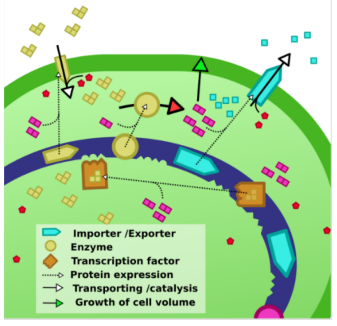

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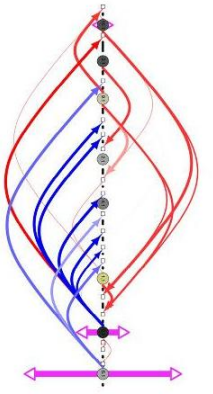
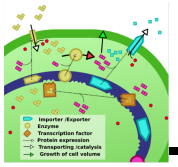


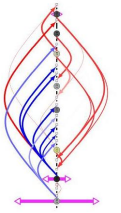
Evolution of complexity
individuals, communities and endosymbiosis

Paulien Hogeweg
Theoretical Biology and Bioinformatics Group, Utrecht University
with thanks to
Jeroen Meijer, Sam von den Dunk, Bram van Dijk
Ben Hesper

,



bottom-up approach to general insights on evolution of biological complexity



"Models should be as simple as possible, but not more so" (Einstein)

empty set in biology?

"What I cannot create, I do not understand" (Feynman)

$- - - >$

Study evolution by evolving a simple "something"
i.e. a thing with some salient features of biological replicators

No a priory defined fitness (what constitutes fitness is a result)

Multiple mutational "operators": (SNP's, dupdels inversions HGT...)

(somewhat) more complex models $- >$ more degrees of freedom for evolution

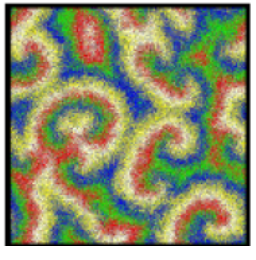
More degrees of freedom appear to lead to more general (and intuitive) results (cf Nobuto Takeuchi)

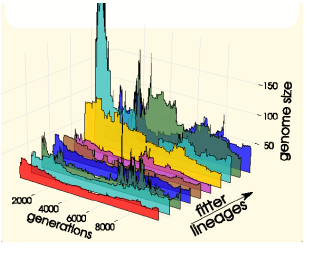
Observe multiple features (complexity) that evolve

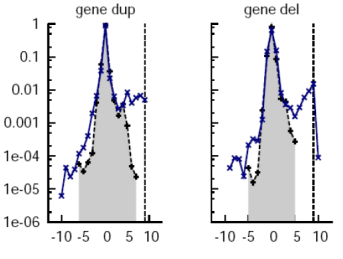
e.g.complexity of mechanisms; complexity of dynamics; genomes phylogeny, ecosystems...

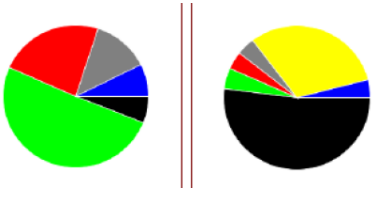
examples of insights emerged from such approach and observed in biological systems

- Multilevel evolution emerges in spatial extended systems, altering **all(most)** evolutionary properties relative to well mixed systems (e.g. hypercycles (Boerlijst & Hogeweg 1991))
- Early (neutral) genome expansion in those lineages which **later** evolve higher fitness (e.g. Cuypers & Hogeweg 2012; Knibbe et al 2007)
- Evolution of evolvability by genome organization, gene regulation, metabolic organization...(e.g. Crombach & Hogeweg 2007,2008)
- interlocking timescales: ecology and evolution; levels van der Laan & Hogeweg 1995)
- Functional role of mutants of quasispecies (e.g. Collizi & Hogeweg 2014)









Today's themes

individual vs ecosystem based complexity
optimization vs speciation
generalist vs specialists

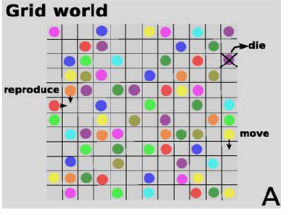
comlexification through endosymbiosis
cell cycle regulation

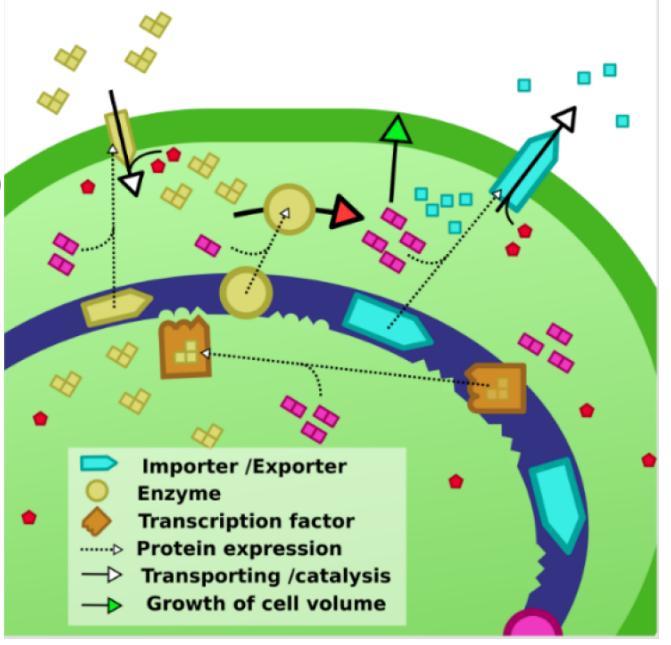
"Virtual Microbes"
a paradigm system for bottom up modeling of multiple modes of adaptation in biological-like systems

Thomas Cuypers and Bram van Dijk

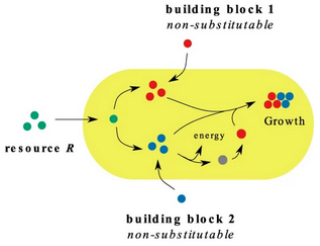
Cell with
Genome with
genes (TFs, pumps, enzymes) with
parameters (Vmax, K, binding)
metabolism
grow and divide
Mutate
(duplication/deletions, HGT, par. changes)

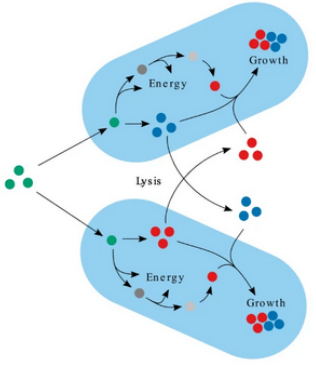
In 'universe'
potential metabolic
reactions
Resource influx
space

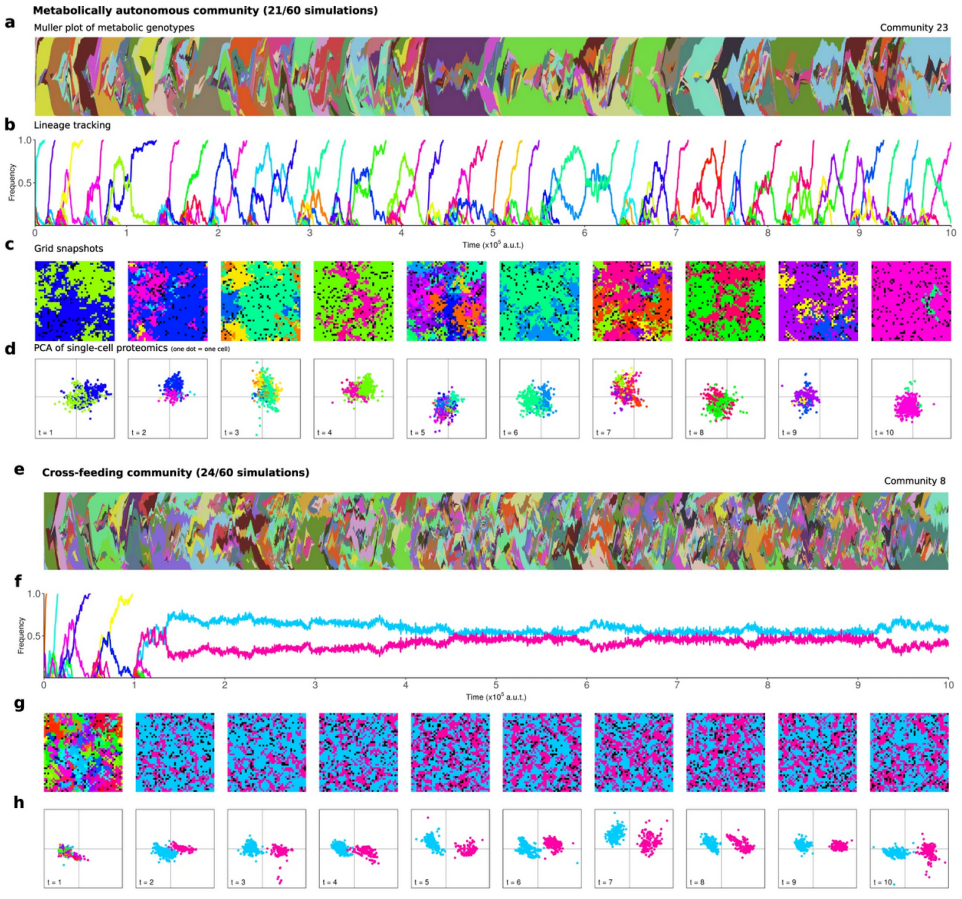




De Novo evolution in a constant environment (1 resource) individual vs ecosystem based complexity

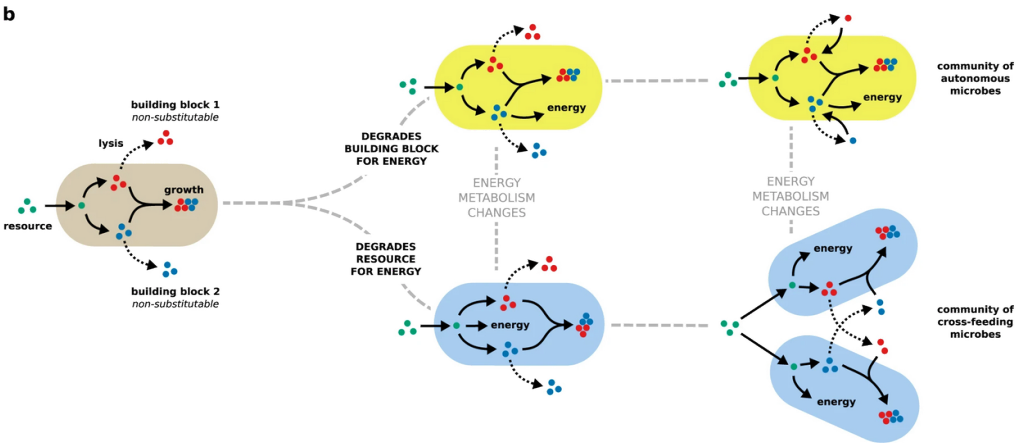


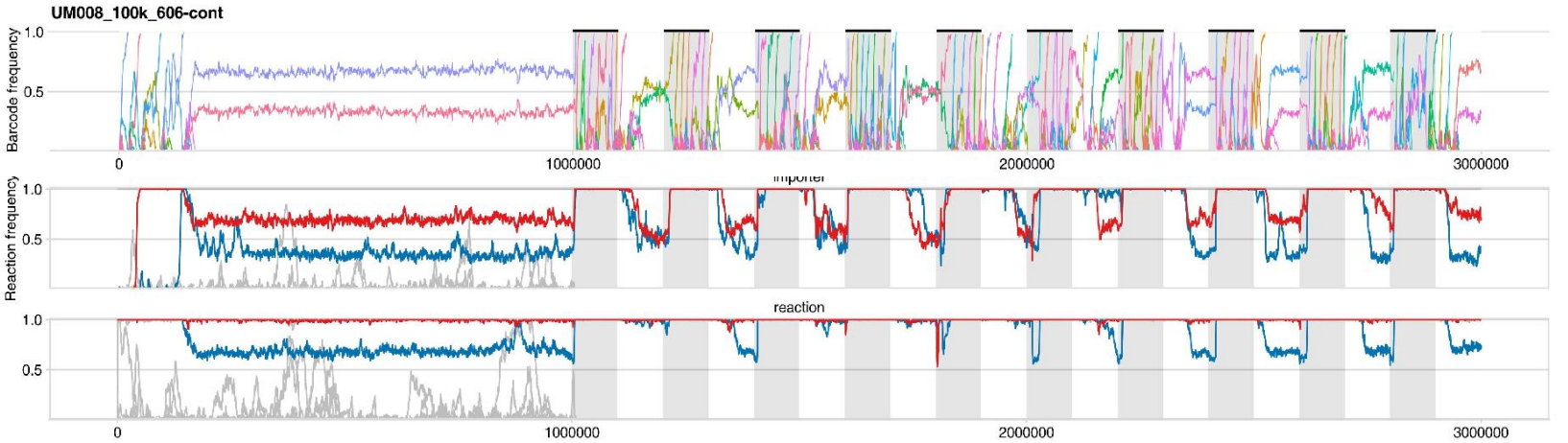




Meijer et al 2020 Nature comm biol

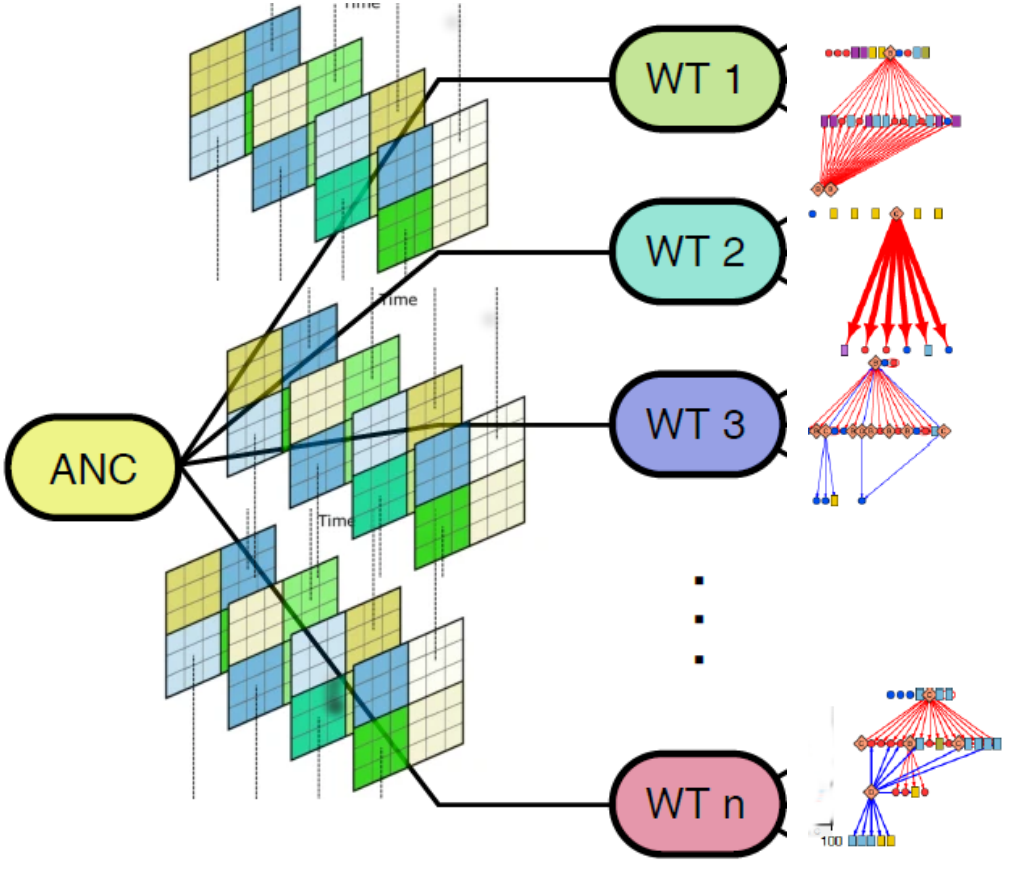
Cross-feeding evolves in 1 of 2 types of metabolism IN SPACE
self-sufficiency regained when mixed (switching)

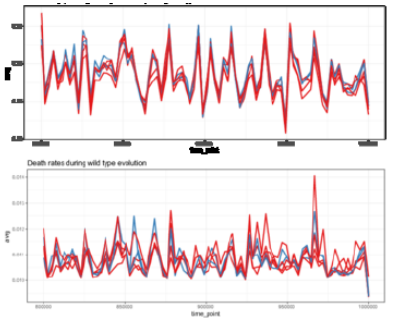




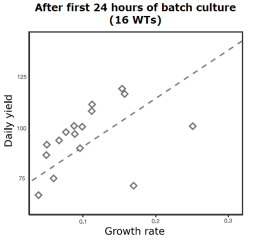
De Novo **Evolution in variable environments**

"WHAT" has evolved?, How to observe?





Similar "fitness"



Dissimilar "fitness"

Harsh, fluctuating environment **Identical for all replicates**

Experimental evolution: starting with pre-evolved "wildtypes"

Well known example of experimental evolution:

Long term evolutionary experiment (LTEE) (Lensky 1991)
One strain of E.Coli is evolving in lab-conditions since 1988
(>70000 generations) in 12 replicates
in a serial transfer protocol (diluted in new medium very 24 hours)
still adapting (getting "better")
Continued new ways of observing & new insights

This case study:

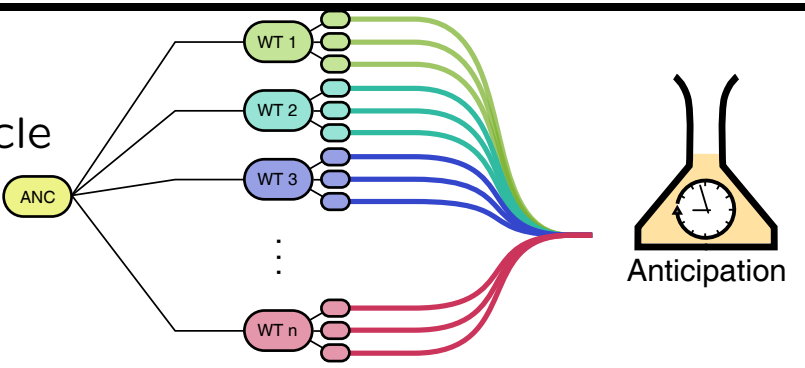
In silico evolution of the above pre-evolved "wildtypes"(WT 1-16)
in similar serial transfer protocol

study "generic" features of such an evolutionary process
To WHAT does the population adapt?
HOW does it adapt?
Multiple observables
Similarities/differences to E. coli?

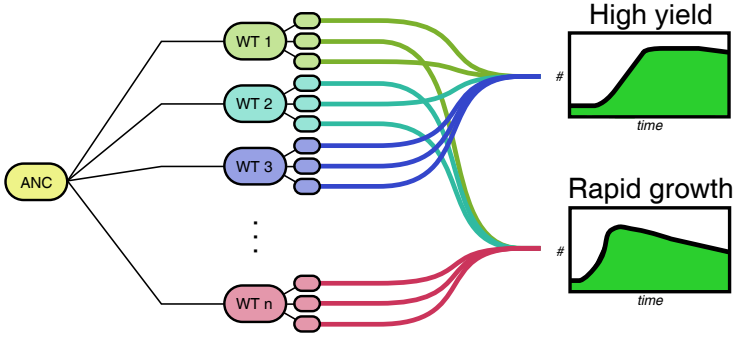
{ van Dijk et al BMC evol bio 2019

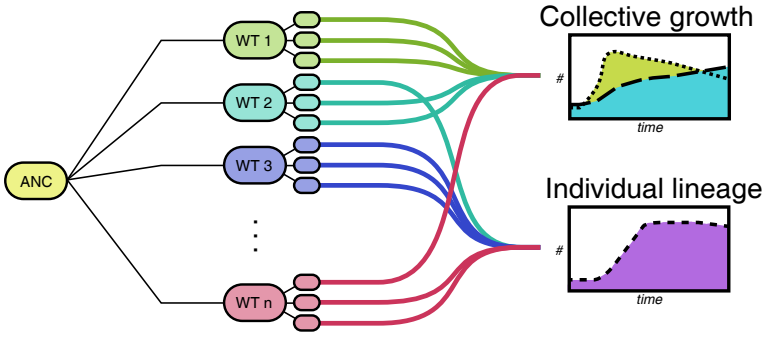
Multiple ways to tune growth to 24hr cycle through regulation or speciation with high growth rate OR high yield

Diversified evolved wildtypes
all evolve anticipation of 24 hr cycle
emerged fitness determinant

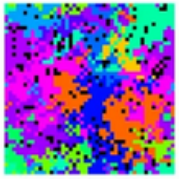


BUT in different ways

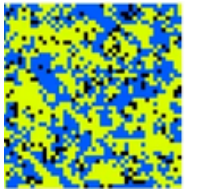




Some WT's adapt in a predictable way , others in very different ways
predictibility is an unpredicable outcome of evolution



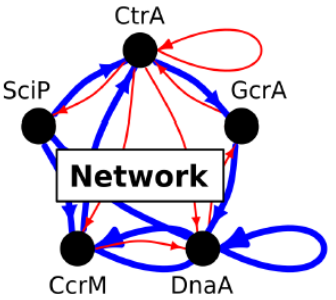
Conclusions/Observations



- What is fitness / what has evolved not obvious
- Autonomous and Collective "problem solving" (metabolism)
  "easy" alternatives
- Non-autonomy not because of lack of genes...
- Spatial embedding, also without spatial patterns important
- Evolutionary attractors can be characterized as a combinatorial set of a limited set of alternatives
- Trade-off's not innate but evolved properties
- GRN very variable (presence and shape)
- Predictability, even in well defined environments depends on prior evolution *Predictability is an unpredictable outcome of (prior) evolution*

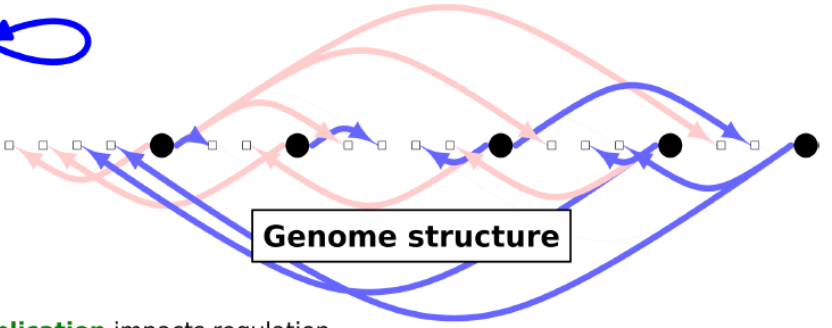
modeling evolution of cell cycle control

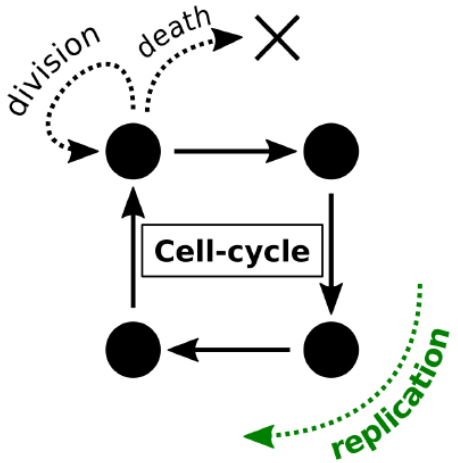
Caulobacter crescentus



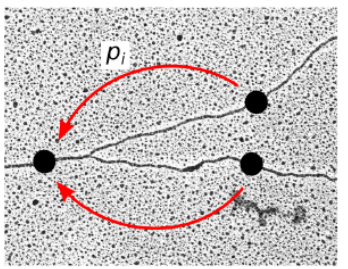
Sanchez-Osorio *et al.* (2017)

▷ Mutations
- small (e.a. bitstrings)
- large (e.a. organization)

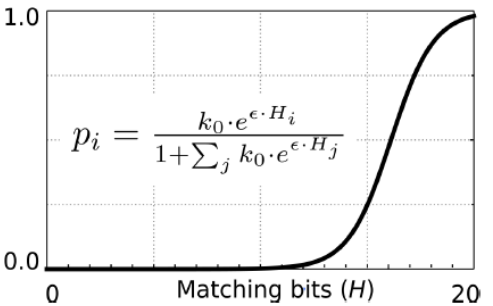




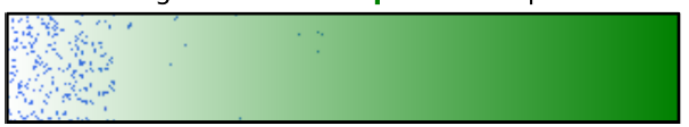
Replication impacts regulation



▷ Stochastic binding

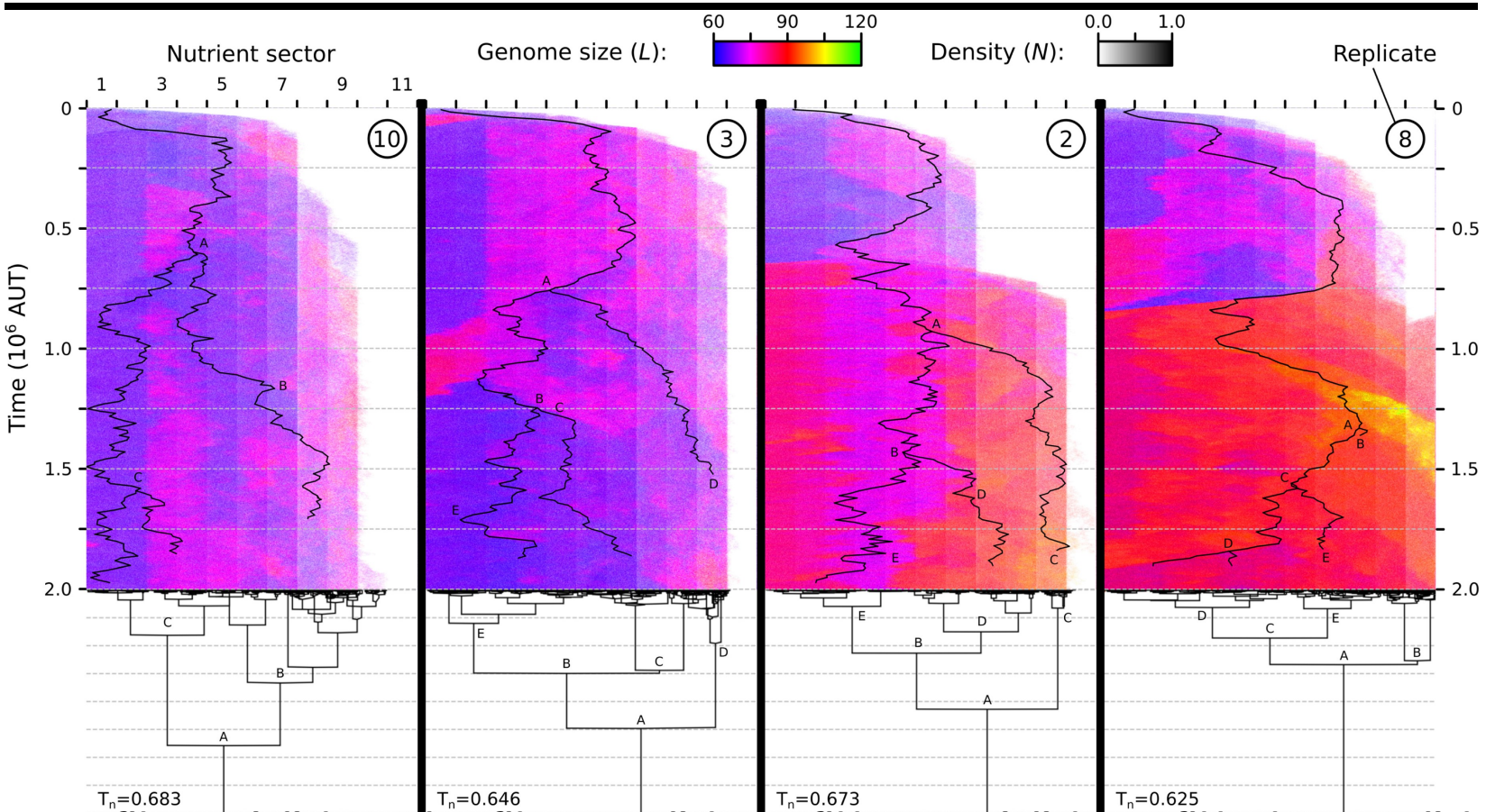


Nutrient gradient sets **replication** speed



von den Dunk, Snel & Hogeweg 2022 GBE

Evolution of cell cycle control: adaptive genome expansion in generalists and specialists



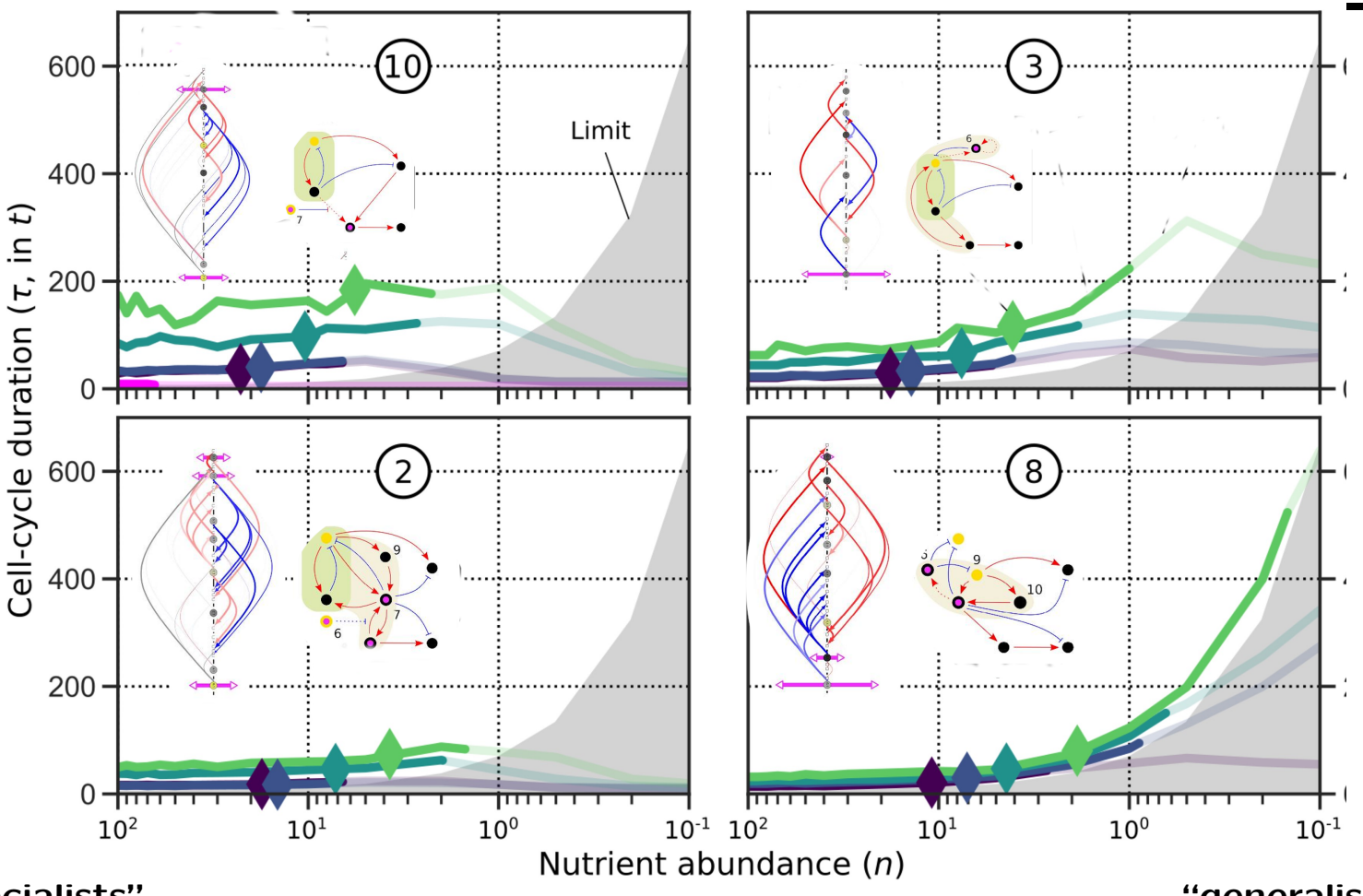
unfit specialist
pop: 42%
genome 70

lessfit generalist
pop 57%
genome 68

fitter specialist
pop 58%
genome 82

fittest generalist
pop 78%
genome 81

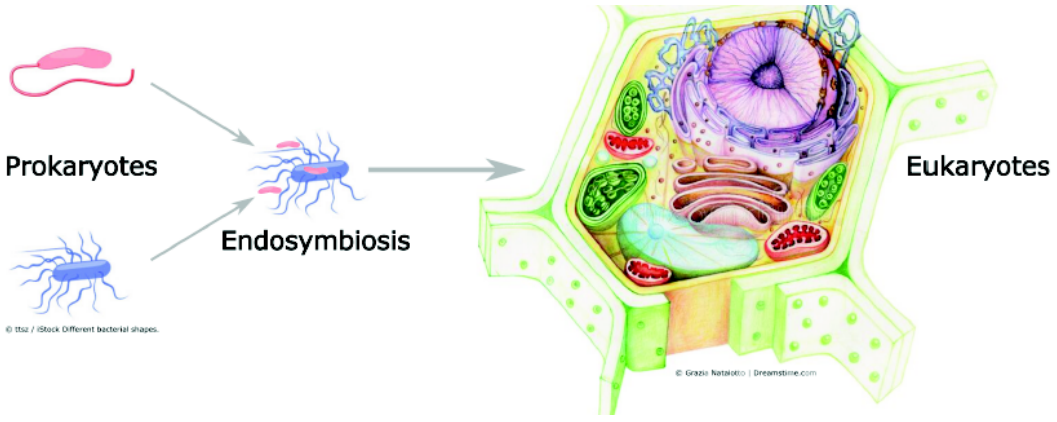
Gene regulatory network AND genome structure together achieve cell cycle control under different nutrient condiditions



“specialists” **“generalists”**

evolution of cell cycle checkpoint

Eukaryogenesis: prototype of evolution of complexity



Endosymbioses of mitochondria pivotal event
early? late? Intermediate

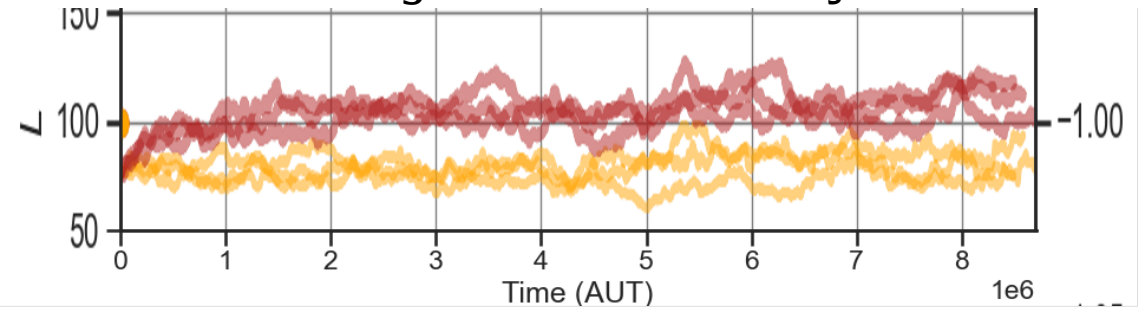
Here we explore:
evolution after obligate endosymbiosis
of cc regulating "prokaryotes"

Trigger for increasing complexity???

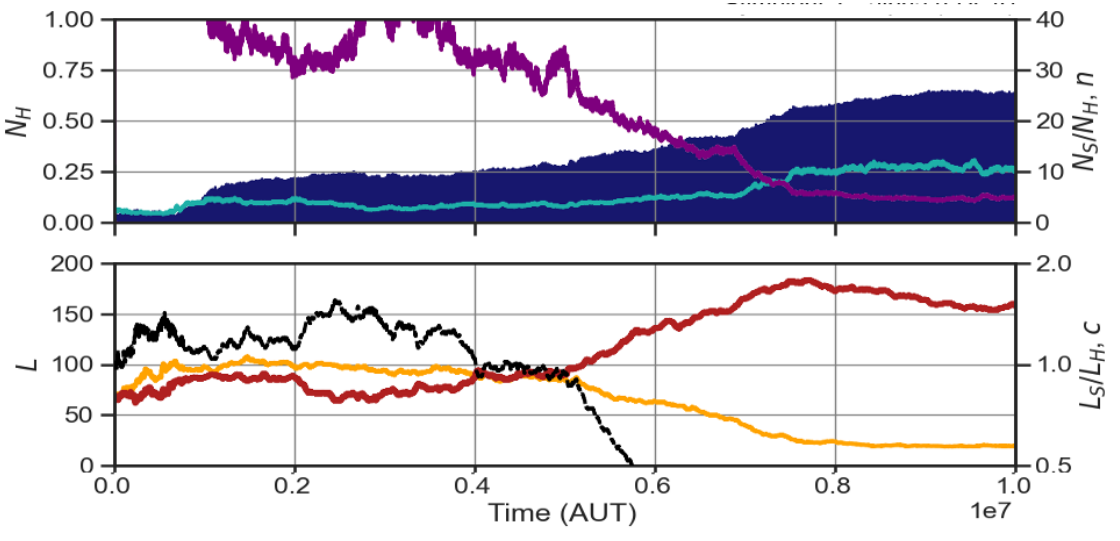
von den Dunk, Snel, Hogeweg in prep

upon endosymbiosis host genome expansion

identical fit generalist host and symbiont



identical ancestral host and symbiont

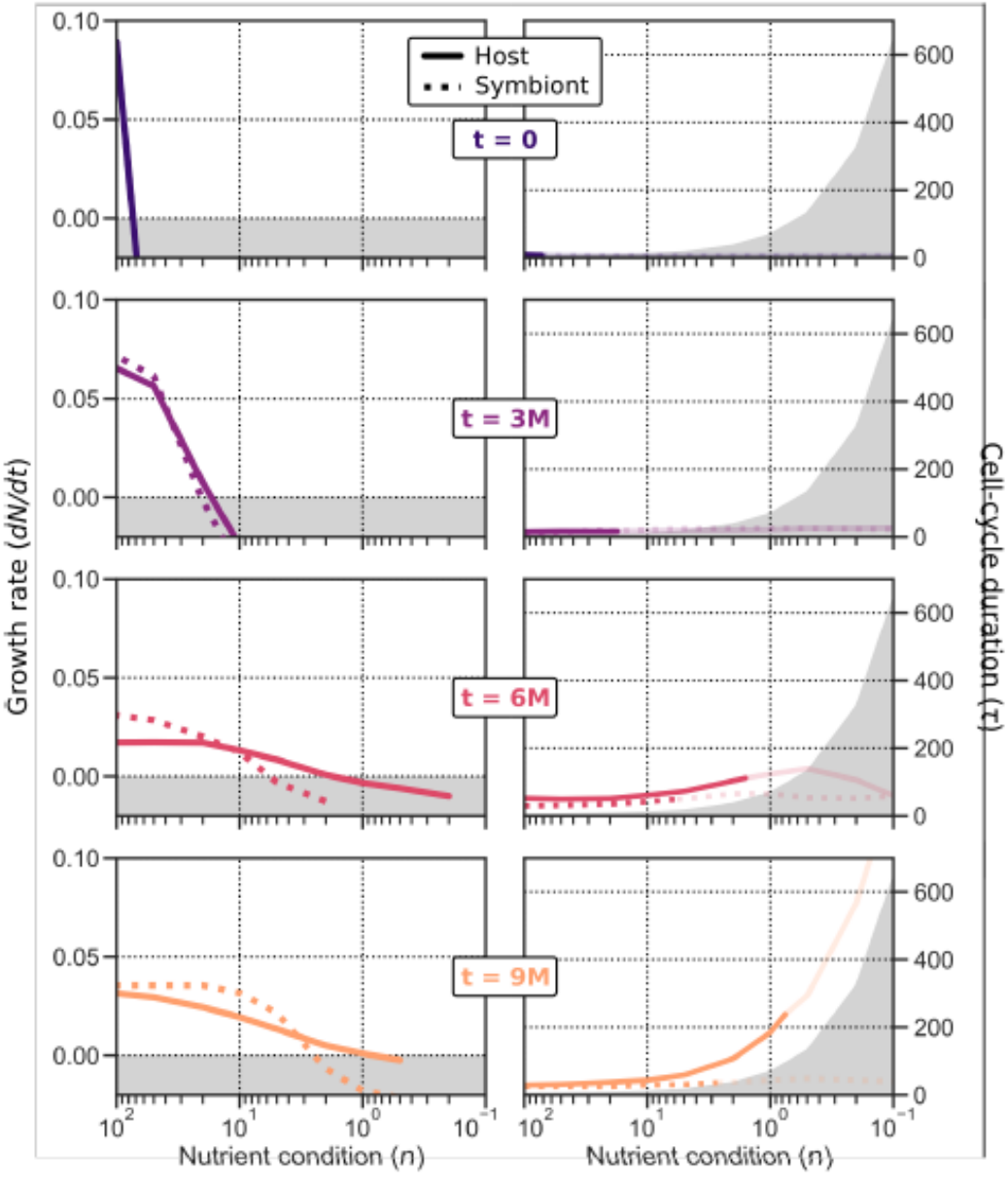


TUNING OF
HOST AND
ENDOSYMBIONT
CC

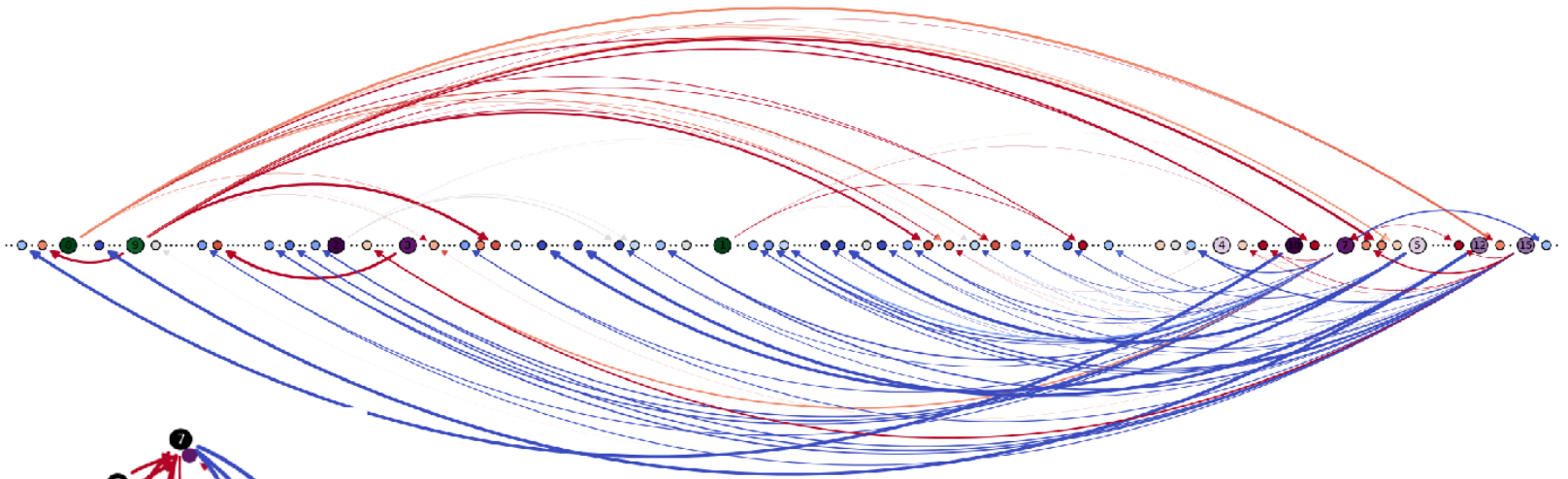
Initially identical cc
often death after division
because no endosymbiont
in daughter cell

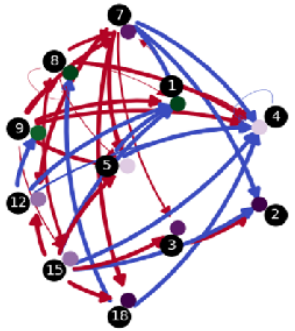
differentiation growthrate
host slower and “flatter”

Equillibrium:
nutrient homeostasis by
regulation of # mitochond

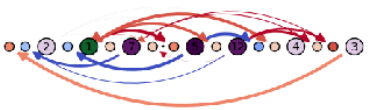


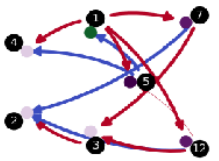
Evolved expanded cc network of “Eukaryotic cell” and reduced, specialist cc network of “mitochondria”





Evolved "Eukaryotic cc regulation"





Evolved "mitochondrial cc regulation"

conclusions

- Generalist and specialist adaptive strategies contingent alternatives
- CC regulation evolves by genome structuring in consort with GRN
- Adaptive limited genome expansion in prokaryotes under strong selection for small genomes
- Upon endosymbiosis relaxed selection for fast replication
  (tuning of replication rates takes precedent)
  $- - - >$ genome expansion facilitated
  (neutral and as mechanism for slowing down(?))
- From earlier work:
  large genomes facilitate adaptation later on!