Endless evolutionary paths to Virtual Microbes

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OUTLINE

EVOLVABILITY

(micro) organisms show a remarkable ability to adapt rapidly under stress or changing conditions
in vivo

- rapid extensive transcriptional changes (yeast) [1]
- adaptation to experimental condition by parallel gene loss and point mutations (e. coli) [2]

[1] Ferea, 1999
[2] Schneider, Hindré

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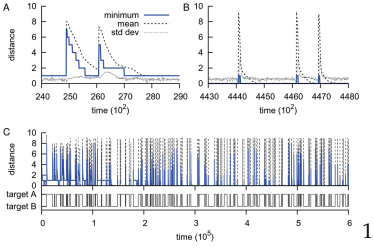
Question: does evolvability evolve?

[1] Ferea, 1999
[2] Schneider, Hindré

IN SILICO

when environment alternates between discreet states

- genome restructuring
- regulatory changes



biases spectrum towards favourable mutations

[1]

[1] Crombach & Hogeweg, 2008

IN BIOLOGY

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Redefined question: how do evolvability, regulation and ecosystem interact?

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- regulation may interfere with evolution of evolvability
- evolution of evolvability can imprint GRN as well as genome structure

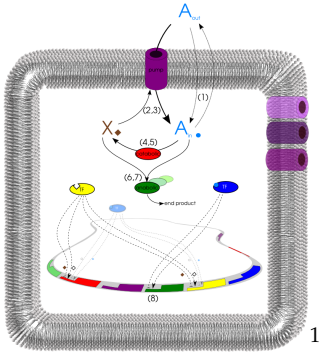
VIRTUAL CELLS

Virtual Cell model has

- TFs sense internal metabolites
- continuous environment
- also drastic environmental change
- evolve for homeostasis

Mutations:

- genome scale → dup, del, invert, translocate
- genes:
  - enzymes → alter metabolic constants
  - sequences → bit string mutations



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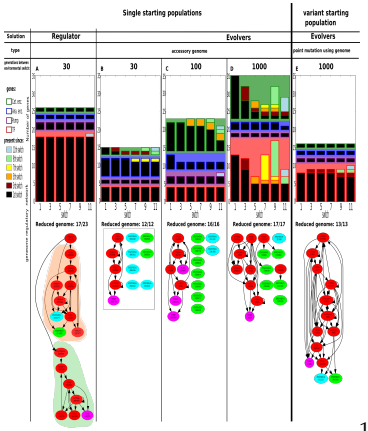
[1] Cuypers & Hogeweg, 2012; adapted from Neyfakh et al, 2006

DIFFERENT STRATEGIES EVOLVE

We observed:

- evolution of *homeostasis* regulation
- fast readaptation when change is drastic
- competition between evolutionary adaptation and regulation (timescales)



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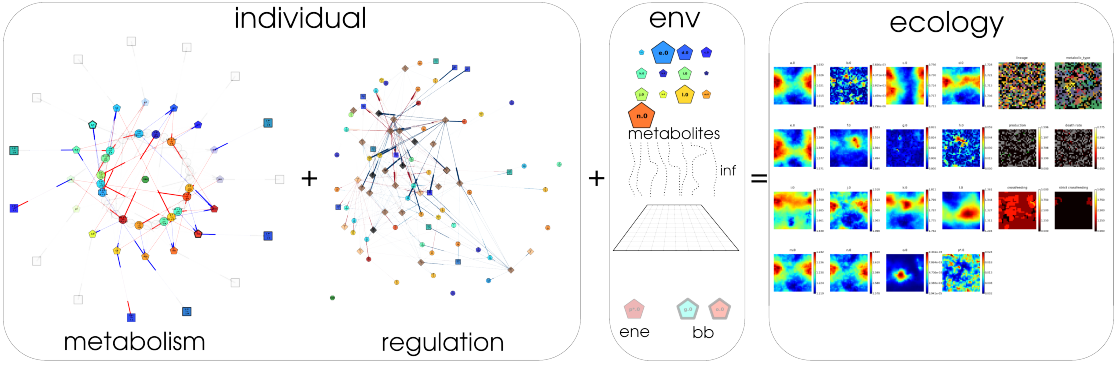
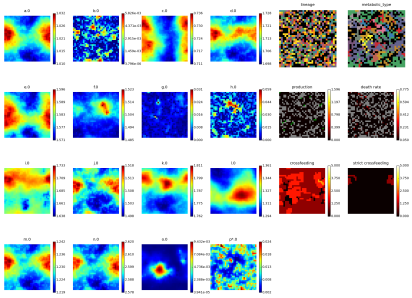
[1] in collaboration with Jaap Rutten (in progress)

TOWARDS VIRTUAL **MICROBES**



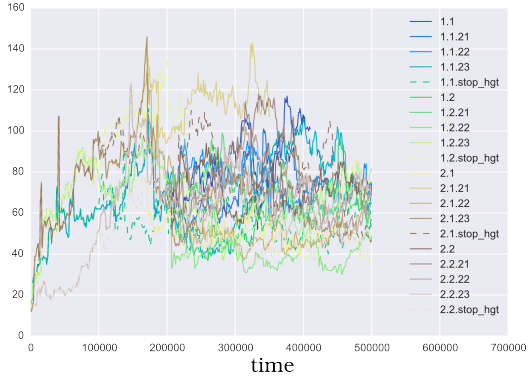
WHAT IS THERE TO DO?



no explicit fitness function that can be optimized (cf. Virtual Cell), instead:

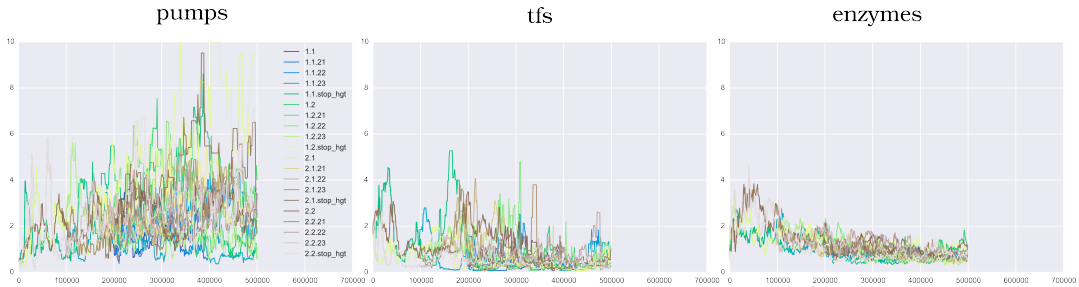
- increase *production* through metabolism
- avoid *toxic* build up of internal metabolites
- *ecosystem* feedback changes the fitness seascape.

COUNTING GENES



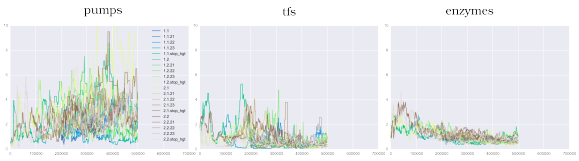
at $t = 200000$ change from fluctuating to constant environment Fast initial increase, and tendency to reduce on long time scale (cf. Knibbe & Beslon, Cuypers & Hogeweg)

GENE EXPRESSION



GENE EXPRESSION

why do pump and enzyme expression have opposite evolutionary pattern?



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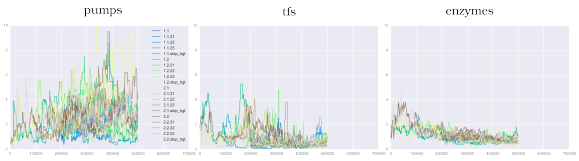

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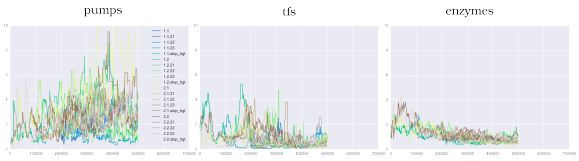

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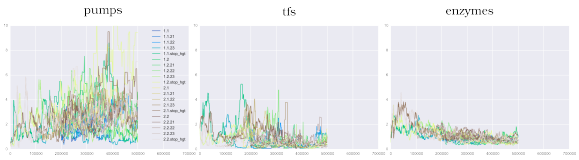

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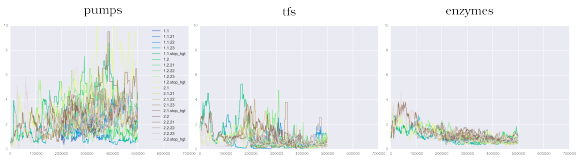

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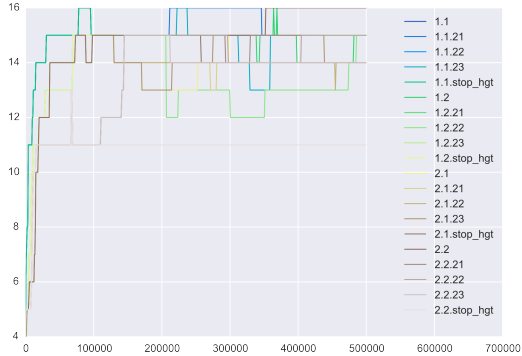
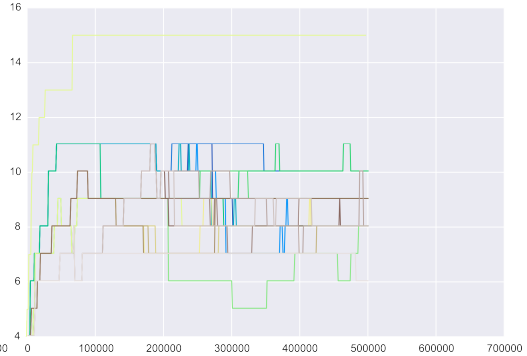
- increasing metabolic enzymes can *dissipate* high resource concentration (metabolic regulation)
- once, established, it becomes safe to pump
- fine tuning of enzymes can minimize cost of expression

EVOLVING RESOURCE EXPLOITATION

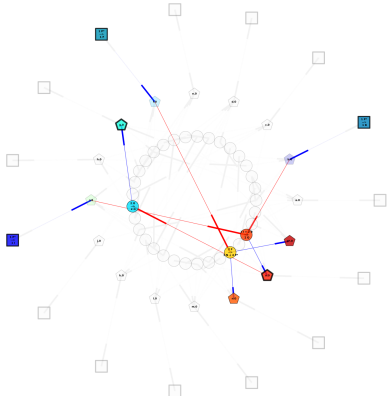
consumed



produced



CONTINUOUS CHANGE IN LINE OF DESCENT



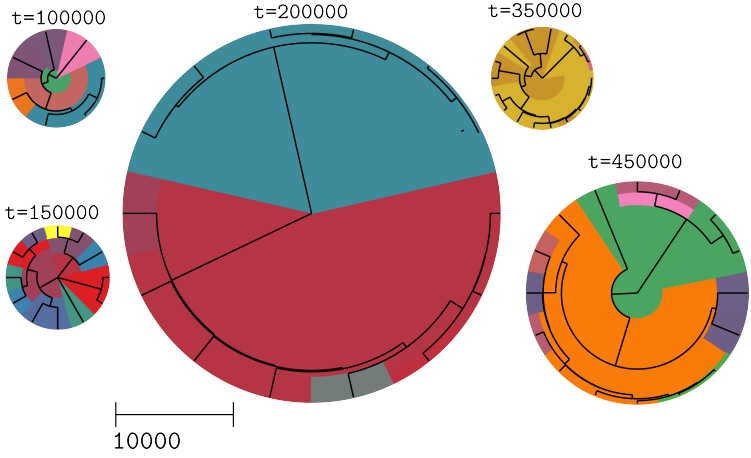
METABOLISMS IN FLUX

even though organisms quickly learn to exploit all metabolites, metabolism network remains in flux.

sustained flux in constant environment

driven by external HGT

WITHIN POPULATION DIVERSITY



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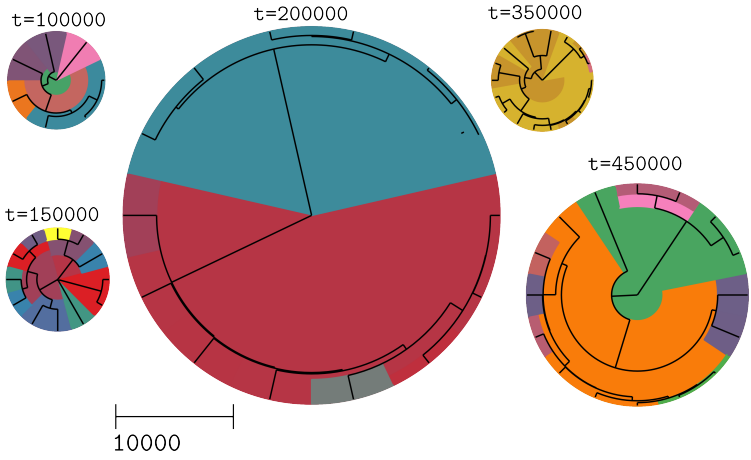
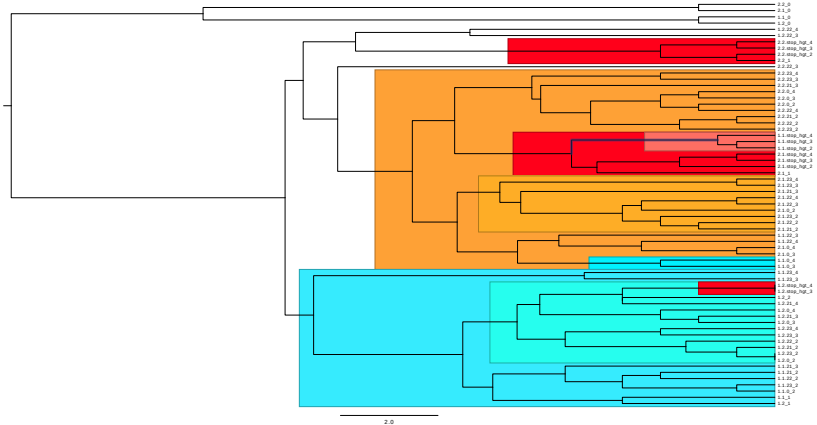


different metabolic types coexist at intermediate evolutionary time scales

BETWEEN POPULATION METABOLIC DIVERSITY



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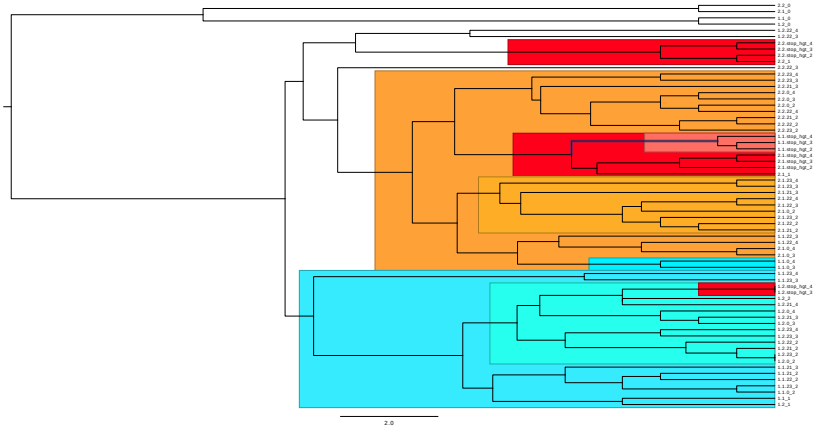
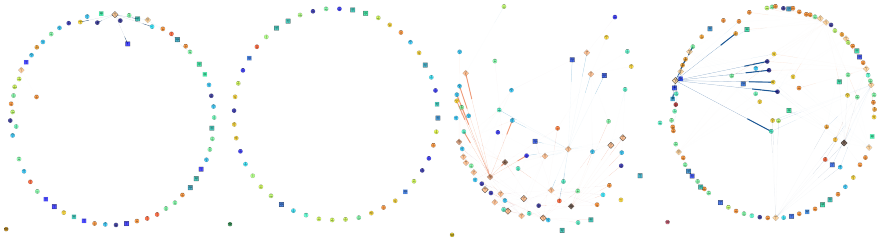


strong evolutionary contingency in evolving metabolisms

WHAT ABOUT REGULATION?



production 0.41
connectivity 0.003

production 0.41
connectivity 0.0

production 0.44
connectivity 0.216

production 0.56
connectivity 0.033

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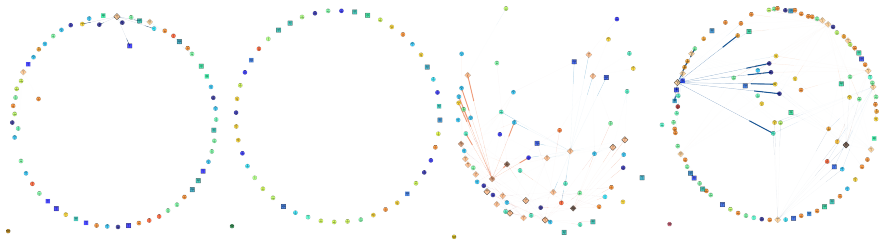

highly variable between evolutionary runs maintenance depends on environmental change

CONCLUSIONS

- microbes quickly evolve metabolic networks
- despite strong selection due to toxicity, high metabolic variation
- metabolisms in flux over evolutionary time
- continuous evolution of population diversity
- strong contingency of evolutionary trajectories

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- Bram van Dijk
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- ECAL organizers

Evolution of Evolution