Neutrality and complex adaptation

Maarten van Elst, Olof Huiberts, and Joyce van Santen

Pál, C., & Papp, B. (2017). **Evolution of complex adaptations in molecular systems.** *Nature ecology & evolution*.

Vosseberg, J., & Snel, B. (2017). **Domestication of self-splicing introns during eukaryogenesis: the rise of the complex spliceosomal machinery.** *Biology direct*.

Hosseini, S. R., & Wagner, A. (2016). **The potential for non-adaptive origins of evolutionary innovations in central carbon metabolism.** *BMC systems biology*.

Complex adaptations

“Complex adaptations are phenotypic traits requiring multiple, specific mutations to yield a functional advantage.” (Pál & Papp)

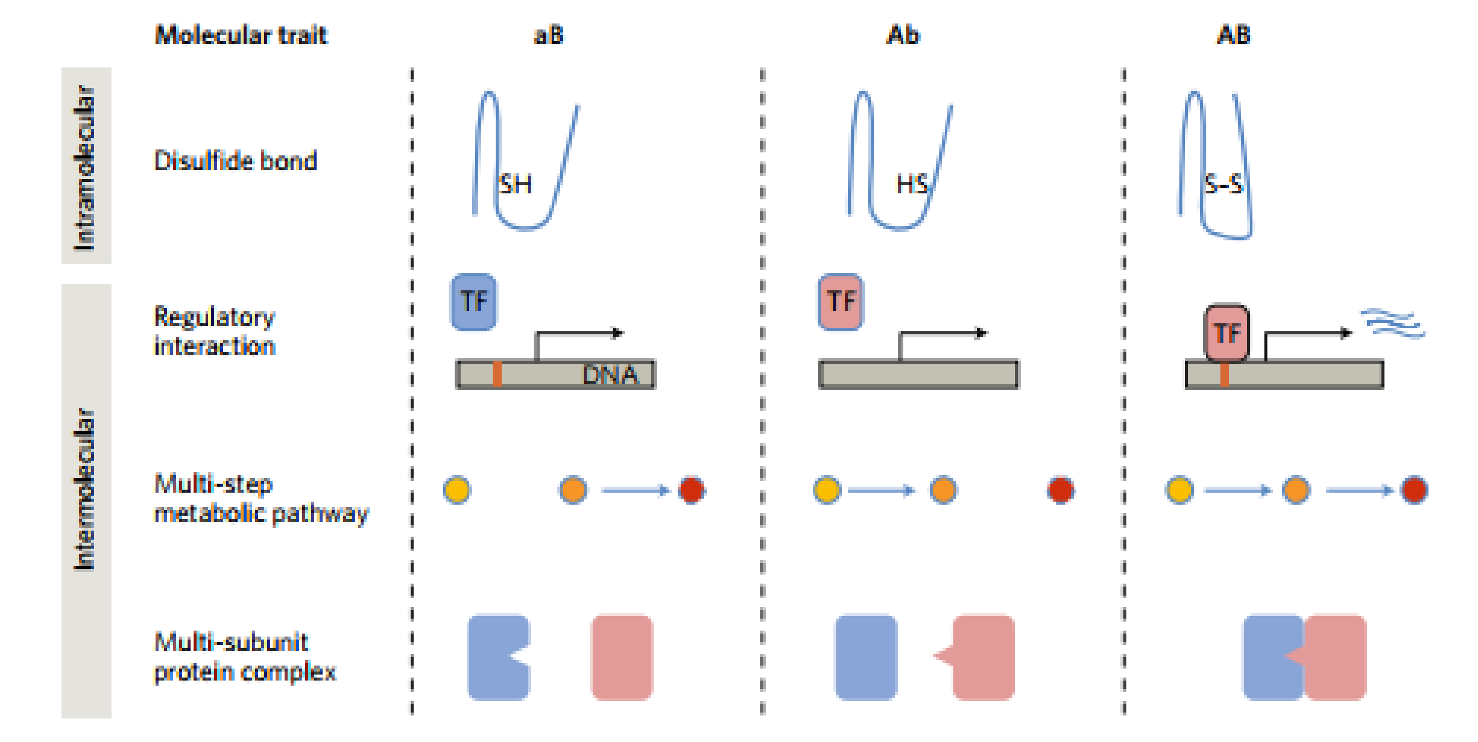
These specific mutations could be seen as neutral; induced by drift and without an individual fitness effect.

To Illustrate:

Genotype/Fitness	a	A (mutated)
b	*Ab* / ***normal***	*Ab* / ***lethal***
B (mutated)	*aB* / ***normal***	*AB* / ***high***

Complex adaptations in molecular systems

- Evolutionary models tend to converge toward local optimum.
- ‘Better’ adaptations in actual Biological (molecular) examples.
- High specificity and ‘chicken or egg’ situations.
- Classification into intra-, inter-, and macro-molecular scales.
- At all scales:
  - *How does an excretion system turn into a flagellum?*
  - Big steps might be necessary (such as HGT).



Molecular trait
aB
Ab
AB
Intramolecular
Intermolecular
Disulfide bond
SH
HS
S-S
Regulatory interaction
TF
DNA
Multi-step metabolic pathway
Multi-subunit protein complex

The unknown antecedent

- **Non-adaptivity**
  - Susceptible to drift, codependency?
  - Laboratory proof only works with high mutation rates
- **Pre-adaptivity (exaptation)**
  - Other functions as a source
- **Dynamic environments**
  - Pre-adaptation but in a specific environment
  - Epistasis
  - Environments simply are dynamic, in itself a mechanism of selection.

Two models proposing the rise of complexity

Domestication of self-splicing introns during eukaryogenesis: the rise of the complex spliceosomal machinery

Julian Vosseberg and Berend Snel

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Neutrality vs adaptivity in the spliceosome and eukaryogenesis

- Complex molecular machine
- Origin is not clear
- Two types of spliceosomes and their introns
- Different outcomes

Adaptive model vs neutral model

- Scenarios for the evolution of the spliceosome
- Adaptive → most prominent and widely accepted
- Efficacy in spliceosomal machines?
- Neutral → drunkard’s walk
- The concept presuppresion

On their own the models are not very concluding and just describing the patterns

Comparing and integrating both models

- Lack of clear benefits
- Compensation for maladaptive features
- No maladaptive features in neutral model
- Integration; Biphasic pattern of evolution

Complexity in metabolism

Hosseini and Wagner *BMC Systems Biology* (2016) 10:97
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BMC Systems Biology

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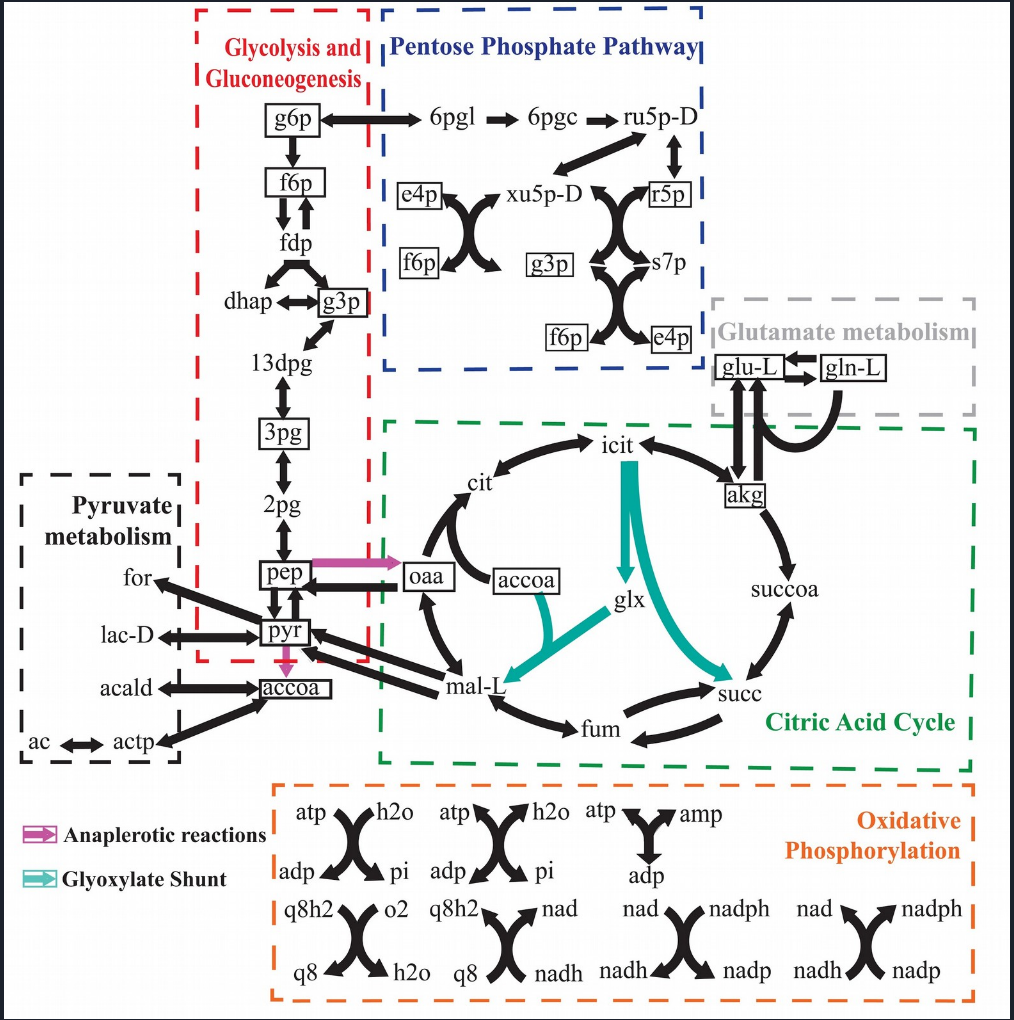
The potential for non-adaptive origins of evolutionary innovations in central carbon metabolism

Sayed-Rzgar Hosseini[1,2] and Andreas Wagner[1,2,3*]

What’s the potential of a biological system for exaptation?

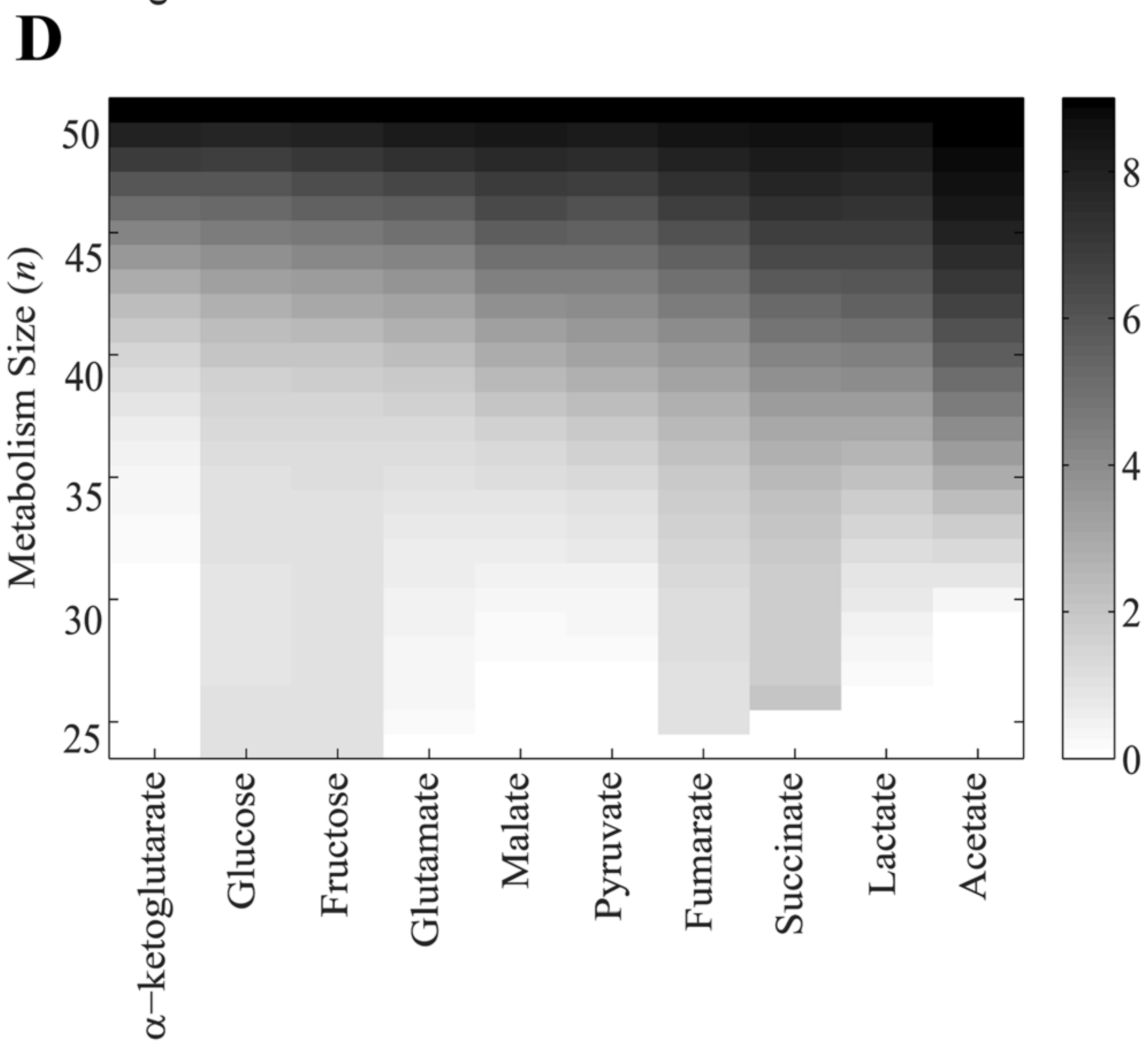
- Exaptation: the process by which features acquire functions for which they were not originally adapted or selected
- Analyzing **central carbon metabolism**
- They used 10^{15} metabolisms and the metabolisms consist of chemical reactions.
- ‘’Each genotype specifies a chemical reaction network that we refer to as a central carbon metabolism.”



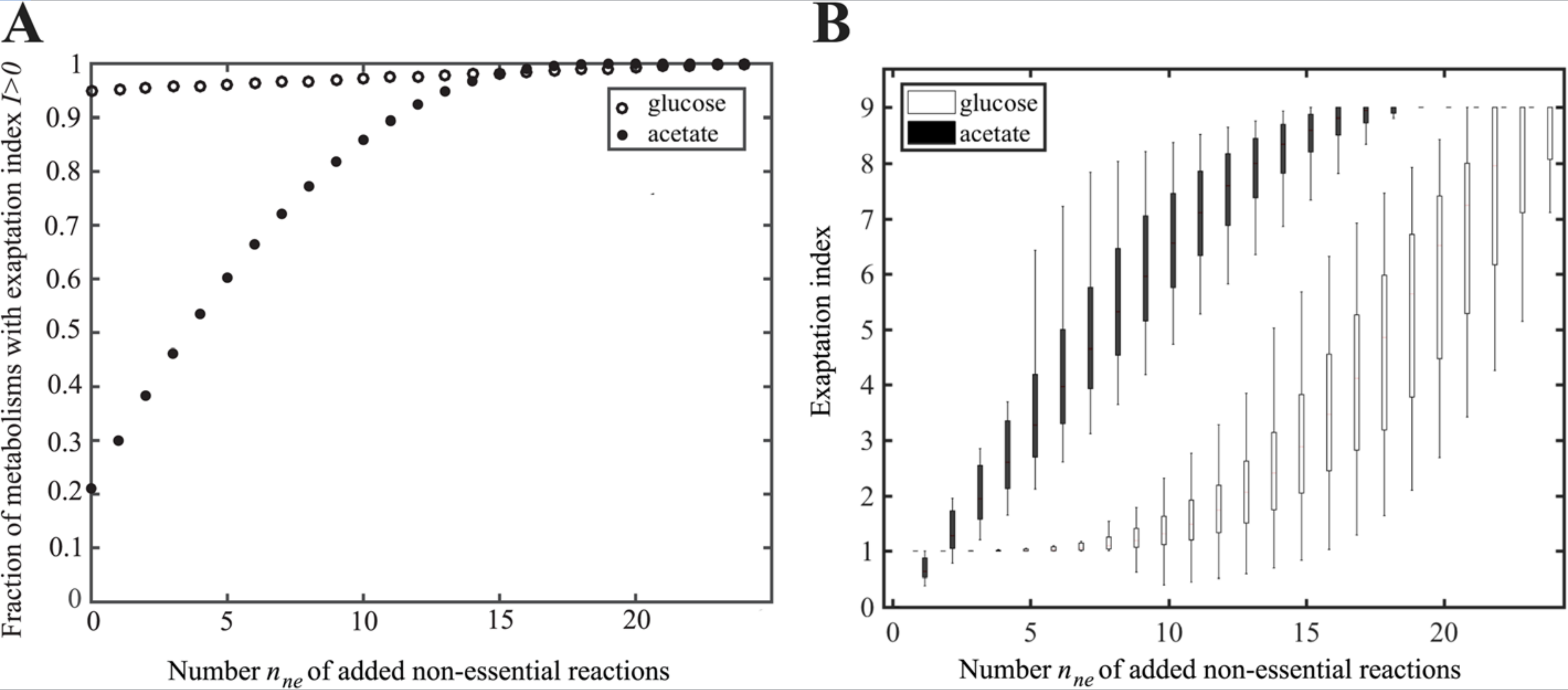
Glycolysis and Gluconeogenesis
Pentose Phosphate Pathway
g6p
6pgl
6pgc
ru5p-D
f6p
xu5p-D
e4p
r5p
fdp
f6p
g3p
s7p
dhap
g3p
f6p
e4p
13dpg
Glutamate metabolism
glu-L
gln-L
3pg
icit
cit
akg
2pg
Pyruvate metabolism
pep
oaa
accoa
glx
succoa
for
lac-D
pyr
acald
accoa
mal-L
succ
ac
actp
fum
Citric Acid Cycle
Oxidative Phosphorylation
atp
h2o
adp
pi
atp
h2o
adp
pi
atp
amp
adp
q8h2
o2
q8
h2o
q8h2
nad
q8
nadh
nad
nadph
nadh
nadp
nad
nadph
nadh
nadp
Anaplerotic reactions
Glyoxylate Shunt

- A metabolism can live on certain carbon sources. In this research they considered 10 carbon sources.
    - D-glucose
    - Acetate
    - Pyruvate
    - D-lactate
    - D-fructose
    - Alpha-ketoglutarate
    - Fumarate
    - Malate
    - Succinate
    - Glutamate

- **Exaptation index (I)** can be between 0 and 9.
- When a metabolism is viable on a new carbon source, then I>0.
- ''We here use the **genotype-phenotype map** of central carbon metabolism to ask how often metabolisms viable on a given carbon source C can survive on one or more other carbon sources Cnew.''
- If a metabolism consists of n=51 then it is viable ons all 10 carbon sources.
- Add non-essential reactions to minimal metabolism → exaptation index rises.



D
Metabolism Size (n)
50
45
40
35
30
25
α−ketoglutarate
Glucose
Fructose
Glutamate
Malate
Pyruvate
Fumarate
Succinate
Lactate
Acetate
8
6
4
2
0


A
B
Fraction of metabolisms with exaptation index I>0
glucose
acetate
Number n_{ne} of added non-essential reactions
Exaptation index
glucose
acetate
Number n_{ne} of added non-essential reactions

Conclusions

The potential of preadaptations rises with the complexity of a metabolism. That is with its number of reactions (the size of the metabolism) and its efficiency.

Metabolic complexity
Metabolic efficiency → The more efficient a metabolism is, the greater is its potential for exaptation.

Limitations of the study

1. No other chemical metabolism
2. No regulation of an enzyme
3. Not all parts of carbon metabolism are considered
4. Catalyzation of a reaction
5. Only 10 carbon sources

The link between neutrality and complexity

Neutrality, pre-adaptivity, and dynamic environments.

Complexity occurs at most biological levels, and evolves ‘similarly’ at these levels.

Molecular mechanisms of complex evolution:

- Permissive mutations for protein stability (e.g. chaperoning activity)
- Many interactions (albeit weak)
- Phenotypic heterogeneity (one gene, two proteins)

Bottom Line

There seems to be more to complex adaptations than gradual evolution. Neutrality plays a role but it is very likely that other factors as discussed also have a big impact on the evolution of complex biological systems.

Discussion

"Several components of the bacterial flagellum share homologous proteins with the type III secretion system, indicating that one evolved from the other" (Pál & Papp, 2017)