Searching for principles of microbial physiology

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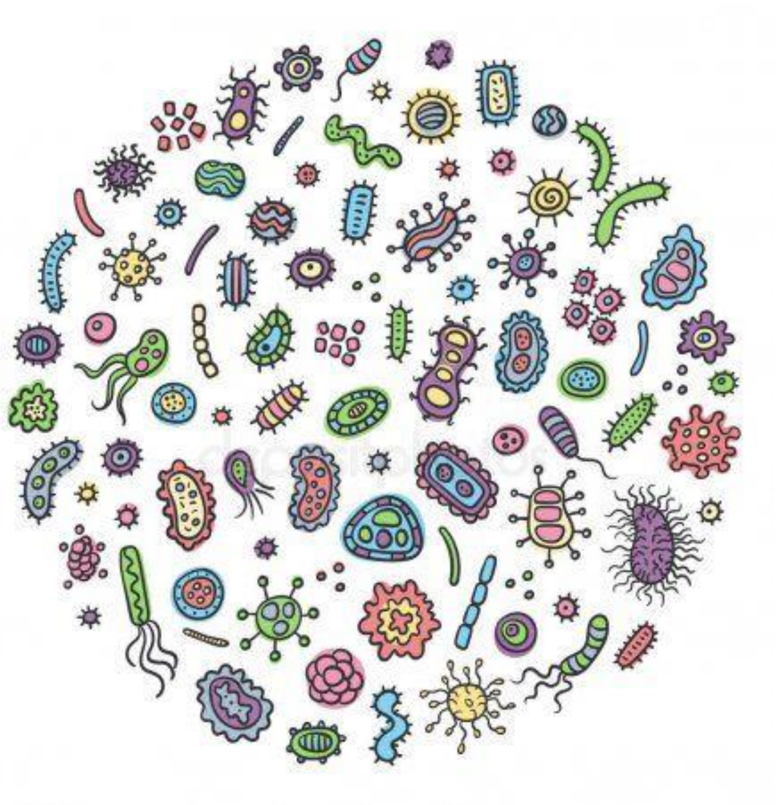
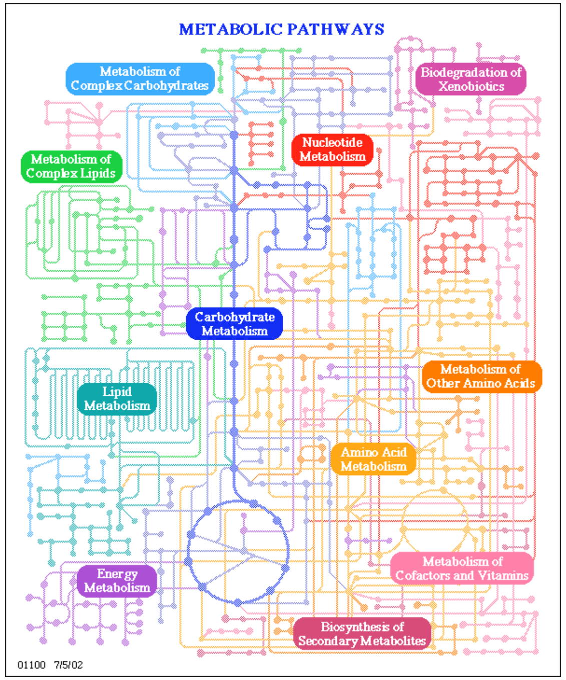
Molecular commonalities across microorganisms

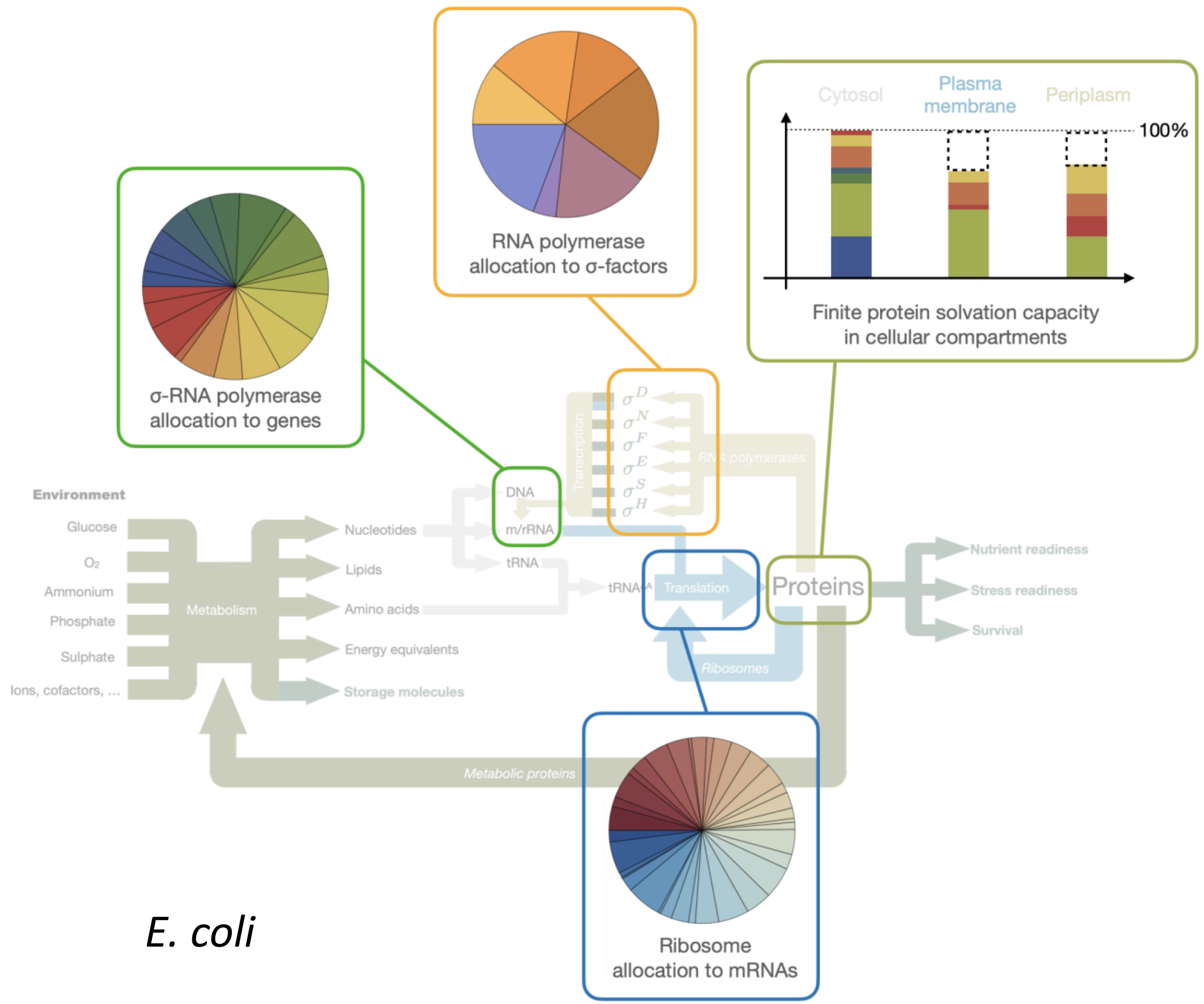




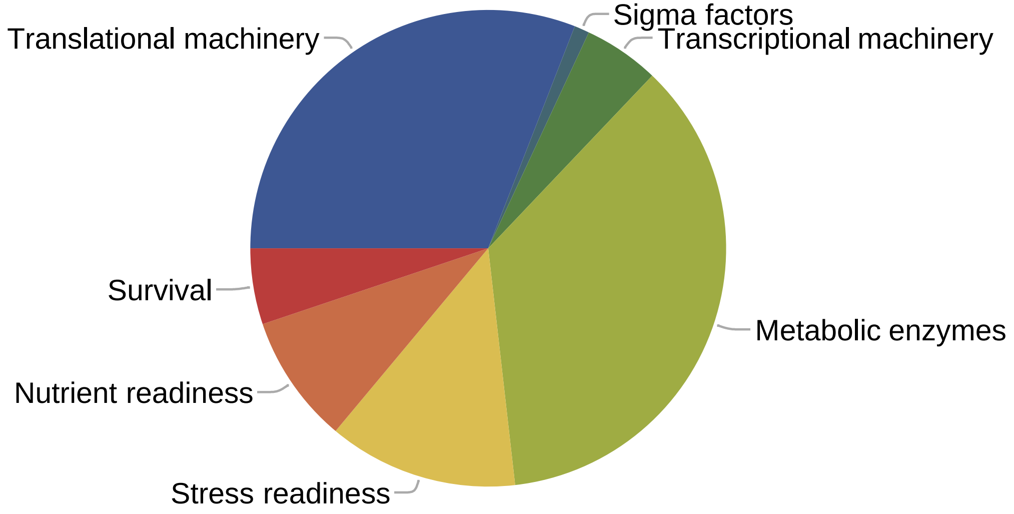
- ✓ Conserved biochemistry and molecular biology
  - ✓ Biosynthesis machinery
  - ✓ Energy conservation and central metabolism
  - ✓ Conserved principles of enzyme kinetics

All microorganisms have a finite biosynthetic capacity

such that the synthesis of one protein is that the expense of others

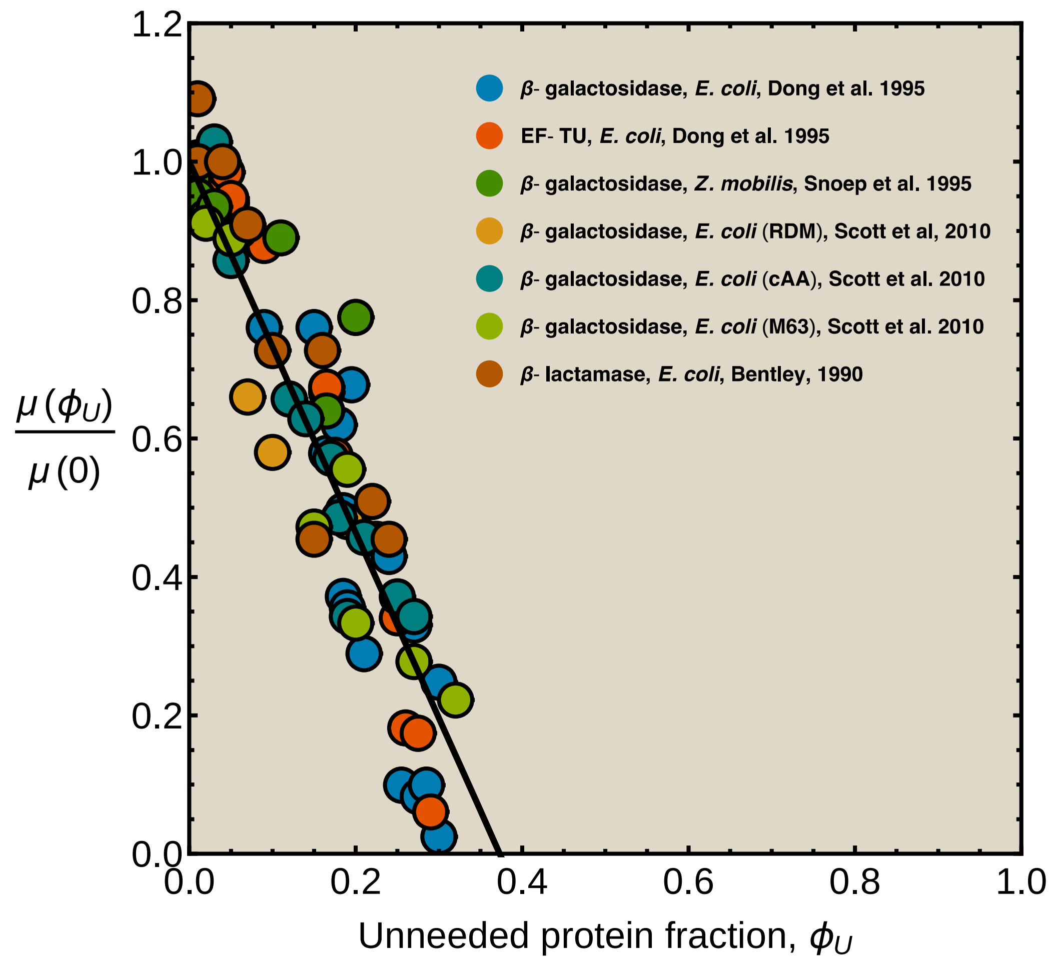


E. coli

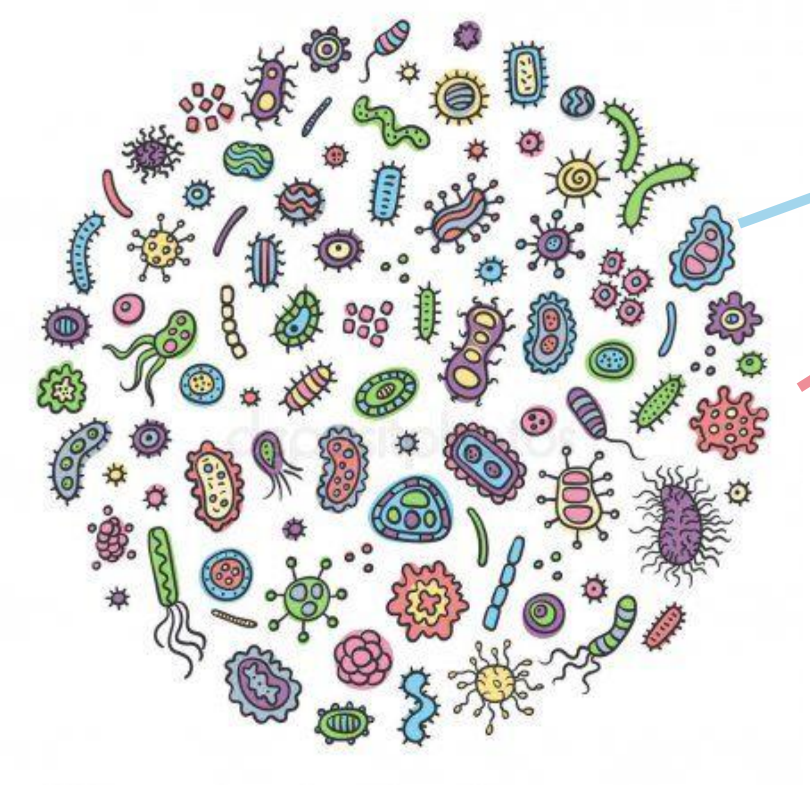


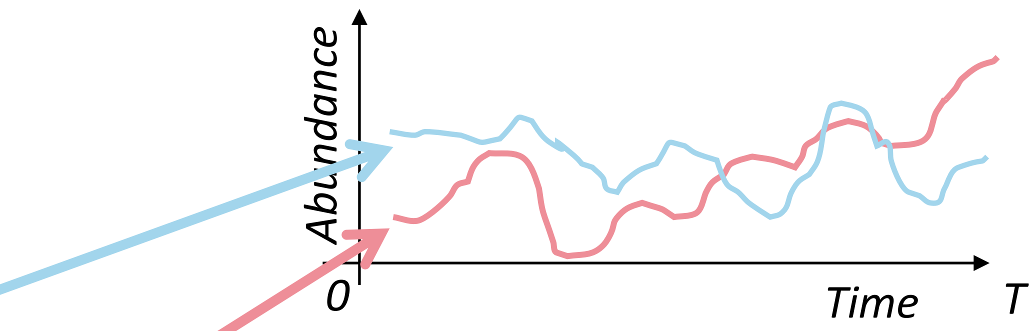
Phenotypic adaptation --
Environment dependent “protein pools”

Unneeded proteins are at the expense of growth proteins in E. coli



Identical fitness measure for all microorganisms





Period of growth, death and stasis

Fitness of  $= \frac{1}{T} \ln \frac{\text{number of } [\text{img 3}] \text{ at time T}}{\text{number of } [\text{img 4}] \text{ at time 0}}$

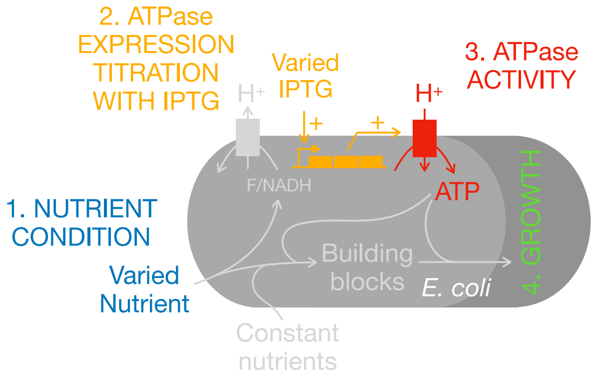
Fitness of  $= \frac{1}{T} \ln \frac{\text{number of } [\text{img 6}] \text{ at time T}}{\text{number of } [\text{img 7}] \text{ at time 0}}$

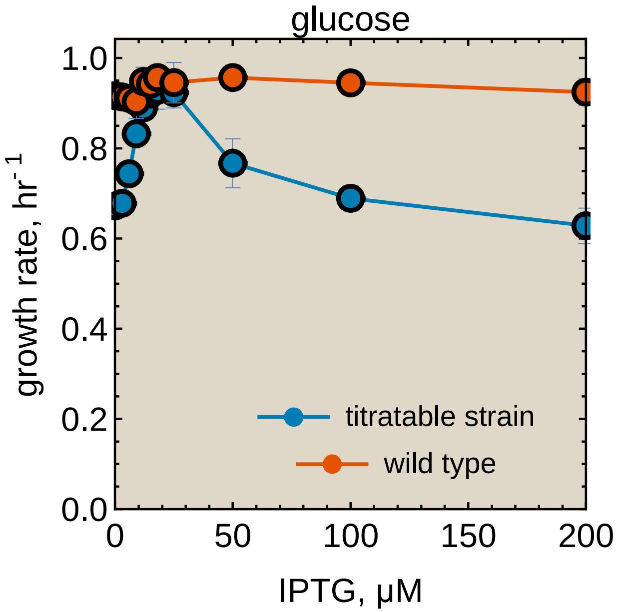
 

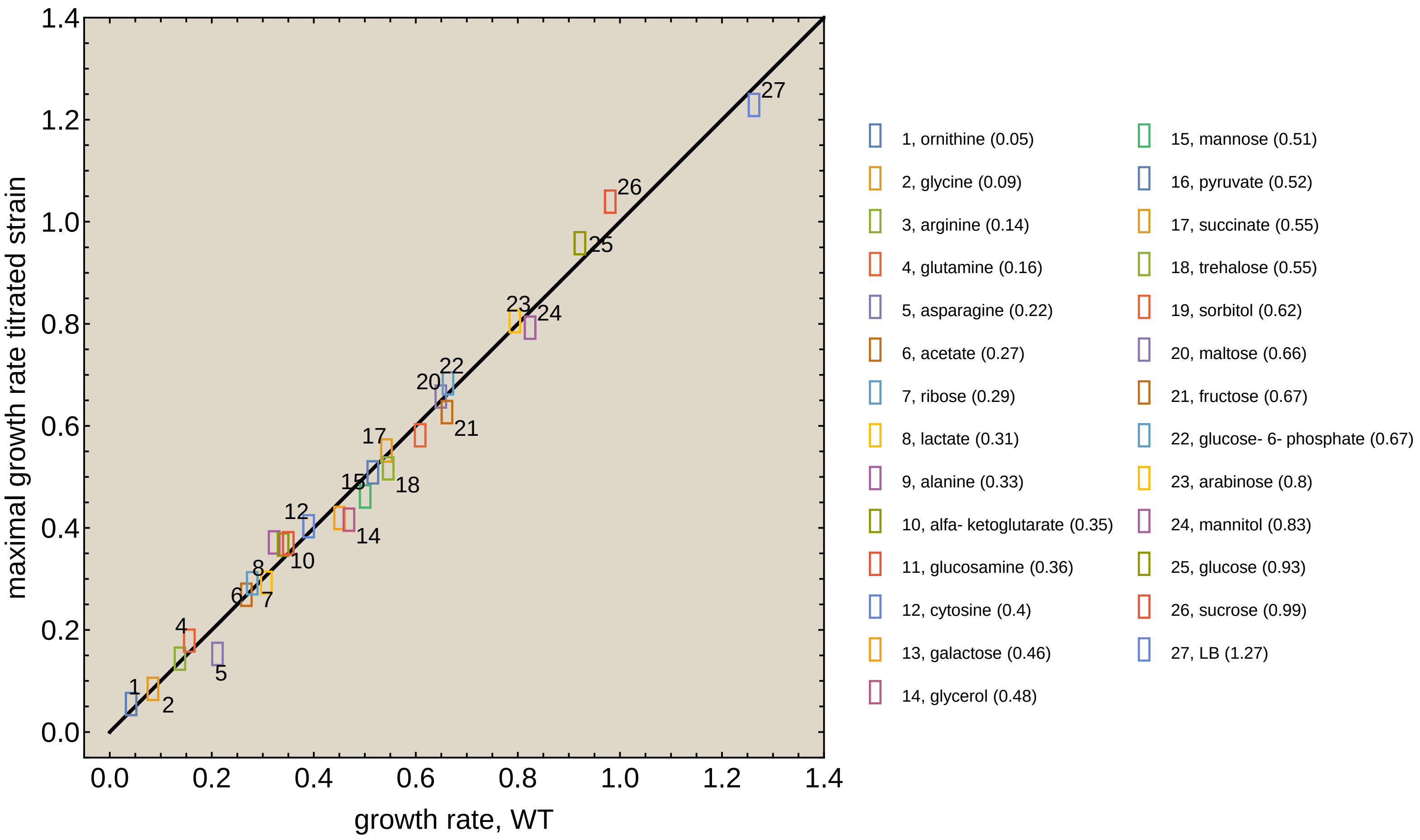
$$\text{Fitness} = \frac{1}{T} \ln \frac{N(T)}{N(0)} = \frac{1}{T} \int_0^T \mu(t)dt = \text{Average growth rate}$$

Protein expression of H-ATPase maximizes growth rate in E. coli

for S. cerevisiae evidence see Keren, et al. Cell, 2016 and for L. lactis evidence see Peter Jensen's papers

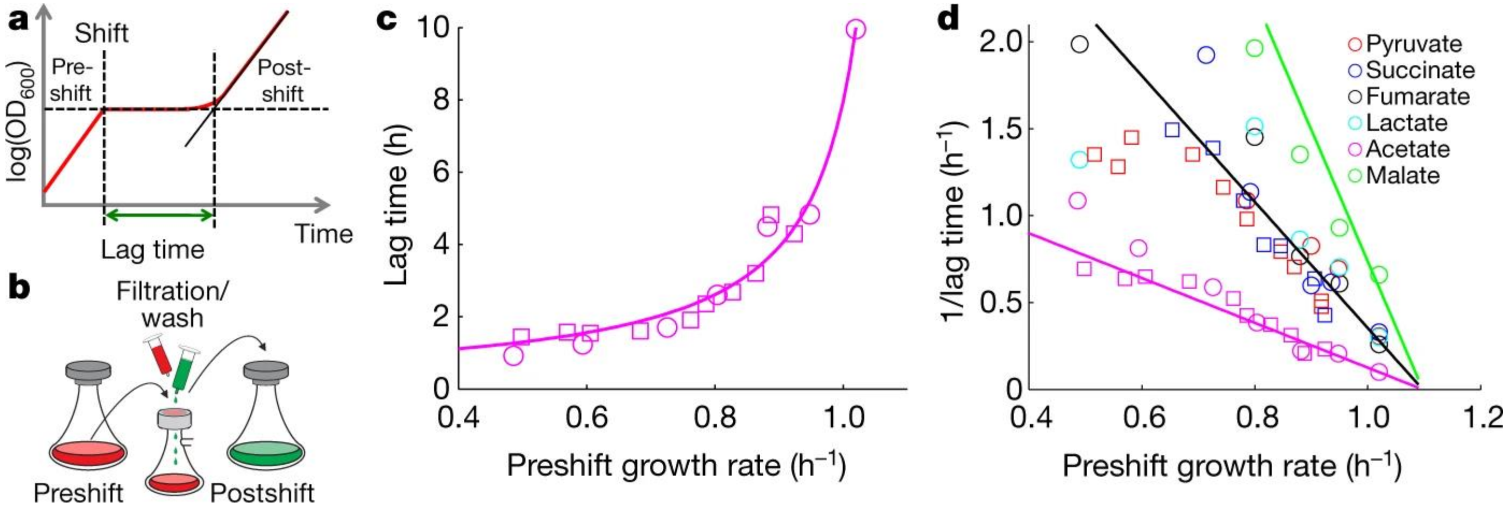






The trade off between growth, stress readiness and adaptation capacity

implied by the finite biosynthetic resources



E. coli study: *Basan et al. Nature, 2020.*

Slower growth of *Escherichia coli* leads to longer survival in carbon starvation due to a decrease in the maintenance rate

Elena Biselli[1,†], Severin Josef Schink[1,2,†] & Ulrich Gerland[1,*]

Environmental Microbiology (2005) 7(10), 1568–1581 doi:10.1111/j.1462-2920.2005.00846.x

Global physiological analysis of carbon- and energy-limited growing *Escherichia coli* confirms a high degree of catabolic flexibility and preparedness for mixed substrate utilization

Microbiology (2004), **150**, 1637–1648 DOI 10.1099/mic.0.26849-0

Specific growth rate and not cell density controls the general stress response in *Escherichia coli*

Julian Ihssen and Thomas Egli

Swiss Federal Institute for Environmental Science and Technology, PO Box 611, Überlandstrasse 133, CH-8600 Dübendorf, Switzerland

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APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Apr. 2006, p. 2586–2593 Vol. 72, No. 4
0099-2240/06/$08.00+0 doi:10.1128/AEM.72.4.2586–2593.2006

Specific Growth Rate Determines the Sensitivity of *Escherichia coli* to Thermal, UVA, and Solar Disinfection

Michael Berney, Hans-Ulrich Weilenmann, Julian Ihssen, Claudio Bassin, and Thomas Egli*

Swiss Federal Institute of Aquatic Science and Technology (Eawag), Überlandstrasse 133, P.O. Box 611, CH-8600 Dübendorf, Switzerland

The trade off between growth, stress readiness and adaptation capacity

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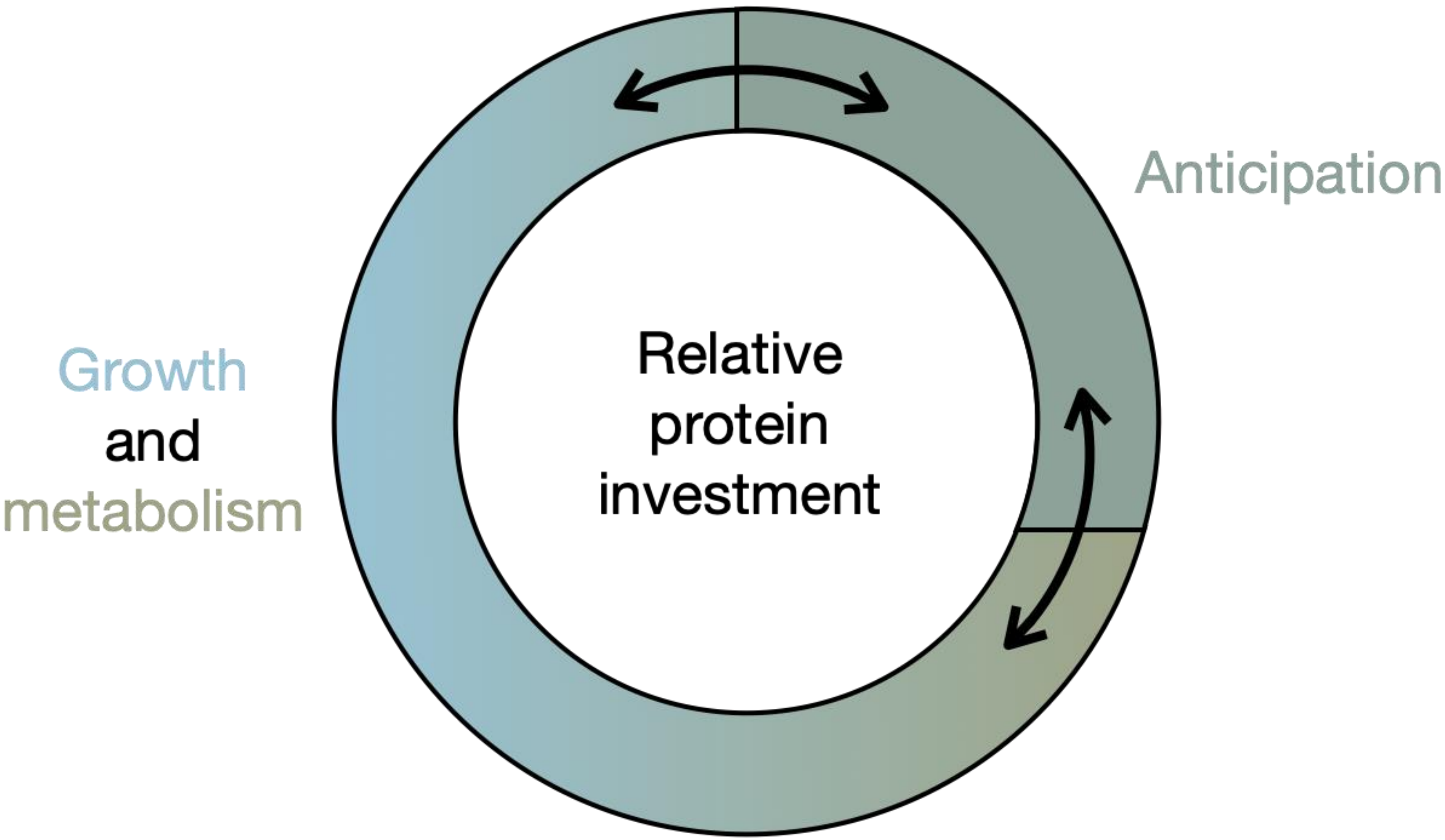
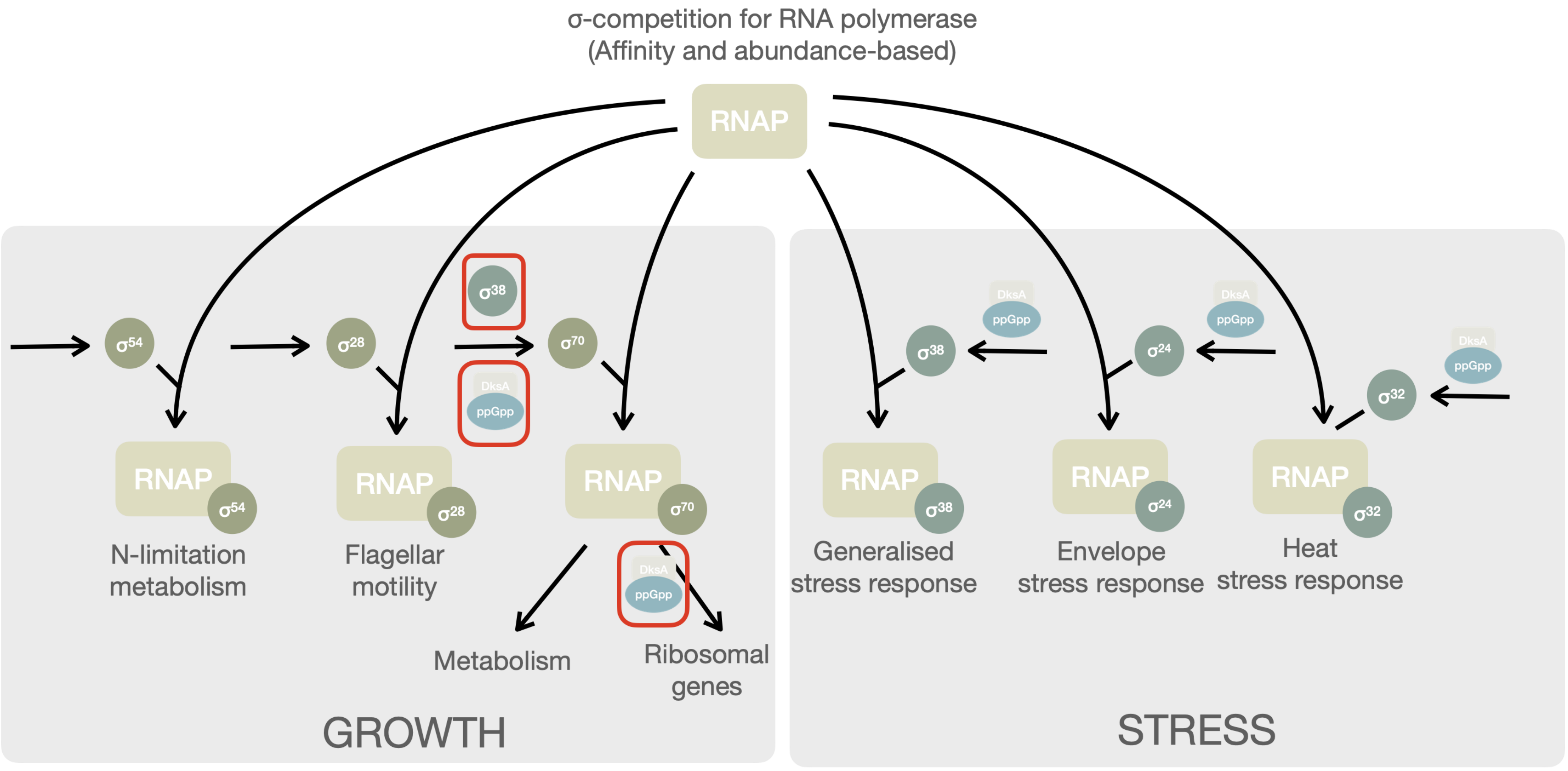


Molecular "hardwiring" of the trade off in E. coli via RNA-pol competition

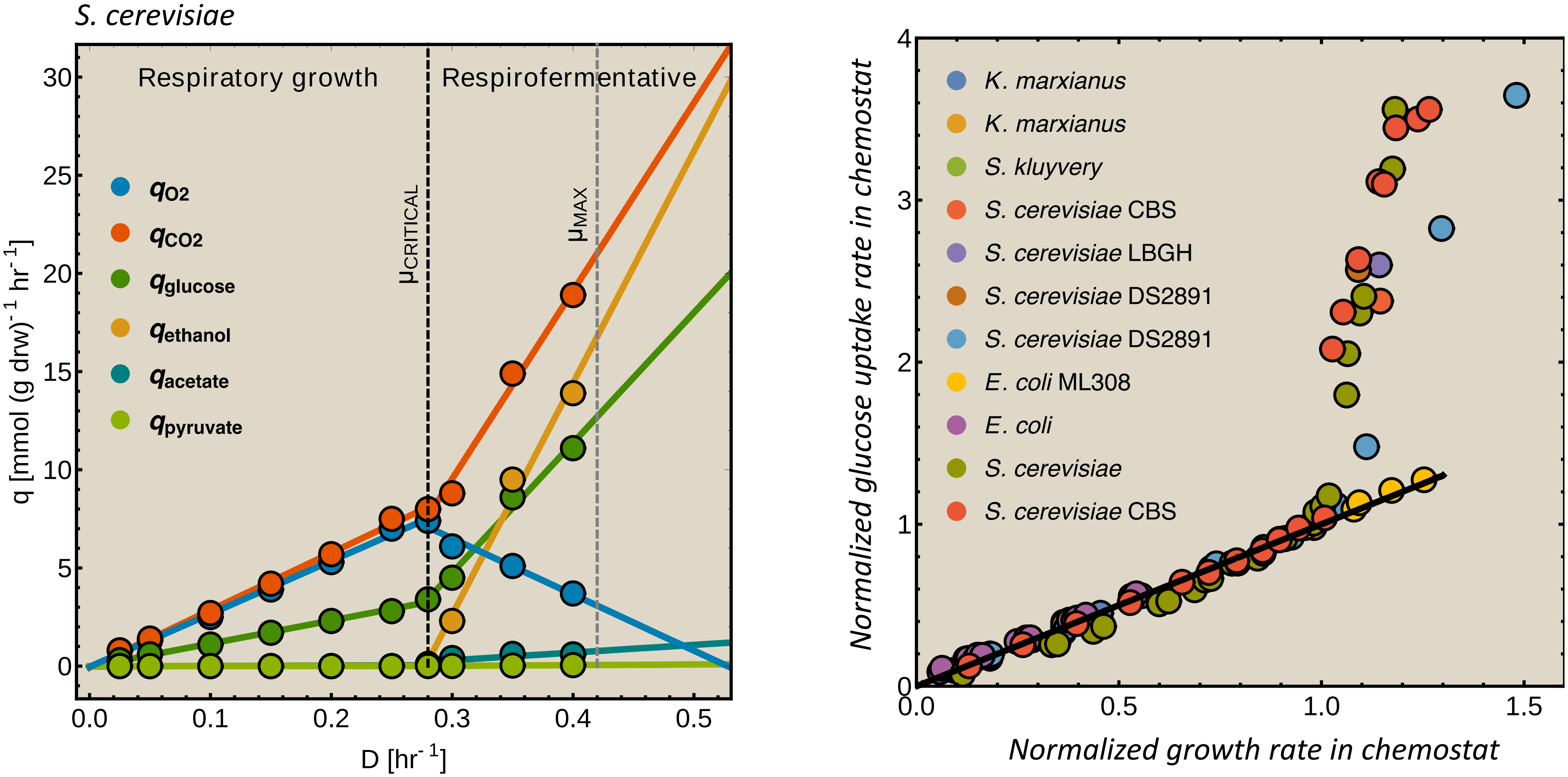
σ-factors are required, transient subunits of RNA polymerase in E. coli



In lab-evolution experiments, growth-vs-stress "rebalancing" mutations were found in sigma factors and RNA pol.

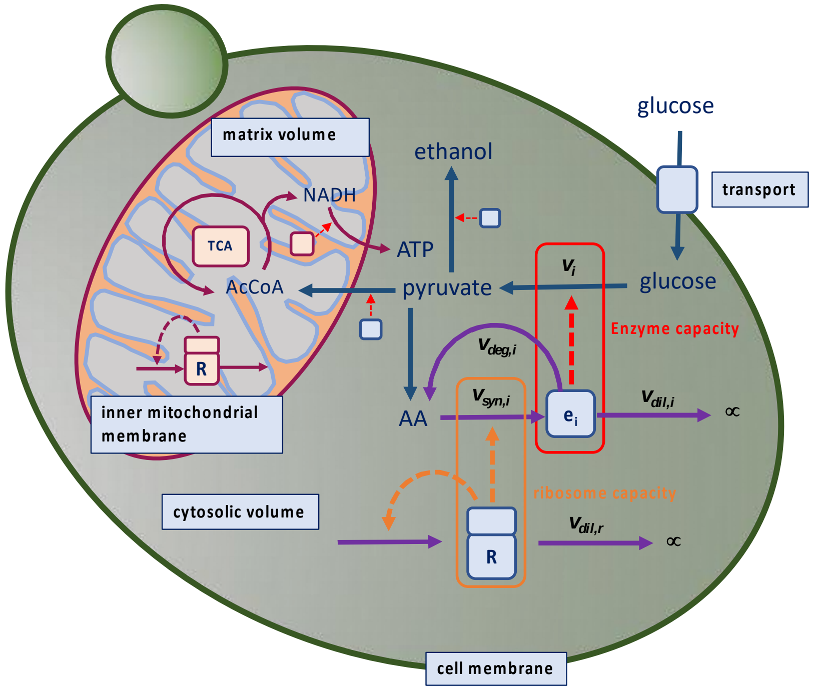
Commonality of overflow metabolism at fast growth

for L. lactis example see Goel et al. Molecular Microbiology 2015

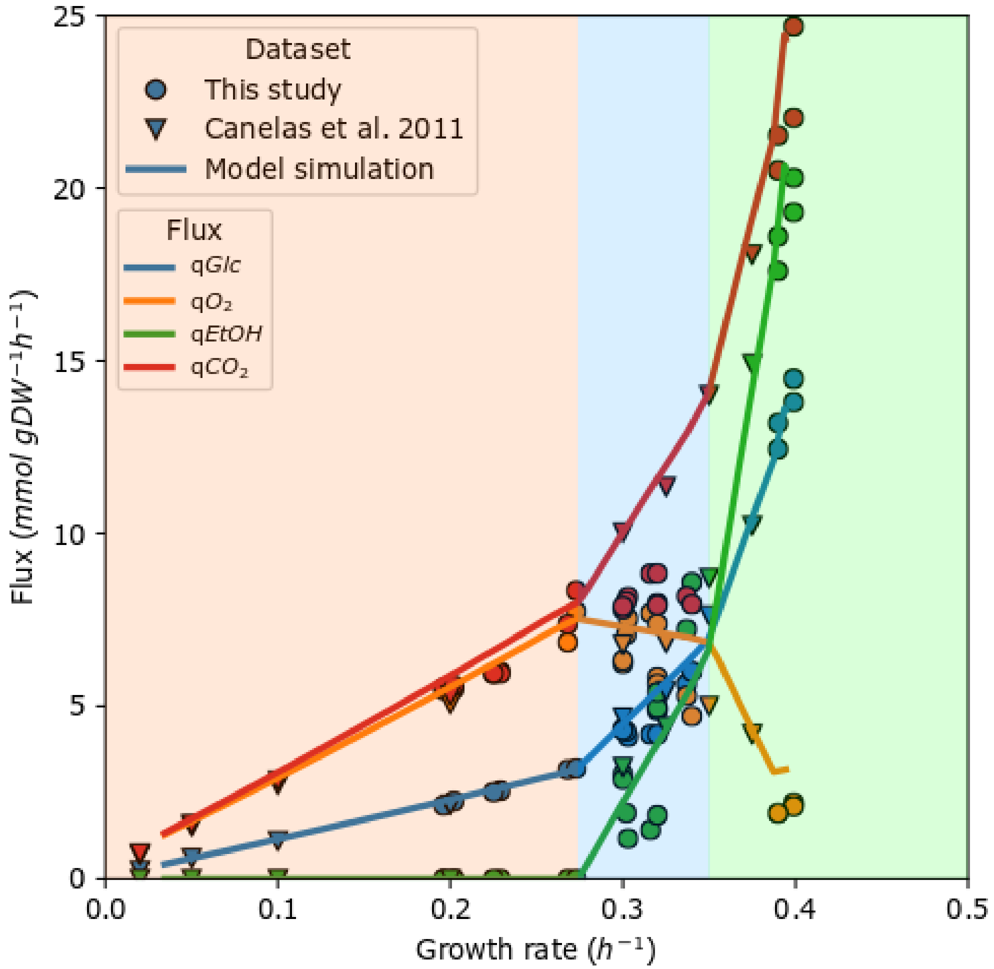


Optimal allocation of biosynthetic resources can explain overflow metabolism at fast growth

Elsemman, Prado, Griagatis et al, BioRxiv preprint, 2021.

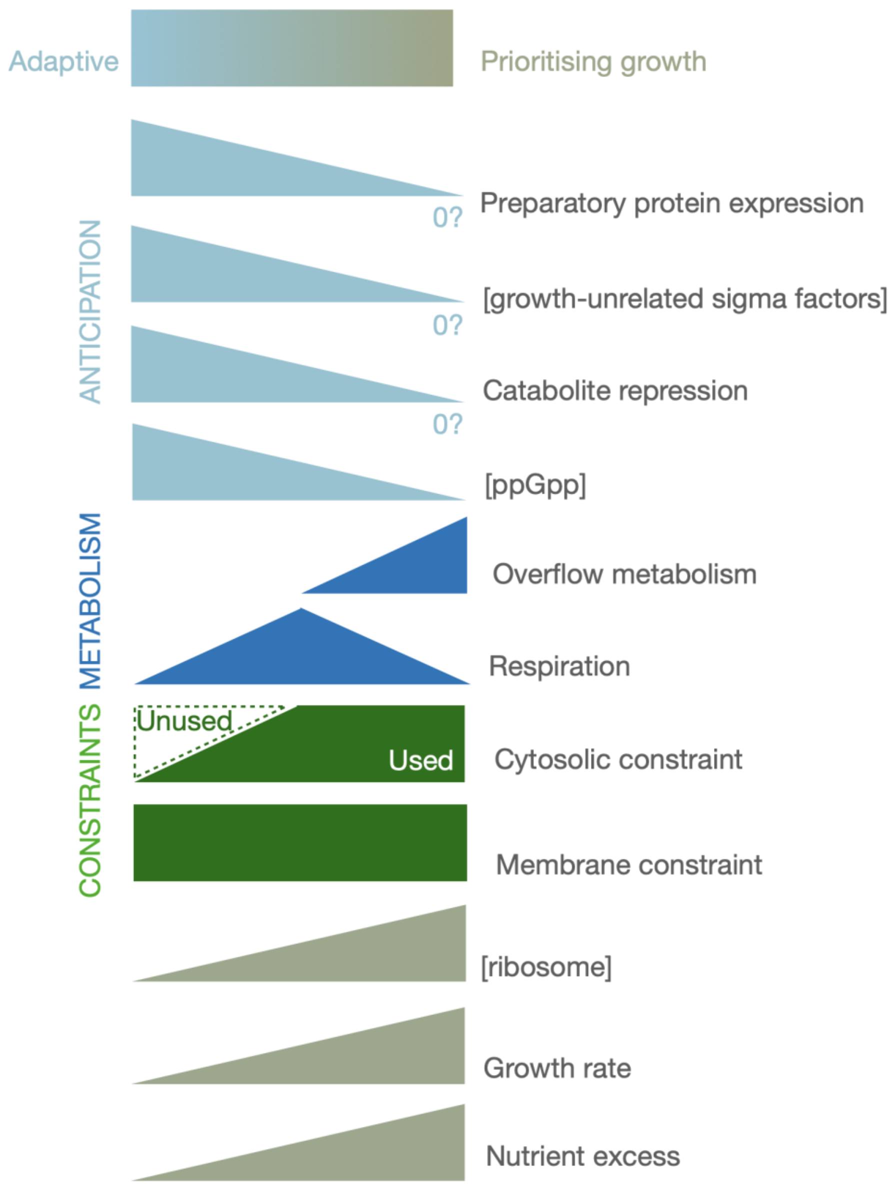


Mathematical model of metabolism, Protein synthesis and protein-expression constraints.



Growth rate is an "order parameter" for E. coli

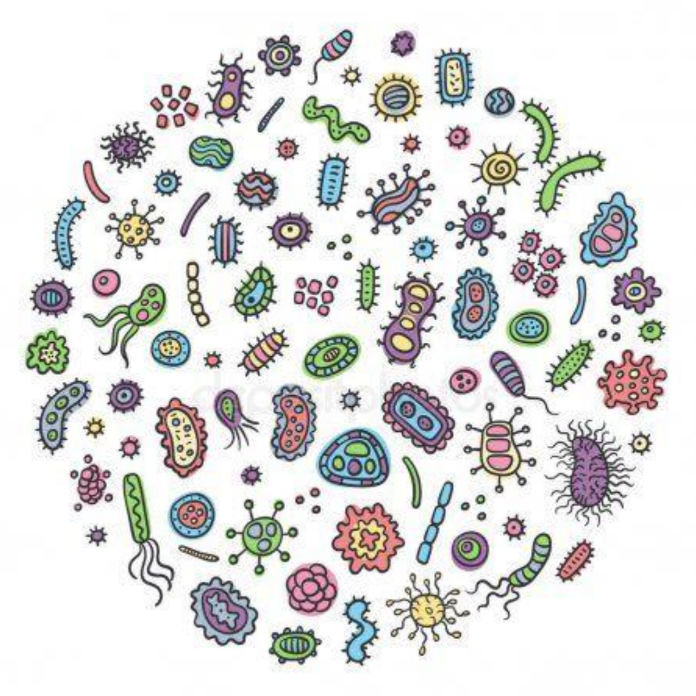
(and likely also for S. cerevisiae)



But not all microorganisms are like E. coli and S. cerevisiae

Commonalities

- ✓ Biochemical kinetics
- ✓ Biosynthesis
- ✓ Finite biosynthetic resources
- ✓ Fitness measure



Possible differences

- ✓ Protein expression as function of growth rate
- ✓ Absence of overflow metabolism
- ✓ Unneeded protein response of growth rate
- ✓ Anticipation behavior at slow growth

Likely cause:
differences in their environment (niches)

The field is biased to fast growing microbes in constant conditions.

Microbial fitness strategies are likely niche dependent

Microbial fitness strategy ≅ Microbial physiology

Mostly (same) feast environment

☑ Growth investment
☐ Stress readiness
☐ Nutrient readiness
☑ Tiny persister cell-fraction

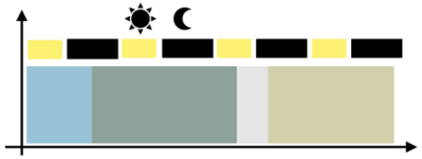
Growers,
Poor adaptors to new conditions,
e.g. ?? *Lactococcus lactis*, *Methanococcus maripaludis*

Unpredictable environment

☑ Growth investment
☑ Stress readiness
☑ Nutrient readiness
☑ Phenotypic diversification

Growers first,
Reasonable adaptors
Future preparation whenever possible
e.g. *Escherichia coli*, *Saccharomyces cerevisiae*

Periodic (energy) environment with an unpredictable component



☑ Growth investment
☑ Stress readiness
☑ Nutrient readiness
☑ Phenotypic diversification

Growers and storers during the day,
Survive during the night
Future preparation whenever you can
e.g. *Synechococcus elongatus*

Mostly famine environment

☐ Growth investment
☑ Stress readiness
☑ Nutrient readiness
☑ Phenotypic diversification

Survivors
Future preparers
Good adaptors
e.g. many soil bacteria

Famine Nutrients Stress Day Night

Conclusions

1. Commonalities exist across microorganisms.
   - ❑ Microbes are nearly identical in their basic metabolism, biosynthesis and biochemistry.
   - ❑ Natural selection selects microbes with the highest average growth rate.
   - ❑ All microbes suffer from finite biosynthetic resources.
   - ❑ Expression of proteins is at the expense of others (the growth-stress-adapt trade-off).
2. Niche-specific physiological phenomena.
   - ❑ Unneeded protein reduces growth rate.
   - ❑ Optimal expression of a needed protein maximizes growth rate.
   - ❑ Overflow metabolism can result from optimal allocation of finite biosynthetic resources.
   - ❑ *E. coli* (and *S. cerevisiae*?) are opportunistic and prioritize growth over future preparation.
3. The physiology (metabolic and stress protein expression) of *E. coli* and *S. cerevisiae* can be predicted by optimal allocation of finite biosynthetic resources to maximize growth rate.
4. The physiology of model microorganisms likely still reflects their natural niches such that *E. coli*, *S. cerevisiae*, *B. subtilis*, and *S. elongatus* (and *L. lactis*) experience the same protein-expression constraints, but nonetheless behave differently.

Thanks to .....

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