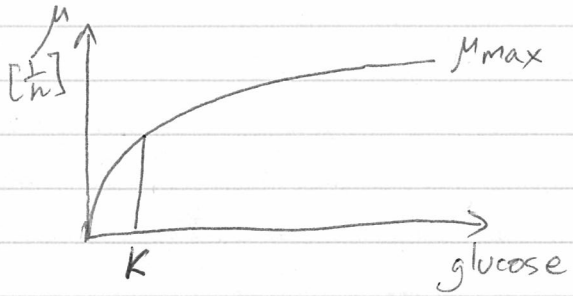
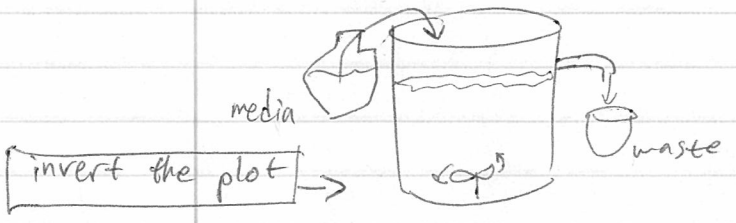
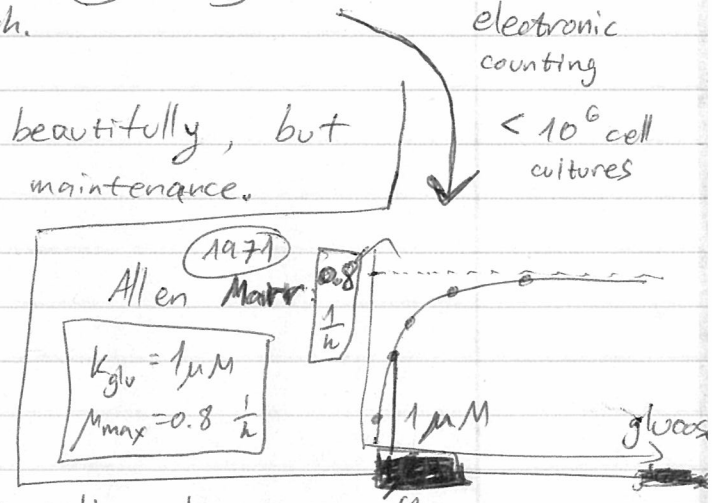
cell physiology: 1949 the growth of bacterial coltures



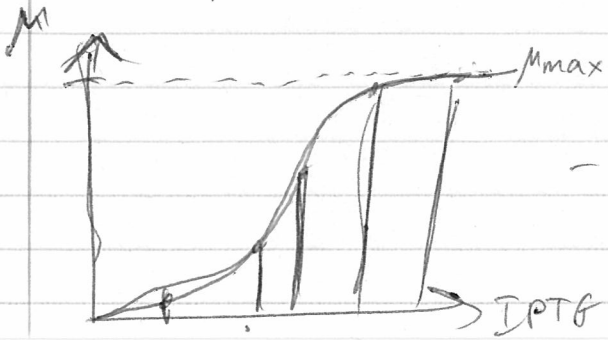
~~Two ways to measure that: batch and chemostat.~~

- It's very difficult to control (μ) using carbon limitation in batch.
- Also, chemostats work beautifully, but require high volumes and maintenance.



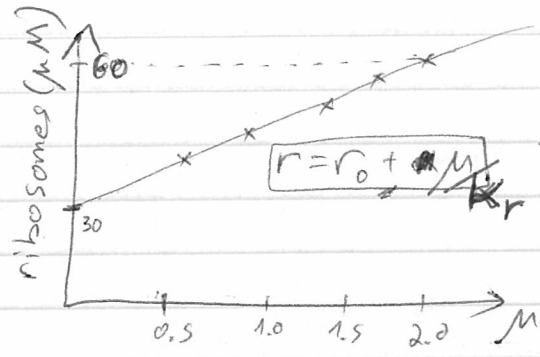


- Clever solution, artificially decrease the maximal uptake rate of glucose by controlling the expression of the trasporter with IPTG



- same [glucose]

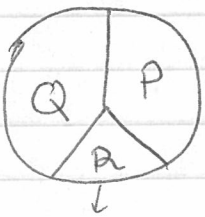
Ribosomes as a function of growth rate:



Marr (1991) – changing media quality

Terry Hwa, Matthew Scott, Carl Gunderson Science 2010

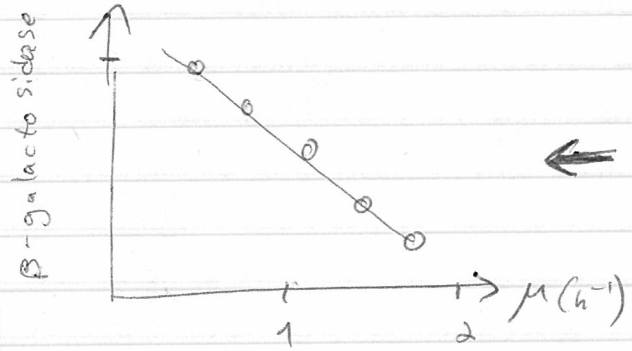
fixed increases with μ



$1 = \phi_Q + \phi_R + \phi_P$ – therefore, must decrease

$\phi_P = 1 - \phi_Q - (\phi_{R_0} + K_r^{-1} \cdot \mu)$

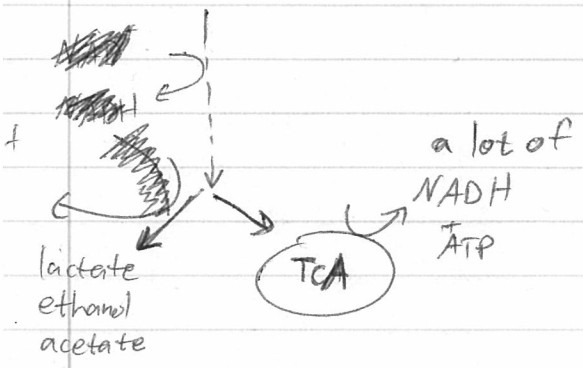
$\phi_P = \phi_{P_0} - K_r^{-1} \cdot \mu$ $\quad$ $\phi_{P_0} = 1 - \phi_Q - \phi_{R_0}$



← a constitutive gene associated with ϕ_P

✡ Physiology fact: maximizing yield is not always the chosen strategy:

- Cancer cells – Warburg effect (lactate)
- Yeast cells – Crabtree effect (ethanol)
- Bacteria like E. coli – overflow metabolism (acetate)



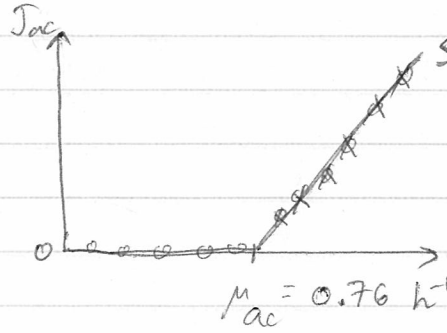
1 not enough oxygen?

2 membrane surface area?

Is this really sub-optimal? ↗

✡ rate vs. yield hypothesis. ← 3

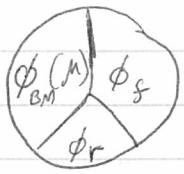
✡ Markus' work Basan et al. 2015 Nature



changing "μ" by limiting the uptake of carbon

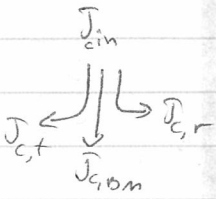
↓

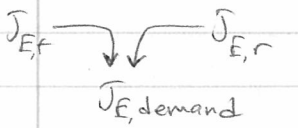
why?



resource $1 = \phi_f + \phi_r + \phi_{BM}$

carbon balance (controlled) $J_{c,in} \geq J_{c,f} + J_{c,r} + J_{c,BM}$





energy balance $J_{E,demand} \leq J_{E,f} + J_{E,r}$

assumptions: $\phi_{BM} = \phi_0 + \gamma \cdot \mu$

$J_{c,BM} = \beta \cdot \mu$

$J_{E,demand} = \sigma \cdot \mu$

$J_{c,f} = \kappa_f \phi_f$ $\quad J_{c,r} = \kappa_r \phi_r$

$J_{E,f} = \varepsilon_f \cdot \phi_f$ $\quad J_{E,r} = \varepsilon_r \phi_r$

$\phi_f = 1 - \phi_0 - \gamma \cdot \mu - \phi_r$

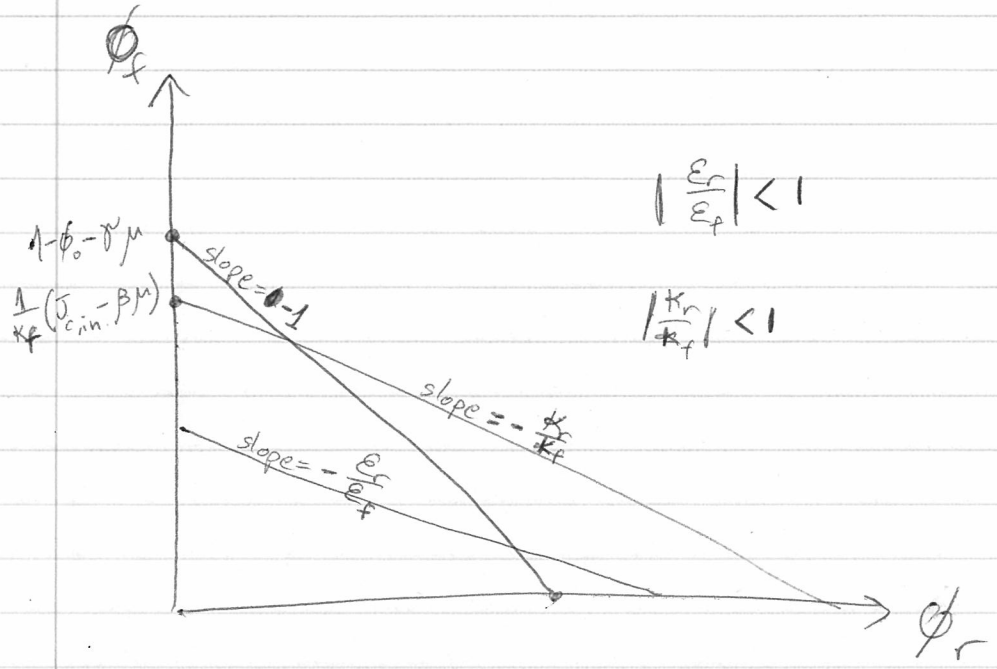
$\phi_f \leq \frac{1}{\kappa_f} \left[J_{c,in} - \beta \cdot \mu - \kappa_r \cdot \phi_r \right]$

$\phi_f \geq \frac{1}{\varepsilon_f} \left[\sigma \cdot \mu - \varepsilon_r \cdot \phi_r \right]$

$\kappa_r < \kappa_f$: respiration is carbon efficient

$\varepsilon_r < \varepsilon_p$: respiration requires more enzymes/protein for the same ATP flux

(V)



$\left|\frac{\varepsilon_r}{\varepsilon_f}\right|<1$

$\left|\frac{\kappa_r}{\kappa_f}\right|<1$

Is there a way to see [redacted] what ε_f, [redacted] K_r and K_f are from enzyme properties?

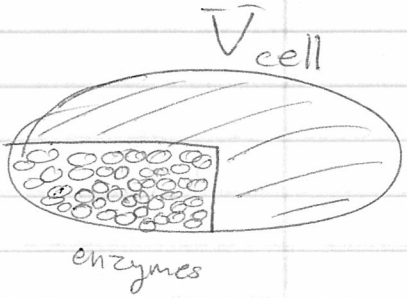
① have a full kinetic model and simulate the flux.

② use simplified kinetics, e.g. assume saturation.

Beg et al. 2007 PNAS

$$\sum_i V_i \, n_i \leq V_{cell} \left(\cdot \frac{1}{4}\right)$$

V_i: molar volume; n_i: copy number; V_{cell}: cell volume dedicated to enzymes



[redacted]

$$|v_i| \leq [\text{redacted}] \, k_{cat,i} \cdot n_i$$

v_i: flux

$$S \cdot v = 0$$

maximize $v_{biomass}$