virtual microbial eco-evolutionary dynamics

evolution predictable???

Course Computational Biology 2025; Paulien Hogeweg;

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TODAY

focus on metabolism

(1) de novo evolution in artifical metabolic uviverse
(possible reactions cf KEGG but much smaller)
what will happen when the tape is playes N times?

(a) from identical initial conditions in a constant environment
(b) from identical initial conditions in a strongly variable environment and brought in lab conditions (LTEE)

(2) What should we expect to evolve after WGD of YEAST
using its metabolic network as starting condition
what will happen when the tape is playes N times?

Compare to what happed in the unique case of YEAST on earth

(3) "causal drift": what changes in metabolic rates cause diabetis?

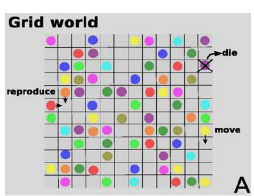
“Virtual Microbes”
a paradigm system for bottom up modeling of multiple modes of adaptation in biological-like complex complex adaptive systems

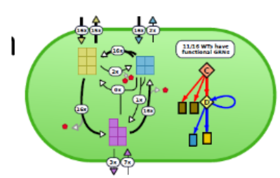
Thomas Cuypers and Bram van Dijk

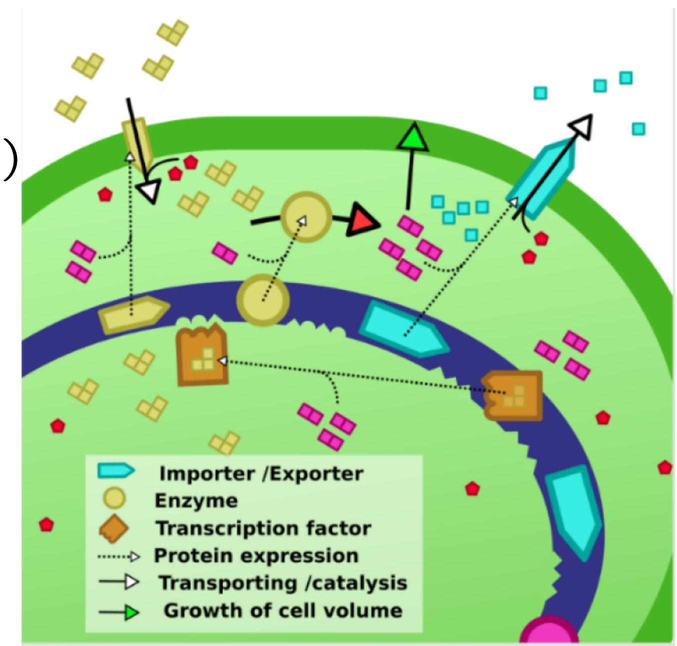
NO PREDEFINED FITNESS

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







Metabolic universe

{Meijer , v. Dijk & H. 2020

Table 1 Metabolic universe: Using VirtualMicrobes, we generated an artificial biochemistry comprised of 9 metabolites, 8 importers, 8 exporters and 43 conversion reactions, with two non-substitutable building blocks and a single energy molecule.

From: Contingent evolution of alternative metabolic network topologies determines whether cross-feeding evolves

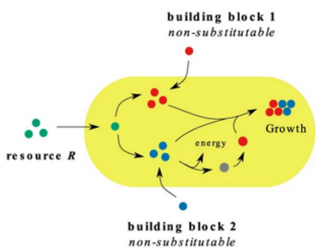
Metabolite	Class	Diffusion rate	Degradation rate	Toxicity	Mass	Influx rate
R	Resource	0.011	0.0003	0.077	9	0.002
B1	Building block	0.011	0.0100	0.058	8	0
B2	Building block	0.012	0.0100	0.103	8	0
E	Energy carrier	0.050	0.1000	0.065	1	0
M1	–	0.014	0.0006	0.105	6	0
M2	–	0.019	0.0003	0.080	4	0
M3	–	0.013	0.0006	0.079	7	0
M4	–	0.014	0.0014	0.158	6	0
M5	–	0.016	0.0008	0.047	5	0

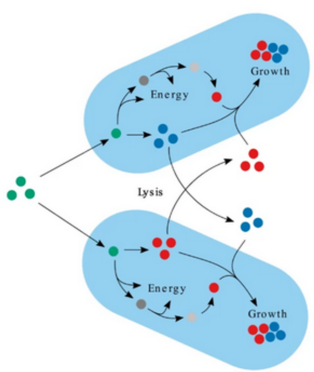
Reactions				
R → B2 + E	B1 → M4 + 2 E	M1 → M2 + 2 E	M2 + M5 → B1	M3 + M5 → R
R → B1 + E	B1 → M5 + 3 E	M2 + M3 → B1	M2 + M5 → M1	M3 → M5 + 2 E
R → M1 + 3 E	B2 → M1 + 2 E	M2 + M3 → B2	2 M1 → R	M3 → M4 + E
R → M2 + 5 E	B2 → M2 + 4 E	M2 + M5 → M4	2 M2 → M1	M4 → M2 + 2 E
R → M4 + 3 E	B2 → M3 + E	M2 + M4 → M3	2 M2 → B1	M4 + M5 → B2
R → M5 + 4 E	B2 → M4 + 2 E	M2 + M5 → M3	2 M2 → B2	M4 + M5 → R
R → M3 + 2 E	B2 → M5 + 3 E	M2 + M4 → B2	2 M2 → M4	M4 + M5 → B1
B1 → M1 + 2 E	M1 + M4 → R	M2 + M5 → B2	2 M2 → M5	M5 → M2 + E
B1 → M2 + 4 E	M1 + M2 → M3	M2 + M5 → R		
Importers: one for each non-energy metabolite (8 total)				
Exporters: one for each non-energy metabolite (8 total)				

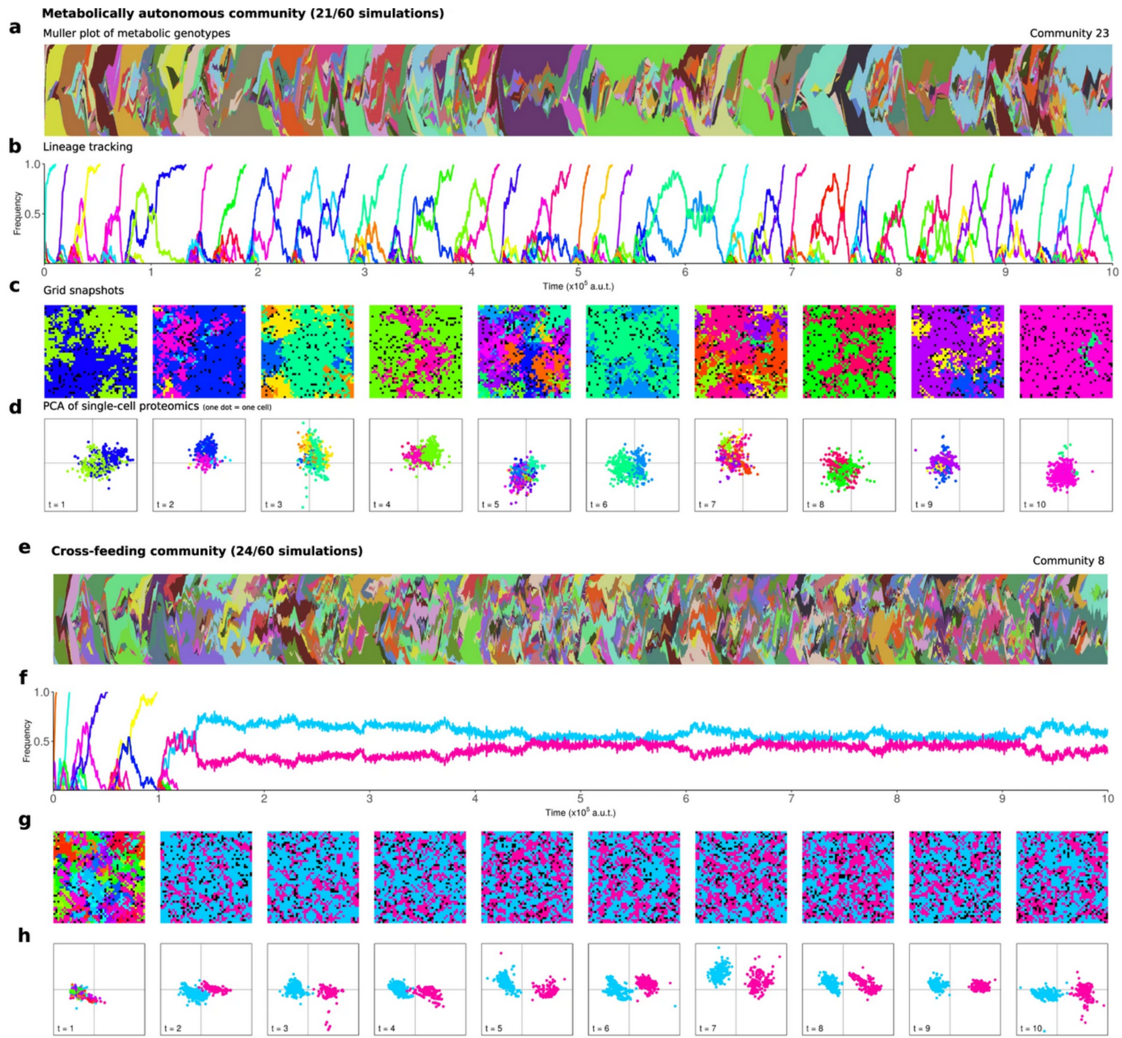
De Novo evolution in a constant environment (1 resource)

Meijer , v. Dijk & H

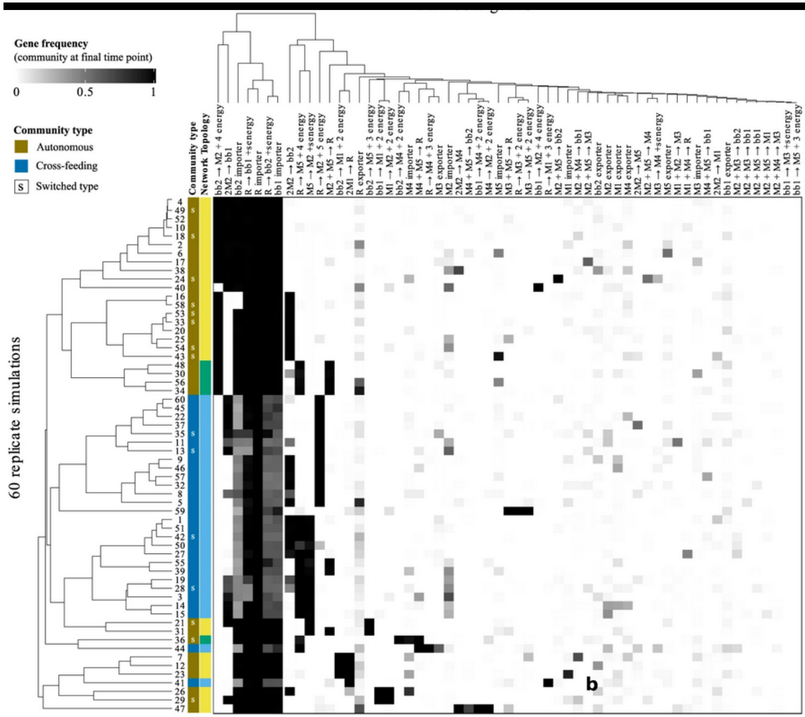
2020

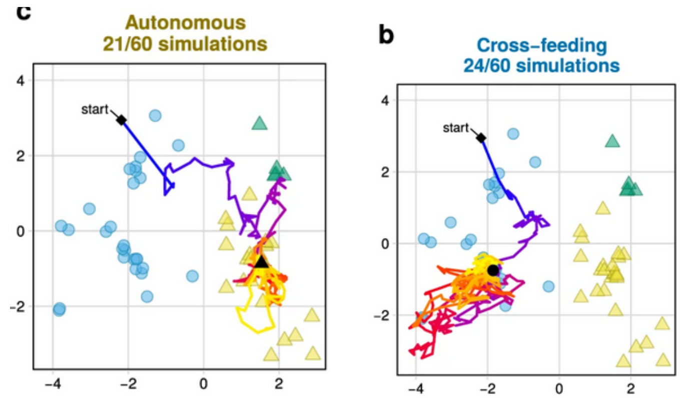






2 types of Evolved metabolism generate predictable ecosystems





"core, shell and cloud"

U-like-shape of pangenome

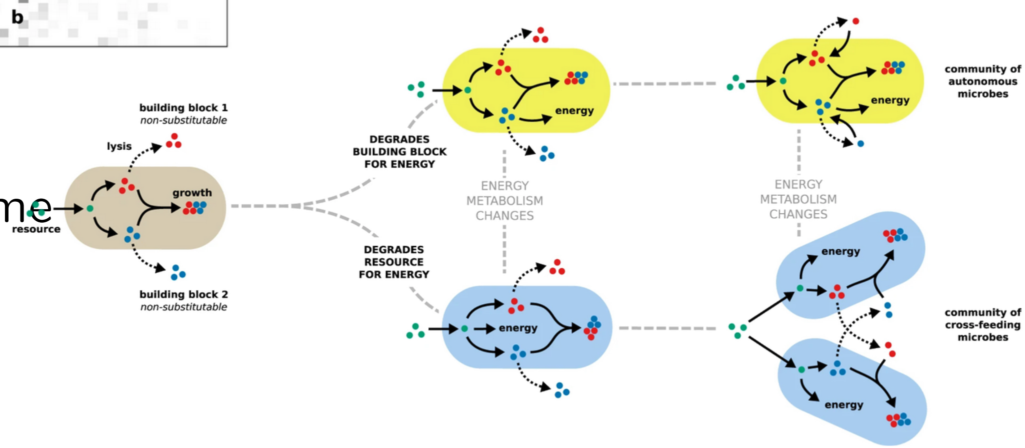
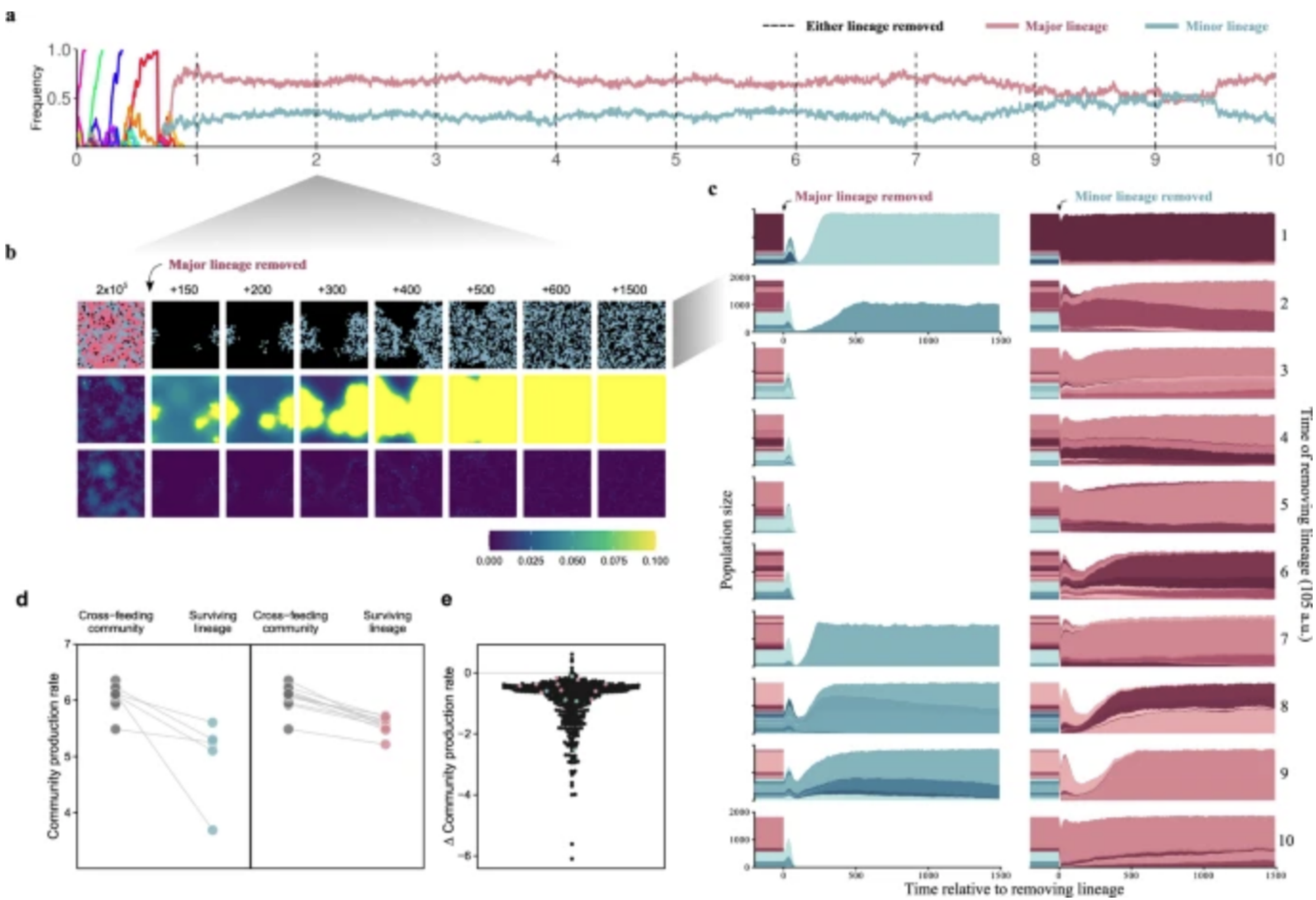
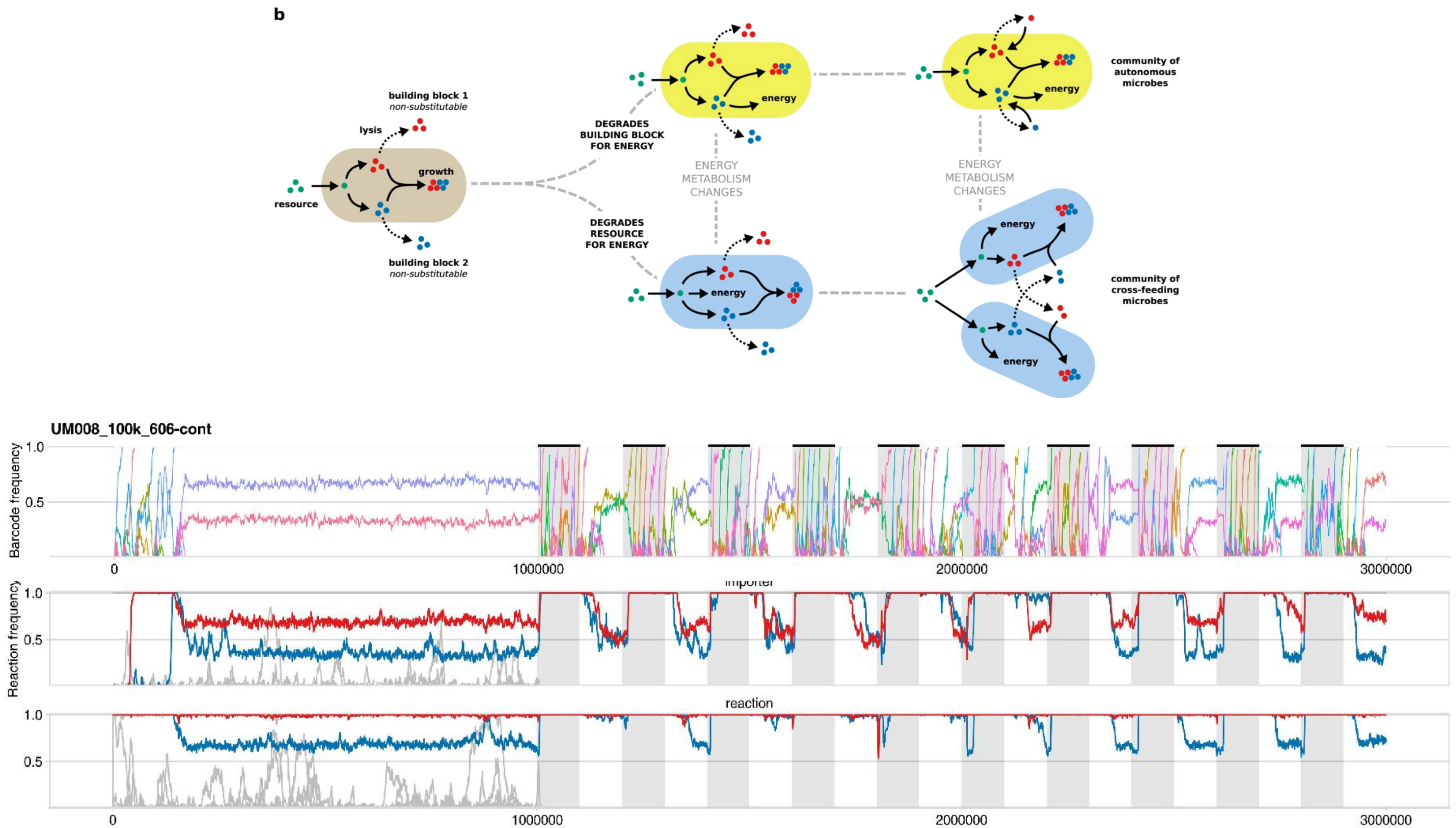


Fig. 3: Metabolic dependencies in cross-feeding communities.



Cross-feeding evolves in 1 of 2 types of metabolism IN SPACE

self-sufficiency regained when mixed (switching)

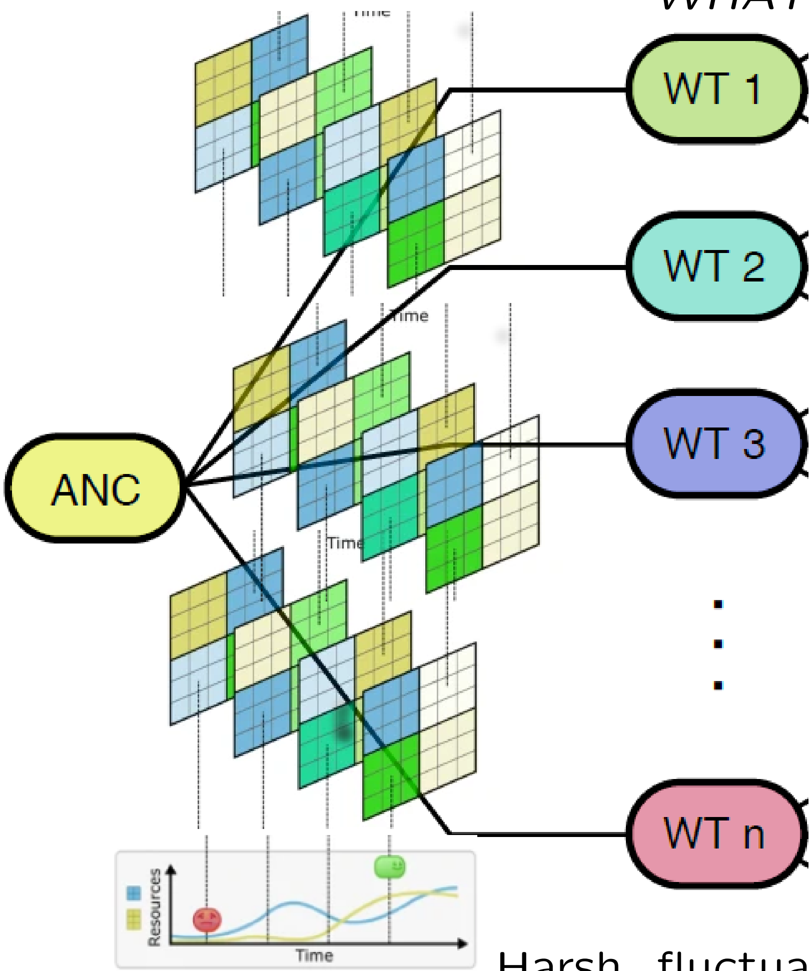


conclusion

- Cossfeeding can evolve in space without explicit costs/tradeoffs or envrionmental variability
- Selfsufficiency can also evolve in exacly the same "universe"
- Crossfeeding and selfsufficiency contingent outcomes from their LUCA
- Crossfeeding and selfsufficiency are predictable outcomes from evolved metabolism
- selfsufficient mutants exist in crosssfeeding ecosystem but do not take over
- switching spatial system (biofilm) to wellmixed lead to switching between crossfeeding and selfsufficincy

De Novo Evolution in variable environment

"WHAT" has evolved?, How to observe?



LCA of evolved population

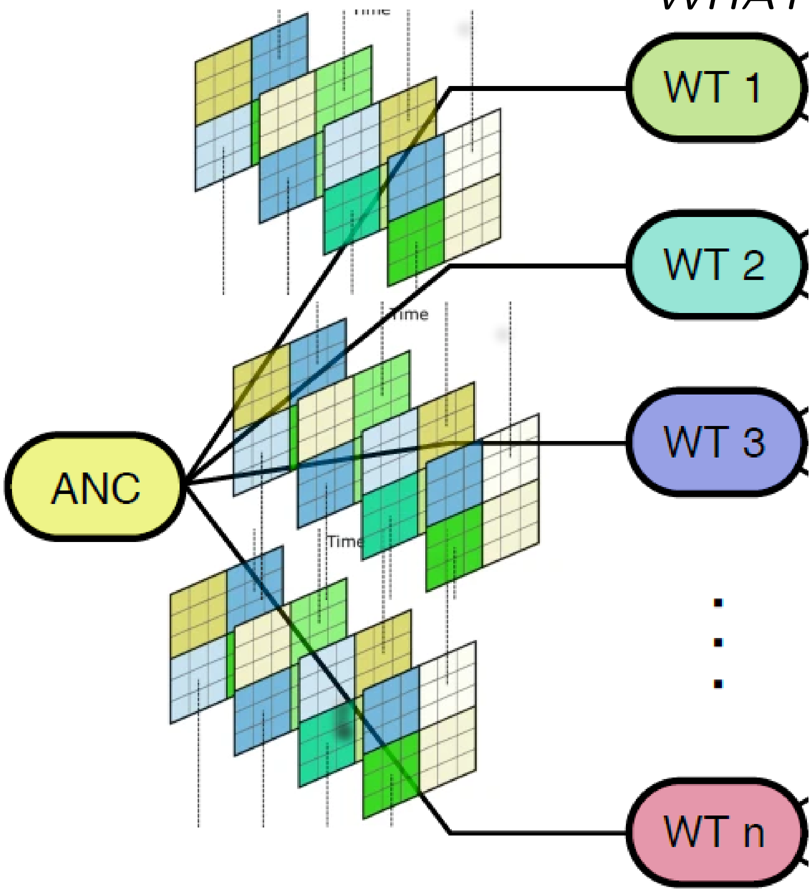
Harsh, fluctuating environment (2 resources)

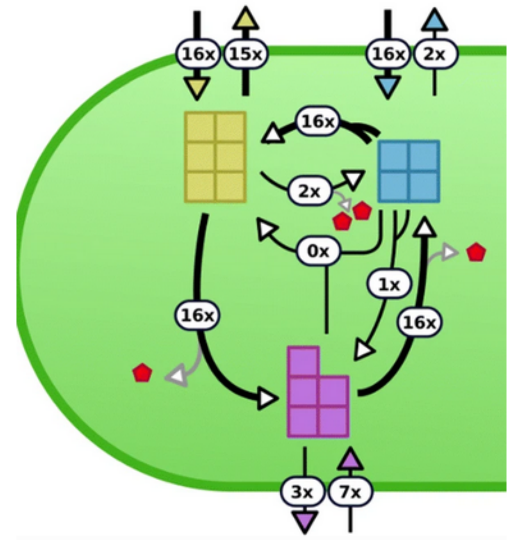
Identical for all replicates

van Dijk et al 2019

De Novo **Evolution in variable environments**

"WHAT" has evolved?, How to observe?





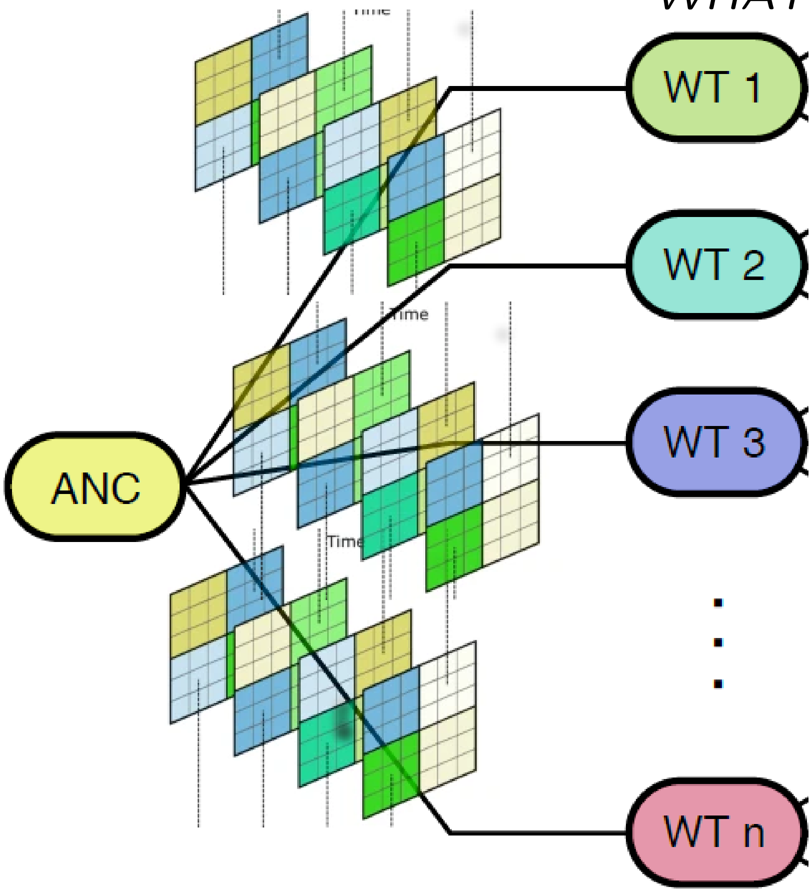
Common metabolic cycle

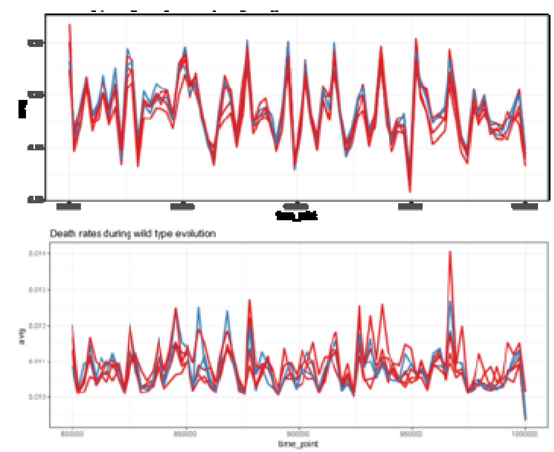
LCA of evolved population

Harsh, fluctuating environment
Identical for all replicates

De Novo **Evolution in variable environments**

"WHAT" has evolved?, How to observe?





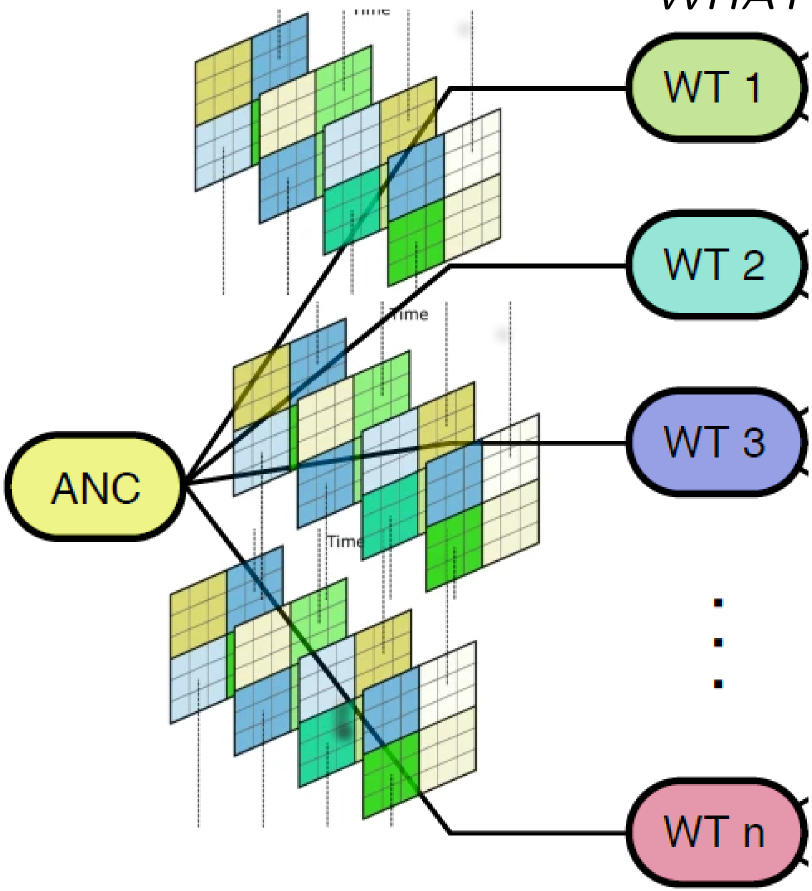
Similar "fitness"

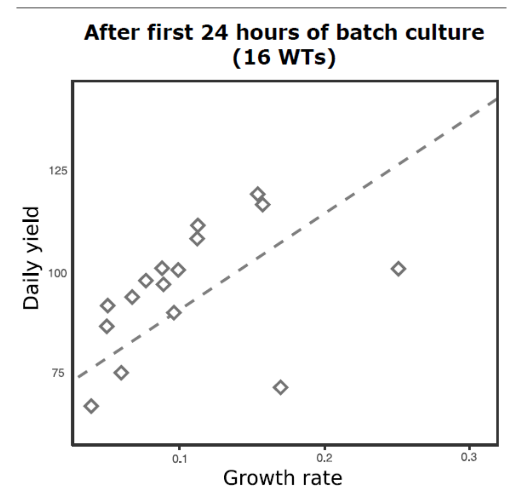
LCA of evolved population

Harsh, fluctuating environment
Identical for all replicates

De Novo **Evolution in variable environments**

"WHAT" has evolved?, How to observe?



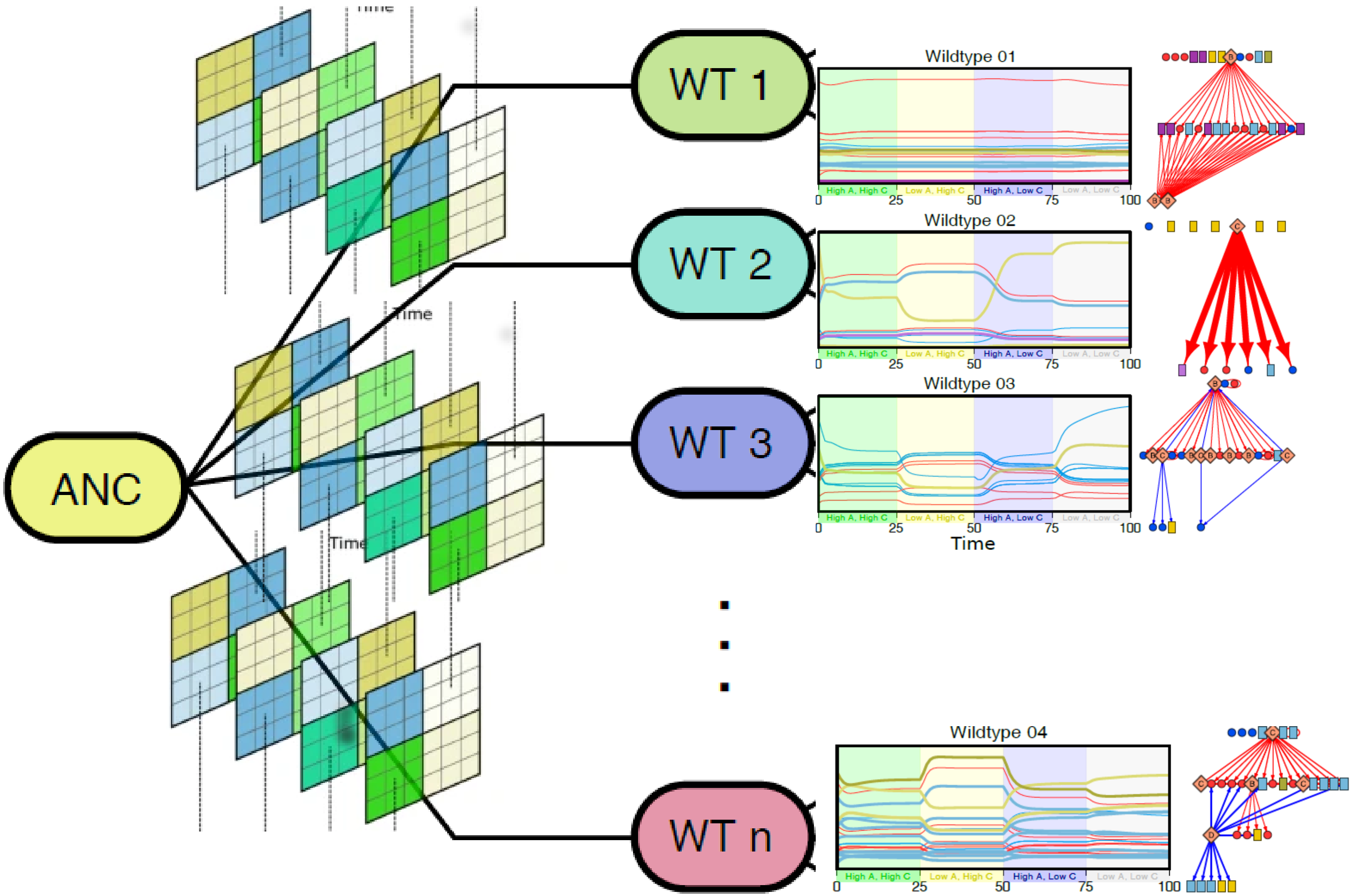


Dissimilar "fitness"

LCA of evolved population

Harsh, fluctuating environment
Identical for all replicates

BUT: very diverse GRN (or none) and metabolic reaction to alternative environments



Experimental evolution: starting with pre-evolved "wildtypes"

Well known example of experimental evolution:

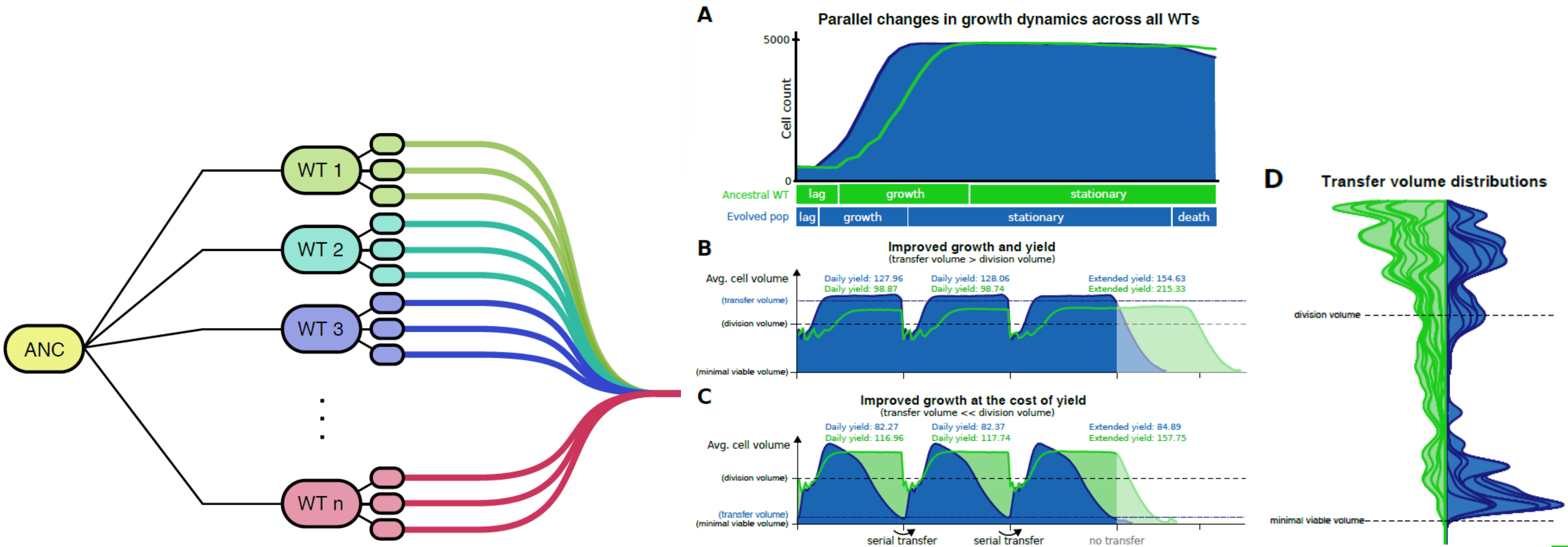
Long term evolutionary experiment (LTEE) (Lensky 1991)
One strain of E.Coli is evolving in lab-conditions since 1988
(>70000 generations) in 12 replicates
in a serial transfer protocol (diluted in new medium very 24 hours)
still adapting (getting "better")
Continued new ways of observing & new insights

This case study:

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

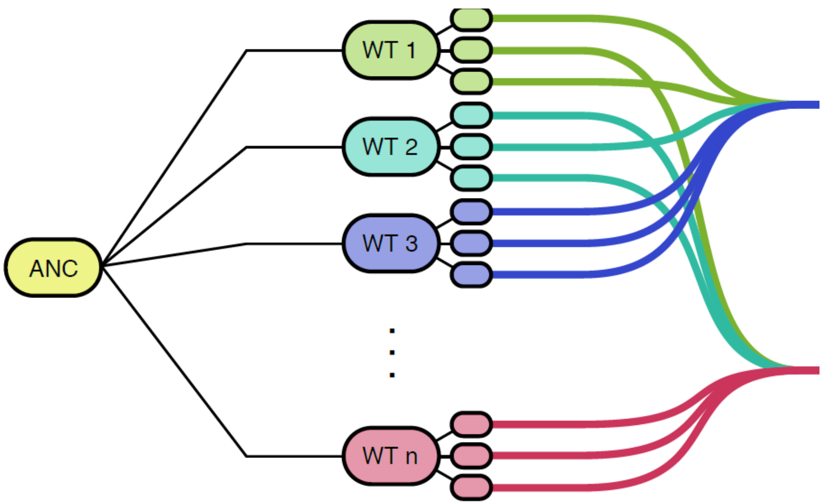
study "generic" features of such an evolutionary process
To WHAT does the population adapt?
HOW does it adapt?
Multiple observables
Similarities/differences to E. coli?

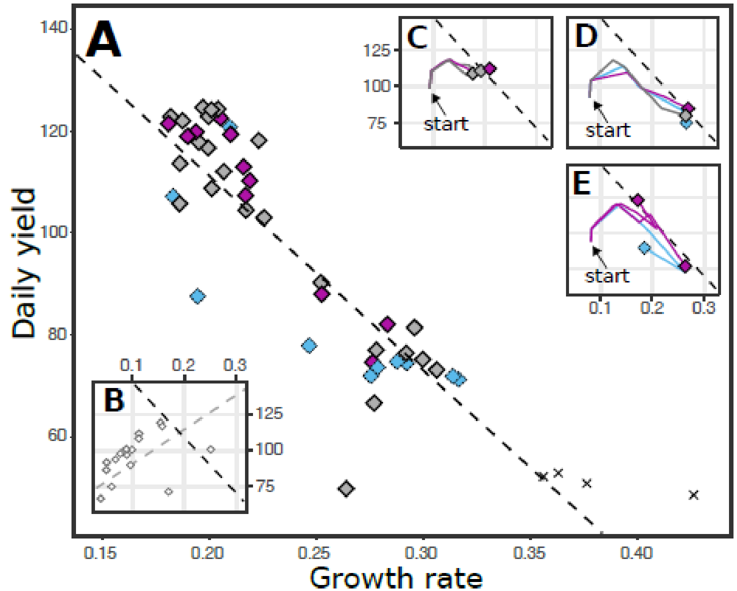
In serial transfer protocol they all evolve to “Trust the hand that feeds them” (anticipate 24 hr cycle)



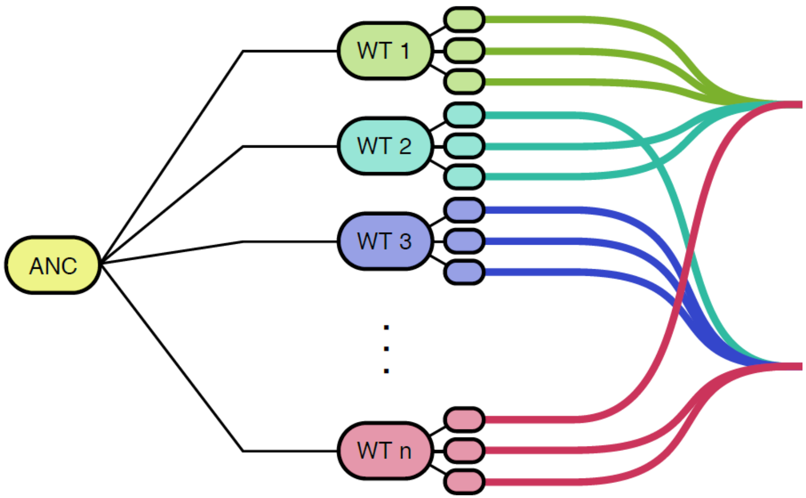
Minimize Lag-phase
Exhaust all food after 24 hours
remaining JUST alive
OR
remaining JUST ready to divide

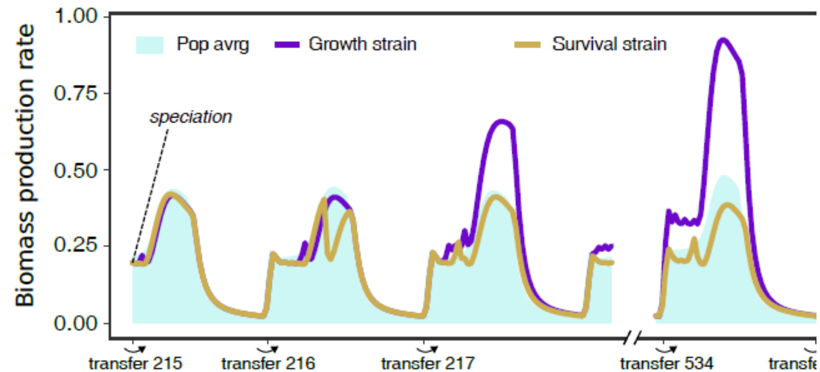
Maximizing growth rate OR Yield
evolved trade-off and distinct strategies

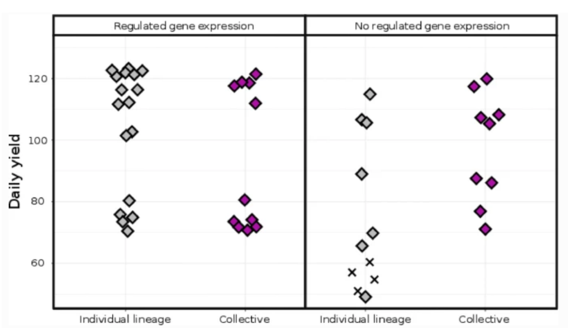


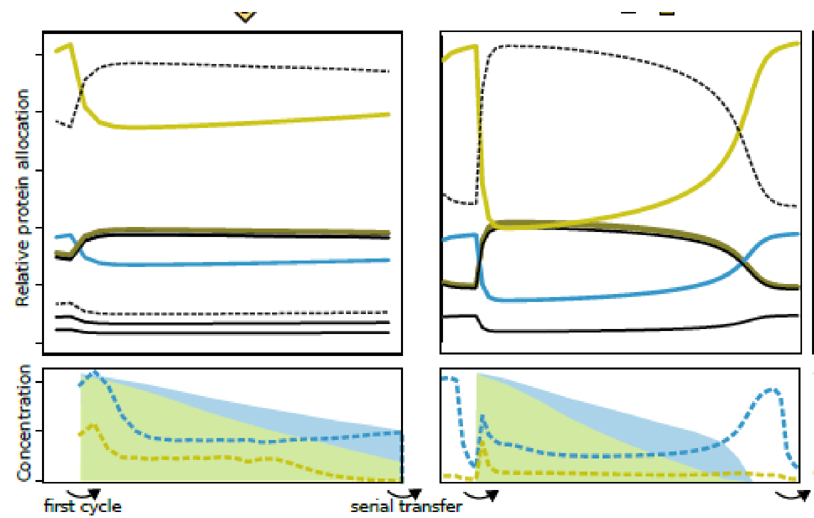


By individual based regulation OR collective tuning









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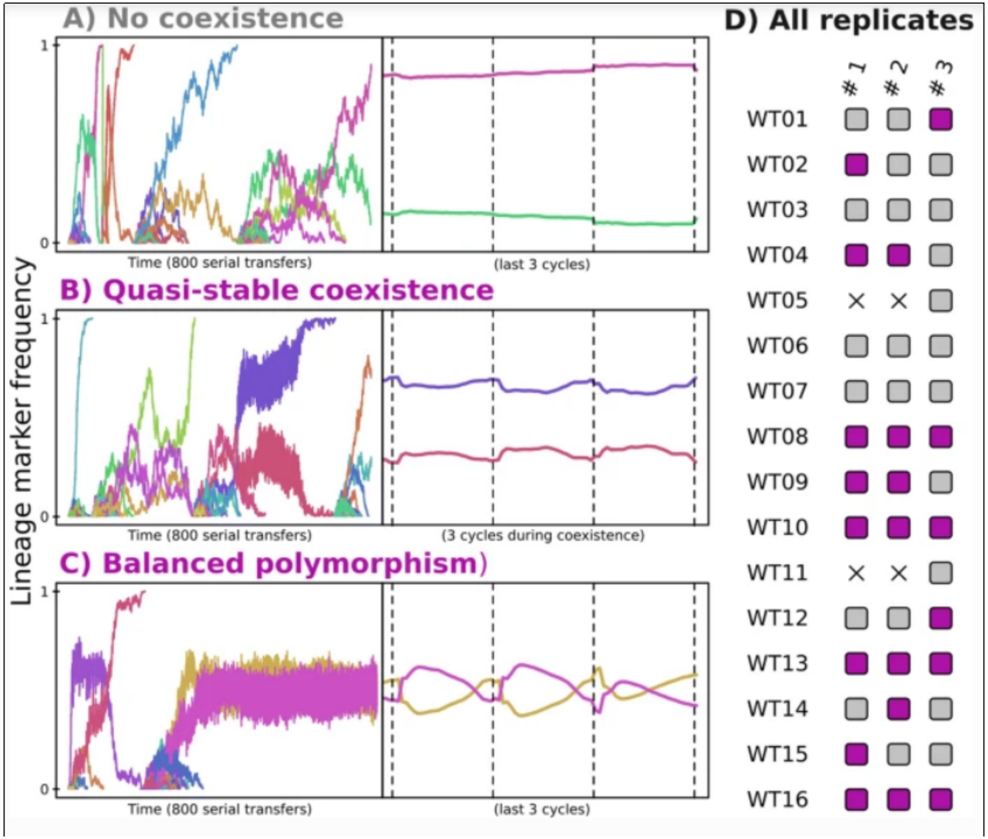
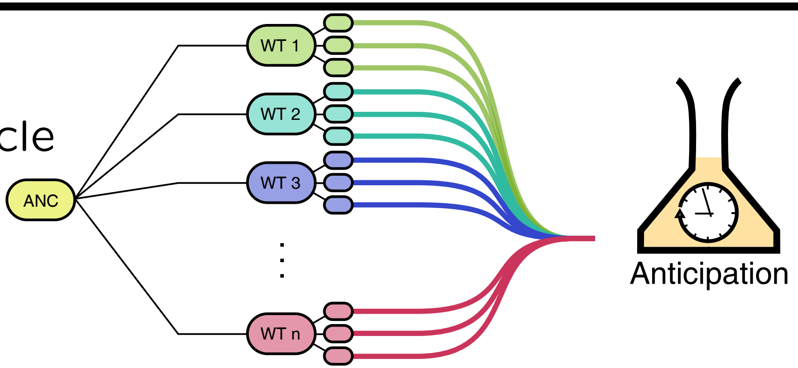
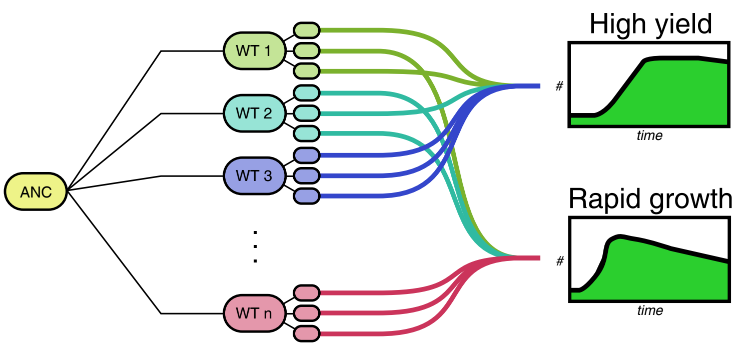


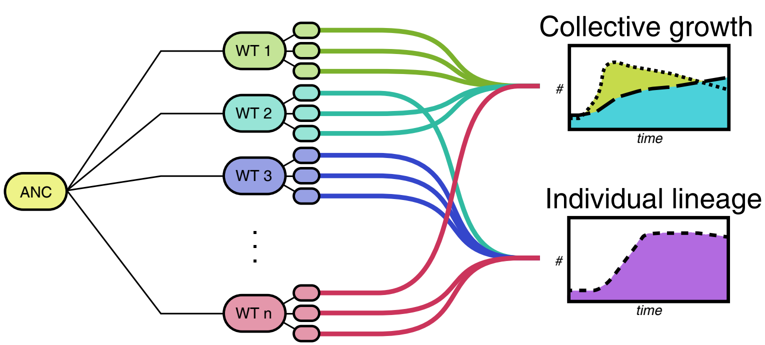
Conclusion
Evolved contingency of predictability combinatorial set of discrete outcomes

Diversified evolved wildtypes
all evolve anticipation of 24 hr cycle
un-predicted predictability



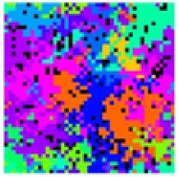
BUT in unpredictable ways



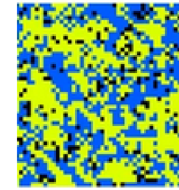


Some WT's adapt in a predictable way , others in very different ways

predictibility is an unpredicable outcome of evolution



Conclusions/Observations



- What is fitness / what has evolved not obvious
- Evolutionary attractors can be characterized as a combinatorial set of a limited set of alternatives
- Autonomous and Collective "problem solving" (metabolism)
  "easy" alternatives
- Non-autonomy not because of lack of genes...
- Spatial embedding, also without spatial patterns important
- 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