H-42

Sviland

Plans for 51

"The prescription or dispensing by a physician of a secret medicine [or other secret remedial agent] of which he does not know the compos. [or the manufacture or promotion of their use] is unethical. —

Andrew C. [illegible]

The Chic. Med. Soc.

1130 VERNON ROYAL LINE U. S. A.

Compound X

1.) Bradley with Gonzales Enzyme B/t, before and after autoclaving. —

2.) make Compound and autoclave it. —

Exp 100 µl Tryptophan-less B/t + Prototrophless strain [2 10^8]

τ = 3 hrs

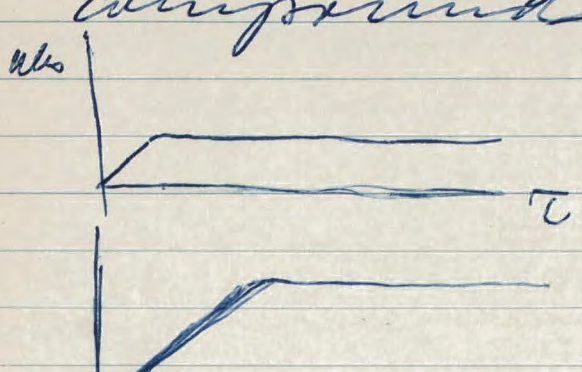
↑↓ Alternative: Phagostat First growth tube B/t; second growth tube B (N limited) gets rid of ammonia

Other method:
Use glucose in first growth tube of thermostat and carbon source limitation in second growth tube; then test with Beckmann; does not work if precursor is withheld as carbon source [in place of testing with Beckmann determine P H.] —

Other method:

In thermostat two strains tryptophaneless and B/34 glucose medium) First grow up tryptophaneless; then inoculate with B/34 (slow grower) and set aside for B/34 with

Effect of N (on level) compound X



~~Effect~~ Outgrowing of precursors

For Nitrogen containing ones use Kjeldahl

For others either established Carbon source and then remove Carbon source

or better

Heavy Water (or Tritium water)

~~and~~ evaporate to dryness repeatedly (washing with ordinary water and determine activity. —

No carbon source left
Extraction or absorption
should permit to
determine precursor

K

For experiment:

To avoid complexation with
precursor do it first (with
either lactate or succinate) as
B with Nitrogen limitation. —

Later: Do it with Tryptophan less
strain comparing lactate
with succinate. (Titration)

Does it go in reverse i.e. if we give arginine do we get ornithine and citrulline prevalent? In this experiment we should have an arginineless bug to eat up arginine in II growth tube and then assay with citrullineless

Metabolic B/1t in I st growth tube; Arginineless in II nd growth tube. — What is taken of Arginineless [with no Arginine in nutrient outflow into I st growth tube]. If E is suddenly increased in I st growth tube is then ~~more~~ ~~arginine~~ rate of arginine outpouring for a while maintained unchanged? or increased!?

mixture of B/1t fast and B/Arg Ratio - 1:1 to 10. —

Can B/~~1t~~fast take away pyrophosphate from B/Arg

Metabolic H

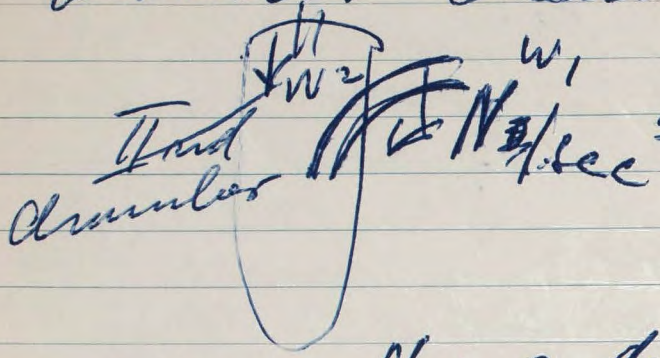
Phagostat. – In first growth tube B/t ~~and~~ tryptlxd and B/t enough Argi- nine to supply 1/2 of orginine in B/t population. – Second growth tube inoculated with Arginine-less /6 and T other with T_6 will be determined. –

Metabolic Oct 6/51

Grow B/t tryptophane lxd and feed Ornithine into I growth tube. Question are citrulline and arginine poured out. assay in second growth tube with a.) citrullineless b.) arginineless

How does out pouring depend on conc. of Ornithine?

Precursor Study with two chamber Chromatograph



$$N + n\frac{dn}{dt}V - n(w_1+w_2) = 0$$

$$n\frac{dn}{dt} = f(c) = n(w_1+w_2) - w_1 n_0$$

$$c_1 w_1 - c_2(w_1+w_2) = a_2 w_2$$

1.) $a_2 w_2 + n_0 w_1 Q \approx n_2 Q(w_2+w_1)$

2.) $n_1 w_1 + \frac{dn_2}{dt} V = n_2(w_1+w_2)$

$$\frac{n_1}{n_2} w_1 + \frac{1}{n_2}\frac{dn_2}{dt} V = w_1 + w_2$$

2.) $$\frac{n_1}{n_2}\frac{w_1}{V} + f(c_2) = \frac{w_1+w_2}{V}$$

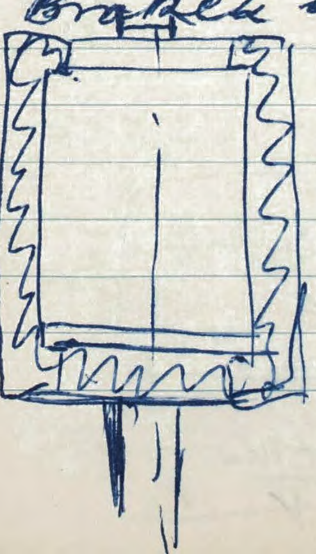
1.) $$n_2 = \frac{a_2 w_2 + n_1 w_1 Q}{Q(w_2+w_1)}$$

$$\frac{n_1}{n_2} = \frac{n_1 Q(w_1+w_2)}{a_2 w_2 + n_1 w_1 Q} = \frac{(w_1+w_2)}{\frac{a_2 w_2}{n_1 Q} + w_1}$$

Anabolic: One chamber chemostat in mixture of B/1t and B/Arg [which seems to maintain itself stationary] how fast does B/1t/Arg vanish?

↑ better:
~~worse~~: Two chamber chemostat
↓ mixture of B/1t and B/1t/Arg determine Arg. titer with array of [illegible] and growth tube in controls: what would be Arg titer for mixture of B/1t and B/Arg?

Fundamental growth in broken up bacteria



lyse with lysogenic strain!!! then see if bacterial synthesis goes on.

Let us set $\frac{W_1+W_2}{V} = 70_{min}$

$$f(c_2) = \frac{1}{70_{min}}\left[1 - \frac{1}{\quad}\right.$$

$$f(c_2)\frac{V}{W_1+W_2} = 1 - \frac{\quad}{\quad}$$

$$\frac{1}{\frac{a_2}{Q}\frac{1}{n_1}\frac{W_2}{W_1}+1} = 1 - f(c_2)\frac{V}{W_1+W_2}$$

$$\frac{a_2}{Q}\frac{1}{n_1}\frac{W_2}{W_1} = \frac{1}{1 - f(c_2)\frac{V}{W_1+W_2}} - 1$$

$$\frac{a_2}{Q} = n_1\frac{W_1}{W_2}\left\{\frac{1}{1 - \frac{f(c_2)}{\frac{W_1+W_2}{V}}} - 1\right\}$$

$$\boxed{\frac{a_2}{Q} = n_1\frac{W_1}{W_2}\,\frac{f(c_2)/\frac{W_1+W_2}{V}}{1 - f(c_2)/\frac{W_1+W_2}{V}}}$$

$$\frac{n_1}{n_2} = \frac{w_1 + w_2}{\frac{a_2}{Q}\frac{w_2}{n_1} + \frac{w_1}{n_1}}$$

$$2) - \frac{w_1 + w_2}{\frac{a_2}{Q}\frac{w_2}{w_1}\frac{1}{n_1} + 1} \cdot \frac{w_1 + w_2}{V} + \frac{w_1 + w_2}{V} = f(c_2)$$

$$f(c_2) = \frac{w_1 + w_2}{V}\left[1 - \frac{1}{\frac{a_2}{Q}\frac{w_2}{w_1}\frac{1}{n_1} + 1}\right]$$

$$f(c_2) = \frac{w_1 + w_2}{V} \cdot \frac{\frac{a_2}{Q}\frac{w_2}{w_1}\frac{1}{n_1}}{\frac{a_2}{Q}\frac{w_2}{w_1}\frac{1}{n_1} + 1}$$

$$f(c_2) = \frac{w_1 + w_2}{V} \times \frac{w_2}{w_1} \cdot \frac{a_2/Q}{n_1} \times \frac{1/n_1}{\frac{w_2}{w_1}\frac{a_2}{Q}\frac{1}{n_1} + 1}$$

$$f(c_2) = \frac{w_1 + w_2}{V}\left[1 - \frac{1}{\frac{a_2}{Q}\frac{1}{n_1}\frac{w_2}{w_1} + 1}\right]$$

$$\frac{f(c_2)}{w_1 + w_2} < \frac{w_1 + w_2}{V}$$

~~$T_{max} = 70$~~

$$\frac{f(c_2)}{\frac{w_1 + w_2}{V}} = \left[1 - \frac{1}{\frac{a_2}{Q}\frac{1}{n_1}\frac{w_2}{w_1} + 1}\right]$$

If a_2 not large enough
n_2 is determined by a_2 (1)
and f is determined by (4)

(1) $a_2 w_2 + \frac{a_1 Q w_1}{n_1} = n_2 Q (w_2 + w_1)$

$$\frac{a_2 w_2}{n_1} + Q w_1 = \frac{n_2}{n_1} Q (w_2 + w_1)$$

$$\frac{\frac{a_2}{Q}}{n_1} w_2 + w_1 = \frac{n_2}{n_1} (w_2 + w_1)$$

$$w_2 \frac{a_2}{a_1} + w_1 = \frac{n_2}{n_1} (w_2 + w_1)$$

$$\frac{n_2}{n_1} = \frac{\frac{a_2}{a_1} w_2 + w_1}{w_1 + w_2} = \frac{1}{\frac{w_1 + w_2}{V_2} - f} \frac{w_1}{V_2}$$

Subst (4)

$$\frac{Q}{Q_1} w_2 \frac{a_2}{a_1} + w_1 = \frac{w_1 + w_2}{\frac{w_1 + w_2}{V_2} - f} \frac{w_1}{V_2}$$

$$w_2 \frac{a_2}{a_1} + w_1 = \frac{1}{\frac{1}{V_2} - \frac{f}{w_1 + w_2}} \frac{w_1}{V_2} = \frac{w_1}{1 - f \frac{V_2}{w_1 + w_2}}$$

~~If the second growth rate >> 0 under~~

these conditions:

2.) $\frac{n_1 w_1}{n_2} + \left(\frac{1}{n_2 + \frac{dw_2}{dt}}\right) V_2 = w_1 + w_2$

$$\frac{n_1}{n_2}\frac{w_1}{V_2} + f_0 = \frac{w_1 + w_2}{V_2} - f_x$$

$$\frac{n_2}{n_1}\frac{V_2}{w_1} = \frac{1}{\frac{w_1 + w_2}{V_2} - f_x}$$

(4) $$\frac{n_2}{n_1} = \frac{1}{\frac{w_1 + w_2}{V_2} - f_x} \times \frac{w_1}{V_2}$$

and if $a_2 w_2 + a_1 w_1 >> (n_2 Q + n_1 Q)_x$

i.e. if a_2 big enough $f(x(w_1 + w_2)$

$f_0 = 70$ min

What holds if a_2 not large enough

and $\frac{w_1 + w_2}{V} > \frac{1}{70 \text{ min}}$?

$$\frac{a_2}{a_1} = \frac{w_1}{w_2} \frac{f\frac{V_2}{w_1+w_2}}{1 - f\frac{V_2}{w_1+w_2}}$$

6

$$f\frac{V_2}{w_1+w_2} < 1$$

for instance for $\frac{V_2}{w_1+w_2} = \frac{\text{20 min}}{0.9 \times 70 \text{ min}}$

and $f = \frac{0.9}{70 \text{ min}}$

$$f\frac{V_2}{w_1+w_2} = 0.9 \times 0.9 \approx 0.8$$

$$\frac{a_2}{a_1} = \frac{w_1}{w_2} \quad \frac{0.8}{1-0.8} = 4\frac{w_1}{w_2}$$

$$\frac{\frac{a_2}{a_1} w_2 + w_1}{} = \frac{w_1}{1 - f \frac{V_2}{w_1 + w_2}}$$

$$1 - f \frac{V_2}{w_1 + w_2} = \frac{w_1}{\frac{a_2}{a_1} w_2 + w_1}$$

$$1 - \frac{w_1}{\frac{a_2}{a_1} w_2 + w_1} = f \frac{V_2}{w_1 + w_2}$$

$$\frac{\frac{a_2}{a_1} w_2}{\frac{a_2}{a_1} w_2 + w_1} = f \frac{V_2}{w_1 + w_2} \qquad (5)$$

for $a_2 <$ ~~[illegible]~~ then what corresponds to w_2 from formula (4) with $f = f_0$

$$\frac{a_2}{a_1} = \frac{w_1/w_2}{1 - f \frac{V_2}{w_1 + w_2}} - w_1/w_2 \qquad (6)$$

first take dry less later 12 hours less than later of B/lt to see if dry measures gets-answered by B/lt in organisms

In experiment of this type it is better to use ~~the~~ Constant Chamber Thermostat for better control at fast growth-rates

Metabolic

Complete synthetic medium
leave out tryptophane
~~my growth~~ gen time max
50 min

between 50 and 70 min of
~~[illegible]~~ gen time for finite amount
of tryptophane what will be
factor of darkening. —

~~Study~~ Precursor

If Precursor made from B/14
with glucose. —
and second ~~[illegible]~~ chemostat ~~is~~
~~[illegible]~~ growth tube is run with
~~[illegible]~~ B he eat up glucose and
lactic acid. Titration
will give quantity of
precursor.

Metabolic.

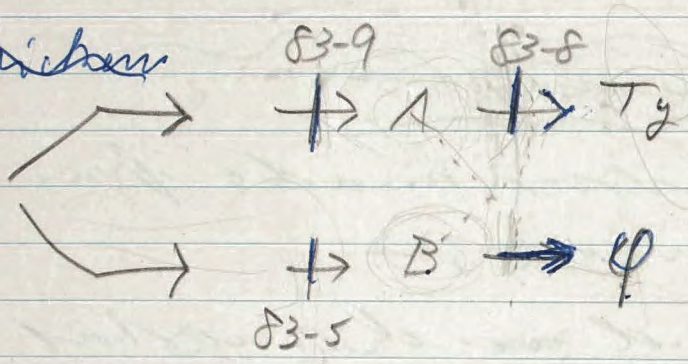
Take B/try + B/14 mixed and
fed with try and tryp respectively

Davis tells this:

Strain δ3-5 Phenylalanine requiring, passes out tyrosine. —

Question: does a cure of ~~[illegible]~~ interest passing out [illegible] 5 mgm/l ?

~~Volwiler~~ Schicham



δ3-9 growing on Ty spells Ø

δ3-9 " on high Ty [10 mg/l] does not excrete Ø

δ3-8 requires Tyrosine does not spell out anything ?

δ3-5 " Ø ~~over~~ spell Ty ,

" with high Ø does not spell Ty

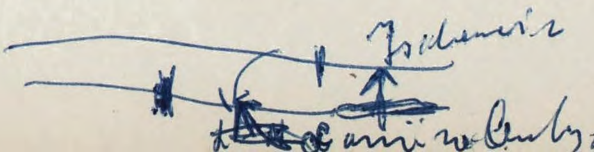
Bernie Davis   Oct 16th/51

1.) ~~Tyrosineless spills out phenyl~~
2.) Tyrosineless spills out ~~alt~~ (alanine) nothing
(Davis interested in product) (No 83-8)
3.) Methionineless does it spill out homocysteine, cystathionine?
[~~not Davis~~ Davis not interested in product

4.)

Davis suggests for proving excretion.

α-aminobutyric acts as a precursor of isoleucine; 97-21 grows equally well on either or on plausible intermediates
(α-keto butyric
(α-keto analogue of IL)
(α-β-dihydroxy " " ")
42-37 grows on IL (sl. faster c̄ leucine + valine as well); not on any others of above.
Either WT or 97-21, growing on 20γ/ml α-NH_2 butyric or more, feeds 42-37.
Chrom. shows excr. to be IL -



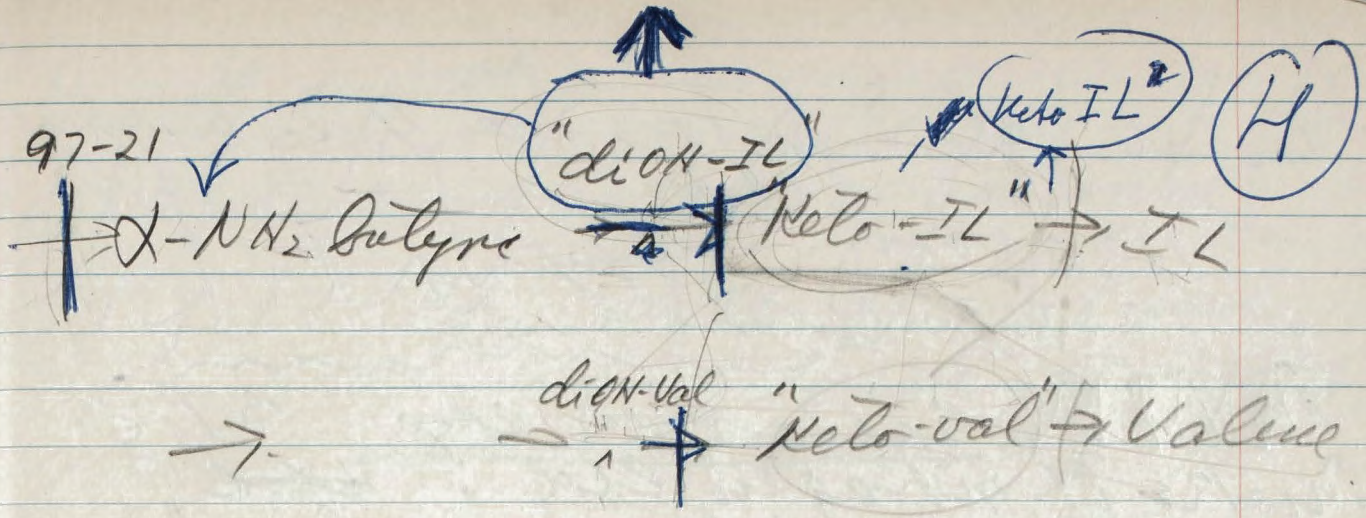
Davis Lysine - less accumulates DAP

X ≠ DAP ≠ Lysine
7 carbon 6 Carbon

Strain 173-25 grows on DAP but also requires Lysine for good growth ; Davis Hinks X includes Lysine formation.

D.A.P. Elizabeth Work

Examine primelic



(4)

97-21, requiring α-NH₂ But, IL, or intermediate, spills out valine
Excess of either α-NH₂ But or IL (100 X/mM) abolishes this excretion.

Bonner
Mut, blocked in IL synth, also requires valine,
This must accum. diOH IL and diOH valine,

Tatum
de Robichon
Umbarger
Davis

Excretion as technique

Berkeley Dept. of Bact
Bact. Dept. [Stanford] Harvard Med

~~Intake 150 mgm/l ~~ " 1/5 cc bodema~~

~~150 x 5000 mgm~~

~~750 gm [illegible]~~

~~[illegible]~~ Excretion exp. B/1t

Make it nitrogen ltd. ~~[illegible]~~ alanine

in presence of Phenyl alanine.

does it pour out?

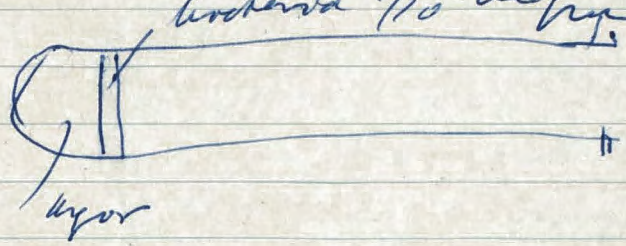
and 1mg/l
pyrophosphate
and without
phenylalanine

Excretion P limited Chlamydomonas
with B/1t + Trypt + phenyl
~~[illegible]~~ alanine. Does it pour
out.

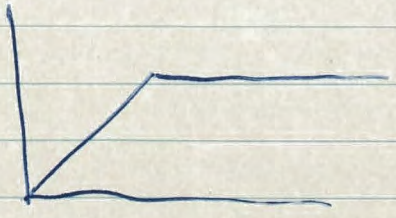
Growth in culture

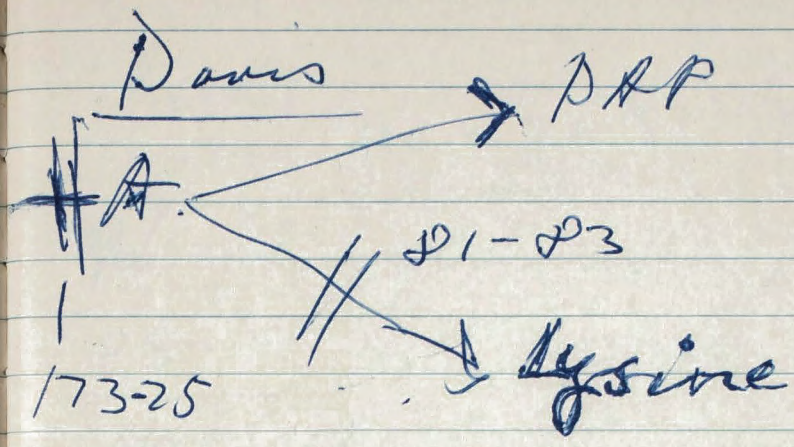
1.) Phage growth [extra handout]

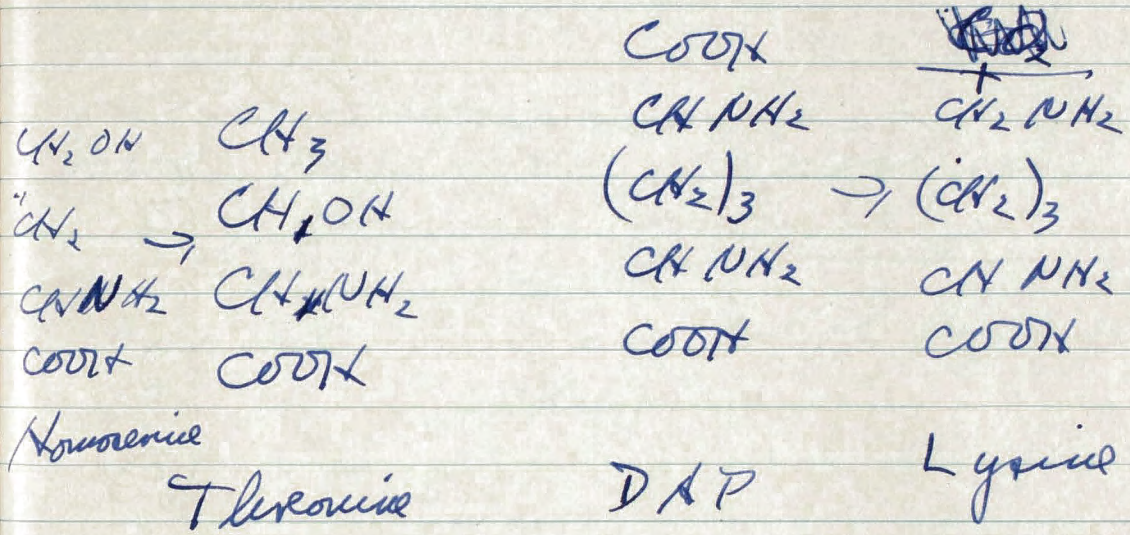
Infect B/2 with T_2 hrt and spin down before lysis, drain off water, add T_2 r and let lyse while spinning. — What about restriction



Extraction exp.
B/1 t with N. Oxygen
low. and Phenylalanine
to suppress tyrosine phenase;
this should now give:




Davis
DAP
M1 - M3
Lysine
1
173-25


COOH
CH NH2
(CH2)3
CH NH2
COOH
CH2 NH2
(CH2)3
CH NH2
COOH
CH2OH
CH2
CH NH2
COOH
CH3
CH OH
CH NH2
COOH
Homoserine
Threonine
DAP
Lysine

Feeds <u>83-9</u> [requires Tyrosine]
Feeds 81-83 } ~~…~~ passes out
feeds 26-26 } (it)
Lysine: ~~at~~ spells out also
for Phenylalanine, and Tryptophane

<u>83-8</u> ~~a~~ (requires Tyrosine)
also feeds 81-83 (lysineless)

~~~~~~

~~Berg~~ professor of Biochem
(C.P.) (Univ of) Iowa <u>Iowa City</u>

Do <u>not</u> grow on Indol Pyruvic
19-2 (Indol)
121-35 ["] or anthr.?
~~~~~~

Tryptophan mutants - coli

~~#5~~

Davis

159-11 Tr⁻ Tryptophan only, no exer.

165A-52 Tr⁻/~~Tyr⁻~~, feeds "indole" to 19-2, 121-35

159-10 Tr⁻/slow indole/fast indole + serine + pyridoxin, no excretion

154-33 Tr⁻/slow indole, no excretion

63-16 Tr⁻/serine + pyr/slow anthranilic (also by indole; exer "indole")

19-2 Tr⁻/indole, exer "anthranilic"

121-35 Tr⁻/indole/anthranilic

156-67 Tr⁻/indole/slow anthranilic.

Excreter of tryptophan (as well as of tyrosine)

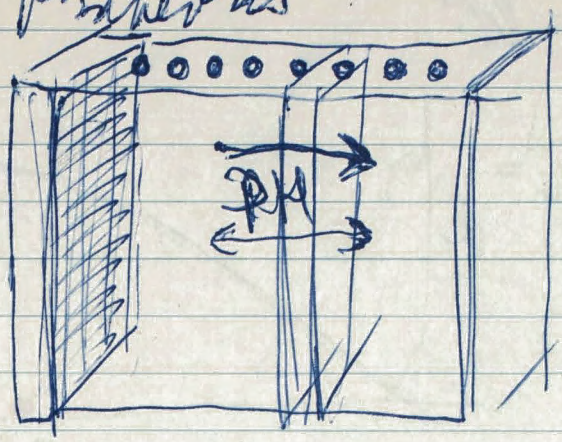
83-5 Phenylalanine⁻

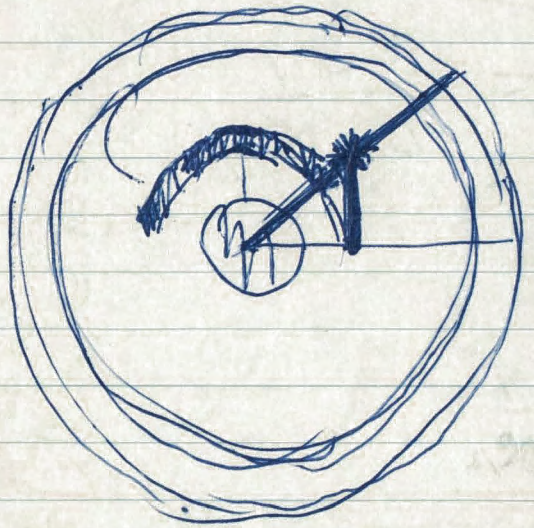
83-9 Tyrosine⁻ (also exc lysine, Val)

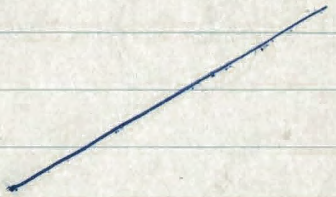
Dick Moder says: 4

Cost of liquid extraction
between 1 to 3 cent per gallon
put through [1 cent per gallon
would be 1 cent per 4 gm or $1 per lb
assuming 1 gm/liter in original juice]
Solid columns sulfonated polystyrenes
[Dow Chemical Co or Resinous Products
Co] are cheaper products sell
for 50 cents to 1$ per lb. If we
need less purification but have
lower conc. to start with may be
our price will be 50 cents/lb. —

Brackets

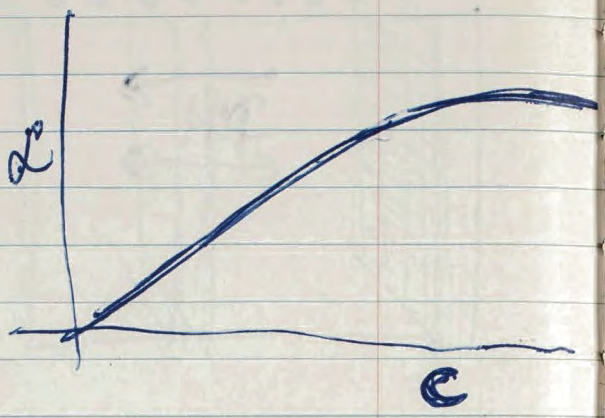






$$\frac{c\alpha_2}{Q_2} = \frac{dp_2}{dt}/\rho_2 = \tau$$

$$\frac{c\alpha_1}{Q_1} = \frac{dp_1}{dt}/\rho_1 = \tau$$



$$\frac{c\alpha_2}{Q_2} = \frac{1}{\tau}$$

$$c = \frac{Q_2}{\tau}\,\frac{1}{\alpha_2}$$

$$\frac{a-c}{Q_2} = \frac{Q_1^0}{Q_2}$$

$$\frac{a}{Q_2} - \frac{1}{\tau}\frac{1}{\alpha_2}$$

$$\frac{Q_1}{Q_2} = f(c)$$

$$\frac{a-c}{Q_2} = \rho_1\left[\frac{Q_1^0}{Q_2} - \varepsilon\right] + \rho_2$$

$$\frac{Q_1}{Q_2} = \frac{Q_1^0}{Q_2} - \varepsilon$$

$$\boxed{\frac{a}{Q_2} - \frac{c}{Q_2} = \rho_1\frac{Q_1^0}{Q_2} + \rho_2 - E\rho_1}$$

Two strain experiments

$$a\dot{\varepsilon} = c\dot{\alpha} + \rho_1 Q_1 \frac{dv}{dx} + \rho_2 Q_2 \frac{dw}{dx}$$

$$\frac{c\alpha_1\rho_1}{Q_1} = \frac{d\rho_1}{dt}$$

$$a - c = \rho_1 Q_1 + \rho_2 Q_2$$

$$\frac{c\alpha_2\rho_2}{Q_2} = \frac{d\rho_2}{dt}$$

$$\frac{\alpha_1}{\alpha_2} = \frac{Q_1}{Q_2}$$

$$\frac{\alpha_1}{Q_1} = \frac{\alpha_2}{Q_2}$$

$$Q_1 \leq 0.2\, Q_2 \qquad \alpha_1 \leq 0.2\, \alpha_2$$

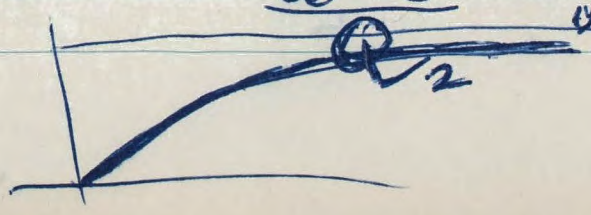
What is $\frac{Q_1}{Q_2}$ & ρ_1 is set by keyst.

cane. $\rho_1 Q_2$ is total keyst.

Q_1 which comes from outside

$$\frac{Q_1}{Q_2} = f(c) \qquad a - c = \rho_1 f(c) Q_2 + \rho_2 Q_2$$

$$a - c = \rho_1 f(c) + \rho_2$$



Good experiment is!

Trypstaphanelen and Strychnine less at fixed & use different amounts of strychnine below the amount contained in trypstaphanelen. —

Observe either rate at which strychnine less is washed out or level at which strychnine-less is maintained. If

a.) If strychnine is maintained strychnine conc c is given by E and we can compute what fraction of strychnine in trypto-phanelen comes from antidote. —

This should be Independent from amount of strychnine supplied. — We can go with strychnine even above strychnine amount conc. a contained in trypstaphanelen. —

The Strand experiment

$$a = c + \rho_1 Q_1 + \rho_2 Q_2$$

$$a - c = \rho_1 Q_1 + \rho_2 Q_2$$

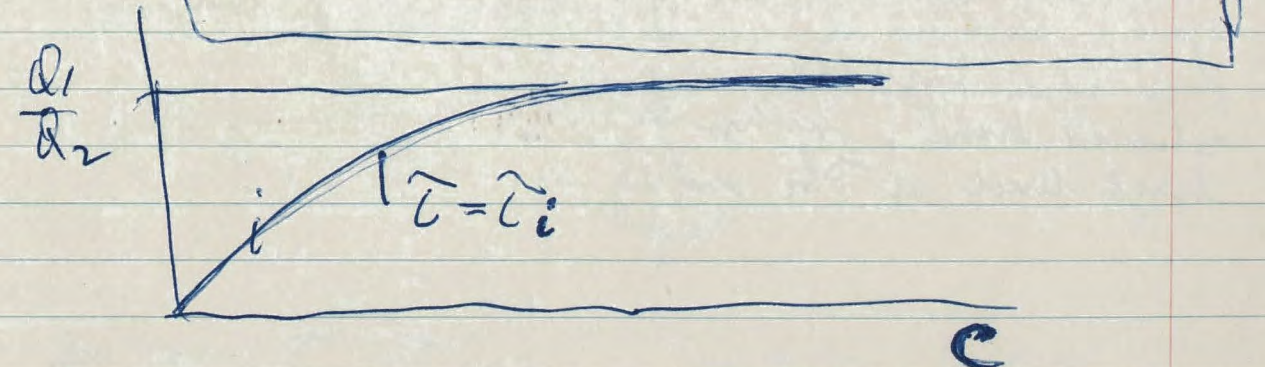
$$\frac{[a-c] - \rho_2 Q_2}{\rho_1} = Q_1$$

change τ will change ρ_2
change a will change ρ_2

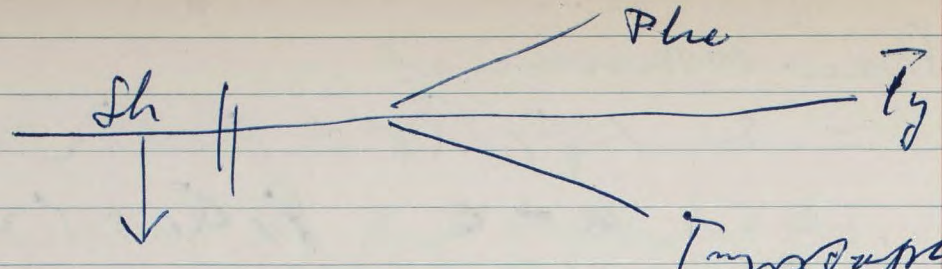
$$\frac{1}{\rho_1}\frac{a-c}{Q_2} - \frac{\rho_2}{\rho_1} = \frac{Q_1}{Q_2}$$

$$\frac{Q_1}{Q_2} = \left\{\frac{Q_1}{Q_2}\right\}_{\rho_2 = 0} - \frac{\rho_2}{\rho_1}$$

$$\frac{Q_1(\rho_2=0) - Q_1}{Q_2} = \frac{\rho_2}{\rho_1}$$

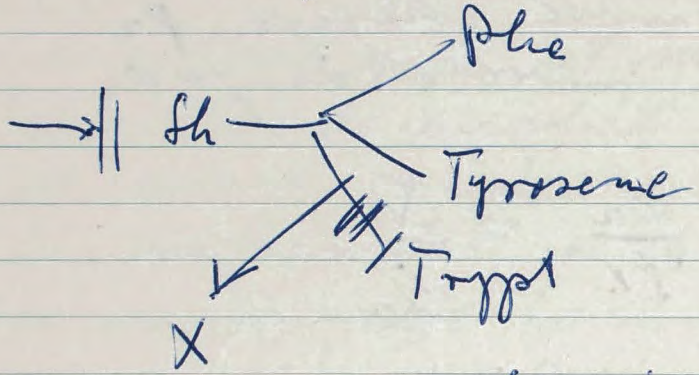


4.)



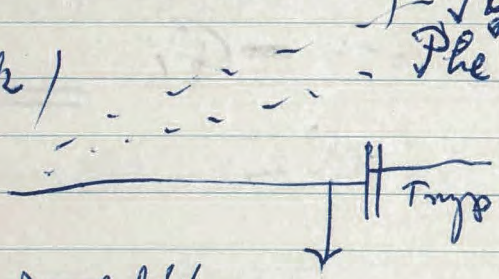
is antagonizing of Sh dependent all ~~Tro~~ levels of Tr, Ty and Phe ?

5.)



is antagonizing of X determined by Shikenwik level (and by ~~Tryptophane~~ Tryptophane Tyrosene and Phe - levels)

6.) (Mondek)

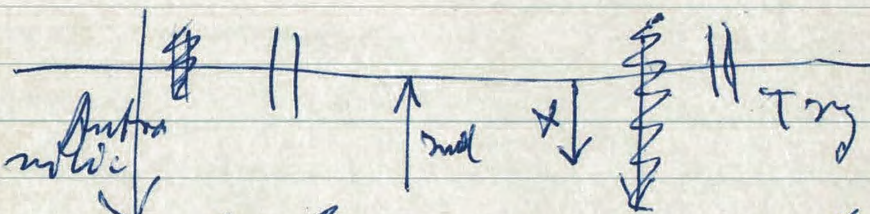


this mutation Tryptophane should have a rather high level of Phe and Ty

Metabolic

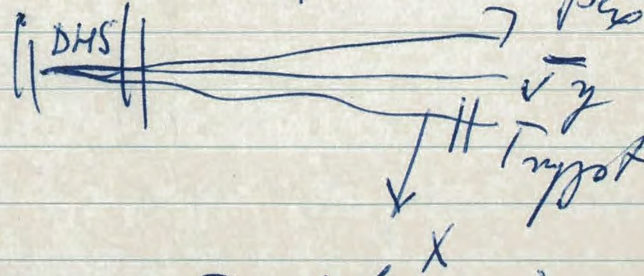
1.) Phe Tyd Chemostat
with B/1, τ ; at lowest values
it may be limited but
at high τ values it will the line
excess tryptophane. Where does it
pour out? If it does not pour out
try at τ = 4 hrs but does pour out of
try at τ = 8 hrs that would show
that it is tryptophane conc. rather
than growth rate that controls
pouring out of precursor. —

2.)



does tryptophane conc. control
outpouring of anthranilic acid. —

3.)



At try τ = 5 hrs is outpouring of
X the same with Tyrosine control
as with tryptophane control

applying this correction it seems
that there is no fall the first hour
then it falls

	0 hr	0.405
	1 hr.	0.394
	2 hr.	0.302
	3 hr	0.211
	4 hr	0.240

18 hypot. = 405
= 376
33 = 271

262 / 0.76 = 358

Thermostat 320
with phenyl alanine and tryptophane (and 500γ/l trypt)
sprinkled at 0 time also into growth tube

0 = 3 hr	0 hr	0.258
	½ hr	0.251
	1 hr	0.213
	2 hr	0.181
	2½ hr	0.106
	3 hr	0.083

345 / 405 =

Main trouble is that
during first hour [298]
junk comes out (abs. at 250)

Summary of post experiments

1.) Sudden increase of tryptophane with B/t start to see if passing out of precursor falls off instantaneously. —
Chemostat No 298 $\bar{\tau} = 3.5$ hrs
{500 µ/l tryptt. [0.149]
Chemostat No 320
tryptt. concentr. suddenly raised from 500 µ/l to 3000 µ/l.
Increase in pers t from 0.149 to 0.169 abs at 280 drops by less than 5% [or 18% from Chemostat sample with Anderson] but abs absorption at 250 rises instead of falling. —
{from 0.365 to 0.385. {
$\frac{-102}{0.263}$ to $\frac{-102}{.283}$
after ca 1 hour Increase rise and oxygen limitation can set in.

$\frac{y_2}{y_1} = \frac{250 \text{ Abs}}{280 \text{ Abs}} = 2.2$ for autolyses

$\frac{x_2}{x_1} = 0.5$ for precursor

$x_1 + y_1 = A_1 \ (280)$

$x_2 + y_2 = A_2 \ (250)$

$x_1 = \frac{2.2\,A_1 - A_2}{1.7}$

Summary of post exp.

2.) Chemostats 323, 324 1 mg/l tryptophane, running at 2 hrs and suddenly switched to 8 or 10 hours.

$\frac{\Delta \text{ at } 280}{\Delta \text{ at } 250}$ is about 2 whereas at $\bar{\tau} = 2$ ratio of [280]/[250] is less than 2.—

For evaluating we use $\Delta 280$ as amount of precursor poured out ~~a~~ 1 hour ~~or~~ or 1½ hour ~~after~~ in sample pushed out after changing $\bar{\tau}$ from 2 hrs to 8 or 10 hours at $\bar{\tau} = 2$ hrs precursor is apparently poured out at the rate of

$$X_1 = \frac{2.2\ 160 - 114}{1.7} = \frac{352 - 114}{1.7} = 140$$

352
114
238

$$\frac{X_1}{2}\ \frac{145}{216} = 0.047$$

Entropy of protein

If protein is formed from amino acids at conc. of 1 g/l [Mol weight 200] we have to compress from one molecule in 10^{-12} cc to one molecule in $(10^{-7})^3$ cc or we have $R \log 10^9 =$

$= R 9 \times 2.3 \simeq R\, 20.7$

or at $T = 300$ $ST \simeq 12000$ cal / Amino acid

Turnover number of chains

Protein molecules N in cubic cm

$N \frac{4 \text{ gram}}{6\,10^{23}} = \frac{1}{3} 10^{-12}$, $\frac{6}{3} \frac{10^{23-12}}{4\,10^4} = N$

$N = \frac{1}{2} 10^7$ / assuming 2000 sec = $\bar{t}$ and 1000 chains

turnover number is 2.5/sec

Synthesis of amino acids. —

assume concentrations of 1 g/l, Mol weight 200 200 Amino acids per enzyme, 10 steps per amino acid

(turnover number of enzyme 2)

how long does it take to synthesize enzyme

Theory of growth:

If case of all another acid molecule is $1/\ell$

To form protein each amino acid has to diffuse to the "hook" of the which is $R = 10^{-7}$ cm, assuming 1000 assembly lines each with 200 hooks, an average amino acid molekulus weight of 200.

$4\pi D \rho R = 4\pi 10^{-5} 10^{12} 10^{-7} = 12$ / sec

$1000 \frac{\text{chains}}{} \times 200 \frac{\text{hooks}}{} \times 2000 \frac{\text{seconds}}{} \; 12 \text{ per sec} \; \frac{200}{6\,10^{23}} \text{ gms}$

$= \frac{10 \cdot 10^{10}}{6 \cdot 10^{23}} = \frac{1}{6} 10^{-12}$ gm

which is almost right the value of $\frac{1}{3} 10^{-12}$ gm. [Taking for R $5 \cdot 10^{-8}$ and for conc $1/\ell$ we get rate higher by factor 15 i.e. $15 \cdot 10^{-12}$ gm.]

Assumption of 1000 assembly lines is very arbitrary × Should one have more than one assembly line for one enzyme? What about mutations, even a fraction of the enzyme produced be altered leaving the rest unaltered?

—

Fast Chemostat. —

When we grow in amino acid mixture we have $\tau = 30$ min
When we grow in minimal medium we have $\tau = 60$ min

How does bacterial density ρ depend on τ?

Let ρ_0 be density for which amino acids are supplied. Let us assume no energy is needed for making ρ_0 bacteria but $A(\rho - \rho_0)$ is needed to make $\rho > \rho_0$ bacteria — and energy supply per hour is $a\rho$/hour

Then for $30'' < \tau < 60''$ we have

$$\frac{d\rho}{dt} = \frac{a}{A}\rho + \frac{\rho_0}{\tau} - \frac{\rho}{\tau} = 0$$

$$\left(\frac{1}{\tau} - \frac{a}{A}\right)\rho = \frac{\rho_0}{\tau}$$

for $\tau = 30''$

$$\rho_{(30)} = \rho_0 \frac{1}{30''\left(\frac{1}{30''} - \frac{a}{A}\right)}$$

from diffusion consideration
~~XXX~~ conc = 1/1 ; $R = 5\,10^{-8}$

$4\pi D\rho R = 4\pi\, 10^{-5}\, 3\times10^{12}\times 5\,10^{-8}$

$12\times 15\,10^{-1} = 18.0$ per sec ~ 20/sec

~~XXX~~ $\times \frac{10\times 200}{20} = 100$ sec this is 20 times faster than necessary.

If each step requires ~~XX~~ one high energy phosphate bond each amino acid would cost ~~XXXX~~ 10^5 cal if ten steps needed & How many steps are needed

1 gm of sugar burned gives 4000 cal/gm or about 4000 ~~30~~ 30 = 120 000 cal/gm per gm Wt. Carbon

or about 10 to 12 high energy phosphate bonds.—

Heat of activation factor

$$e^{-\frac{E}{RT}} = Q_{10}^{-30} \text{ or more general}$$

$$= Q_{\Delta t}^{-\frac{T}{\Delta t}}$$

we can stand only

$$e^{-\frac{E}{RT}} = \frac{1}{20}\,;\quad \frac{1}{20} = Q_{10}^{-30} \text{ or}$$

$$20 = Q_{10}^{30} \text{ or } Q_{10} = 20^{\frac{1}{30}}$$

Metabolic ; is there adaptation? — "Evocation"

Arginine – hypoxanthine system
we grow in <u>second</u> growth
tube at phagostat B/18 ; first
feeder has arginine of 1.2
light equivalent. Both
feeders have 500γ/l hypoxanthine
Work at 2 hrs = $\bar{\tau}$. Change from
first feeder to second feeder
see if bacterial density
falls before it rises ~~to~~
again. — (do it with [illegible]!)
(Schweigert – [illegible])

Denaturing of enzymes

a) very long $\bar{\tau}$ → , lactate ltd chemostat
does viable count and density fall

b) in complete medium + ~~lactate~~ ltd
chemostat ~~compose~~ bacterial titer at 250 and
370

$\rho_{60} = \infty$ or $\frac{a}{A} = \frac{1}{\text{"}60\text{"}}$ 4

$\rho = \frac{\rho_0}{\tau} \quad \frac{1}{\frac{1}{\tau} - \frac{1}{60}}$

$\rho_0 = \rho(30)\ 30 \times \left(\frac{1}{30} - \frac{1}{60}\right)$

or

$\rho = \frac{\rho(30) \times 30 \left(\frac{1}{30} - \frac{1}{60}\right)}{\tau}$

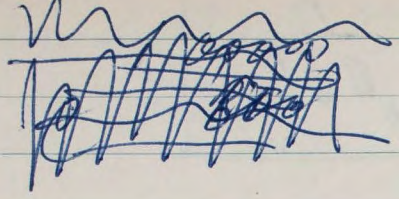
$30 \left(\frac{1}{30} - \frac{1}{60}\right) \rho_{30} = \frac{\rho_0}{30}$

$\rho = \rho_{30} \left(\frac{1}{30} - \frac{1}{60}\right) \frac{30}{\tau} \quad \frac{1}{\frac{1}{\tau} - \frac{1}{60}}$

$\rho = \rho_{30} \left(\frac{1}{30} - \frac{1}{60}\right) \frac{1}{\frac{1}{\tau} - \frac{1}{60}} \frac{30}{\tau}$

$\rho = \frac{\rho_{30}(60-30)}{60-\tau}$ * O.K.

that formula



$e^{\frac{\varepsilon}{RT}}$ $\quad \frac{15{,}000}{600}$

$\frac{e^{\frac{\varepsilon}{RT_1}}}{e^{\frac{\varepsilon}{RT_2}}} = e^{\frac{\varepsilon}{RT_1} - \frac{\varepsilon}{RT_2}}$

$e^{\frac{\varepsilon(T_2 - T_1)}{RT^2}} = e^{\frac{\varepsilon \Delta T}{15{,}000}}$

Example $a = 1 \quad b = 1.5$

$T_{max} = T_0 - \frac{\ln b/a}{b-a} \approx$

$= T_0 - 20 \ln b/a$

$\ln Q_{10}^*$

$10 \ln \ln Q_{10}$

$T_{max} - T_0 \approx$

$T_0 - T_{max} = \frac{\ln b/a}{b-a} = \frac{}{\ln Q_{10}^* - \ln Q_{10}}$

$e^{\frac{\varepsilon_1 \Delta T}{18{,}000}} = 10$

$\frac{\varepsilon}{e^{18{,}000}} = Q_{10} \Big| \frac{\varepsilon}{18{,}000} = \ln Q_{10}$

$a = \frac{1}{10} \ln Q_{10}$

Saturating in bacteria.

Theory $\frac{dx}{dt} = A(T, c)x - B(T)x$

$c = \infty$ $\qquad \alpha = A - B = \frac{1}{x}\frac{dx}{dt}$

$A = A_0 e^{aT}$

$B = B_0 e^{bT}$ $\qquad \alpha = A_0 e^{aT} - B_0 e^{bT}$

$v = \frac{d\alpha}{dt}_{max} = A_0 a e^{aT} - B_0 b e^{bT}$

$A_0 a e^{aT} = B_0 b e^{bT}$

$\frac{A_0 a}{B_0 b} = e^{(b-a)T}$

$T_{max} = \frac{1}{b-a}\left[\ln\frac{A_0}{B_0} + \ln a - \ln b\right]$

T_0

It stops growing at

$A_0 e^{\alpha t} = B_0 e^{\beta t}$

$\frac{1}{b-a}\ln\frac{A_0}{B_0} = T_0$

$T_{max} = T_0 + \frac{\ln a - \ln b}{b-a}$

If α rises by

factor e for $\Delta T = 10^0$ C

then $a \times 10 = 1$ $\quad a = \frac{1}{10}$

If we grow in growth tube at a low c value

$$\frac{1}{x}\frac{dx}{dt} = \alpha = A - B$$

A should be proportionate to c as long below 1/10 of . At some low c value $A - B = 0$ should be reached and if we know c we could compute B. In the Chemostat however c is not predetermined but rather α is predetermined. So the only thing we could expect to see in chemostat is a statistical phenomenon: If there are only a few enzyme molecules of a certain kind and if all remaining the bacterium is dead and the whole count should fall even though individuality does not fall since all important admitted loses in form of proteins. — But is conc. c really higher in Chemostats for large τ than it should be $(\frac{\tau_0}{\tau})$ (assuming no death)?

In our formulae x denotes amount of same enzyme which is present in growth rate determining quantity. If we have low c the growthrate is for $\tau = \tau_0$ determined

$$T_0 - T_{max} = \frac{q_n \ln b/a}{b-a} = \frac{4}{}$$

$$T_0 - T_{max} = \frac{10 \ln \frac{\ln Q_{10}^*}{\ln Q_{10}}}{\ln \frac{Q_{10}^*}{Q_{10}}}$$

$$T_0 - T_{max} = \frac{18000}{\varepsilon_2 - \varepsilon_1} \ln \frac{\varepsilon_2}{\varepsilon_1}$$

$$\approx \frac{18{,}000}{\varepsilon_2 - \varepsilon_1} \ln\left\{1 + \frac{\varepsilon_2 - \varepsilon_1}{\varepsilon_1}\right\}$$

$$\sim \frac{18{,}000}{\varepsilon_1} \approx 10^\circ C$$

---

assuming a solution out of denatured enzyme what fraction is denatured?

$$\frac{dx}{dt} = Ax - Bx$$

$$\frac{dy}{dt} = +Bx$$

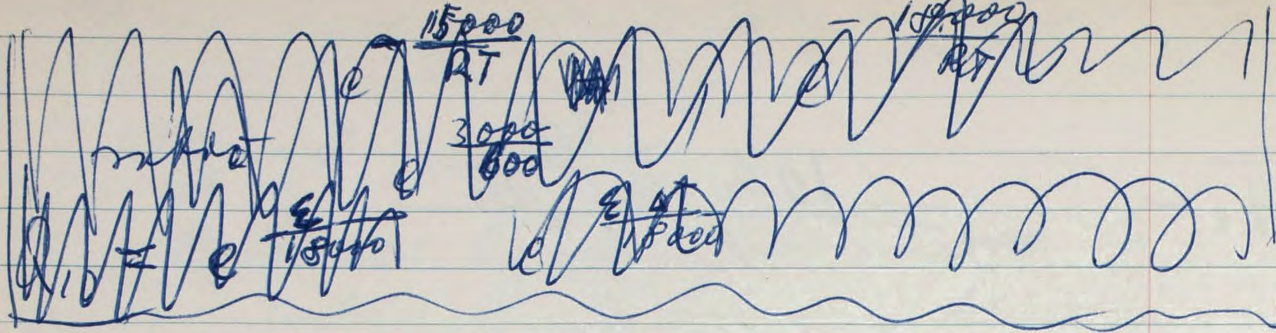
$$0 = \frac{d}{dt}\left(\frac{x}{y}\right) \quad \frac{v}{v}$$

$$- \frac{x \frac{dy}{dt}}{y^2} + \frac{\frac{dx}{dt}}{y}$$

$$x \frac{dy}{dt} = y \frac{dx}{dt}$$

$$xBx = y[Ax - Bx]$$

$$\frac{x}{y} = \frac{A-B}{B}$$



Remark to exp. 296/297

at a given T say 12 hours nitrogen curve c must be ~~the same~~ in two exp (1 and 2) proportionate to precursor level y. So

34 – Bact – $a y_1 = b y_1$
#26 – Bact – $a y_2 = b y_2$

8 mgm/l $= (b-a)[y_1 - y_2]$

Also at 10 hrs precursor at 0.075 || A | $\frac{CA}{CB} = 0.75$
5 hrs " at 0.1 || B |

~~Max~~ c_1 × Precursor$_1$ = c_2 × Precursor$_2$

$0.25 c_1$ = A Precursor$_2$ – A Precursor 1

$$\frac{c_1}{4} = \frac{1}{4}\ \frac{25}{60}\ 20\ \text{mgm}/l\ NH_4Cl$$

$c_1 = 9$ mgm

$c_2 = 6.7$ mgm

an upper curve $c_3 = 1.6 \times 6.7 = 10.7$ mgm/l

$c_3 - c_2 = 4$ mgm

$8 - 4 = 4$ mgm of NH_4Cl

should give 14.5 mgm of Trypt
and this give 0.44 absorption rise T=10

by c and not by enzyme X
It might be that we have

$$\frac{dx}{dt} = F\, cX - BX$$

when X and c are both low
then c is no longer proportional
to $1/\tau$ but

$$\frac{1}{\tau} = Fc - B$$

or $\left(\frac{1}{\tau} + B\right)\frac{1}{F} = c$

going to $\frac{B}{F}$ for $\tau = \infty$.

Can this be tested? requiring hypophosphate for instance

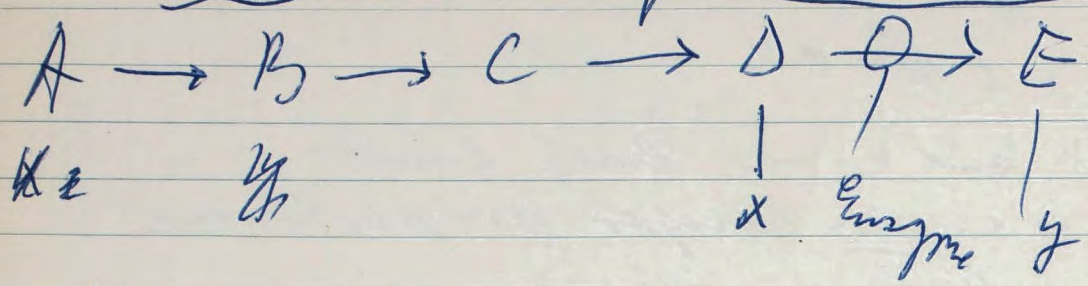
Yes if two strains compete at high τ strain which has lower ~~[illegible]~~ optimum temperature should loose out!

If lower temp strain is bulk of the population to begin with, it will set a comparatively high c at high τ and high temp strain will rise even though at low τ the reverse may hold. —

this experiments could be done with Nitrogen limitations at a Temp where at low τ ~~[illegible]~~, ~~[illegible]~~ they hold a " balance " ?

Jan 52

Trivial regulation



free enzyme molec: b

occupied by y : a

when it is adsorbed to free molec goes to y instantly. —

y evaporates at rate of const. a

$$\frac{dc}{dt} = \text{const}\, a - c_1 x b - c_2 y b$$

$$b = \frac{1}{1 + \frac{c_1 x + c_2 y}{\text{const}}}$$

rate of reaction:

$$c_1 x b = \frac{c_1 x}{1 + \frac{c_1 x + c_2 y}{\text{const}}}$$

If most molec occupied:

$$c_1 x b \approx \text{const}\, \frac{c_1 x}{c_1 x + c_2 y}$$

Observed value is 0.45 . O.K. H

That C_1 should be so high
8 mgm/l NH_4Cl is however rather
surprising

Remark about B/t mutants

only 1 B/t out of 6 examined
proved aut X. — assuming that
all mutants can same locus
affecting same enzyme could
it be that in most mutants
enzyme is non functional
whereas in B/t (X) it disfunc-
tions so that it makes the
wrong compound which has
little affinity to enzyme
and runs out not being
able to regulate. —

$$\text{rate} = \frac{c_1 X}{1 + \underbrace{c_1 X + c_2 y}_{\text{Const}}}$$

$$\frac{\text{rate}}{\lambda'} = \frac{c_1 \lambda_x X}{1 + \underbrace{c_1 \lambda_x X + c_2 \lambda_y y}_{\text{Const}}}$$

$$\lambda' = \frac{\left(1 + \underbrace{c_1 \lambda_x X + c_2 \lambda_y y}_{\text{Const}}\right)}{\lambda_x \left[1 + \underbrace{c_1 X + c_2 X}_{\text{Const}}\right]}$$

$$\lambda' = \frac{\text{Const} + \lambda_x c_1 X + \lambda_y c_2 y}{\lambda_x [\text{Const} + c_1 X + c_2 y]}$$

$$\frac{c_1 x + c_2 y}{\text{Const}} = \text{Const}\left(\frac{c_1 X}{\text{rate}} - 1\right)$$

$$y = \frac{1}{c_2}\left\{\frac{\text{Const}\, c_1 X}{\text{rate}} - \text{Const} - c_1 X\right\}$$

$$\frac{y}{X} = \frac{1}{c_2}\left\{\frac{\text{Const}\, c_1}{\text{rate}} - \frac{\text{Const}}{c_2 X} - c_1/c_2\right\}$$

Theory of regulation [difficulty]

Intermediates X_1, X_2, X_3 etc

cure. X_1 X_2 X_3 etc.

rate of reaction for production of X_i is $f_i(X_{i-1}; X_i)$

1.) assumption X_{i-1} increases with X_i and for X_{i-1} = const.

rate falls by factor $\lambda_i' \leq \lambda_i$ if X_i increases with factor λ_i

X_0 = const and are increase concentration of X_n

we have (as before $f_1 = f_2 = f_3 =$)

$$\frac{f_1'}{\lambda_1'} = \frac{f_2'}{\lambda_2'} = \frac{f_3'}{\lambda_3'}$$

X_{i-1} (X_i) rises by $\lambda_i > \lambda'$

$$\text{rate} = c_1 X_6 = \frac{c_1 X_0}{1 + c_1 X_0 + c_2 y_0}$$

$$\frac{\text{rate}}{\lambda'} = \frac{c_1 \lambda X_0}{1 + c_1 X_0 + c_2 y^*}$$

const const

Penicillin · Polysaccharides
Sucrose + Dextran
Lucanobac · mesinteroides · —
Fermentation products
Starch and Dextrose Industries
Commercial Solvents, Terre Haute,
make of. —
Pharmacia — Sweden

$$\frac{dB}{dA} = k_1 A - l_2 B - k_2 B + l_3 C$$

($k_2 B$ → rate)

$$\frac{dC}{dt} = k_2 B - l_3 C$$

rate

or $k_2 B =$ rate $+ l_3 C$

or $k_1 A - l_2 B -$ rate $= 0$

$$k_1 A = l_2 B + \text{rate}$$

$$k_1 = \frac{l_2 B}{A} + \frac{\text{rate}}{A}$$

$$\frac{k_1}{l_2} - \frac{\text{rate}_1}{l_2 A} = \frac{B_1}{A_1}$$

$$\frac{\frac{k_1}{l_2} - \frac{\text{rate}_1}{l_2 A}}{\frac{k_1}{l_2} - \frac{\text{rate}_2}{l_2 A}} = \frac{B_1}{B_2}$$

rate $= k_1 x - l_2 y$

$2, B_1$

$2 - \frac{\text{rate}}{l_2 A} = 1$

1

$$c_1 x \; b = \text{rate} = \frac{c_1 x}{1 + \frac{c_1 x + c_2 y}{\text{Const}}}$$

$$\frac{1}{\text{rate}} = \frac{1 + \frac{c_1 x + c_2 y}{\text{Const}}}{c_1 x}$$

$$\frac{c_1}{\text{rate}} = \frac{1}{x} + \frac{c_1}{\text{Const}} + \frac{c_2 y/x}{\text{Const}}$$

$$\frac{\text{Const}\; c_1/c_2}{\text{rate}} = \frac{\text{Const}}{c_2 x} + c_1/c_2 + y/x$$

$$y/x = \frac{\text{Const.}\; c_1/c_2}{\text{rate}} - \frac{\text{Const}}{c_2 x} - c_1/c_2$$

W. 2. B.W.

Is this generally true?

$A \rightarrow B \xrightarrow{\text{rate}} C$

~~$\frac{dB}{dt} = k_1 A - \text{rate}$~~

~~$\frac{dB}{dt} = k_2 B$~~

$B \rightarrow$

X_n $\frac{dA}{dt} = 0$

~~$\frac{dB}{dt} = k_1 A - k_2 B - B$~~

~~$0 = k_1 A - k_2 B - \text{rate}$~~

~~$\text{rate} = k_1 A - k_2 B$~~

~~B~~

In Chemical Transformation

$$\frac{dy}{dt} = \frac{w}{V} y + B x$$

$$\frac{dx}{dt} = \left(\frac{\alpha_0 - B}{\tau_{final}}\right) x - \frac{w}{V} x$$

$$= \left(\alpha_0 - \frac{1}{\tau}\right) x$$

$$\tau_{final}$$

$$\sigma = x + y$$

$$\frac{d\sigma}{dt} = -\frac{w}{V}(x + y) + A_0 x$$

$$\frac{1}{\sigma}\frac{d\sigma}{dt} = -\frac{1}{\tau} + A_0 \frac{x}{x+y} =$$

$$= \left(\alpha + B\right) \frac{x}{x+y} - \frac{1}{\tau}$$

$$\frac{1}{\sigma}\frac{d\sigma}{dt} = \left(\alpha + B\right) \frac{x/y}{x/y + 1} - \frac{1}{\tau}$$

$$= \left(\alpha + B\right) \frac{1}{1 + \tau_{fin} B} - \frac{1}{\tau}$$

or for $\frac{1}{\sigma}\frac{d\sigma}{dt} = 0$

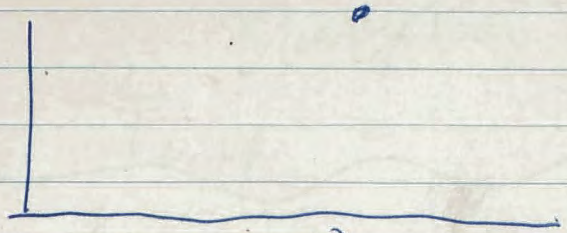
$\tau = \tau_{instt}$

$$\frac{1}{\tau_{instt}} = \frac{\alpha + B}{1 + \tau_{fin} B}$$

$$\tau_{instt} = \frac{1 + \tau_{fin} B}{\alpha + B}$$

Denaturing Exp

Can be computed from "initial" slope



$$-\frac{dx}{dt} = A^{(i)} x_A - B x$$

$$\frac{dy}{dt} = B x$$

$$\frac{1}{\tau} = A(\tau) x_A - B x_A$$

$$\frac{1}{\tau_{min}} = A_0 x_A - B x_A$$

$$\frac{1}{\tau} - \frac{1}{\tau_{min}} = A\tau - A_0$$

$$\frac{x}{y} = \frac{A_0 - \left(\frac{1}{\tau_{min}} - \frac{1}{\tau}\right) - B}{B}$$

$$\frac{\dot{x}}{y} = \frac{A - B}{B}$$

(in steady-state:)

$$A_0 - \frac{1}{\tau_{min}} - B = 0$$

$$\boxed{\frac{x}{y} = \frac{1}{\tau B}}$$

Yale

annual Rev of

Plant ~~ecological~~ Reviews

Biochemistry

Best test for theory is determine rate of fall of the number to short time τ as a function of how long we stay at τ_2. —

If the very time spent at τ_2 then — rate

$$\frac{dx}{dt} = A(\tau_2)x - Bx = \left(\frac{1}{\tau_2} - \frac{1}{\tau_{min}} + \alpha\right)x$$

$$A(\tau) \qquad \frac{1}{\tau_2} - \frac{1}{\tau_{min}} + A_0$$

$$\beta = \left[\alpha - \left(\frac{1}{\tau_{min}} - \frac{1}{\tau_2}\right)\right]t$$

$$B = \frac{1}{\tau_2}$$

$$x = x_0 e^{\beta t}$$

$$y = \frac{Bx_0}{\beta}\left[e^{\beta t} - 1\right] + y_0$$

$$\frac{x}{y} = \frac{e^{t/\tau_2}}{\frac{y_0}{x_0} + \tau B\left[e^{t/\tau_2} - 1\right]} =$$

$$\frac{x}{y} = \frac{e^{t/\tau_2}}{\frac{y_0}{x_0} + \tau_2 B\left[e^{t/\tau_2} - 1\right]}$$

for instance

for $\alpha = 2B$

$\alpha = B^* = \frac{1}{\tau_0}$

$$\tau_{cntp} = \frac{\frac{\tau_{final}}{\tau_0} + 1}{2} \tau_0$$

$$T_{cntp} = 3\tfrac{1}{2}\,\tau_0$$

Question how long does it take to reach a growth rate $\frac{1}{\tau^*}$ if we dump from a chemostat which runs at τ_2 into a flask.

τ_0 is minimum generation time answer see for flask

$$\frac{\tau^* - \tau_0}{\tau_0} = \frac{(\tau_2 B - \tau_0)\, e^{-t/\tau_0}}{\tau_0 + 1}$$

about 3 hours [$B = 1/\text{hr}$; $\tau_0 = 1$ hour

$\tau_2 = 6$ hrs]

gives $\frac{\tau^* - \tau_0}{\tau_0} \approx \frac{1}{10}$

$$\frac{1+t/\tau_2}{1+\frac{(1+\tau_2 B)\,t/\tau_2}{1+\frac{y_0}{x_0}}} \cdot \frac{1}{1+\frac{y_0}{x_0}}$$

$$\frac{1}{1+\frac{y_0}{x_0}} \times \left\{1+\frac{t}{\tau_2}\left(1-\frac{1+\tau_2 B}{1+\frac{y_0}{x_0}}\right)\right\}$$

$$\frac{1+\frac{y_0}{x_0}-\tau_2 B}{1+\frac{y_0}{x_0}} = \frac{\frac{y_0}{x_0}-\tau_2 B}{1+\frac{y_0}{x_0}}$$

$$= \frac{1}{1+\frac{x_0}{y_0}} - \frac{\tau_2 B}{1+\frac{y_0}{x_0}}$$

$$\frac{1}{1+\frac{y}{x}} \simeq \frac{1}{1+\frac{y_0}{x_0}} \left\{1+\frac{t}{\tau_2}\left(\frac{1}{1+\frac{x_0}{y_0}} - \frac{\tau_2 B}{1+\frac{y_0}{x_0}}\right)\right\}$$

$$\frac{L}{\sigma}\frac{d\sigma}{dt} = (\alpha_0 + B)\,\frac{x_0/y_0}{1+x_0/y_0}\left\{1+\frac{t}{\tau_2}\left(\frac{1}{1+\frac{x_0}{y_0}} - \frac{\tau_2 B}{1+y_0/x_0}\right)\right\}$$

for small t/τ_2

$$\frac{\frac{x}{y}}{\frac{x}{y}+1} = \frac{1}{1+\frac{y}{x}}$$

$$\approx \frac{1}{1+\frac{y_0}{x_0}+\tau_2 B\left(e^{t/\tau_2}-1\right)}{e^{t/\tau_2}}$$

$$\boxed{\frac{\frac{x}{y}}{\frac{x}{y}+1} = \frac{e^{t/\tau_2}}{e^{t/\tau_2}+\tau_2 B\left(e^{t/\tau_2}-1\right)+\frac{y_0}{x_0}}}$$

or for small t/τ_2

$$\approx \frac{1+t/\tau_2}{1+t/\tau_2+\tau_2 B\, t/\tau_2+\frac{y_0}{x_0}}$$

$$\approx \frac{\tau_2+t}{\tau_2+t+B\,t\,\tau_2+\tau_2\frac{x_0}{y_0}}$$

$$\approx \frac{\tau_2+t}{\tau_2+t+(B\tau_2)t}$$

$$\boxed{\frac{1}{\alpha}\frac{dy}{dt} = (\alpha+\beta)\frac{1}{1+y/x}}$$

$$\approx \frac{1+t/\tau_2}{1+\frac{y_0}{x_0}+(1+\tau_2 B)\frac{t}{\tau_2}}$$

for $t = \infty$

$$\frac{\frac{x}{y}}{1+\frac{x}{y}} = \frac{1}{1+\tau_2 B}$$

~~for instance~~ for instance

for instance drawing first lamp turns off $\tau_1 = 2$ hrs

$\frac{x/y}{1+x/y}$ for $\tau = 2$ hrs is $\frac{1}{1+\tau B} = \frac{1}{1+2'' B} = \frac{1}{1+\tau_1 B}$ $\quad \tau_1 = 2$

If we now switch to $\tau_2 = \infty$ hours for some t and then switch back to some τ hours (or t hours) we have:

$$\frac{1}{\sigma}\frac{d\sigma}{dt}_{\text{initial}} + \frac{1}{\tau} = (\alpha + \beta)\frac{1}{1+2''B}$$

initial rate of fall

$$\times \frac{1}{e^{-t/\tau_2} + \frac{(1+\tau_2 B)(1-e^{-t/\tau_2})}{1+2''B}}$$

$$= (\alpha + \beta)\frac{1}{1+\tau_2 B}$$

for $t/\tau = \infty$ and for $e^{-t/\tau_2} = 1/2$

$$= (\alpha+\beta)\frac{1}{1+\tau_1 B}\frac{1}{1/2 + 1/2\frac{1+\tau_2 B}{1+\tau_1 B}}$$

$$= (\alpha+\beta)\frac{1+\tau_1 B}{1+\tau_1 B + 1+\tau_2 B}$$

$$\frac{\frac{x}{y}}{1+\frac{x}{y}} = \frac{e^{t/\tau_2}}{e^{t/\tau_2} - 1 + \tau_2 B e^{t/\tau_2} - \tau_2 B + 1 + \frac{y_0}{x_0}}$$

$$= \frac{1}{1+\frac{y_0}{x_0}} \frac{1}{\frac{e^{t/\tau_2} - 1 + \tau_2 B e^{t/\tau_2} - \tau_2 B}{1+\frac{y_0}{x_0}} + 1}$$

$$= \frac{1}{1+\frac{y_0}{x_0}} \frac{1}{e^{-t/\tau_2} + \frac{1 - e^{-t/\tau_2} + \tau_2 B - \tau_2 B e^{-t/\tau_2}}{1+\frac{y_0}{x_0}}}$$

$$= \frac{1}{1+\frac{y_0}{x_0}} \frac{1}{e^{-t/\tau_2} + \frac{1 - e^{-t/\tau_2} + \tau_2 B (1 - e^{-t/\tau_2})}{1 + y_0/x_0}}$$

$$= \frac{1}{1+\frac{y_0}{x_0}} \frac{1}{e^{-t/\tau_2} + \frac{(1+\tau_2 B)(1 - e^{-t/\tau_2})}{1 + y_0/x_0}}$$

or first approx. for small t/τ_2

$$\approx \frac{1}{1+\frac{y_0}{x_0}} \left\{ 1 - \frac{1+\tau_2 B}{1 + y_0/x_0} \, t/\tau_2 \right\}$$

Metabolic

Arginine synthesis may be a function of arg. concentration

Experiment: A Chemostat with B/t (which can make arginine) and a concentration of arginine such that the fraction of arginine contained in the B/t which comes from the outside is $X \cdot (1-X)$ is synthesized by the bacteria. We measure the concentration c of arginine in the outside (in the growth tube of the Chemostat) by matching how fast an arginineless strain present grows [$\alpha = f(c)$]

We then may write

$$\frac{X}{c} = \beta(c - i)$$ where i is the arg. conc inside the bacteriums

P. T. O.

~~In fact those~~

$$= (\alpha + \beta) \frac{1}{\frac{1+\tau_1 B + 1+\tau_2 B}{2}}$$

~~or death after~~ or growth rate

~~a after with the~~ after this time

$(e^{+t/\tau_2} = 1/2)$ at which τ_2 is ~~the~~

~~arithmetic~~ such that the

corresponding generation

time is arithmetic mean

between τ_1 and τ_2

$$\frac{X_1}{X_2} = \frac{c_{1m} - i_{1m}}{c_2 - i_2} = \frac{c_1/i_1 - 1}{\frac{c_2}{i_1} - \frac{i_2}{i_1}}$$

$$\frac{i_2}{i_1} = \frac{c_2}{c_1}\frac{c_1}{i_1} - \frac{X_2}{X_1}\left(\frac{c_1}{i_1} - 1\right)$$

$$\frac{i_2}{i_1} < \frac{c_2}{c_1}\frac{c_1}{i_1}$$

for small X_2 and large X_1

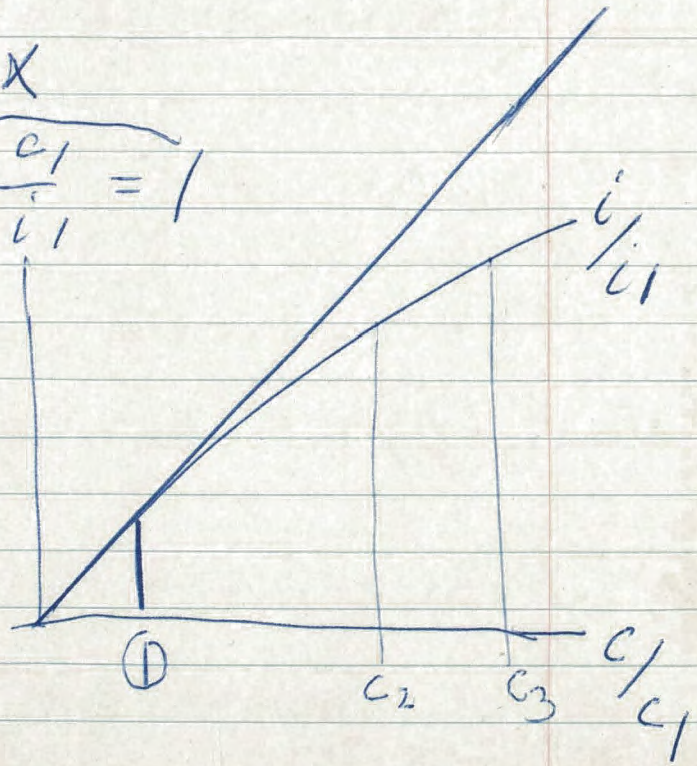
$$\frac{c_1}{i_1} = 1$$

$$\frac{i_2}{i_1} < \frac{c_2}{c_1}$$

$$\frac{i_3}{i_1} < \frac{c_3}{c_1}$$

by analogy:

$$\frac{i_3}{i_2} < \frac{c_3}{c_2}$$



We then have:

$$x_1 = \tau\beta(c_1 - i_1)$$

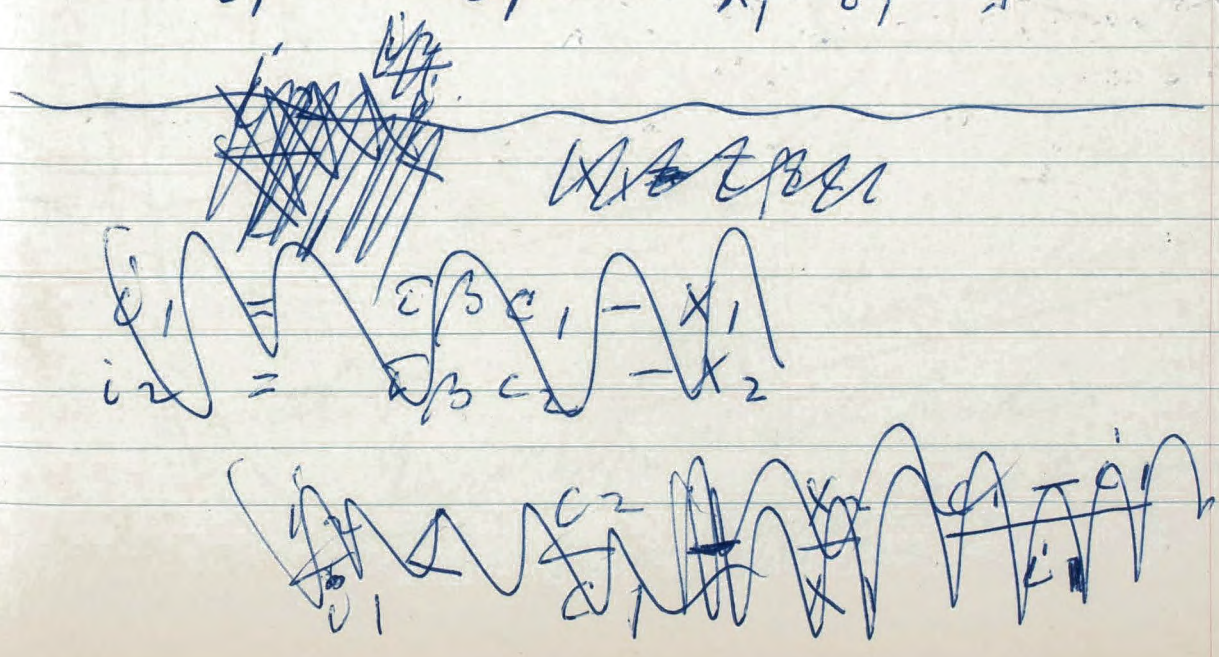
$$x_2 = \tau\beta(c_2 - i_2)$$

$$\frac{x_1}{x_2} = \frac{c_1 - i_1}{c_2 - i_2} = \frac{\frac{c_1}{i_1} - 1}{\frac{c_2}{i_1} - \frac{i_2}{i_1}}$$

$$\frac{x_1}{x_2}\left(\frac{c_2}{i_1} - \frac{i_2}{i_1}\right) = \frac{c_1}{i_1} - 1$$

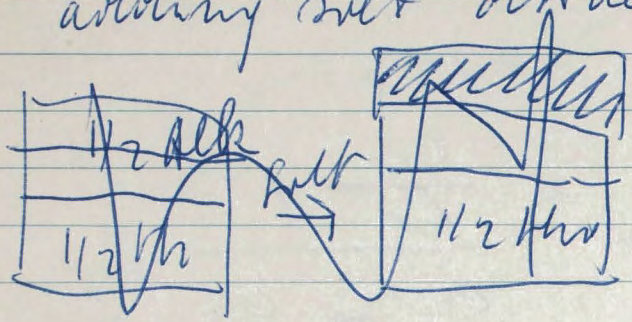
$$\frac{x_1}{x_2}\frac{i_2}{i_1} = \frac{x_1}{x_2}\frac{c_2}{i_1} - \left[\frac{c_1}{i_1} - 1\right]$$

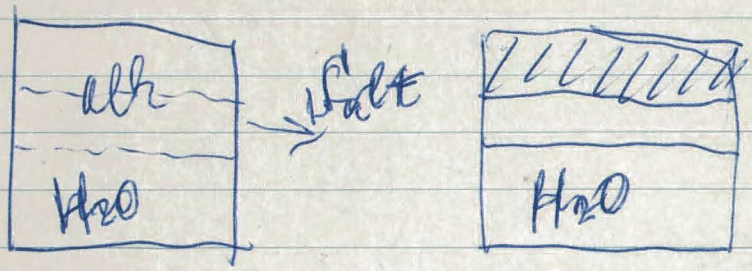
$$\frac{i_2}{i_1} = \frac{c_2}{i_1} - \frac{x_2}{x_1}\left[\frac{c_1}{i_1} - 1\right]$$



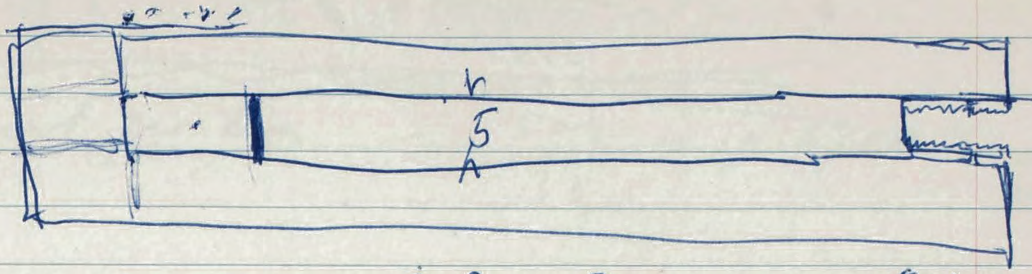
Assume

adding salt dissolves 1/2 of alcohol





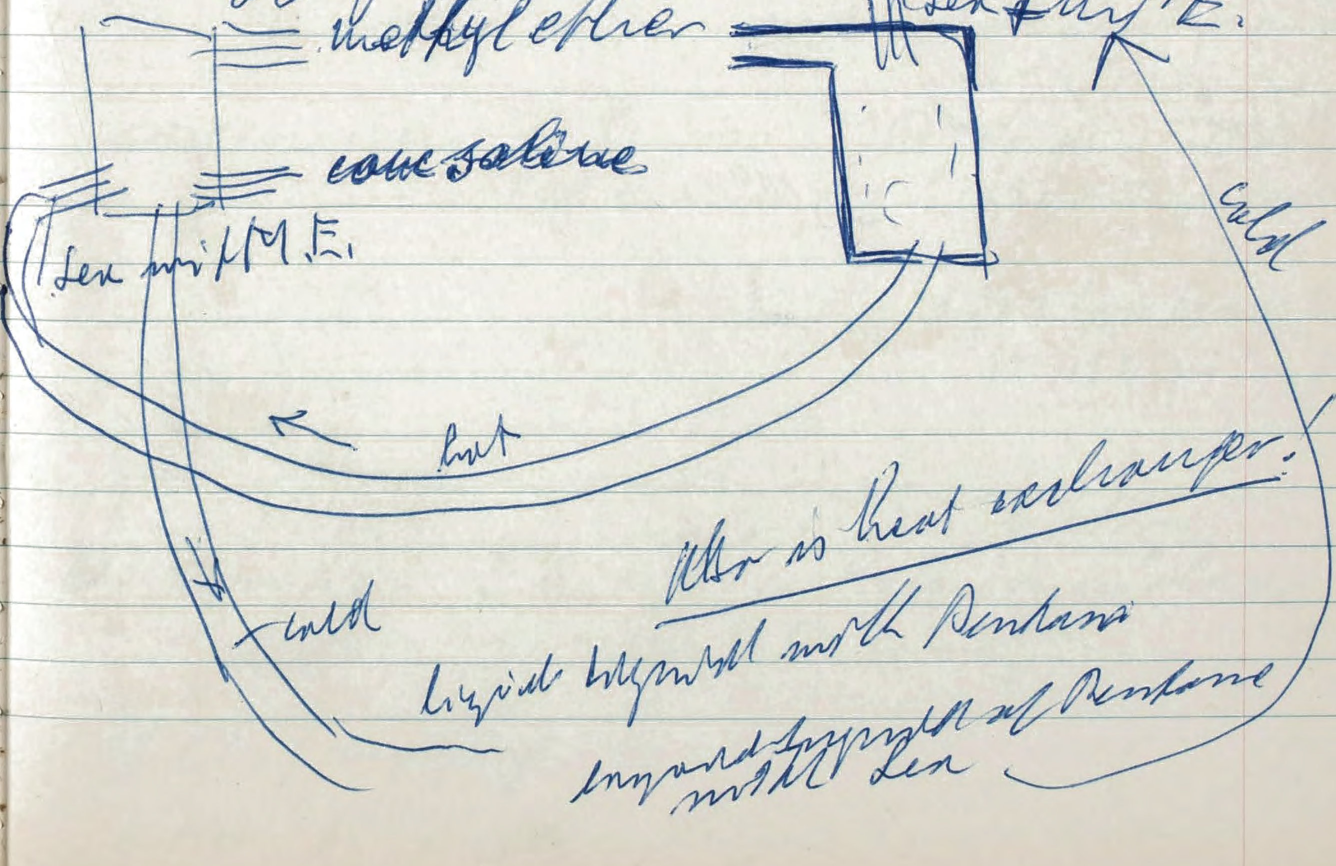
„Frozen" Sperm



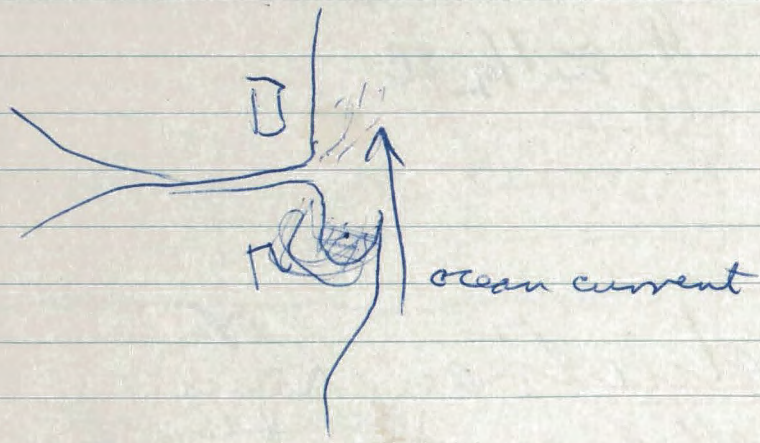
$0.2\,cm^2 \times 20 = 4\,cm^3$

$\frac{4}{10} \approx 1/2$ cc

Energy production (Hum)



breeze maker!



$15/ton 1500

+3,000

Sea water purification

Evaporate $5 a ton for crude salt

50 cent per ton or $\frac{50¢}{30}$ = 1.7 cent/ton of water

~~2000~~

25 kg 10 km³ 10,000 kg

Upgrade 1 cent per KWh

$100 acre foot / per

an acre of solar still ~~[illegible]~~ yields 4-6 acre feet /yr
4000 sq m. under ~~[illegible]~~ steady winds

an acre costs ~ $10,000 @ 10%/yr $1000/yr cost
cost of water is $167-250 per acre ft.

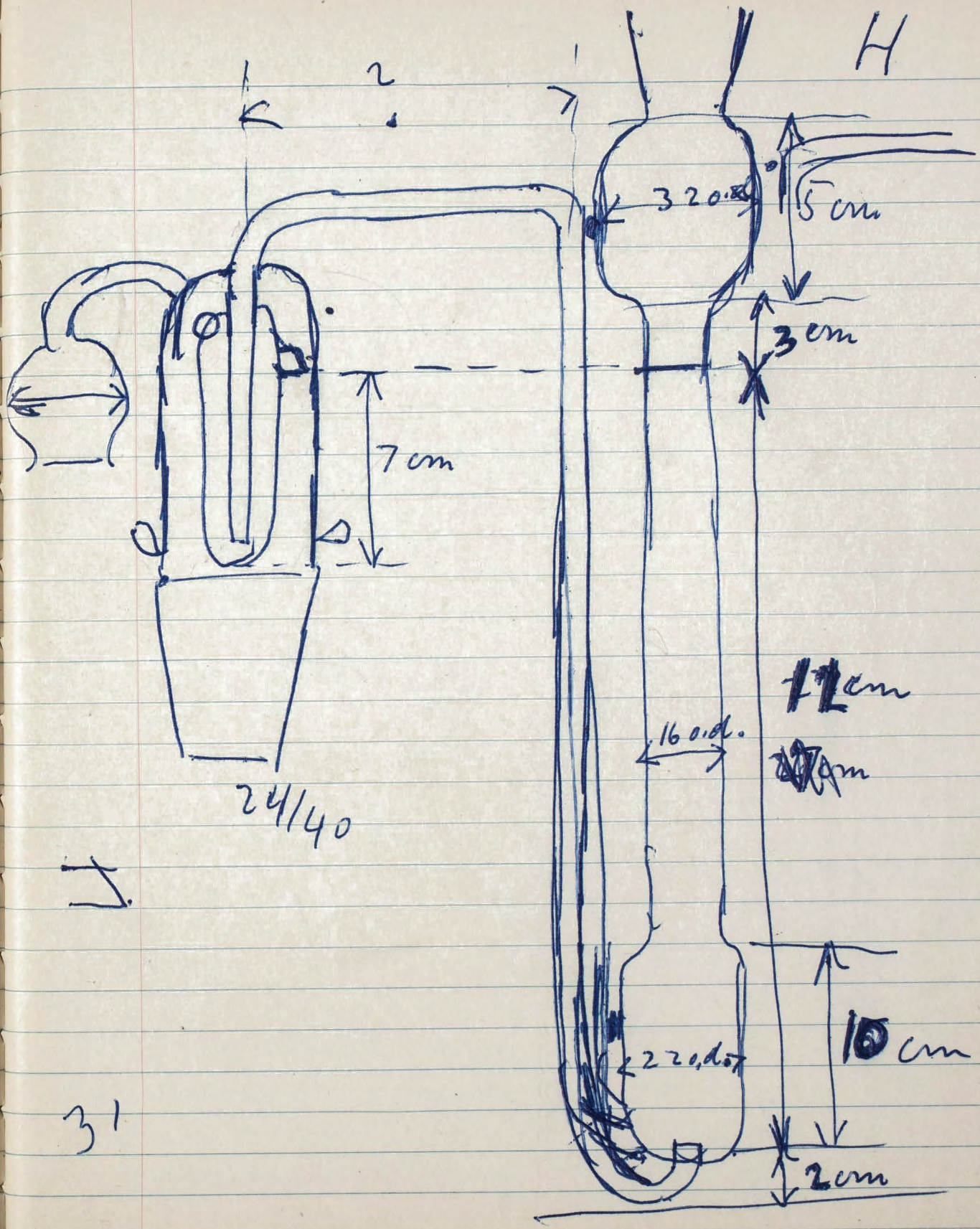
1300 tons/acre ft

12-19¢ per ton of water

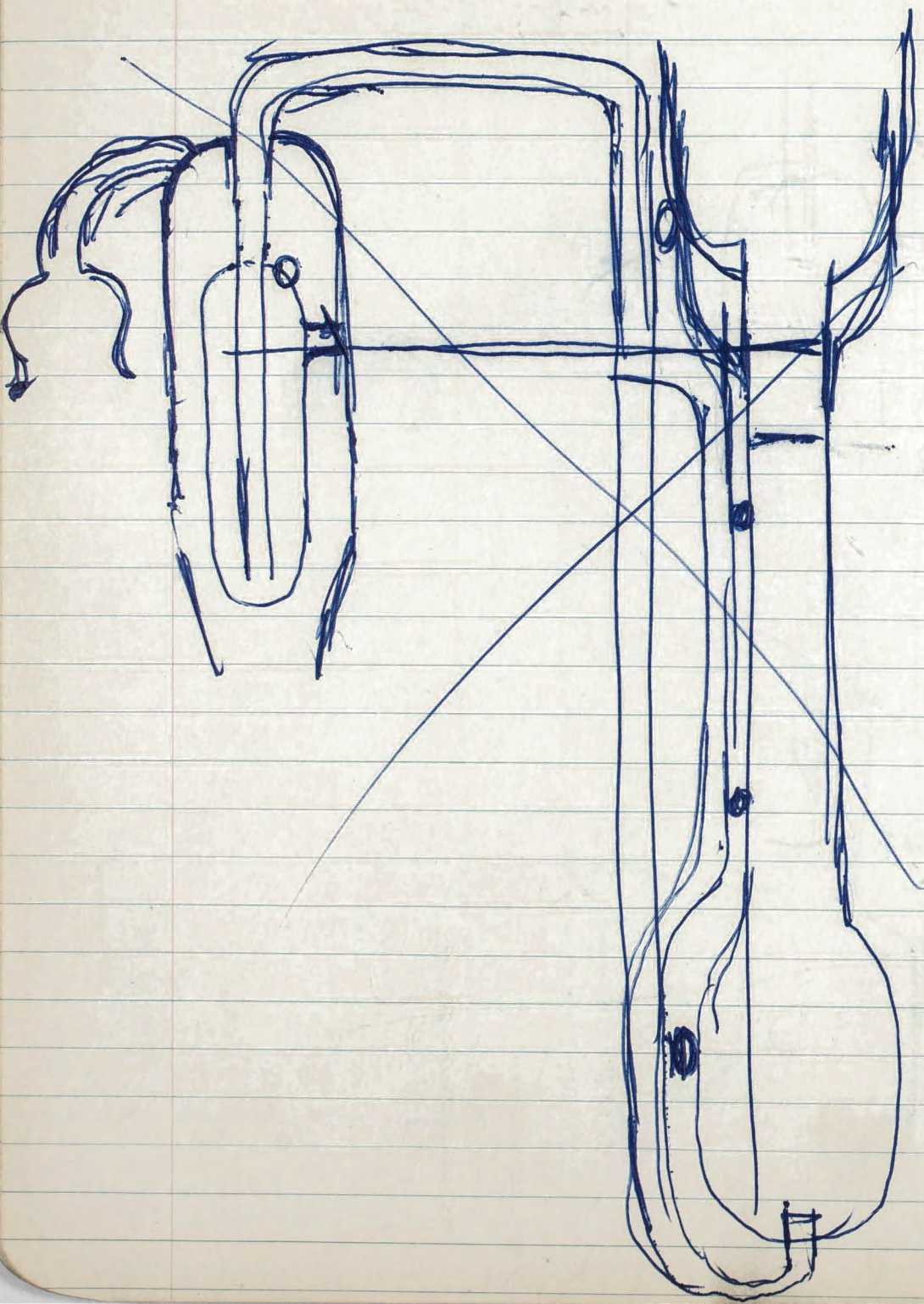
A month ago in science! inhibitor
Hesperidin inhibitor to hyaluronidase ×
Time magazine [St Louis]

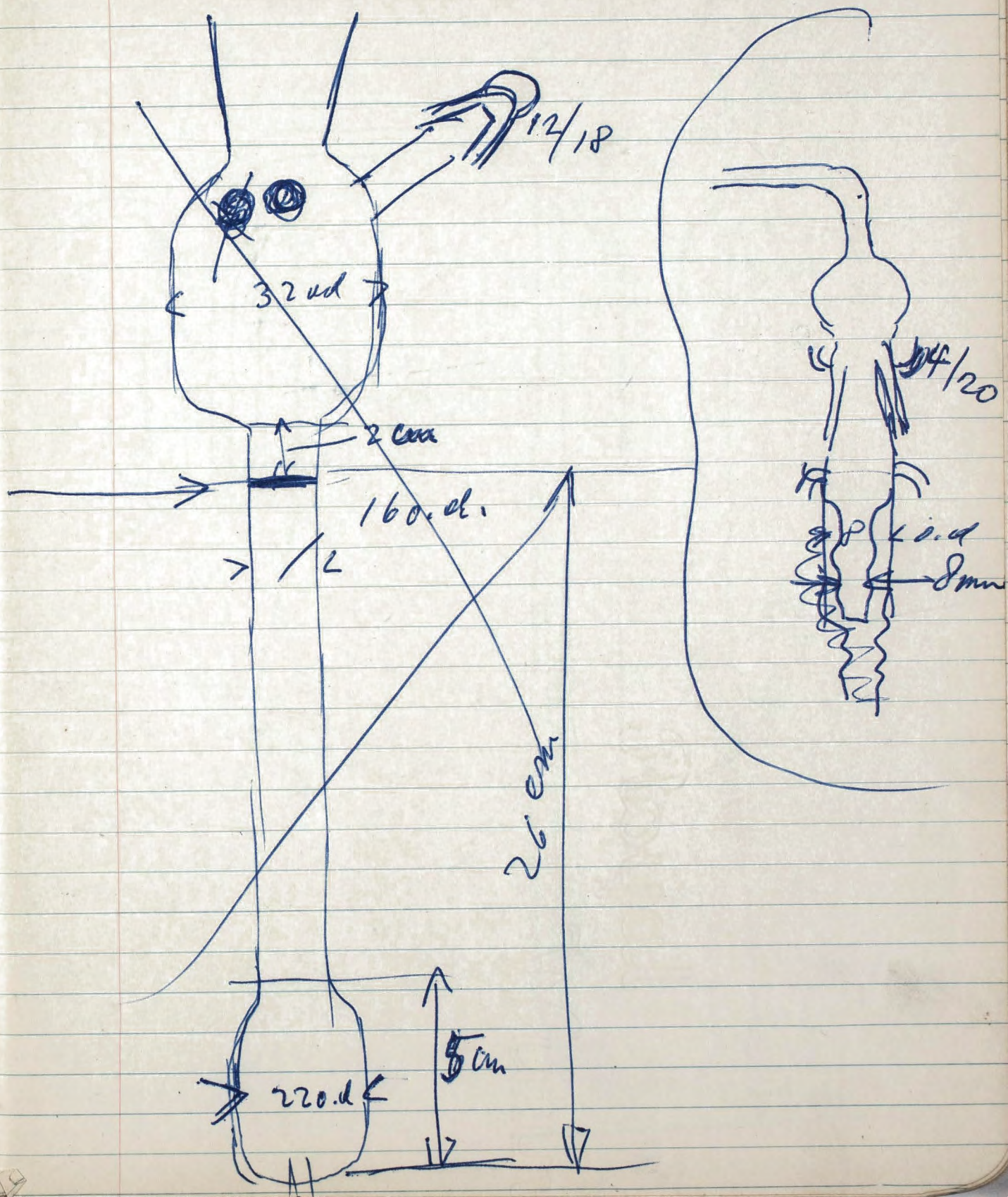
Vold (Emergency)

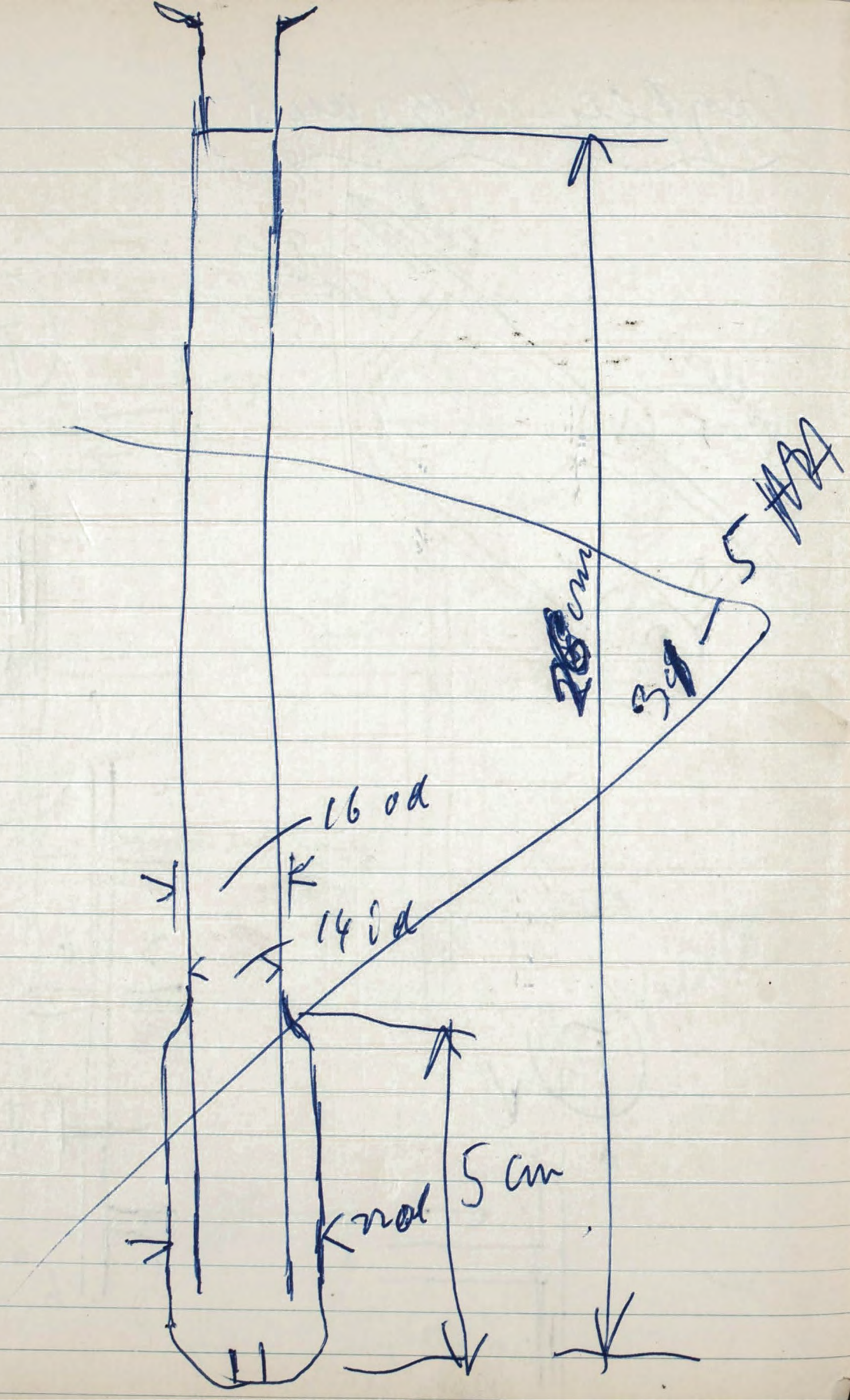
Arthur D. Little Chem. Eng. News
Febr.



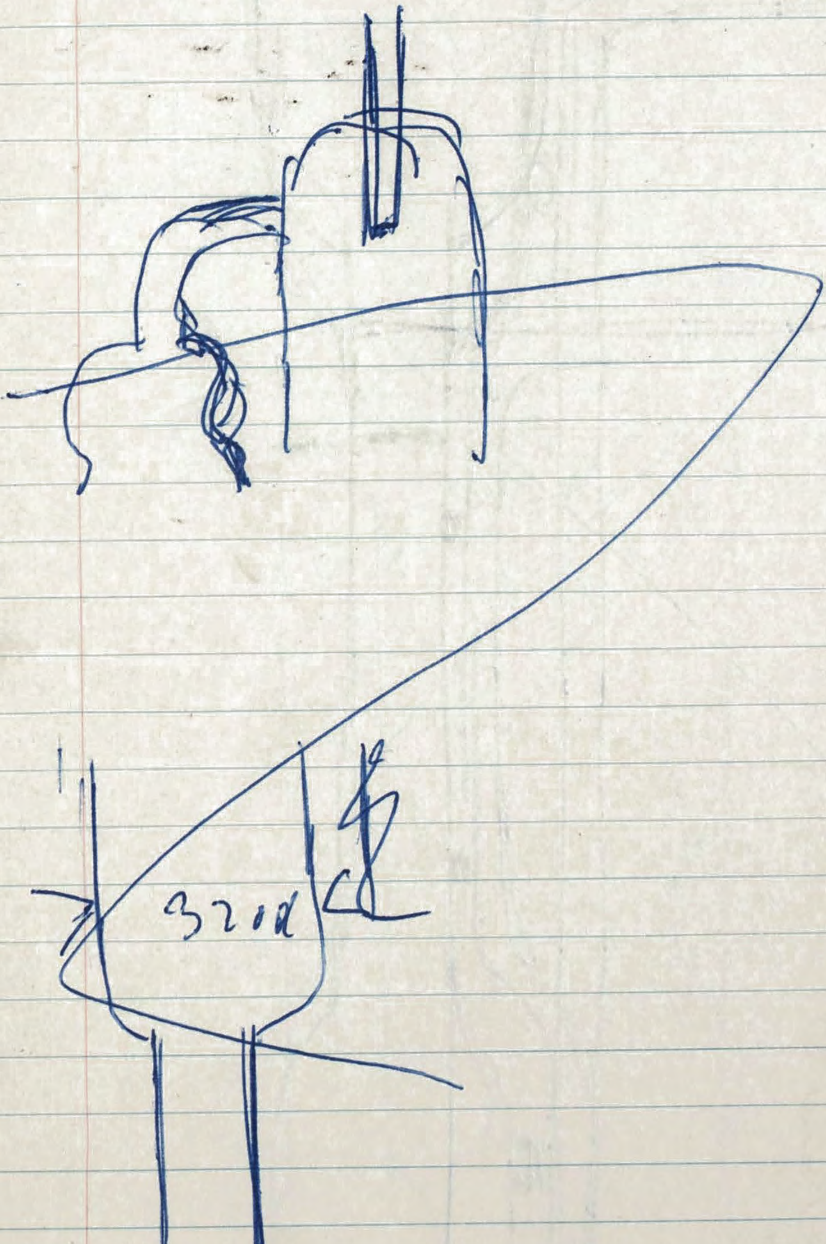
J.

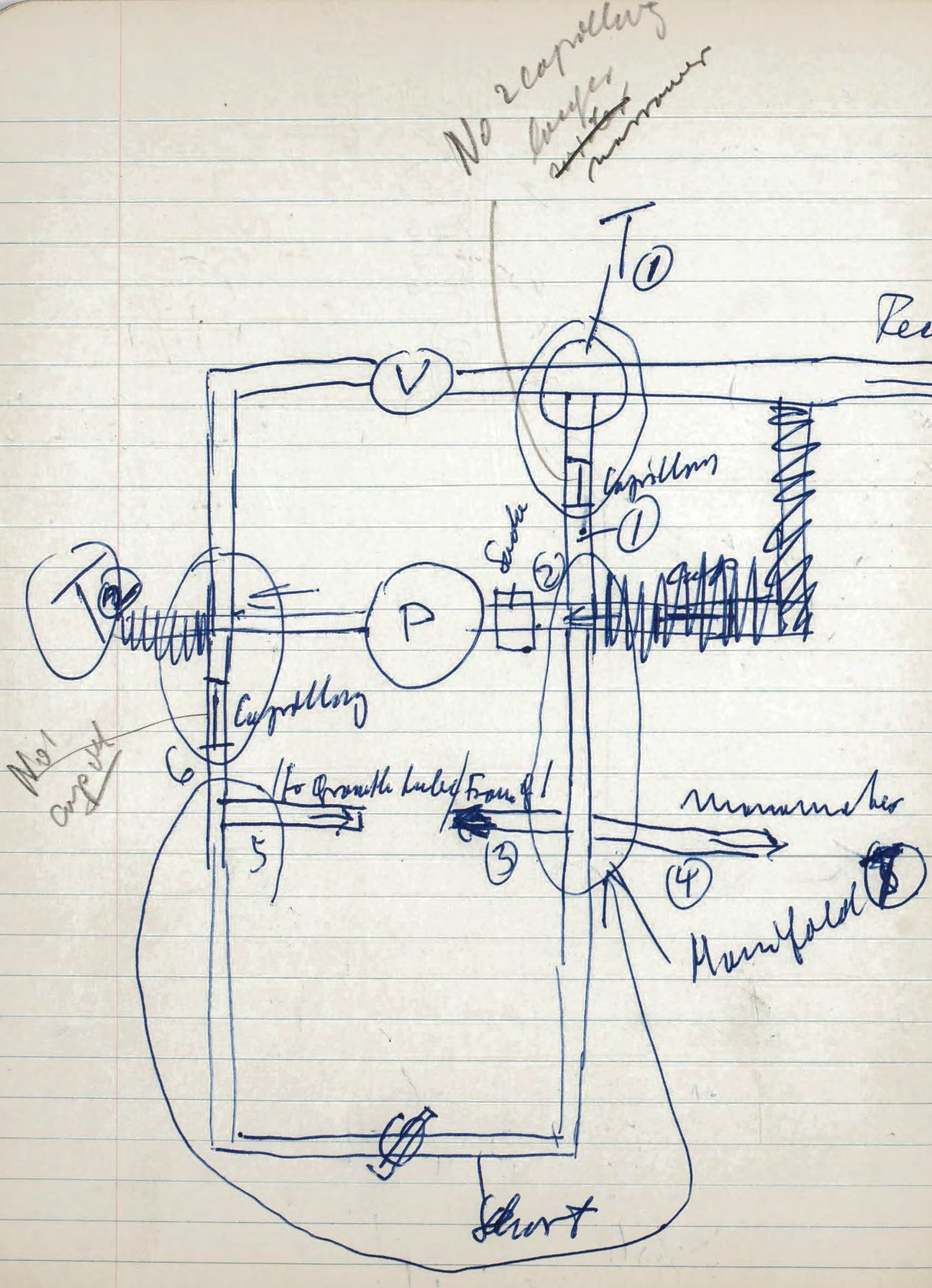



12/18
32 ud
2 cm
160 ud.
26 cm
5 cm
220 ud
10/20
10 ud
8 mm

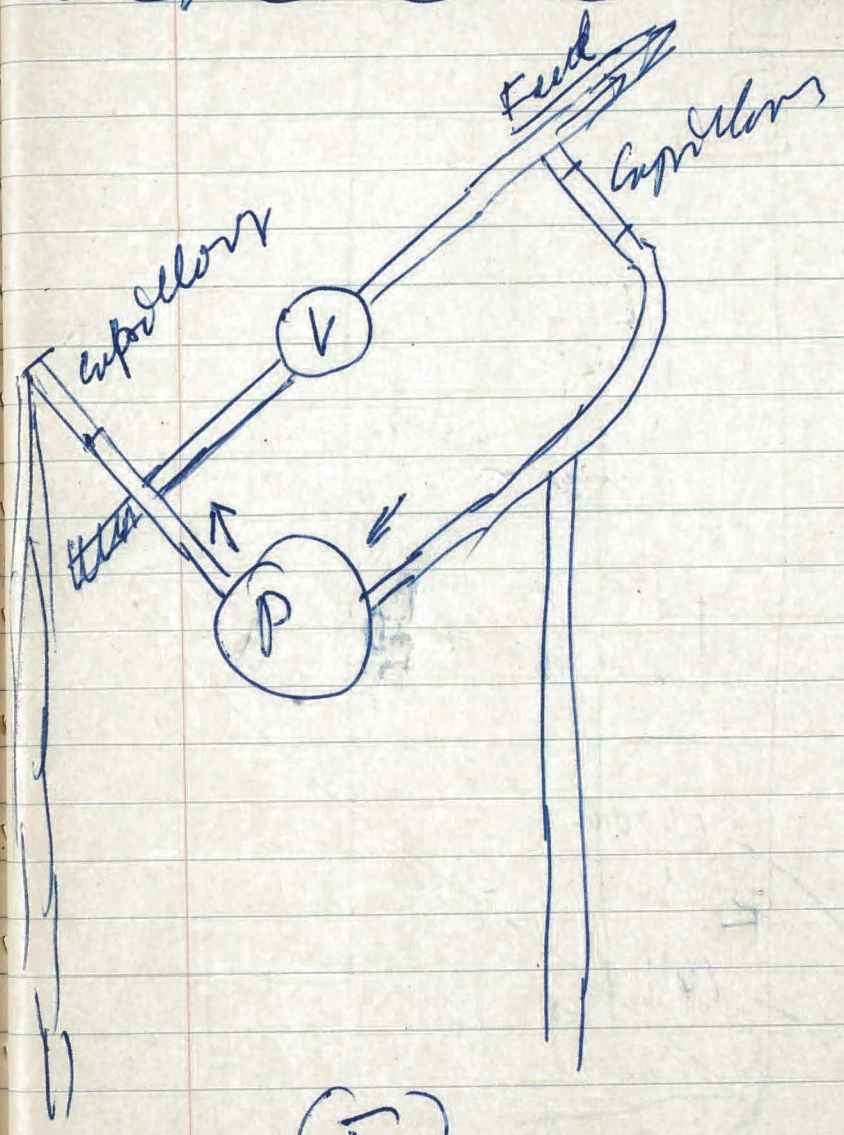

16 od
14 od
rod
5 cm

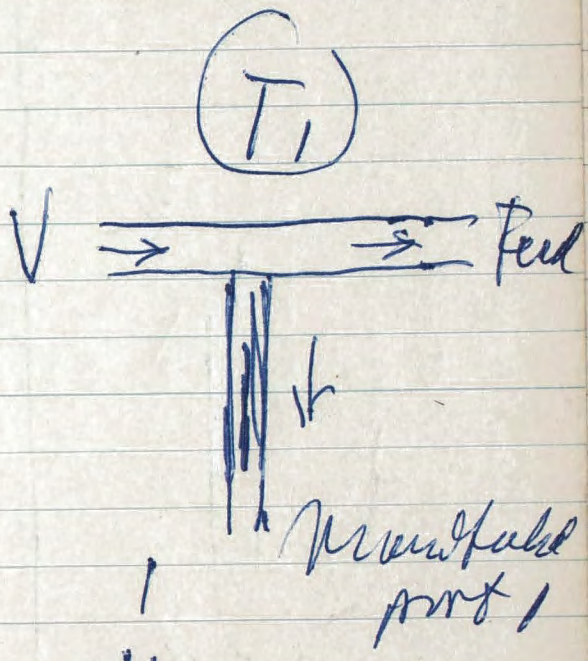
~~[illegible]~~

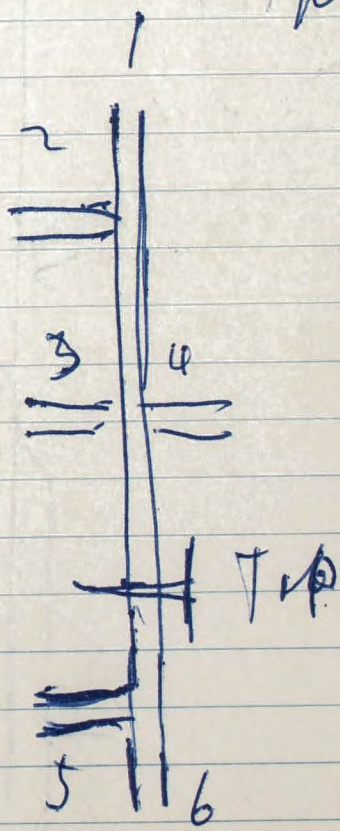

320d

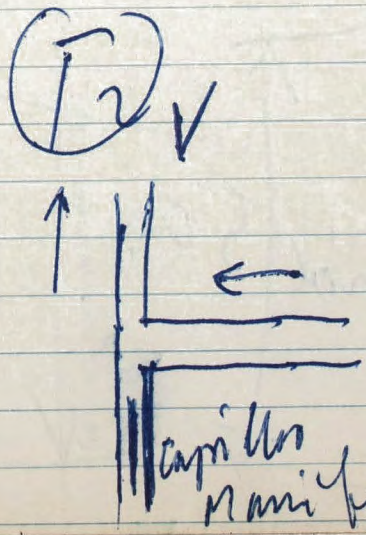

No 2 capillary
T
1
Reed
V
Capillary
1
Solder
2
T
2
P
Capillary
No 1
capillary
6
To throttle body from #1
5
3
4
Manifold
Short

Oxygen layout









Pay
Grinker Mitchell Res
Lawrence Kolb. Menger

Levine (Harry) Shelton Clark
Plastics manufacturer
New England

~~Selzabeccia~~

Ralph Connor
Vice Pres. in charge of Res.

SZILARD

Oct-50