E. Description of Specific Growth Rate – Unstructured Models

1. Limiting Substrate Concentration

That is, $\mu = f(S)$

Empirical Models are Used:

a) Monod $\mu = \dfrac{\mu_{MAX}\, S}{K_S + S}$

K_S = "Monod Constant" (typically very small)

So, $\mu \approx \mu_{MAX}$

For multiple substrates… $\mu = \dfrac{\mu_{MAX}\, S}{K_S + S} \dfrac{O}{K_O + O}$

b) Modified Monod

$$\mu = \frac{\mu_{MAX}\, S}{K_S + K_{S0}S_0 + S}$$

S_0 = Initial Substrate Concentration

c) Blackman

$\mu = \mu_{MAX}$ If $S \geq 2K_S$

$\mu = \frac{\mu_{MAX}S}{2K_S}$ If $S < 2K_S$

No transition between 0^{th} and 1^{st} order

d) Tessier $\mu = \mu_{MAX} (1 - e^{-KS})$

e) Moser $\mu = \frac{\mu_{MAX} S^N}{K_S + S^N}$ Same as Monod when N=1

f) Contois $\mu = \frac{\mu_{MAX} S}{K_{SX} X + S}$ Predicts $\mu \propto \frac{1}{X}$ at low S

Predicts $\mu \rightarrow 0$ at high X

Comments

Monod most commonly used model

Blackman is discontinuous

Contois often preferred for wastewater treatment. Also, unlike other models in a continuous process it allows for effluent concentration (S_{OUT}) to be dependent of influent concentration (S_{IN})

Contois and Tessier show most gradual decrease in specific growth rate at low substrate concentrations

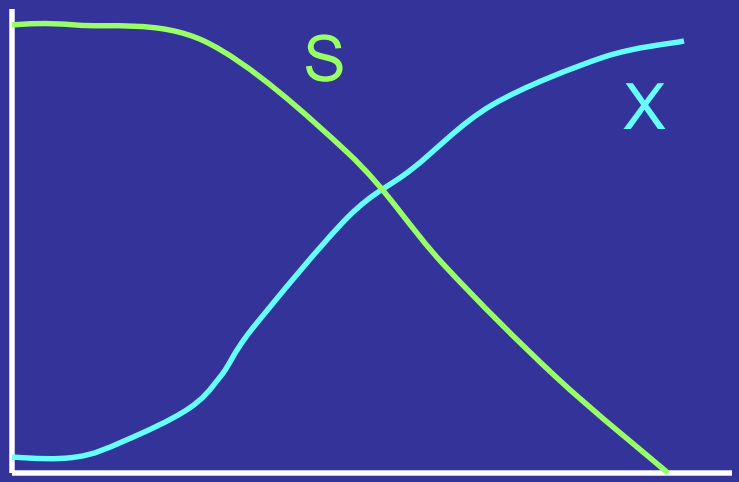
Moser most general

All models are very similar

How are parameters determined?

1) Measure S and X as a function of time

Time	S	X
t_1	S_1	X_1
t_2	S_2	X_2
t_3	S_3	X_3
t_4	S_4	X_4
…	…	…



And then estimate a specific growth rate at each time…

Time	S	X	μ
t_1	S_1	X_1	
t_2	S_2	X_2	μ_2
t_3	S_3	X_3	μ_3
t_4	S_4	X_4	μ_4
…	…	…	

Recall… $\frac{1}{X}\frac{dX}{dt} = \mu$

If time intervals are all equal, integrating (e.g., t_1 to t_3)…

$$X_3 = X_1 e^{\mu_2(t_3-t_1)}$$

So… $$\mu_2 = \frac{\ln(X_3) - \ln(X_1)}{t_3 - t_1}$$

Method subject to significant error because S, X values are not always precise.

2) Fit one of the above models [$\mu = f(S)$ or $\mu = f(S, X)$]

Method doesn't work very well for K_S because its value is so small that $\mu \approx \mu_{MAX}$ for the entire experiment.

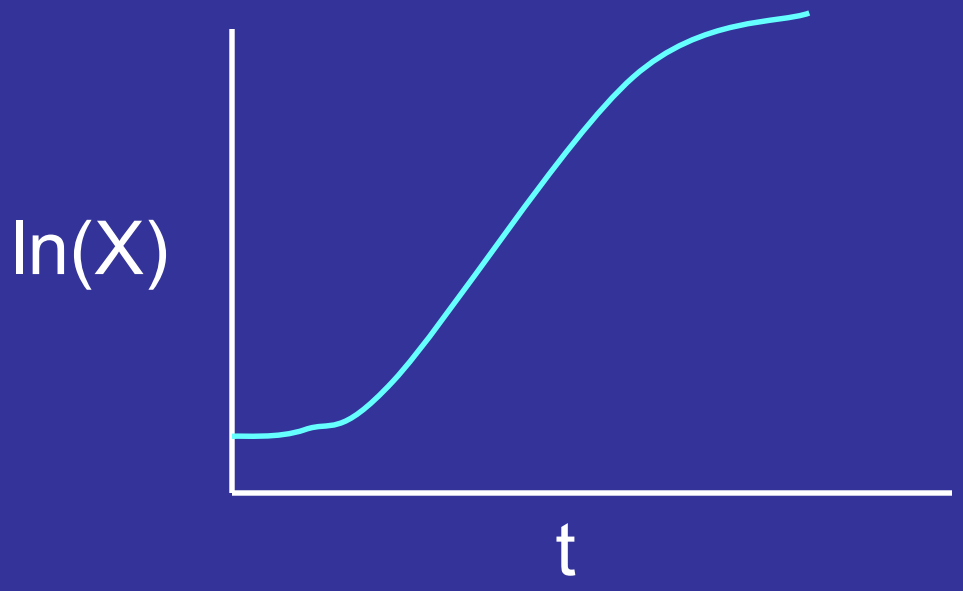
…but, it is very easy to calculate μ_{MAX} and to determine when lag, exponential and stationery phases occur.

$$\frac{1}{X}\frac{dX}{dt} = \mu$$

Integrating…
(indefinite interval during exponential growth)

$$\ln(X) - C = \mu_{MAX} t$$

Plot of ln(X) versus t will provide a slope of μ_{MAX}



2. Inhibitors

The presence of a chemical "inhibitor" (I) or substrate (S) or product (P) can reduce the cell growth rate. At sufficiently high concentration, cell growth ceases. Empirical models are again used, and they have the general property:

$$\lim_{I \to \infty} \mu = 0$$

a) Substrate Inhibition
Monod-like "Noncompetitive"

$$\mu = \frac{\mu_{MAX}\, S}{K_S + S} \frac{K_S'}{K_S' + S}$$

b) Substrate Inhibition
Monod-like "Competitive"

$$\mu = \frac{\mu_{MAX}\, S}{K_S \left(1 + \frac{S}{K_I}\right) + S}$$

c) Product Inhibition
Monod-like “Noncompetitive”

$$\mu = \frac{\mu_{MAX}\, S}{K_S + S} \frac{K_P}{K_P + P}$$

d) Product Inhibition
Monod-like “Competitive”

$$\mu = \frac{\mu_{MAX}\, S}{K_S \left(1 + \frac{P}{K_P}\right) + S}$$

e) Product Inhibition
Exponential

$$\mu = \frac{\mu_{MAX}\, e^{-\frac{P}{K_P}}}{\left(1 + \frac{K_S}{S}\right)}$$

f) Inhibition
Monod-like “Noncompetitive”

$$\mu = \frac{\mu_{MAX}\, S}{K_S + S} \frac{K_I}{K_I + I}$$

g) Inhibition
Monod-like “Competitive”

$$\mu = \frac{\mu_{MAX}\, S}{K_S \left(1 + \frac{I}{K_I}\right) + S}$$

Note that an inhibitor can be intentionally added to “force” a low growth rate, or to cause the substrate to be diverted to more product at the expense of growth.

3. Temperature

a) Ratkowsky Equation
(J. Bacteriol. 1982, 149:1-5)

$\mu^{1/2} = b(T - T_0)$ when $T > T_0$

$\mu^{1/2} = 0$ when $T < T_0$

This equation does not predict a maximum

Only useful for $T < T_{OPTIMAL\ GROWTH}$

b) Arrhenius Equation (like Enzyme Denaturation)

$$\frac{dX}{dt} = \mu X - \alpha X$$

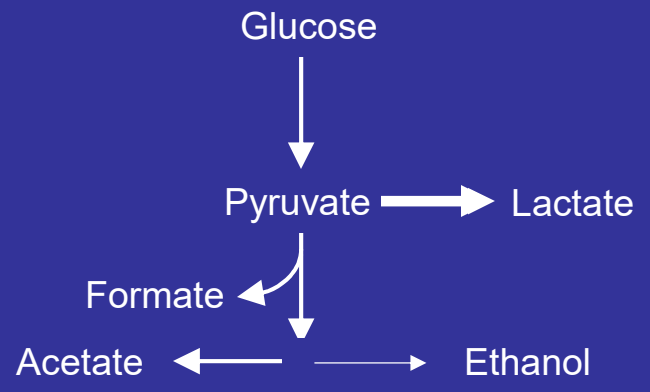
Activation: $\mu = A_a e^{-E_a/RT}$ $E_a = 18$ kcal/mol

Death: $\alpha = A_d e^{-E_d/RT}$ $E_d = 70$ kcal/mol

c) Other Comments

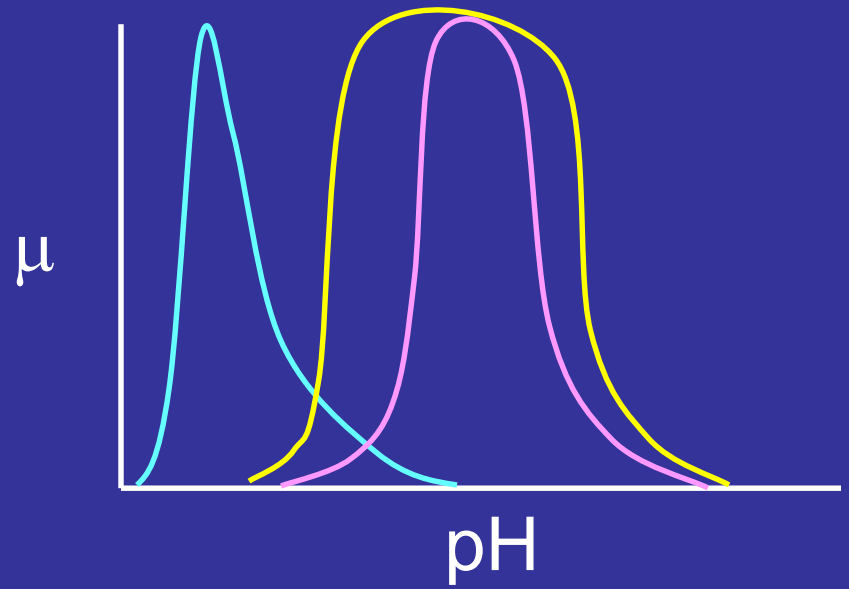
Temperature influences some enzymes more than others. Thus, the formation of product may be affected by temperature quite differently than cell growth. The consequence of this situation is:

$$Y_{P/S} = f(T)$$



Also, $Y_{X/S}$, $m_S = f(T)$

4. pH



Essentially impossible to predict

5. Logistic Equation

A different approach entirely

Specific growth rate is related to the carrying capacity

Carrying capacity (X_∞) is the maximum cell mass concentration that the environment can support.

$$\mu = k(1 - X / X_\infty)$$

$$\frac{dX}{dt} = kX(1 - X / X_\infty)$$

Integrating ($X = X_0$ @ $t=0$)…

$$X = \frac{X_0 \, e^{kt}}{1 - \frac{X_0}{X_\infty}(1 - e^{kt})}$$

6. Summary of Modeling Batch Growth – Unstructured Models

Growth

$$\frac{dX}{dt} = \mu X - \alpha X$$

Substrate Utilization

$$Q_S = m_S X + \frac{\mu X}{Y_{X/S}} + \frac{Q_P}{Y_{P/S}}$$

Product Formation

$$Q_P = Y_{P/X}\, \mu\, X$$ (Growth-Associated)

Specific Growth Rate

$$\mu = \frac{\mu_{MAX}\, S}{K_S + S} \frac{K_P}{K_P + P}$$

Volumetric Productivity

$$\Pi = P/t_{FERM}$$