Paul Steiner
Prof. of Path
Eldnor Humphreys Chicago

leukemia in virus
Matthew Block 3182 S. Holly $\boxed{\text{M 107}}$
SK 6-6328

Herman Hoster
Bibliography of Hodgkins. —

Milt Verner says James Crostie
Univ of Wash Seattle
Hematologist (dept of Med)
T.M. 52

reticulum cells ~~lymphoblasts~~. [mesoderm]

opinion
thus of
disease

the
metabolic
role

Harold
~~[illegible]~~
Pathologist - Stewart at
Nat. Cancer ~~Bethes~~
Inst.

Healthy lymph node into
patient + cord serum

unwitting
~~the tumor~~
the wrong
lymph node
region

Wurmck

TA57905

5726 Drexel (W.)

Biochemical Bio-
physica acta
~~abstracts of biochem.~~

Phils
Adm 2401
J 312

Nordik
Midd ~~2~~ 1958
Sat 2540

2338
2971

Sunyside Pux
5318 S. Cornell
Mi 38320 until Aug 15.

arch Meder Fa 45531 (E. Unger)
Berkeley 2524
(Warring Str.
Thornwald 3 62 65
July Aug

Arnold (Oak Ridge)
Eberts (Indiana)
Lindslide (Syracuse)
Eden (~~Ar~~ Bethesda)
Asmund (Oak Ridge
Mahler (India)
Gibbs (Brookhaven)
~~Joe Hoffmann~~
Dan Tosteson
((Bentley Glass))

50%
50%
25%

L16415

526

211

Ch 72200

SZILARD

Gr 83246

583 Urain
Bunge
6 2900
Tax
20909
28000
69558
~~2900~~

Volumes

40% of total (Galvestone)
extracellular 20 – 25%
of total body vol
30% Muscle Volume

At rest 1/3 of vol in
muscle

Thyroid removal
drop bas. met. rate to 60%

Grose, meltbold Maldre

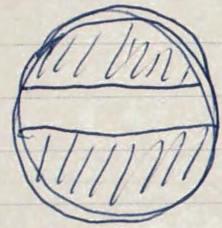
Stress 1/2 to 2/3 4

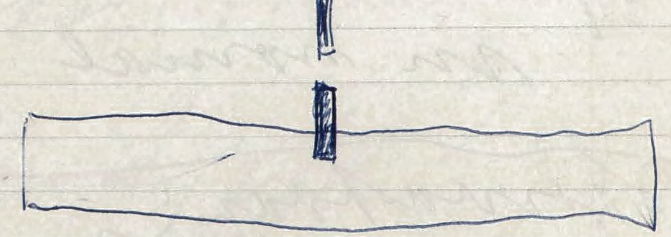
of 2000 Cal were glucose
in normal

Starvation:
less 1/3 glucose

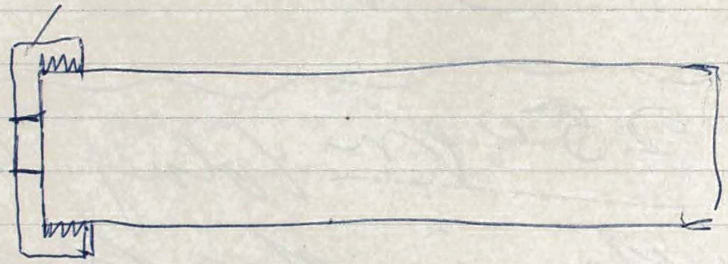
5 250 gm body sugar
made in diabetic
liver. —
1000 Cal

1 hr 1.5 gm glucose (kg/hr
for maximum insulin / does
it not apply?)
In no liver ~~At~~ 0.5 gm
Lundsgaard Copenhagen





plastic



Jerman ; Buffer

Ion exchange resin for tissue culture

short mesh → IR 45 ??

(Rochm & Haas)

$N(CH_2-CH_2OH)_3$

tri ethanolamine

$pH = 7.9$

or

$NH_2-\overset{O}{\overset{\|}{C}}-CH_2-NH_2$

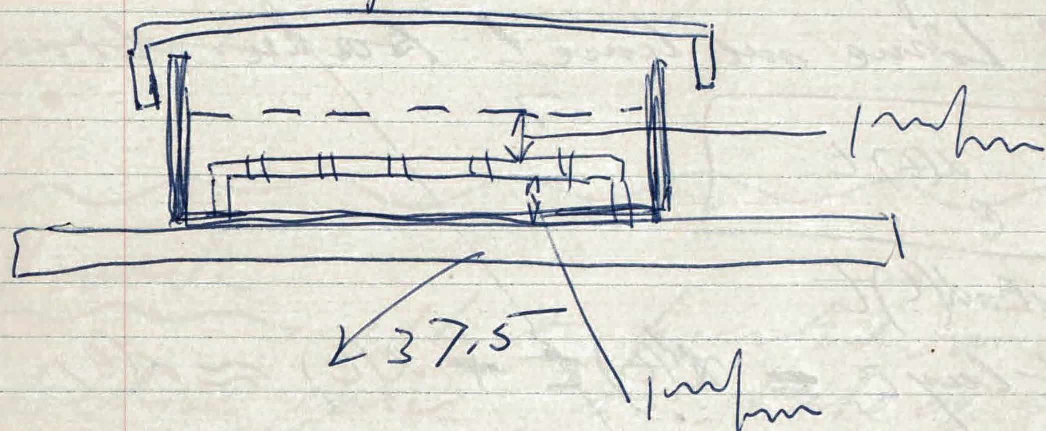
glycine amide pH 7.5 to 8

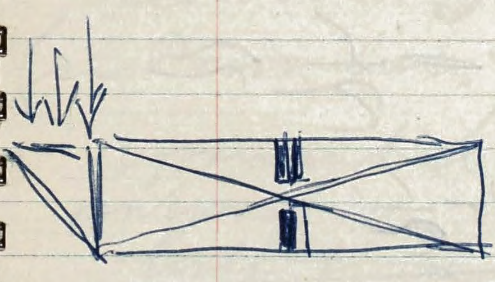
32 liter

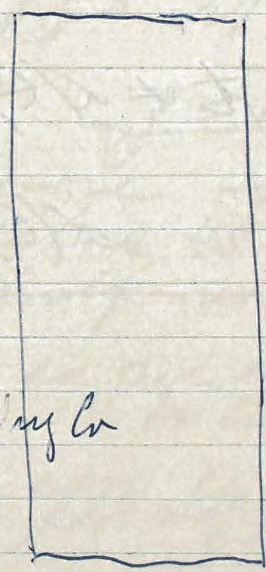
$\boxed{32\ gm}$

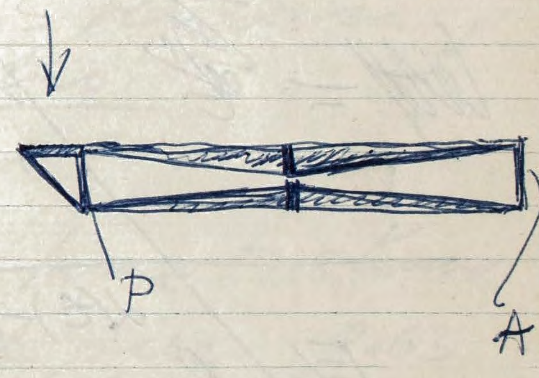
Febr 21/55

Single Cell dances!

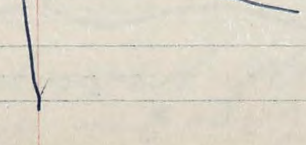








Abegg Fellows Printing Co
Key 4 4054
1454 Welton Str.



Exp. No 8

$\frac{d}{dt} \log E$ = ~~[illegible]~~

corrected for ~~[illegible]~~

for 3.2 [illegible]

at which time we have ! saturation

$$\boxed{E = e^{\alpha(t) t}}$$

$$\log E = \alpha(t) t$$

$$\frac{d}{dt} \log E = \alpha'(t) t + \alpha(t) \approx \alpha(t)$$

$\cancel{N e^{\beta t}}$ Interesting value

$\cancel{e^{\alpha t}}$

$$\cancel{\log N} = \cancel{\frac{\log}{\alpha}} \quad \alpha'(t) t + \alpha(t) - \frac{1}{\tau} \approx$$

$$\alpha(t) - \frac{1}{\tau}$$

$$E/B \quad e^{\alpha(t) - \frac{1}{\tau}}$$

246

[illegible] [illegible]

Lloyd O Timblin Jr.
Bureau of Reclamation
Be 3-3611, EX541

Novick

What function of lactose conc. is rate of lactose splitting in suspension of adapted cells?

Inducer 5 10^{-5} M ~~[illegible]~~ β thio m. g. ~~Exp~~ No5
(in broth less) $g = 1.88$ hrs

exponential rise after 10 to 20
saturation value 45
~~half time~~ half value time 7.5 hours
gen. time of exponential rise in chemostat 0.63 hours
δ = gen time of exp. enzyme rise 0.47 hours corrected for mortality rant
Silard factor $\frac{\text{gen time}}{\delta} = \frac{g}{\delta} = 4$

Nitrogen control

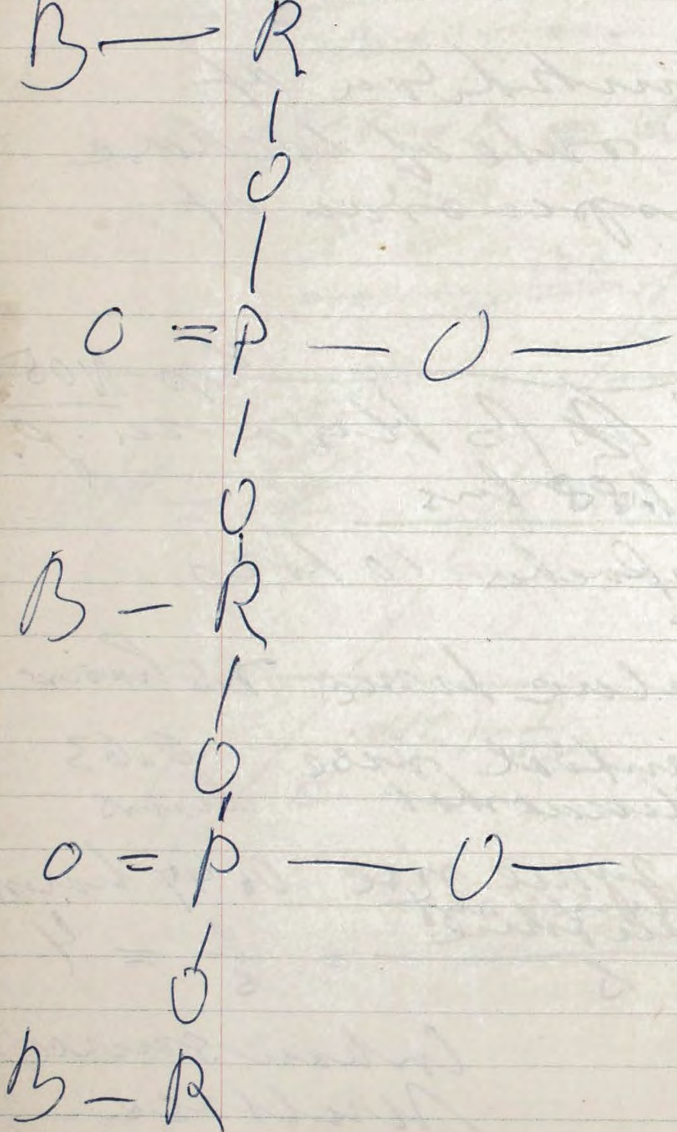
Carbon source
Maltose

bacterial density
Beck = 0.182 at 350

$E/B = At$

$E = e^{\alpha t} At$

Watson-RNA



ORGEL
oxfd

George)
Widaver
(Kinlaw)

Moldave &
Heidelberger
p. 679
J.A.C.
76 1954

RNA made by DNA may have base ratios characteristic of DNA whereas virus RNA may have no base ratios.—

80-30 in 45°

1935-36

H.

E is hubal enzyme in best tube

$e^{\beta(t)t}$

$\beta \longrightarrow \alpha$

$\beta' \longrightarrow 0$

Gain is chem. $e^{(\beta(t)-\alpha)t} = Z$

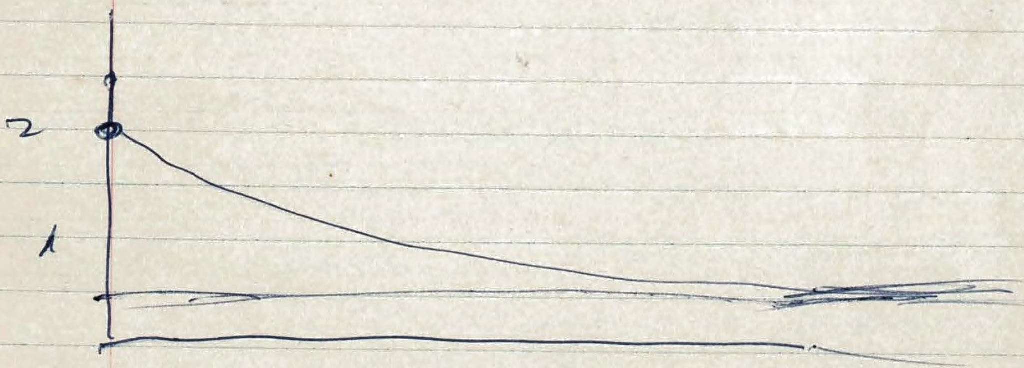
$\log Z = [\beta(t) - \alpha]\, t$

$\frac{d}{dt} \log Z = \beta(t) + \beta'(t) \cdot t - \alpha \simeq \beta - \alpha$

1 + 0.2 x 3

β starts with 2.1 ... 1

0 hrs ... at 3.5 hrs



Novick:
$m_{\|}$ linear regulation
z enzyme on demand

$$\frac{dn}{dt} = P - \frac{z}{\tau} = K$$

$$K + \frac{z}{\tau} = P$$

P is production per unit.
z is enzyme per unit.

Shehler [B. b.]

Murray Edeen / Princeton / dept of math

Morton Gibbs

St. Francisco Apr. 12

~~Kestler [illegible]~~

~~[illegible]~~ $(y \times E)$

$$\frac{y \times E}{\cancel{x}} = k$$

assumption that anyone ~~[illegible]~~ ~~with indirect multiples~~ [illegible]

$$\frac{k = \cancel{A} \pm e^{\alpha t}}{\tau}$$

~~In Saturation~~

$$\frac{E}{B} = C \qquad \frac{dE}{dt} = \frac{\beta}{\tau} N \frac{y}{N} + \frac{kN}{\tau}$$

(multiplying units independent of $\frac{E}{N}$ dependent only on Ind./N

In Saturation

$$\alpha = \cancel{[illegible]} \; \frac{1}{E}\frac{dE}{dt} = \frac{\beta}{\tau} N \cdot \frac{y t}{\cancel{N} E} + \frac{KN}{\tau E}$$

In Stat. stat ~~[illegible]~~ state;

$$\frac{1}{E}\frac{dE}{dt} = \alpha$$

(multiplying units proportional to $\frac{y}{N}$ ~~[illegible]~~ $\frac{E}{N}$

Before saturation

$$\frac{1}{N}\frac{dE}{dt} = \frac{\beta}{\tau} \cancel{N} \frac{yE}{N} + \frac{k \cancel{N}}{\tau}$$

Platt is every H
mutation an inversion?

Mutation sensitivity in
phage at time would decide this! —
Agent X rays. But why ~~are~~ is
mutation rate linear with intensity?
It could be deletion rather than
inversion.
Would fit with Horvick-Sutland law
of mut. rate ~~per~~ per ion track!
For certain fraction of time in sensitive
state. —

Phage by using thymineless tryptophane less mutant!

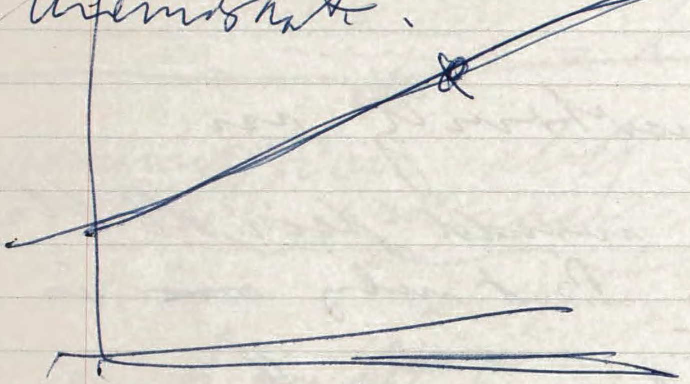
P. → DNA → P → DNA

↓

P

$$E = E_0 + e^{\alpha t}$$

In Chemostat!



at low inducer and enzyme in Chemostat:

$$\frac{dE}{dt} = \cancel{\frac{1}{\tau}E} + \frac{KN}{\tau} - \cancel{\frac{E}{\tau}}$$

$$\frac{dE}{dt} = \frac{\beta^*}{\tau} N \frac{y}{N} \frac{E}{N} + \frac{KN}{\tau} - \frac{E}{\tau}$$

$$\frac{1}{E}\frac{dE}{dt} = \left(\frac{\beta^*}{\tau}\frac{y}{N} - \frac{1}{\tau}\right) + \frac{KN}{\tau E} = \frac{1}{\tau}\left(\beta^*\frac{y}{N} + \frac{K}{\frac{E}{N}} - 1\right)$$

$$\beta^* \frac{y}{N} = 1$$

1

$N = e^{\alpha_0 t}$

Saturation

Y is inducer amount

$$\frac{dE}{dt} = \frac{\beta}{\tau}\frac{NY}{N} + \frac{KN}{\tau} \qquad \beta = 1$$

$$\alpha = \frac{1}{E}\frac{dE}{dt} = \frac{\beta N}{\tau}\frac{\cancel{YN}}{E} + \frac{KN}{\tau E}$$

$$\alpha = \frac{\beta}{\tau}\frac{Y}{N}\frac{1}{\frac{E}{N}} + \frac{K}{\tau}\frac{1}{\frac{E}{N}} \qquad \beta^{+} = K$$

$\frac{Y}{N} \ll E/N$ $\qquad E/N = \frac{Y}{N} + K$

Be (in linear region?)

$$\frac{dE}{dt} = \frac{\beta^{*}}{\tau} N \frac{E}{N} + \frac{KN}{\tau}$$

$\frac{E}{N} \approx \frac{Y}{N}$ $\quad$ if enough inducer and enzyme = to enzyme*

If no inducer

$$\frac{dE}{dt} = \frac{K_0 N}{\tau}$$

$$\frac{1}{E}\frac{dE}{dt} = \frac{K_0 N}{\tau E} = \frac{K_0}{\tau}\frac{1}{\frac{E}{N}} = \alpha$$

$$\frac{E}{N} = \frac{K_0}{\alpha\tau}$$

check : in chemostat

$$\frac{dE}{dt} = kN$$

$$\frac{dE}{dt} = \beta E - \frac{1}{\tau} E + kN \qquad \beta = \frac{1}{\tau}$$

~~[illegible]~~ !

mass action law : fight by molding pl [illegible] [illegible]

$$k_1 a_1 b_2 = k_2 c \qquad \frac{k_2}{k_1} = M$$

$A = a + c$

$B = b + c$

$$(A - c)(B - c) = M c$$

$$AB - Bc - Ac + c^2 = Mc$$

$$(M + A + B) c = AB + c^2$$

$$c^2 - (M + A + B) c + AB = 0$$

$$X^2 - (M + A + B) X + AB = 0$$

$$a X^2 + b X + c = $$

$$x = \frac{-b \pm \sqrt{b^2 - 4c}}{2}$$

$$\frac{b^2}{4} \mp b\sqrt{\quad} + \frac{b^2 - 4c}{4} \qquad - \frac{b^2}{2} \pm b\sqrt{\quad} \qquad \frac{+4c}{4}$$

$$X = \frac{M + A + B \pm \sqrt{(M + A + B)^2 - 4AB}}{2}$$

$$(M + [A + B])^2 = M^2 + 2M(A + B) + [A + B]^2$$

$$M^2 + A^2 + B^2 .$$

At first no inducer 4

$$\frac{y}{N} = g^{t/\tau}$$

$$\frac{dE}{dt} = \frac{1}{\tau} N g^{t/\tau} + \frac{kN}{\tau}$$

In chemostat

$$\frac{dE}{dt} = \frac{1}{\tau} N g^{t} + \frac{kN}{\tau} - \frac{E}{\tau}$$

100

$$\frac{1}{E}\frac{dE}{dt} = \frac{1}{\tau}\left[\frac{g^{t/\tau}}{E/N} + \frac{k}{E/N} - 1\right] = \alpha\left[g^{t/\tau}\right.$$

10

$$= \frac{1}{\tau}\left[\frac{g^{t/\tau}}{k} + \frac{k}{k} - 1\right]$$

at $t = 0$

100

let $\frac{g}{k} = 40$

$k = 10$

$\frac{E}{N}$ at $t = 0$ $= k$

$$\frac{g}{k} = 4$$

Saturation $E/N >> Ind/N$

$$\frac{dE}{dt} = \frac{\beta}{\tau}\frac{Y/N}{\frac{M}{E/N}+1}N + \frac{kN}{\tau} \qquad \beta = 1$$

$E/N >> 1$

$Y/N >> E/N$

$$\frac{dE}{dt} = \frac{\beta}{\tau}\frac{E/N}{\frac{M}{Y/N}+1}N + \frac{kN}{\tau}$$

for $S/N <<<< M$

$$\frac{dE}{dt} = \frac{\cancel{\beta}}{\tau}\frac{E/N}{\frac{M}{gt}+1}N + \cancel{\quad}(k_0+Jt)\frac{N}{\tau}$$

In chemostat:

$$\frac{d}{dt}\log E = \frac{1}{\tau}\frac{gt}{M} - \frac{1}{\tau} + \frac{[k_0+Jt]}{\tau}\frac{1}{E/N}$$

~~Exponential part:~~ ~~stage~~ large $k_0 e^{4\alpha t}$

~~Const~~ i.e. $E = \frac{dY}{dt}$

~~Constit~~ $\quad x \quad \frac{E\ E}{\frac{M}{i}+1} - gS$

$$= \frac{dY}{dt}$$

$$\left(1-\frac{C}{A}\right)\left(\frac{B}{A}-\frac{C}{A}\right)=\frac{MC}{A} \qquad \frac{B}{A} \ll 1$$

~~[illegible]~~ $C \neq B$ if $M \gg 1$?

$$\frac{B}{A}-\cancel{\frac{C}{A}}+\cancel{\left(\frac{C}{A}\right)^2}-\frac{C}{A}\frac{B}{A} \cong \frac{M}{A}\frac{C}{A}$$

$$C \cong \frac{B}{M}$$

and for $\frac{B}{A} \ll 1$ but $M \ll 1$

$$\frac{B}{A}-\frac{C}{A}+\cancel{\left(\frac{C}{A}\right)^2}-\cancel{\frac{C}{A}\frac{B}{A}}=\frac{M}{A}\frac{C}{A}$$

$$\frac{B}{A}=(M+1)\frac{C}{A}$$

$$\boxed{C=\frac{B}{\frac{M}{A}+1}}$$

holds for all M if $\frac{B}{A} \ll 1$

and if $\frac{A}{B} \ll 1$

$$C=\frac{A}{\frac{M}{B}+1}$$

small M is tight binding

$$\frac{d^2}{dt^2}(E/N) = g\frac{dy}{dt} = \frac{gE}{\frac{M}{i}+1}\,E/N$$

w

$$y'' = wy$$

$$\boxed{y = e^{kt}}$$

$$w = k^2$$

$$k = \sqrt{w}$$

$$ke^{kt}$$

$$k^2e^{kt}$$

$$K = \sqrt{\frac{gE}{\frac{M}{i}+1}} \cong \text{Const}\sqrt{i}$$

~~suggested~~

(compressed

~~several~~ 4 & 5

very boring

evaluate

$$a - by = \frac{dy}{dt}$$

$$y = C(1 - e^{-kt})$$

$$y' = Cke^{-kt}$$

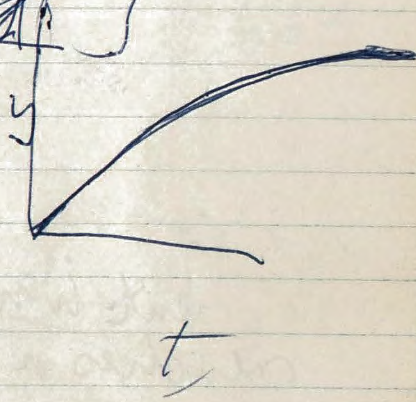
$$a - Cb + Cbe^{-kt} = Cke^{-kt}$$

$$K = b \qquad Cb = a$$

$$C = \frac{a}{b}$$

$$\boxed{y_\infty = \frac{1}{\theta} \frac{FE/N}{\frac{M}{i} + 1}}$$

$$\frac{dy}{dt} = b\,\frac{a}{b} = a$$



1.) $$\frac{dy}{dt} = \frac{FE/N}{\frac{M}{i} + 1}$$

for $t = 0$

$$E/N = K_0$$

$$\frac{dE}{dt} = \frac{1}{\tau} \frac{E/N}{\frac{M}{S/N} + 1} N + (K_0 + gS) N$$

2.) $$\frac{dE/N}{dt} = \frac{1}{\tau} \frac{E/N}{\frac{M}{S/N} + 1} + (K_0 + gS)$$

Approximation

2(a) $$\frac{dE/N}{dt} \cong K_0 + gS$$

$$RNA \rightarrow P \rightarrow RNA \rightarrow P \text{ —}$$

$$\downarrow \qquad\qquad \downarrow$$

$$P_y \qquad\qquad P \qquad\qquad T$$

RNA

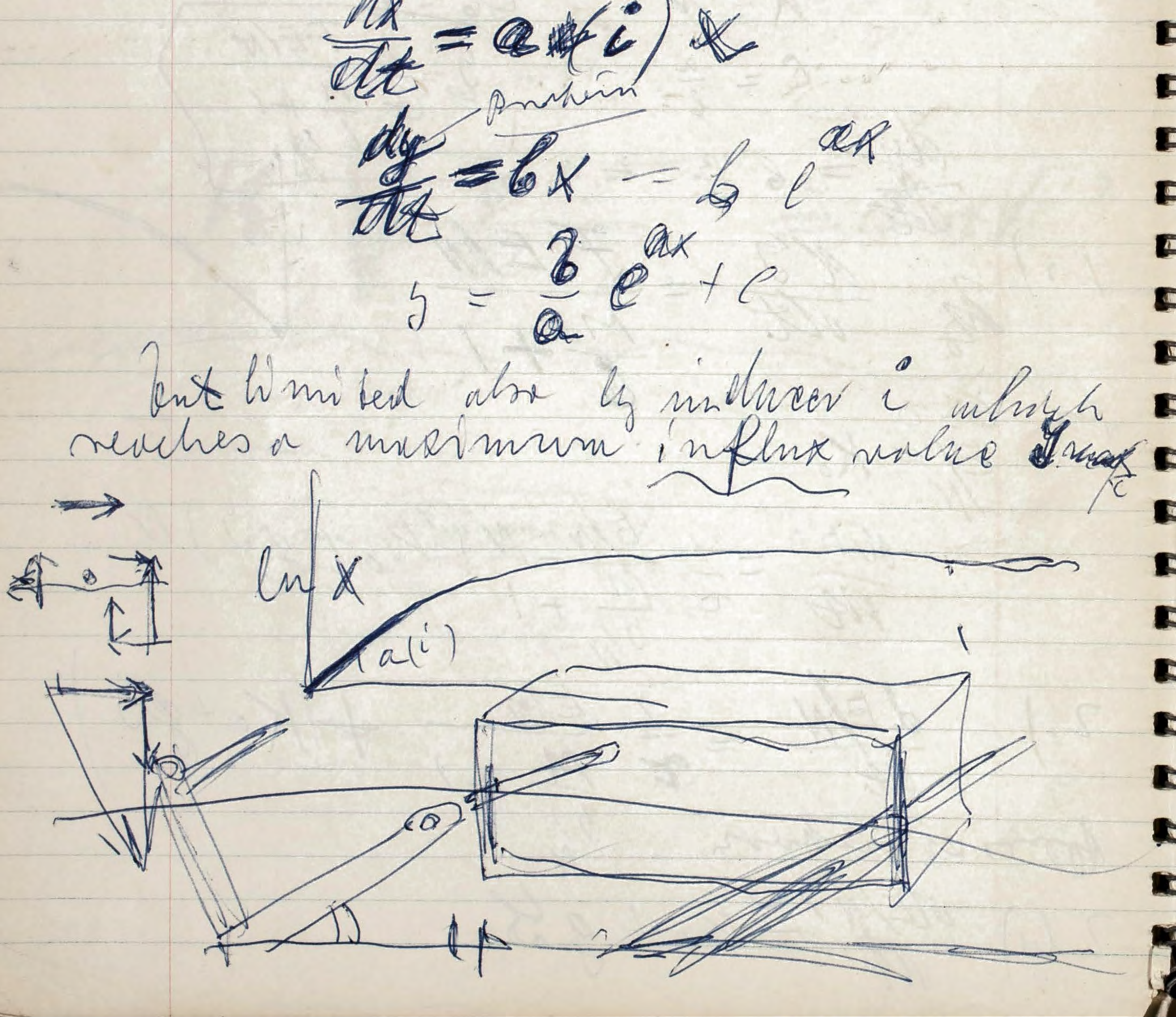
$$\frac{dx}{dt} = a(i)\,x$$

protein

$$\frac{dy}{dt} = bx = b\,e^{ax}$$

$$y = \frac{b}{a}\,e^{ax} + c$$

but limited also by inducer i which reaches a maximum influx value I_{max}



Question: DNA makes RNA

x $\qquad$ y

$\frac{dy}{dt} = ax$ $\qquad$ DNA makes Protein

$x = e^{\alpha t}$ $\qquad$ y $\qquad$ z

$y = \frac{a}{\alpha} e^{\alpha t} - \frac{a}{\alpha}$

$\frac{dz}{dt} = by$ $\qquad$ $z = \frac{ab}{\alpha^2} e^{\alpha t}$

$$\frac{d}{dt} E = aN$$

$$E = \frac{a}{\alpha} e^{\alpha t} - \frac{a}{\alpha} \simeq \frac{a}{\alpha} \alpha t = at$$

~~the myth of ... and~~

$$\frac{dE}{dt} = a - \frac{E}{\tau}$$

$$E = a\tau\left(1 - e^{-\frac{t}{\tau}}\right)$$

$$\frac{dE}{dt} = a e^{-\frac{t}{\tau}} = a - a\left(1 - e^{-\frac{t}{\tau}}\right)$$

Mrs Knudsen En3-2666

Pepsi Cola

Mr Domek Olmelas

Norwich

Assumption: Mar 20/55

RNA is made so that $[RNA]/N = Gt + R_0$

and $\frac{dP}{dt} = b[RNA]$

then $\frac{P/N}{Gb\tau} = t + \left(\frac{R_0}{G} - \tau\right)\left(1 - e^{-t/\tau}\right)$

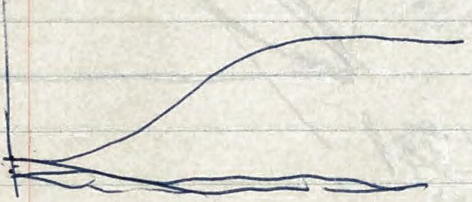
linear off the bat! for $G\tau = R_0$

at first $\frac{dX}{dt} = aX$ $\qquad \frac{X}{N} = e^{(a-\alpha)t}$

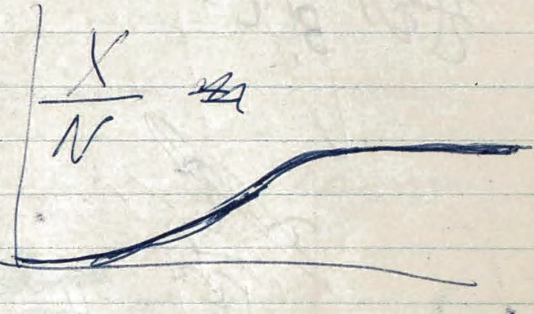
later $\frac{dX}{dt} = aiN$ $\qquad \frac{X}{N} = ai$

$\frac{dE}{dt} = bX$

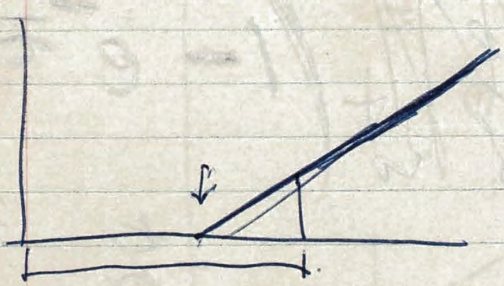
$\frac{1}{N}\frac{dE}{dt}$

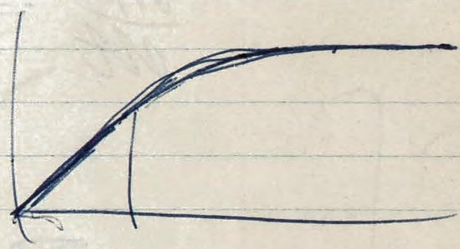


$\frac{X}{N}$

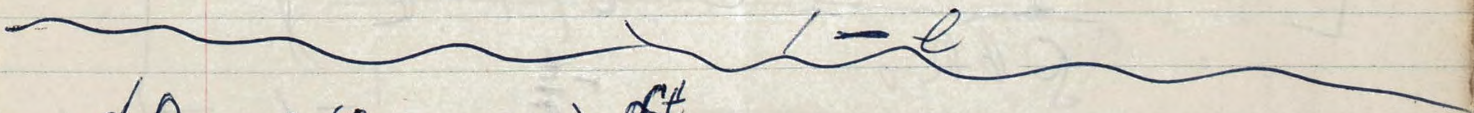


t



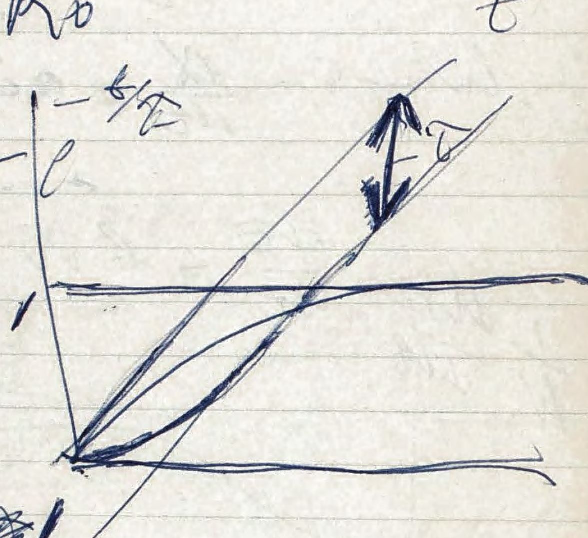


$1 - e^{-\alpha t}$



$$\frac{dP}{dt} = b\,(Qt + R_0)\,e^{\alpha t}$$

$$\frac{P}{\rho b R_0} = t - \tau(1 - e^{-t/\tau})$$



$$\frac{\tau t}{\tau^2}$$

For $\frac{R_0}{g\tau} \ll 1$

slope = 0 for $t = 0$

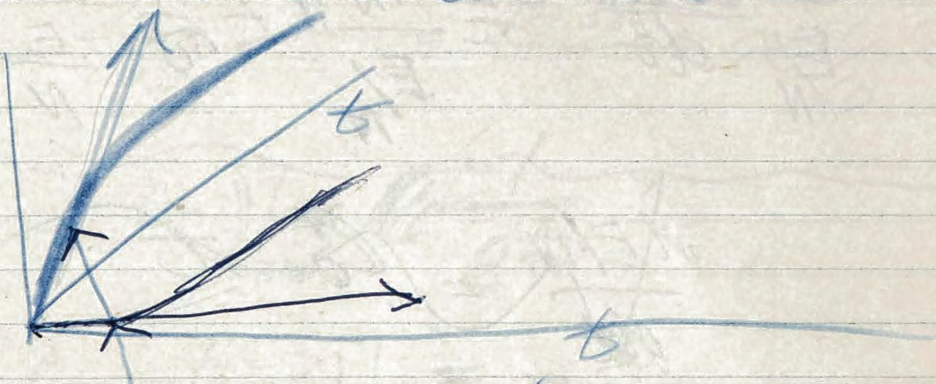
$$\frac{dP}{dt} = \frac{1}{\rho b R_0}\left(1 - e^{-\frac{t}{\tau}}\right)$$

$$\left[\quad \frac{P}{\rho b R_0} = t - \tau(1 - e^{-t/\tau}) \quad\right]$$

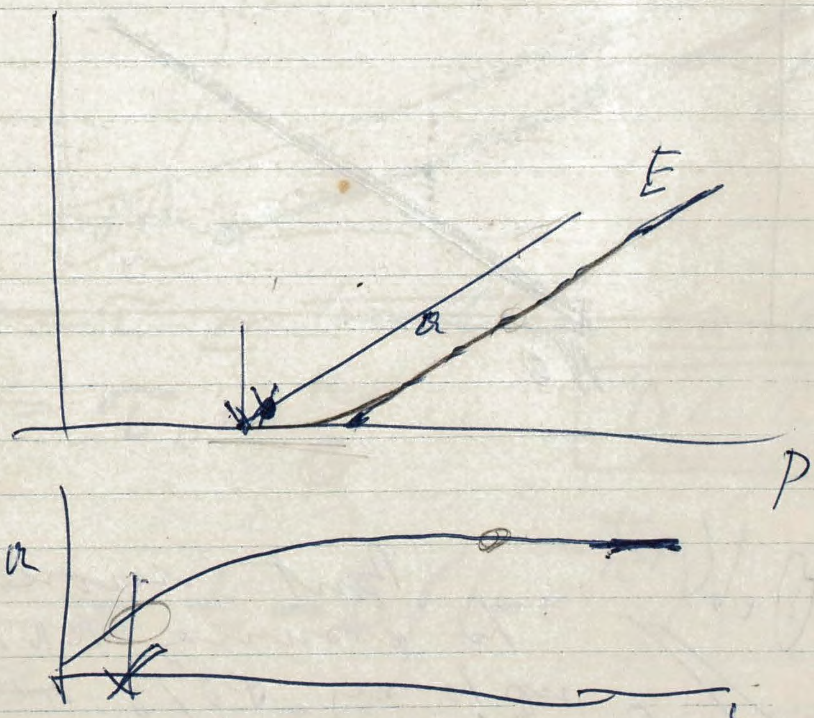
for $t = \tau$ $\quad$ " $= \tau e^{-\frac{t}{\tau}} = \tau e^{-1} = \tau \frac{1}{2.73}$

for $t = \frac{\tau}{2}$ $\quad$ " $= \tau e^{-1/2} - \frac{\tau}{2} = \tau\left(e^{-1/2} - \frac{1}{2}\right)$
$= \tau$

Ro is defined
as RNA/N at time 0 when
P = 0



slope at time zero
$= \dfrac{Ro}{G\tau}$
in place of $\frac{1}{}$



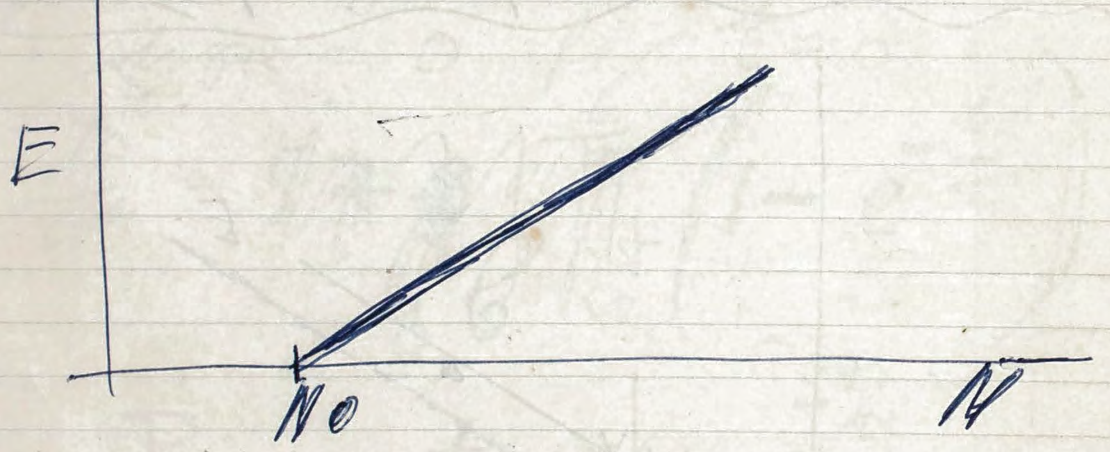
Saturation (?)

$$\frac{1}{E/N}\frac{dE/N}{dt} = \frac{1}{c}\frac{I_N N}{E/N} + \frac{K}{c}\frac{1}{E/N}N = \frac{\text{Const}\,N}{E/N}$$

$$\frac{dE/N}{dt} = \cancel{\text{Const}}$$

$$\frac{dE}{dt} = \text{Const}\; N$$

$$E = \text{Const}\,N - \text{Const}\,N_0$$



O.K. But more correct to assume RNA is up to say 80% ~~remaining~~

$$\frac{1}{RNA/N}\frac{d\,RNA/N}{dt} = \frac{\text{Konst}}{RNA/N}$$

4

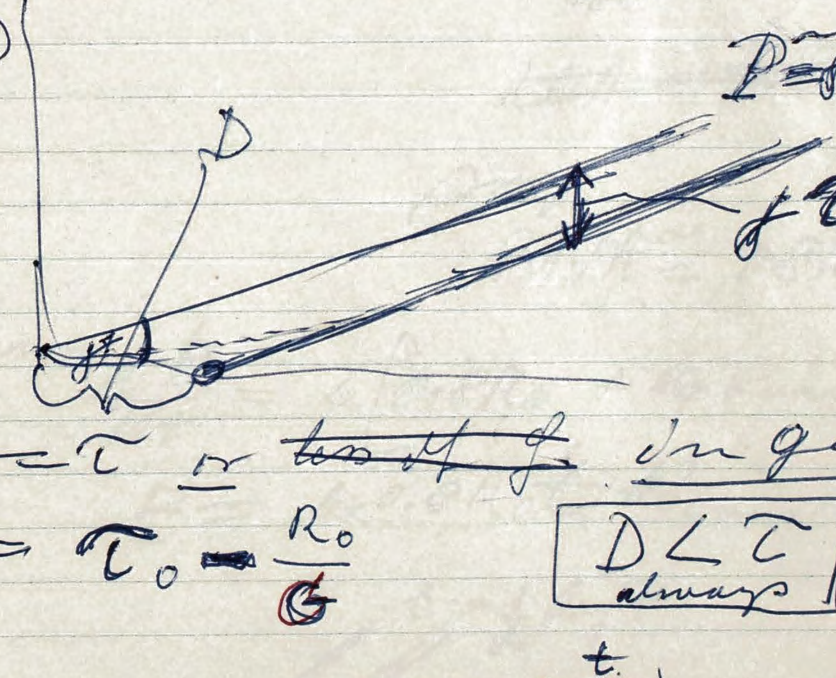
~~1.6×1.8~~
~~96~~
~~256~~

~~1.7~~ ~~1.7~~
~~1.18~~
~~289~~

(1) $= \frac{1}{1.65} - \frac{1}{2} = \frac{0.35}{} \approx \frac{1}{10}\tau$

$$\boxed{\begin{aligned}&\frac{1}{\tau}\left[\frac{P}{\rho b R_0} - (t-\tau)\right] = \frac{1}{e^{t/\tau}} \\ &\ln\frac{1}{\tau} + \ln\left[\frac{P}{g b R_0} - (t-\tau)\right] = -\frac{t}{\tau}\end{aligned}}$$

or P



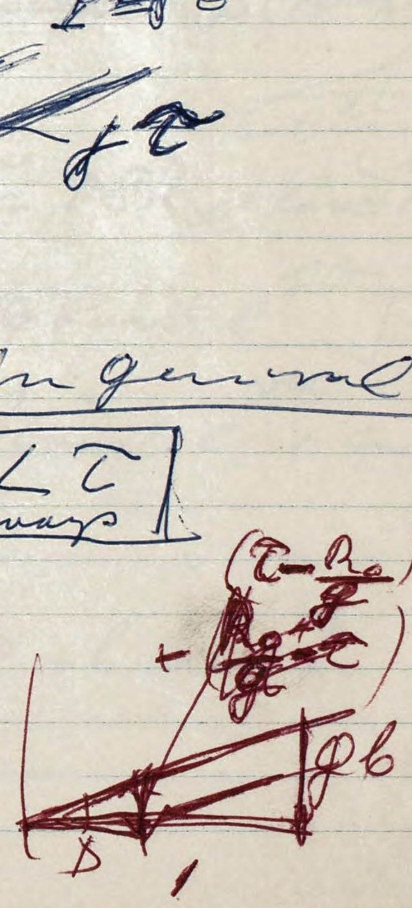
D = τ or ~~...~~ In general

$D = \tau_0 - \frac{R_0}{G}$ $\boxed{D < \tau \text{ always}}$

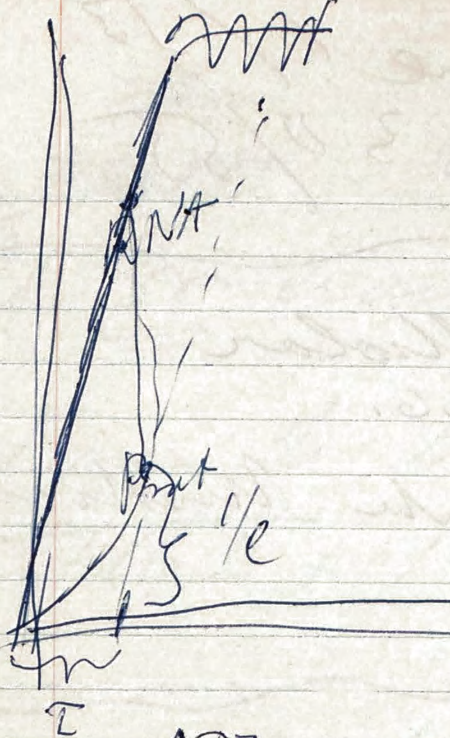
and

$$\frac{P/N}{G b \tau} = t - D\left(1 - e^{-\frac{t}{\tau}}\right)$$

$D = \frac{\tau - \frac{R_0}{g}}{g b \tau} \approx 0$ for large g



H



if flat: nothing
one ~~first~~ ~~a~~ generation or

$\frac{d[P]}{dt} = 6[RNA]$

$\frac{d[RNA]}{dt} = \text{konst}\, e^{\alpha t}$

~~$RNA = (0.8R_\infty + \text{konst}\, e^{\alpha t})$~~

say

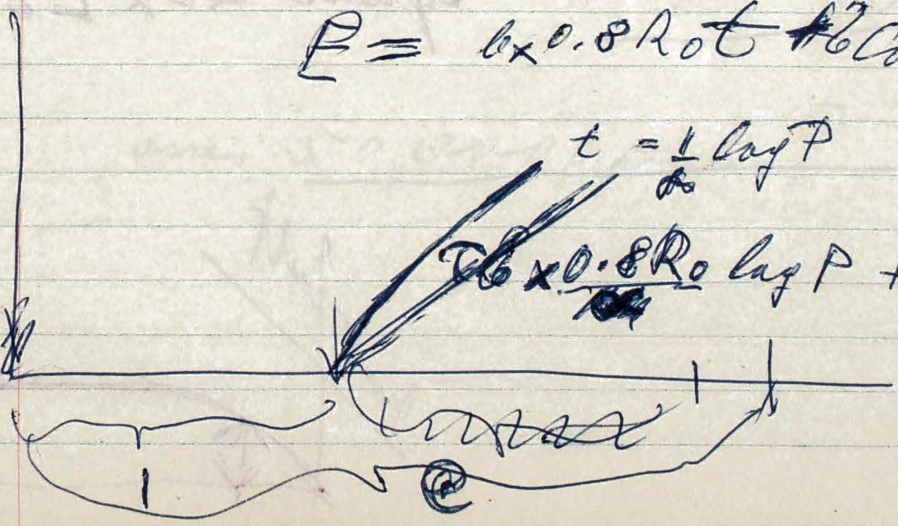
$RNA \simeq 0.8R_\infty + \text{konst}\, e^{\alpha t}$

Protein $\frac{dP}{dt} = 6\left[0.8R_0 + \text{konst}\, e^{\alpha t}\right]$

$P = 6 \times 0.8 R_0 t + \frac{6}{\alpha}\text{Const}\, e^{\alpha t} + \text{const}$

$t = \frac{1}{\alpha} \log P$

$\frac{6 \times 0.8 R_0}{\alpha} \log P + 6\,\text{Const}\, P$



Norwich ~~May 30/55~~ June 1/55

$i_{critical} \sim 10^{-5}$ Molar
J.M.G.
Lactate Medium

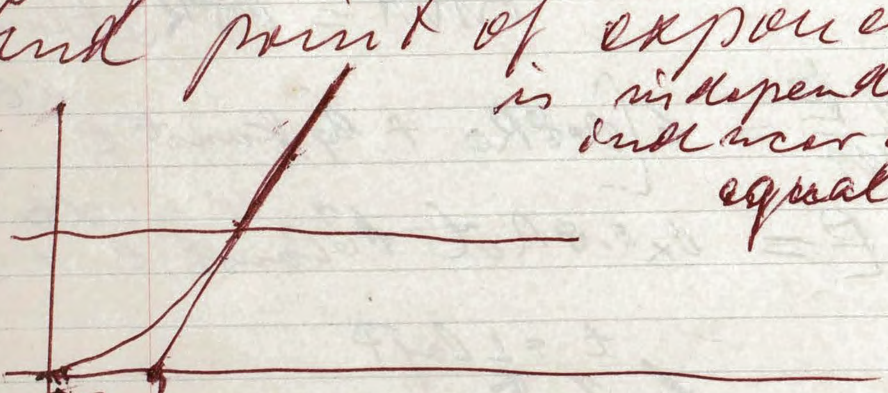
Exp.

$$\frac{L\,dE}{E\,dt} = \alpha\left(i\,\delta_0 - 1\right)$$

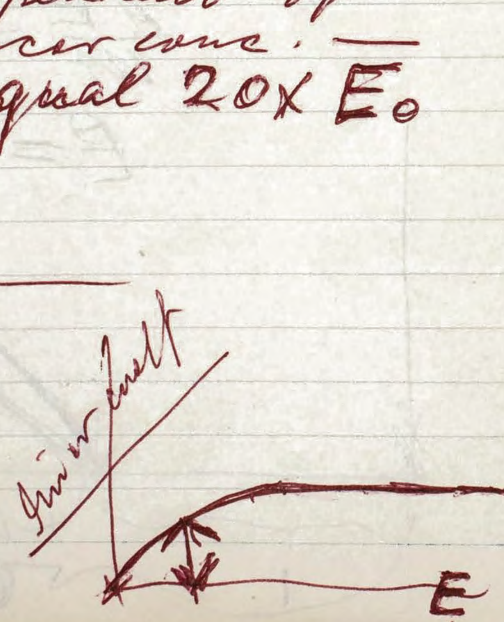
~~tested~~ tested up to 50 i_c

for 50 i_c it rises factor e
in 5 minutes

End point of exponential
is independent of
inducer conc. —
equal 20 x E_0



τ =



~~40~~ +

1hy ~~20,000~~ 20.000 000

$\frac{1}{60}$% ~~Br~~ bones and liver
→ 10 or 20

1 hour D burned ~~over~~ flesh.

TUGD + 1 UGT = 22.000 Tons

The inception

7000 sq miles ~~[illegible]~~ ~~=~~ ∞
5.000~~0~~
~~2,000~~

$[\int n t]_t^{\infty}$ $t^{0.2}$

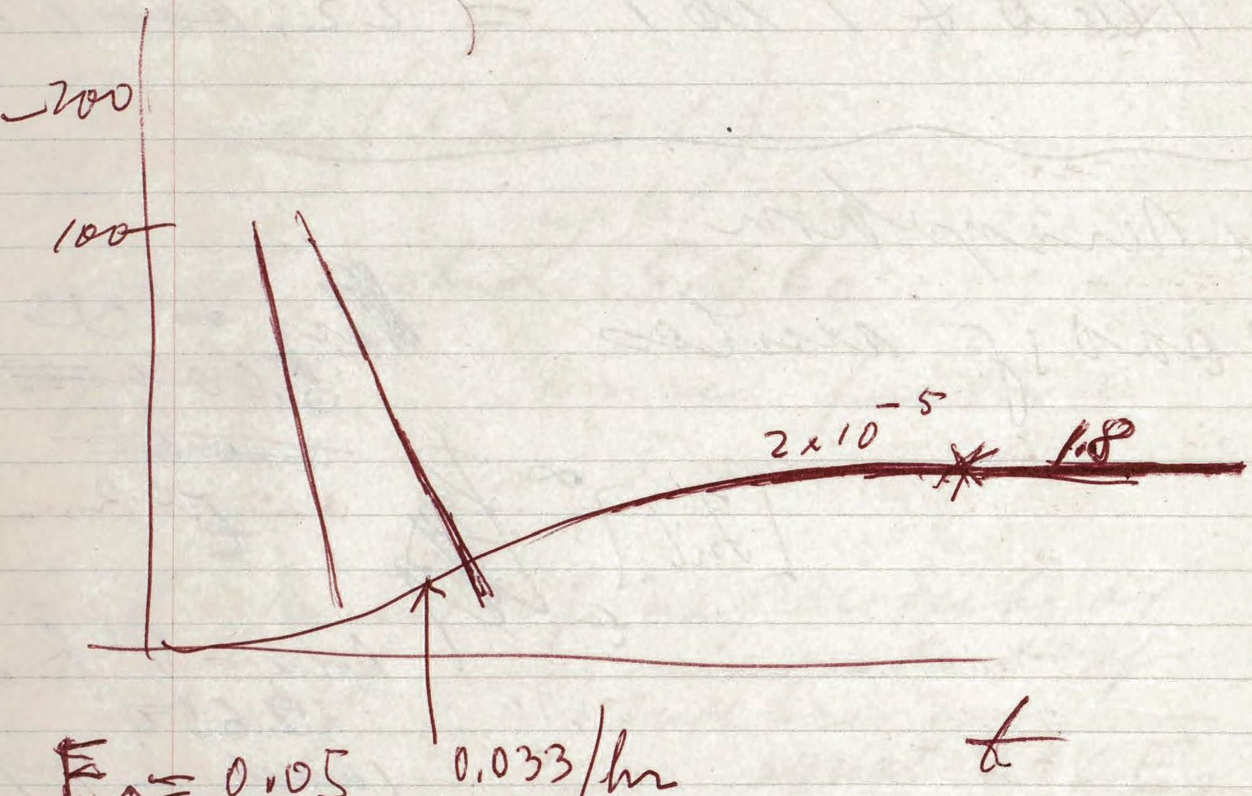
1 day - 4inf
~~2~~650
1 week hr inf
1850

ones 50,000 (miles)^2 ~~[illegible]~~
250 R
~~[illegible]~~

Cont.

$$\frac{dE}{dt} = + \overset{20}{K}E - \frac{E}{Y}$$

130/gen



$E_0 = 0.05$

0.033/hr
0.083/gen

Slope of linear goes between 2^{nd} and 3^{rd} power saturation; how does it depend on inducer conc.?

Summary

"Enzyme" reproduces itself not quite but reproduction rates: i.

5×10^{-4}	$\frac{137}{200}$ in saturation
2×10^{-4}	
10^{-4}	0.86 in saturation
5×10^{-5}	0.80 in saturation
2×10^{-5}	0.46 in saturation
5×10^{-6}	$\approx$ 0.62 (from expfall)

in linear region (lowest exp. for $i = 2\,10^{-5}$)

Theory:
Linear production on same template; both inducer and enzyme must sit on template at a fixed number of points.   P.T.O.

Number of sites occupied by inducer on template is a function of i rises very rapidly from $i = 2\,10^{-5}$ to $5\,10^{-5}$.
This number determines at what E exponential ends and linear region begins.

It is ~~not~~ quite clear why at lower number of sites occupied by inducer there should be saturation of all points be reached at a lower number of enzyme molekules (E). — this is however an experimental fact — to be checked

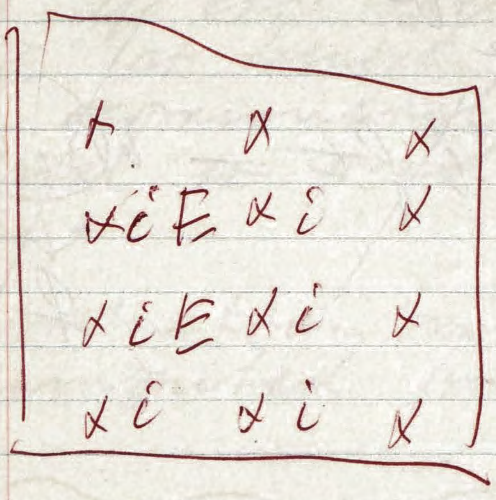
[illegible] hypoth.

i	Exp. reg. per gen	Intersect	Linear prod / g	Sat.	Repr. rate on Sat	E_0
$5\,10^{-4}$	31.6	12'	146	200	$\frac{137}{200}$	2.24
$2\,10^{-4}$	26	30'	94	190		2.35
10^{-4}	5.31	96'	26	180	0.86	2.02
$5\,10^{-5}$	1.98	150'	5	50	0.90	2.04
$2\,10^{-5}$	0.5	114'	0.083	1.8	0.96	2.5

1/2 of Sat at 3 hrs

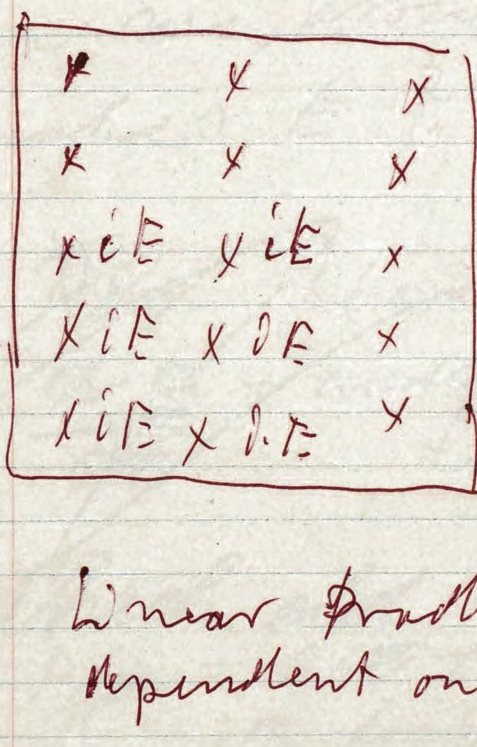
This is even confirmed by full experiment E falling [illegible] 10 to 99 with 97%

Zero level 0.05



for low energies

"linear" production proportionate to E



for high energy

Linear production ind. of E dependent on i alone

Each iE point produces E at a rate which is a function of i (and is about proportional to i but rises faster than i

$$\frac{d}{dt}\left(\frac{u}{v}\right) = \frac{u'v}{v^2} - \frac{u}{v^2}v'$$

$$= \frac{N}{N^2}\left[\cancel{}(b R_0 + b \beta t - 2 R_0 \alpha t)\right.$$

β

H

End of exp region is defined as E at which production computed from exponential region is equal to prod. from linear term.

Reproduction rate in saturation is computed from linear production

~~value~~

Can we assume that ~~RNA~~ makes E? for linear rise?

~~$R(NA) = \text{Const}_1 + \text{Const}_2$~~

~~$\frac{dE}{dt} = \text{const} \, kR - \frac{E}{g}$~~

Check old result:

$P/N = 6bE\,t \quad = 6R_0 t$

$\leftarrow$ for $g\tau = R_0$

$\frac{d}{dt}\frac{P}{N} = 6R_0 = \quad (g t + R_0)\,N$

$\frac{1}{N^2}\left(N \frac{dP}{dt} - P\frac{dN}{dt}\right) = \frac{1}{N^2}\left[e^{\alpha t}\,6R - N\,6R_0 t\,\alpha N\right]$

$N^2/R_0 t$

[illegible]

1.) Liver removal gives rise of amino acid level
2.) Sleep: Paradoxes
3.) Glucose: take Brain slices from dog maintained at low blood sugar level

Another exp. with Co_2 in chemostat at 10^{-4} inducer gives good repeat of earlier experiment intercept 1.6 hours for τ = 2.5 hours

at 9 hours 1/2 value of saturation

In second flask experiment higher E values for same inducer curve, (49 in place of 14)

$\boxed{\text{but at } 1 \times 10^{-5}}$ → Gen

		E	E
Gen	9.9	3.7	185
	19.8	8.7	133
	29.7	9.5	79
	~~44. 2²~~	~~10.1²~~	~~49²~~

and for " induced at

repeat 96%

Nonrich Cabal Sprung

not the O_2

		(Y) Flush	(E) Level
~~F~~lask	a.) induced [10^{-3}]	0	0.06
	b.) induced [10^{-3}]	10^{-5}	92
	c.) ~~[illegible]~~ induced [10^{-3}]	$2 \cdot 10^{-5}$	96
		(Y) Flush	E Level
	d.) not ind [0]	0	
	e.) not ind [0]	10^{-5}	1.4
	f.) not ind [0]	$2 \cdot 10^{-5}$	14.5

related to 0.1 Beckmann

Paget ~~[illegible]~~ old units 2.8 X

10 open of close

i	τ	$t(E/2)$	g	Start	E_0	a	E
$5\,10^{-5}$ No ~~16~~ No con	2.04	11 hrs	5.0%/gen	3 hr	2.5	1 mμ	42
~~[illegible]~~							

Chemostat

i	τ	$\frac{t}{\cancel{tdbl}}$ ($t/2$)	g	start	τ_0	H a	E_g
(15) $5\,10^{-4}$ $N_2\,CO_2$	2.24	80 m	65/hr	15 min	~~13~~ min	1 mgm	140
51 CO_2 + Jun 6 10^{-4}	2.5	9 hrs	~~26~~.4/gen	2 hrs	1.6 hrs	1/2 mgm	150
37 CO_2 $2\,10^{-4}$ May 28	2.35	1.2 gen	~~42~~ 44/gen	3/4 hr	30 min	1/2 mgm	190
35 No CO_2 $2\,10^{-4}$ May 10	2.10	2.12	59/gen	95 min	65 min	1 mgm	185
34 $2\,10^{-4}$ No CO_2	2.7	14 hrs	12.4/gen	6 hrs (rose to 160 when C. Uradhlin)	6.3 hrs	1/2 mgm	85
~~33 No CO_2 $2\,10^{-4}$~~	~~3.06~~		~~14.7~~			~~1/4 mgm~~	~~88~~
(No CO_2) 24 $5\,10^{-4}$	2.02	4.7 hrs	~~65~~/gen ~~32~~ 65/gen	2 hrs	1 3/4 hrs	1/2	194

i is Umolar TMG.

Man

circulatory arrest with
survival 15-38 min at 20-30°C
Swan et al Arch. Surg. 138 360-376
$\boxed{\text{Fibrillation below } 25°C}$
Lynn et al, surface cooling Ann. R. Coll
Surg. Engl.
14 267-275, 1954
also Lancet 2 1011/1953

Neurological damage Dog
Jensen & Parkins 1954 Fed. Proc. 13 75

Hamsters: Smith, Al Nature. Lond.
173 1136-37/1955

Edholm Practitioner 168 583-592
(Rapid rewarming difficult)/1952

~~Rat Lack after 10 hr 12 temp at 15°-18°C Adolph~~

Proposed exp.
Sleep at low temp does it replace sleep
" Low Temp aging + X rays is it like Aging

~~R.K. Andjus~~ Hibernation

Ref: The Journ. of Physiology Vol 128!

(28 June 55)

R.K. Andjus & Audrey U. Smith. p. 446–2–472

Andjus & Al p. 541–546

Andjus p. 547–556

Andjus ed. J. Physiol. 123

R.K. Andjus Nat. Inst for Medical Research Mill Hill N.W.7. 66-67 P / 1954

H

Dogs [isolated blood circulation]

Delorme E.J. 1952 Lancet 263 814–15

Gollan F. 1954 Fed. Proc. p. 184; 544 [1 hour at 1°C – oxygenation]

Juvenelle, Lind, & Wegelius (1954) Amer Heart Journ. 47 692–736

~~Von Wertz 1954 Arch. exp. Path. Pharmak. 222, 78–79~~

~~Rats~~ BMR rat cal/m²/24 hr ~ 700

Man 3000

ratio = 4

Rats at 15–18°C live for 10–12 hrs

X Adolph Amer Journ of Phys 155 378–87 / 1948

" 161 359–73 / 1950

Dogs. Benitte Arch. Exp. Path. Pharm. (German) 222 20–41 (1954)

Urea can increase his
Heat prod 18 fold

Arrhenius-like rate as function
of Temp. graph int. Heat 2. f.
phys Chem Biol 1 491, 1914

Data on Hibernation &
Literature:

Paul O. Chatfield, 163 p. 566-574 / 1950
Charles P. Lyman
Harvard Med School Am. Journ of Phys

Data: — Cooling of Dogs from
takes ~~½~~ hour & to 25 kg dogs
to $\frac{1}{2}$ cool 10°C in 0°C water

H

Cr[illegible] flow 5%

Hibernation Davison The
Textbook of Gen Phys. Blakiston
N.Y.

Mariquant 80kal / kg / 24 h

Man $\frac{2000}{70} = 30$ kal / kg / 24 h

27 = $R_1^3 / R_2^3 = 27^{2/3}$ 9

mouse ~~[illegible]~~ produces 3 X as much heat. —

~~Shivering~~ In hibernation
metabolic rate falls [illegible]
70.!

Ratio ~~Dorf~~ / Man ≈ 3.5

Dorf / Man ≈ 1.3 70 cal / 24 h
0.73

Law: Heat Prod = k Weight

or $\frac{\text{Heat Prod}}{\text{Weight}^{0.73}} = 70 \text{ cal} / 24 \text{ hrs}$

$\boxed{25}$ gm Prot. $\boxed{5 \text{ gm } \cancel{N} \text{ Urea}}$ / day

$\boxed{550}$ ~~g~~ A $\frac{1500 \text{ gm}}{7} \approx 200$ gm fat burned

1 kg 9000

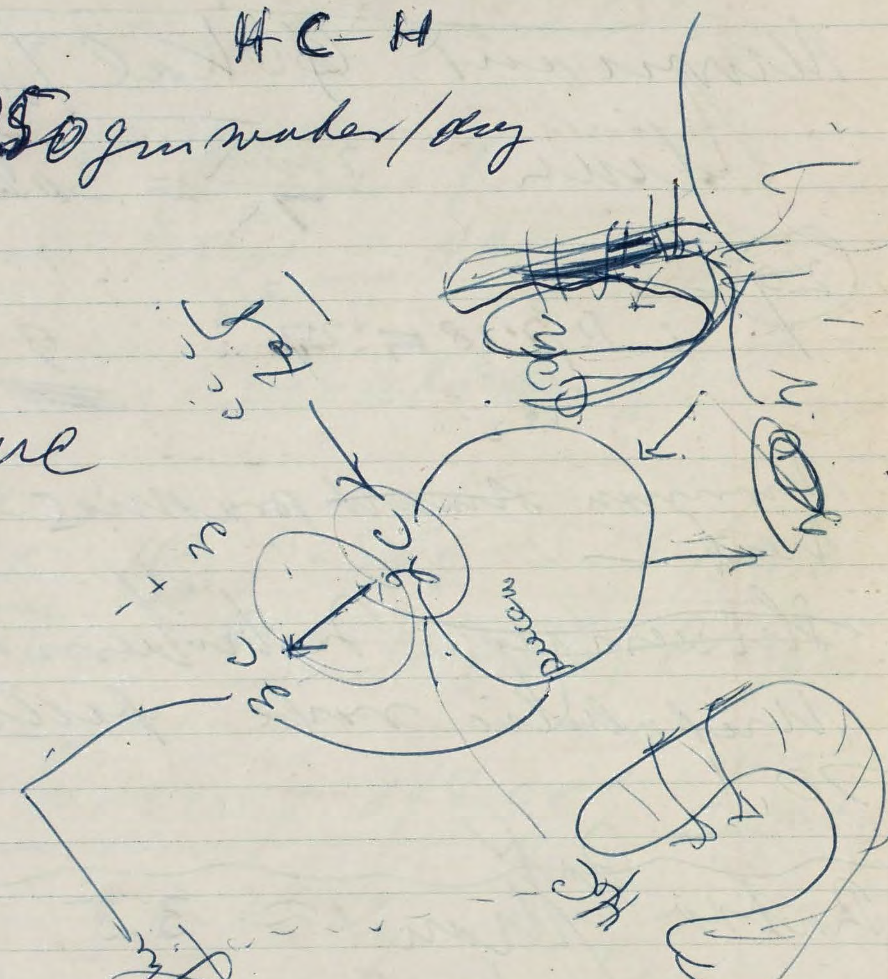
$\boxed{14000}$

$HC-H$

250 gm water / day

7th and

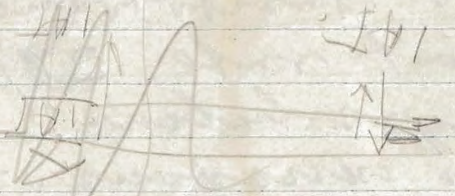
multip. lure



LS

1 hour for 70 kg ~~dog~~ man
30°C difference removes

$\boxed{700 \text{ Cal}}$



by heater around bladder
input at 20°C difference
(5 to 25°C) in 20 min =
= 100 Cal and in 1 hour =
300 Cal

this can be cut by factor 2 at least

because at 25°C heart
does not need

Heart holds $\boxed{150 \text{ cc}}$

~~775 cc 70 4800~~

Basic met. rate turned
allow loss of 30 lb in 9 months

rat at 15°C $\frac{1}{7}$th of normal (after first shivering)

Heart rate   Data from p. 585 168
Proc Nat Acad Sci (?) 1952
at 30°C heart rate 30/min
Shivering stops below 34°C
rectal; semi conscious. –
Animals at 20°C metabolic
rate 1/5 of normal

Data: from Ann. R. Coll Surgeons England 14, 1954 p269

Oxygen cons falls linearly:
from 8.2cc at 38°C
to 0.62 at 14°C

$10\,cc$ $10^5\,cc$

10^{-4} 5 liter 5000

$\boxed{1\,cc}$/min ~~36~~

60 cc

H

June Am. Journ. Phys.

Data: ~~from~~ Juvenelle
Am Heart Journal. Vol 47; 1954

1/10 Blood circulation sufficient at 15°C uses $\frac{400}{3}$ cc/min for 25 kg Dog at 15°C ~ 1/20th of normal
& Bodies could be held at 15°C indefinitely.

Through femoral vein catheter into inf. vena cava

---

went down to 9°C with recovery

La press Medicale (Aug) 1952

~~Arch. f. exp. Path. u. Pharm.~~

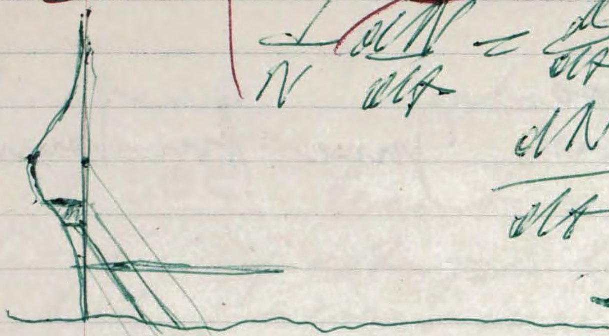
Data: Vol 222 / 1953/54

Metabolic rate, hypernating marmont $\frac{1}{50}$ / ~~1/30~~ of normal

but

$\cancel{f(n) = e^{-\alpha n}}$

$\cancel{-\alpha(1-e^{-\beta n})\,n}$



$$\frac{1}{N}\frac{dN}{dt} = \frac{d}{dt}\ln N = -Ae^{\alpha t}$$

$$\frac{dN}{dt} = -AC_2\, e^{\{\alpha t - \frac{A}{\alpha}e^{\alpha t}\}}$$

$$N = C_2\, e^{-\frac{A}{\alpha}e^{\alpha t}}$$

$t = 50;\ Ae^{\alpha t} = \frac{1}{100}$

$\alpha \approx \frac{1}{10}$

$Ae^{5} = \frac{1}{100}$

$A \approx \frac{1}{100}e^{-5}$

$$Z = \alpha t - \frac{A}{\alpha}e^{\alpha t} \qquad Z = \alpha t - 1$$

$$0 = \alpha - Ae^{\alpha t} \qquad \alpha = Ae^{\alpha t}$$

$$\alpha = Ae^{\alpha t}$$

$$\frac{\alpha}{A} = e^{\alpha t}$$

$$\frac{1}{10}\,100e^{5} = e^{\alpha t}$$

$$2.3 + 5 = \alpha t$$

$$\frac{7.3}{\alpha} = t$$

$\alpha t = 7.3$ and $e^{\alpha t} = e^{7.3}$

Limits

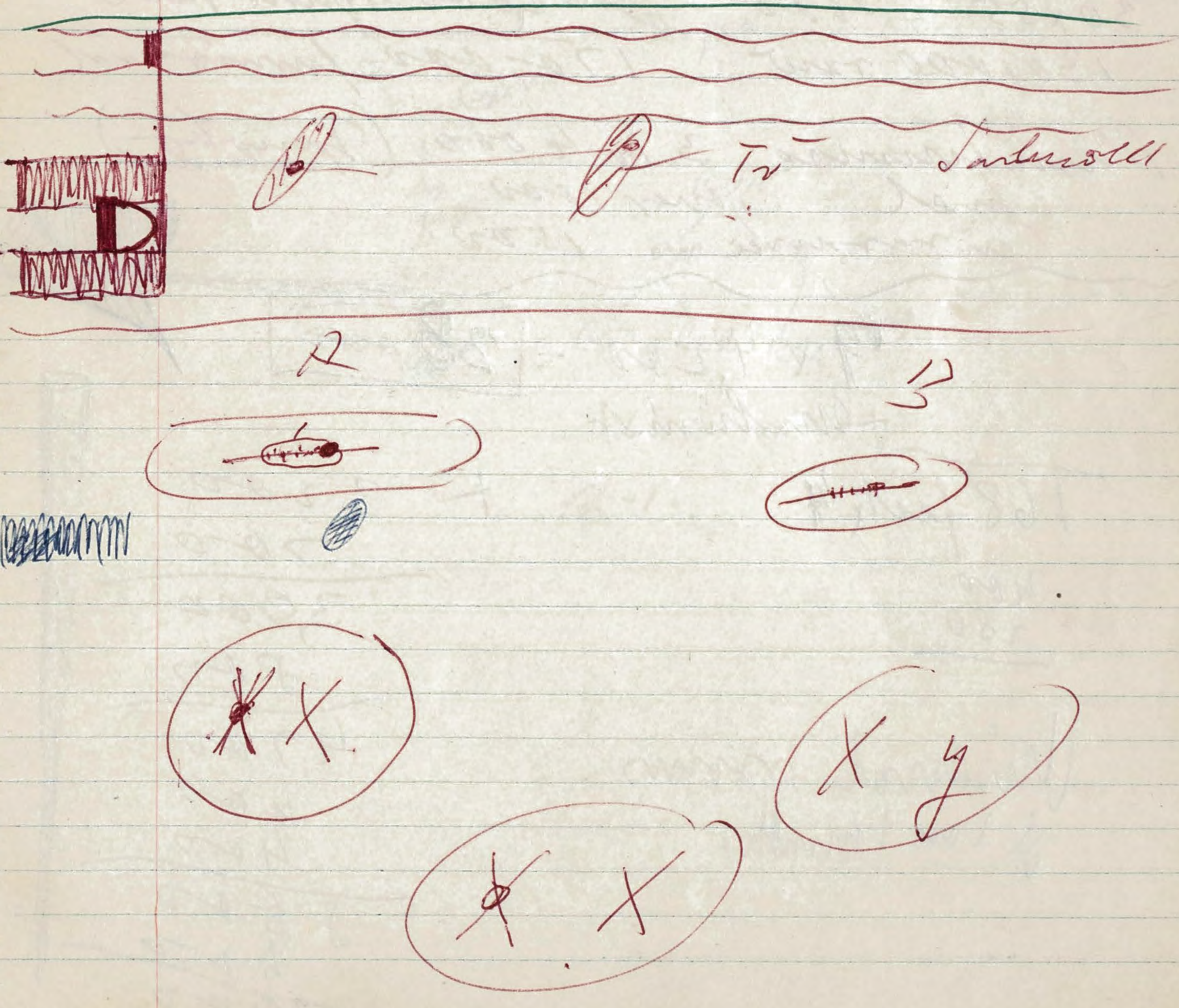
T.B.

H

8 to 10 mgm / kg Standard
5% to 10% / will not respond

2% will keep   Katalase diminished

B6 30 mgm / person / day
Pfizer



21st & 22nd

H. J. Muller H. v. Neumann

Bernard Davis [illegible]

~~Pauling H. J. Muller H. C. Urey~~

Harrison Brown, F Lippmann

(Cyril Smith)

~~1500 library~~

Overlap

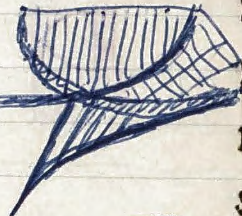
30x55 = 1600 2000 square feet

130,000 raw 170,000 furnished

Maintenance 3 to 4000 (Janitor included)

fuel over 1000

insurance 1500



9 x 4,200 = 38,000

+ [illegible]

168 feet x 4

.400

280

+ 3200

700

3,900

800

4,700

400

400

5,500

[illegible]

6900

Animal rooms

$1000 / months

P

H

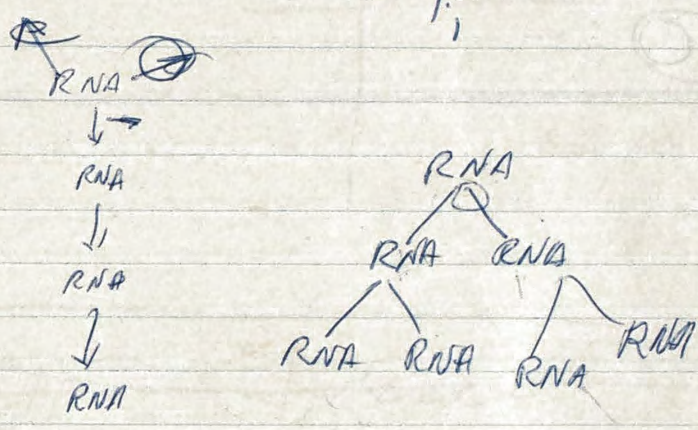
RNA

$RNA_1 \rightarrow RNA_1'$

$\rightarrow P_1'$

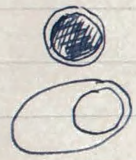
$RNA_1 \rightarrow RNA_1''$

$\rightarrow P_1''$



$n-1$

Beck Wolldam A.E.C. (Ochoa) || UCLA Staff-Warren

Lymphocytic 30 to 60 days	Granulocytic ↓ 48 hours
Simmons (Norman)	
30%	70%
	

A → B

O

B*

A

wild type

A group selected
inhibited by Hammersdine
in individual medium

H.

A group mutant mutation of hammersdine
is retarded in growth rate

1 mg per 1 × 001

55

22 30

~~Pathology 5 men $15,000~~
~~for animals~~

$$e^{\frac{t}{\tau}} = N$$

$$\frac{ds}{dt} = \left(kN - \frac{s}{\tau}\right)$$

A and B brother rabbits

Rabbit

A skin → B + 8 days + 7 days || +4 days skin ↓

~~lymphocytes~~

← lymphocytes 100+500 × 10^6 cells

auto transplant

[delayed skin test]
1 to 2 days

lymphocytes transport sensitivity

plasma cells make circulating antibody

70 plasma cells / 5000 b.m. cells
in bone marrow
go up in case of infection
parallel to antibody titer

multiple myeloma (plasma cells proliferate in foci)
0.5 gms % normal γ glob in serum
10 gms % in multiple myeloma

lymphocytic leukemia

H

Cortisone affects phagocytes

exposure 1.) india ink
2.) cortisone } same effect on delayed skin tests.

Hypersensitivity in skin graft lasts 3 months – B Meanble

In man lymphocytes can be killed
in Rabbit lymphocytes must live

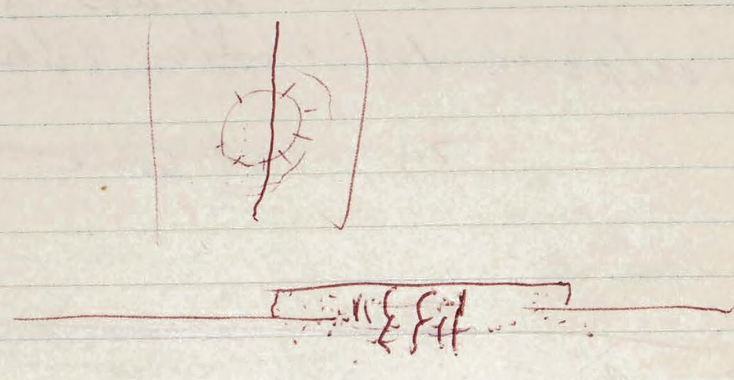
Abe White lymphosarcoma

Cortisone little lower cells

Allergy for inst: hay fever
{ Arthus type : horse serum into Rabbit skin sens.
{ Anaphylaxis

Delayed type ~~sens~~ sensitivity
Adjuvant diseases

A
B
C
D
E
F
G



Am. Journal of Medicine
H. Sherwood Lawrence N.Y.U.

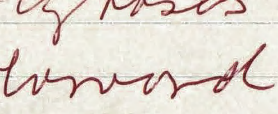
Can you transfer skin sens. (delayed)
through lymphocytes A → B → C → D →

Moen Johnson

Freund
Monocytes do
the phagocytoses
A. H. Coons Harvard

Skin reaction (delayed) due to reaction
of antigen with already sensitised lympho-
cytes. —

Benjamin Zweifach [Phys]



$$1 - e^{-\frac{t}{\tau}}$$

$1 - \frac{1}{2.7} = .37\%$

$\frac{100}{27} = 3$

81

$\cancel{140}$ 190 $\cancel{14}$ 2189

63%

$\leq \tau$

54

70. 63

44.1 less

o.k.

Nov 5/55

Exp: after Debrost

B/r 10^{-3} TTC

compressed	1:2 dil	density before dil density 159
108.3/147	54.4	~~147~~ (undiluted
	1:3 dil	
104/144	69.4	144
	1:4 dil	
106.6/143	79.9	143
	1:8 dil	
114/152	100	152
	1:16	

standardized for Bacterial density of 100 gives for saturation (74) (Maxwell relaxation step)

(standardised for 125 :)

at $2\,10^{-4}$

diluted 1:8 x

~~density 155~~

	density	
125	155	gives for standard density

Novick-Szilard theory of saturation:

Assumption:

$D(i_0-i)$ is influx of inducer.

Inducer is rapidly converted into i^* therefore inducer disappears from interior of bacteria at the rate at which i^*N increases

$$D(i_0-i) = \frac{d}{dt}(Ni^*) = \frac{i^*}{\tau} + \frac{di^*}{dt}$$

$$\text{and } \frac{di^*}{dt} = \alpha z\frac{di}{dt} + \alpha i\frac{dz}{dt}$$

(?) assuming (?) that equilibration is so fast that $i^* = \alpha i z$ at all times

$$D(i_0-i) = \frac{d}{dt}(Ni^*) = \frac{i^*}{\tau} + \alpha z\frac{di}{dt} + \alpha i\frac{dz}{dt}$$

(and $i^* = \alpha i z$)

$$D(i_0-i) = \frac{\alpha i z}{\tau} + \alpha z\frac{di}{dt} + \alpha i\frac{dz}{dt}$$

$$\boxed{\frac{D\tau}{\alpha}\left(\frac{i_0}{i}-1\right) = z + z\tau\frac{1}{i}\frac{di}{dt} + \frac{dz}{dt}\tau} \quad (1.)$$

for i const $z = z_0$,

$$\boxed{\frac{D\tau}{\alpha}\left(\frac{i_0}{i_c}-1\right) = z_0} \quad (2.) \qquad \boxed{z + \frac{D\tau}{\alpha} = \frac{i_0}{i}\frac{D\tau}{\alpha}}$$

→ In stationary state for two different i_0 values i_1 and i_2 we have:

N-S theory of shape

$$\frac{\left(\frac{i_1}{i_c}-1\right)}{\frac{i_2}{i_c}-1} = \frac{Z_1(\infty)}{Z_2(\infty)} = \frac{i_1-i_c}{i_2-i_c}$$

~~...~~ for $\frac{z}{z_0}=\frac{1}{2}$ i may be computed as follows:

we write (2) as $\frac{\Delta\tau}{\lambda}\underbrace{\left(\frac{i_0}{i_c}-1\right)}_{\Delta} = z_0 = \frac{\Delta\tau}{\lambda}\Delta$

(2) or $\frac{\Delta\tau}{\lambda} = \frac{z_0}{\Delta}$

and (1) we may now write

$$\frac{z_0}{\Delta}\left(\frac{i_0}{i}-1\right) = z\left(1+\frac{1}{i}\frac{di}{dt}\tau\right) + \frac{dz}{dt}\tau$$

and for $z = z_0/2$

$$\left(\frac{i_0}{i}-1\right) = \frac{1}{2}\Delta\left(1+\frac{1}{i}\frac{di}{dt}\tau\right) + \overset{K(1/2)}{\frac{dz}{dt}\tau}\,\frac{\Delta}{z_0}$$

In first approximation we may compute now $\frac{di}{dt}$ ~~$\frac{dz}{dt}$~~ from

$$\left(\frac{i_0}{i}-1\right) = \frac{z}{z_0}\Delta$$

$$i_0 - i = \frac{z}{z_0}\Delta i \quad \text{or} \quad i = \frac{i_0}{\frac{z}{z_0}\Delta+1}$$

$$\frac{di}{dt} = -i_0\left(\frac{1}{\frac{z}{z_0}\Delta+1}\right)^2\frac{dz}{dt}\frac{\Delta}{z_0}$$

$$\frac{di}{dt}\frac{1}{i}\tau = -\frac{1}{\frac{z}{z_0}\Delta+1}\overset{K(1/2)}{\left(\frac{dz}{dt}\tau\right)}\frac{\Delta}{z_0}$$

N-S theory of shape

H

so that we have

$$(1) \quad \left(\frac{i_0}{i} - 1\right) = \frac{1}{2}\Delta - \frac{1}{2}\Delta \frac{1}{\frac{Z}{Z_0}\Delta + 1} K(1/2)\frac{\Delta}{Z_0} + K(1/2)\frac{\Delta}{Z_0}$$

B

is $\frac{1}{B}$ larger than 1, if so we are
is B smaller than 1, if so we are
worse off than first approximation!

$$~~\Delta~~ \quad B = \frac{1}{2}\Delta \frac{1}{\frac{Z}{Z_0}\Delta + 1} = \frac{1}{2}\Delta \frac{1}{\frac{1}{2}\Delta + 1}$$

$$\frac{1}{B} = 1 + \frac{1}{\frac{1}{2}\Delta} >> 1$$

– trouble. –

150 = }
150 = } 300.000 →

50/100

royalty - income
20% 80% =

Pat such Streptomycin went to Waksman + Staff

Balance went to Public Research to said foundation or to Institute associates

3
36 older Station Sci.
25
150
50/65 Group
figure out #1

70 younger Sci.
75 10
2

Proper Human understanding

Group one

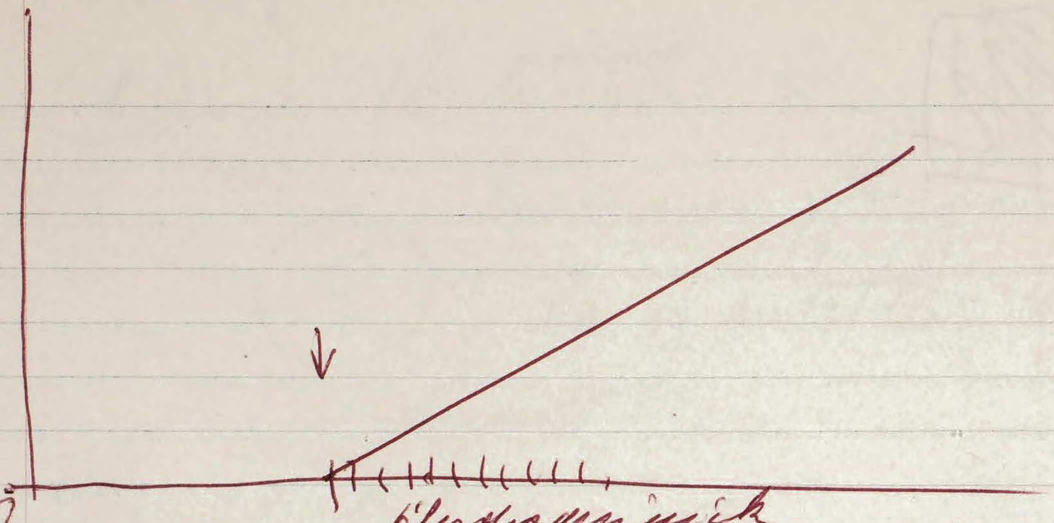
(1) He is entitled to
Insurance for family
(2) ? He is entitled to
Security

(a) He can buy an annuity.

or

if he interest in Royalty
equal agreed annuity
then annuity is cancelable -
because royalty is his security

1st Proper bond -
Endowment is unnecessary
what is necessary is
1st Principal of Division
~~#~~ 2nd #1
3rd #3
4th Home for Project
5 10 years of assured
income
6. Public funds



~~Trans~~

$\cancel{W} \rightarrow X$

Strain ~~#~~ $\boxed{83-1T}$

at 43° enzyme goes to pot 80% in our (in vitro)

Experiments in culture strain to destroy enzyme ~~overnight but~~ at 43°C and determine lag 3 transfers. — in presence of "three amino acids" — (and absence) Tryptophan Tyrosine and Phenylalanine

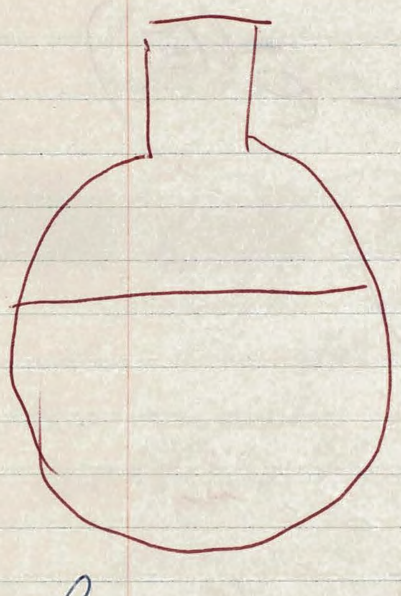
Pantothenic Mutant Strain 88-1T

80% of enzyme leading pantothenic acid. — ~~t~~

~~CoA~~ ~~with~~ ~~ruscimube as~~ carbon — ~~furnace~~

without CoA (pantothenic acid is part of it) can not grow on succinate. –

determine enzyme in Buffer



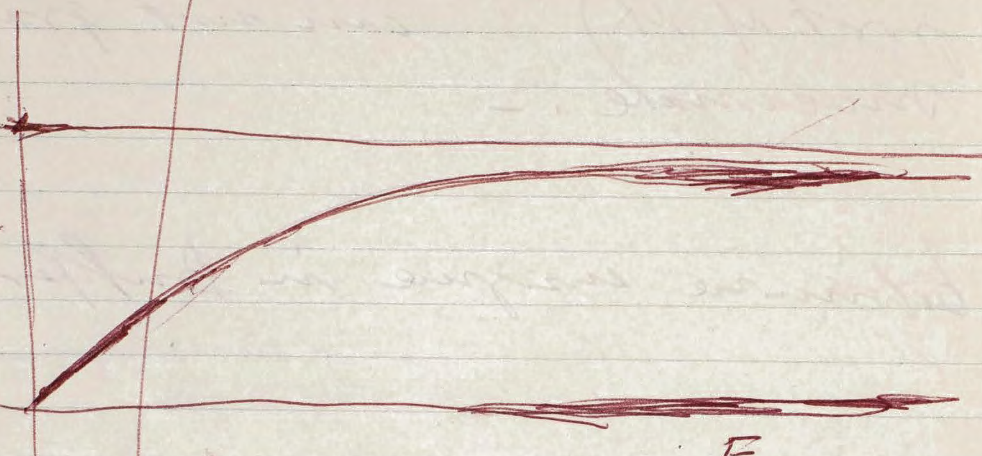
Lactose delayed mutant for Novick

Monod $lac^{-E} \longrightarrow lac^{-Et}$

Fatal assumption

$$\frac{dS}{dt} =$$

$\frac{dE}{dt}$



$$A - Ae^{-bE} = A\left(1 - e^{-bE}\right)$$

$$\frac{dE}{dt} = A\left(1 - e^{-E}\right)$$

$$\frac{dE^*}{dt} = \frac{dE}{dt} - \frac{E^*}{\tau} = K$$

$$A\left(1 - e^{-bE}\right) - \frac{E}{\tau} = K$$

Norwich – Mass 14

look for ~~all~~ microbiograph
with penicillin method
after Thomas, after isolations
in chemostat [after UV]

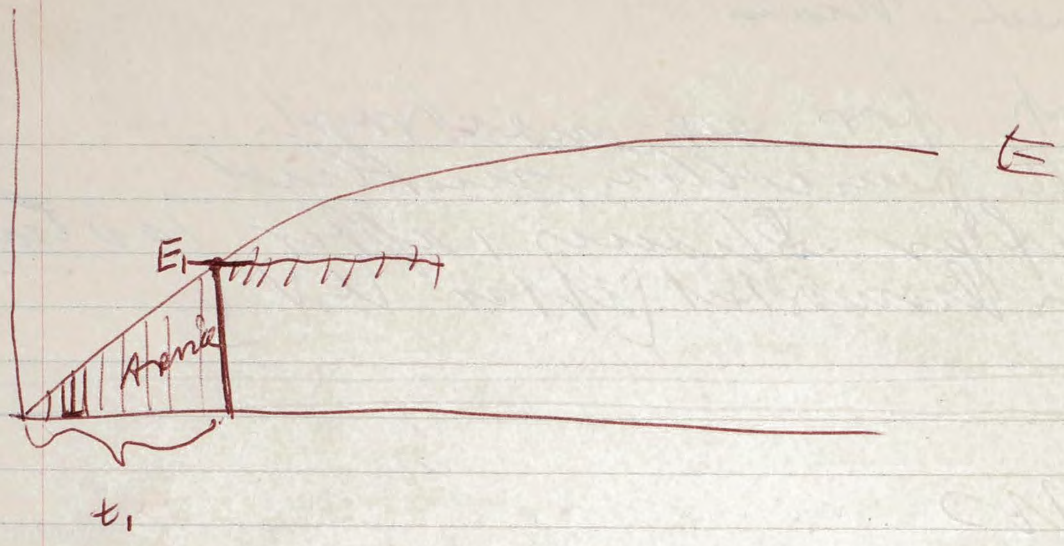
Mass

$H\text{-}DHS \nrightarrow S$

when this goes it grows !!

~~[illegible]~~: If enzyme can
duplicate at $5\ 10^{-5}$ M inducer
why should it ~~[illegible]~~ at $5\ 10^{-4}$ inducer
so much inducer that the Novo
coeff. falls off? must
answer: enzyme ~~[illegible]~~ binds unnecessarily
much enzyme.

~~[illegible]~~



w Area + $\underline{E_1 \tau w}$

Res + excess prod − excess lost = Ens prod

$\frac{E_0}{2} \tau w < \downarrow < E_0 \tau w$

In one gen: ~~[illegible]~~ $\frac{E_0}{2} \tau w$

$E_0 \tau W + E_0 \tau W - \frac{E_0}{2} \tau W$ > Ens prod.

$E_0 \tau W + E_0 \tau W - E_0 \tau W$ < Ens prod

$1.5 E_0 \tau W$ > Ensz prod. in one gen > $E_0 \tau W$

Unnecessl rel.

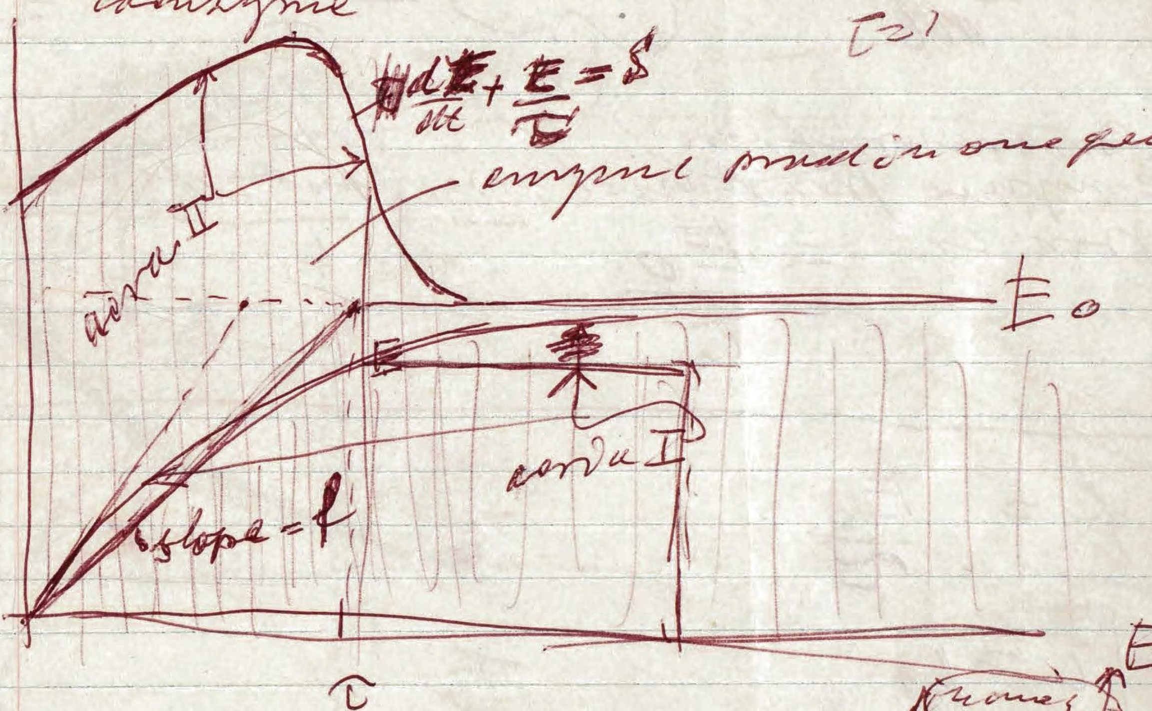
(H)

Theory of saturation:

A coenzyme is made at the rate of $\frac{dF}{dt} = f$

saturation (reserve) $= f\tau (= E_0)$

When enzyme reaches saturation ~~enzyme~~ enzyme is made at same rate as coenzyme



E(prod) = enzyme produced in n gen. is = area × W

~~the~~ Coenzyme produced $= n\, f\tau\, \tau \frac{W}{V}$

Coenzyme lost: at zero time concentration is E_0 ($= f\tau$) if conc. does not fall until $t = \tau$ coenzyme lost is $E_0 \tau W$ but if conc. of coenzyme falls linearly to 0 in one generation then average lost is $\frac{E_0 \tau W}{2}$

$$\frac{dy}{dt} + \frac{1}{\tau} y = S^*(t)$$

y is conc of crocus, (starts out with E_0)

$$\frac{dy}{dt} = \underbrace{\overset{\frac{E_0}{\tau}}{f} - S(t)}_{S^*} - \frac{y}{\tau}$$

~~In saturation from~~

(Enzyme produced per unit time per cc $= \frac{E_0}{\tau}$

$$f = \frac{E_0}{\tau}$$

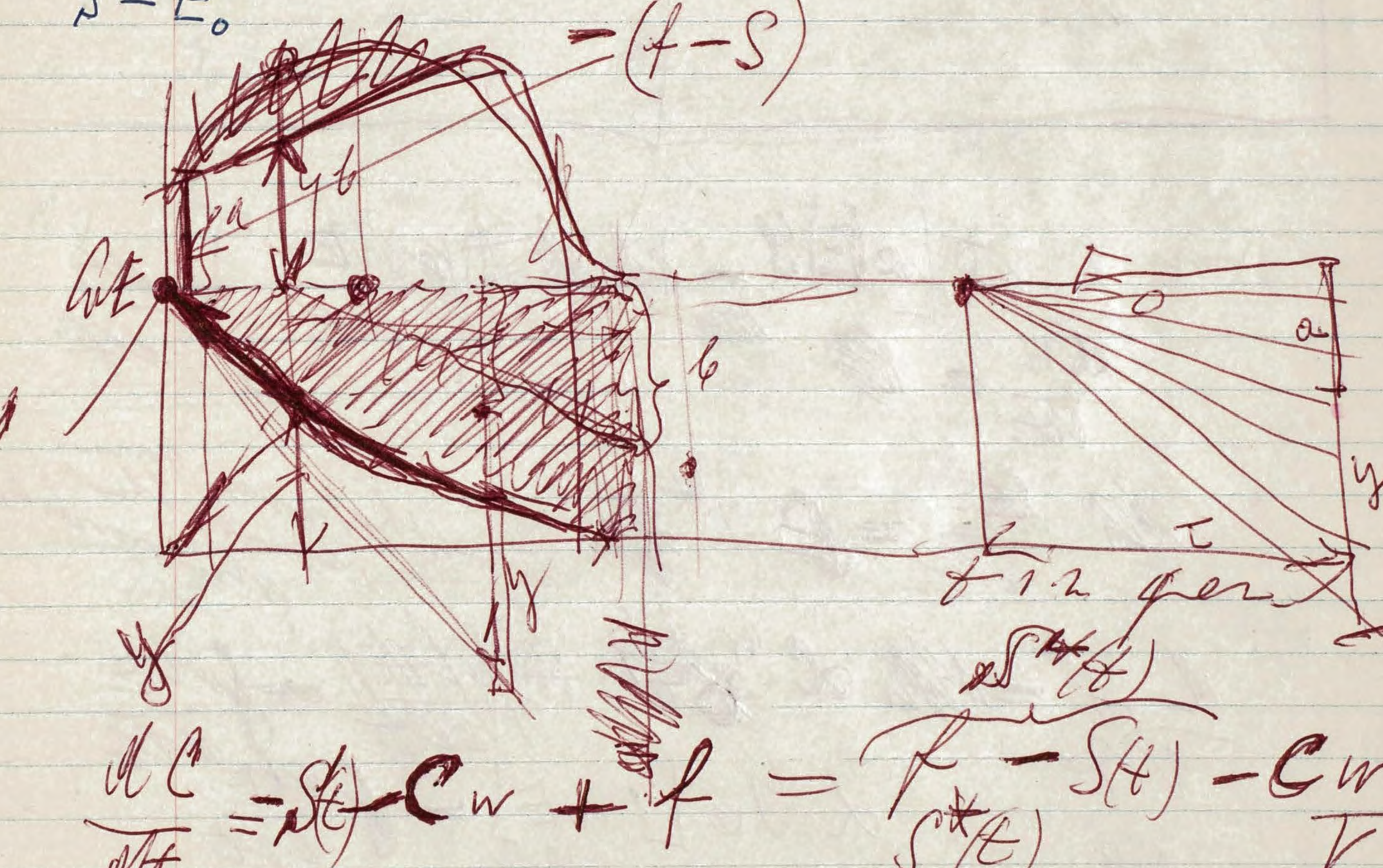
set $\boxed{\tau = 1}$

H

The concentration of the co-enzyme F $\left(\frac{dF}{dt} = f\right)$ can be computed from the synthetic rate $\left\{\frac{dE}{dt}\right\} = S$ ~~in one Bact.~~

At time zero $F = ft$

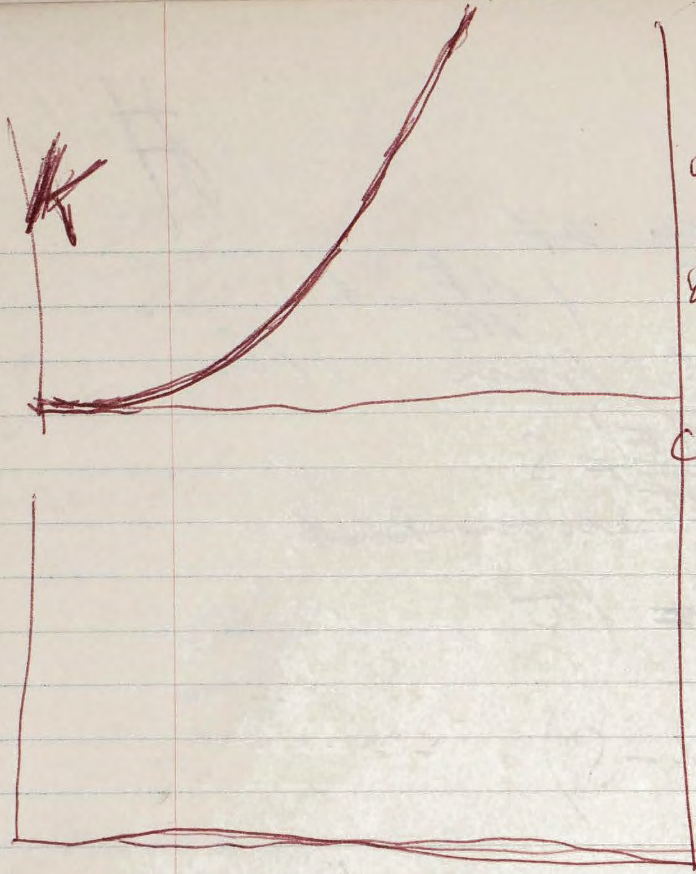
$S - E_0$



$$\frac{dC}{dt} = S(t) - Cw + f = \overbrace{f}^{S^*(t)} - S(t) - \frac{Cw}{V}$$

$$\frac{dy}{dt} = S(t) - \ldots f - S(t) + \ldots$$

$$\frac{dy}{dt} = S^*(t) - y/\tau$$



$y = 1 - e^{-t}$

$\frac{dy}{dt} = e^{-t}$

$e^{-t} =$

transport $[\alpha E) Y - \cancel{\ldots} \frac{dE}{dt}] = \frac{dy}{dt}$

$\frac{dE}{dt} = \cancel{B}$

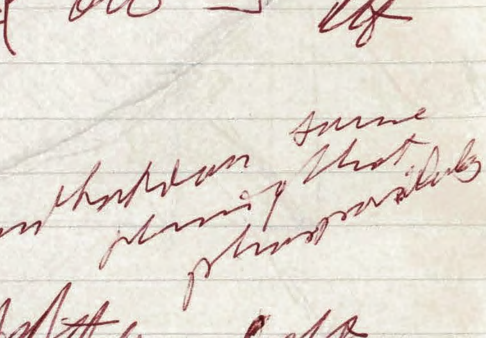
$\frac{dE}{dt} = \beta y^*$ linear that one same storing that phosphorylation

$\frac{dy^*}{dt} = \alpha Y_0 \cancel{\ldots} - f \frac{dE}{dt}$

$\alpha Y_0 [1 - E] - f \frac{dE}{dt}$

$\frac{dy^*}{dt} = \alpha Y_0 [\;] - f \beta y^*$

$\frac{dy}{dt} = \text{const} - k y$



4

exponential rise

a $y_1 \| e^{\alpha t} = z \qquad \frac{dz}{dt} = \alpha e^{\alpha t} = \alpha z$

b.) $y_2 \| e^{\beta t} = z \qquad \frac{dz}{dt} = \beta e^{\beta t} = \beta z$

c.) $\qquad \frac{dz}{dt} = \frac{\alpha}{y_1}[z\, y_1]$

$\qquad \frac{dz}{dt} = \frac{\beta}{y_2}[z\, y_2]$

But why should for different y z_0 (where linear region starts) be the same

when phosphorylated [illegible]
gets [illegible]

$$\frac{d\cancel{B_p}}{dt} = a\mathcal{Y}_0 \qquad \frac{\mathcal{Y}_p(\infty)}{N} = a\mathcal{Y}_0 - \alpha$$

$$\boxed{\mathcal{Y}_p \alpha N = \frac{a\mathcal{Y}_0}{\alpha}}$$ in stationary state

$$\frac{d\mathcal{Y}_p}{dt} = \frac{a\mathcal{Y}_0}{\alpha}$$

at what enzyme conc does $\mathcal{Y}^*$ become const

$$\frac{d\mathcal{Y}^*}{dt} = \frac{b}{\alpha}\mathcal{Y}_p E_{\text{cons}}$$

$$\frac{dE}{dt} = \mathcal{J}e^{\mathcal{Y}^*}$$

$$\frac{d\mathcal{Y}_p}{dt} = a\mathcal{Y}_0 - \frac{d\mathcal{Y}^*}{dt}$$

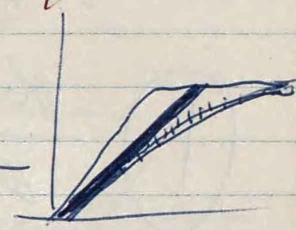
$$\frac{d^2\mathcal{Y}^*}{dt^2} = b\frac{d\mathcal{Y}_p}{dt}E$$

$$\frac{d^2\mathcal{Y}^*}{dt^2} = ab\,\mathcal{Y}_0 E - b\frac{d\mathcal{Y}^*}{dt}E$$

~~$\frac{dS^*}{dt} = A\,\mathcal{Y}_0 E -$~~ 4

~~T M G is phosphorylated~~

At low conc. transport phosphorylated



$$\frac{d\mathcal{Y}_p}{dt} = \underline{a\mathcal{Y}_0} - b\,\mathcal{Y}_p E^*$$ ~~sets upper limit for~~ in stationary

$$\boxed{b\,\mathcal{Y}_p E^* = a\,\mathcal{Y}_0}$$

transport.

Transport

$\mathcal{Y}_p$

$$\frac{dS^*}{dt} = \text{consts}\ \mathcal{Y}_p E - \frac{dE}{dt}$$

$$\frac{d(S^*N)}{dt} = a\,\mathcal{Y}_0 \frac{E}{N} N - \frac{d(EN)}{dt}$$ I

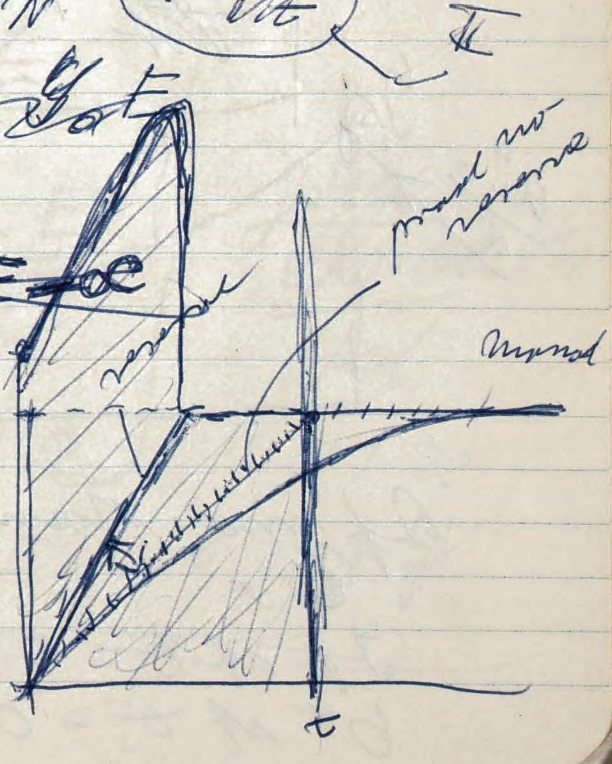
$$\frac{dS^*}{dt} + k\,S^* = a\,\mathcal{Y}_0 t$$

~~$\frac{dS^*}{dt} = a\,\mathcal{Y}_0 E + c$~~

maybe $\frac{dS^*}{dt} = \cancel{a\mathcal{Y}_0}$

II

$$\frac{dS^*}{dt} = a\,\mathcal{Y}_0$$



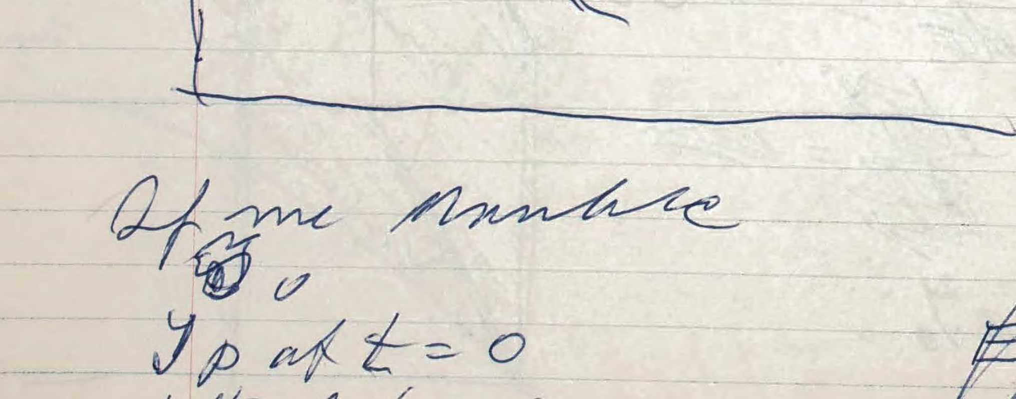
$$\frac{d(Y_p N)}{dt} = (aY_o \ldots \frac{d}{dt}(N y^*)$$

(1) $$\frac{dy_p}{dt} + \alpha y_p = aY_o - \frac{dy^*}{dt} - \alpha y^*$$

$$y(max) = \frac{aY_o}{\alpha}$$

$$\frac{d(Y_p N)}{dt} = aY_o - bY_pE$$

$$\boxed{\frac{dy_p}{dt} + \alpha y_p = aY_o - bY_pE}$$



[illegible] [illegible]

Y_o

Y_p at $t=0$

y^* at $t=0$

E at $t=0$

$$y_p(\max) = \frac{a y_0}{\alpha} = y^*(\max)$$

$$\frac{d(y^* N)}{dt} = b y_p E N$$

$$\cancel{\frac{dy^*}{dt} + \alpha y^* N = b y_p E N}$$

$$\frac{dy^*}{dt} + \alpha y^* = b y_p E \quad \cancel{\text{constant } E}$$

$$\cancel{\frac{dy_p}{dt} + \alpha y_p = a y_0 \cdots = b y_p E}$$

$$\frac{dE}{dt} = f(y^*) \approx \delta y^*$$

for y_p constant

and $y^* <<$

$$\frac{dy^*}{dt} \approx b y_p^{\max} E$$

$$\frac{dE}{dt} = \delta y^* + \frac{E}{\tau}$$

$$\frac{d^2E}{dt^2} = \delta \left(\frac{dy^*}{dt}\right)$$

gives exponential

rise

$$y'' + \alpha y' = b y_p E' - b y_p \delta y'$$

$$0 = b y_p' E + b y_p E'$$

$$0 = b \cancel{y_p'} E + b y_p [\delta y^* + E]$$

11

~~[illegible]~~ The "Intercept"

RNA ~ Protein problem*

$$\frac{RNA}{N} = Gt + R_0$$

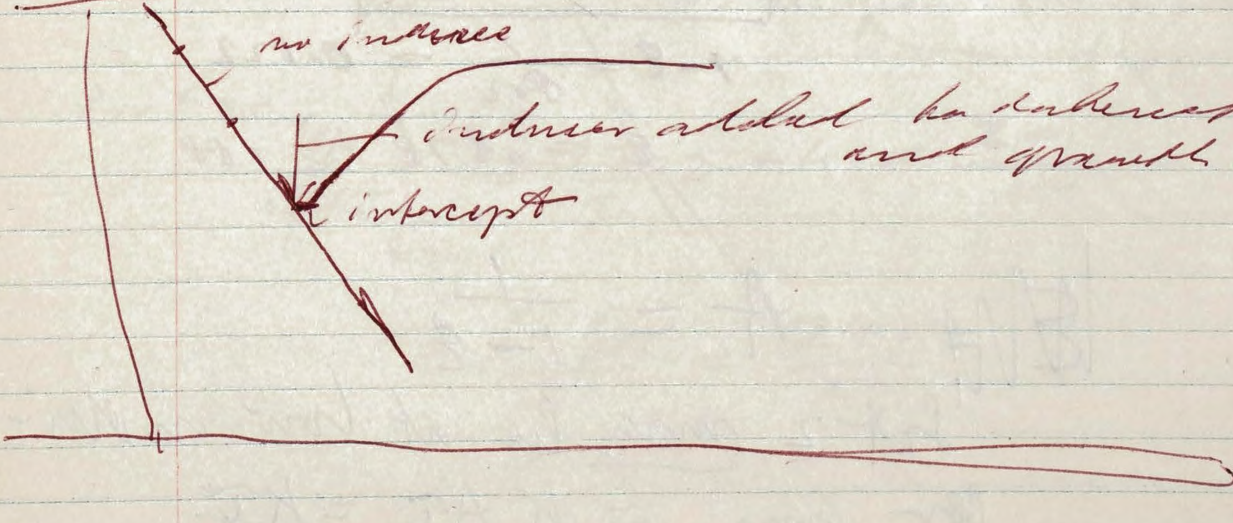
$$\frac{dP}{dt} = bGt + bR_0 \quad \Big| \quad \frac{1}{b}\frac{dP}{dt}\frac{1}{Gt} = \frac{[RNA]}{bg\tau}$$

for $t = 0$

Compare $\frac{R_0}{G}$ with τ !

Experiment proposed !

Put inducer in tank of chemostat so that saturation be at about 5 or 10 then use an inducer for which saturation is at 50 (for [illegible] thyo[illegible] #a)



~~In experiment of Fig 1 in first paper in Science:~~

~~$z(\infty) = 21$~~

~~$A = 8.2$~~

~~$1-\varepsilon = \frac{21}{8.2} = \boxed{0.256}$~~

~~$\varepsilon = .744$~~

$$\begin{array}{r} 1000 \\ 256 \\ \hline .744 \end{array}$$

~~Conclusion $\varepsilon > .744$~~

For saturation

$$\frac{dz}{dt} = 0 = \frac{\varepsilon - 1}{\tau} z_\infty + K$$

for $t = 0$ $z = 0$

$$\frac{dz}{dt} = \frac{\varepsilon - 1}{\tau} z + K = \frac{z_\infty}{A\tau}$$

so that

$$\frac{1-\varepsilon}{\tau} \cancel{z_\infty} = \frac{\cancel{z_\infty}}{A\tau}$$

$$\boxed{1 - \varepsilon = \frac{1}{A}}$$

$$1 - \varepsilon = \frac{1}{8.2} = 0.122$$

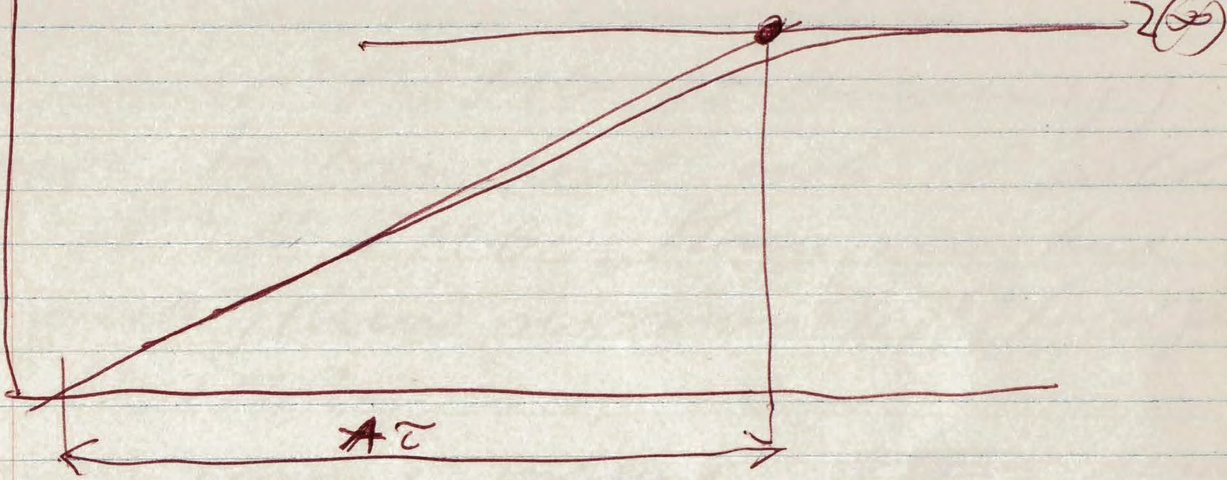
$$\varepsilon = .878 \approx .88$$

$$A = \frac{1}{1-\varepsilon}$$

Sat z may be at low inducer conc. $= K A \tau = \frac{K\tau}{1-\varepsilon}$

The duplication ~~factor~~

Note. of saturation is due to $\varepsilon < 1$



$$s' = k + \frac{\varepsilon z}{\tau}$$ modified (2)

$$\frac{dz}{dt} = s' - \frac{z}{\tau}$$ (1)

$$\left(\frac{dz}{dt}\right)_{\text{total}} = \frac{\varepsilon - 1}{\tau} z + k = \cancel{z(\infty)}$$

For sat $$\frac{dz}{dt} = 0 = \frac{\varepsilon - 1}{\tau} z + k = 0$$ (α)

For $t = 0$ $$\left(\frac{dz}{dt}\right)_{t=0} = \frac{\varepsilon - 1}{\tau} z + k = \frac{Z(\infty)}{A\tau}$$ (β)

$$\frac{1-\varepsilon}{\tau} = \frac{Z(\infty)}{A\tau}$$

or $$1 - \varepsilon = \frac{Z(\infty)}{A}$$

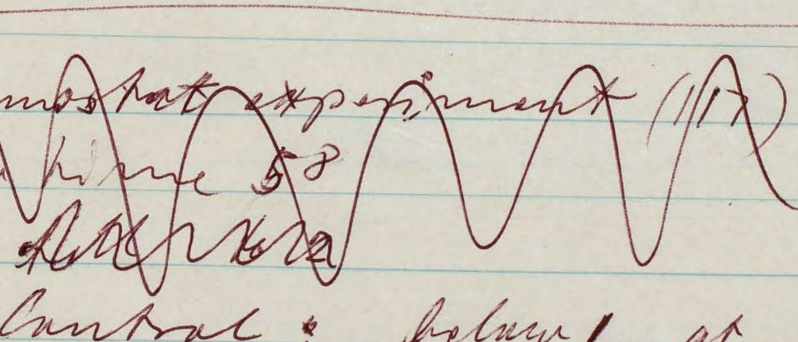
Saturday Oct 29/55

Culture (~~ice box~~ ~~for week~~) III/e~ B/r III EA
~~history: and transferred to~~

B/r into 10^{-3} M TMG (15 doubling) through 4 transfers each 10^6 fold in 10^{-5} M TMG then ice box for week, then regrown (10^6 fold) in 10^{-5} M TMG.

freshly growing culture ~~density~~ density until 195 activity $\boxed{76 \text{ and } 82}$

Diluted 6:14 in F grew to density 195 activity 37, 38,
inoculated into four tubes
1:10^6 into 10^{-5} M TMG grown to 195 activity 112, 120
1:10^7 " " " " activity 87, 88 old medium

Chemostat experiment (II)
rerun ... 58

~~A...~~
Control: below 1 at

Chemostat, originally 58
~~sat~~ washed but regrown 23 inoculum
lunch an old beaker 36:45

Intercept once more;

$$\frac{[RNA]}{N} = gt + R_0$$

$$\frac{dP}{dt} = \frac{[RNA]}{\tau} = \frac{gt + R_0}{\tau} N$$

$$\frac{d}{dt}\frac{P}{N} = \frac{gt + R_0}{\tau} - \frac{P}{\tau}$$

$$\frac{d\,P/N}{dt} = \frac{gt + R_0}{\tau} - \frac{P/N}{\tau}$$

$k\tau = 1$

$$P/N = gt - g\tau\left(1 - e^{-\frac{t}{\tau}}\right)$$

$$\cancel{\mathrm{const}\; gt}$$

$$\cancel{g + g\tau}$$

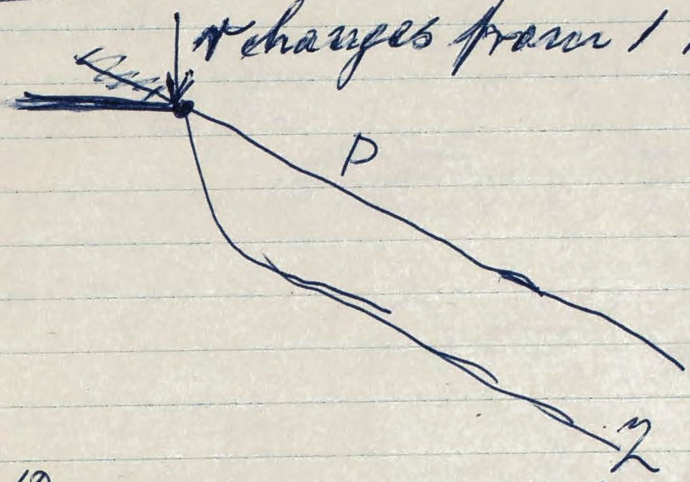
$$\cancel{g} + \frac{g\tau}{\tau} e^{-\frac{t}{\tau}} =$$

$$= \cancel{\frac{gt}{\tau}} - \cancel{\frac{gt}{\tau}} + g\left(1 - e^{-\frac{t}{\tau}}\right)$$

O.K.

$\underline{H}$

Mirando:



$$\frac{dD}{dg} = \varepsilon D - D = (\varepsilon - 1) D$$

$$\frac{dz}{dg} = rD - z$$

$$Z = \frac{rD_0}{\varepsilon} e^{(\varepsilon-1)g} + \left(Z_0 - \frac{rD_0}{\varepsilon}\right) e^{-g}$$

$$D = D_0 e^{(\varepsilon-1)g}$$

$$\frac{D}{Z}(t=\infty) = \frac{\varepsilon}{r}$$

Shape of curve :

$$D(i_0 - i_c) = \beta i_c z_0 \qquad \beta/D = \frac{i_0 - i_{cr}}{z_0}$$

$$\beta i_c z_0 + D i_c = D i_0 - \cancel{\beta i_c z_0}$$

$$i_c z_0 \left(\frac{\beta}{D} + 1\right) = i_0$$

$$i\, z \left(\frac{\beta}{D} + 1\right) = i_0$$

$$\frac{i_c z_0}{i\, z} = 1$$

$$\frac{i}{i_c} = \frac{z_0}{z}$$

$$\left(z\frac{\beta}{D} + 1\right) i = i_0$$

$$\boxed{i = \frac{i_0}{z\frac{\beta}{D} + 1}}$$

$$\frac{(\ )\,i}{(\ )\,i_{cr}} = 1 \rightarrow \frac{i_0}{i_{cr}}$$

$$\frac{i}{i_{cr}} = \frac{z_0 \beta/D + 1}{z\frac{\beta}{D} + 1}$$

$$z_{cr}\frac{\beta}{D} + 1 = \frac{i_0}{i_{cr}} \qquad \boxed{\frac{i}{i_{cr}} = \frac{z_0\beta/D + 1}{z\beta/D + 1}}$$

Wavelet theory

~~Sa~~ Saturation occurs when $\dot{i}$ falls to $\dot{i}_{crit} = \dot{j}$ ~~for saturation~~

$$D(\dot{i}_0 - \dot{i}_1) = \beta \dot{i} z$$

for saturation ($\dot{i}_{crit} = \dot{j}$)

$$D(\dot{i}_0 - \dot{j}) = \beta \dot{j} z$$

$$\frac{z_1}{z_2} = \frac{\dot{i}_1 - \dot{j}_1}{\dot{i}_2 - \dot{j}}$$ 0.1 / 1 $\dot{j}$ is about 5 10^{-6} TMG

Simplest assumption: i^* is a weak inducer and

$B = K i^* + \dot{i}$ has ~~same~~ critical value B for which K becomes 0. — $B = k^* i z + \dot{i}$

$$\left(D(\dot{i}_0 - \dot{i}) - \beta \dot{i} z\right) N = \frac{d}{dt}(N \dot{i})$$

$$D(\dot{i}_0 - \dot{i}) - \beta \dot{i} z = \frac{1}{N}\frac{dN}{dt}\dot{i} + \frac{d\dot{i}}{dt}$$

$$D(\dot{i}_0 - \dot{i}) = \frac{\dot{i}}{\tau} + \beta \dot{i} z$$

this term new

$$D\left[\dot{i}_0 - \dot{i}\left(1 + \frac{1}{D\tau}\right)\right] = \beta \dot{i} z$$

~~$\frac{D}{R} 4\pi R^2 t = \frac{4\pi R^3}{3}$~~ ~~$\frac{3}{RH}$~~ $t = \frac{R^2}{3}\frac{1}{D}$

~~Fort~~ For to diff
~~Ro~~ ...
for

$$\frac{\ell}{c}\,0 = 1 + \sigma \qquad \text{and say } \sigma = 0.2 \text{ and } \frac{\ell\, o}{\sigma\, \omega} = 2$$

$$0.2 = \cancel{1.5}\,\frac{2}{2_0} - \frac{2}{2_0} \cdot \frac{2}{2\,2_0}$$

$\gamma = 0.4$

Experiment ~~with temp. sensitive lactose+ mutant~~ :

2.) How to pick the "back mutant" to temp. independence (lac+): a.) put 10^6 bacteria with TMG on mother plate and let it multiply by 100. b.) replica plate on plate, no TMG, with limiting maisnate to express mutant and then spray lactose. c.) Colonies indicate which region of mother plate to pick for subculture"

3.) ~~Subcult~~ ~~Subcult~~ Subculture is plated on mother plate containing TMG (& carbon source), From mother-plate are made ~~three~~ replicas, one on TMG agar and ~~two~~ on plate with limited maisnate and after a few generation these two plates ~~&~~ are sprayed with lactose, —

1.) How to pick temperature sensitives: Plate UV-d population at 27° (10 bact.) ; pick positives with lactose the only ~~carbon~~ source for carbon source, make replica plates and incubate at 37

H

$$\frac{i}{i_{cr}} = \frac{z_0\beta/\Delta + 1}{k\, z_0\beta/\Delta + 1} = A$$ fixed slope

$$z_0\beta/\Delta + 1 = A(k\, z_0\beta/\Delta + 1)$$

$$i\, z\frac{\beta}{\Delta} + i = i_0$$

$$\frac{i_0 - i_{cr}}{i_{cr} z_0} = \beta/\Delta$$

$$\boxed{\frac{i}{i_{cr}}} = \frac{i_0}{i_{cr}} \Big/ \frac{z}{z_0}\frac{i_0 - i_{cr}}{i_{cr}} + 1$$

$$\frac{i}{i_0} = \frac{1}{\frac{z}{z_0}\frac{i_0}{i_{cr}} + 1 - \frac{z}{z_0}}$$

$$\boxed{\frac{i_0}{i} = \frac{z}{z_0}\frac{i_0}{i_{cr}} + 1 - \frac{z}{z_0}}$$

$k \sim 5$
$\sim 10 - 10^{-6}$

$$\frac{i_0}{i} = \frac{z}{z_0}\frac{i_0}{i_{cr}} + 1 - \frac{z}{z_0}$$

rework Naudet's theory with

$$D(i_0 - i_c(1+\tfrac{1}{D\tau})) = \beta i_c z_0$$

$$D(i_0 - i(\quad)) = \beta i z$$

$$\boxed{\frac{\frac{i_0}{i_1}-1}{\frac{i_0}{i_2}-1} = \frac{z_1}{z_2}}$$

$$\frac{\frac{i_0}{i}-(\quad)}{\frac{i_0}{i_c}-(\quad)} = \frac{z}{z_0}$$

$$\frac{i_0}{i} = \frac{z}{z_0}\left(\frac{i_0}{i_c}-(\quad)\right)+(\quad)$$

$$\frac{i_0}{i} = \left(1-\frac{z}{z_0}\right)\left(1+\frac{1}{D\tau}\right)+\frac{z}{z_0}\frac{i_0}{i_c}$$

$$1.2 = 1.2 - \frac{z}{z_0}1.2 + \frac{z}{z_0}1.5 \quad 1.5$$

$$0.3\frac{z}{z_0}$$

$$\frac{i_0}{1+\frac{1}{D\tau}}/i = \left(1-\frac{z}{z_0}\right)+\frac{z}{z_0}\left(\frac{i_0}{i_c}\frac{1}{1+\frac{1}{D\tau}}\right)$$

which is old Naudet result! (no gain)

For new Naudet-Siloso theory

see middle of Book

~~New Novick à la Sutland~~

H

$$\cancel{D(i_0 - i)N = \frac{d}{dt} N i^* = \frac{i^*}{\tau} N + N \frac{di^*}{dt}}$$

$$\cancel{D(i_0 - i) = \frac{i^*}{\tau}}$$

$$\cancel{i^* =}$$

$$\cancel{\beta i z N = \frac{d}{dt} i^* N = \frac{i^*}{\tau} N}$$

~~Growth of i^* is indirect but made~~

Sutland – Novick theory

$$D i_0 = \beta i z$$

$$D i_0 = \beta i z$$

$$D i_0 = \beta i_{cr} z_0$$

$$\frac{D}{\beta} \frac{i_0}{i_{cr}} = z_0$$

$$\frac{D}{\beta} \frac{i_0}{i_{cr}} = z_0$$

$$\frac{i_0}{i} = \frac{\beta}{D} z$$

$$\frac{i_0}{i} = \frac{z}{z_0} \frac{i_0}{i_{cr}}$$

$$\frac{1.2}{1.5} = \frac{z}{z_0}$$

5 years, 750,000 } **Brandeis**
300000,

15,000 $\boxed{300000}$

(4) Rucker:

72000 (60000 + $\overset{E.E.}{12000}$)

(4 MD or PhD) | Fellows [5 PhD]

6 Techn

1 Secr

Director
Business Mgr } Adm [2700 sq feet]
5 secretaries

[very crowded]

(4-5 grad) Students needs $1\frac{1}{2}$ times space twice as much space

shares ~~stockroom~~ downstairs

Sterilizing equipment

outside grants 10000 7000

17000

about ½ plus undispendables (10000)

~~Total~~ 22000 not salary includes extra ordinary Ind. [illegible] equipment.

Security for Inst
~~Constitutional~~ Pledges:
1.) unspent income until Endowment of 2.0 million accumulated ×

2.) ~~In any one year no l~~
For a number of years ~~[illegible]~~
no less than 150 000 a year
except ~~if last three years~~
~~average income~~ if years
income less than 250,000 and
if in addition last five years
income less than 300,000

(Kornberg)
RNA ~~Haberland~~ DNA
Uracil Cytosine ||| Thymidine Cytos

H 5,000 Davis

~~26~~

on grants 25-30,000
3 techn dishwasher
1 1/2
4 PhD

Outside grants
total: 40000
+ 4000
4000
8000

control this E. E.

200
200
400
200
200
600
200
200
200
400
200
200
200

Instal Equipp
ment!
20,000

400
1000
2000
$\boxed{3400}$ sq foot

de Bodo
600

Jones 4200

Mass + tech
Adams + tech
McR. —
Fresco —
Davis + tech
1 secretary
1 1/2 dishwasher
Gr. Jomolinsky —
F Gorini
Gr. Kalen
Gr. Lettner

10 PhD | [3 Staff]

1 Salary 38,000
− 10
28,000
+ 7000
35000
+ 3000
$\boxed{38,000}$

without de Bodo
from School
none for
equipment

X1 1150,000

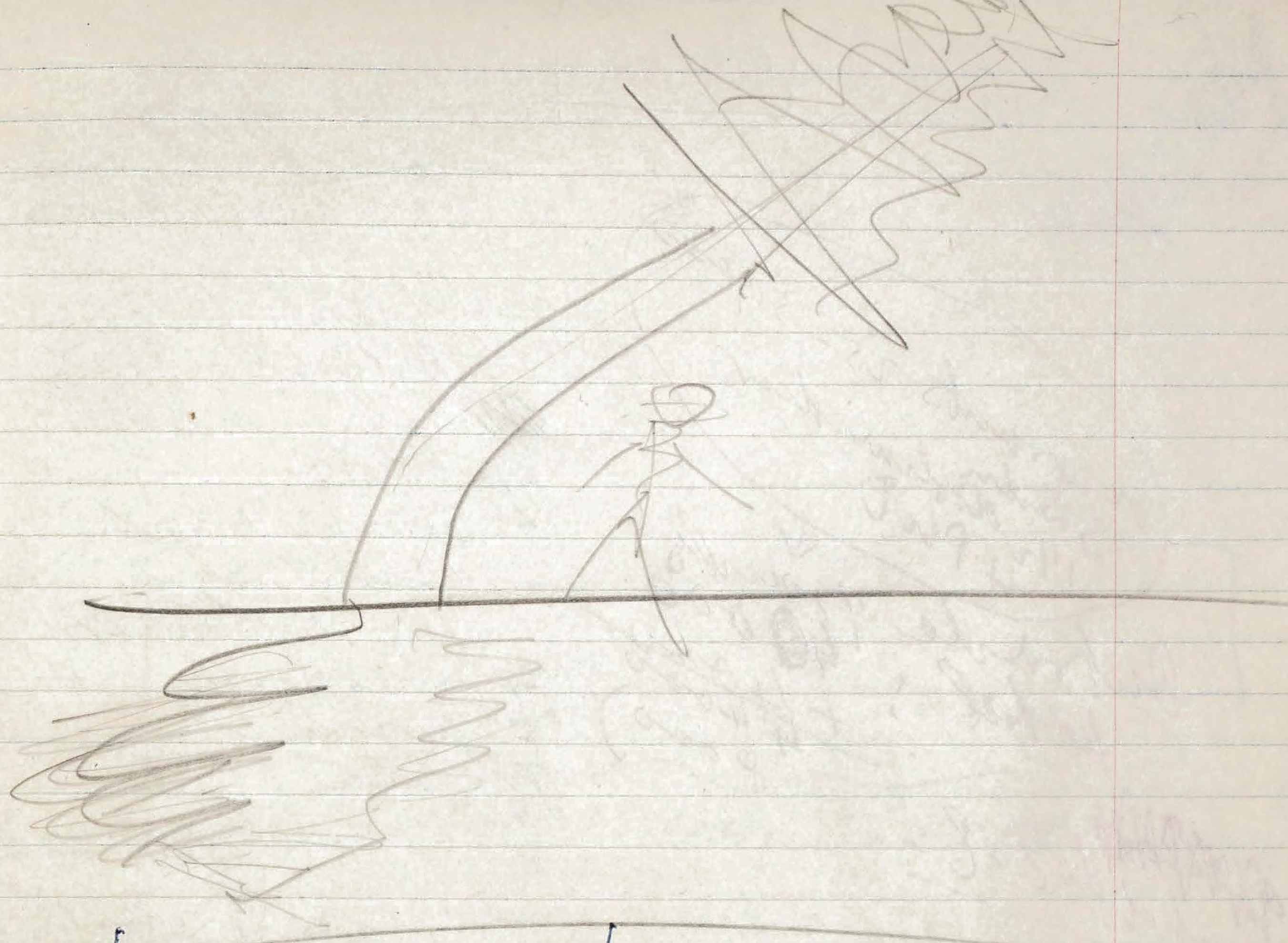
H

200,000

1 or 20 15 oooo, 3000000

4000

330 = 4 00



nuevo Arenas

Freund

Negative: Kidney F
liver F
ovary ≠
skin F
lens (no damage)
uterine muscle
? adrenals ?
Bone marrow
Thymus {Guinea pigs (Carter / Utah)}
Pancreas
Pituitary
Parathyroid
Spleen, lymph gland
Prostate
Breast

Positive: Whole testes / Sperm
Species specific (no damage by antibody)
Thyroid
lens (antibody)

Brain
Thyroid
nerve
Uvea
} damage
organ specific

Heterologous

modify body proteins;

Cavelti

Thomas

Jules Freund
Chief of Div. of applied Immun.

Mrs Shelley P.

H

Dr. Moore (George E) Roswell Park

Roswell Park Mem. Inst. Buffalo —

{ Bressman
{ Jim Holland }
Urbach
Hoshke

Cancer
550 Bed

Boddick — Karl Meyer

Mir State Univ.

Charles Doon; Dean of Med School

Rolling Riv. Rehab. Disease Dept
St. Vincent's Hospital

Mass Gen. Hospital.

Butler || Mt. Sinai

Gregory Pincus
Sept 11–17

Worcester
Inst of Exp. Biolo
Shrewsbury Mass
222 Maple Ave

Is excess heat produced by

chronic myelogenous leukemia
irradiation of spleen helps!! only

acute myelogenous leukemia

increase metabolic rate
bigger than temperature would
warrant

Mrs Winthrope ~~~~ Salt Lake City
Leon Jacobson
Carl Moore Wash Univ. St. Louis
no Dameshek (William)
Paul Steiner Chicago
Elmer Humphreys
David Karnofsky ~~~~ Mem Hosp N.Y. Memorial
no Burchenall
Austen Weisberg Western Reserve Cleveland
Lockhard Conley Johns Hopkins
Arnold Rich " "
Shils Warren Harvard

Clement Finch Univ. of Wash Seattle
William Bloom