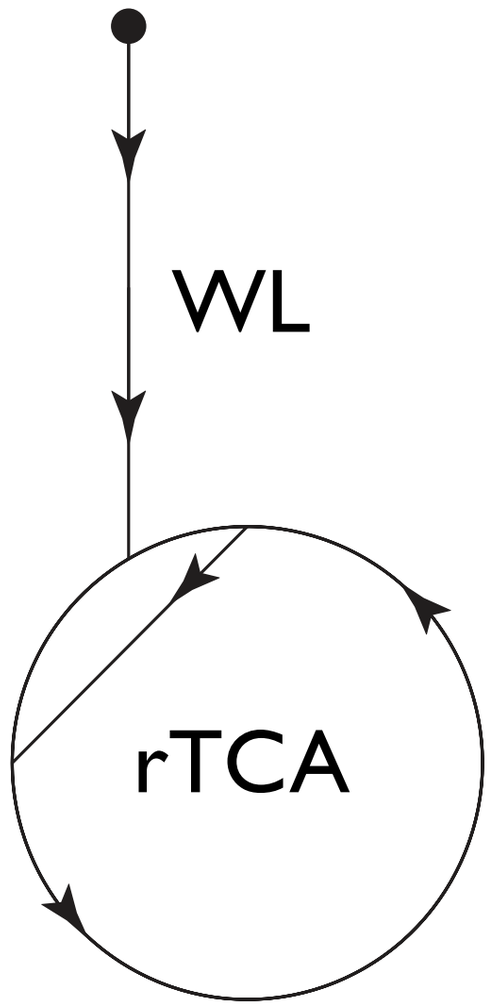
Kinetic feedback

Metabolism is an "onion" with a heart of carbon-fixation - peeling back its layers tells a story of emergence

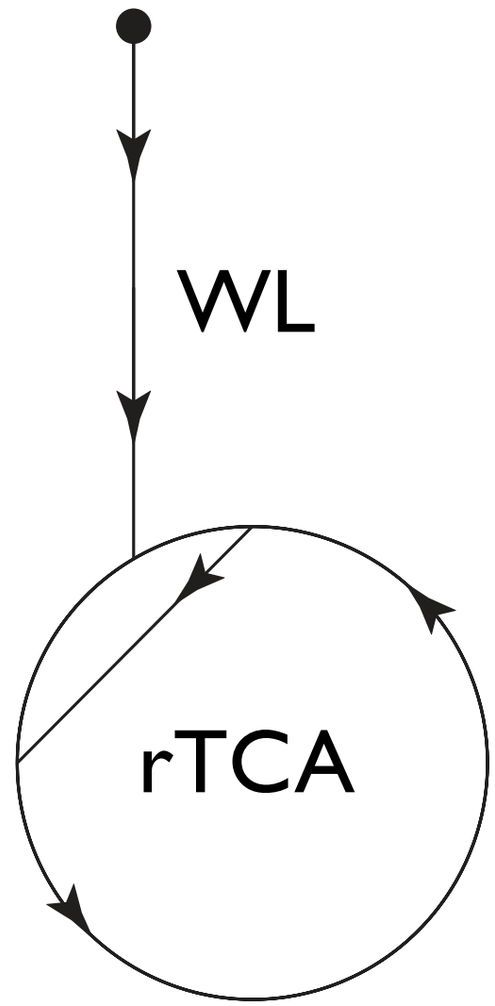


Kinetic feedback

Looking for the geochemical roots of metabolism

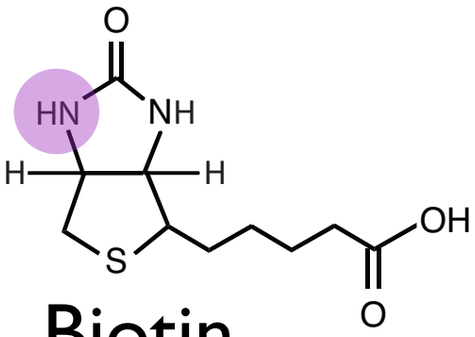


Looking for the geochemical roots of metabolism

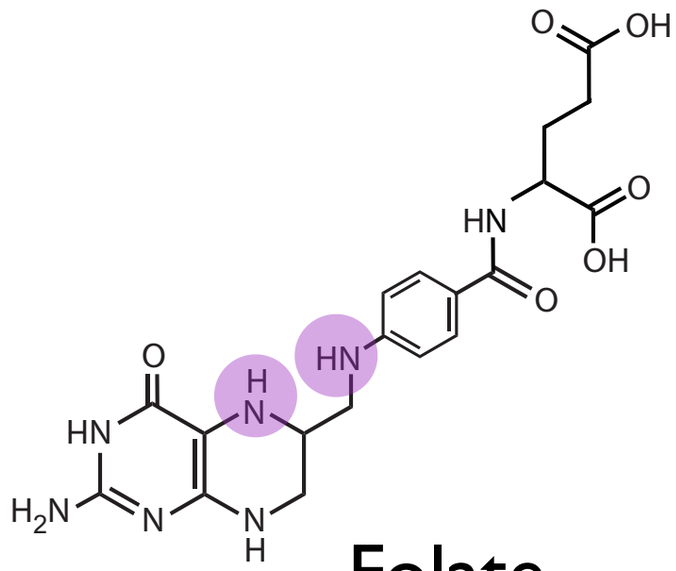


How does biology catalyze this chemistry?

Looking for the geochemical roots of metabolism



Biotin



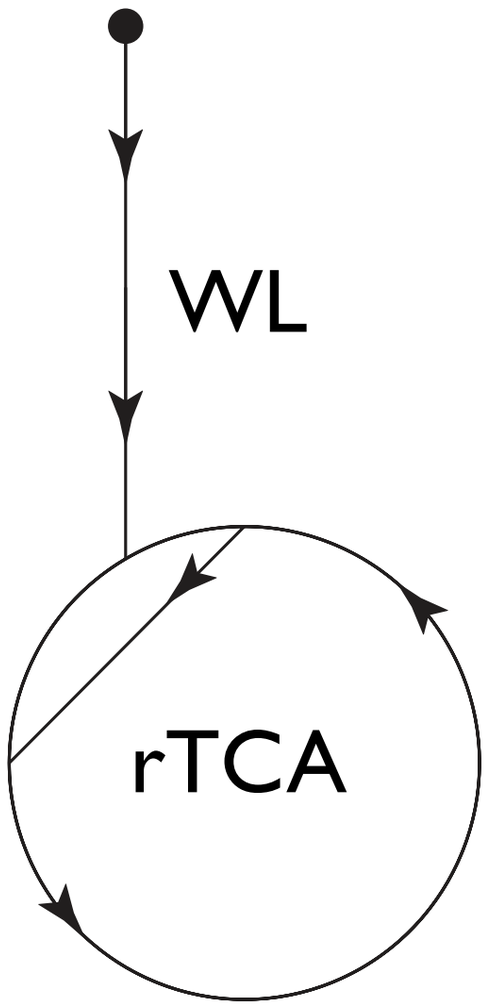
Folate

$Ni\text{-}Fe_4S_5$

Co^+

$Ni\text{-}Ni\text{-}Fe_4S_4$

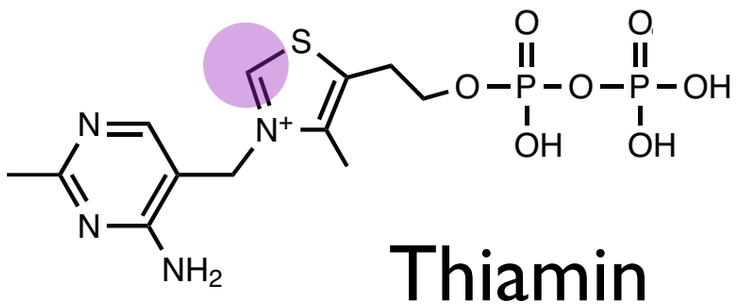
WL



HS-CoA

Fe_4S_4

$Ferredoxin\text{-}Fe_4S_4$



Thiamin

Did metallo-enzymes, N-heterocycles, and alkyl-thiols
"lift metabolism off the rocks"?

Conclusions

- Integrating phylogenetic and metabolic reconstruction leads to a "metabolic tree of life"

- Phylometabolic tree of carbon-fixation connects all forms and identifies environmental driving forces for divergences

- Findings suggest that geochemical perturbations of carbon-fixation pathways resulted in many of the deepest branches in the tree

- Character of root suggests that metabolism can be explained as feedback stabilization of autocatalysis initially facilitated by minerals

Acknowledgements and references

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- Harold Morowitz
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- You!

References:

Braakman & Smith (2012), "The emergence and early evolution of biological carbon-fixation", PLoS Comp Bio 8, e1002455

Braakman & Smith (2013), "The compositional and evolutionary logic of metabolism", Physical Biology 10, 011001