SZILARD

1155E 5464

301 Kent ||

Zirkel

GRA-1166 Bakery 102
Use Stke B

up to day!

Lewis Gleeck
~~[illegible]~~
9 o'clock

Simeon Leland.

Simmini day 2nd // on Ambassador
Hotel N.Y. –

{ (11) AM

Mm 57358

~~6 pm~~ 6 pm

PL 28576

$$\frac{dz}{dt} = K(1 - \lambda z^*) - \frac{z}{\tau}$$

(2)

first process:

$$i z^* = (z - z^*)\,\text{Const.}$$

$$z^* = \frac{z}{i + \text{Const}}$$

(3)

$$\frac{dz}{dt} = \left(1 - \frac{\lambda}{i + \text{Const}} z\right) - \frac{z}{\tau}$$

for $i = 0$

$$z = k\tau - k\tau\frac{\lambda}{c} z$$

$$z + k\tau\frac{\lambda}{c} z = k\tau$$

$$z = \frac{k\tau}{1 + k\tau\frac{\lambda}{c}}$$

$$K = \frac{k_0}{\tau}$$

$$K - \frac{\lambda K}{i + C} z = \frac{z}{\tau}$$

$$z_\infty = k_0\left(1 - \frac{\lambda}{i + C} z_\infty\right)$$

$$z_\infty\left(1 + \frac{\lambda k_0}{i + C}\right) = k_0$$

$$z_\infty = \frac{k_0(i + C)}{i + C + \lambda k_0}$$

$$\frac{z_\infty}{z_0} = \frac{i + C}{i + C + \lambda k_0}$$

$$K_\infty = z_\infty\left(\frac{1}{\tau} + \frac{\lambda K}{i + C}\right)$$

$$k_0 = \left(1 + \frac{k_0 \lambda}{i + C}\right) z_\infty$$

$$k_0 = \frac{i + C + k_0\lambda}{i + C} z_\infty$$

$$z_\infty = \frac{k_0(i + C)}{i + C + k_0\lambda}$$

(4)

$$z_\infty = k_0$$

$$\cancel{\frac{dz_\infty}{di} = \frac{d}{di}\left\{\frac{k_0 i}{i+C+k_0\lambda} + \frac{k_0 C}{i+C+k_0\lambda}\right\}}$$

$$\frac{dz_\infty}{di} =$$

$$i + C = x$$

$$= \frac{dz_\infty}{d(i+C)} = \frac{k_0 x}{x + k_0\lambda} = \cancel{\frac{k_0}{x+k_0\lambda}}$$

$$\frac{d}{dx}\frac{u}{v} = \frac{-uv'}{v^2} + \frac{u'v}{v^2}$$

$$= \frac{k_0}{x+k_0\lambda} - \frac{x k_0}{(x+k_0\lambda)^2}$$

$$= \frac{k_0}{n} - \frac{(n-1)k_0\lambda}{(n)^2}\, k_0$$

$$\frac{1}{2}\frac{dz}{di} \cong 1$$

$$z_\infty = \text{const}\; e^{i}$$

$$n - 1 = \frac{k_0\lambda}{i+C} = \frac{k_0\lambda}{i + z_0\lambda}$$

say $k_0 = 10000$ $\quad n \cong 10$ for $i = \frac{1}{10} k_0\lambda$

4a

for $i = 0$

$$Z_0 = \frac{K_0 C}{K_0 \lambda + C}$$

$Z_0 \ll C K_0$

$Z_0 K_0 \lambda + Z_0 C \cong K_0 C$

$Z_0 K_0 \lambda \cong K_0 C$

$$\boxed{Z_0 \lambda = C}$$

4b

for $i = \infty$

$Z_\infty = K_0$

4c

$$Z_\infty = \frac{K_0}{2} = K_0 \frac{i + C}{i + C + K_0 \lambda}$$

$$\frac{i_2 + C}{i_2 + C + K_0 \lambda} = \frac{1}{2} \quad \text{or}$$

$$\boxed{i_2 + C = K_0 \lambda}$$

$$Z_\infty = \frac{K_0}{n} \quad \Big\| \quad \frac{i_n + C}{i_n + C + K_0 \lambda} = \frac{1}{n}$$

$$\boxed{[i_n + C](n-1) = K_0 \lambda}$$

5

4

(1) $$\frac{dz}{dt} = K\left(1 - \frac{\lambda z}{i + c}\right) - \frac{z}{\tau}$$

$$c = z_0 \lambda$$

$$(n-1)(i + \lambda c) = K_0 \lambda$$

$$\boxed{\frac{dz}{dt} = K\left(1 - \frac{\lambda z (n-1)}{K_0 \lambda}\right) - \frac{z}{\tau}}$$

$$\tau = \frac{1}{10} \text{ of } \frac{K}{n-1}$$

6

Demonstrate

$\boxed{K_0 = K\tau}$

$$i z^* = (z - z^*) C$$

$$z^* = \frac{zC}{i + C} \qquad (3)$$

$$g^* = \frac{z}{\frac{z}{i+C} + z}$$

$$g^* = \frac{z(i+C)}{zC + z(i+C)} \qquad (4)$$

for $Cz \ll z(i+C)$

$$\boxed{g^* \approx 1 - \frac{C}{z(i+C)} z \qquad (5)}$$

Stationary state:

$$K\tau g^* = z_\infty \qquad (6)$$

for $i = 0$

$$K\tau - \frac{K\tau}{zC} z_\infty \cong z_\infty$$

$$K\tau \cong \left(1 + \frac{K\tau}{zC}\right) z_\infty \qquad (7)$$

$$z_\infty = z_0 = \frac{K\tau}{1 + \frac{K\tau}{zC}} = \frac{K_0 zC}{zC + K_0} = \frac{zC}{1 + \frac{K_0}{zC}}$$

$$z_0 + z_0 \frac{K_0}{zC} = K_0 \qquad z_0 \ll K_0 \qquad \boxed{z_0 \cong zC}$$

Stationary state:

for $i = \infty$ $\quad z_\infty = K_0 \qquad (8)$

$$\frac{z_0}{K_0} + \frac{z_0}{zC} \cong 1 \quad , z_0 = zC$$

Tu Wed
$\frac{12}{19}$ %

De Novo —

$$g^* z^* = (g - g^*) z$$

$$(z^* + z) g^* = g z$$

$$g^* = \frac{g z}{z^* + z} \approx \qquad g = 1$$

$$1 - g^* = 1 - \frac{z^*}{z^* + z}$$

(8-9)

$$g^* z^* = (g - g^*) z \qquad g = 1$$

$$(z^* + z) g^* = g z \qquad \text{or } \lambda z \ll 1$$

(1) $$g^* = \frac{z}{z^* + z} \approx 1 - \frac{z^*}{z} \quad \text{for } z^* \gg z \qquad (1a)$$

$$\lambda = \frac{1}{z} ; \quad g^* \approx 1 - \lambda z^*$$

$$\frac{C}{K} \frac{dz}{dt} = K g^* - \frac{z}{\tau} \qquad (2)$$

$$z_\infty = \frac{k_0}{n}$$

$$\left(k_0 - \frac{k_0}{n}\right)(i+c) = \frac{n k_0^2}{n^2}$$

$$\frac{n k_0 - k_0}{n}(i+c) = n\frac{k_0^2}{n^2}$$

$$(n-1)\cancel{k_0}(i+c) = n\frac{k_0}{n}\cancel{k_0}$$

$$\cancel{(k_0 - z_\infty)(i+c) = 0}$$

$$k_0 g^* = z_\infty$$

$$k_0 \frac{(i+c)}{n z_\infty + (i+c)} = z_\infty \qquad z_\infty > n(i+c)$$

$$n z_\infty > i+c$$

note $f = n$

$$\eta(i+c) = \frac{k_0}{n(n-1)}$$

$$\frac{dz}{dt} = \frac{k_0 \frac{k_0}{n(n-1)}}{k_0 z + \frac{k_0}{n(n-1)}} - z$$

~~Check 4.10~~

4

calculate in frame (stationary state)

$$k_0 g^* = \cancel{\frac{k_0}{n}} = Z_\infty = \cancel{\frac{k_0}{n}}$$

$$g^* = \frac{\eta(i+C)}{Z + \eta(i+C)} = \frac{i+C}{nZ + i + C}$$

$$\cancel{\boxed{\frac{\eta(i+C)}{\frac{k_0}{n} + \eta(i+C)} = \frac{1}{n}}}$$

$$i + C$$

SS

$$\boxed{\frac{k_0 \eta(i+C)}{Z_\infty + \eta(i+C)} = Z_\infty}$$

$$\frac{k_0}{i+C}\left(1 - \frac{Z_\infty n}{i+C}\right) = Z_\infty$$

$$k_0 = Z_\infty + \frac{Z_\infty n k_0}{i+C}$$

$$k_0 \eta(i+C) = (Z_\infty)^2 + Z_\infty \eta(i+C)$$

$$(k_0 \eta - Z_\infty \eta)(i+C) = Z_\infty^2 \qquad \boxed{Z_\infty = \frac{k_0}{n}}$$

$$\left(k_0 - \frac{k_0}{n}\right)\eta(i+C) = \frac{k_0^2}{n^2}$$

$$\boxed{(n-1)\eta(i+C) = \frac{k_0}{n}}$$

$$k_0 \eta(i+C) = Z_\infty^2 + Z_\infty \eta(i+C)$$

$$k_0(i+C) = nZ_\infty^2 + Z_\infty(i+C)$$

$$(k_0 - Z_\infty)(i+C) = nZ_\infty^2 \qquad nZ \ll 1$$

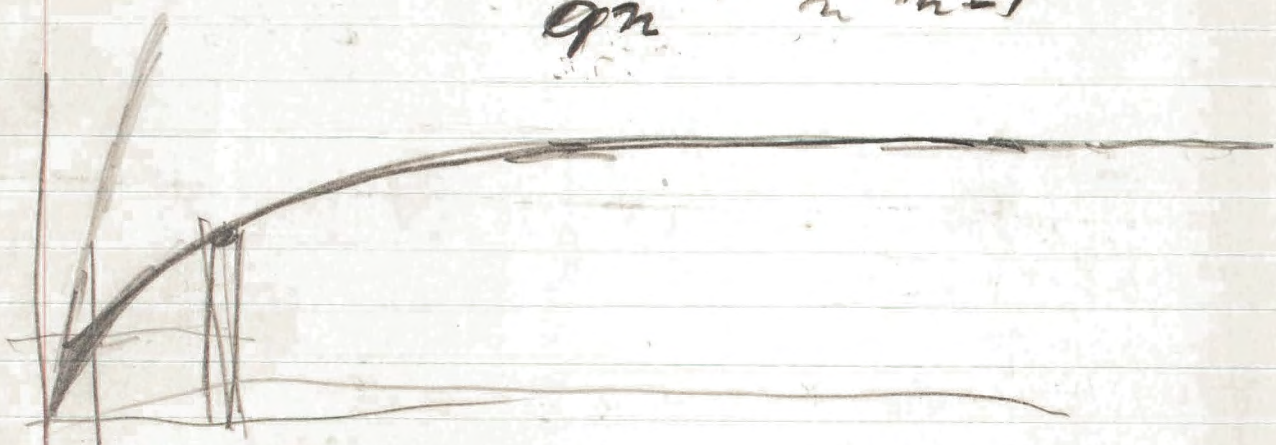
$$K_0 g^* = K_0 \frac{\frac{K_0}{n}\frac{1}{n-1}}{(n-1)\frac{K_0}{n} + \frac{K_0}{n}\frac{1}{n-1}} = \frac{K_0}{n}$$

$\underline{\underline{0.K.}}$

$$\log z = \frac{K_0}{10n}$$

$n = 10$

$$g^* = \frac{\frac{K_0}{n}\frac{1}{n-1}}{\frac{K_0}{9n} + \frac{K_0}{n}\frac{1}{n-1}}$$



at 1/9 of z_∞ slope

$\left(\frac{1}{n-1} \text{ of } z_\infty\right)$ $\quad g^* = 1/2$

Check $i + c = x$?

$$\frac{1}{n} = \frac{x}{x + \lambda k_0}$$

$$1 = \frac{n x}{x + \lambda k_0}$$

$$x + \lambda k_0 = n x \qquad (n-1)x = \lambda k_0$$

$$i + c = \frac{\lambda k_0}{n-1}$$

O.K.

Check:

$$k_0 g^* = z_\infty = \frac{k_0}{n}$$

$$g^* = \frac{1}{n}$$

$$\frac{1}{n} = \frac{\eta(i+c)}{\frac{k_0}{n} + \eta(i+c)}$$

$$\frac{1}{n}\frac{k_0}{n} + \frac{1}{n}\eta(i+c) = \eta(i+c)$$

$$\frac{k_0}{n} = (n-1)\eta(i+c)$$

$$\frac{1}{n-1}\frac{k_0}{n} = \eta(i+c)$$

~~O C A~~

~~O C C A~~ A has no effect

O → om → C → citr A → arg.

A* + [A arginine] free

citrullin indirect/ ~~A C A~~ [citrullin A] ~~indirect~~ ~~bound~~ ~~bound~~

C* + [C citrulline] free

O* +

precise! $\underline{\underline{i = 0}}$

check: $k_0 g^* = z_0$

$$g^* = \frac{\eta c}{2+\eta c} \qquad k_0 = \frac{z_0}{g^*} = \frac{z_0(z_0 + \eta c)}{\eta c}$$

$$\eta c = \frac{z_0}{k_0}(z_0 + \eta c)$$

$$\left(1 - \frac{z_0}{k_0}\right)\eta c = \frac{z}{k} z_0$$

$$\eta c \approx \frac{z}{k} z_0$$

$$\boxed{k \eta c \approx z_0^2}$$

approx:

for i_∞ ; $z_\infty = Kg = A$

$$\boxed{\frac{dz}{dt} = Kg\,\frac{\eta(i+c)}{zc+\eta(i+c)} - \frac{z}{t}}$$

for i for which $z_\infty = \frac{A}{n}$

$$\cancel{A}\,\frac{\eta(i+c)}{\frac{A}{n}c + \eta(i+c)} = \frac{\cancel{A}}{n} \qquad \left(z = \frac{A}{n}\right)$$

$$\cancel{\eta(i+c)}$$

$$\cancel{\eta}(i+c) = \frac{A}{n}\frac{c}{n} + \frac{1}{n}\eta(i+c)$$

$$(n-1)\,\eta(i+c) = \frac{A}{n}c$$

$$\eta(i+c) = \frac{1}{(n-1)}\frac{A}{n}c$$

$$\frac{dz}{dt} = Kg\,\frac{\frac{1}{n-1}\frac{A}{n}\cancel{c}}{\frac{1}{f}\frac{A}{n}\cancel{c} + \frac{1}{n-1}\frac{A}{n}\cancel{c}} - \frac{\frac{1}{f}\frac{A}{n}}{t}$$

$$\boxed{\text{if } z = \frac{1}{f}z_\infty = \frac{1}{f}\frac{A}{n}}$$

for $f = n-1$; $\frac{dz}{dt} = \frac{1}{2}Kg$

~~for n = 2~~

DeNuo

$$\rho^* z^* = (\rho - \rho^*)\,\eta$$

strong buildup
η small

$$\rho^* z^* = \rho\eta - \rho^*\eta$$

$$\rho^*(z^* + \eta) = \rho\eta$$

$$\rho^* = \rho\,\frac{\eta}{z^* + \eta}$$

$$\lambda = \frac{1}{\eta}$$

$$i z^* = (z - z^*)\,c$$

$$i z^* + c z^* = z c$$

$$z^*(i + c) = z c$$

$$z^* = \frac{z c}{i + c}$$

$$\frac{dz}{dt} = K\rho^* - \frac{z}{\tau}$$

Stationary states

$$K\tau = K_0$$

$$K\tau\,\rho^* = z_\infty$$

$$K_0\,\rho^* = z_\infty$$

$$\rho^* = \rho\,\frac{\eta}{\frac{zc}{i+c} + \eta}$$

$$K_0\rho = A$$

$$K\rho^* = K_0\rho\,\frac{\eta(i+c)}{zc + \eta(i+c)} = z$$

$\frac{dz}{dt}$ is $\approx \frac{A}{\frac{n-1}{2}+1} - \frac{A}{2n}$ for $z = \frac{A}{2n}$ for large n

corresponding "Mound & slope" would be $\frac{A}{n}$

$$\frac{2A}{n+1} - \frac{A}{2n} = \left(\frac{4n - (n+1)}{2n^2 + 2n}\right) \times A$$

$$\cong \frac{3n}{2n^2} \quad \text{or} \quad \frac{3}{2}\frac{A}{n}$$

or $\frac{3}{2}$ × "Mound & slope" at

1/2 Saturation.

M3

Also

$$\frac{dz}{dt} = Kg \frac{\frac{1}{n-1}\frac{A}{n}C}{2C + \frac{1}{n-1}\frac{A}{n}C} - \frac{z}{\tau}$$

$$\frac{dz}{dt} = Kg \frac{1}{\frac{2A(n-1)n}{A} + 1} - \frac{z}{\tau}$$

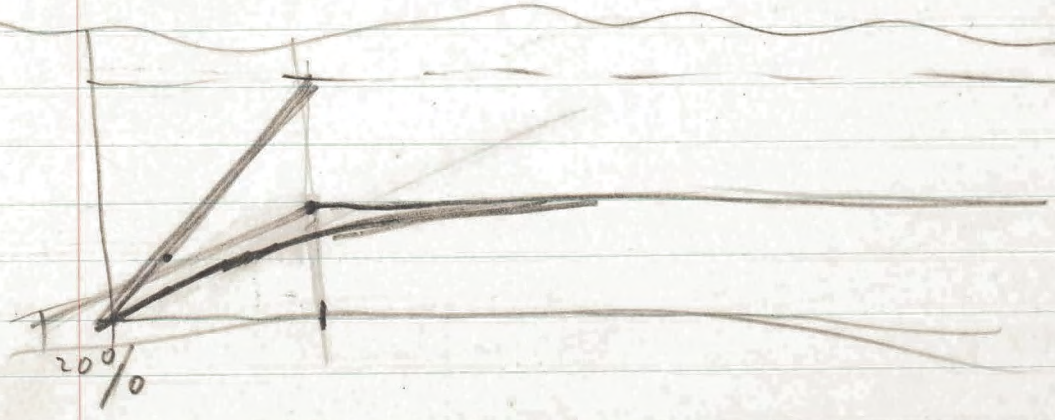
$\tau = 1$

$\frac{dz}{dt}$ is $= 0$ for $z = \frac{A}{n}$

" is $\cong \frac{Kg}{2}$ for $z = \frac{A}{n}\frac{1}{n-1}$

" is $= \frac{5}{12}Kg$ for $z = \frac{A}{2n}$ and $n = 2$

$$\frac{2}{3} - \frac{1}{4} = \frac{5}{12} \qquad \frac{Kg}{\frac{1}{2}+1} = \frac{Kg}{4}$$



integrate

Milt:

Conspicuous can not be better than an indurable mutant or. —

In indurable strain growing on system galactose should not effect rise of mutant mutable cells

---

ML 30 ind by MB and lact +

↓

ML3 not ind. by MB. does not grow on lactose and lact − (Crispaic)

not indurable by MB but grows on 10^{-2} M lactose but ind by low lactose (not const) but does it show Monod relationship Ritland says

not mutantable!

References for Monod's views

Jacques Monod, Germain Cohen Bazire, Melvin Cohn, Biophysica & Biochem Acta p. 585. 7 / 1951 see page 597 and summary. see quotes by this paper

for $i = 0$ saturation! H

$A g^* = Z_0$ gives

$$\frac{\eta(i' + i)}{Z_0 i + \eta(i' + i)} = \frac{Z_0}{A}$$

$$\frac{\eta}{A} = \frac{Z_0}{A}\left(\frac{Z_0}{A} + \frac{\eta}{A}\right)$$

$$\left(\frac{Z_0}{A}\right)^2 + \frac{\eta}{A}\frac{Z_0}{A} = \frac{\eta}{A}$$

or if $\frac{Z_0}{A} \ll \frac{\eta}{A}$

Approximate

$$\frac{1}{\frac{Z_0}{\eta} + 1} = \frac{Z_0}{A}$$

$$1 - \frac{Z_0}{\eta}$$

$$\left(\frac{Z_0}{A}\right)^2 = \left(1 - \frac{Z_0}{A}\right)\frac{\eta}{A}$$

$$\boxed{\frac{\eta}{A} = \frac{Z_0^2}{A^2}\,\frac{1}{1 - \frac{Z_0}{A}}} = \cancel{\frac{Z^2}{A^2}\,\frac{A}{A - Z_0}}$$

$$\boxed{\frac{\eta}{A} \approx \left(\frac{Z_0}{A}\right)^2}$$

Enzyme Kinetics:

S conc. of substrate

e " of total enzyme

p " complex $= [eS]$

$e-p$ " free enzyme $\boxed{= e^*}$

$$K_1 e^* S = K_2 p = K_2 [eS]$$

$$\frac{K_2}{K_1} = K_s$$

$$p = [eS] = \frac{e_x S}{K_s + S} \quad \Bigg| \quad e^x = e - \frac{e_x S}{K_s + S}$$

$$e^* = e \left\{ \frac{K_s}{K_s + S} \right\}$$

velocity of reaction $V = C[eS]$

$$v = C \frac{e_x S}{K_s + S} = C \frac{e}{\frac{K_s}{S} + 1}$$

for $S \to \infty$ $V_{max} = Ce$

~~for S finite~~ and thus

$$V = \frac{S V_{max}}{K_s + S}$$

P.T.O.

(H)

New assumption to get Monod Kinetics:

$\cancel{x\ \ = \text{Const}}\ K_0 g^*$

$i\,x^* = (x - x^*)c$

$$x^* = \frac{xc}{i+c} = \frac{D K_0 g^* c}{i+c}$$

$$g^* = g\,\frac{\eta}{x^* + \eta}$$

$$g^*(x^* + \eta) = g\eta \quad \Big\| \quad g^* x^* + g^* \eta = g\eta$$

$$x^* = \frac{(g - g^*)\eta}{g^*} = \left(\frac{g}{g^*} - 1\right)\eta$$

$$\left(\frac{g}{g^*} - 1\right)\eta = \frac{D K_0 g^* c}{i+c}$$

this gives

→ Monod Kinetics

Reality in between?? : NO.

~~[illegible]~~

~~[illegible]~~ because this does not give the right $\hat{\eta}$ dependence. –

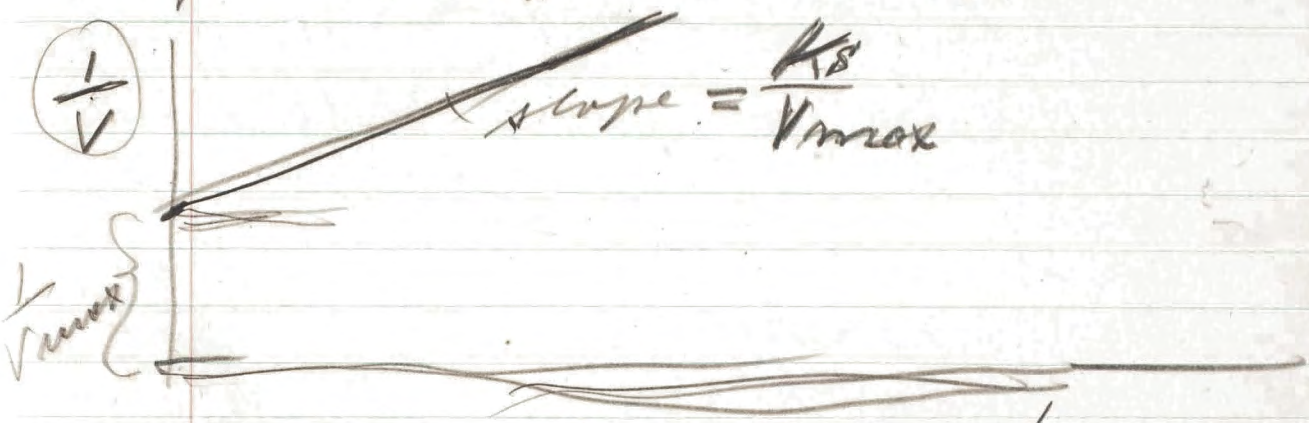
K_3 can be made very small by using a bimolekular reaction $[Se] + T = e + [ST]$ measuring ~~and without taking~~ reaction rate for very low conc. T once for low S ~~a~~ giving V and once for $S = \infty$ giving V_{max} in formula (1)

substrate

(1) and $K_S = S\left(\frac{V_{max}}{V} - 1\right)$

To find it write:

$$\frac{1}{V} = \frac{K_S}{V_{max}}\frac{1}{S} + \frac{1}{V_{max}}$$



~~Assumption~~
~~that assumption we shall make is that~~

However in such a reaction we must really write

$$K_S = \frac{K_2 + K_3}{K_1}$$

where K_3 is the rate at which S^* is transformed into S^*

Tolmadge

(1)

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tangstate matrix assigns
~~as tangstate short time~~

TE ~~TE-J~~

in this combination
Tangstate decays

TE-J

Tangstate
not destroyed

---

species dependence of antigen
"The nat. sel. theory of antibody formation"

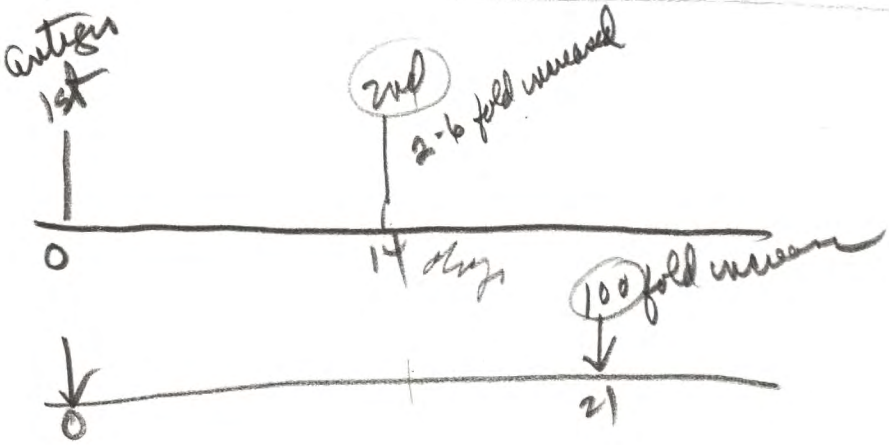
Organic strain no variability

(molecule of antigen 100 000
~~Orp E strain~~ toxin antibody
ovalbumin = 1:5000
but really 4 g% is gone
secondary

maximum titer the same for both (2)

1 mgm ovalbumin into rabbit gives almost max titer

Question?



T = template (decays) G = antigen

S = negative template

A = antibody

$T + S \rightleftarrows TS$

T and S decay

$A + T \rightleftarrows AT$

$T + AA \rightarrow A$

$T \rightleftarrows S$

$G + A \rightleftarrows AG$

$G + S \rightleftarrows GS$ (im possible decays)

(3)

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1 mg Bovine albumin in rabbit gave (detection
1 μg antigen N per ml serum

at this ~~amount~~ concentration in test tube
~~is required to bind~~ 50% antibody
is combined with antigen.

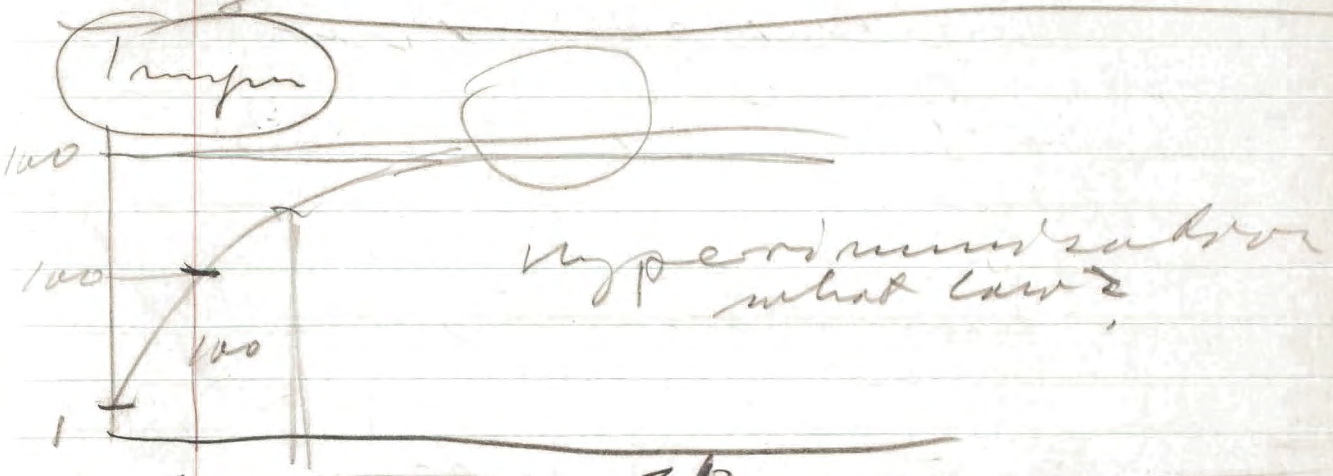
$$K = \frac{(G)(A)}{AG}$$

Assumption: antigen does not enter cells, antibody does

this selection theory explains obtaining higher combining power antibody through selection

Immunity

work barium albumine
anamnestic reaction gives
100 fold the primary titer
this should hold in general
for the tightly fitting antibody



10^6 red cells $10^{3/12}$ Antigen molecules

$10^{12} \times 10^{5} \frac{10^{17}}{6\ 10^{23}}$ gm

effect within the spleen

10^6 red cell (sheep) $= 10^{-4}$ cc packed red cells
10^7 cells/(mm)^2

Rabbit ~~bros~~ 120 cc serum
or 40 cc in one batch
filter ~ instead of centrifuging

Immunity Apr. 5/57

Experiment for Talmadge:
Inject ovalbumin [antigen] at time 0 (in primary or secondary) and at time $t = \tau$ inject antibody against ovalbumin + then head radioactive amino acid and determine new antibody by measuring activity of specific precipitate as function of τ

Wissler: antigen sheep red cells | hyphood lac.

Wissler uses β-lactoglobulin

Experiment for Talmadge:
Immunize Rabbit with an antigen to have high antibody titer. Now prepare antiserum (horse) against Rabbit Globulin and by injecting it into rabbit remove rabbits own antibodies from circulation. Is there ~~a~~ an enhanced antibody production (anamnestic response) to ~~the~~ chosen antigen — [This is better than bleeding!]
Use this method to reduce titer of antibody after 16 days (after primary injection) to reduce antibody titer before 2nd injection of antigen.

Immunity

A good immunostoc serum may give 1 mgm antibody / 10 to 15 mgm / cc total g glob / cc

Rabbit — all intravenous injections

1. Passively transfer rabbit anti sheep rbc antibody
2. Primary injection c 100 x minimum immunizing dose (10^8)
3. No detectable primary response

4. Divide animals into two groups

Group A

(a) Compare response to second injection of rbc with 1st normal (untreated) animals → no difference (normal anamnestic response for binding antibody is 5-10x primary)

Group B

Passively transfer rabbit antibody 2nd time
Inject 100 x min dose 2nd time
Detectable response of combining antibody

---

1 mgm Bovine serum alb. min sensitize for sec. response intravenously.

ML 308

constitutive ip Z level reduced
to $\frac{1}{8}$ by lactose; to $\frac{1}{2}$ by 10^{-3} galactose
10^{-4} Mol

True for 3 different strains. —
TMG restores Z activity fully
TPG also raises Z activity
Question: if we thus use TPG
can bacterium grow in lactose
as sole carbon source? Tells us where
by nitr. —

Q. Constitutive makes inducer?
Yes, because if Z were changed
lactose ~ TMG should play
no role

Enzymes in cryptic.

Assumptions 1. Const. it. and inducable make inducer but inducable has an enzyme destroying that inducer ; TMG block destroying enzyme ! What does TPG do ? No good

~~2.) without cryptic, bacs~~

~~Also constit which is blocked by~~ test. tube

~~Assumption~~

~~by lactose should not be reinduced by T.P.G~~

Assumption 2 : Const. makes inducer while the inducable does not ~~[and real inducer makes with enzyme forming rates]~~ Question depressed by Lactose ?] Yes I hope

$$\left(E \xrightarrow{nat} S\right) = E + nat\,S^{*}$$

because otherwise why does lactose depress non cryptic constitutive ?

Can be saved, if we assume that real inducer is made out of TMG by enzyme E_3 and this is blocked by TPG.

Lactose depresses constitutive because it depressed production

Nakoroom 4/p m Biochem
Central Not the R. i. S.
Janine Bernheim

inducable strain, induced
by TMG what does lactose do

Van Potter

Yates & Pardee 1956 J. of Biochem.

of real inducer $[E_1 \cdot \overset{nat}{I}_{ind}] = E_1 + \overset{nat}{I}_{ind}$
$E_1 + \text{Lactose}] = [E_1 \text{ Lactose}]$

(~~the~~ E_1 might be identical with E_3.)

Real inducer interacts with poss gene

---

assumption 2 confirmed
Can we assume that real and hist ind interacts with paragene?
(For this case and in assumption 1 paragen is unchanged. —)

The perfect mystery:
Y not inducible by melibiose
(ML 31)

Everyone

The best way to keep young is to associate with youth and the worst way to grow old is to try to keep up with youth.

Ann II McCoy p. 9 June 2 / 56

$\bar{\tau} = 2.5$ hr

density 188

500 g/l Methionine

W-14

$5 \cdot 10^{-4}$ TMG at 10^{05} AM

~~145 PM~~

11 AM	12^{30}	14^{45} PM	16^{20}	23^{25}
10.3	21.0	25.3	28	27.3

7.6 assume 5 min lag

17.2 – 17.6

~~1/10 of ceiling~~

~~1.82~~

milk says, ceiling (38) for density 188 maximum

~~1.83~~ ~~150~~

W-14

lactate limitation

28 %

$\bar{\tau} = 2.5$ hrs

$2 \cdot 10^{-4}$ M density 155

Start 10^{05} AM

11 AM	12^{30} AM	14^{45} PM	16^{00} PM
17.1	28.2	38	41

assume 5 min lag

should be

26

11.5

Mult Exp Febr 21/57

B const. lines pumps always

induced

cutting 375

lactate 10^{-3} M pushes

it down to 58

TMG 10^{-4} M raises it to 64.3

at 1/2 gen 61.3

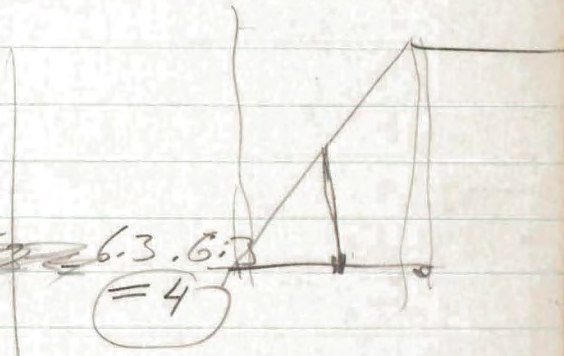
at 1 gen 63.5

total rise = 6.3

at 1/2 gen = 3.3

at 1 gen = 5.5. ~~6.3~~ 6.3. 6.3

= 4



TMG = $5 10^{-4}$ M raises it to 75 − 58 = 17

1/2 gen 69 − 58 = 11

1 gen 73.5 − 58 = 15.5 | should be 11.7

Cy says look at:

Unsolved Bases in Ochoa

A U A	C A G	U
G U G	~~U C G~~	
C U C		
A U G	C G A	
G U A	C A A	
A U C	C G G	
C U A	C A U	
C U G	C U A	
G U C	C U U	
	C A C	
	C C A	
	C C C	
		I

~~1 A and 1 U at least!~~

~~U A U~~	~~U U C~~	~~A U C~~
~~U U A~~	~~U U A~~	G
~~U U G~~	~~U A U~~	~~A A U~~
	~~U~~	

4

RNA → Enzyme

E + S = [ES] → RNA

Rivolt model

→ inoperates when coupled with Inducer

Edward, assume: Febr 23/57

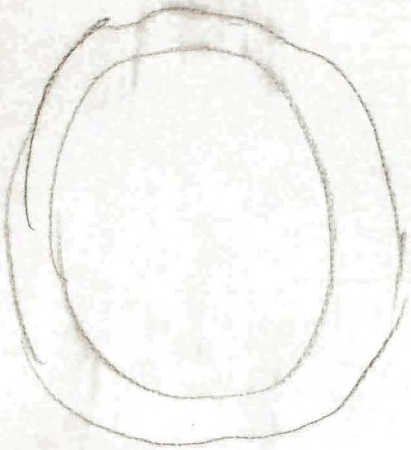
~~RNA~~ ~~no~~ Paragen makes polypeptide; ~~Polypeptide makes paragen~~ – Paragen ~~thing~~, Polypeptide rolls up if combined with inducer – not otherwise.

	U, C, A, G.		UCA	U	CUA
UUU	ACA	CAA	UCG	U	AUC
CCC	ACG	CGG	UAA	U	CUC
	GCA	ADC	UCC	U	AUA
	CCC	GGC			

lancine - machine -
- tr lancine

1064

Step' fee



Clausen

N.Y., an 6 77

Meaver

Bonnesbure

4

Prediction:
real enzyme at 1/2 ceiling
pushed there with T.M.G.
should respond ~~with~~ to
T.P.G. by increased enzyme
level because ~~we are~~
TPG combines with
β galactosidase and
we have assumed that
TMG is transformed
by some enzyme
into natural inducer

Could it be that Z is
produced by the real
enzyme ~~that~~ also high TPG

!! Theory: real inducer is produced
TMG blocks Z and raises level of TPG

THE QUADRANGLE CLUB
CHICAGO

(1)

Nulp
~~III~~ rd cop. Feb 23
Constitutive + lactose
depressed 30 or to 46
~~TMG~~ 10^{-4} M
IPG
Propagated this strain added
new saturation: 80
at 1 gen 79
at 1/2 gen 72

Strain not inducible by methylose
(lac mutant ~~K12~~ K12) called: 22-41/a
↓
22-41
J.P.G $5 10^{-5}$ M

---

62 x 63

THE QUADRANGLE CLUB
CHICAGO

(2)

Wolf

The Constitutive mutants to strain which can not grow on lactose (because it is not induced in) will be used to repeat Foster Hinshelwood's rise [when depressed by lactose and relieved by TMG]

~~Suppose the strain ML 30 mutants~~
to ML 3 non inducible by methylthiogalactoside [ML 30 inducible by TMG and by Methylthiogalactoside but does not split it]
is Lac⁻.
A mutant derived by Wolf (ML 3 Gray strain Fever in 10^{-4} M) grows on lactose which has no pumps, is not maintained by TMG. (10% of wild

P.T.O.

(3)

In MLS Methodose does not induce enzyme.

In many strains it does.

Wilde Notes of Mitt

Theory:

Natural inducer is split by β galactosidase and β galactosidase ~~combines with TMG~~ and TMG blocks the β galactosidase not in

In ordinary enzyme Real inducer is made out of TMG

(*Reprinted from Nature, Vol.* 170, *p.* 926, *November* 29, 1952)

Anti-mutagens

WHILE studying the mutagenic action of various purine derivatives on bacteria, we came across a new phenomenon : we found that certain nucleosides can act as anti-mutagens.

Following the discovery[1] that caffeine—a purine derivative—increases the mutation-rate in fungi and in bacteria, we began a quantitative study of the mutagenic action of purine derivatives. Such a study has been made possible by the use of a constant flow device, called the 'Chemostat'[2-4], which maintains a stationary bacterial population growing at a fixed rate that can be set at will. The concentration of the bacterial population maintained in the growth tube of the 'Chemostat' is determined by the input concentration of one of the required nutrients, called the controlling growth factor, and the growth-rate is fixed by the rate at which fresh nutrient flows into the growth tube.

A variety of different mutations will occur at different rates in such an otherwise stationary population, and if one plots the concentration of one particular type of mutant against time, one should obtain a straight line which rises with a slope that is determined by the mutation-rate. This holds for each type of mutant which grows at the same rate as the parent strain, that is, if there is no selection for or against the mutant. If there is selection against a mutant, the concentration of that mutant will remain stationary after an initial rise.

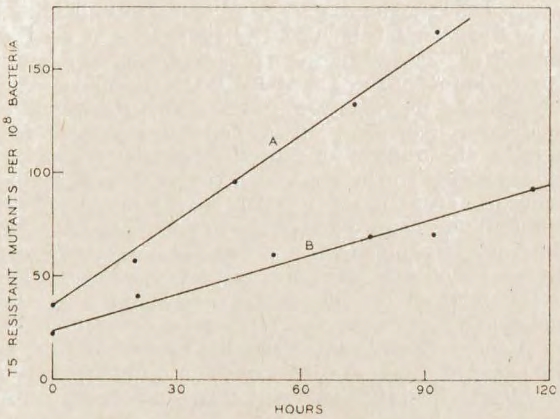


Fig. 1

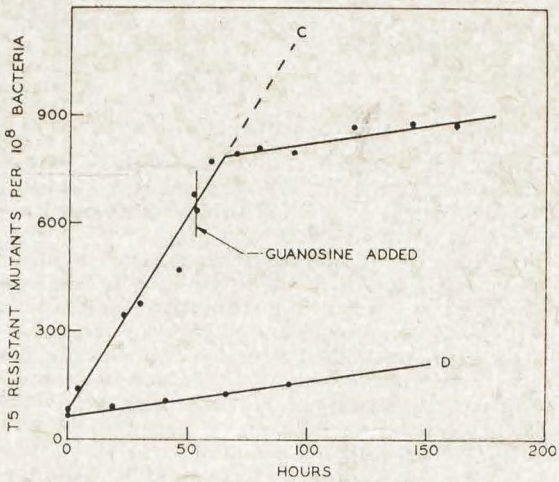


Fig. 2

In the experiments to be reported here, we used a strain of *E. coli* (*B*/1*t*) requiring tryptophane, and used tryptophane as the controlling growth-factor. This organism is sensitive to the bacteriophage *T*5. Mutants resistant to *T*5 present at any given time in the population growing in the 'Chemostat' can be scored by colony count simply by adding a small quantity of the virus *T*5 to an aliquot at the time of plating; in the presence of the virus, only the resistant mutants will grow out into colonies.

As we reported earlier[3], mutation to *T*5 resistance occurs at a constant rate independent of the rate at which the bacteria grow, that is, independent of the generation-time of the bacteria. By plotting against time the number of *T*5-resistant mutants present in the growth tube of the 'Chemostat', one obtains curve *A* of Fig. 1. The slope of this straight line gives a mutation-rate $\mu = 1 \cdot 4 \times 10^{-8}$/bacterium/hr.

When the nutrient medium contains theophylline (a dimethylxanthine) in a concentration of 150 mgm./l., the number of mutants rises very quickly, corresponding to the straight line *C* in Fig. 2, giving a mutation-rate of $10 \cdot 7 \times 10^{-8}$/bacterium/hr. This represents a seven-fold increase in the mutation-rate, which we attribute to the mutagenic action of theophylline. However, if the nutrient contains, in addition to 150 mgm./l. of theophylline, 50 mgm./l. of the nucleoside guanosine, the number of mutants rises much more slowly, as shown by line *D* in Fig. 2. The slope of this line corresponds to a mutation-rate of about 1×10^{-8}/bacterium/hr., indicating that

guanosine, in the concentration used, completely counteracts the mutagenic action of the theophylline.

In the experiment mentioned earlier, which is described in the upper curve in Fig. 2, the bacterial population is first grown (at a generation-time of 3·2 hr.) in the presence of 150 mgm./l. of theophylline with no guanosine present. After 53 hr., guanosine is added to give a concentration of 150 mgm./l. For the first 53 hr. and for a short time thereafter, the number of mutants follows the straight line *C*, which gives a mutation-rate of $10{\cdot}7 \times 10^{-8}$/bacterium/hr. ; but afterwards the number of mutants follows another straight line which gives a mutation-rate of less than $1{\cdot}5 \times 10^{-8}$/bacterium/hr. The two straight lines intersect, not at the time when the guanosine is added, but about 12 hr. later.

In order to explain this 12-hr. delay in the fall of the mutation-rate after adding guanosine, we do not have to assume that it takes that time for the guanosine to counteract the mutagenic effect of theophylline, but may attribute the delay to the fact that mutations are not immediately expressed in the phenotype of the bacteria. When the guanosine is added, the mutations induced by theophylline may very well cease to occur ; but the mutations induced prior to the addition of guanosine continue to be expressed phenotypically for a period of about 12 hr.

The results shown in Fig. 2 have to be interpreted as an actual reduction of the mutation-rate by guanosine ; that is, they cannot be attributed to a selection against the bulk of *T*5-resistant mutants resulting from the presence of guanosine. It is easy to show that if such a selection were responsible for the low mutation-rate shown by line *D* in Fig. 2, then in the upper curve in Fig. 2 the number of mutants resistant to *T*5 should fall steeply after adding guanosine at the 53rd hour.

The concentration of guanosine needed to counteract the mutagenic effect of 150 mgm./l. of theophylline is quite low. For a concentration of about 2 mgm./l. of guanosine, the rate of mutation induced by theophylline falls to one-half.

The other normally occurring purine ribosides were examined for anti-mutagenic action at concentrations of 5 mgm./l. At this concentration adenosine and inosine are strongly anti-mutagenic against theophylline, whereas xanthosine has no such activity. In contrast to inosine itself, its components, that is, the free purine hypoxanthine and the free sugar ribose, are not anti-mutagenic even at concentrations of several hundred milligrams per litre.

A concentration of 500 mgm./l. of guanosine gives

practically complete suppression of the mutagenic action of the following purine derivatives (at concentrations of 150 mgm./l.) : theophylline, caffeine, theobromine, paraxanthine, and 8-azaguanine. But tetramethyluric acid and benzimidazole retain more than half their mutagenic effect.

One may ask what effect guanosine has on the spontaneously occurring mutations. As can be seen from line *B* in Fig. 1, 50 mgm./l. of guanosine gives a mutation-rate of $0 \cdot 6 \times 10^{-8}$/bacterium/hr., that is, one-half to one-third as much as the spontaneous mutation-rate derived from curve *A*. This shows that guanosine in the concentration used reduces the mutation-rate to *T*5 resistance appreciably below the spontaneous mutation-rate.

AARON NOVICK
LEO SZILARD

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University of Chicago,
Illinois.
July 30.

[1] Fries, N., and Kihlman, K., *Nature*, **162**, 573 (1948). Demerec, M., Bertani, G., and Flint, J., *Amer. Naturalist*, **85**, 119 (1951).

[2] Novick, A., and Szilard, L., *Science*, **112**, 715 (1950).

[3] Novick, A., and Szilard, L., *Proc. U.S. Nat. Acad. Sci.*, **36**, 708 (1950).

[4] Monod, J., *Ann. Inst. Pasteur*, **79**, 390 (1950). Novick, A., and Szilard, L., *Cold Spring Harbor Symp. Quant. Biol.*, **16**, 337 (1951).

Printed in Great Britain by Fisher, Knight & Co., Ltd., St. Albans.

4

RNA → Enzyme

E + S = [ES] → RNA

Built model

unpoisons when coupled with Inducer

Evolved, Assume: Febr 23/57

~~RNA m~~ Paragen makes Polypeptide; ~~Polypeptide makes paragen~~ – Paragen ~~Hangs~~, Polypeptide rolls up if combined with inducer – not otherwise.

	U, C, A, G		UCA	U	CUA
UUU	ACA	CAA	UCG	U	AUC
CCC	ACG	CGG	UAA	U	CUC
	GCA	ADC	UCC	U	AUA
	CCC	GGC			

Apr 23 Forward phasing

$$\begin{cases} (z - z_1 - z_2)\, i = z_1 \alpha \\ (z - z_1 - z_2)\, y = z_2 \beta \end{cases}$$

$$z i - z_2 i = (\alpha + i) z_1$$

$$\begin{cases} z_1 \\ z y - z_2 (y + \beta) = y z_1 \end{cases}$$

$$z \frac{i}{\alpha + i} - \frac{z_2 i}{\alpha + i} = z - z_2 \frac{y + \beta}{y}$$

$$z \frac{1}{\frac{\alpha}{i} + 1} - \frac{z_2}{\frac{\alpha}{i} + 1} = z - z_2 (1 + \beta / y)$$

$$1 + \frac{\alpha}{i} = r \qquad 1 + \frac{\beta}{y} = R \qquad R > 1$$

$$z - z_2 = z r - z_2 r R$$

$$(R r - 1) z_2 = (r - 1) z$$

$$z_2 = \frac{r - 1}{R r - 1} z$$

$$z_1 = \frac{R - 1}{R r - 1} z$$

$$z^* = z \left(1 - \frac{r - 1}{R r - 1} - \frac{R - 1}{R r - 1} \right)$$

$$\boxed{z^* = z \frac{1 + R r - r - R}{R r - 1}}$$

Lockwood Theory Apr 23

Prorepressor makes Polypeptide equilibrium

Polypeptide builds up at slow rate but also combines with prorepressor; when inducer attached does not combine with prorepressor. —

TPG acts two ways blocks enzyme and thus prevents destruction of nat. inducer and blocks polypeptide also

Nat. inducer y is made at rate ν and destroyed at rate εz^*

$$\frac{dy}{dt} = \nu - \varepsilon z^* - \frac{y}{\tau}$$

$[t=0 \quad y = y_0]$

$$\varepsilon z^* = \nu - \frac{y}{\tau}$$

$$y = \nu\tau - \varepsilon\tau z^*$$

Stationary state

$$K_1(z^* i) = K_2(z_1 z^*)$$

$$\begin{cases} z^* i = [z_1]\alpha \\ z^* y = [z_2]\beta \\ z_1 + z_2 + z^* = z \end{cases}$$

$$\frac{\lambda}{\varepsilon} - s_1 s_2 z = z \frac{1}{\underbrace{1+\frac{i}{\alpha}}_{r} + s_3 z}$$

$$\frac{\lambda}{\varepsilon} r + \frac{\lambda}{\varepsilon} s_3 z - z\, s_1 s_2 r - z^2 s_1 s_2 s_3 = z$$

$$\frac{\lambda}{\varepsilon} r = \left(1 + s_1 s_2 r - \frac{\lambda}{\varepsilon} s_3\right) z + z^2 s_1 s_2 s_3$$

Try again Shortcuts

Start. $y_0 = \lambda\tau - \varepsilon\tau z_0^*$

$$z_0^* = z_0 \frac{1}{1+\frac{i}{\alpha}+\frac{y_0}{\beta}}$$

$$y_0 \cong \frac{z_0}{\text{Const}\,\tau}$$

$$y_0 = \lambda\tau - \varepsilon\tau z_0 \frac{1}{1+\frac{i}{\alpha}+\frac{y_0}{\beta}}$$

$$y_0 = \lambda\tau - \frac{\varepsilon}{c\varepsilon} y_0 \frac{1}{1+\frac{i}{\alpha}+\frac{y_0}{\beta}}$$

$$\tau y_0 + \frac{y_0^2}{\beta} = \lambda\tau\tau + \lambda\tau\frac{y_0}{\beta} - \frac{\varepsilon}{c} y_0$$

$\tau y_0 = \lambda\tau\tau$

P.T.O.

~~Check~~:

$$r = 1 + \frac{\alpha}{i} \qquad h = 1 + \frac{\beta}{g}$$

$$z^* = z \frac{\frac{\alpha}{i}\frac{\beta}{g}}{\frac{\alpha}{i} + \frac{\beta}{g} + \frac{\alpha}{i}\frac{\beta}{g}}$$

$$z^* = z \frac{1}{1 + \frac{i}{\alpha} + \frac{g}{\beta}}$$

Approx. assumption:

$$\boxed{\frac{dz}{dt} = \text{Const}\, g - \frac{z}{\tau}}$$

Sat. state $\varepsilon z^* = h - \frac{g}{\tau}$

$$\frac{h}{\varepsilon} - \frac{g}{\varepsilon}\frac{1}{\tau} = z \frac{1}{1 + \frac{i}{\alpha} + \frac{g}{\beta}}$$

$$\text{Const}\, g = \frac{z}{\tau}$$

$$g = \frac{z}{\text{Const}\,\tau} = s_2 z$$

~~s_1~~

~~$\text{Const}\,\tau = s_2$~~

$$\frac{h}{\varepsilon} - \frac{z}{\text{const}}$$

$$\frac{h}{\varepsilon} - s_1 g = z \frac{1}{1 + \frac{i}{\alpha} + \frac{g}{\beta}}$$

$$\begin{cases} s_2 = \frac{1}{\text{Const}\,\tau} \\ s_1 = \frac{1}{\varepsilon\tau} \end{cases}$$

$$\frac{s_2}{\beta} = s_3$$

Solution

~~Transp~~ Theory from

scratch: y = nat. number one

i = TMG one.

$$\frac{dy}{dt} = \lambda - \varepsilon y z^* - \frac{y}{\tau}$$

$$\boxed{\text{Stat. } y = \frac{\lambda\tau}{\varepsilon\tau z^* + 1}}$$

$$y = \frac{\lambda\tau}{\dfrac{\varepsilon\tau z_0}{r + \dfrac{y}{\beta}} + 1}$$

z_0 = const y

$$\frac{\lambda\tau\left(r + \dfrac{y}{\beta}\right)}{\varepsilon\tau z_0 + \left(r + \dfrac{y}{\beta}\right)} = y_0$$

$$\lambda\tau r + \lambda\tau\frac{y_0}{\beta} = \varepsilon\tau z_0 y_0 + y_0 r + \frac{y_0^2}{\beta}$$

$$(\lambda\tau - y_0)\, r = \varepsilon\tau z_0 y_0^2 + \left(\lambda\tau - \frac{\lambda\tau}{\beta}\right) y_0 + \frac{y_0^2}{\beta}$$

$$r = \frac{\quad}{\lambda\tau - y_0}$$

sign wrong

$$\zeta_0 r + \frac{\zeta_0^2}{\beta} = \lambda\tau r + \lambda\tau \zeta_0 - \varepsilon\tau z_0$$

$$\varepsilon\tau z_0 = \lambda\tau r + \lambda\tau \zeta_0 - \frac{\zeta_0^2}{\beta} - \zeta_0 r$$

$$z_0 = \frac{\zeta_0}{\text{Const}} \quad \Big\| \quad \frac{\varepsilon}{\text{Const}} \zeta_0 = \lambda\tau r + \lambda\tau \zeta_0 - \frac{\zeta_0^2}{\beta} - \zeta_0 r$$

$$\frac{\varepsilon}{\text{Con}} \zeta_0 - \lambda\tau r - \lambda\tau \zeta_0 - \zeta_0 r = -\frac{\zeta^2}{\beta}$$

Determine i as a function of z_0!

$$\zeta_0 r + \frac{\zeta_0^2}{\beta} = \lambda\tau r + \lambda\tau \frac{\zeta_0}{\beta} - \varepsilon\tau z_0$$

$$(\zeta_0 - \lambda\tau) r =$$

$$(\lambda\tau - \zeta_0) r = \frac{\zeta_0^2}{\beta} - \frac{\lambda\tau \zeta_0}{\beta} + \varepsilon\tau z_0$$

$$r = \frac{\frac{\zeta_0^2}{\beta} - \frac{\lambda\tau}{\beta}\zeta_0 + \varepsilon\tau z_0}{\lambda\tau - \zeta_0}$$

$$r = 1 + \frac{i}{\alpha}$$

$$\cancel{\frac{dr}{di} = \frac{\lambda\tau}{\alpha} \simeq \frac{2\cos}{2\,\mathrm{const}\,\varepsilon\tau\, y_0 \frac{dy}{di} - \frac{1}{\beta}\frac{dy}{di}}}$$

$$\cancel{\frac{\lambda\tau\beta}{\alpha} \sim \left(2\beta\,\mathrm{const}\,\varepsilon\tau\, y_0 - 1\right)\frac{dy}{di}}$$

$$\boxed{\frac{y_0}{\lambda\tau} \ll 1}$$

$$\frac{dr}{dy} = \frac{1}{\alpha}\frac{di}{dy} \simeq \frac{\lambda\tau}{\alpha}\frac{di}{dy} \simeq$$

$$\simeq 2\tau\,\mathrm{const}\,\varepsilon\tau\, y_0 - \frac{1}{\beta}$$

Let us write $y_0 - \underbrace{y_0[i=0]}_{} = D$ $\quad y^0$

$$y - y^0 =$$

$$= \lambda\tau\left[\frac{\tau + y/\beta}{\varepsilon\tau\,\mathrm{const}\,\tau\, y + \tau + \frac{y}{\beta}} - \frac{1 + y^0/\beta}{\varepsilon\tau\,\mathrm{const}\,\tau\, y^0 + 1 + \frac{y^0}{\beta}}\right]$$

$$y^0 = \frac{1 + y^0/\beta}{m\left(1 + \frac{y^0}{\beta}\right) + 1 + \frac{y_0}{\beta}}$$

$$\lambda\tau\, r + \frac{\lambda\tau}{\beta} y_0 = \varepsilon\tau z_0 y_0 + y_0 r + \frac{y_0^2}{\beta} \quad H$$

$$(\lambda\tau - y_0)\, r = \varepsilon\tau z_0 y_0 + \frac{y_0^2}{\beta} - \frac{\lambda\tau}{\beta} y_0$$

$$\left(1 - \frac{y_0}{\lambda\tau}\right) r = \frac{\varepsilon\tau}{\lambda\tau} z_0 y_0 + \underbrace{\frac{\beta y_0^2}{\lambda\tau\beta} - \frac{y_0}{\beta}}$$

$$\left(1 - \frac{y_0}{\lambda\tau}\right) r = \varepsilon\tau z_0 \times \frac{y_0}{\lambda\tau} + \frac{y_0}{\beta}\left(\frac{y_0}{\lambda\tau} - 1\right)$$

$$\left(1 - \frac{y_0}{\lambda\tau}\right) r = \varepsilon\tau z_0 y_0 - \frac{y_0}{\beta}\left(1 - \frac{y_0}{\lambda\tau}\right)$$

$$r\left(1 - \frac{y_0}{\lambda\tau}\right) = \frac{1}{\lambda\tau}\left(\tau\, \text{Const} \times \varepsilon\tau + \frac{1}{\beta}\right) y_0^2 - \frac{y_0}{\beta}$$

$$r = \left\{\frac{1}{\lambda\tau}\left(\qquad\right) y_0^2 - \frac{y_0}{\beta}\right\} \frac{1}{1 - \frac{y_0}{\lambda\tau}}$$

large

$$r \cong \left\{\frac{y_0}{\lambda\tau}\, \varepsilon\tau\, \text{Const} \times \tau\, y_0 + \cancel{\frac{y_0}{\lambda\tau}\frac{y_0}{\beta}} - \cancel{\frac{y_0}{\beta}}\right\} \cancel{\frac{1}{1 - \frac{y_0}{\lambda\tau}}}$$

for $\varepsilon >> \beta$

$$r = \frac{1}{\lambda\tau}\left\{\tau\, \text{Const}\, \varepsilon\tau\, y_0^2 + \frac{y_0}{\beta}\left(\frac{y_0}{\lambda\tau\cancel{\beta}} - \cancel{1}\right)\right\} \frac{1}{1 - \frac{y_0}{\lambda\tau}}$$

Manual: Room 1105
Mutter
6-3266

K for enzyme

TMG M/100

TDG M/500 has no effect on cryptic

TPG M/2000 has effect on cryptic

TPEthylG M/50000 weak inducer

pumpless constitutive
inhibit of with galactose!

Question: those which combine strongly with enzyme and are not inducers (TDG), for instance, need not be inhibitors of cryptic. —
But TDG aut to help lactose (rgalactose) inhibited constitutive pumpless strain. —

Ben Acceraff

Inappropriate for
TMG

Pulmudye

4

a

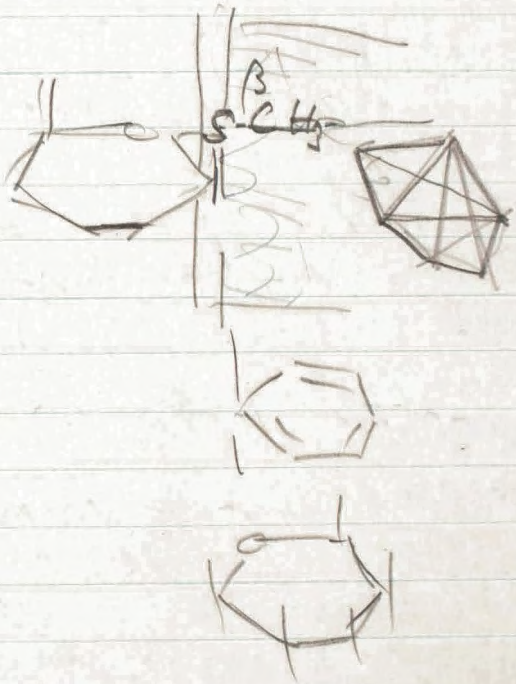
A B

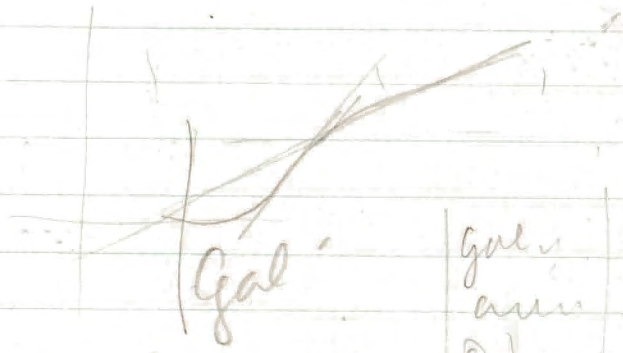
antiserum a

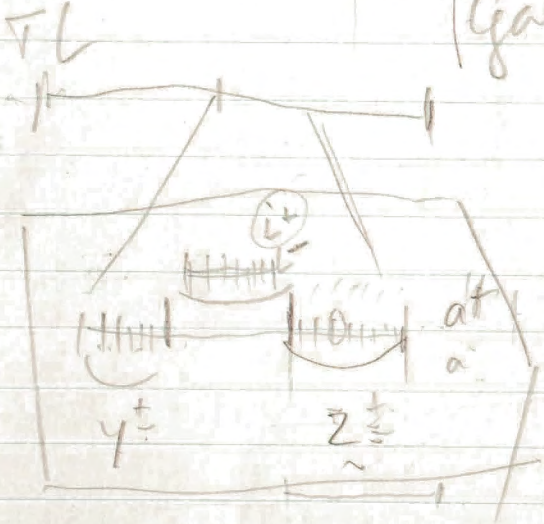
10 (A) → a → + B

ex rabbit + A.S. A

+ A







Gal
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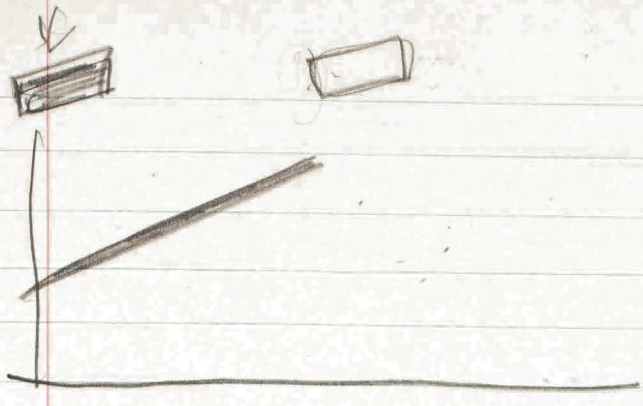
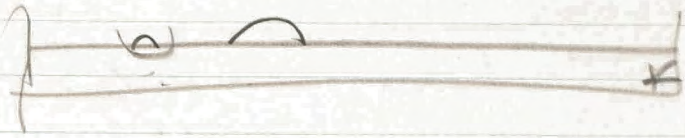
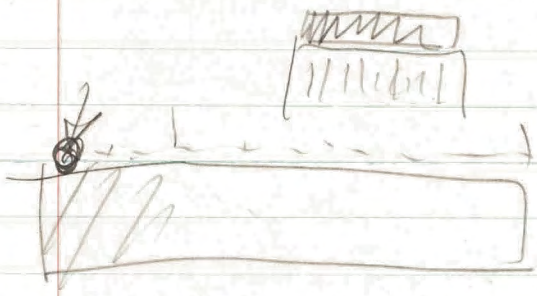
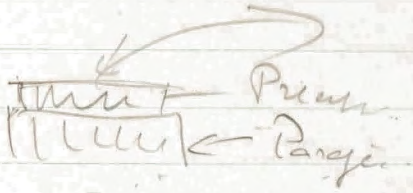
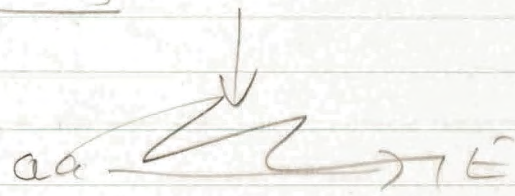
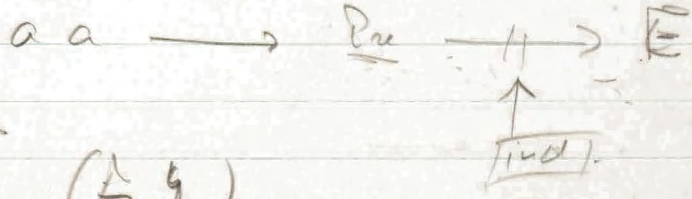












$\boxed{E^*}$ (E ↯)

$$y + G \rightleftharpoons Gy \rightleftharpoons y' + G$$

Histidine

glycine
NH_{4}
Hist. a

$\rightarrow$

glycine
Hist.

Check Mull results;

Eilard Arrny

$$\frac{dh}{dt} = Kg \frac{\eta(1+c)}{2c + \eta(1+c)} - \frac{z}{\tau}$$

for $\tau = 1$;

For

$$2\frac{dx}{dt} = \frac{1}{f}\, 2\omega = \frac{1}{f}\,\frac{A}{n}$$

$$\frac{dn}{dt} = \frac{A}{\dfrac{2(n-1)\,n}{A} + 1} - \frac{2}{\tau}$$

for large n

$$\frac{dn}{dt} \approx \frac{A}{\dfrac{2(n-1)}{f} + 1} - \frac{2}{\tau}$$

$$\approx A\,\frac{f}{n-1+f} - \frac{2}{\tau}$$

for $\dfrac{n-1}{f} \gg 1$ $\boxed{\text{for } \tau = 1}$

$$= \frac{A}{n}\left[\frac{f\,n}{n-1+f} - \frac{1}{f}\right]$$

for $\left.\begin{matrix} n = 10 \\ f = 2 \end{matrix}\right\}$ $\dfrac{20}{11} - \dfrac{1}{2} \approx \dfrac{3}{2}$ "Normal" shape

for $\left.\begin{matrix} n = 10 \\ f = 4 \end{matrix}\right\}$ $\dfrac{40}{13} - \dfrac{1}{4} \approx 2$ "minimal" shape

W-2241 grows on Melibiose which induces permease

W-2242

Novick thinks TMG* induces permease I

Conference Mar 15

(has. prompts)

Weak Const. → 20% of "ceiling"

10^{-4} TPG reduces to 1% of "ceiling" down to zero

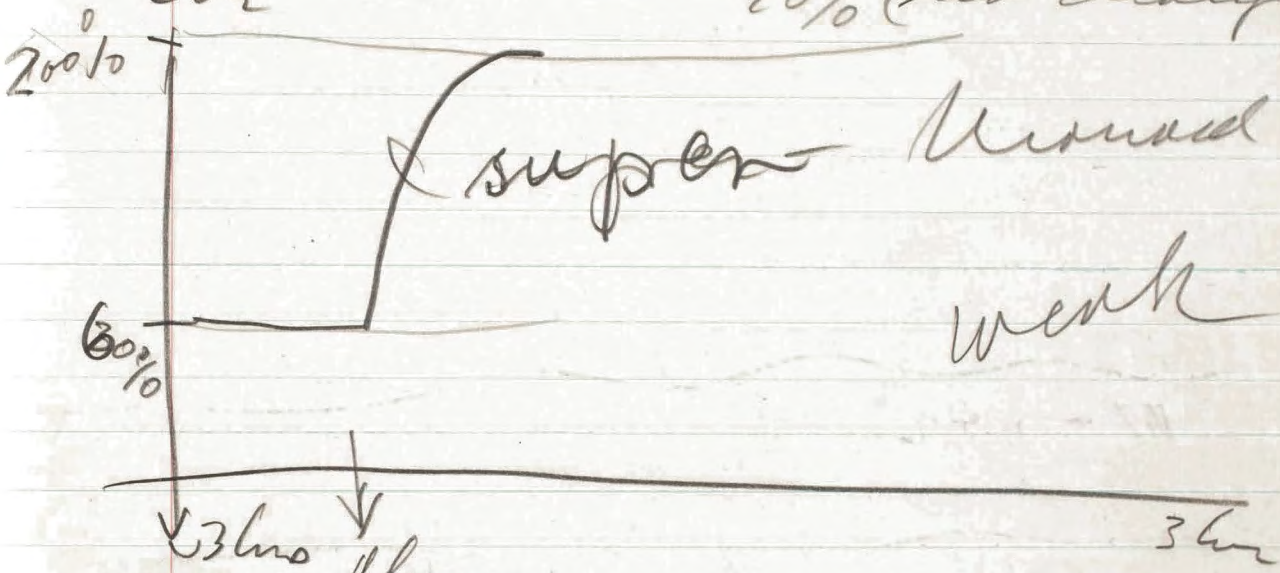
$5\ 10^{-4}$ glucose

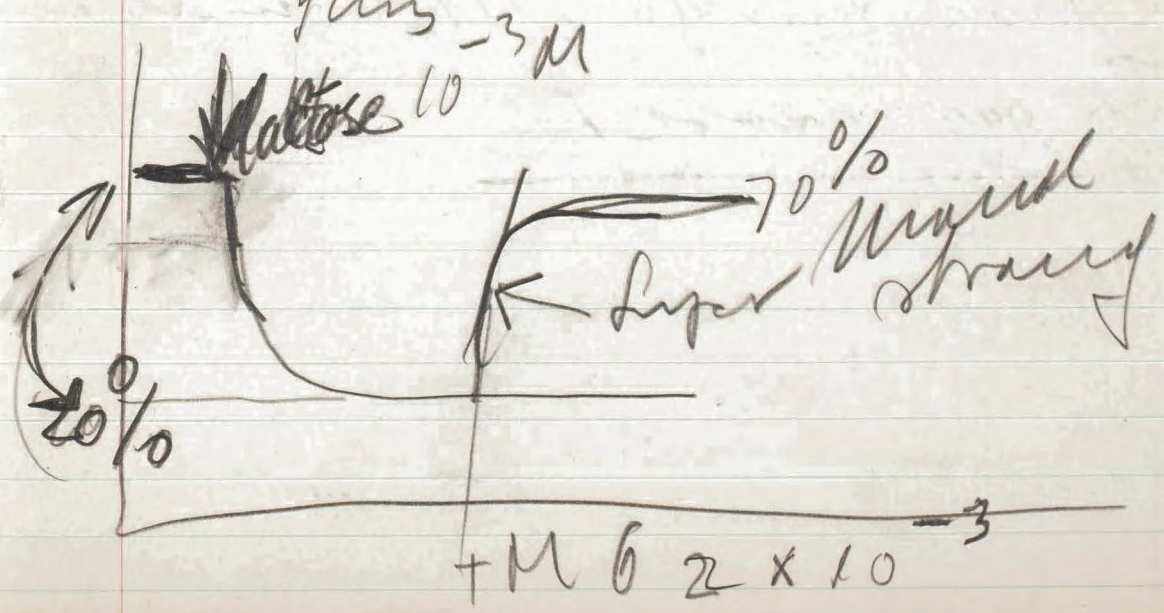
7×10^{6} TMG

200% of ceiling

CO_2

20% (no change)

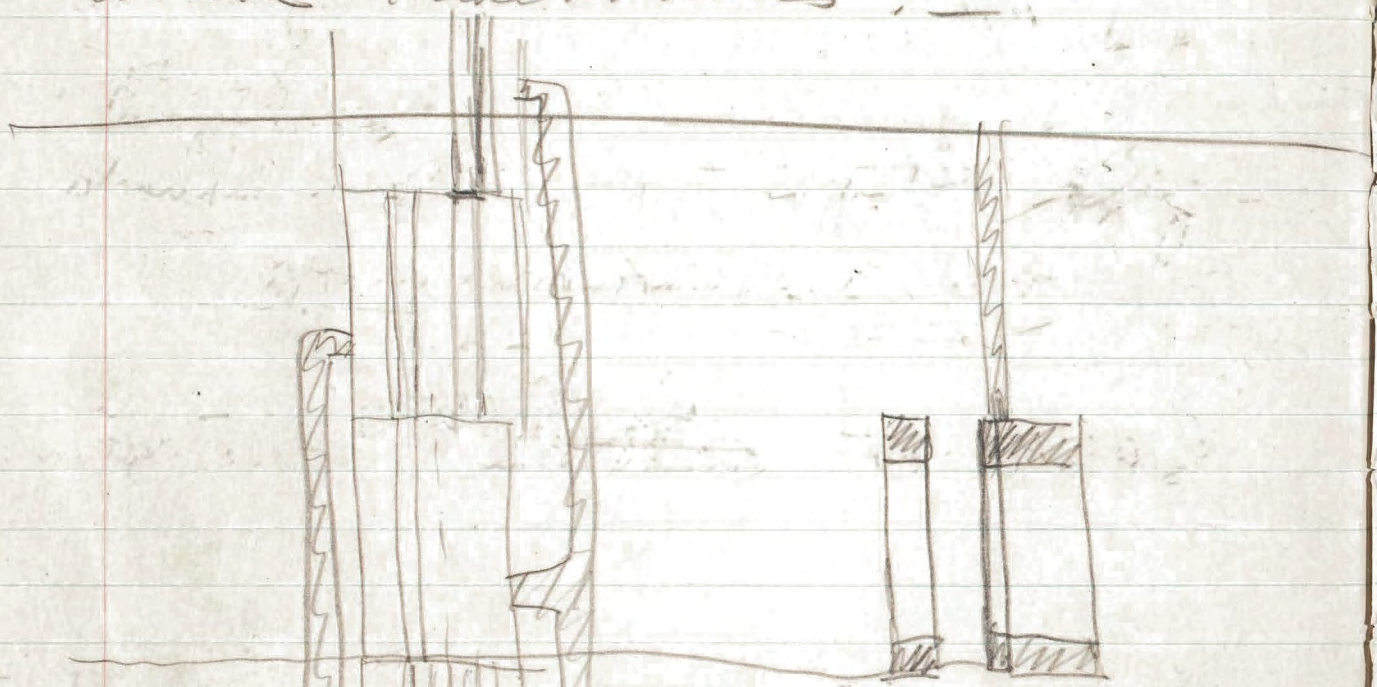




$$K = \frac{[ES]}{[E][S]}$$

1 st he / 133,000 enzyme mol wt / 8 or 6 for 800,000 mol. weight

Vessine inactivates. —



UDPgal + β gal + poly
→ poly-galact + UDP

TPG and IMG
can not conjugate
in cytoplasm

cytoplasm: const.
inhib. of galac
~~not conjugated~~

UDPG = uridine diphospho glucose
UDPGal - " " galactose

β-galactosidase

Possible not ind
- α-galactose-1-PO_4
- uridine diphosogalactose

Utilization of galactose (man, yeast, coli)

uid.

1.) galactose + ATP $\xrightarrow{\text{gal-kinase}}$ gal-1-PO_4 + ADP

2.) galactose 1 PO_4 + UDPG $\xrightarrow[\text{uridyl transferase}]{}$ UDPgal + gluc-1-PO_4 (small trace)

into cell

Z

constit (coli)

3.) UDPGal $\xrightarrow[\text{const.}]{\text{epimerase}}$ UDPG.

UDPG + PP $\xrightarrow[\text{const.}]{\text{uridine DP glycosyl pyrophosphatase}}$ UTP + gluc-1-PO_4

the ind?

1.) Question: Principles — how T.M.G. can it be overcome by galactose?

2.) Galactose ind. chemostat what does c in growth tube do if TMG is added?

3.) Does "real inducer" inhibit the enzyme?

4.) Cryptic (abs.) is depressed by galactose

gal Trans is induced by galact. if grown in succin

~~10 inches~~ ~~20 cm~~

$400\,cm^2 \times 1\,cm \approx 1/2\ kg$

One burst 1100 Watt sec

Apr 27/57

Cryptic, cant strong,
should not be inhibited by
T.P.G when grown on maltose
Galactose should inhibit it
but this is lifted by TPG
[not lifted by TMG]

In cryptic Galactose inhibition
should not be lifted by TMG

We can understand why TPG
induces weak const. (abnormal enzyme)

Nuts: Supernatant: ~~[illegible]~~ | Non-cryptic |

1.) with TMG (low) (in weak const)
2.) or Lactose depressed strong const with TMG
3.) Galactose depressed " " with TMG

2MBV

10^6 Rep

1 el Stat

30 Volt x 1 el Stat. x 10^6

$\frac{30 \times 10^6}{3109}$ Watt sec

$\frac{1}{100}$ Watt sec 1 cc air

10 Watt. sec

50% eff.

20 Watt

20,000 Watt

1 cc

1 kg/sec

60 000 input

3 kg/sec // 3600 x 3 ≈ 10000 kg/hr

60 cent. steel lining

plastics

600 units

1 city block 3 story bldg
WISTAR

1/2 IIIrd floor McLimans
4,100 000 x 3 1/2 % 140,000
70,000 —
+ 25 000 from Press

Billingham Oct 10th

isogenic mice

3 month, — within one month kills

(normal)
virus — vesicular stomatitis (horse)
intravaginally (no antibodies,
or hexapyrene treated for two month
prior to virus — ~~two~~ nothing
2,4 C treated 3 month with hexapyrene
and then re fed with virus
virus multiplies on cervix
(pass in carcinoma cells)
malignancy will develop

malignancy implanted of labia
skin in another isogenic mouse
after 3 ~~trans~~ passage we make
ascites tumor [intraperitoneally]
transplant into a mouse (no skin)
mouse under skin

Theory

Results in remarkable const. 4

because if stage of increase of TMG is added we assume with high TMG destruction by Z is stronger than regular destruction. In this strain regular destruction is inherently weak and this is reason for const. nature. —

~~Upon adding~~ Initially however, when Z is still low, even at high TMG, ~~destruction~~ regular destruction predominates (other wise ~~rate~~ growth rate should in the absence of TMG. regular destruction even higher.

I assume it does initially, why not and then fall? — does it?

and that TMG increases production rate. This would account for positive & dependence but how can TMG increase production rate? Clearly by inducing the enzyme that 'produces' the NS

Tumor will disappear. — Take lymphnodes cell (of B mouse) and inject it into isogenic A mice with ascites; same out; tumor activity in A mice (lymphnode other not survive)

isogenic mice treated with benzpyrene + lymphnodes from other strain of mice (B) (also control)
with normal lymphnodes
~~After inoculation~~
isogenic mice painted for 3 month during with once a week intolerant B lymphnode was given intraperitoneally. — develops lymphoma intraperitoneally

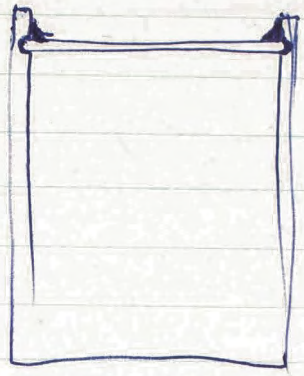
---

controls a.) benzpyrene and inj. normal lymphnodes

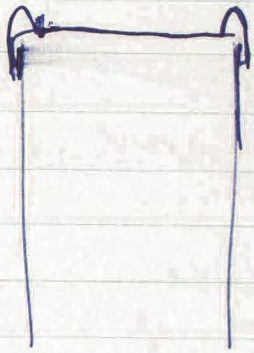
b.) no benzpyrene and intolerant lymph node

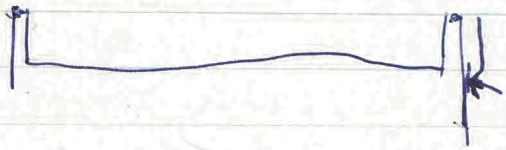
(isogenic CBH)
B strain = ACR (not isogenic)

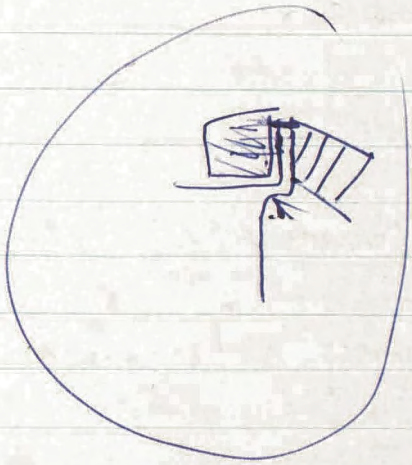
Smakup.

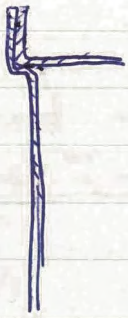


polyethylene-tape









Ulr

Ulr can measure the antitoxin to toxoid 25×10^{-4} microgram antibody (nitrogen) Antus within 2 hrs.

H & Y immunized with Rabbit and vice versa in hypergammaglobulinemia

[In experiment inject human antigen]

delayed type hypersensitivity appears in 4 days in guinea pig

To transfer D.H. in Man may take 100 cc [packed leucocytes $\frac{1}{10}$ cc]

To desensitize use human. guinea pigs

→ Salvin (Montana) Rocky Mtn Lab. || Hamilton ||
Colin Mackenzie

Pace

In actively immunized (intramuscular) Rabbit (trained) there is no delayed type reaction (not much)
(Schick positive means the lad in diphtheria toxin gives reactions. and has no antitox)

Another series

Strain: PRI strain (not dog.)
from A to B inject ascites
after 7 days inject West Nile
virus which destroys
tumor; B now resistant
broadly to ~~tumor~~ a
variety of tumors
If no virus treatment
but tumor represses
only narrow intolerance
ensues

Take a mouse with
spontaneous tumor. (not PRI strain)
and treat it as above
tumor [not transplanted
tumor because smaller. —

with tumor ascites)

HERRIOT Hirschfeld

Å 10 mμ

100,000

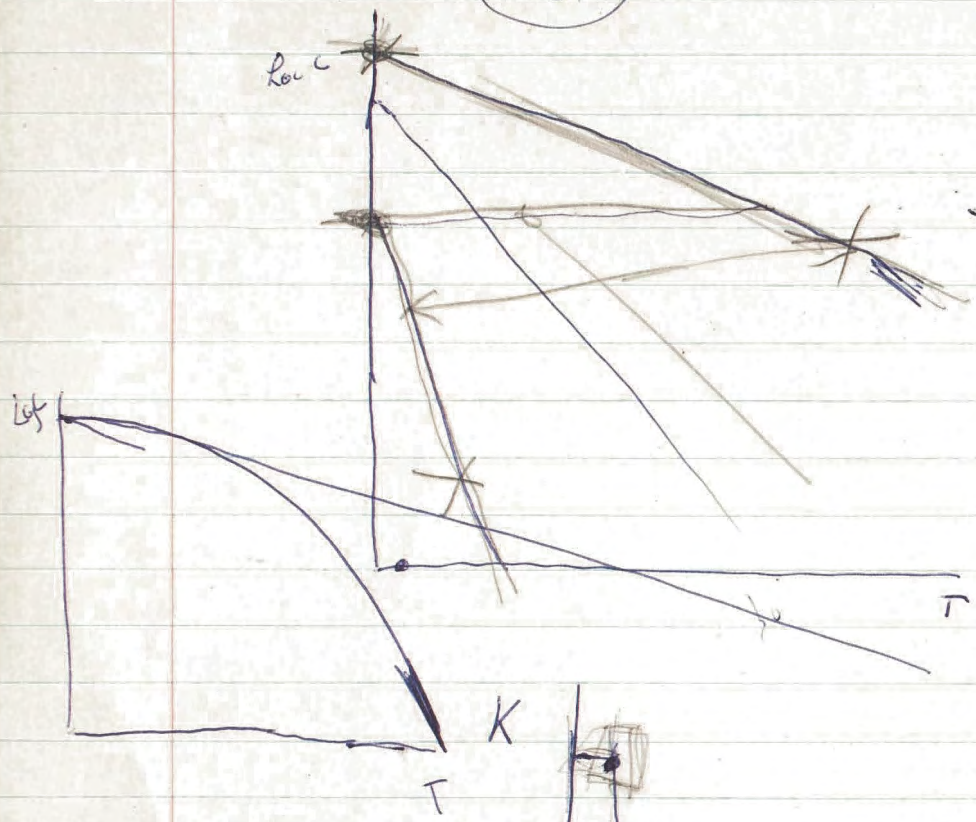
10,000

250 Å

P

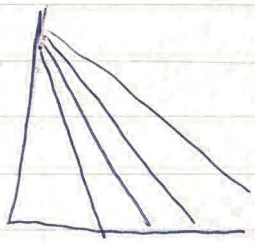
251

$C = C_0 10^{-\boxed{K}t}$



$-\frac{dc}{dt} = ct\,\frac{C}{C_0}$

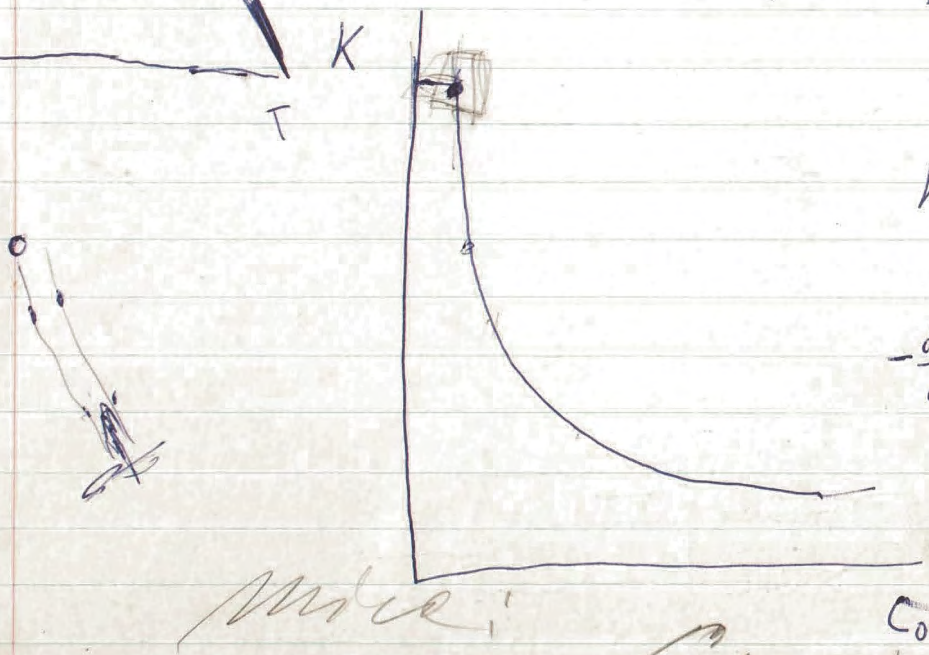
$C_0 = C + P$



K

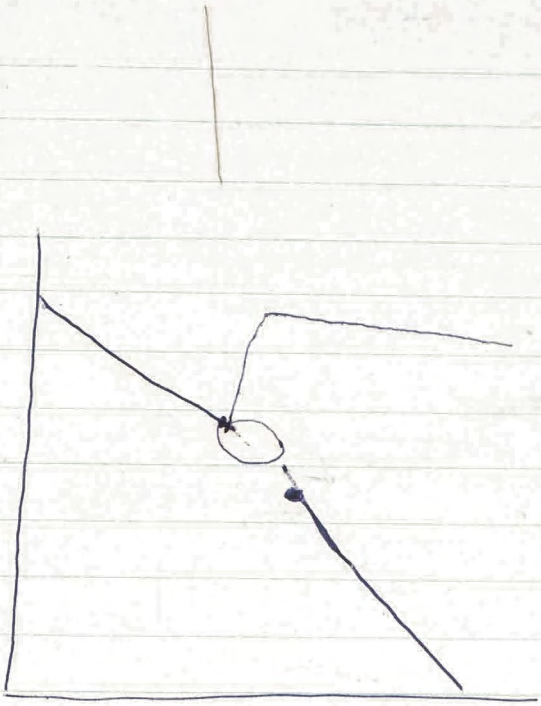
$K \times C_0 = ct$

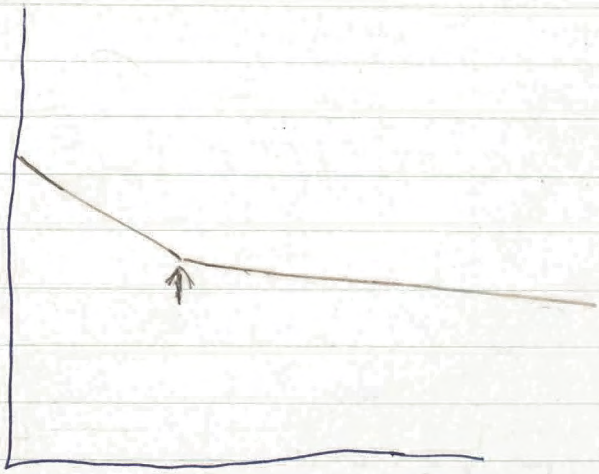
$-\frac{dc}{dt} = ct\left(1 - \frac{P}{C_0}\right)$

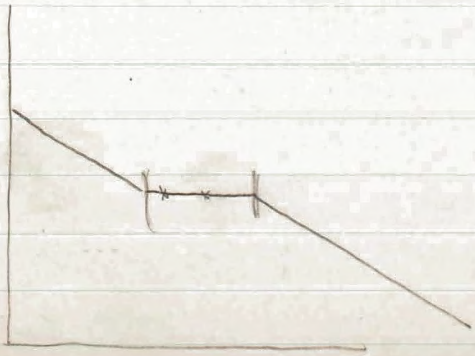


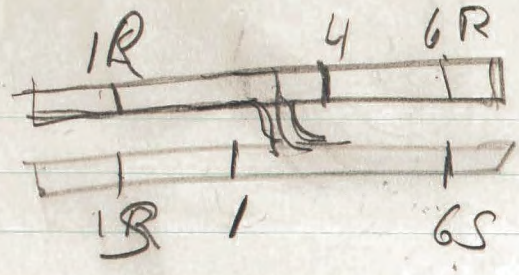
Mole:

200 mgm Carbon / 100 mgm moight

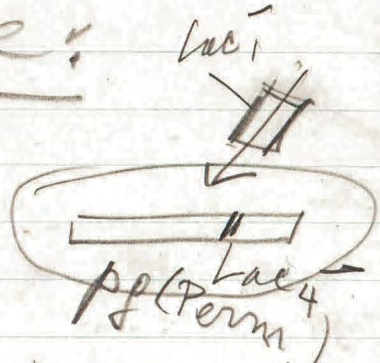






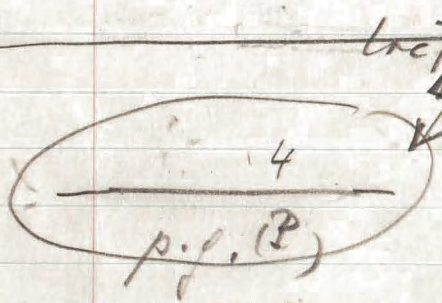


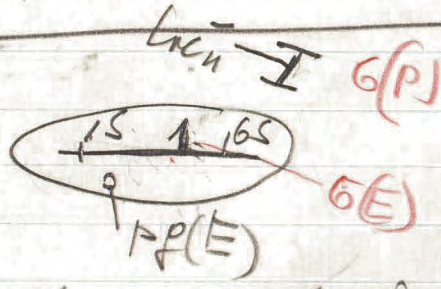
Alternative:



≠ —

little p.g for any lac4 lots p.g Perm	lac1 lots of Perm



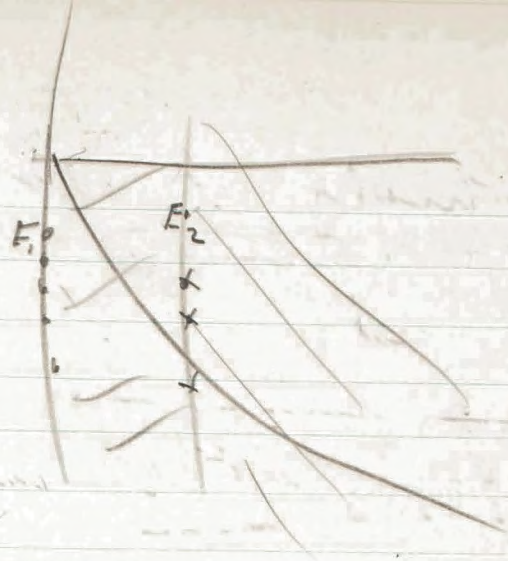


majority	minority
lac4 6(P) μ·6(P) much pumps few p.g(E)	6(E) μ·6(P)

majority	minority
6(E) μ·6(E) few pumps much p.g(E)	6(P) μ·6(E) many pumps few p.g(E)

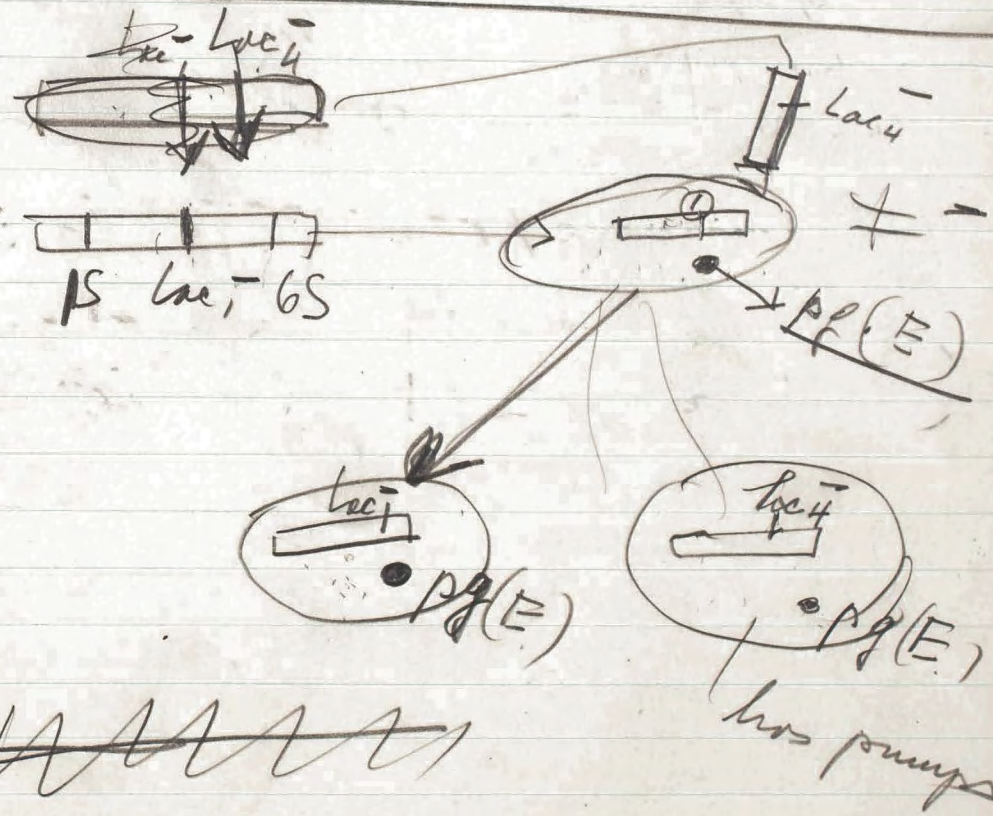
Paper

Mult:



Pulser:

Humphrey



Exp. Wolf Apr 5/87

1.) Study kinetics in changing τ, transition to next ~~st~~ 2 level, in ~~cons~~ perfect cryptic

2.) Effect of TDG on 3 ~~into~~ neck constitutive. Does it prevent leaking out of induction?

3.) Select cryptic (perfect) from const. mtk TMG, lactose and Melibiose.—

4.) In W2241 Does Melibiose abolish conversion TMG to TMG* ?

{ Does bryophenoxide ~~into~~ ~~fore~~ abolish it?

Immunology

J. Sterzl and M. HRUBEŠOVÁ
Inst. of Biol.,
Czech Acad. of Science
Praha

Folia Biologica p. 193
Vol I 1955
Fasc 4

also
Tom II Fasc 1 1956 p. 21

Taffner (Weigle Dixon)

Why does young rabbit not form antibodies? Czech exp. and fact that transplanted thymus gland (from non immunized rabbit) gives different results makes me suspect that yeast extract would help young rabbit.

~~Basic fact for~~

For Werner test

Strong const. not inhibited by TPG.

Note A Class of Gal when grown on succinate ~~[illegible]~~ in the presence of galactose gets induced. —

Note Test ~~[illegible]~~ inhibition ~~of st~~ of permease in strong const

~~TPG~~ should inhibit growth on galactose

{ Local lac argument }

Note no galactose depression of induction by transferring to lag galactose

Note check with Alr that no TDG brought up of weak constitutive depression by galactose or lactose (non cryptic.) with Dulbecco

Note check whether induction in weak const. || as Werner thinks || shows super induced induction by TDG.

Theory:

TDG is not reacting with 3rd enzyme but with β galactosidase! This explains why TDG in work chest. gives Emp mononol kinetics. Exp to do: Cyphic add TMG now TDG should give mono-mononol kinetics. —

~~Theory:~~

TMG gives Monod kinetics in cyptic and only if concentration is high enough to slow growth.

Fit indicates E, and E2 because a β-galactosidase inhibitor

TP Ethyl G M/50000 should be used in place of TMG present

4 incl 5
Thesis

For c/o Cristo Pinheiro
Dept. of Finance) Pittsburgh W.
"The University"

Nelson 330 pm R.J. ~~Small Class~~
Wed. Nov 6

645 Pk. Ave 845 pm Hans H. Wales
Room 1403 &

Monday Nov 4th Amphitheatre A 5 pm
630 W 168th Street

~~240 Ave~~ Room 240 Pappenheimer Library

Measures

3 teaspoon	1 tblsp.
4 tblsp	1/4 cup
2 tblsp	= 1 ounce
1 cup	1/2 pint
2 cups	1 pint
4 "	1 quart

Newdale book:

Russian drug
Phthivazid
a benzaldehyde hydrazon of INH

English drug Smith & Nephew
Nupasal Salicylaldehyde
hydrazon of INH
(Salizith in USA.) made by Nypera U.S.A.
America

3 to 6 cents Piridoxin 50 to 100 mgm / person
16 to 20 mgm INH / kg
3 to 6 cents

~~4~~XXXX (4X) skins
Intrans ~~Charith~~ Schmid's Co N.Y 3 Lora #1

for Viscanti
Carnatron Company

Room 21 Lowenthal
Barry

Leo Lowenthal

r: 1214 Contra Costa Drive
El Cerrito, Cal.
LAndscape 6-5607

o: Departments of Speech and/or Sociology
University of California
Berkeley 4, Cal.
ASberry 3-6000 X13-449, 13-450

Sherwood Lawrence
Am. Journ. of Medicine
Vol 20 p. 240 (March) 1956

Frederic J. Lewy M.D. (Ha 56090)
765 No Broadway Hastings on Hudson
N.Y. & Am. Heart Ass. E. 23rd.

419

M. Fr. Morning-Bandler

S/15/57

Involved E 2-1881
School Du 8-4511 Found

452 The Rockefeller
49 W 49 Street
New York 20 N.Y.

Dean Rusk

Women Women

Evening
Mon
Wed p.m.
Fri.

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345 E 46th N.Y. 17 N.Y.

Ford Foundation
Mr. Peak Vice Pres
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