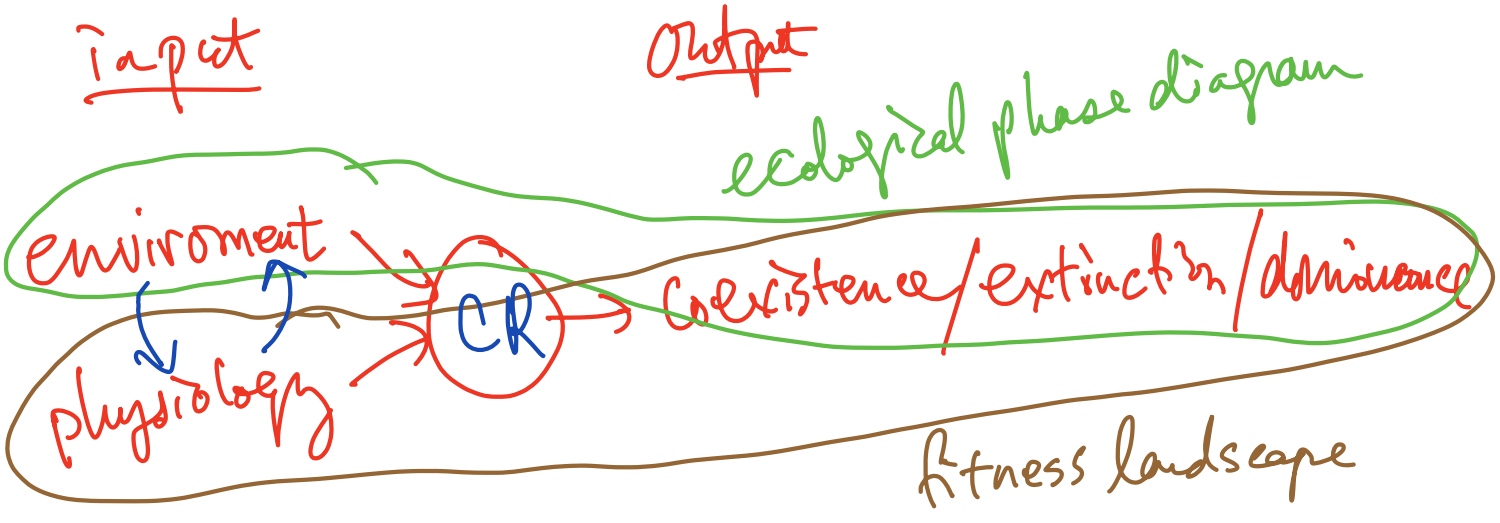
II. Consumer-Resource Model

- gLV model describes effective pairwise interactions between species; doesn't address mechanistic origin
- "random interactions" leads to global instability for large number of interacting species (May, 72)
- incorporate more realistic interactions:
  - → Competition for nutrients (Sec IIB)
  - → Collaboration to scavenge (Sec IIC)

Want to know



⇒ focus on planktonic, microbial systems where the effect of nutrient on growth is reasonably understood

⇒ focus on exponential growth and neglect stationary phase + cell death

A. Intro to CR Model

1. Bacterial growth physiology

a) Overview of bacterial growth: cell + medium → cells

Medium ingredients:

- nutrients [CO_2, methane]
  - C: sugars (glucose, fructose, ...), acids (acetate, succinate, ...)
  - N: ammonium (NH_4^+), nitrate (NO_3^-), ...
  - mixed C/N: amino acids, nucleotides, ...
  - phosphate, sulfate, ... [O_2], [CO_2]
- micronutrients: metal, vitamins
- buffer (pH range, capacity)
- osmolarity

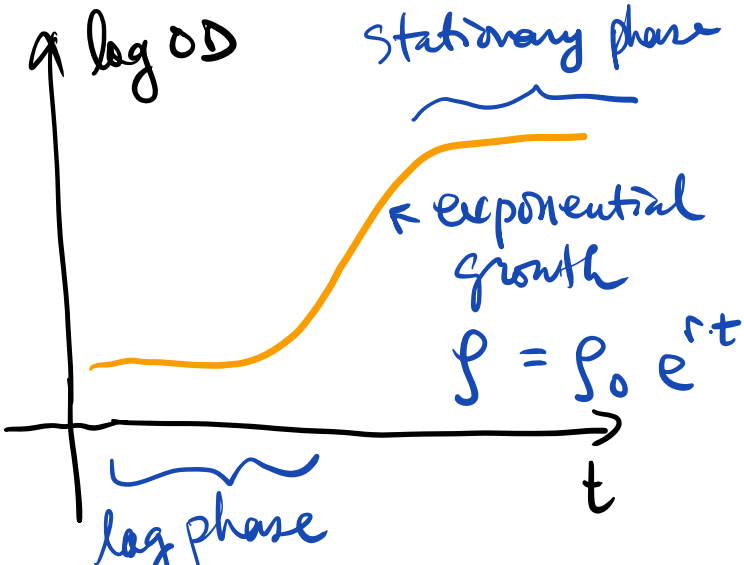
Growth venue:

- batch culture growth

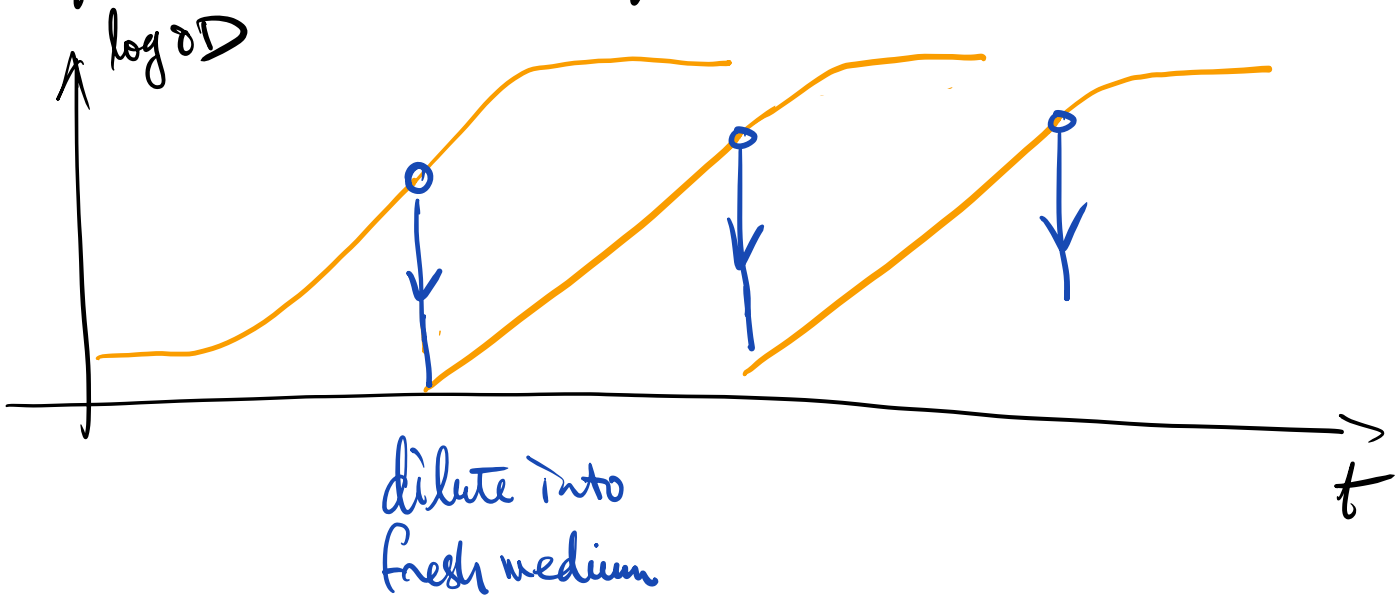
optical density: biomass density
= mass/cell × cell/ml
= ρ

$\tau \propto$ cell density if cell size const.

1 ml culture at $OD_{600} = 1$:
0.5 mg drymass
(in 1 g of water)

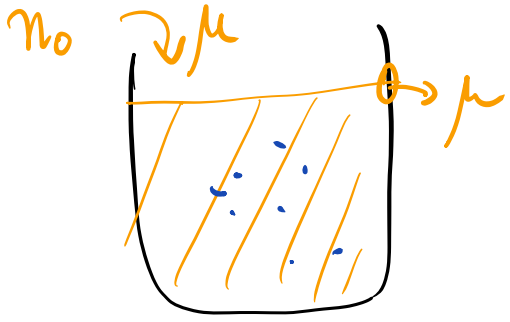


- growth-dilution cycle



⇒ Steady state growth (balanced growth)
if lag and stationary phase avoided.

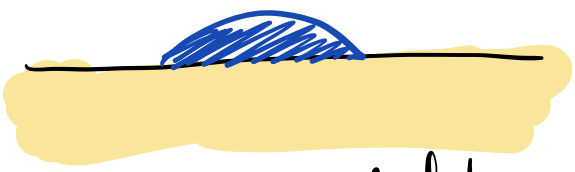
- Continuous culture (chemostat)



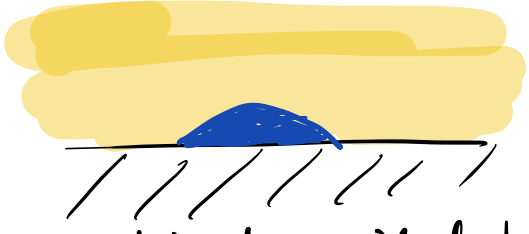
slow relaxation
towards steady state
if close to washout limit.

Above are all planktonic growth

bacteria growth on solid substrate



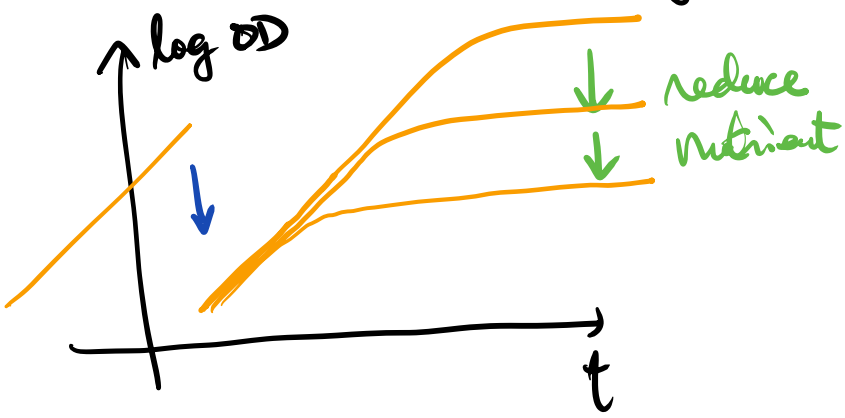
nutrient provided by Subs.

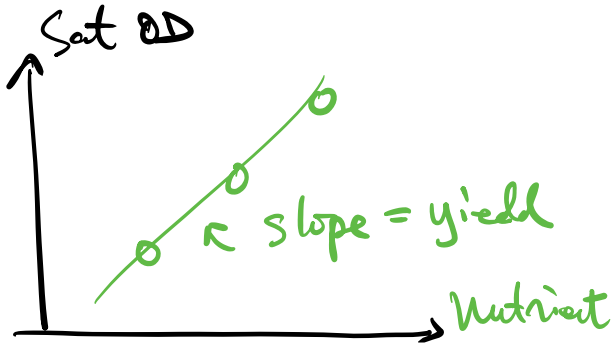


nutrient provided by fluid

batch culture growth

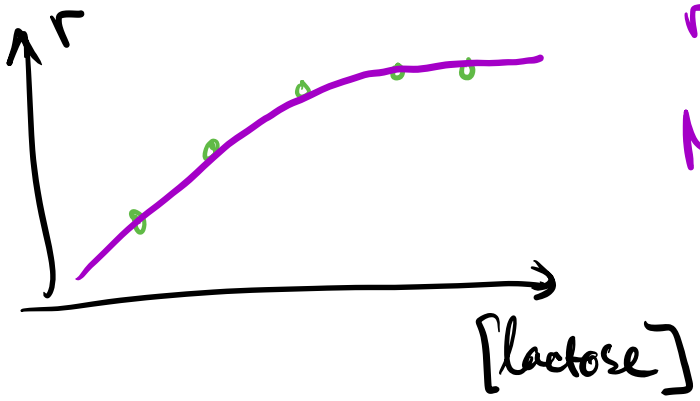
(with enough cycling to enter steady state)





for E. coli, $Y_{glc} \simeq$ 1OD/5mM glucose $= \frac{0.5\,mg\ DW}{5\,\mu mol \times 180\,g/mol} \simeq 0.5\,\frac{g\,DW}{g\,glucose}$

→ nutrient conc also affect growth rate



$r = r_0 \frac{n}{n+K_M}$

Monod growth kinetics (1942)

r_0 sat. growth rate

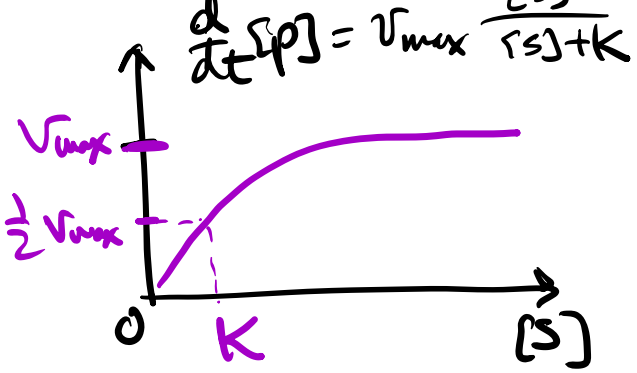
K_M Monod constant.

Same form as Michelis-Menten enzyme kinetics:

$$E + S \underset{k_{1-}}{\overset{k_{1+}}{\rightleftharpoons}} E\cdot S \xrightarrow{k_2} E + P.$$

$$\frac{d}{dt}[P] = k_2 \cdot [E\cdot S]$$

$$\frac{[E\cdot S]}{[E]_{free}\cdot[S]} = \frac{k_{1+}}{k_{1-}}$$



↑ Michaelis const.

$$[E]_{tot} = [ES] + [E]_{free} = [ES] + \frac{[ES]}{[S]}\frac{k_{1-}}{k_{1+}}$$

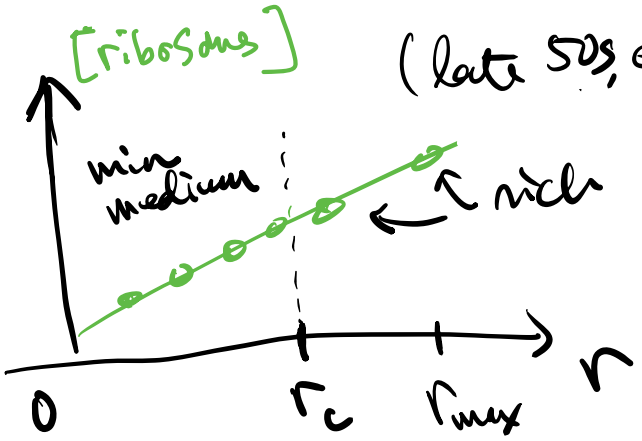
$$[ES] = \frac{[E]_{tot}}{1 + \frac{k_{1-}}{k_{1+}}/[S]}$$

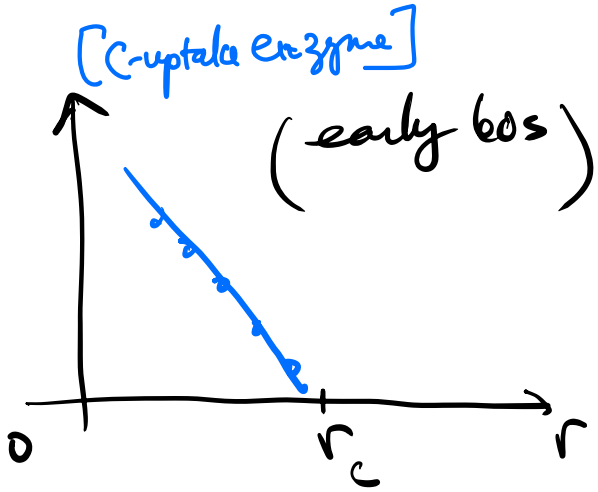
$$\rightarrow \frac{d}{dt}[P] = \underbrace{k_2[E_{tot}]}_{V_{max}} \cdot \frac{[S]}{[S] + \underbrace{k_{1-}/k_{1+}}_{K}}$$

but what does MM kinetics has to do with cell growth ??

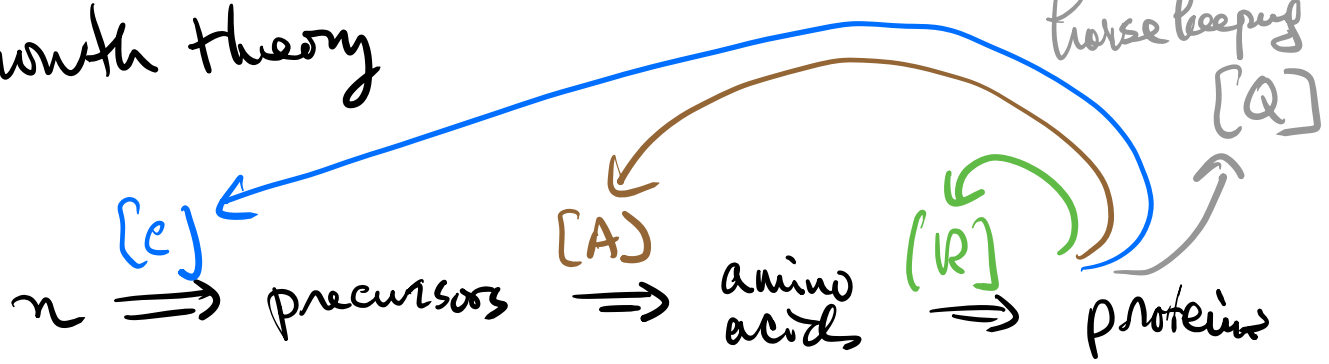
growth limited by nutrient uptake ?
(e.g. E = uptake enzyme?)

b) bacterial growth laws





growth theory



total cell mass $\simeq$ total protein mass $= M$.

total ribosomal mass $= M_R$

total mass of protein X $= M_x$

$\frac{dM}{dt} = k_R M_R$ k_R: Specific rate of ribosome activity or translational elongation rate

exponential growth $\frac{dM}{dt} = r \cdot M = k_R M_R(t)$

$\Rightarrow \frac{M_R(t)}{M(t)} = r/k_R$

↑ ribosomal mass fraction.

$\propto [R]$ since M/water is invariant

∥ total protein conc.

gene regulation:

$\frac{dM_i}{dt} = \chi_i k_R M_R$ ← fraction of ribosomes synthesizing protein i.

$\rightarrow \frac{M_i}{M} = \chi_i$ sets the conc of protein i

What should protein conc be set to?

Carbon uptake flux: $w_c M_c = -\frac{dn_c}{dt} = Y_c^{-1} \frac{dM}{dt}$

↑ Specific uptake rate

$Y_c \frac{dn_c}{dt} + \frac{dM}{dt} = 0$

$\rightarrow \frac{M_c}{M} = \frac{r}{w_c Y_c} \equiv \frac{r}{k_c}$

Internal flux balance: $k_c M_c = k_A M_A = \frac{dM}{dt}$

$$\rightarrow \frac{M_A}{M} = \frac{r}{k_A}$$

Overall constraint:

$$\frac{M_c}{M} + \frac{M_A}{M} + \frac{M_R}{M} + \frac{M_Q}{M} = 1$$

Assume $\frac{M_Q}{M} = \text{const}$ (expt: $\frac{M_Q}{M} \approx 50\%$)

$$\frac{r}{k_R} + \frac{r}{k_c} + \frac{r}{k_A} = \phi_{max} = 1 - \frac{M_Q}{M}$$

↑ fraction of proteome available to growth-dependent processes

rich medium: $k_c = \infty$, $k_A = \infty$.

$r = r_{max} = k_R \phi_{max}$ ($\approx 2/h$ for E. coli)

min medium with best C-source: $k_c = \infty$.

$$r = r_c = \frac{\phi_{max}}{k_R^{-1} + k_A^{-1}} \equiv k_{RA} \phi_{max}$$

min medium with "poor" C-source: small k_c

$$\frac{r}{k_c} + \frac{r}{k_{RA}} = \phi_{max}$$

$$r = \frac{k_{RA} \phi_{max}}{1 + k_{RA}/k_c} = r_c \frac{x}{1+x}$$

$x = \frac{k_c}{k_{RA}}$: carbon "quality" (glucose $x \approx 10$, $r \approx r_c$)

- Relation between C-proteins and GR?

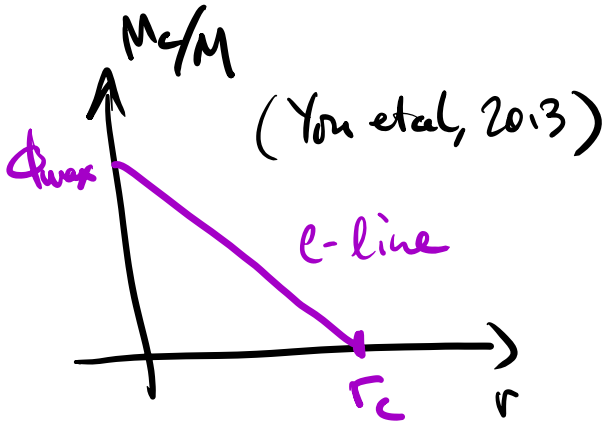
under C-limitation (changing C-sources, i.e., k_c)

$$\frac{M_C}{M} = \phi_{max} - \frac{M_R}{M} - \frac{M_A}{M}$$

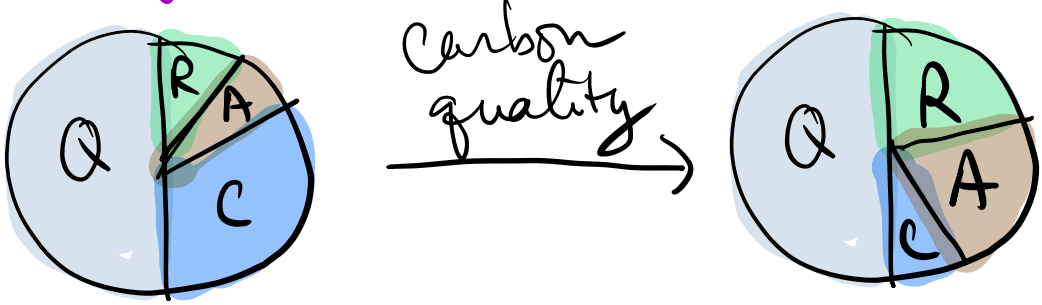
$$= \phi_{max} - \frac{r}{k_{RA}}$$

Since $r_c = k_{RA}\phi_{max}$.

$$\frac{M_C}{M} = \phi_{max}\left(1 - r/r_c\right)$$



→ explains "catabolite repression"
an ubiquitous phenomenon in microbial.



- Conc dependence of GR?

include MM kinetics of uptake protein

$$k_c \to k_c \frac{n}{n+k_c} \quad \text{or} \quad k_c^{-1} \to k_c^{-1}\left(1+\frac{k_c}{n}\right)$$

$$\to r = \frac{r_c}{1+\frac{k_{RA}}{k_c}\cdot\left(1+\frac{k_c}{n}\right)} = \frac{r_c}{1+\frac{k_{RA}}{k_c}+\frac{k_{RA}}{k_c}\cdot\frac{k_c}{n}}$$