rK selection theory simplified by trading-off growth rate and efficiency

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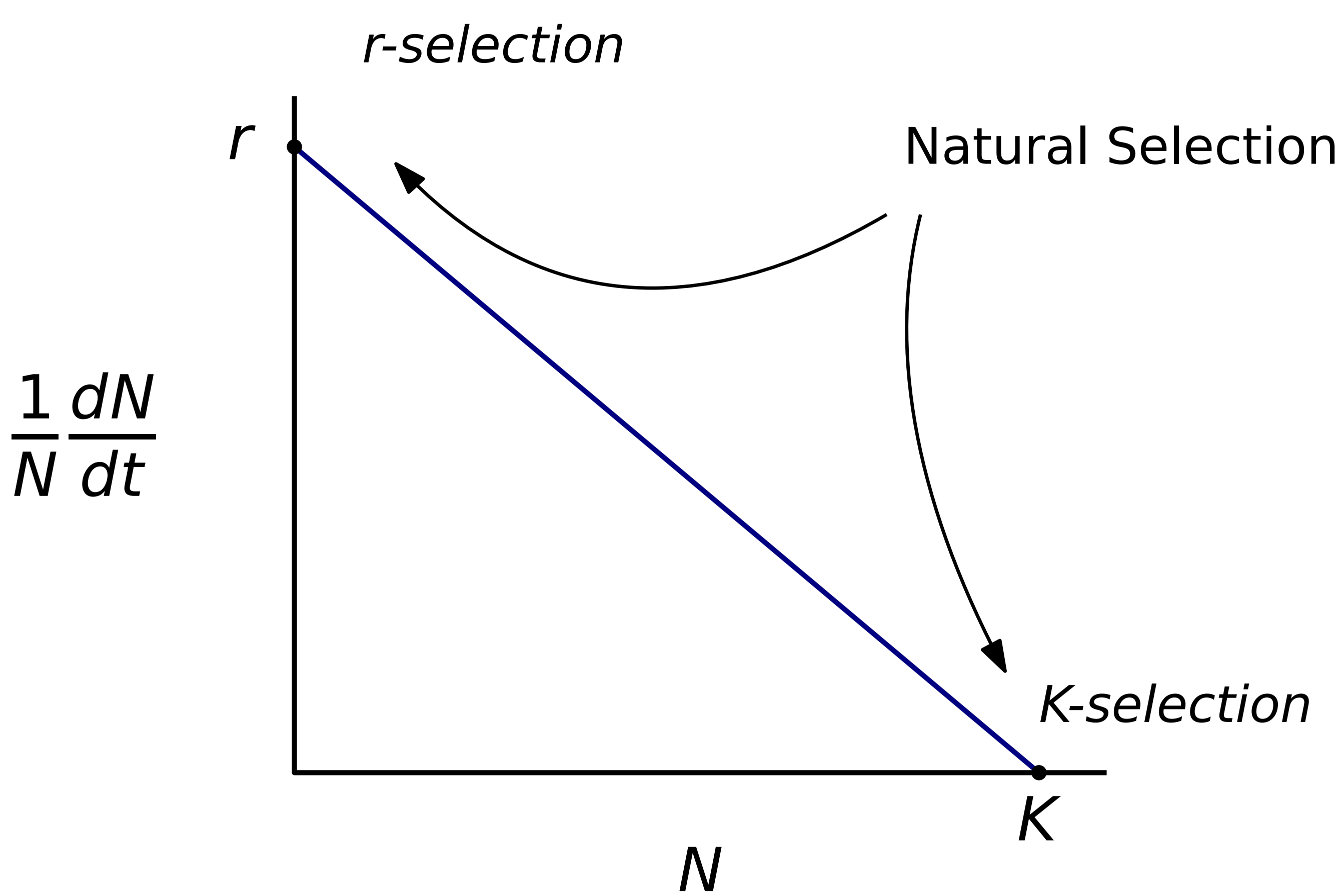
Engineering and Physical Sciences Research Council

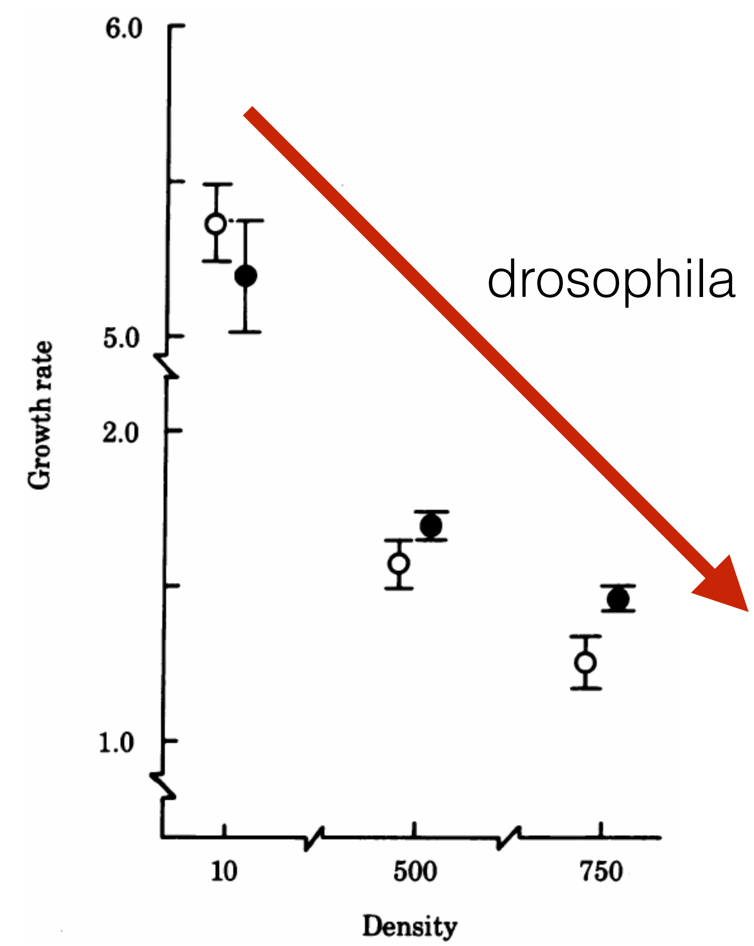
UNIVERSITY OF EXETER

ecology textbooks:



$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right)$$

data:



Mueller and Ayala (1980)

…so far, so good

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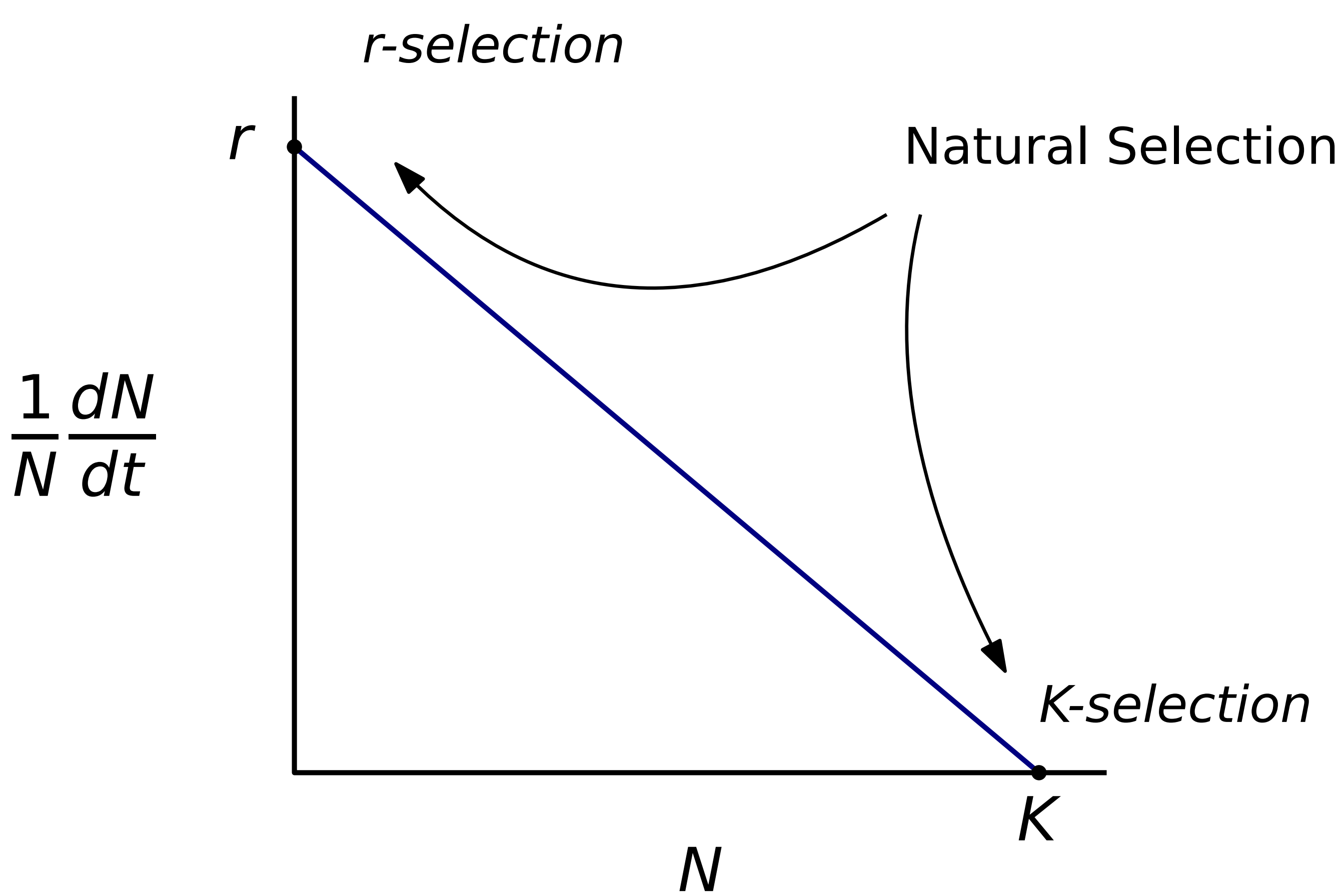

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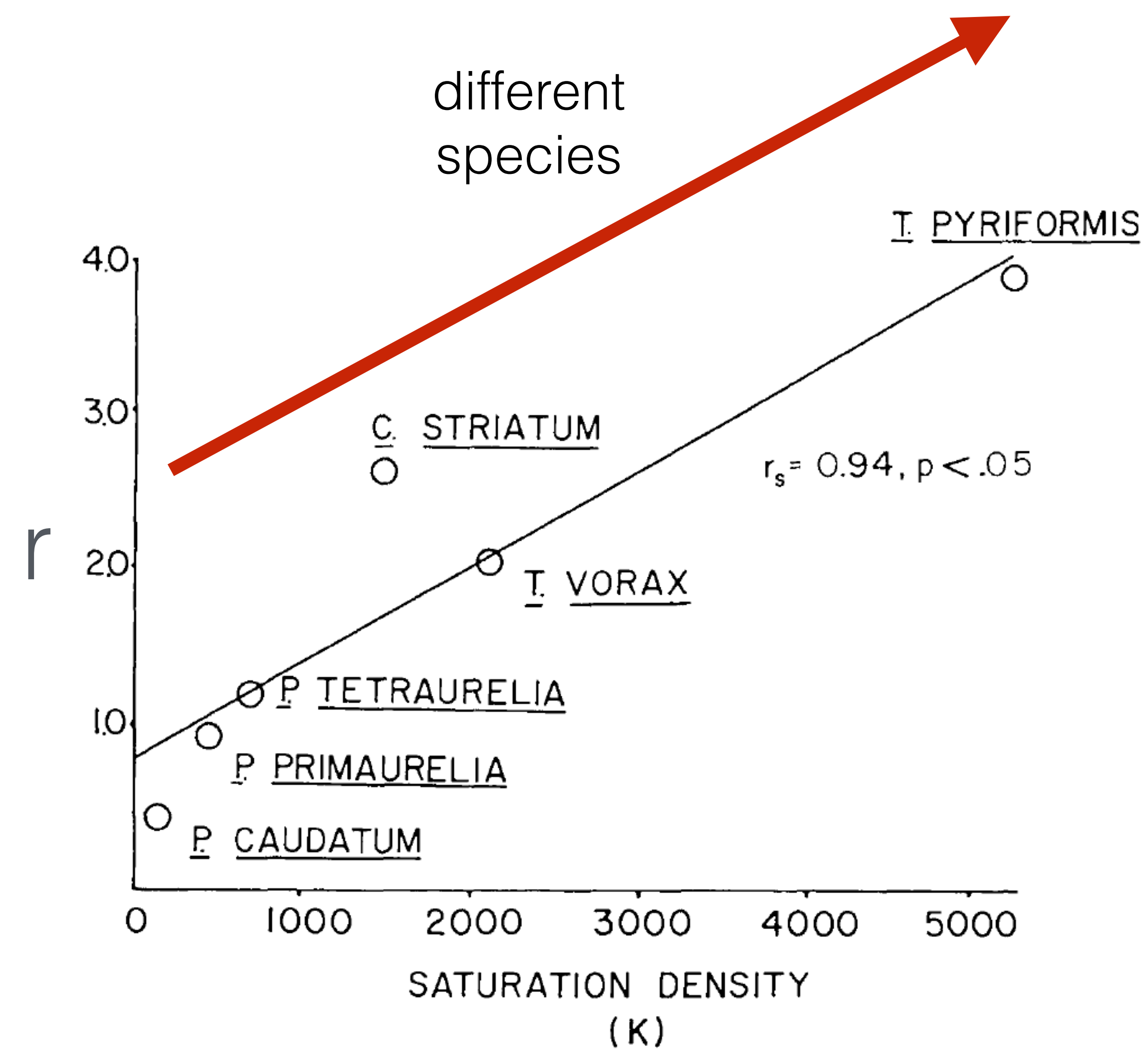
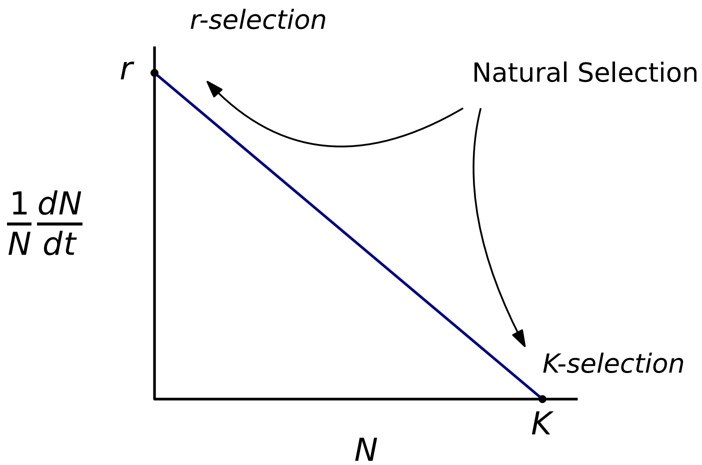


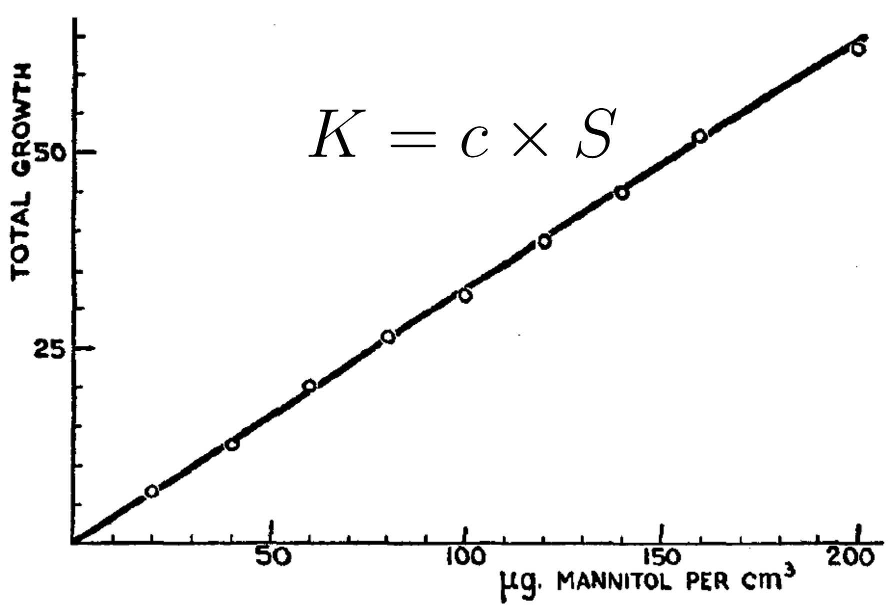
Luckinbill (1979)

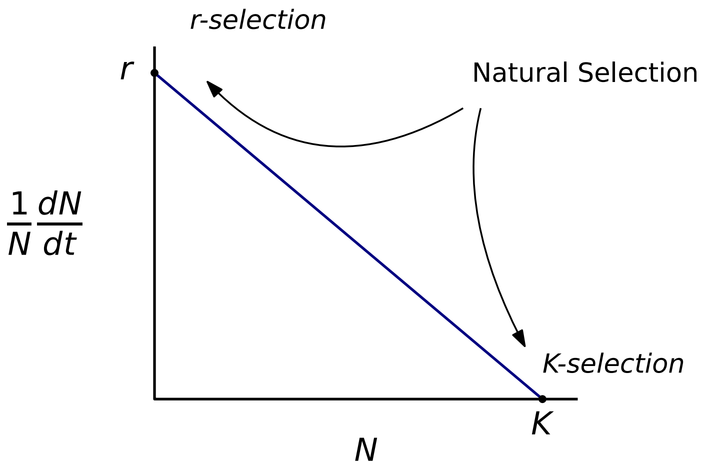
...not so good



…there is a theoretical ‘**but**’ to this too**:**

$$\begin{aligned} \text{population size} &= K \\ &= \#\text{cells} \\ &= \#\frac{\text{cells}}{\text{sugar}} \times \text{sugar} \\ &= c \times S \\ &= \text{efficiency} \times \text{sugar} \end{aligned}$$





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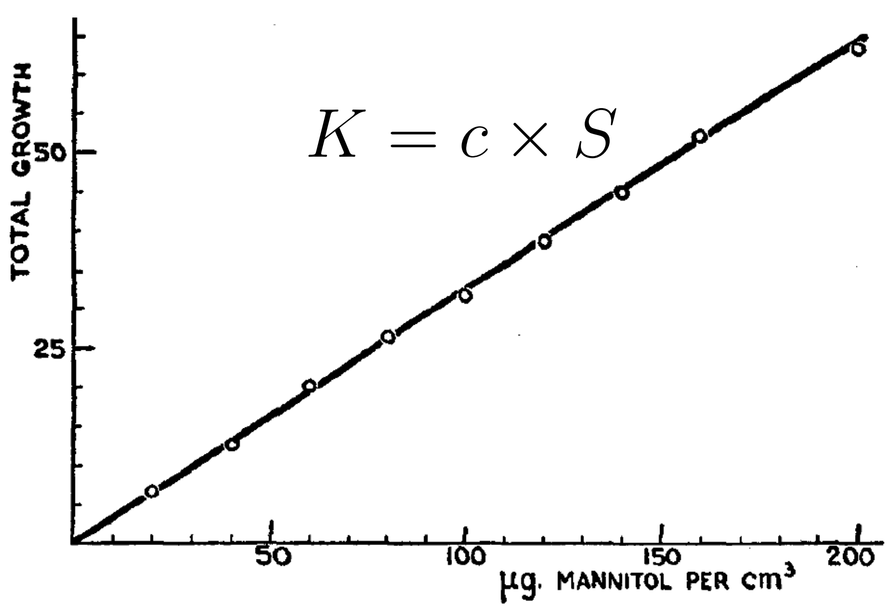
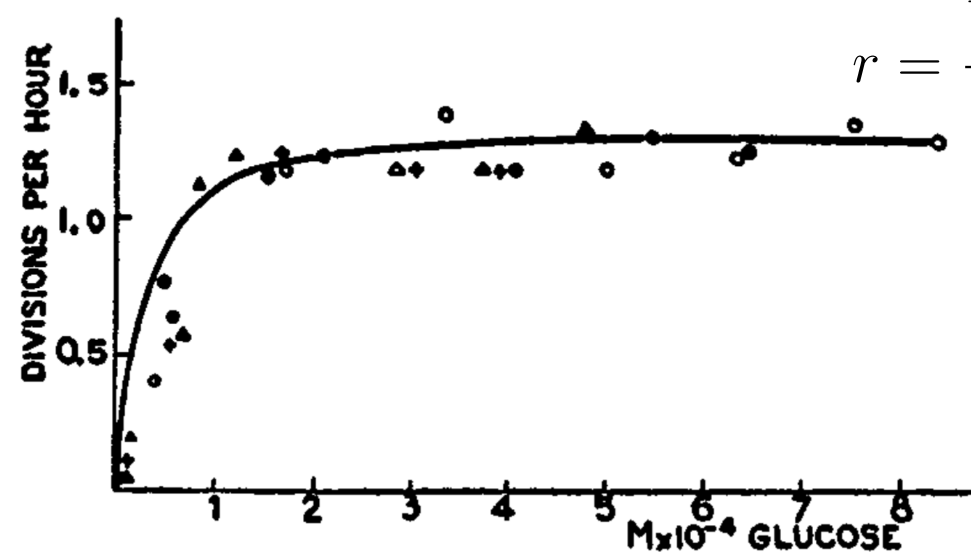


$$K = c \times S$$

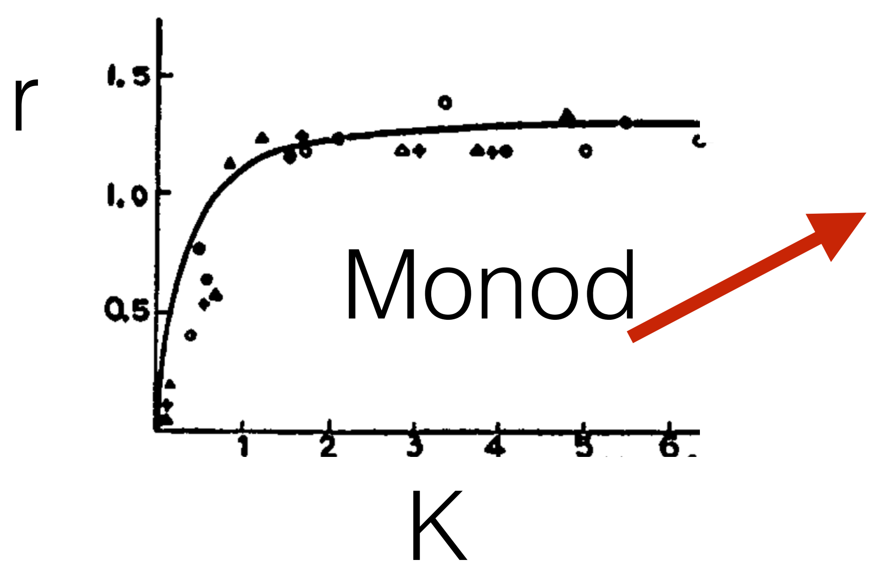
$$
\begin{aligned}
\text{growth rate} &= r = r_{\max}\frac{S}{k+S} \\
\text{max. growth rate} &= h^{-1} \\
&= (\text{sugar}^{\text{out}} \rightarrow \text{sugar}^{\text{in}}) \rightarrow (\text{sugar}^{\text{in}} \rightarrow \text{biomass}) \\
&= (\text{sugar} \cdot \text{cell}^{-1}\text{h}^{-1}) \times (\text{sugar}^{-1}\text{cell}) \\
&= \frac{V_{\max}S}{k+S} \times \text{efficiency}
\end{aligned}
$$



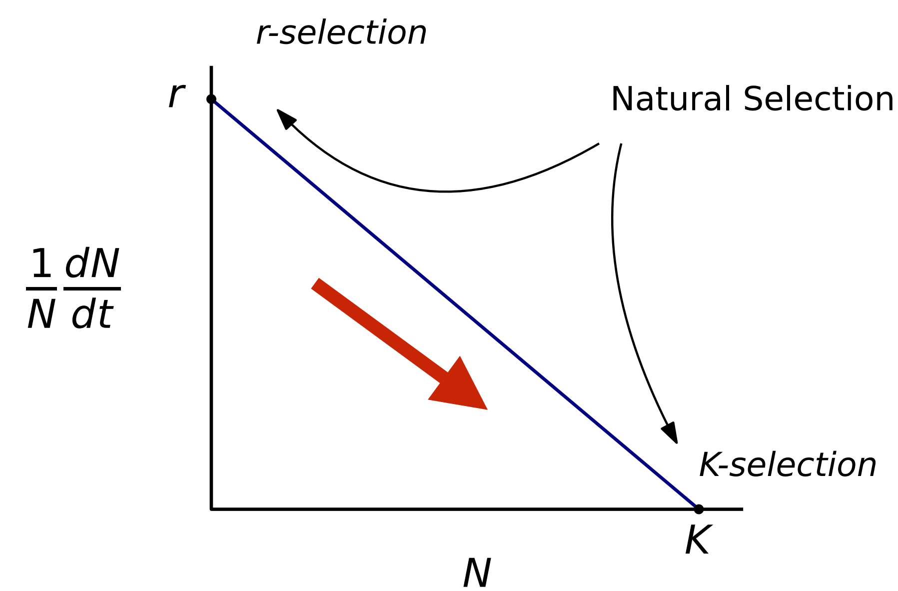
$$r = \frac{V_{\max}S}{k+S} \times c$$

the theory ‘**but**’:

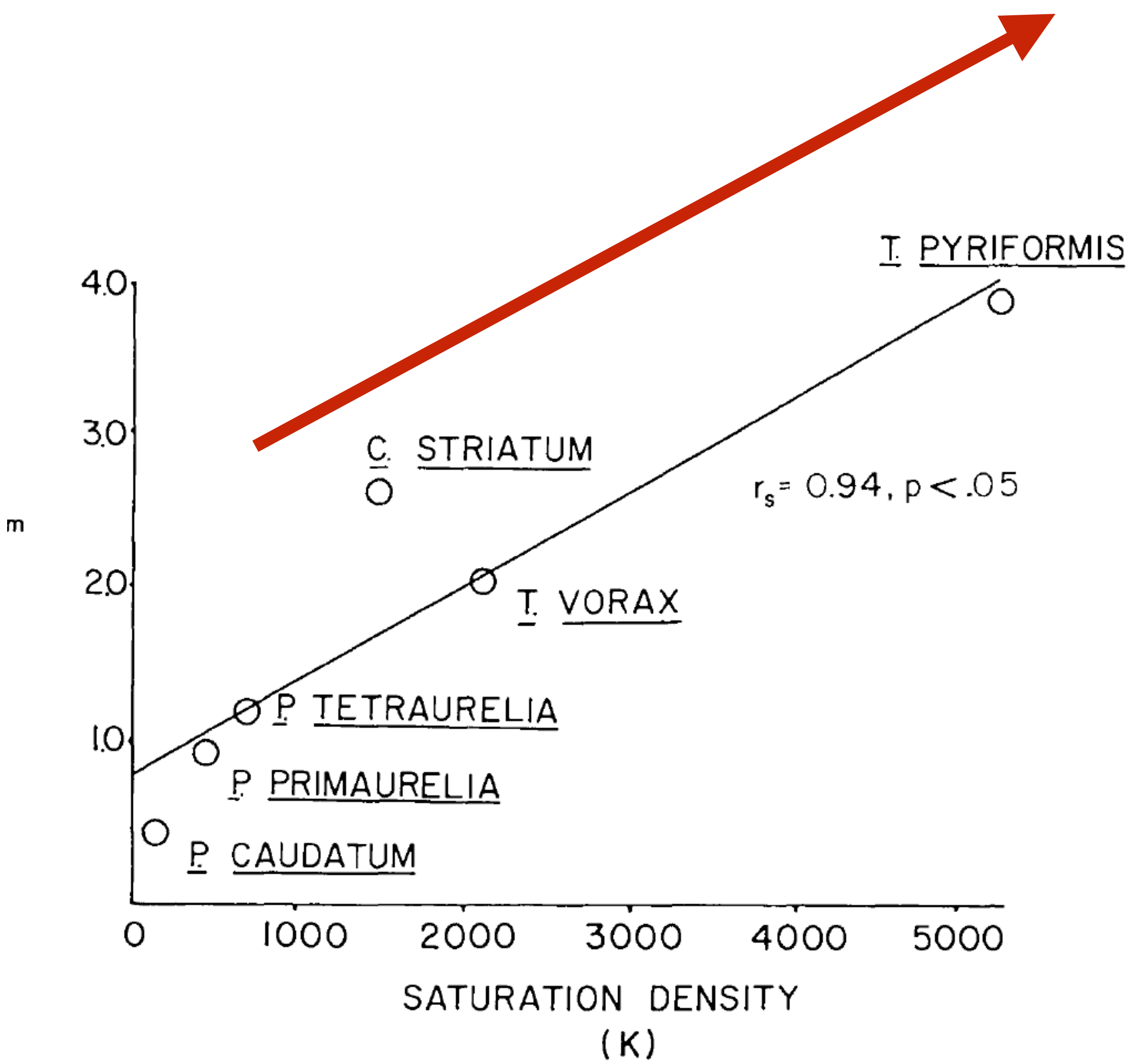
$$K = c \times S \qquad r = \frac{V_{\max} S}{k + S} \times c \qquad \Longrightarrow r(K) = \frac{V_{\max} K}{kc + K}$$



$\neq$

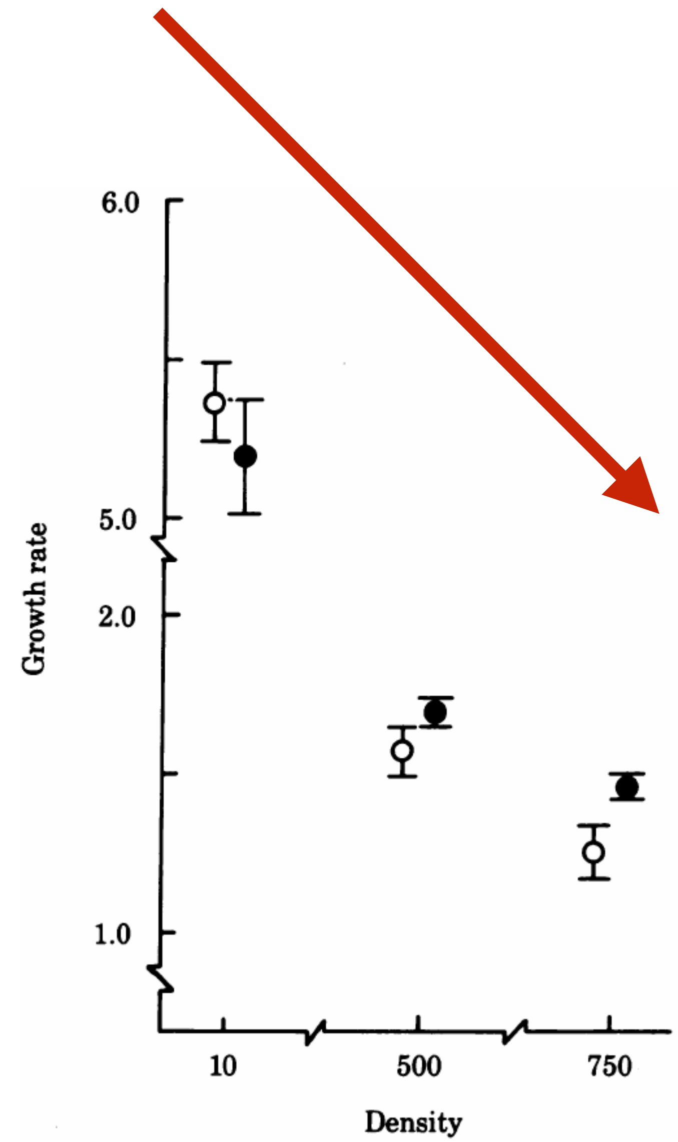


recall the data ‘**but**’:



Luckinbill (1979)

≠



Mueller and Ayala (1980)

We need to unify all this…

Let's start by getting clean data on r and K:

"We conclude that **under circumstances of carbon limitation the cells have formed translation machinery during the slow growth which is not used to maximum efficiency**, but is rapidly converted to maximum efficiency when the environment is enriched." — Koch, AR and Deppe, CS. *J Mol Biol* **55**, 549–562 (1971).

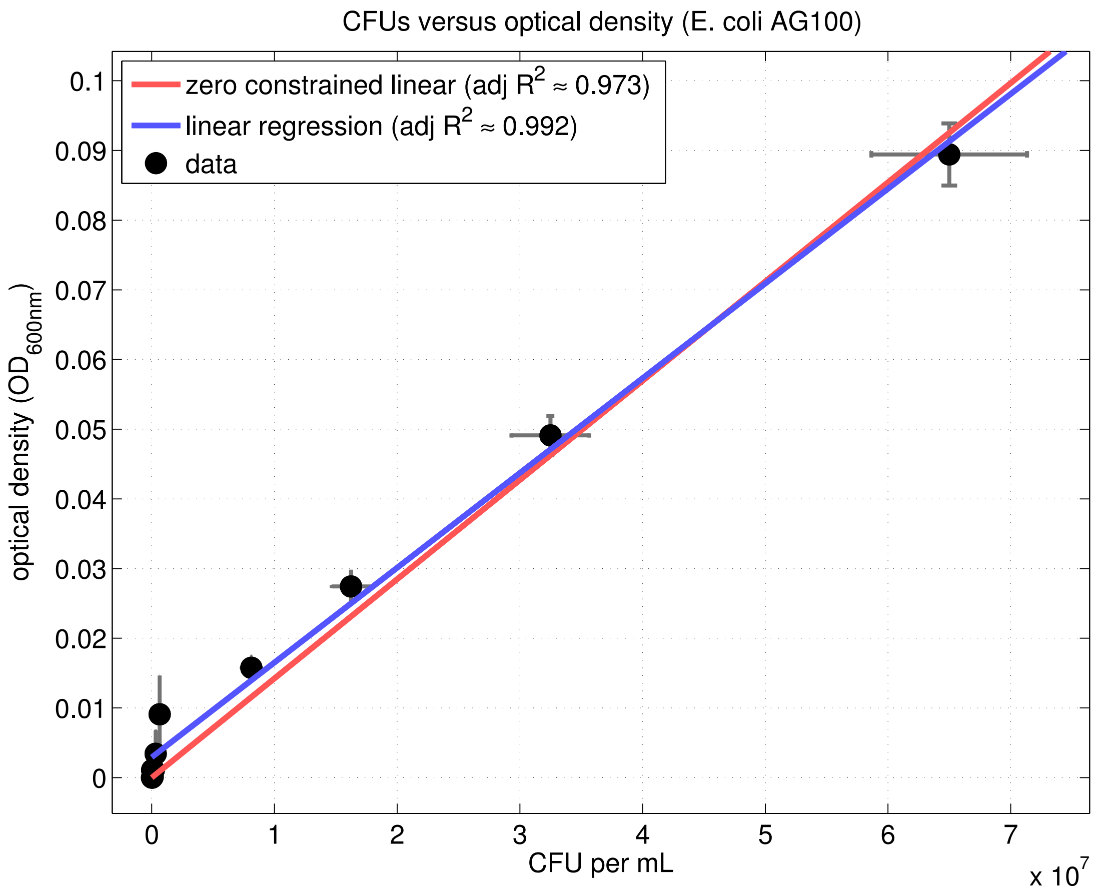
"Inadequate regulation of the expression of additional plasmid-borne rRNA operons in *Escherichia coli* was exaggerated at slow growth rates (...). These observations are consistent with the hypothesis that **multiple rRNA operons constitute a metabolic burden at slow growth rates**." —Stevenson, BS and Schmidt, TM. *J Bacteriol* **180**(7), 1970–1972 (1998)

So, manipulating rrn operon # should affect **r** & **efficiency**:

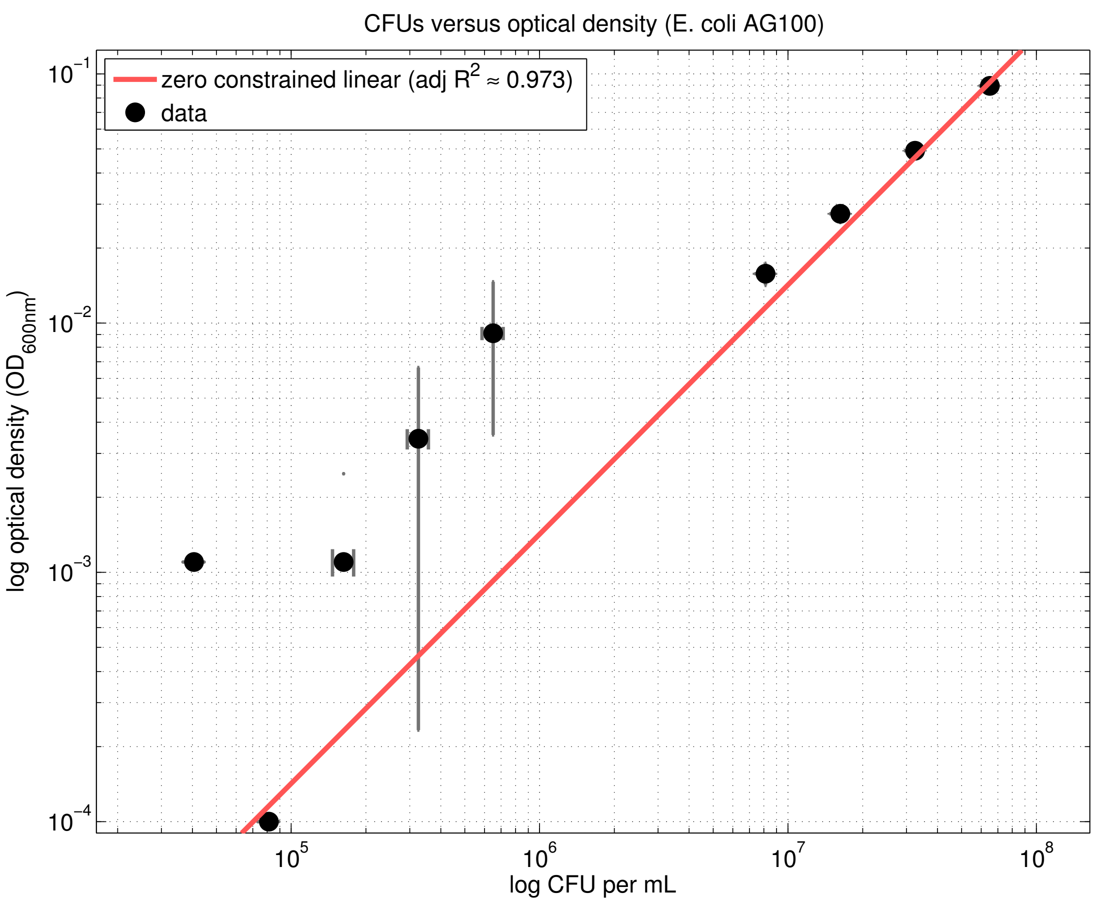
Nonoptimal Microbial Response to Antibiotics Underlies Suppressive Drug Interactions

Tobias Bollenbach,[1] Selwyn Quan,[3] Remy Chait,[1] and Roy Kishony[1,2,*]
[1]Department of Systems Biology, Harvard Medical School, 200 Longwood Avenue, Boston, MA 02115, USA
[2]School of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138, USA
[3]Department of Chemical and Systems Biology, Stanford University, 318 Campus Drive, Stanford, CA 94305, USA
*Correspondence: roy_kishony@hms.harvard.edu
DOI 10.1016/j.cell.2009.10.025

A decent enough proxy: OD ~ cells per ml



(a)

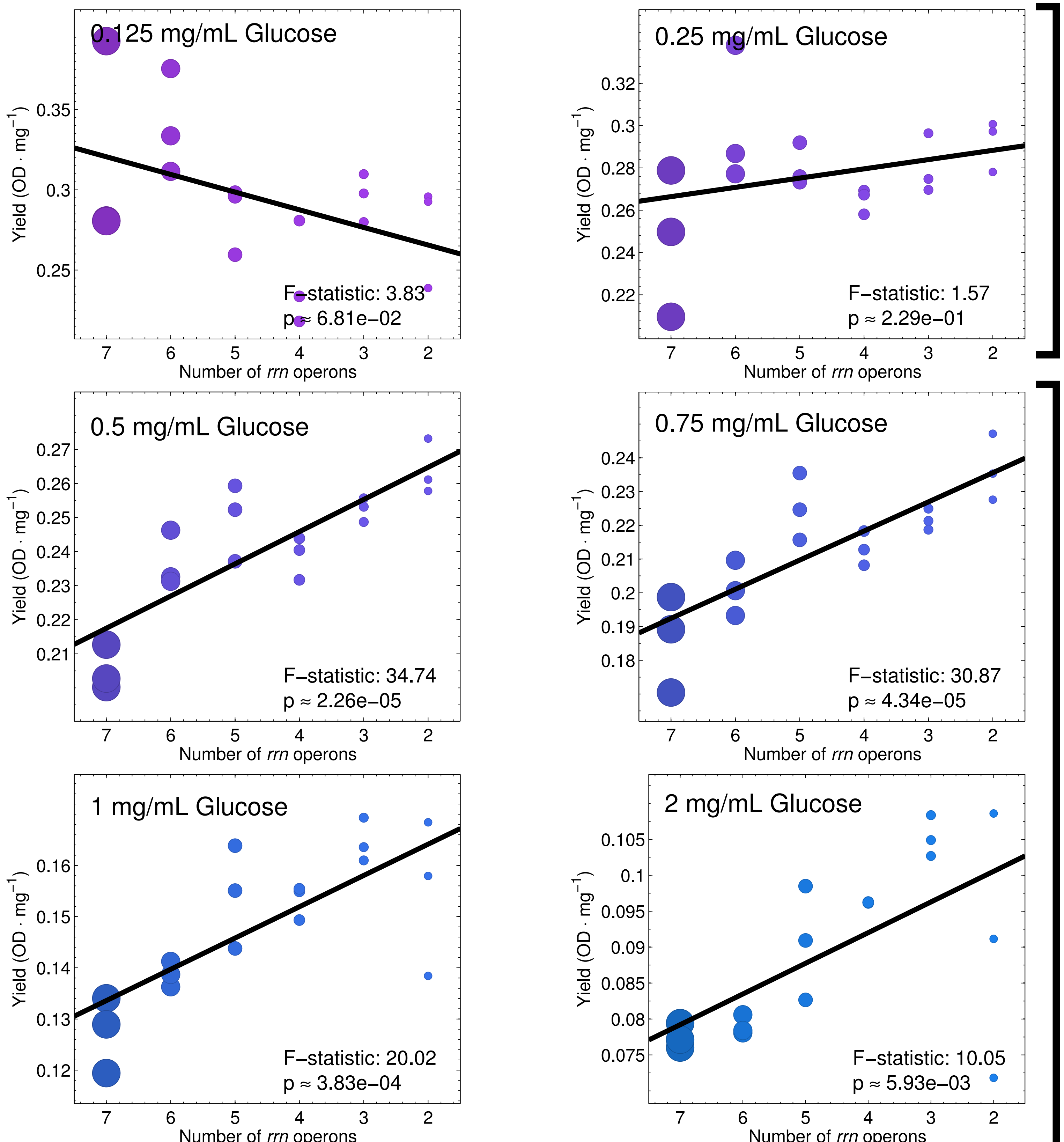


(b)

rrn operon # affects efficiency:

= biomass **yield**

biomass yield



not significant

significant

As K ~ efficiency **x** sugar, we can change glucose & rrn operon # to manipulate **r** and **K** together, voila!… **:**

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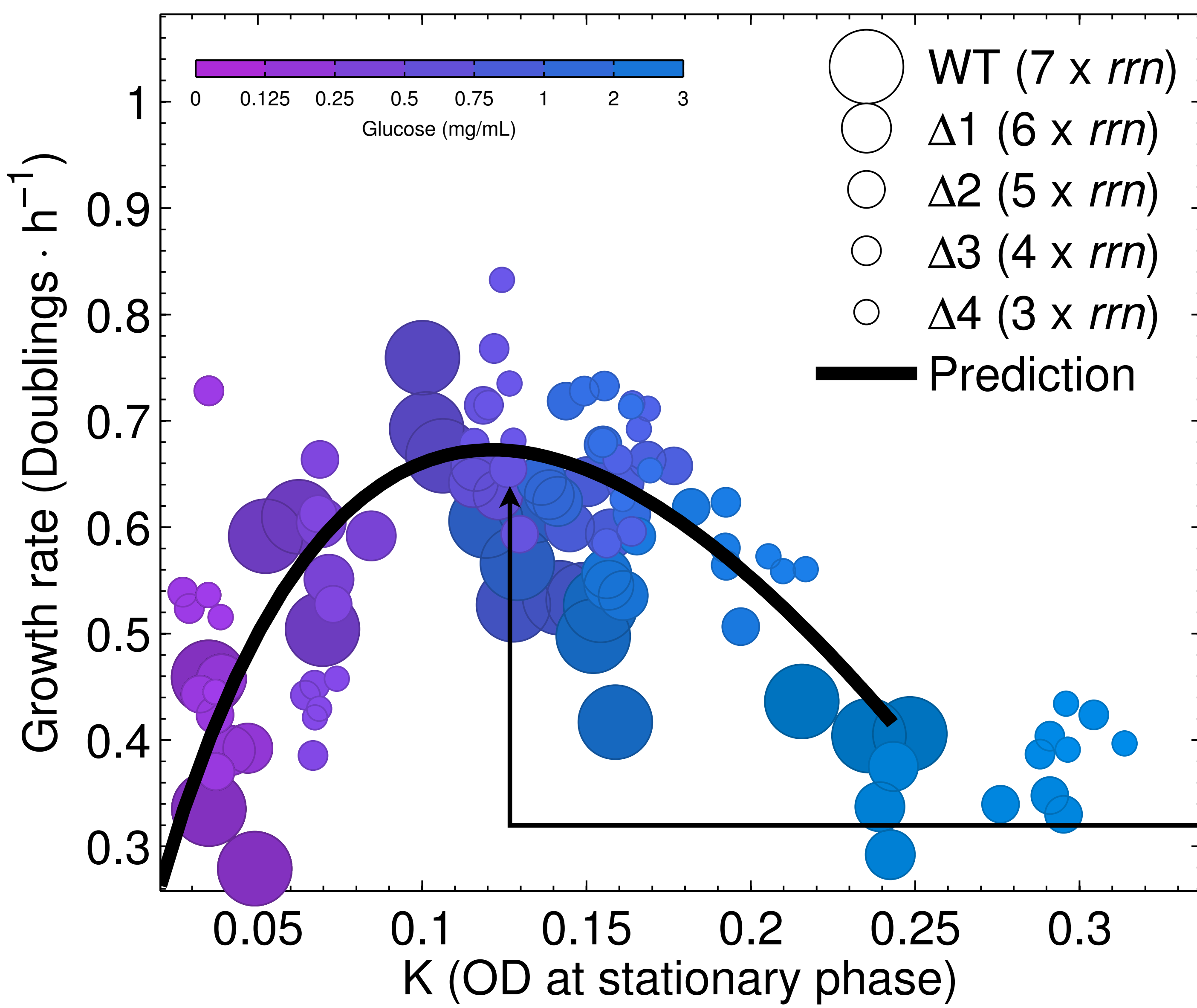
data in M9 + glucose



similar optimal r for similar K
@ different rrn # and different Glu

As K ~ efficiency **x** sugar, we can change glucose & rrn operon # to manipulate **r** and **K** together, voila!… **:**

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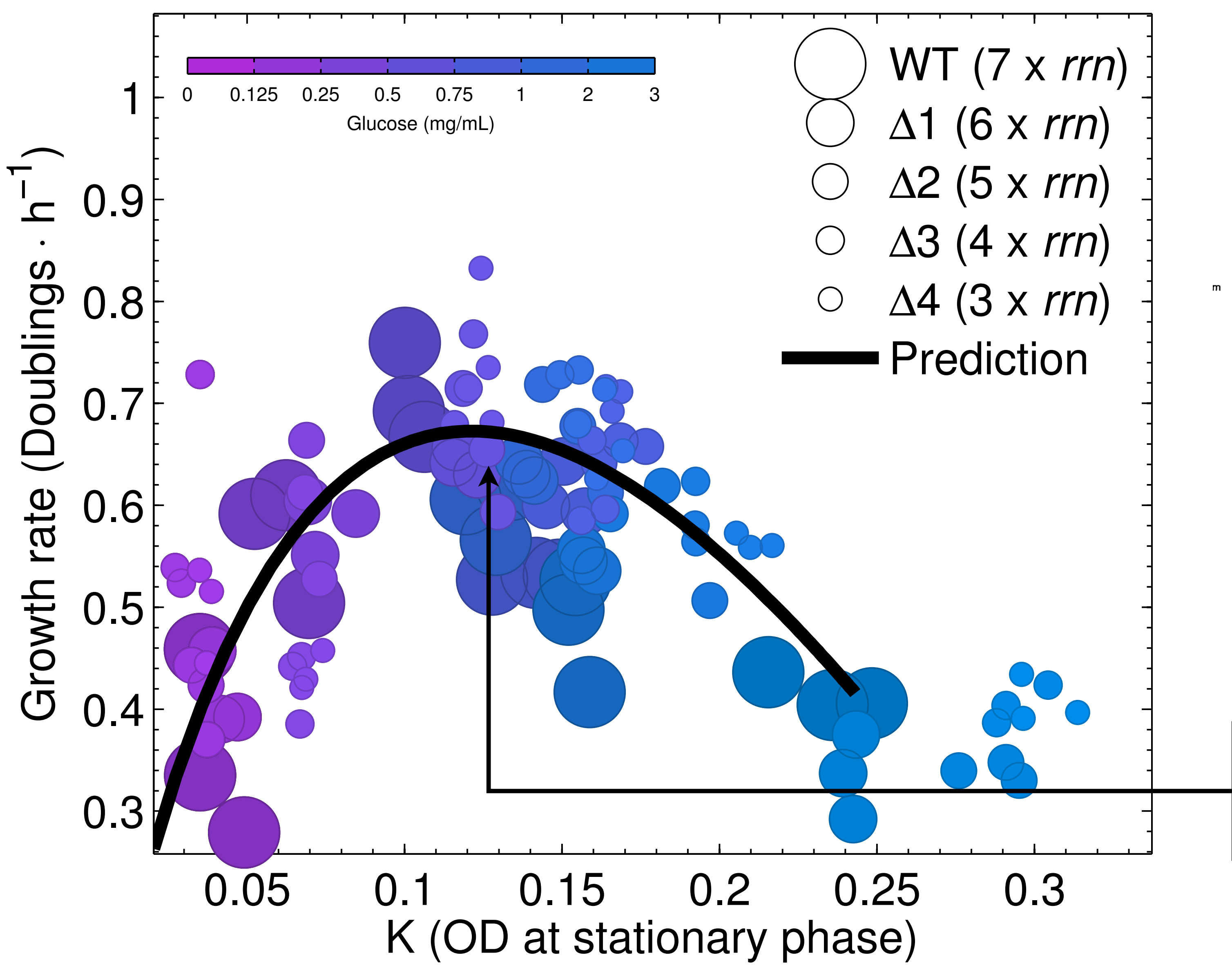
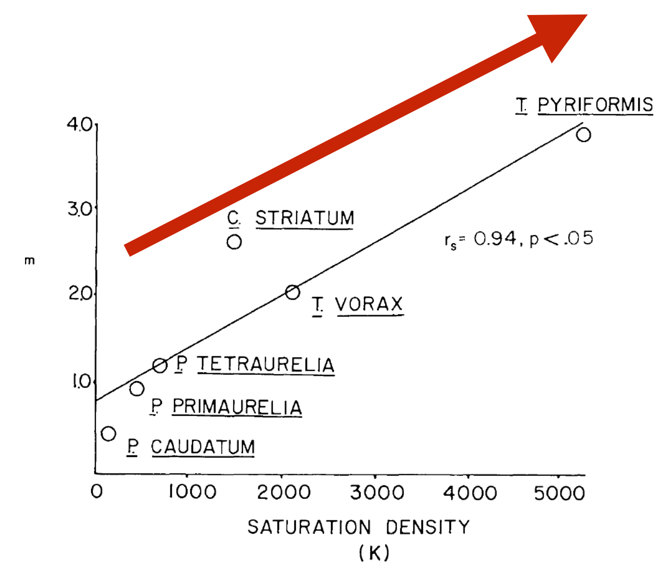
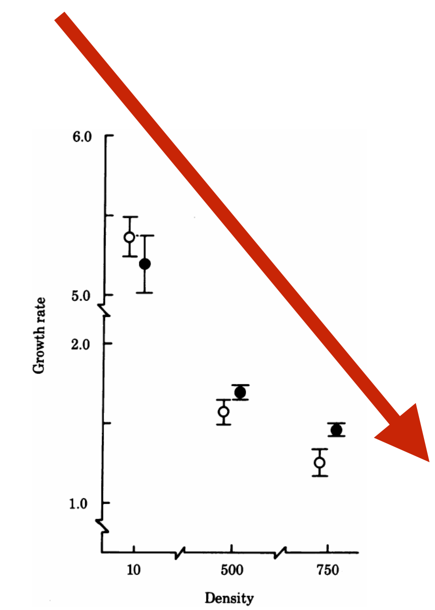




Luckinbill (1979)



Mueller and Ayala (1980)

similar optimal r for similar K
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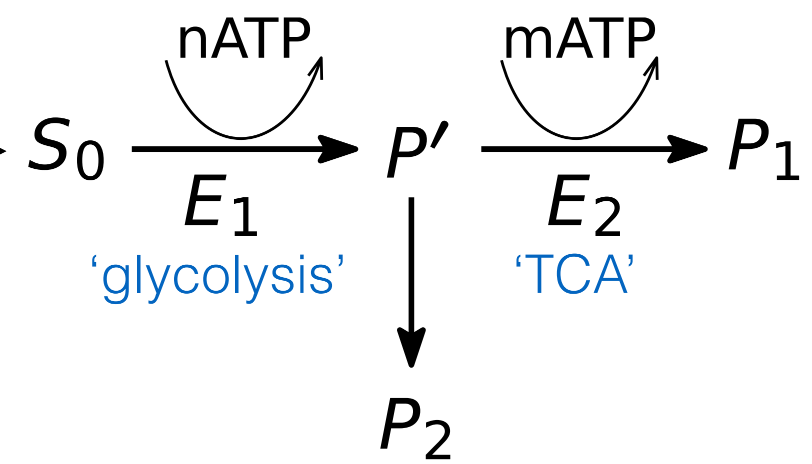
This 'unifies' prior data, now for the theory…

$$\begin{aligned}
\text{population size} &= K \\
&= \#\text{cells} \\
&= \#\frac{\text{cells}}{\text{sugar}} \times \text{sugar} \\
&= \#\frac{\text{cells}}{\text{ATP}} \times \frac{\text{ATP}}{\text{sugar}} \times \text{sugar} \\
&= c(A) \times A(S) \times S \\
&= \text{efficiency}(\text{sugar}) \times \text{sugar} \\
&= c(S) \times S
\end{aligned}$$



Efficient $= c_{hi} = nATP + mATP$ Inefficient $= c_{lo} = nATP$

$$\Downarrow$$

RYTO: $$c(S) = c_{\text{hi}} \frac{1}{1 + p \cdot S} + c_{\text{lo}} \frac{S}{1 + p \cdot S}$$ + Monod…

4-parameter Monod-like model:

$$r(S) = \frac{V_{\max} S}{k + S} \times c(S) \quad \& \quad K = c(S) \times S$$

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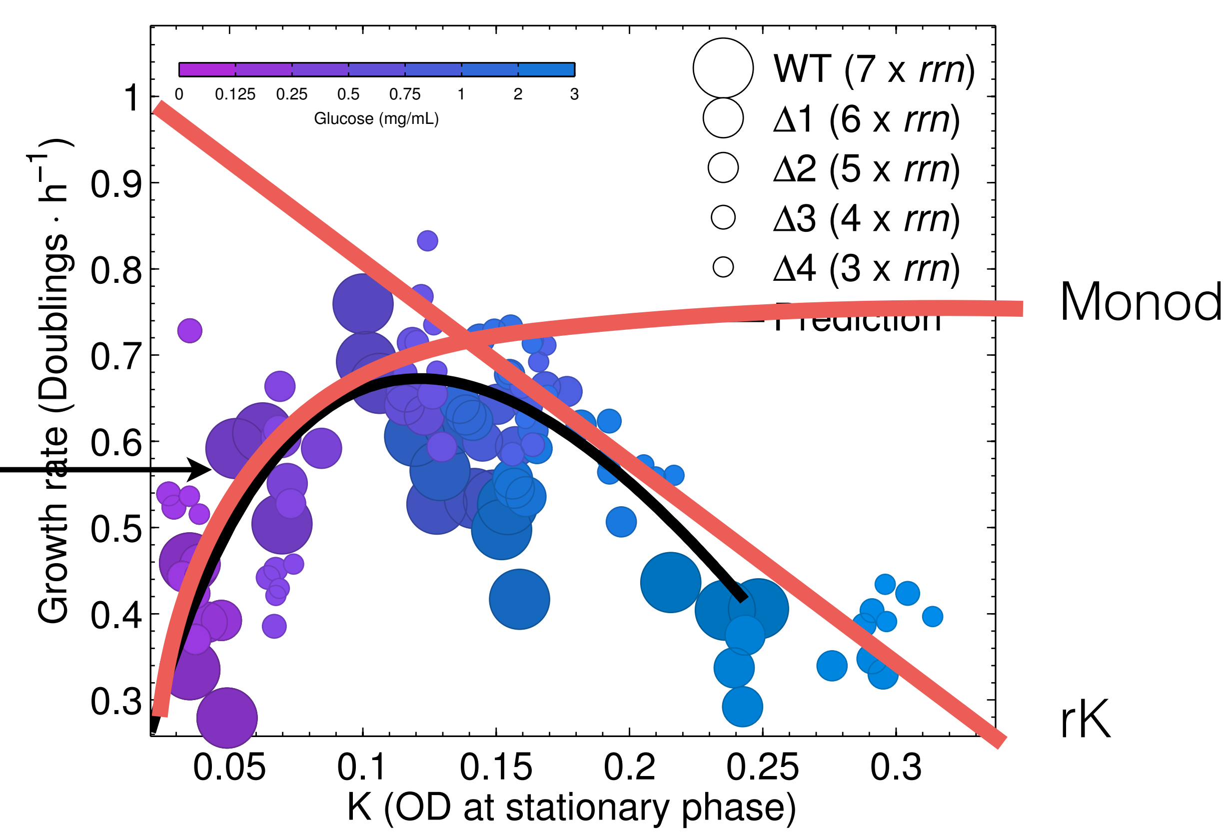
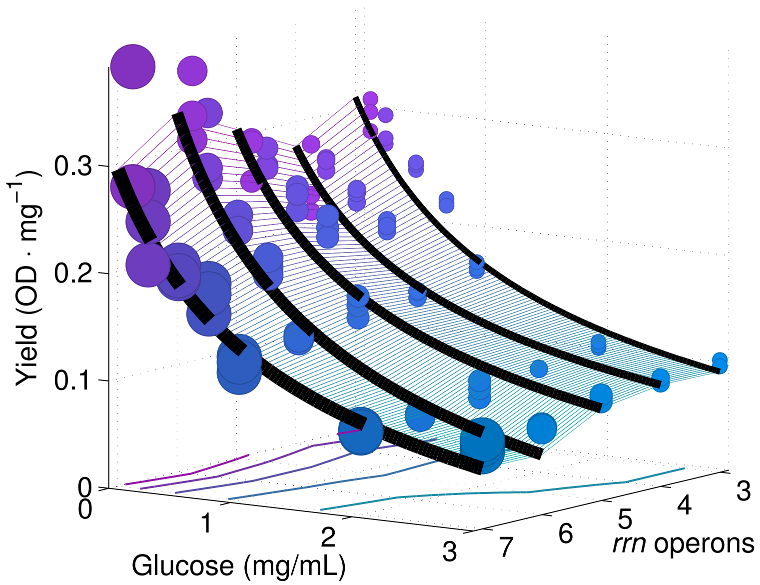
where $$c(S) = c_{\text{hi}} \frac{1}{1 + p \cdot S} + c_{\text{lo}} \frac{S}{1 + p \cdot S}$$

MLE prediction from
a training dataset



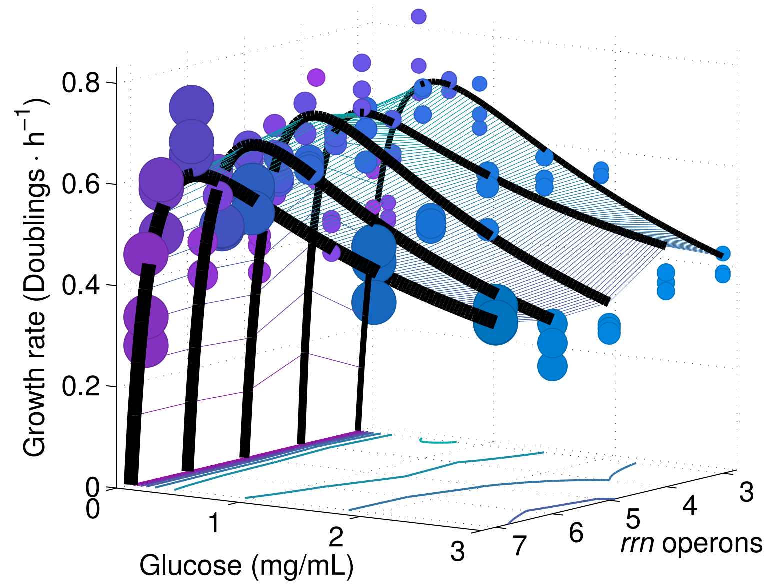
within-strain rate-yield TOs:

$$c(S) = c_{\mathrm{hi}} \frac{1}{1 + p \cdot S} + c_{\mathrm{lo}} \frac{S}{1 + p \cdot S}$$



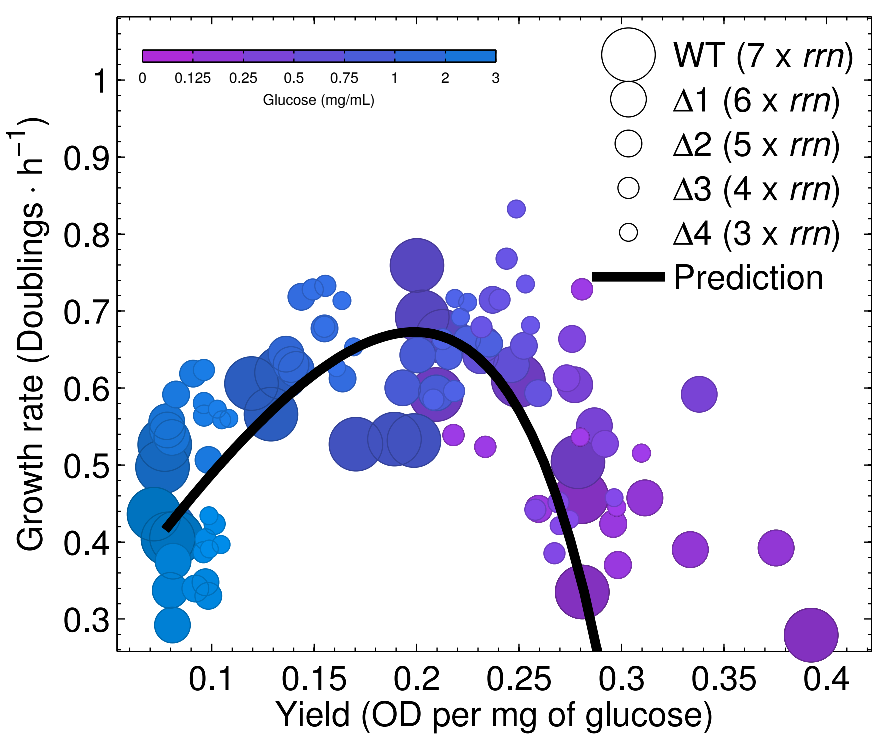
…gives optimal growth rate…

$$r(S) = \frac{V_{\mathrm{max}} S}{k + S} \times c(S)$$

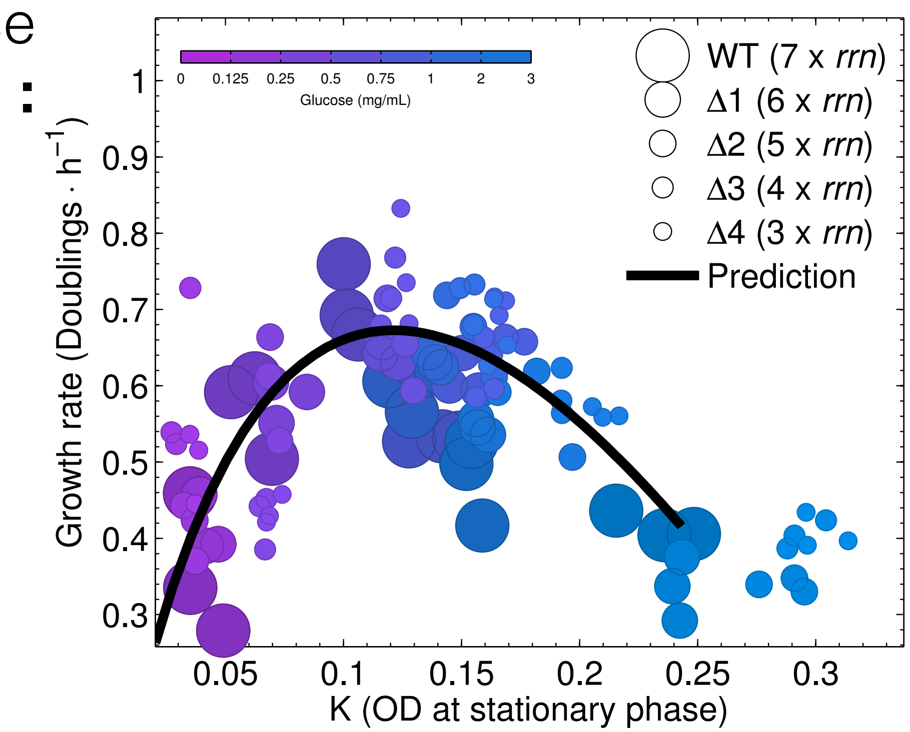


we see a within-strain RYTO in **every** microbial species and this, added to Monod, creates the ‘rK parabola’ …

…this gives a rate yield parabola…



…whence rK :



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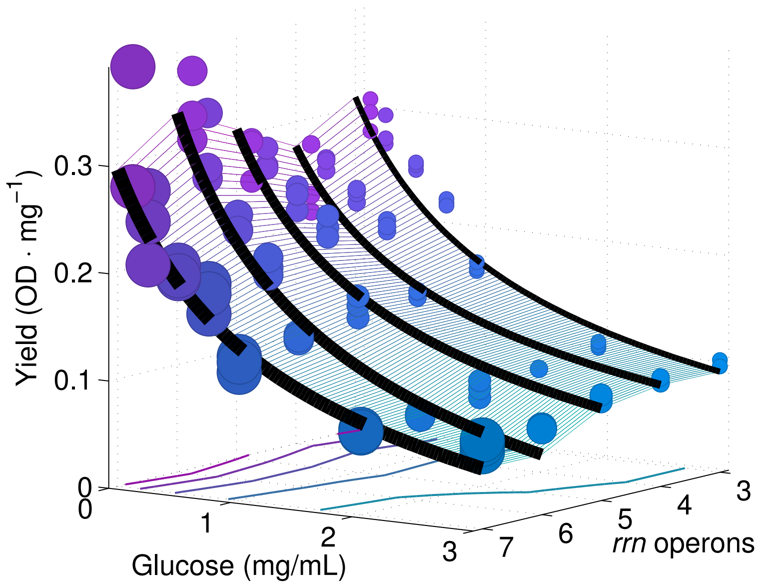

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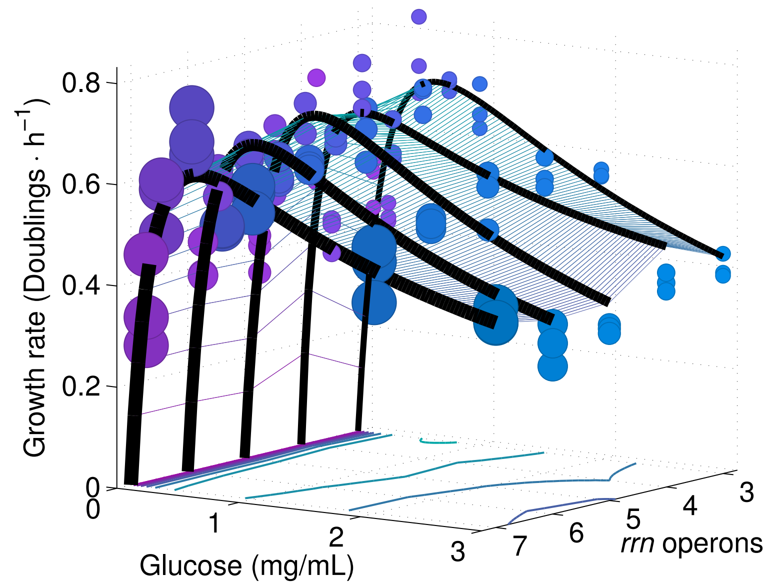

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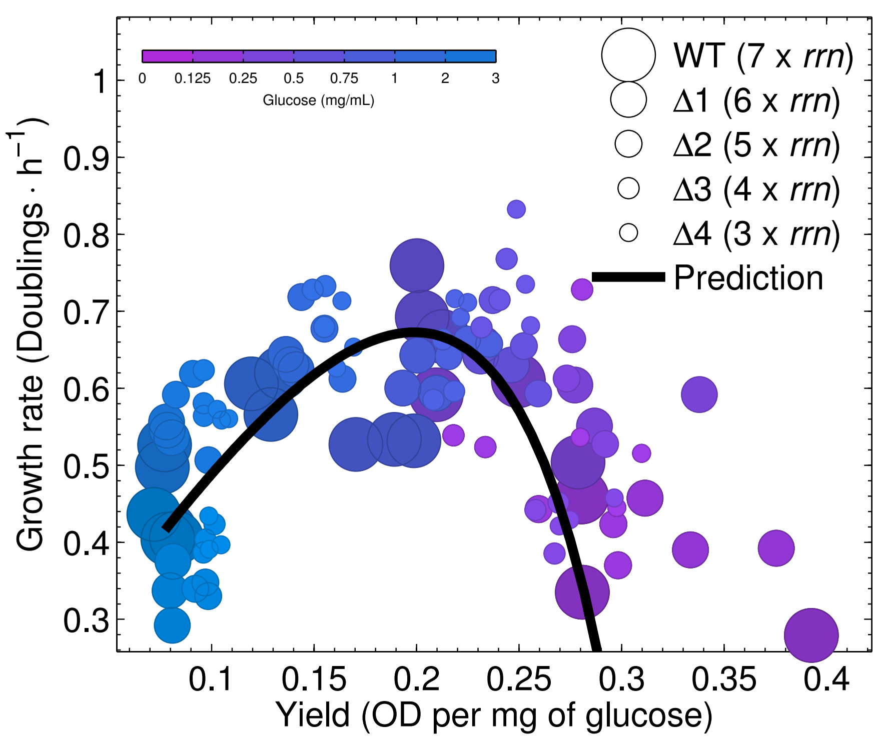

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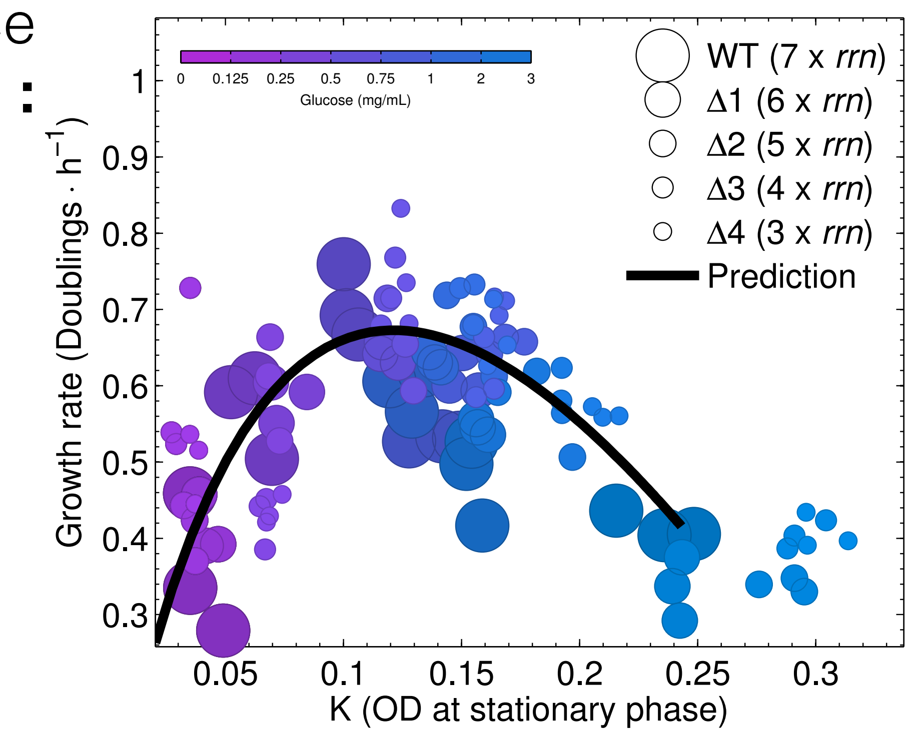

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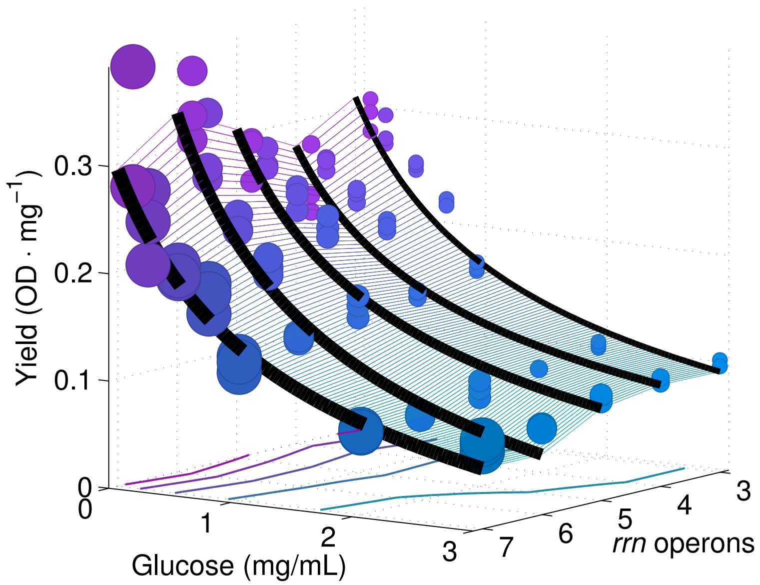

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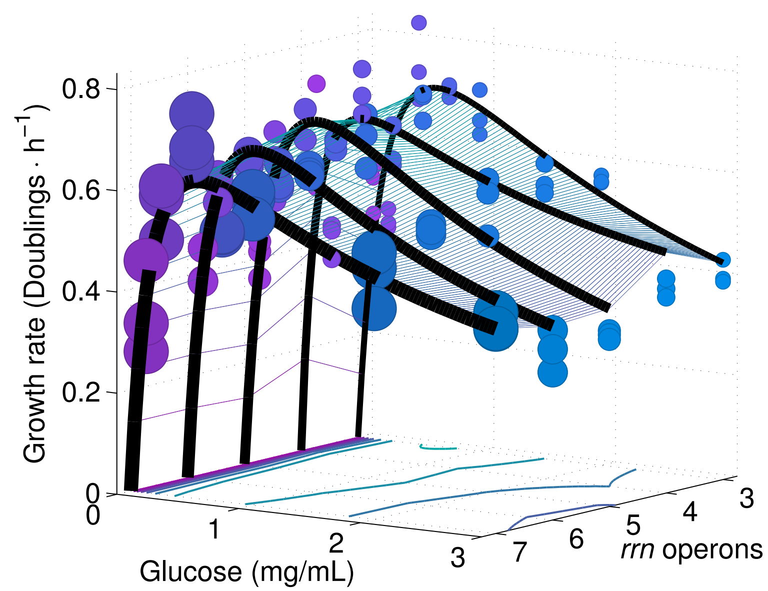

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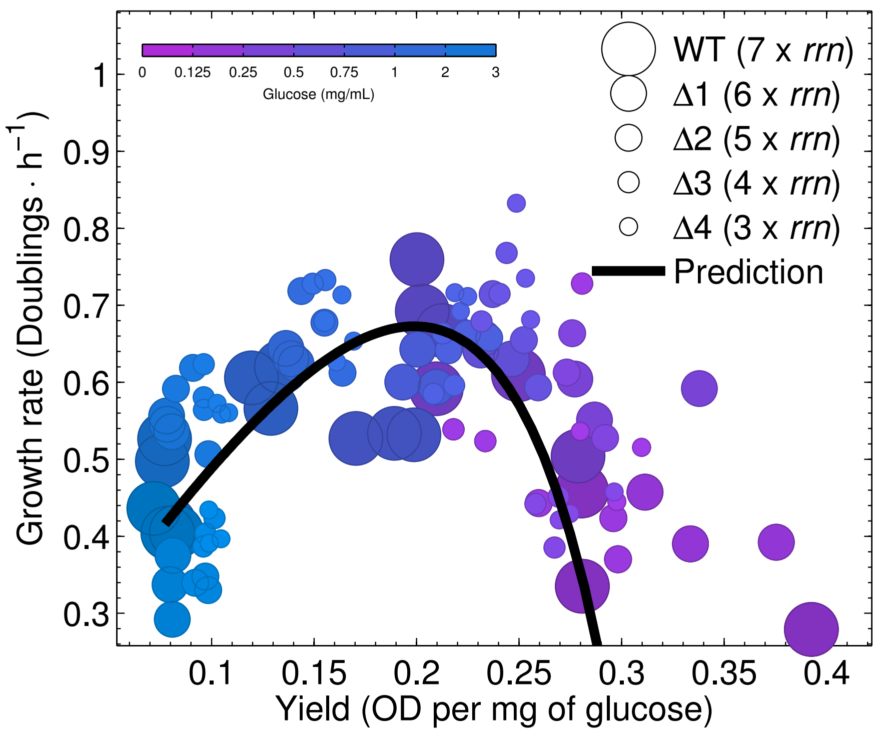

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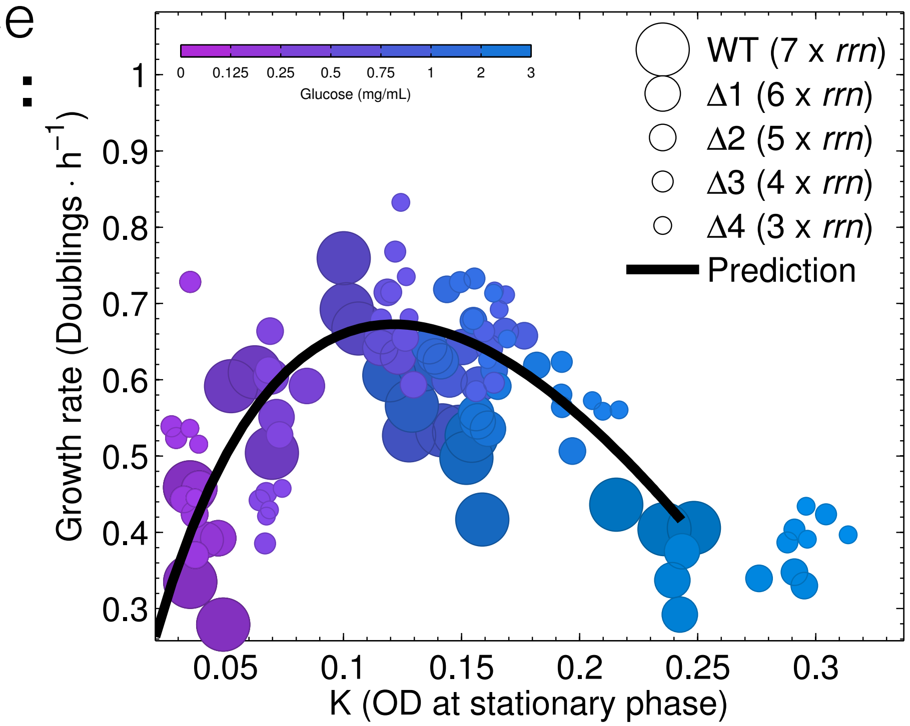

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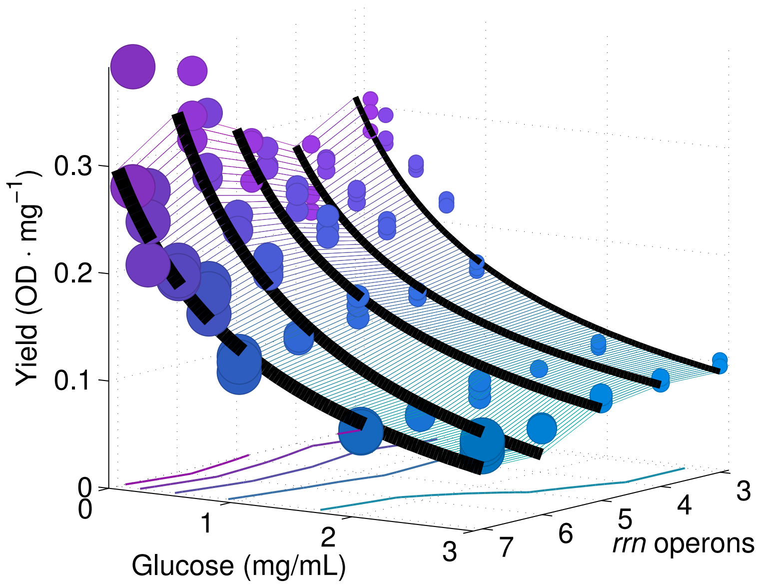

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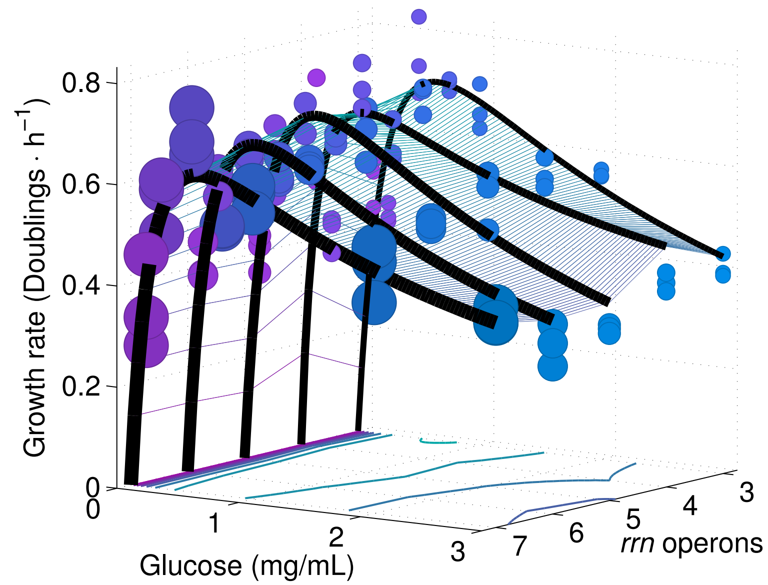

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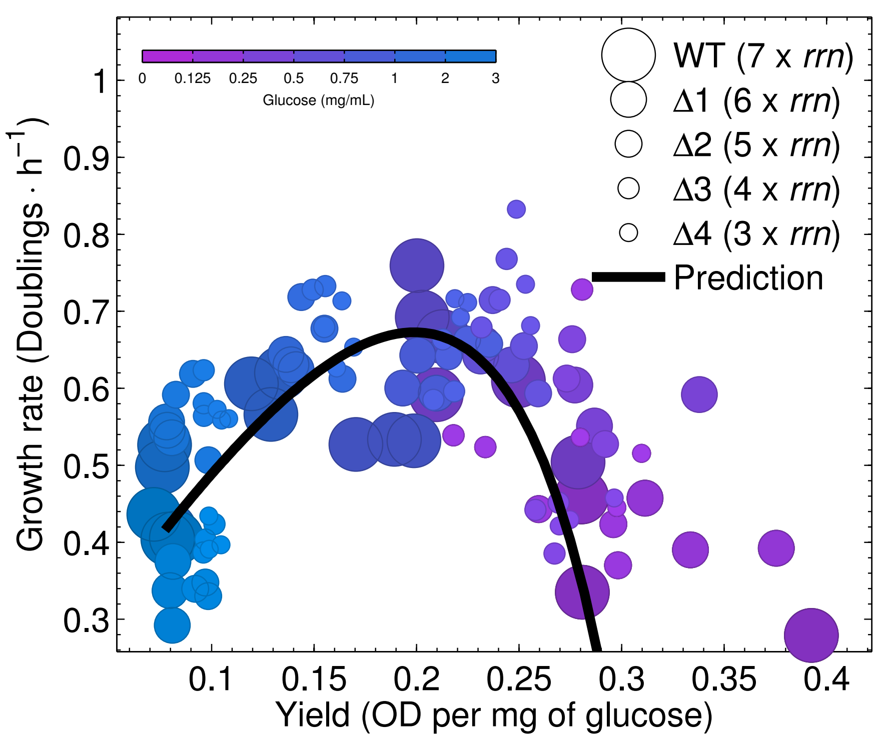

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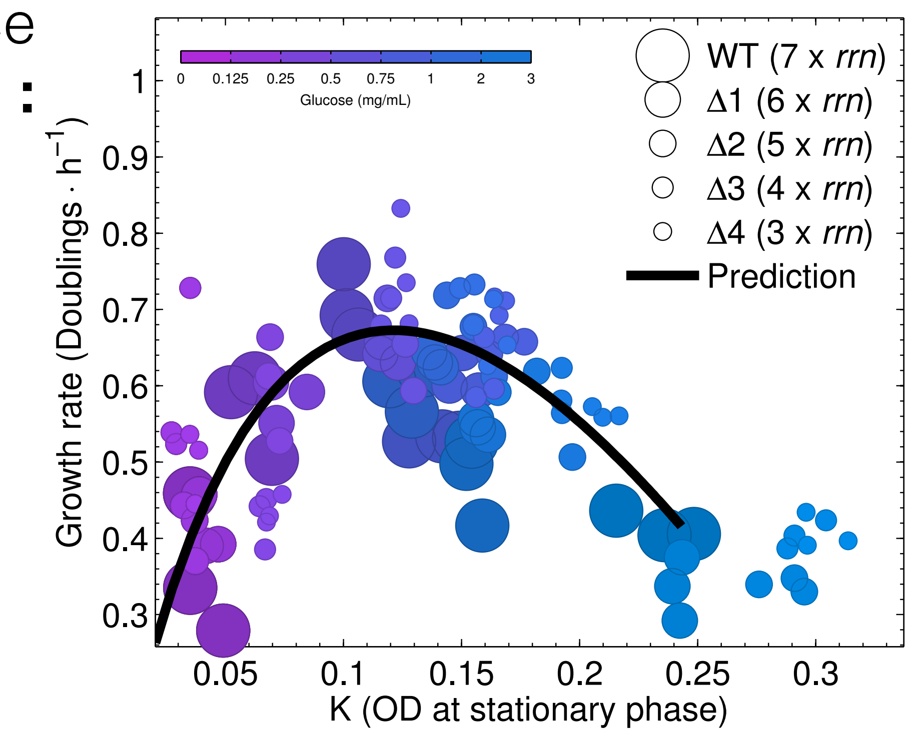

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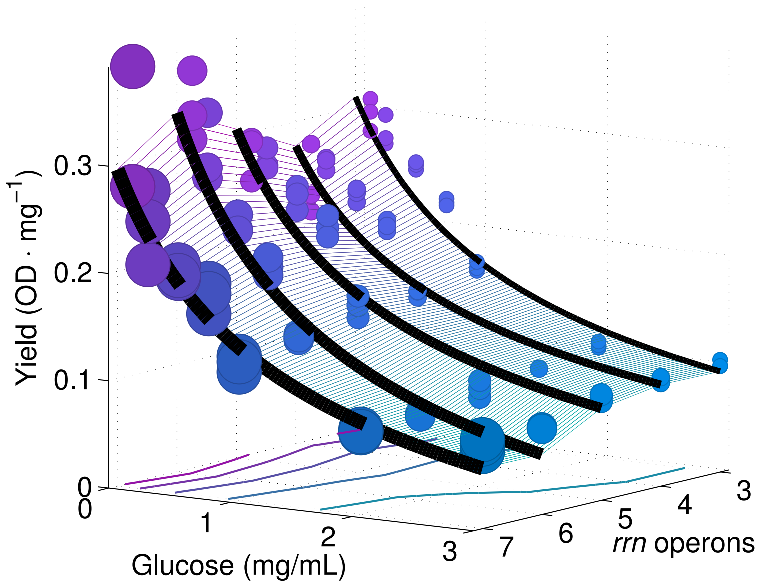

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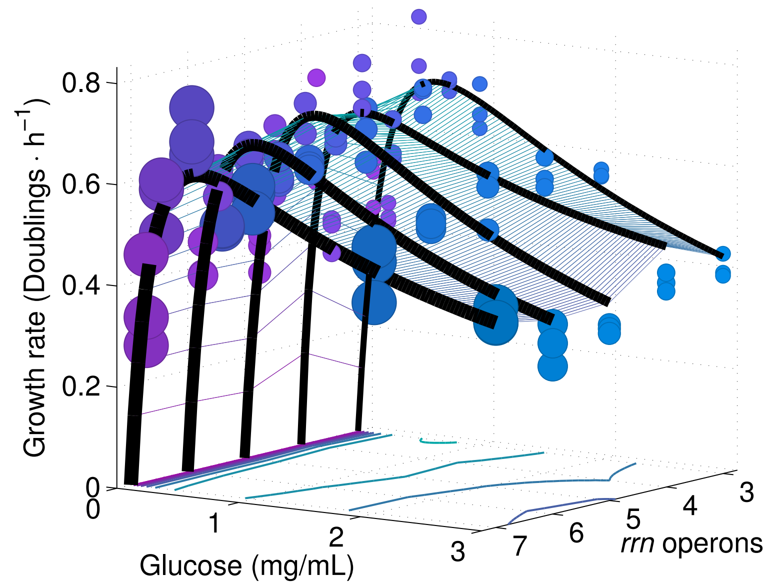

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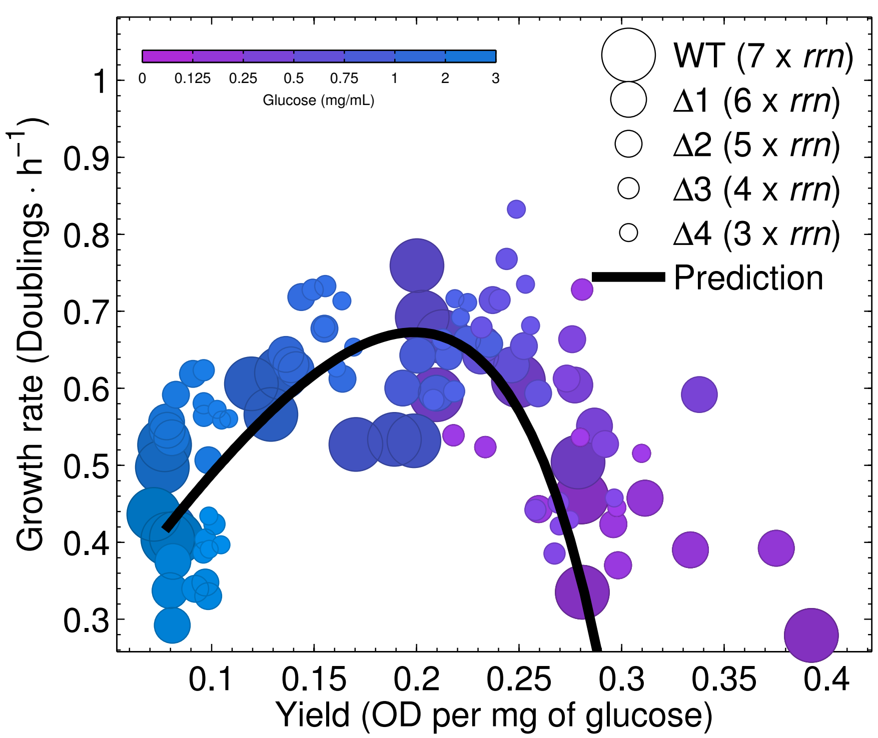

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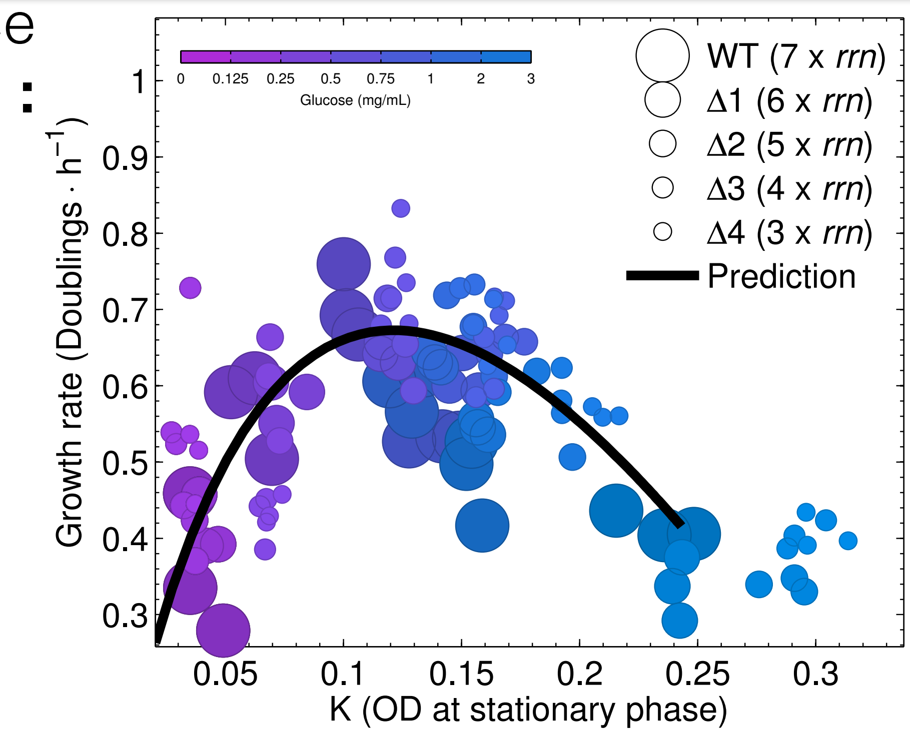
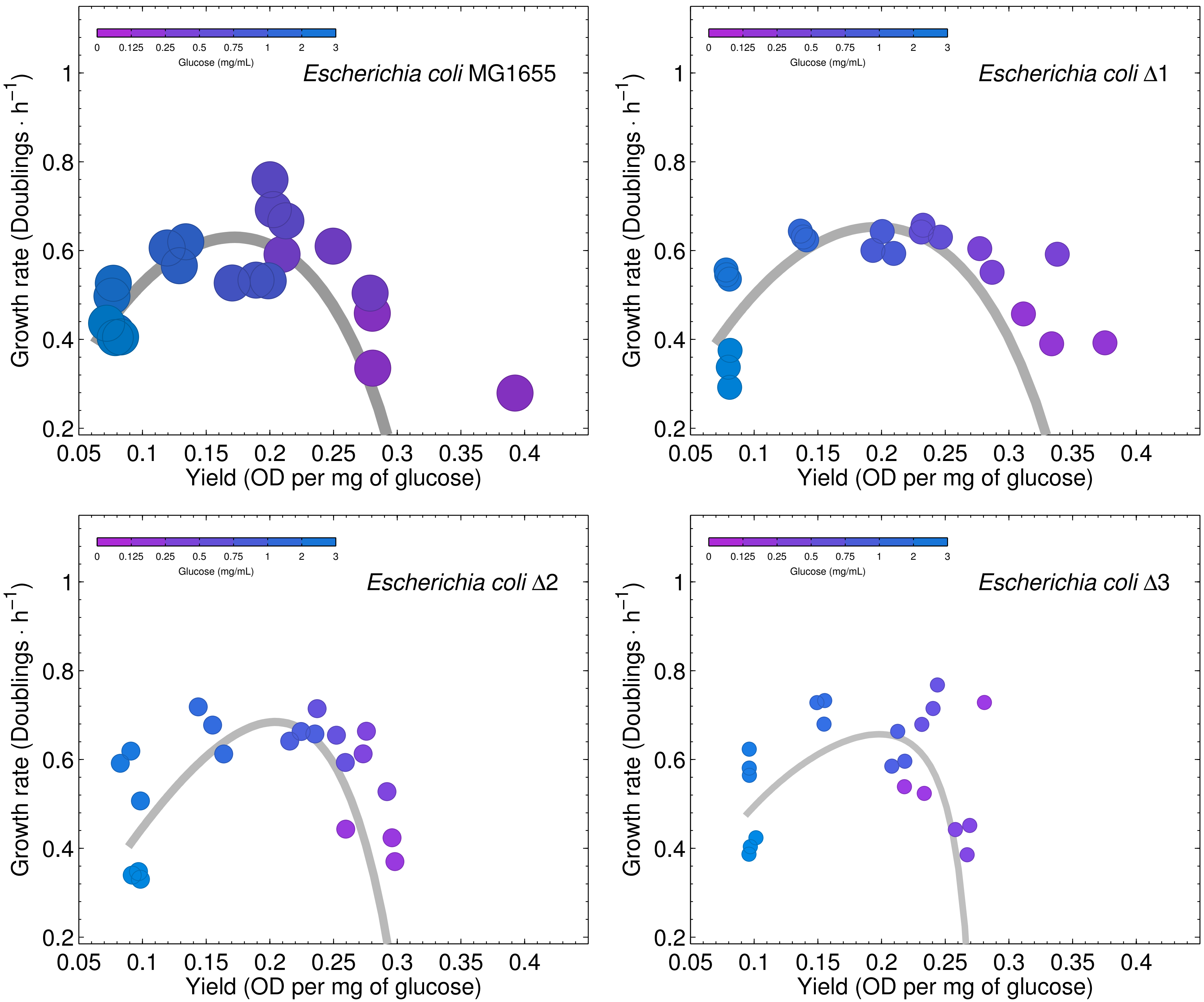
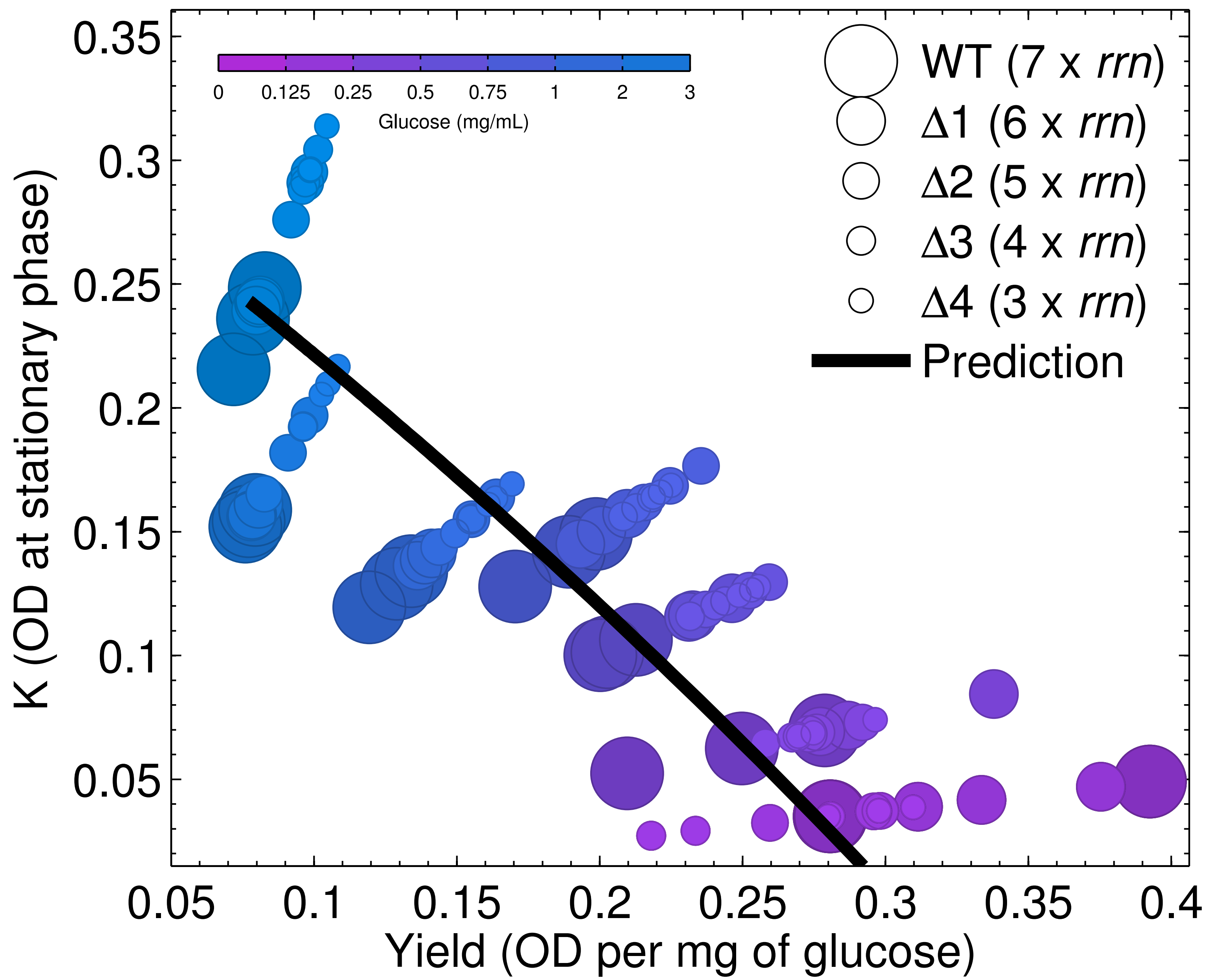
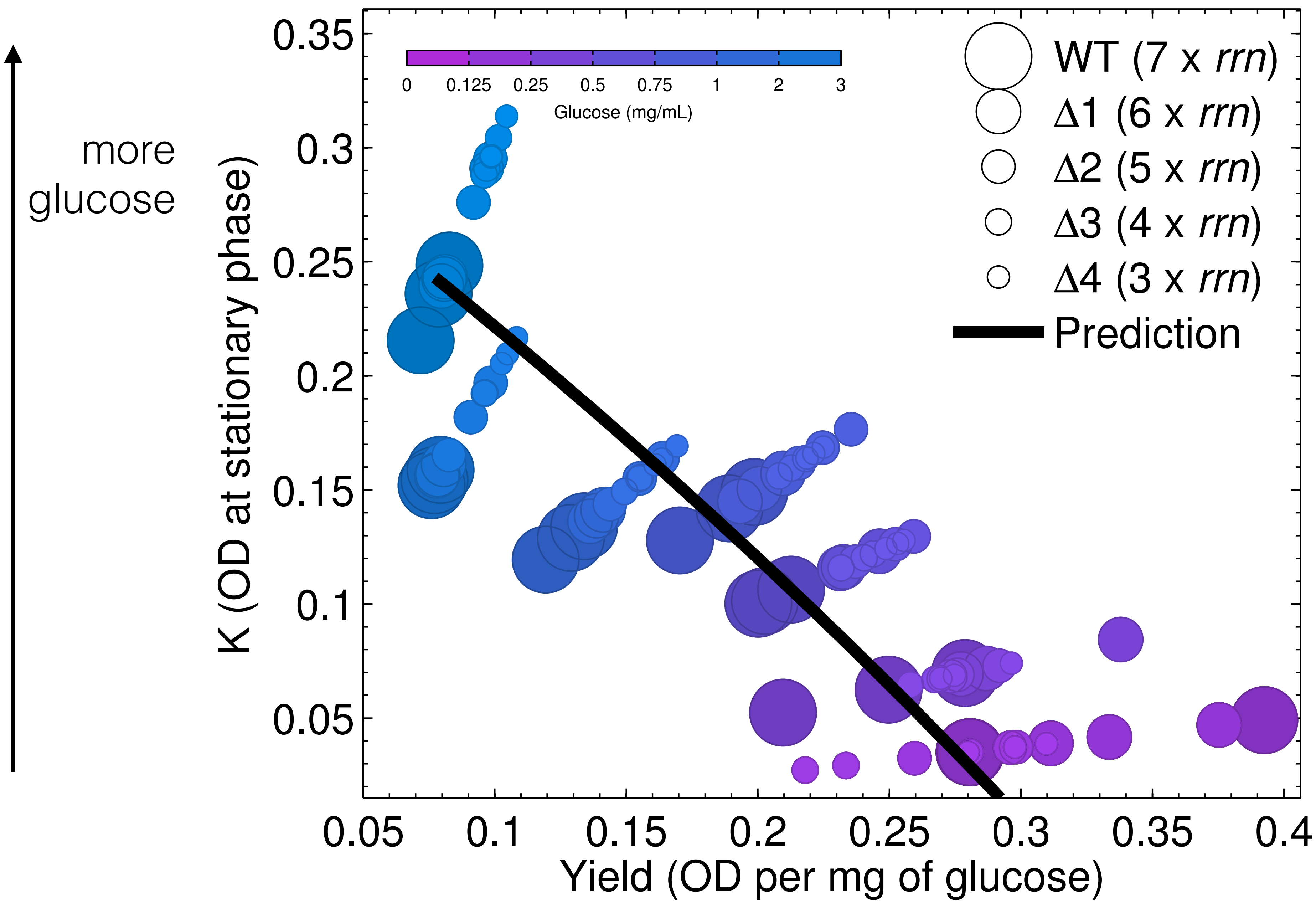


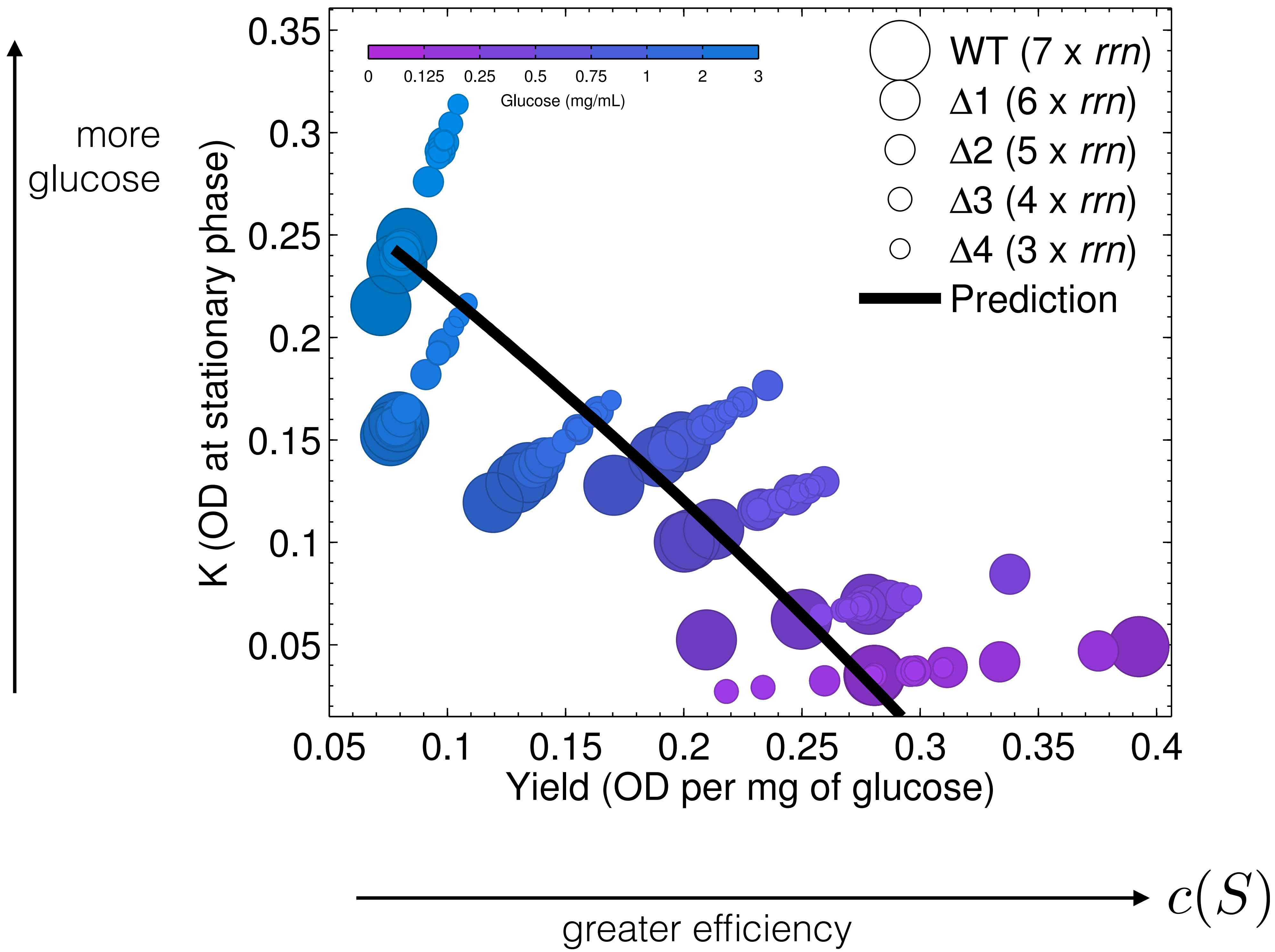
All the strains have a similar RY parabola:



Our Monod-like ‘metabolic model’ misses many features, after all, it contains no info about rrn # … :




more glucose
K (OD at stationary phase)
Yield (OD per mg of glucose)
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0
0.125
0.25
0.5
0.75
1
2
3
Glucose (mg/mL)
WT (7 x *rrn*)
Δ1 (6 x *rrn*)
Δ2 (5 x *rrn*)
Δ3 (4 x *rrn*)
Δ4 (3 x *rrn*)
Prediction



more glucose
K (OD at stationary phase)
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0 0.125 0.25 0.5 0.75 1 2 3
Glucose (mg/mL)
WT (7 x *rrn*)
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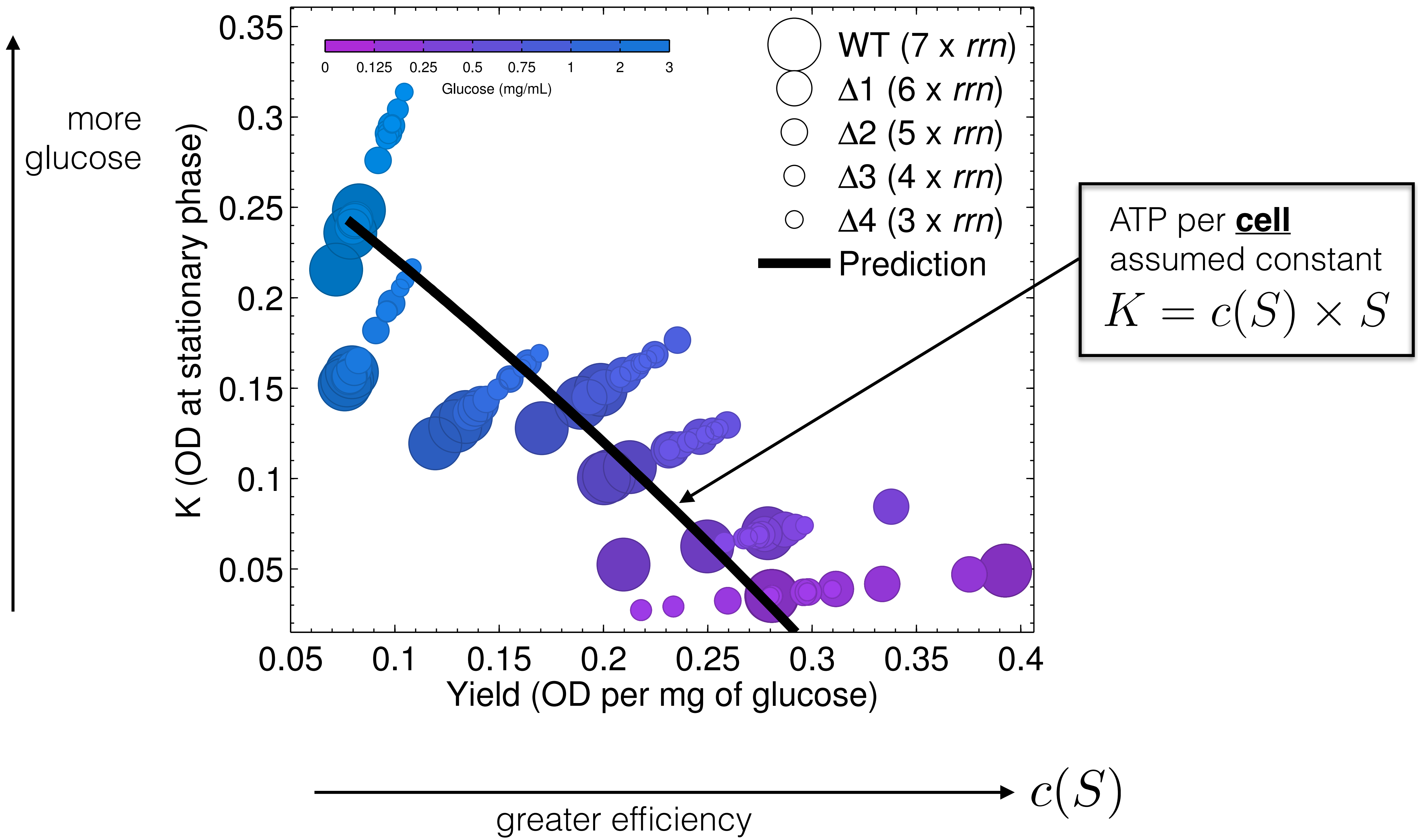
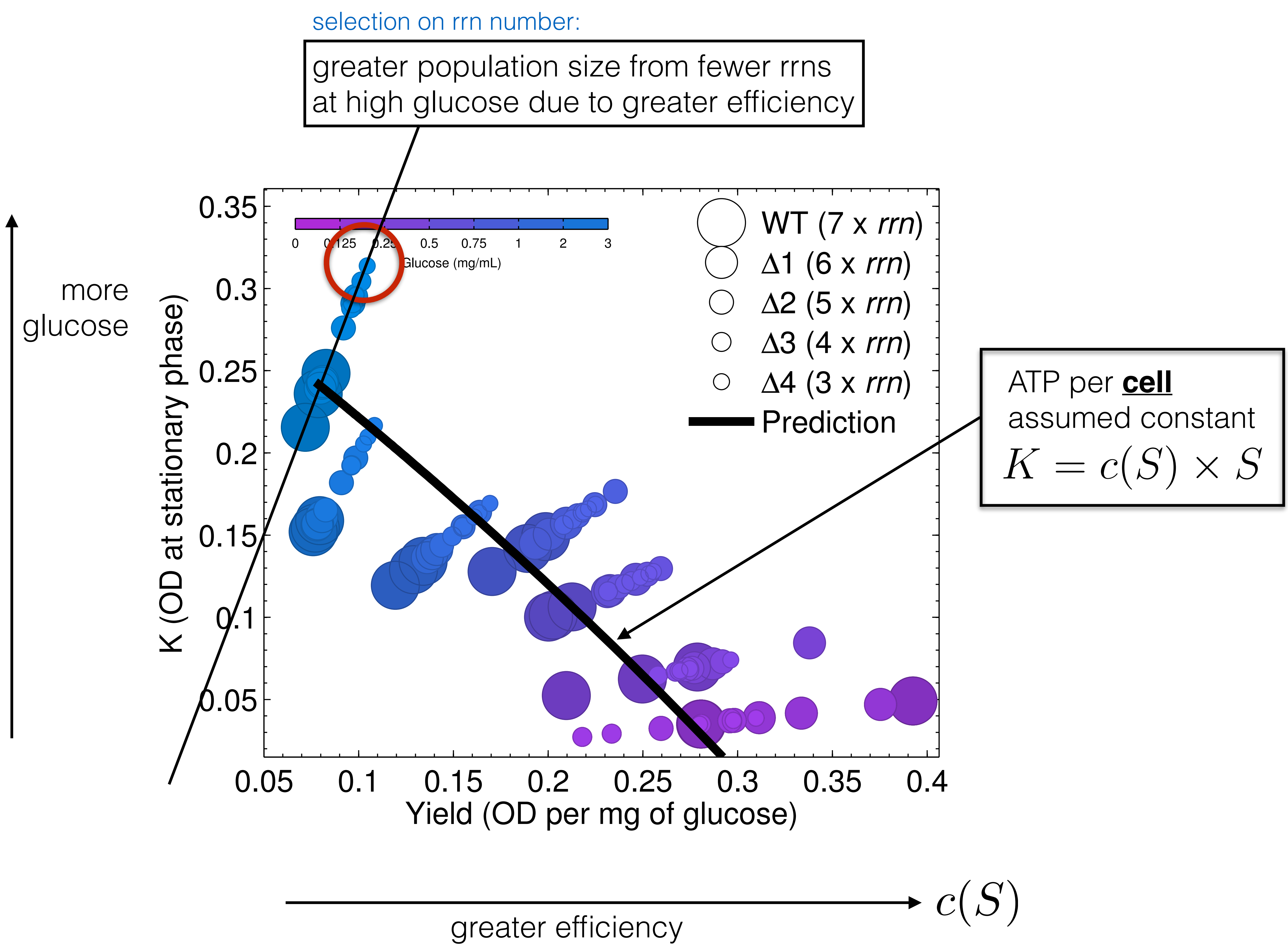
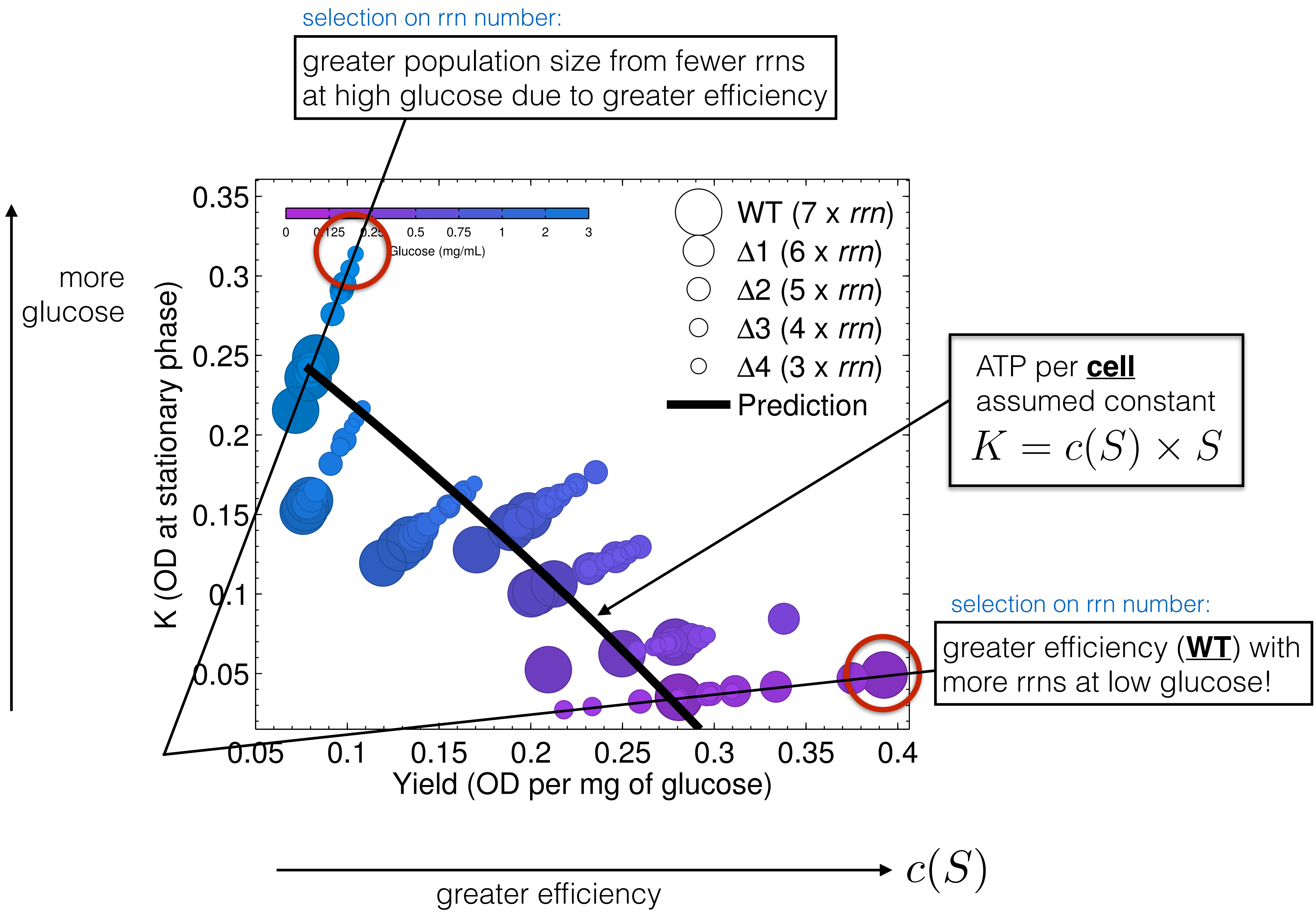
Prediction
0.05 0.1 0.15 0.2 0.25 0.3 0.35 0.4
Yield (OD per mg of glucose)
$c(S)$
greater efficiency

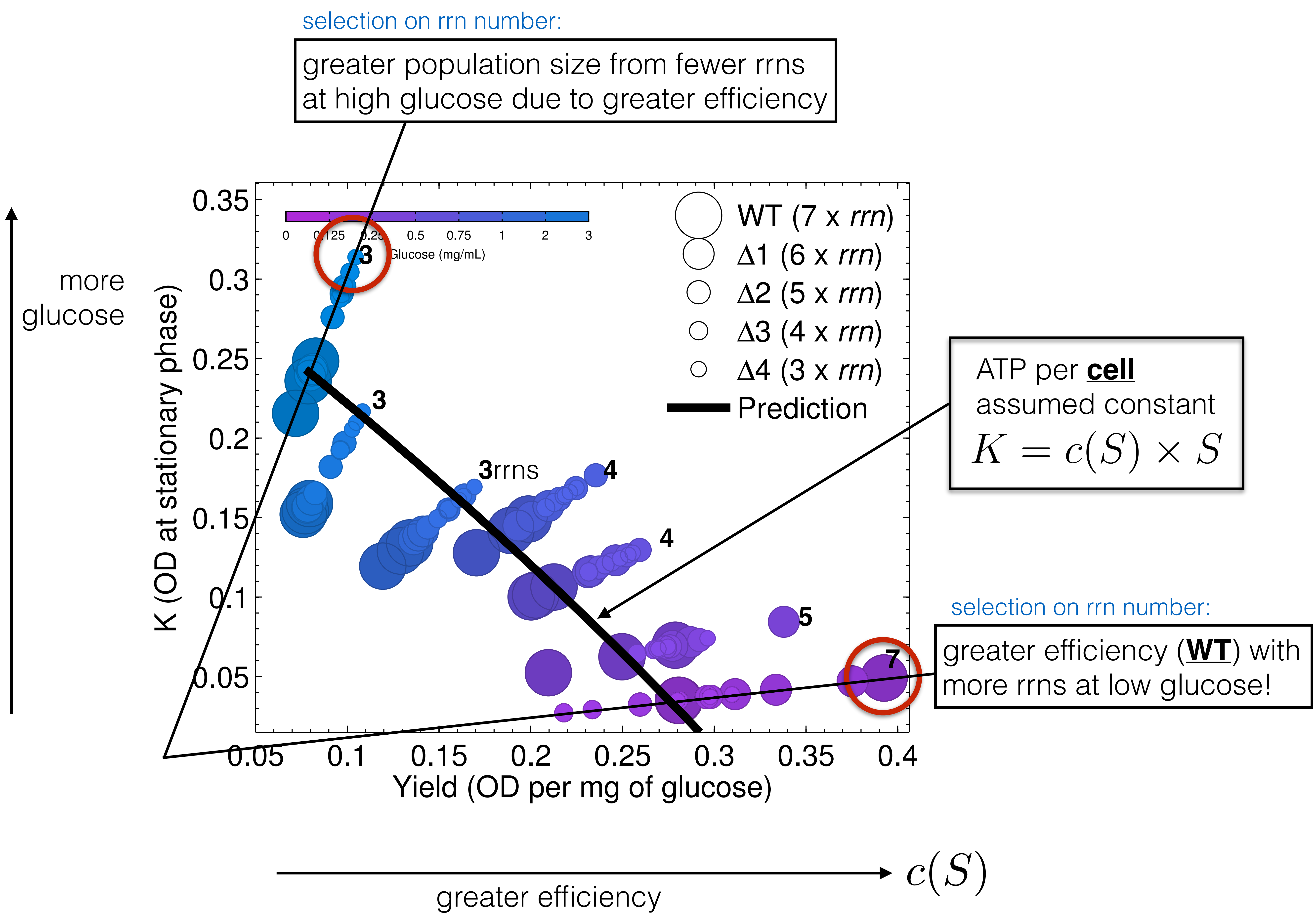


more
glucose
0.35
0.3
0.25
0.2
0.15
0.1
0.05
K (OD at stationary phase)
0 0.125 0.25 0.5 0.75 1 2 3
Glucose (mg/mL)
WT (7 x *rrn*)
Δ1 (6 x *rrn*)
Δ2 (5 x *rrn*)
Δ3 (4 x *rrn*)
Δ4 (3 x *rrn*)
Prediction
ATP per **cell**
assumed constant
$K = c(S) \times S$
0.05 0.1 0.15 0.2 0.25 0.3 0.35 0.4
Yield (OD per mg of glucose)
$c(S)$
greater efficiency

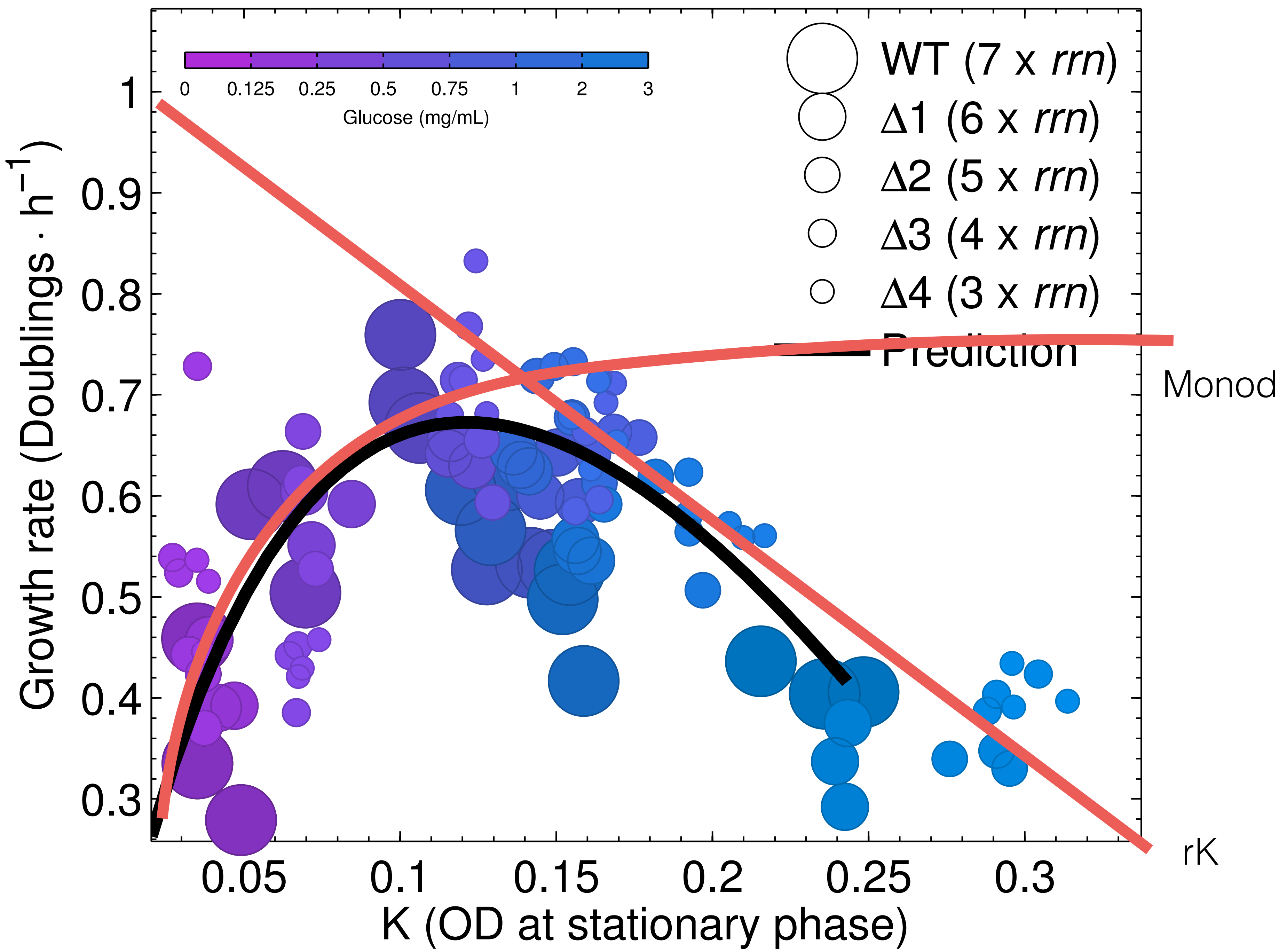

selection on rrn number:
greater population size from fewer rrns at high glucose due to greater efficiency
more glucose
K (OD at stationary phase)
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0 0.125 0.25 0.5 0.75 1 2 3
Glucose (mg/mL)
WT (7 x *rrn*)
Δ1 (6 x *rrn*)
Δ2 (5 x *rrn*)
Δ3 (4 x *rrn*)
Δ4 (3 x *rrn*)
Prediction
ATP per **cell** assumed constant
$K = c(S) \times S$
0.05 0.1 0.15 0.2 0.25 0.3 0.35 0.4
Yield (OD per mg of glucose)
greater efficiency
$c(S)$



selection on rrn number:
greater population size from fewer rrns at high glucose due to greater efficiency
0 0.125 0.25 0.5 0.75 1 2 3
Glucose (mg/mL)
WT (7 x rrn)
Δ1 (6 x rrn)
Δ2 (5 x rrn)
Δ3 (4 x rrn)
Δ4 (3 x rrn)
Prediction
ATP per cell assumed constant
$K = c(S) \times S$
selection on rrn number:
greater efficiency (WT) with more rrns at low glucose!
more glucose
K (OD at stationary phase)
0.35 0.3 0.25 0.2 0.15 0.1 0.05
0.05 0.1 0.15 0.2 0.25 0.3 0.35 0.4
Yield (OD per mg of glucose)
greater efficiency
$c(S)$



selection on rrn number:
greater population size from fewer rrns at high glucose due to greater efficiency
more glucose
0 0.125 0.25 0.5 0.75 1 2 3
Glucose (mg/mL)
WT (7 x rrn)
Δ1 (6 x rrn)
Δ2 (5 x rrn)
Δ3 (4 x rrn)
Δ4 (3 x rrn)
Prediction
3
3
3rrns
4
4
5
7
ATP per cell assumed constant
$K = c(S) \times S$
selection on rrn number:
greater efficiency (WT) with more rrns at low glucose!
K (OD at stationary phase)
0.35 0.3 0.25 0.2 0.15 0.1 0.05
0.05 0.1 0.15 0.2 0.25 0.3 0.35 0.4
Yield (OD per mg of glucose)
greater efficiency
$c(S)$



Conclusion: everyone was right somewhere!

There is a rate-yield parabola, so there is an rK parabola.

Finally, even the Rate-Yield Trade-Off (RYTO) had proven elusive…

a RY parabola predicted before…

Cooperation and Competition in the Evolution of ATP-Producing Pathways

Thomas Pfeiffer,[1]* Stefan Schuster,[2] Sebastian Bonhoeffer[1]*†

Heterotrophic organisms generally face a trade-off between rate and yield of adenosine triphosphate (ATP) production. This trade-off may result in an evolutionary dilemma, because cells with a higher rate but lower yield of ATP production may gain a selective advantage when competing for shared energy resources. Using an analysis of model simulations and biochemical observations, we show that ATP production with a low rate and high yield can be viewed as a form of cooperative resource use and may evolve in spatially structured environments. Furthermore, we argue that the high ATP yield of respiration may have facilitated the evolutionary transition from unicellular to undifferentiated multicellular organisms.

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Experimental Tests for an Evolutionary Trade-Off between Growth Rate and Yield in *E. coli*

Maja Novak,[1,*] Thomas Pfeiffer,[1,2,†] Richard E. Lenski,[3,‡] Uwe Sauer,[4,§] and Sebastian Bonhoeffer[1,||]

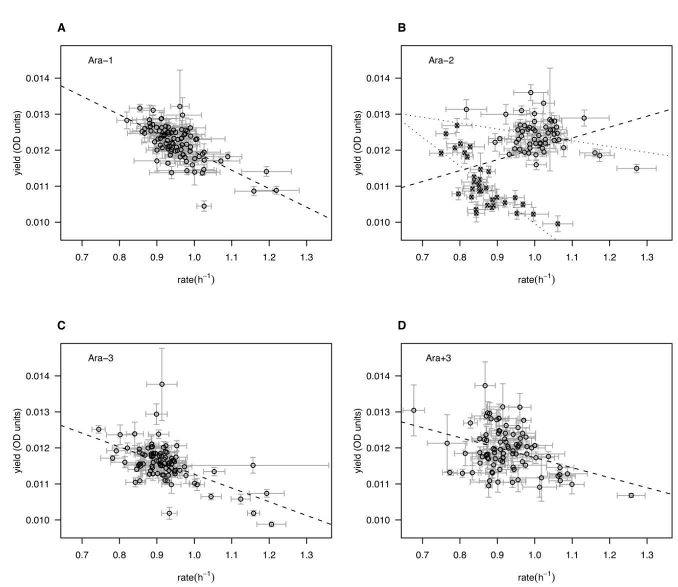

Figure 4: Trade-off between growth rate and yield across clones within particular evolved populations: growth yield versus rate estimated for 92 clones sampled from each of four populations at generation 20,000 (*A*, Ara − 1; *B*, Ara − 2; *C*, Ara − 3; *D*, Ara + 3). Each value is the mean of up to five measurements. Error bars represent standard errors. Three of the four populations show a highly significant negative correlation (*dashed lines*). The remaining population shows a significant positive correlation over all clones (*B*, *dashed line*), but it has been previously shown to have evolved a stable dimorphism. Based on their rate and yield data, we grouped the clones of this population into two clusters, referred to as cluster 1 (*circles*) and cluster 2 (*crosses*). Within both clusters, we observe a significant negative correlation (*dotted lines*). Details on the clustering algorithm and all statistical results are given in the text.

weak RYTO

RYT-Up in data & a theory parabola!

ARTICLE

BIOTECHNOLOGY and BIOENGINEERING

A Hidden Square-Root Boundary Between Growth Rate and Biomass Yield

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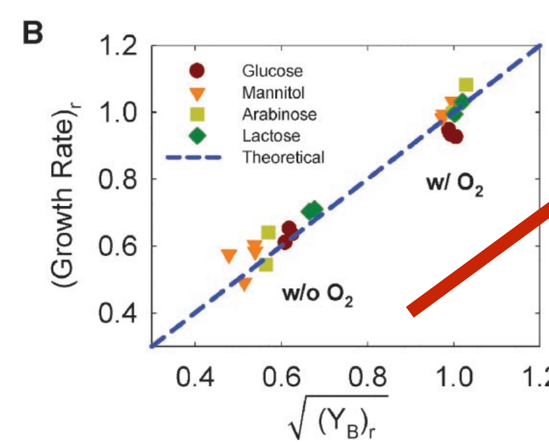

Figure 2. Square relationship between growth rate and biomass yield. **A**: The relative (denoted by subscript r) growth rate and the relative biomass yield in glucose followed the square-root relationship when cultured with or without amino acid (AA) supplementation or oxygen. The rates and yields were normalized to the wild-type values under aerobic conditions without AA supplements. All AA indicates all 20 amino acids were added to the culture while "some AA" indicates only some of the amino acids were added. **B**: The relative growth rate and the relative biomass yield followed the square-root relationship when cultured in various sugars with or without oxygen. The growth rate and biomass yield for each sugar is normalized against the aerobic condition in the same sugar.

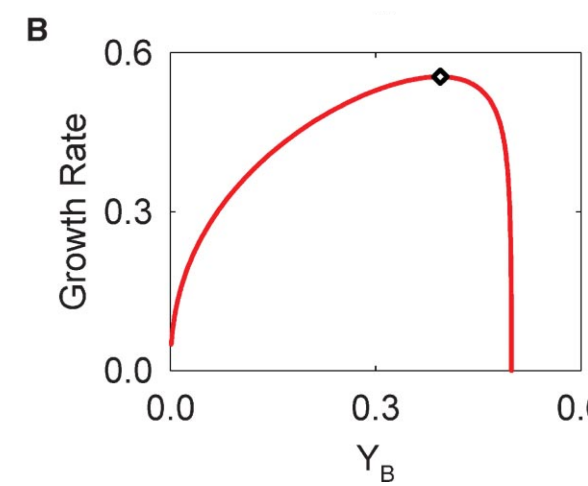

Figure 3. **A**: A typical effect of protein overexpression on yield. $(Y_B) = 0.5 - (1 + \exp(-6R_m + 6))^{-1}$. When protein synthesis rate (R_m) increases, the biomass yield decreases because of higher energy demand and potential saturation of downstream metabolic pathways. **B**: When the relationship in (A) is substituted in Equation (4), a maximum growth rate (open diamonds in A and B) occurs at a sub-optimal yield. Trade-off occurs when the growth rate and the yield of the strain starts on the right side of the maximum growth rate. [Color figure can be seen in the online version of this article, available at www.interscience.wiley.com.]