A-42

[illegible] II

Szilard
1155 E 57th Str
Chicago 37 Ill

Hydrazine

Bridge Travel Bureau 10^{30} AM

8 pm

M. Lowenmanns Dept. Store

Hollander 7137

Szilard

1155 E 57th Str.

Chicago 37

[6615 Murphy]

Ill

W. Bgr.

Office Ext 6611 [LD220 Oak Ridge]

5⁰⁰ Oak Ridge 56045 Home

630 Alexander Hotel.

815

Upton Yockey

Norman Anderson
directly graduates

Wrote: Herman Kahn
Santa Monica Cal.

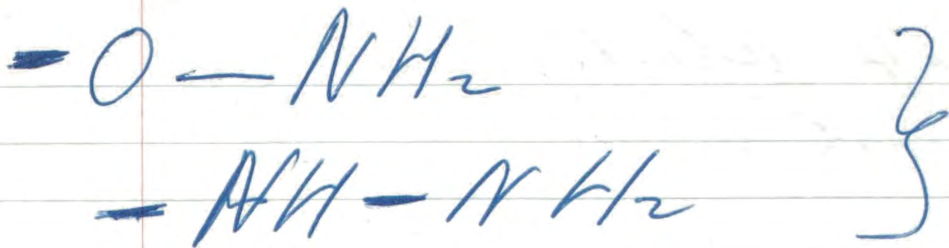
Dun [illegible] sessins

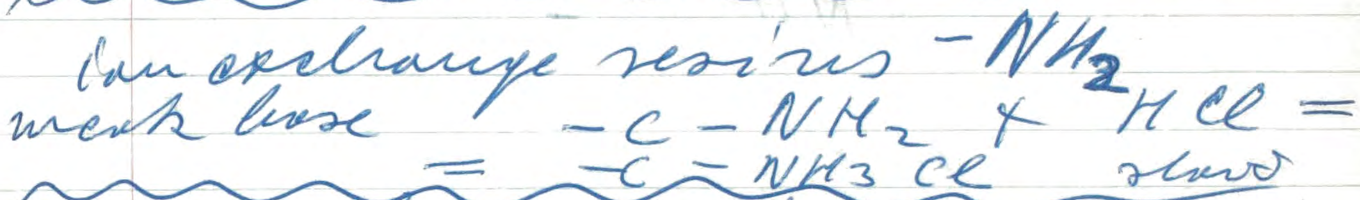
Kunin p Ungers

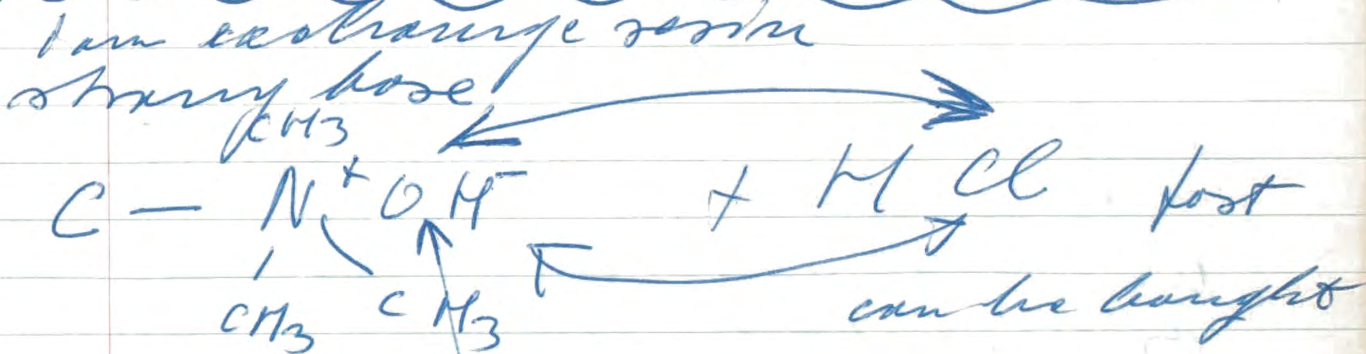
Inhn Walleystons

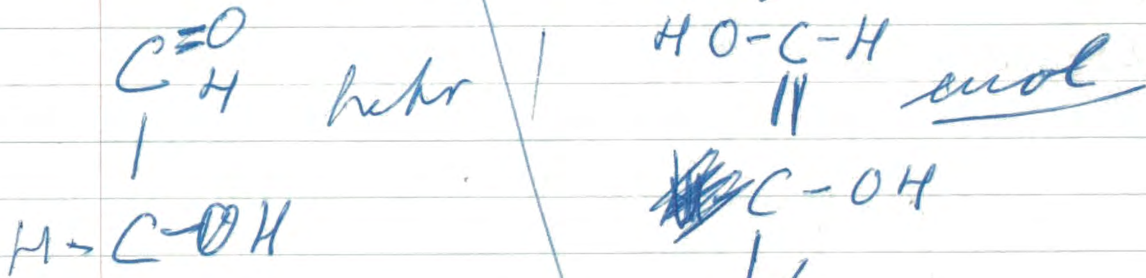
N.4 [illegible]

1950



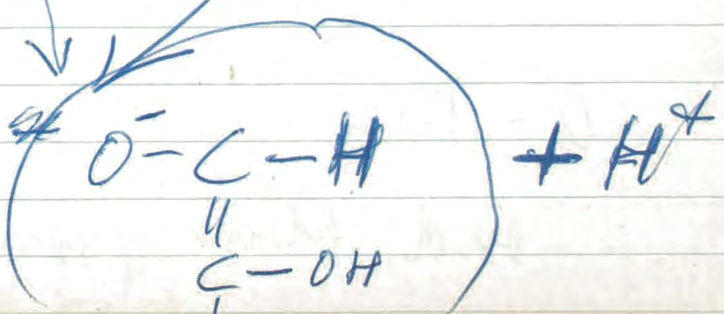




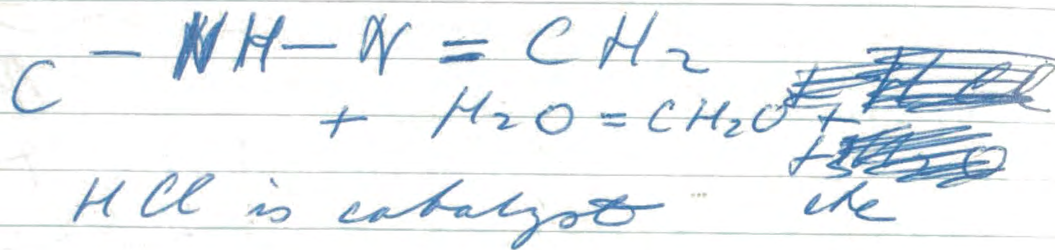


1.) Cl^- may compete

2.) at what pH ??
[illegible]

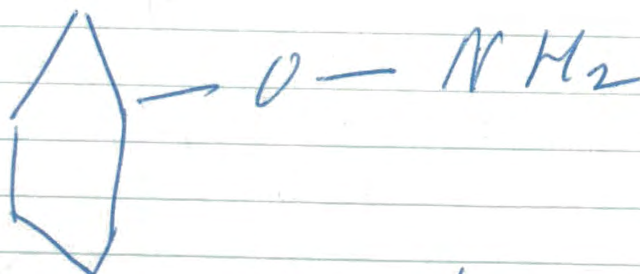


to take off blocking group boil with HCl + steam to boil off formaldehyde



(better block first with formaldehyde but acetone or acetaldehyde.)

Same with

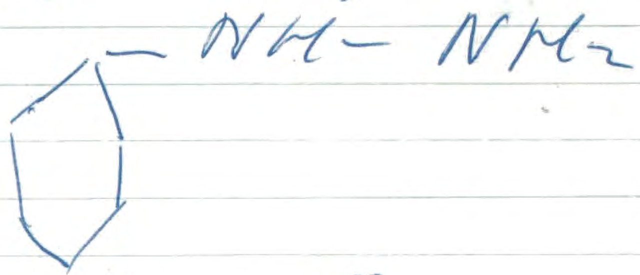


O-phenyl hydroxyamine

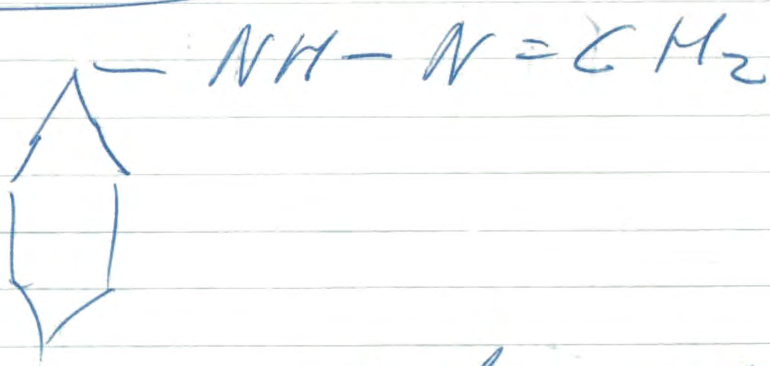
and block, condense, unblock

Resin

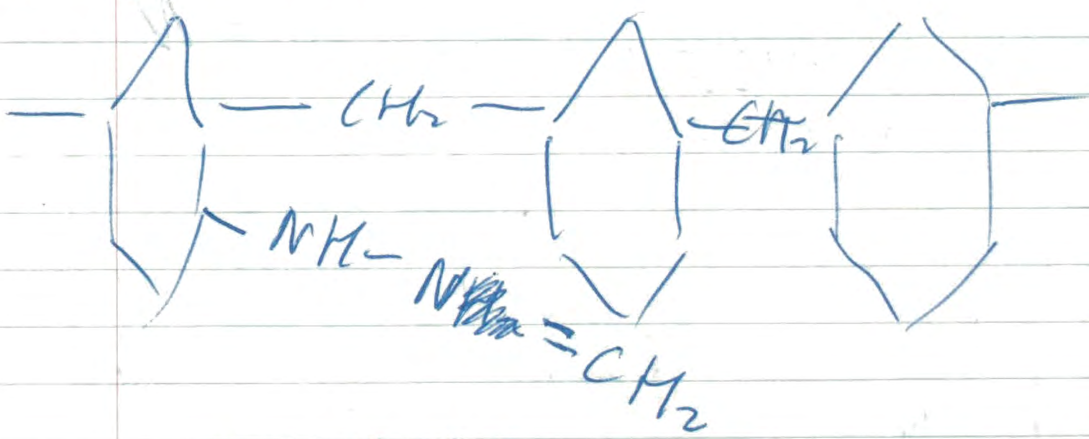
Phenyl Hydrazine



add formalin

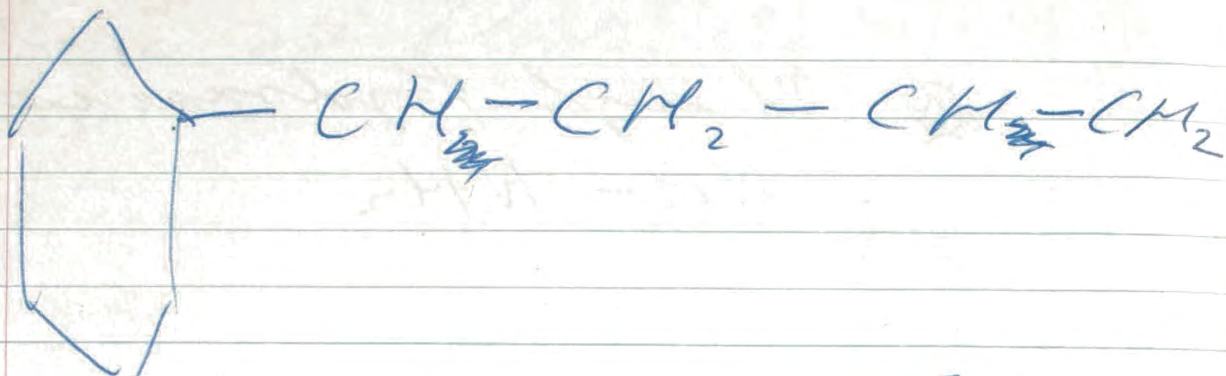


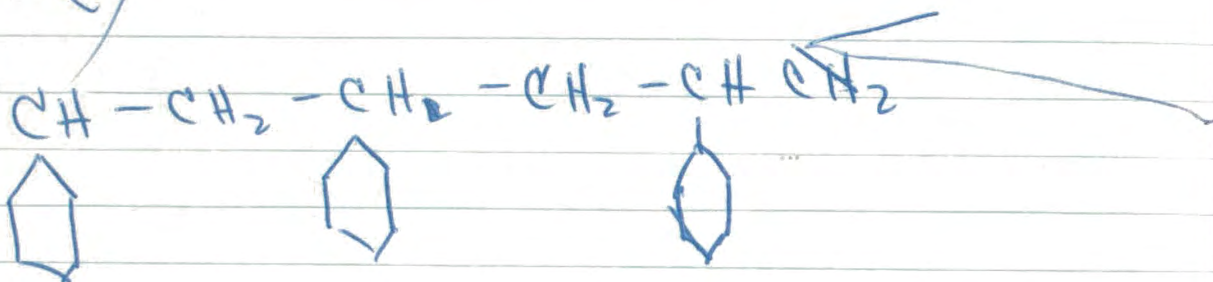
polymerize with formaldehyde

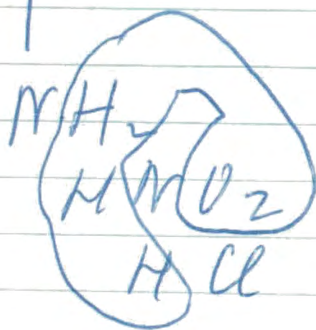


water soluble   long molecule

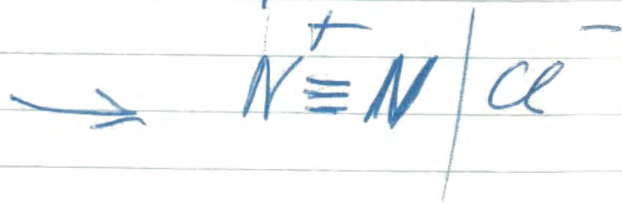
more formaldehyde gives
cross linkages

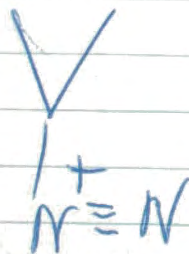




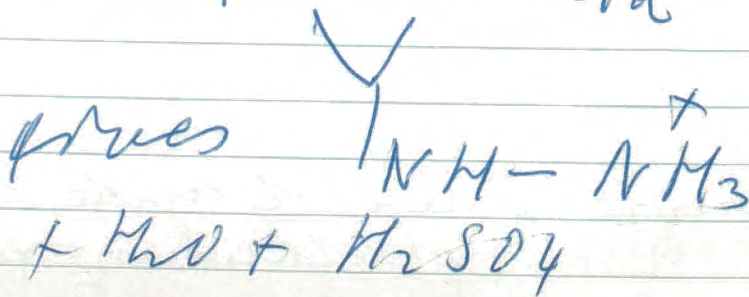


→



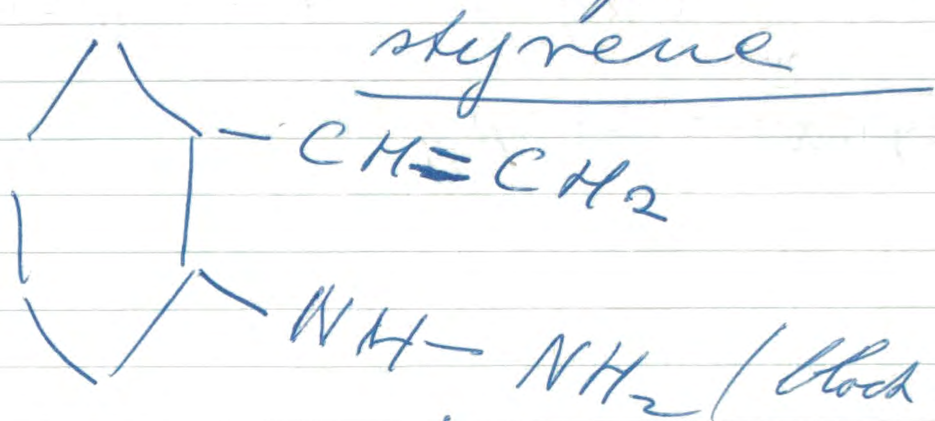


reduced with H_2SO_3
Sulfurous acid

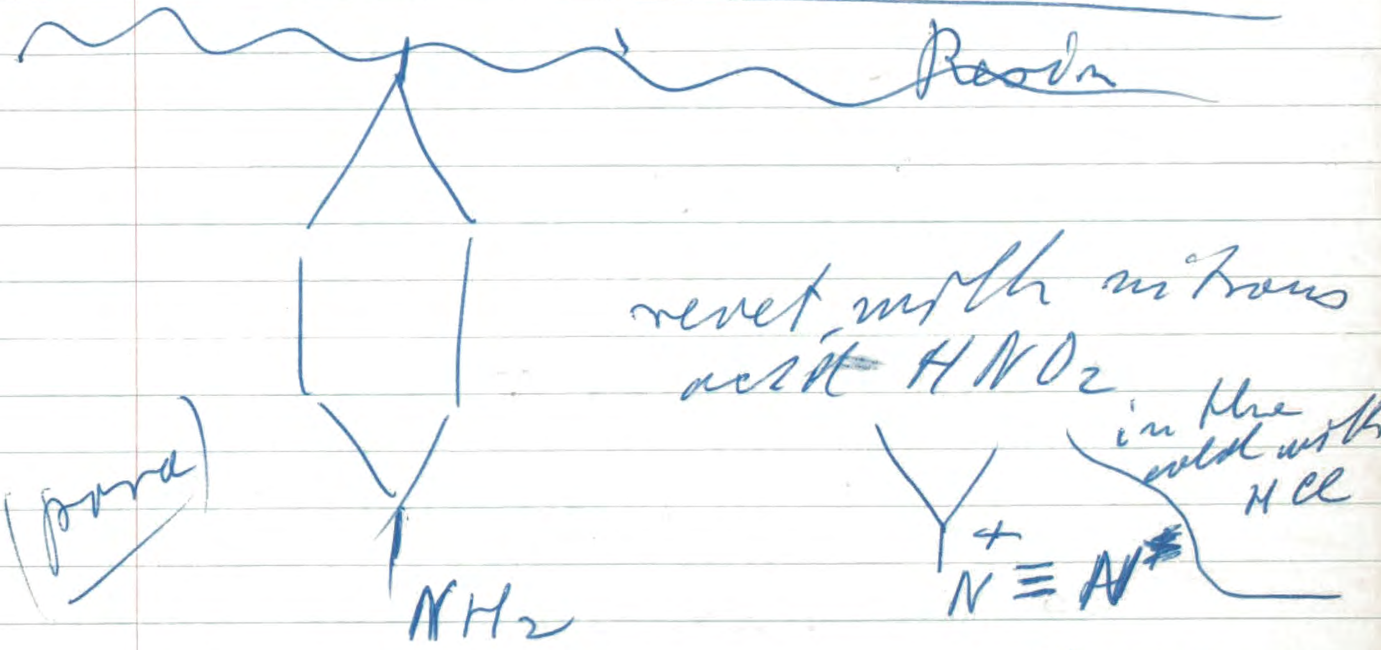


This was bakelite type resin

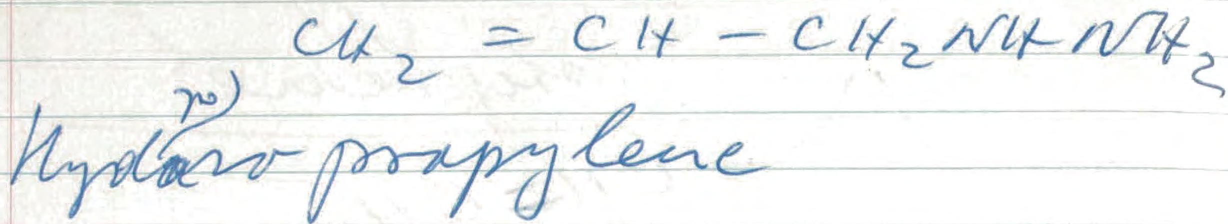
styrene



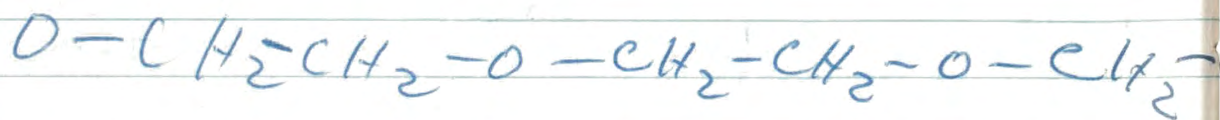
to condense first heat (ortho hydrazino styrene)
see also para-, meta-

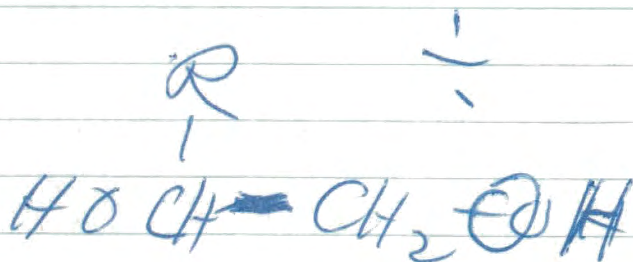


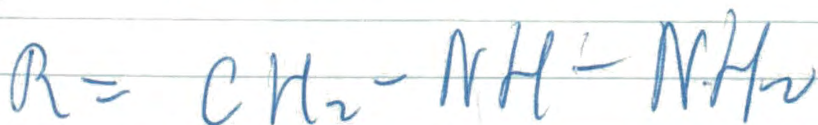
Any resin with aromatic amino group (Eastman Kodak?)

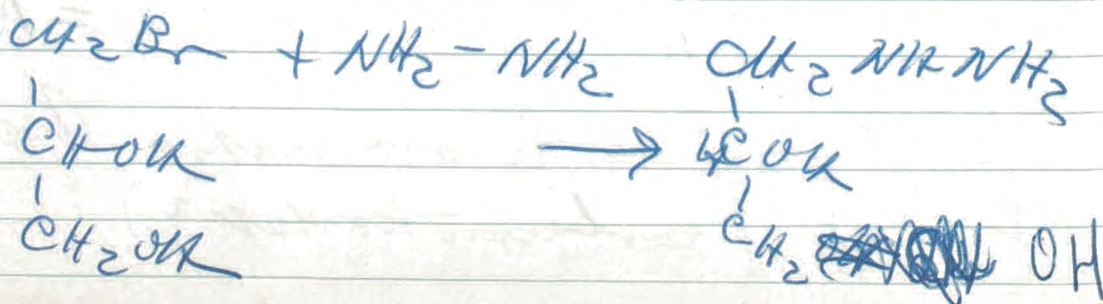


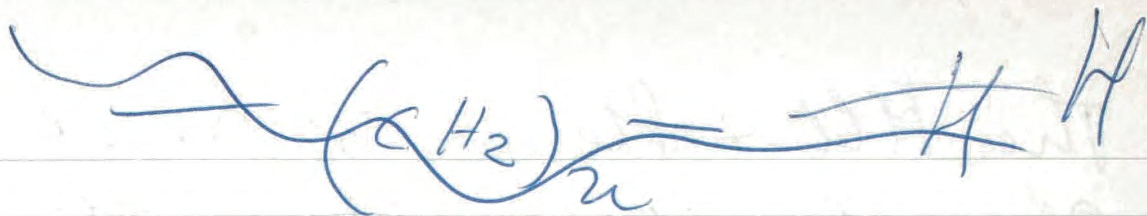
polyethyleneglycols



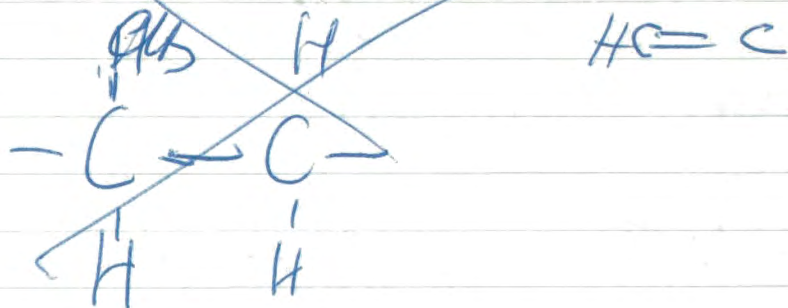


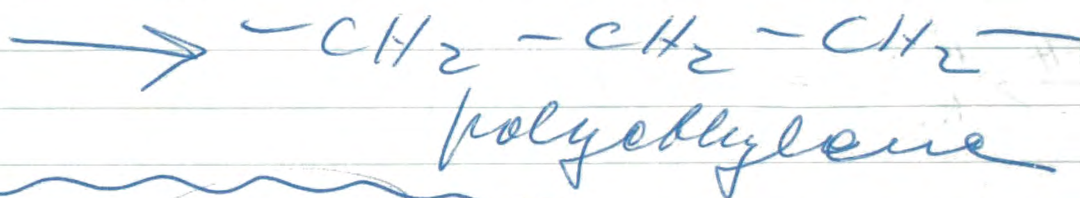




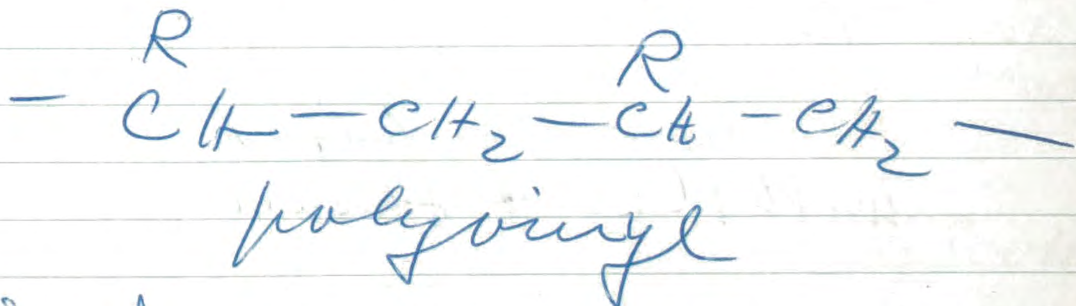


~~Polyvinyl Resins~~





vinyl group

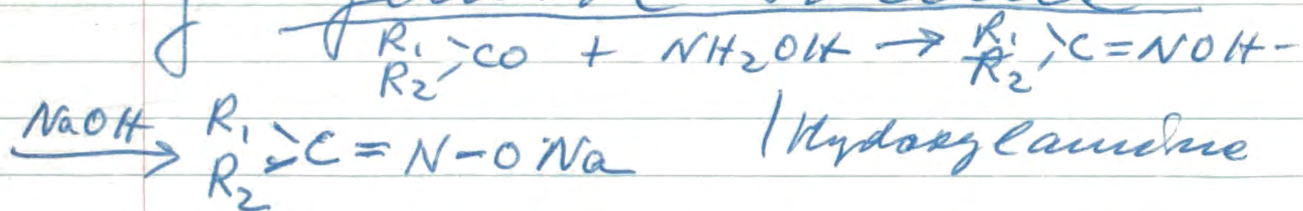


For instance

The HCl + Steam ~~of~~ treatment should come *after* polymerization.—

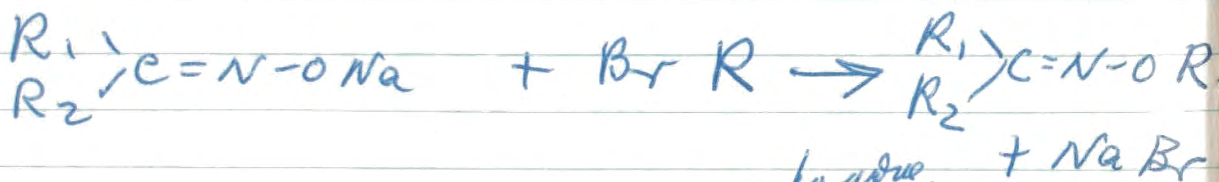
Some way for introducing

$-O-NH_2$ group into benzene ring: General Scheme

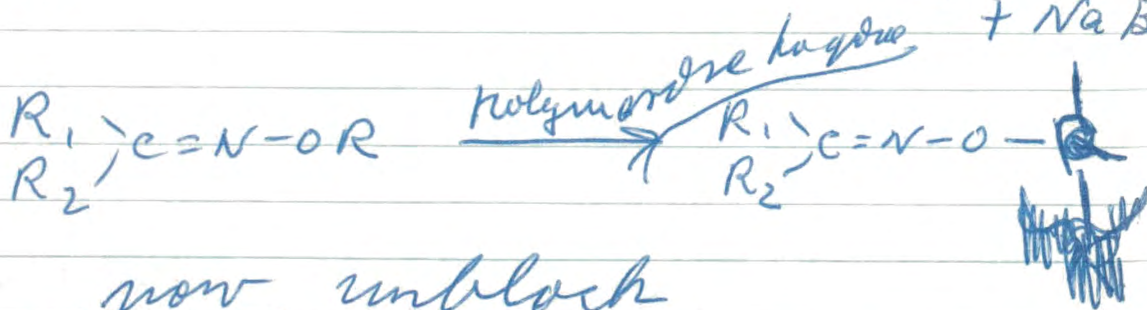


$$\frac{R_1}{R_2}\!>CO + NH_2OH \rightarrow \frac{R_1}{R_2}\!>C=NOH \xrightarrow{NaOH} \frac{R_1}{R_2}\!>C=N-ONa$$

/ Hydroxylamine



$$\frac{R_1}{R_2}\!>C=N-ONa + BrR \rightarrow \frac{R_1}{R_2}\!>C=N-OR + NaBr$$

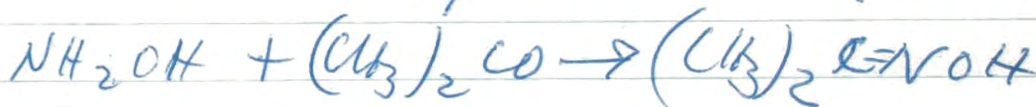


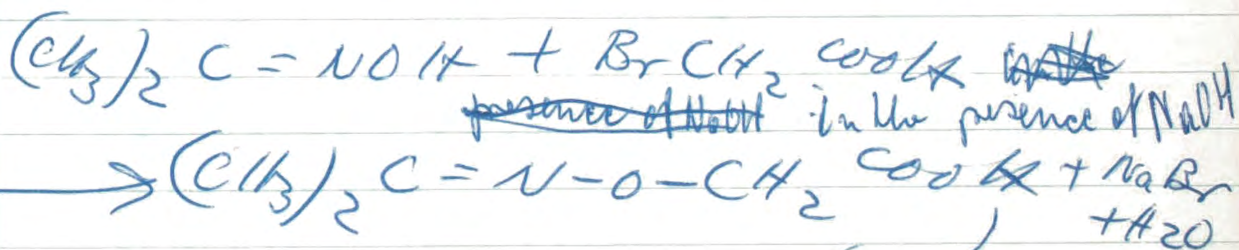
$$\frac{R_1}{R_2}\!>C=N-OR \xrightarrow{\text{polymerize together}} \frac{R_1}{R_2}\!>C=N-O-\text{(ring)}$$

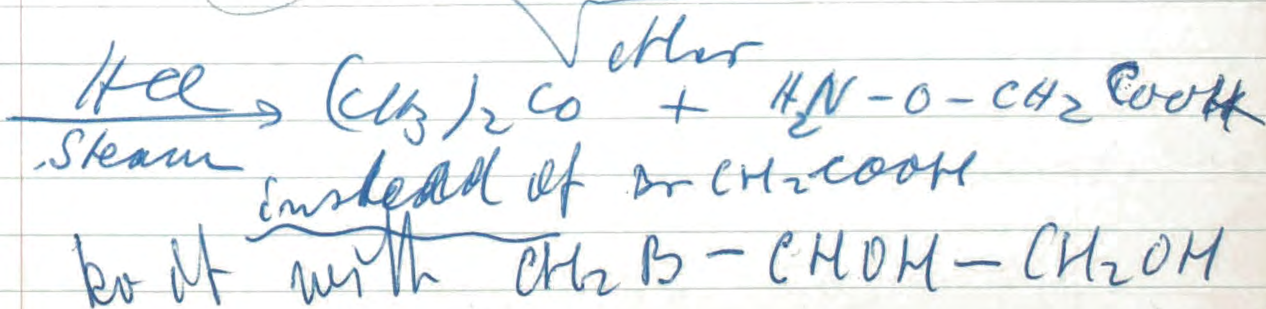
now unblock with HCl + Steam

General Scheme for Hydrazine:

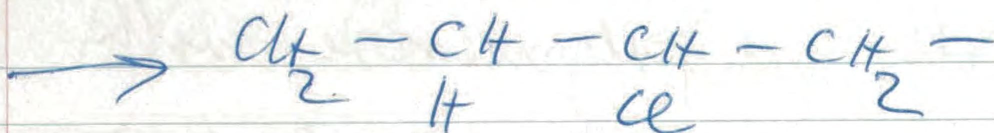
Normally you polymerise with heat. If it does not stand heat substitute one OH with Cl and polymerise with NaOH in the cold. —







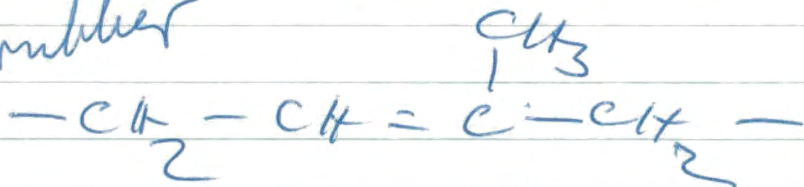
Hydrogenate

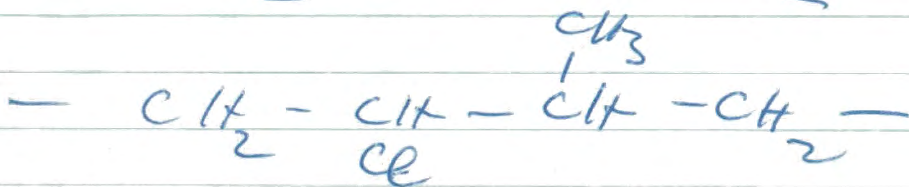


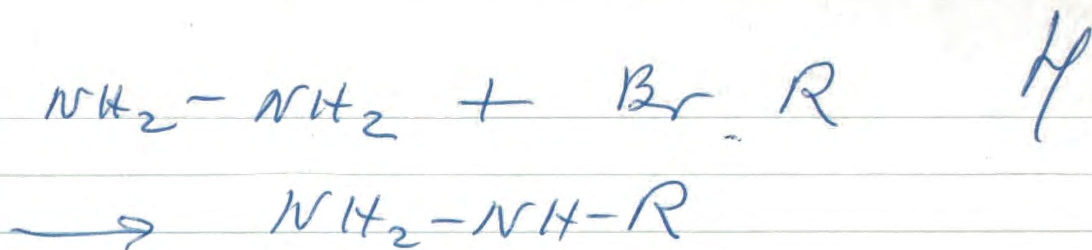
treat with hydrazine

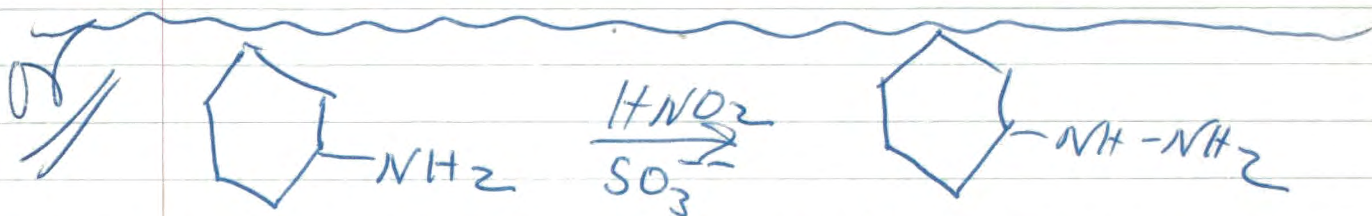
Would rubber hydrochloride react with hydrazine?

rubber





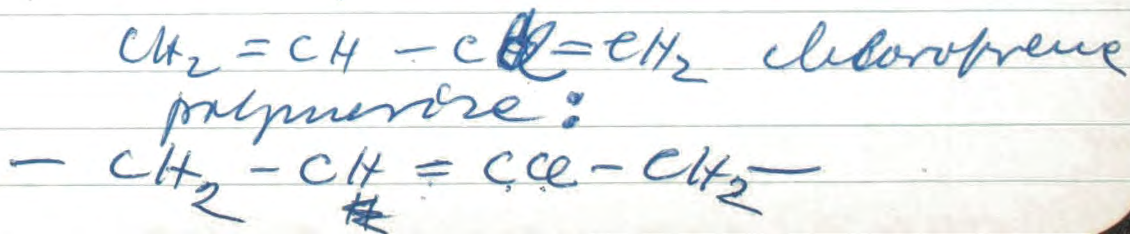




as discussed before [in the finished polymer]

~~[crossed out]~~ does not work except with aromatic amines

Chloroprene rubber would it react with hydrazine? as follows (maybe)



Soluble polymers

methyl cellulose
couple with

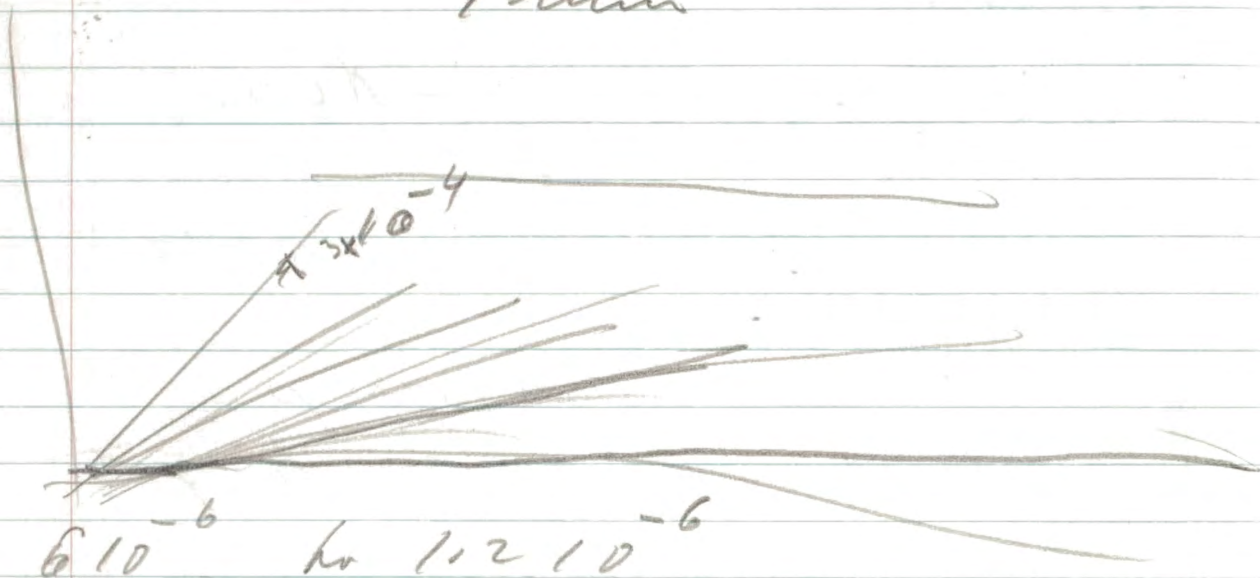
strong NaOH) (10% or/100 cc)
at ~ 100° C
reduce to amino group
and treat with HNO_2 to get
— NH — NH_2

see Campbell, Lerman etc.
Proc. Nat. Acad. 1951 or 52 or 50

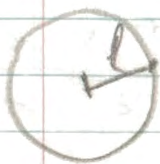
$5\,10^{-4}$ TMG $= S_0$ for max rate

$5\,10^{-4}$ 1/2 cells induced

7 min



$6\,10^{-6}$ to $1.2\,10^{-6}$

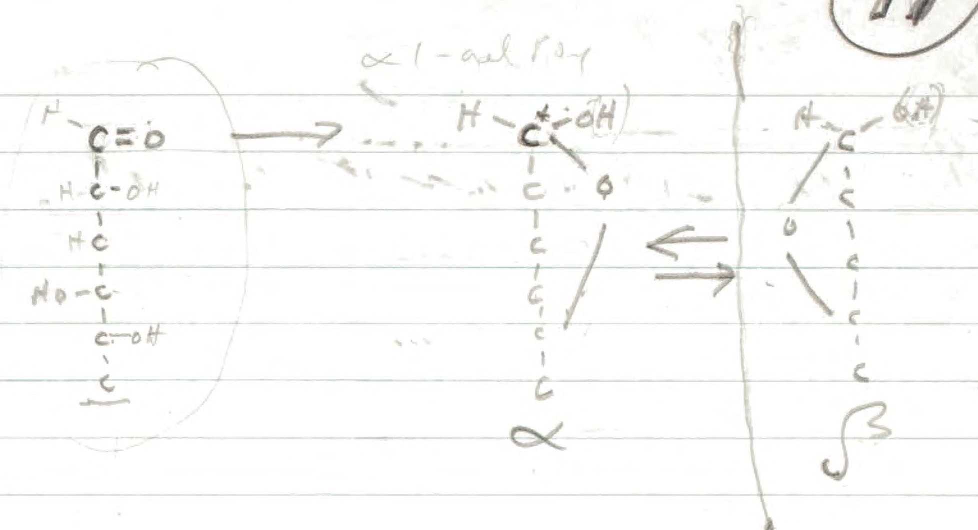


per sec per cm

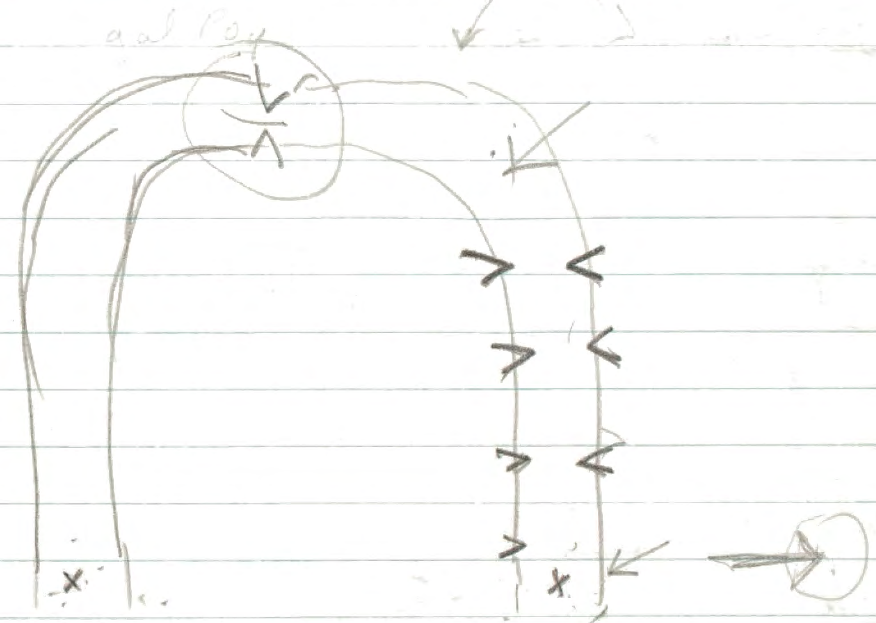
$\frac{gm}{cm^3}$ D. cm l/sec

sec cm^2

H



α gal 1 PO_4 → β gal + PO_4

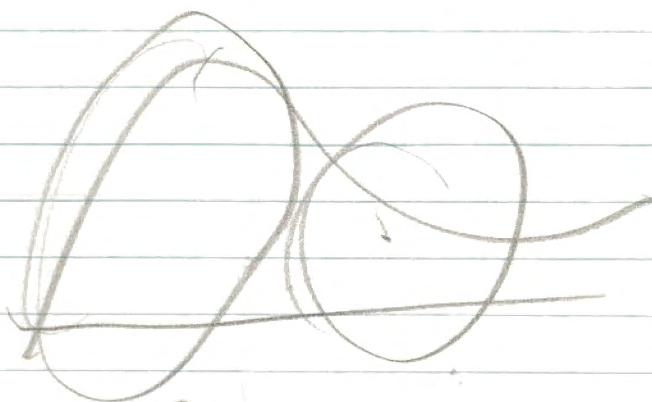


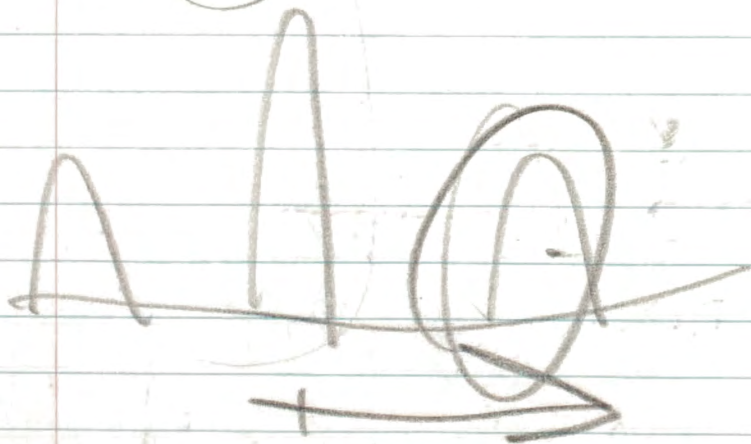
$5\,10^{-6}$ TMG maintain 7% 4% | 3%

$5\,10^{-4}$ TMG 50%

$35 - 5\,10^{-4}$ M

ag + ab — K — ag. ab.





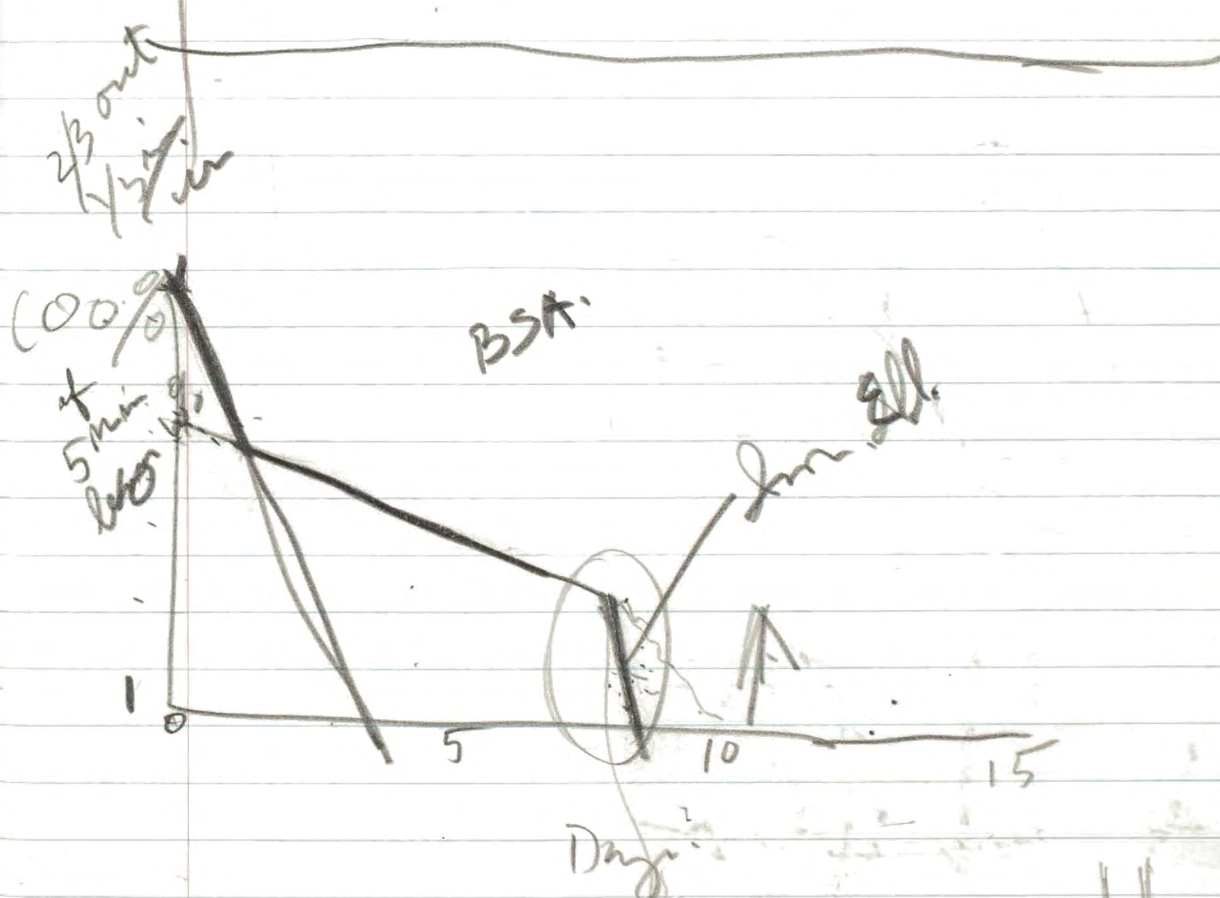
2.5 Kilo   Richard Fair H

do Resp

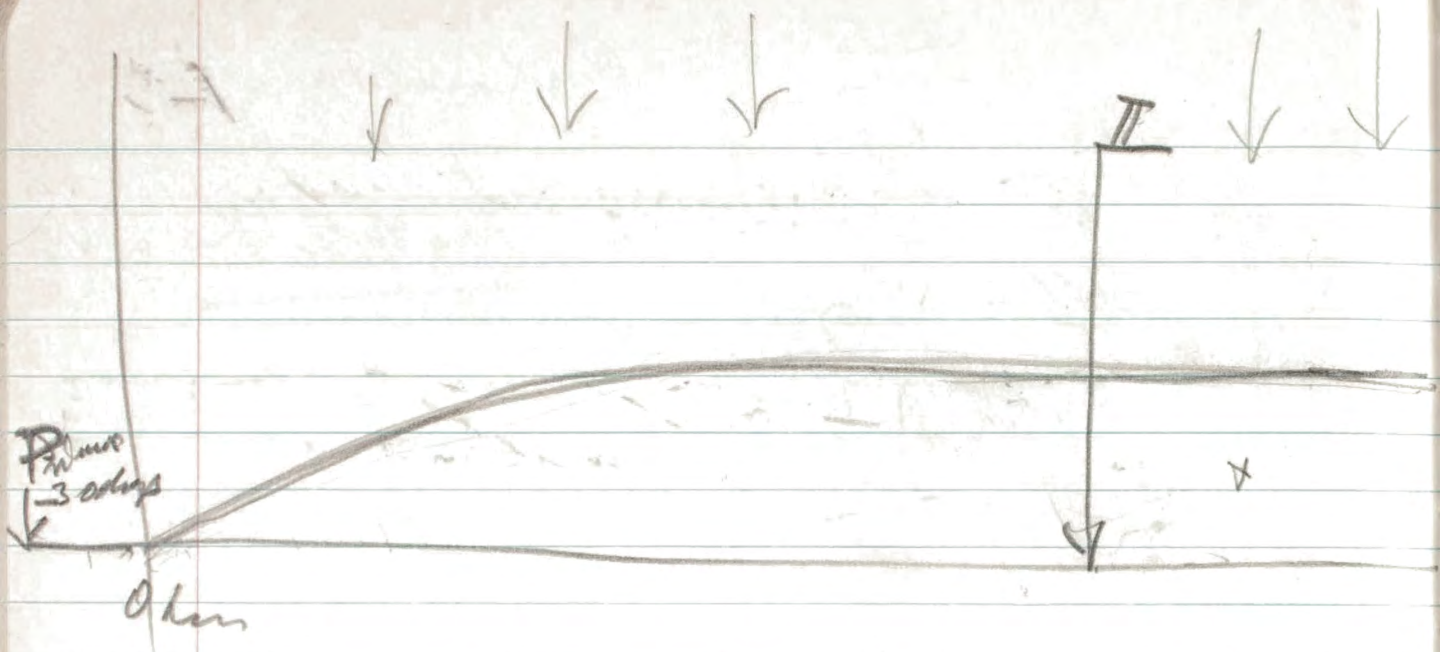
6 γ – 1/24
30 γ = 1/20
160 γ = 75%
8000 γ – 100%

Rabbit i.V.

B.S.A



Eric Nelson C. P. Miller's Lab



Charles Stewart, Brown, inbred rabbits

Kaller

CBA + X ray + C3H

Sarcoma 1A no growth for 1 month

lymphomas of CBA now 1A takes off and grows

myleran - treatment

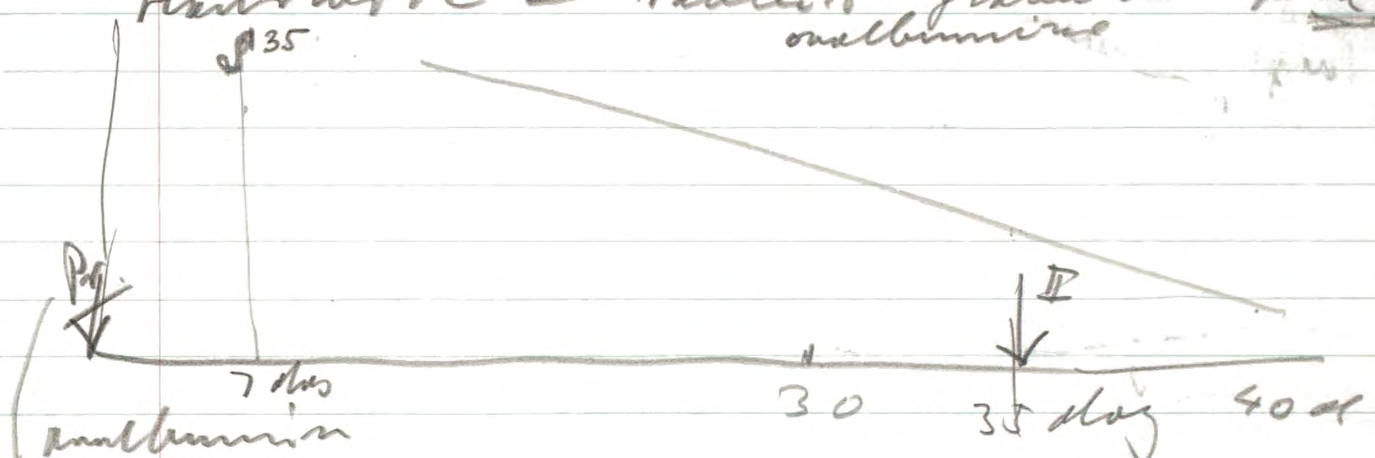
Gatlinburg

Quarton (B.) to Talmadge 4.

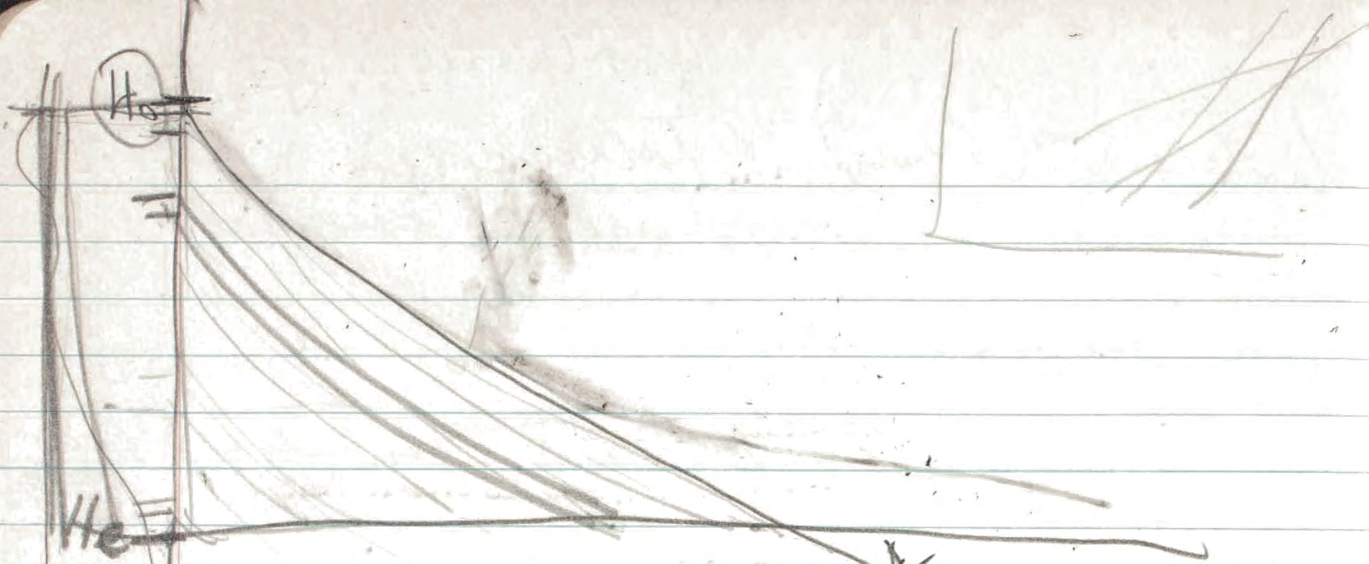
can secondary response be evoked by haptens?

Use Bivalent hapten

Hammerstr — rabbit globulin life 6d



12,000 }
8,000 }



A B C D nucleotides

$p(H)$ probability dist of organism in H

x = age, dose, etc $\quad q$,

l = no in pop

$$H = \sum_i p_i \log_2 p_i - H_m$$

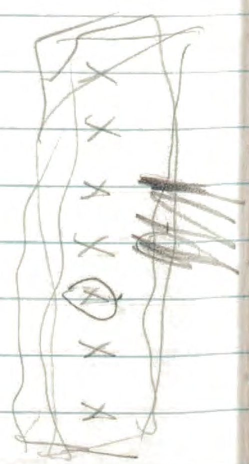
$$H_m = q \log_2 q + (1-q) \log_2 \left(\frac{1-q}{3}\right)$$

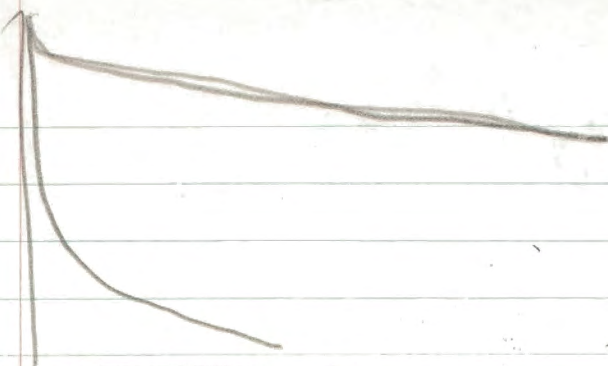
10^{-8} $\quad q = 1/4$ noisy

$$\frac{dq}{dt} = -J(t)\, q + \frac{J(t)}{4}$$

$$\frac{dp}{dt} = -J(t)\, p + \frac{J(t)}{4}$$

J = const





7 70 h

68

H.P. Yockey

H marine 800 r

spleen

DNA

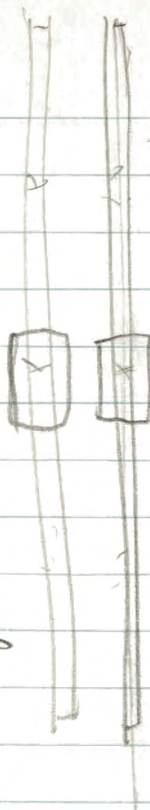
RNA

1 amino

protein

$$\frac{1}{\ell}\frac{d\ell}{dt} = \rho(H_e)\frac{dH}{dt}\Big|_{H_e}$$

$$\rho(H)\,dH\Big|_{t=0} = \rho(H_e)\,dH\Big|_{H_e}$$



$$\frac{1}{\ell}\frac{d\ell}{dt} = \text{const}$$

$$\frac{1}{\ell}\frac{d\ell}{dt} = J_0\, t\, [\text{const}]$$

$$\log\frac{\ell_0}{\ell} = \frac{J_0}{2}(\text{const})\, t^2$$

I $f(t)$

$$J(t) = J_1 t + J_2 t^2 + J_3 t^3 \text{ —}$$

$\log S = \text{Const} \sum J t^2$

$S = \frac{e_0}{e}$

~~Dose~~ 10 μ. $\frac{1}{1000}$

$\frac{1}{2}$ (10⁶) / 25

Coons, J. E. Med. 104. (1955)

Toxoid

Tinct: 1000 x first

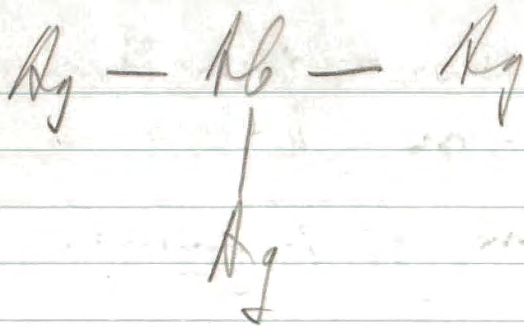
nul albumin

20,000

Stetson nul albumin +

[illegible] 4 + toxoid

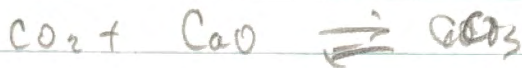
Anderson Edinburgh or Glasgow
on Rabbit Blood groups
Imm. Path. Bact Sell
2 1955 ?



Ab BSA
Serial Absorption → (Nonfitting (Coeff) ½

Ab N/ml

Total Ag − Free = Bound /



(no control of total globulin!!)

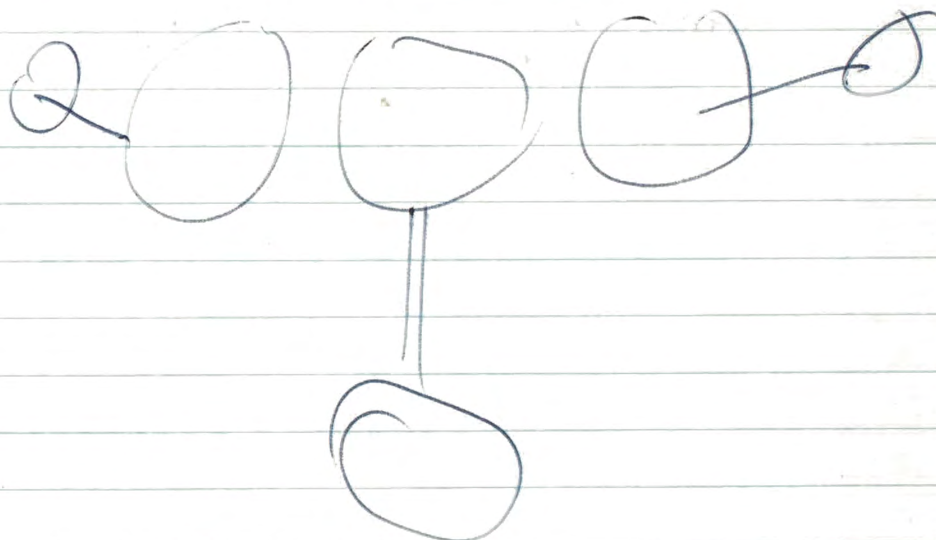
4

Cohn Bar Harbour
T+B Sawdon " "

Recent issue of Genetics
Science last Summer

Compton

Arsenylic acid —



25 years fr.

200,000 Curies / a year

may be ten times

Savannah 10,000 Curie a day

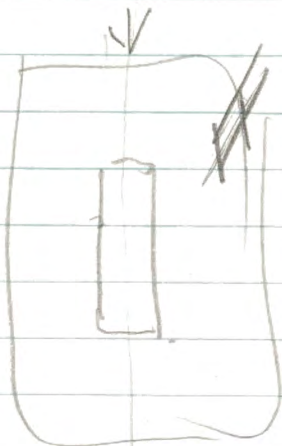
Cres. between .1 and .5
30 year half life

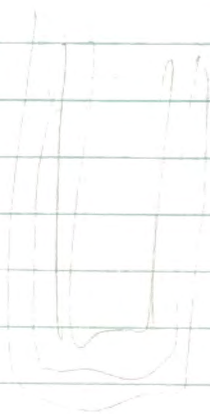
~~$0.50~~ 10 to 50 cents a curie for Sr.

(Start August)

1 year Ruthenium (106)

(Sr. Fl)





Radioisotope Dept.

Cerium 144 275 days
25 x times as much as Sr.
oxide

Aging of isogenic mice; M
Russel

[illegible] Chapter 22 Caw
E.V. Cowdry 1942
The Williams & Wilkins Co

Triploid salamander

10^{-7} per hour per locus | 10^{-8}
10^4 loci
down to $\frac{1}{e}$ in 11.4 years | 114 years

~~Russel~~, Upton
D_2O ~ $20/lb → $10/lb
Snell
1:5000

Arthur F. Rupp
Oak Ridge National Laboratory

Swartout

1 megacurie per square mile
100 Curie / day

Mutation rate
$25 \; 10^{-8}$ per r per locus

on insensitive spermatogonia

cell death (death ~~[illegible]~~ in division)
l.d. 50% in 22 r
diploid
sensitive to killing

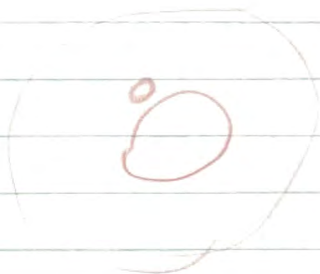
Upjohn dist. of Biological 4

Allen Kimball

Russel - Proc. Nat. Acad.

neutron irrad non isogenic
20 days per rep. to father
0.08% life per rep.—
[31 reps. and 100 rep. neutrons]
19 to 23 days]

X rays - 5



800 r to father — 50% loss of embryo
2-6 days after irrad
therefore less
Mouse sensitive to X rays -
~~Mother irrad shortly before~~

Henry Quastler Information Theory and Biology:

Julian Bigelow Inst of Advanced Studies.

C. W. Sheppard [Oak Ridge]

Inchey M

Isogenic mice! (inbred only)

William S. Murray
Joseph Hoffman
Cancer Res. Vol. 1 298 1941

~~William S. Murray~~
~~Can Vol 1. p123, 1941~~

~~"Isogenic" mice~~

H

age t

Turkamdatch Sr^{90}

~~2.27 Mev~~ max → 28 years of daughter
mean 0.7 Mev

1/2 thickness 130 mgm/cm²

14 gm Sr

2500 Curies ~ 14 gm

1 Curie $4\ 10^{10}$ dis per sec

10^6 R per min

1 R is 1 el stat unit. :

$3\ 10^9$ el stat Coulomb

30×10^6 x

100 erg / gm water ~ 1 R

10^6 R / min 10^8 ergs / gm / minute

$4\ 10^{10} \times 0.7 \times 1.6 \times 10^{-6} \times 60$

~ 1 C = $3\ 10^4$ R / min or 40 C needed

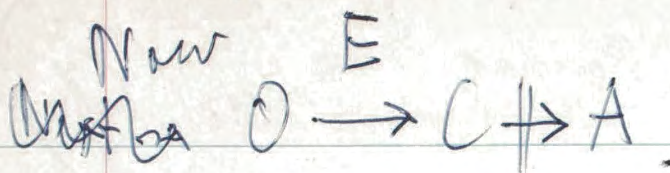
Anderson by Pentex Inc.
Kankakee Ill. (H)

Bovine S. A.
35% of sol. is B.S.A.
1 gm B.S.A has a vol.
0.75cc in sol.

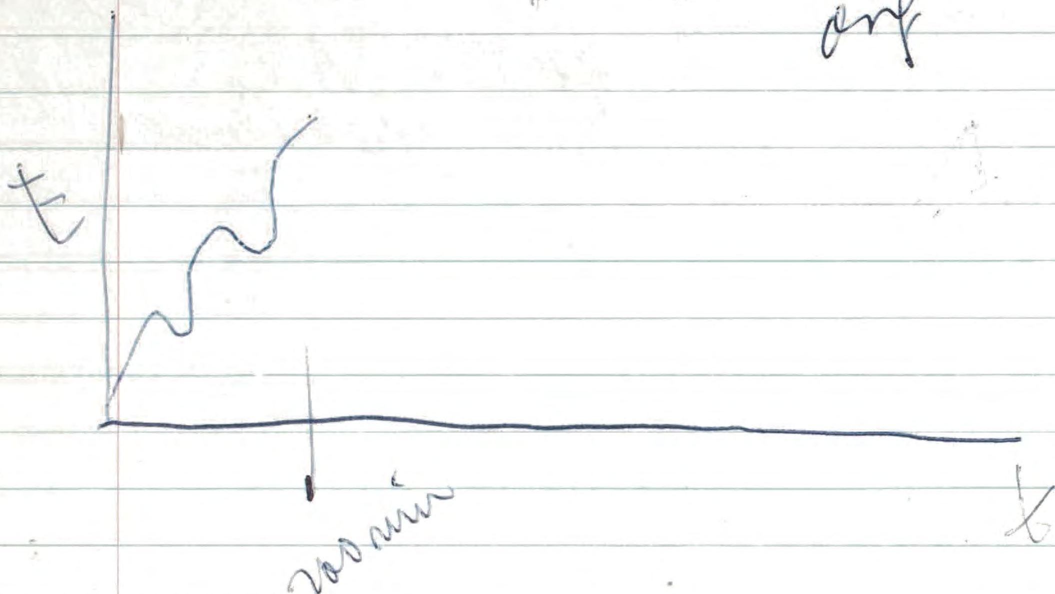
Sucrose
80%
60% sucrose ~ 1.235 density at
0°C

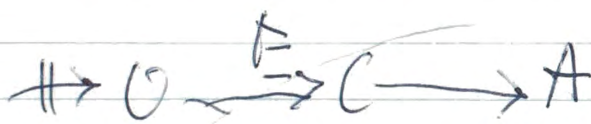
IMEV = 1.6 10^{-6} ergs [illegible]

Händler ([illegible]) Hofman



org line





org line

Turbowerkel

Heat

100 Curves

4 10^6 erg/sec

1 Joule ⇒ 1 Watt

~~Heat Heat Joule~~

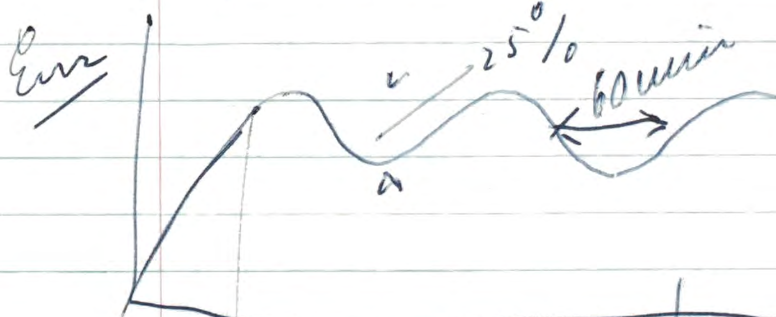
1 million cells × 1 min = 10^6 min

Histidine mutant. (wild type ~~allowed~~) Ames

O ~~Ex~~ C . A

→ →

nothing occurrences in lab by Ang. in Chemost.



$\tau = 400 \times 1.44$ min.

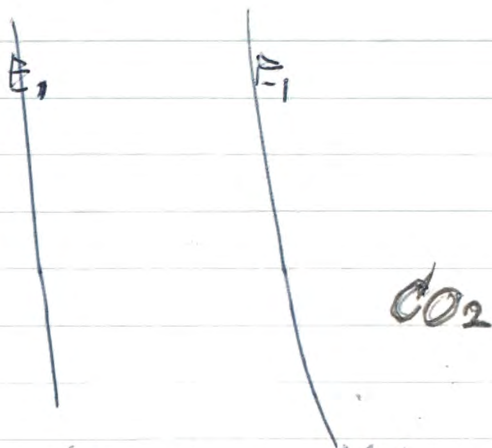
~~Measure~~ Measure rate of
inactivation of inducer by
K W2241a with or without glucose

Measure if in presence of glucose
constitutive, strain leak out
compound!
This is way to get out real inducer
activate it with alkaline hydrolysis!

Milt says TDG induces
the constitutive. (kicks up pumps)

2:35 Max Tischler (virus unit) Vice Pres.
Merck-Sharp and Dohme
Rahway

Merilt. The Pump Apr. 16/57



Applications 1.) ML 3 (abs. suppt.)
2.) W 2241a (K12) (abs. suppt.)

2.) W 2241 (E) is inhibited by CO_2 in TMG (10⁻⁴ TMG and air gives 25% of ceiling + 4% CO_2 drives this down to 10% of ceiling.)
Supernatant has inactive inducer. (Try this with TPG to see spectrum and show that it is either soluble.)

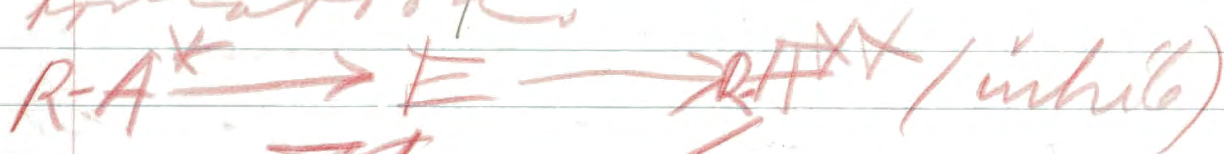
- (can be activated with alkaline (pH 12) hydrolyses for 15 min)

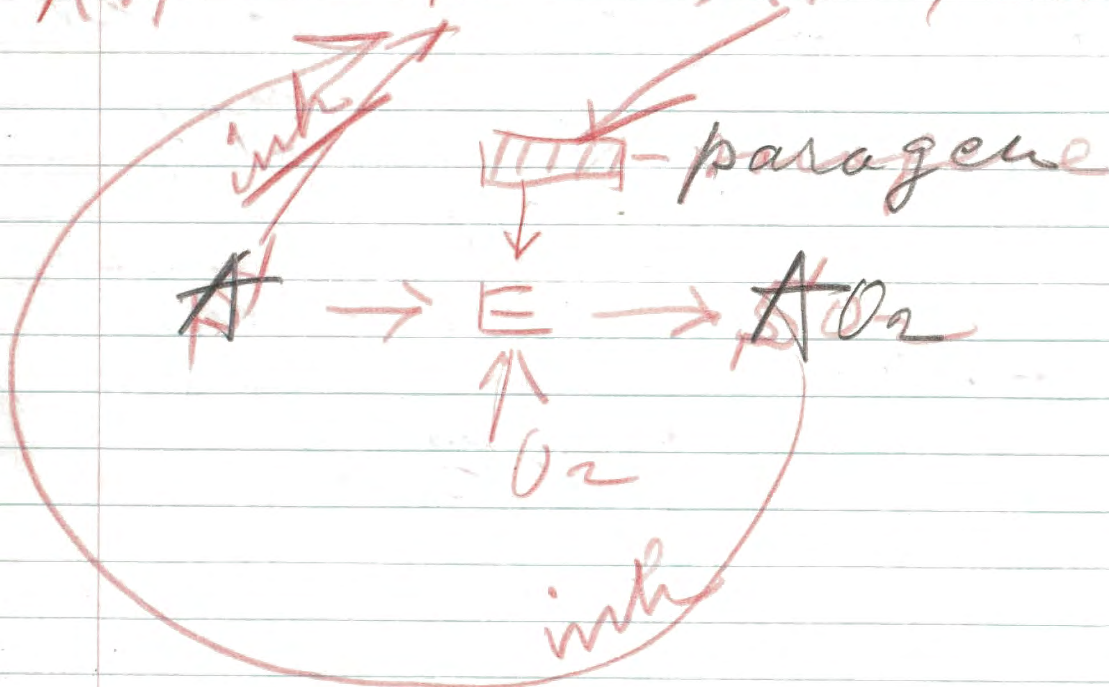
1.) ML 3 is slightly stimulated with 4% CO_2

Ideas:

Anagene II

General theory of adaptive enzyme formation:





Maas 2

H

Exp.: to mutant in arginine system to auxotroph after it back mutates in the same gene should be a slow grower not because the enzyme less active but because enzyme is inhibited at lower arginine conc. —

Novick technik with Tryptophane less at 1/2 of Arg. opt. ~~solut~~ should reveal it. ~~The all~~ To show that not all 3 enzymes are affected but only ~~a~~ one is necessary. —

Urgent experiment:
Is antibody released in anamnestic
Reaction of newly formed antibody?

Why not assume
young animal makes

R* – Hapten which is permanently
fixed in precursor – antibody
– complex
Exciting Hapten also may make
R* Hapten (Chase)

44

10 much
antigen
Antibody ~~in blood~~
paragen II

R_0 pre- Hapten → E → Hapten — R_0

antigen

~~call attention of E + antigen stimulated~~
~~call attention~~
tolerance because lots of E must be present.

paragen II

Antibody
~~[illegible]~~

Chose! R_0^* — Hapten is made in interstitial
remains bound to paragene antibody complex

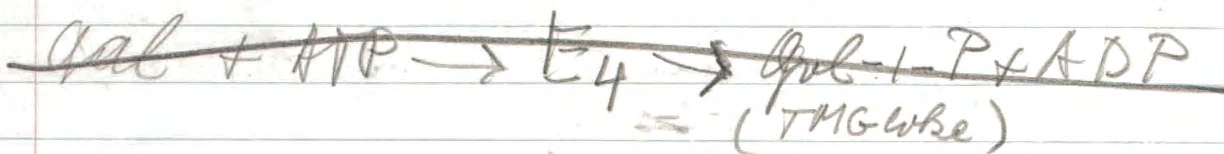
Do we get anamnestic reaction if we first inject antibody (not antigen!)?

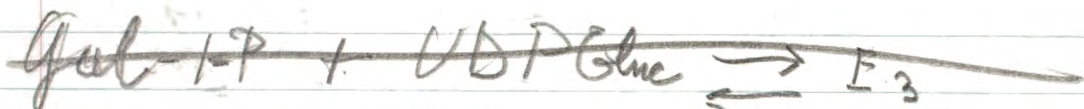
paragen

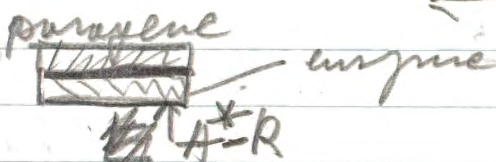
E

antigen

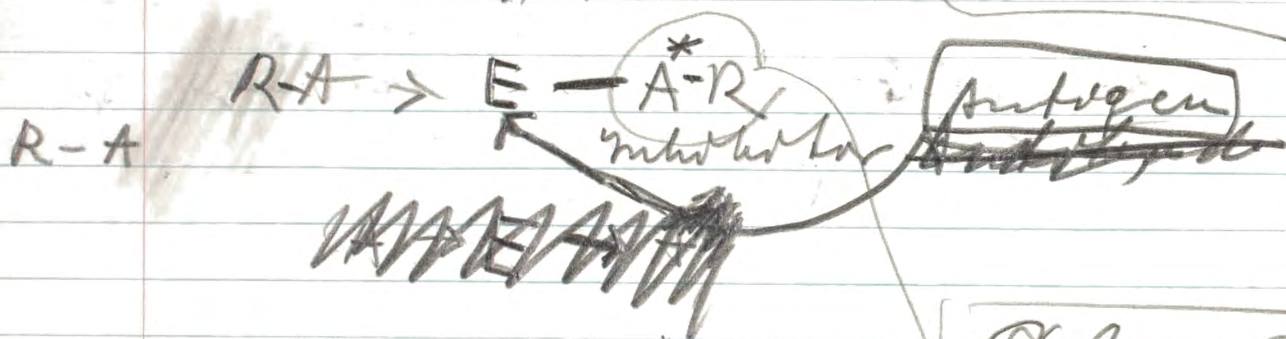
Hapten — R



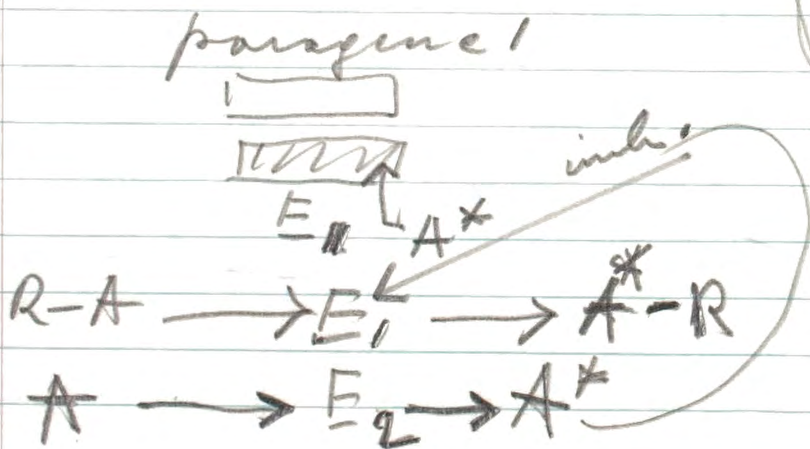




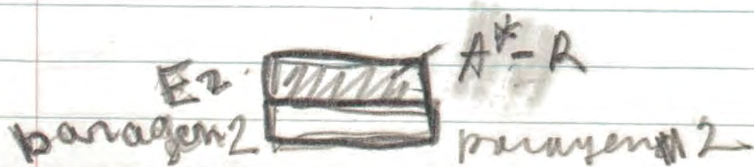
Scheme ①



Scheme ②



UDPA-R



Inhibitor Q

Unusual relationship H

TMG → 1.) combines with the enzyme E ~~[illegible]~~

2.) combines ~~with the pare-~~ paragenic ~~form~~ (Z)

competes with inhibitor Q — combines with Z* (...)

3.) combines with paragenic Z*

4. combines with enzyme Z*

got reduction (with TMG) in para ~~unusual~~ unusual Z

Gal + ATP $\xrightarrow{E_4}$ Gal-1-P + ADP $\underset{\leftarrow}{\overset{E_3}{\rightleftarrows}}$ UDPGal

TPG

UDPGal $\overset{E_2}{\rightleftarrows}$ UDPGluc + PP $\overset{E_1}{\rightleftarrows}$ UTP + Gluc-1-P

TMG Gal-1-P

R

P5

E_5 (β-galactosidase

UPDGal - R

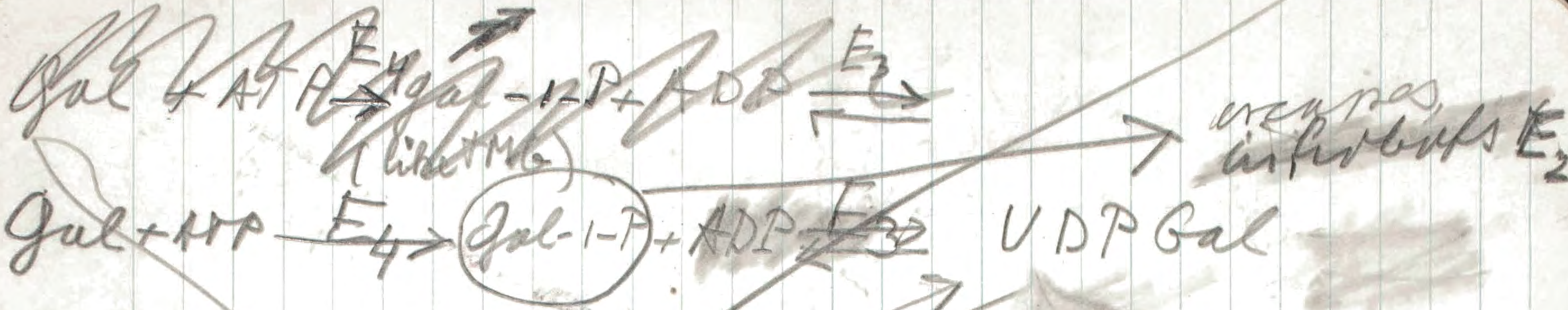
TMG, TPG,

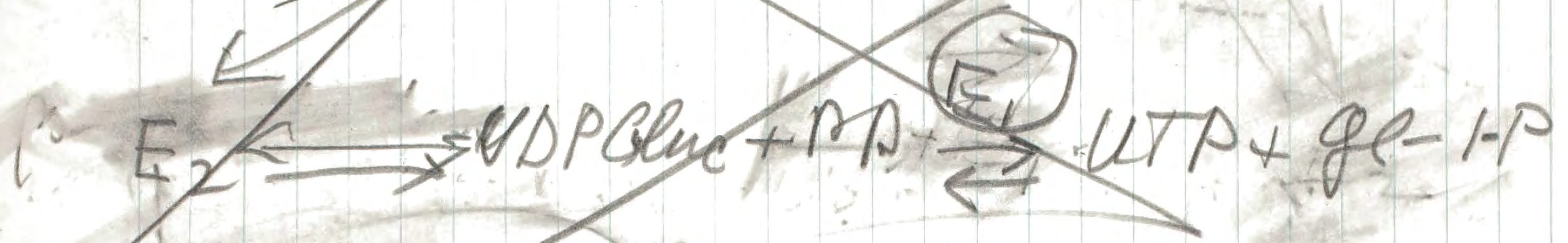
TPG

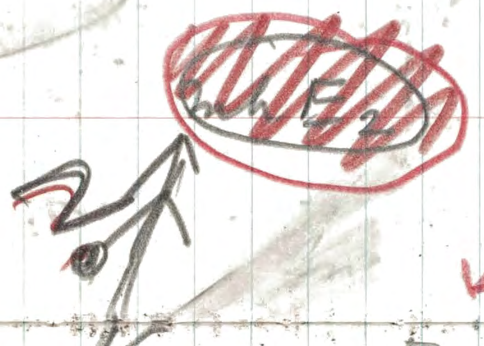
E_6

Polymer

paragen 5







If blocked here
galactose induces

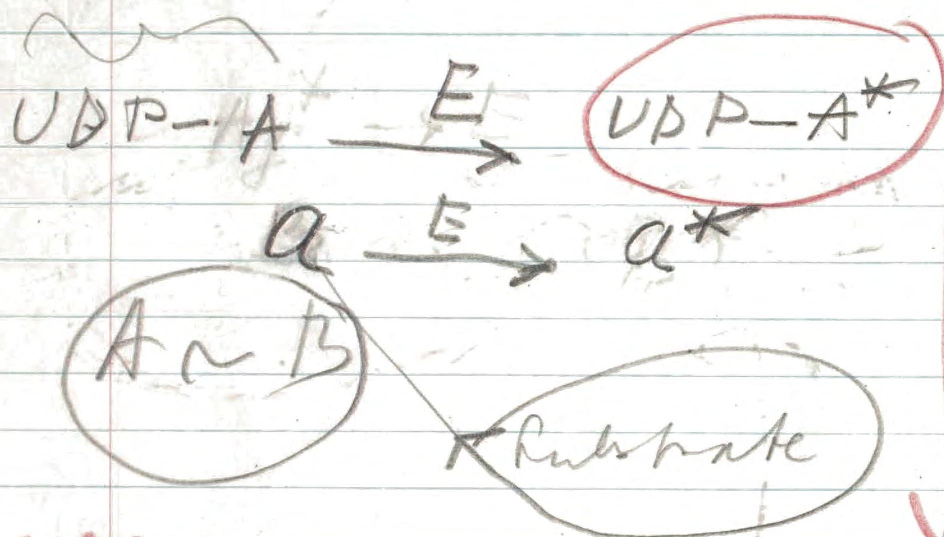
Adaptive enzymes:

Forget

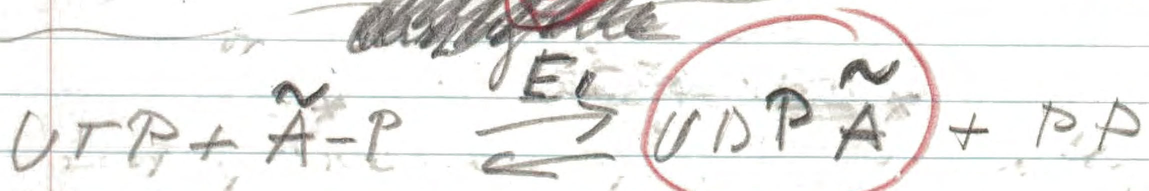
low conc.

$$UDP-A \xrightarrow{E} UDP-A^*$$ inhibitor

$$a \xrightarrow{E} a^*$$



Write for UDP = R

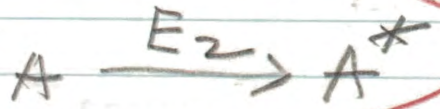


$$UTP + \tilde{A}-P \underset{}{\overset{E_1}{\rightleftharpoons}} UDP\tilde{A} + PP$$

$$A \xrightarrow{E_2} A^*$$

E_2 can be antibody

$\tilde{A}$ resembles A or A*



(H)

Antibody formation

Cell (1)

proenzyme

Antibody

$UDP-A_g^*$ —Antibody or other enzyme→ $UDP-A_g^{**}$

Cell 2

A_g

Chose feeding makes $UDP-A_g^*$ from hapten

I version

other enzyme

~~Antibody~~

$UTP + A_g^*-P$ ⇄ $UDPA_g^* + PP$

Ag

inhib

II reaction

II reaction (not analog to A.g.)

Gould

Antibody formation:

1) anamnestic response

cells which contain "antibody" are ~~an~~ or q stimulated to proliferate when "antigen" is given; these cells (increased in number) ~~later~~
can now make more antibody
when antigen tied up E, ,

2) ~~these phenomenon~~
young animals & abundant
production of ~~[illegible]~~ quasi-hapten — cells produce "antibody" purposely to exclusion of all other proteins and are destroyed.

3) these phenomenon when hapten is fed | in which
is made purposely | correct
ties up pyrogens permanently.
If a non immune lymphoblast is transplanted one again can get sensitivity / death with (?)

Question
Does T.P.G. show
growth in agytic (in wild
type)
Wolt says no!

---

4) Wolt says:
Loran - Medawar
Take spleen cell from ~~from~~
immunized animal (cell should
make antibody) ~~transfer~~
transferred to newborn - no
antibody is produced (check)

Adaptive enzymes: Gorini
Werner says there are cases:
When "Arginine" (Not really arginine)
does not push enzyme level
below wild type but enzyme
level shoots up if ~~mutant~~
~~grows on~~ auxotroph grows
and exhausts growth factor.
If all Arginine has to be made
and of enzyme making it is satura-
P.T.O.

continued:
at [illegible] "arginine" level of work
type then this is to be expected.

When ~~[illegible]~~ cistrons get separated
and cooperate; one makes the
"enzyme" which makes says "arginine",
the other makes ~~a~~ ~~[illegible]~~
~~compound that~~ an enzyme ~~that~~
catalyses the coupling of ~~[illegible]~~
~~[illegible]~~ ~~of~~ which make an
arginine analog which interferes
the enzyme that couples
the "arginine" with ~~[illegible]~~ UDP
that is in another gene

Charles Yanofsky Western Reserve
p. 147 Enzymes Units of Biol
neurospora Structure & Function
Indole + L Serine + pyridoxal phosphate → L Tryptophane

td₂₄ a temp. sens. mutant
is the enzyme in vitro temp. sens. ?

write ~~that~~ UDP = R

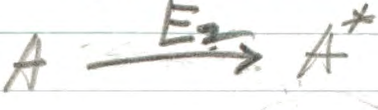
$UTP + \tilde{A} - P \xrightarrow{E_1} UDP\tilde{A} + PP$ ~~prep fat~~ theory

~~[illegible]~~ TH-protein or in case of enzyme synthesis (H)

$A \xrightarrow{E_2} A^*$

$A = A^* \propto \tilde{A}$

write for $\tilde{A}$ $\tilde{H}$ for antigen H-Protein for hapten H



$UDP\tilde{A}$

All within one cell, no diffusion of $UDP\tilde{H}$ from cell to cell.

~~[illegible]~~ Table from [illegible]

Table IV	Konst (10^{-4} M)	ratio
~~[illegible]~~ TMG	120	(1)
PTG	10	12
Pollys Thiogal.	0.15	800
TDG	160	0.8

?

Adaptive enzymes

Seymour Cohen [Mil's idea]

15T⁻ mutant

~~amine UDP cytosine ... controls~~

~~Thymine synthesis / ...~~

This cell does not ~~make~~ ~~...~~ thymine

but if infected with T2, T4, or T6

it does. — T2 etc. does not make

cytosine it make hydroxymethyl

of cytosine. If UDP-cytosine

~~...~~ represses enzyme formation

(~~the~~ an enzyme which ~~makes~~ is involved in thymine

synthesis) or just inhibits such

an enzyme we have explained

this. —

Adult Breeding (Amsst)

Yanofsky. Assume Good

~~If~~ the gene make tryptophane synthase I and adjacent ~~gene~~ enzyme II which complexes tryptophane w UDP

Now assume further II is super efficient in mutant and makes UDP tryptophan very fast & depending on the mutant one or another tryptophane analog is needed to inhibit it! Hence the different suppressors for the different mutant!

There is ~~not~~ no suppressor for ~~td~~ td$_{24}$ which is temp.

Somehow: There should be no suppressors for temp sensitive enzymes! Each mutation in this case is a genuine back mutation.—

Read Crum's paper

~~Important for Talmage theory: young animal must not be like X-rayed animal~~

~~assumption in young animal some co-factor missing. When antigen is given it is taken up by cells. Antibody is required = co-factor ~~[illegible]~~ missing cell makes lots of poly-peptide which does not roll up and destroys cell~~ Good

Ed Lord Theory

correction young animal can couple UDP to any Hapten. Real Hapten UDP couples with pyrogen-enzyme forever.

Antibody is formed only after ~~enzymes which make UDPA diminish in number.~~ ~~cells are~~ or after conc. of ~~[illegible]~~ UTP in cell falls.

Somehow young animal can detach Hapten

Say 100,000 (poor) Haptens made

and " γ-globulins

Control for Sz. (H)

antibody:

Isogenic mice: if one mouse given antigen and then lymphoblasts is transferred to another mouse — if pseudohaptens can freely diffuse — it should not keep on making fresh antibody. — [what about facts relating to Rabbits?]

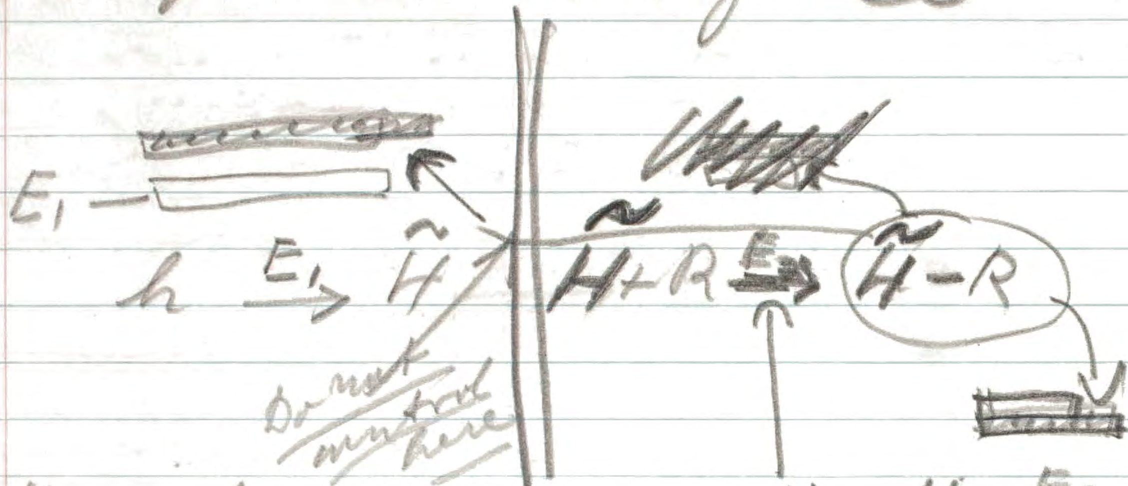
see Harris & Harris
Fed. Proc., 10. 409. 1951
also Harris, Harris and Farber
J. Immunology 72:148 1954
T. N. Harris Philadelphia Penna

Terminology

A = Pseudo hapten = $\tilde{H}$
[illegible] gen: H-Protein

[illegible] theory:
assumption UDP-$\tilde{H}$ does not diffuse from cell to cell!

Adaptive enzymes



Essential enzymes H $H_1 \xrightarrow{E_3} H_2$

Acetyl ornithine $\xrightarrow{E_4}$ O $\xrightarrow{E_r}$ C → E_r ~~[illegible]~~ Arg

Acetyl O $\xrightarrow{E}$ orn → citr. → A

Conceivable: R + A → E_R → ~~[illegible]~~ RA

A-PO_4 + UTP = UDP-A + PP

If E_R saturated

~~Question does Phenyl ethyl TG~~

slow growth of coli?

UDPH

~~paragen 50000 paragenes~~ 4

of 100000 ~~paralustrogens~~ made

50,000 but very well ~~and these~~

50,000 paragens therefore

became permanently inactive

antigen production by remaining

50 000 paragenes is inhibited

by deadly getting ~~Haptens~~

remaining UDP-Haptens —

Suspension X-rayed Rabbit

does not phagocytise antigen

well.

~~Question~~ Expo: Young animal

— would yeast extract enable it

to make antibody? should not!

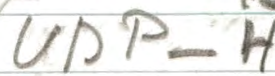
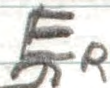
Bernet point mutation!!

X-rays on Tr should be

tried!!

Antigen

coupling Enzy.

$\tilde{H}+R \rightarrow \tilde{H}-R$ ⟷ UDP–$\tilde{H}$

E_R

paragen

E (antibody)

H–Pr. = antigen

Embryo

If Hapten is fed

H–R inhibits

irreversibly with paragen–protein complex

Adaptive enzyme

$\tilde{H}+R \xrightarrow{E_R} \tilde{H}-R$

antiferred. Substrate

$H_1 \xrightarrow{E} H_2$

$\tilde{H}+R \xrightarrow{E = E_R} H-R$

The $E_r = E$

UDP Gal is ~~not~~ probably inhibitor
of Z for Lactose does not
inhibit synthesis of
enzyme though it produces
~~Gal and~~ galactose and
glucose.

D methyl thio gal has sensitive
affinity for enzyme Z it
should induce and slow growth;
does it? If it does not
induce we are in trouble and
would say then UDP gal is
inhibitor.

and amino acid something
higher than (AA + B)
becomes low and ~~enzy~~
enzyme shoot up.

~~Amper~~

uracil

C – C – C – C – C – O – P(=O)(OH) – O – P(=O)(OH) – O – Gal.

~~[illegible]~~

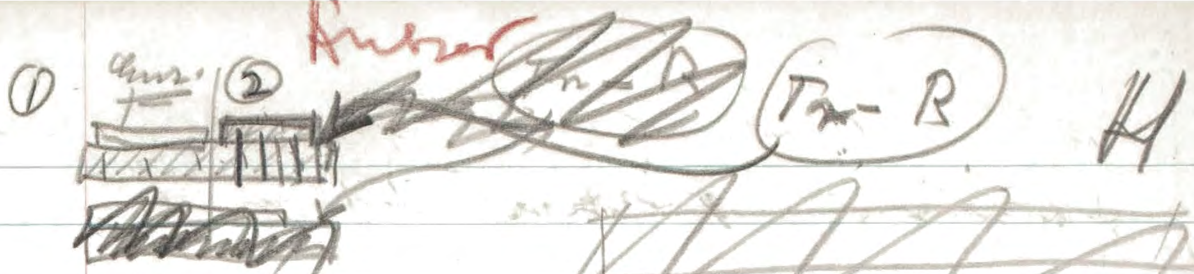
acid anhydride

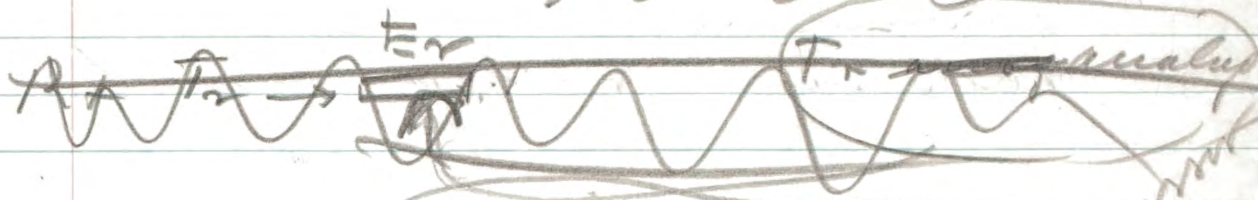
C – C – C – C – C – O – P(=O)(OH) – O – C(=O) – CH(NH_2)R

ATP + Aminoacid $\xrightarrow{E}$ AP-Aminoacid + PP

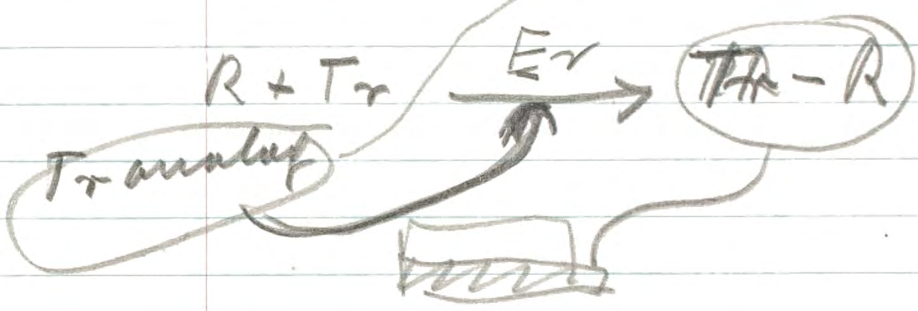
A = adenosine

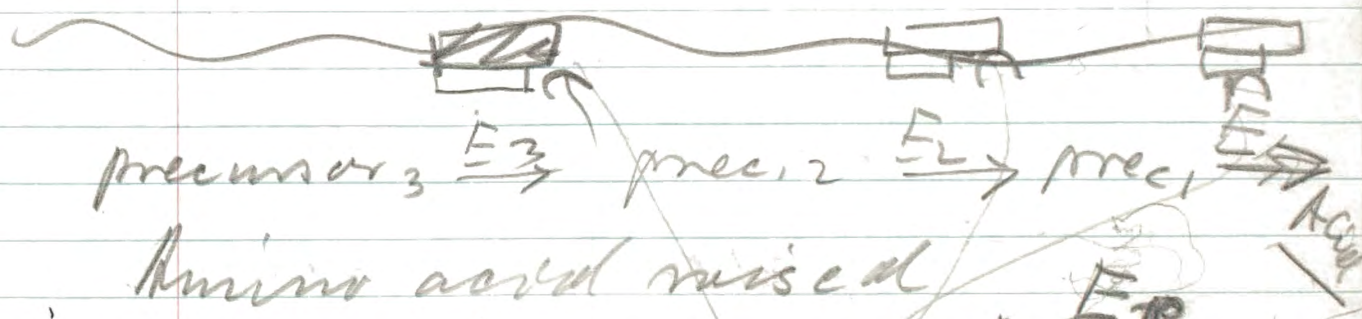
Adenylaminoacid

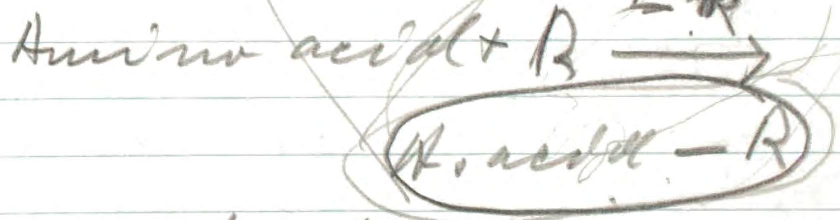




made by suppressor gene







If Er is saturated in growth on minimal med. no repression of enzyme in Amino acid added

But if mutant used that requires amino-acid

an inhibitor for [illegible] of growth ~~[illegible] product~~ (because no [illegible] is made
Further:
~~[illegible]~~
~~When [illegible]~~
When Lac$_4^-$ grows on inositate TPG must inhibit growth,
~~[illegible]~~

Antibody formation
Tolerance
Hapten does not destroy [illegible]

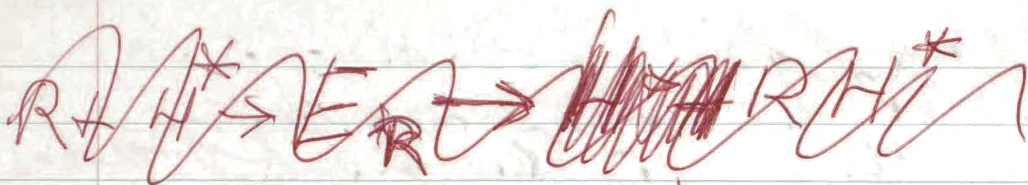
Hapten*(H*) represses
but if antigen penetrates to [illegible] [young animals] it [illegible] permanently perhaps also [illegible] [illegible].
Similarly in those phenomenon where a hapten capable of attachment to protein [illegible] is fed and diffuses into [illegible] containing

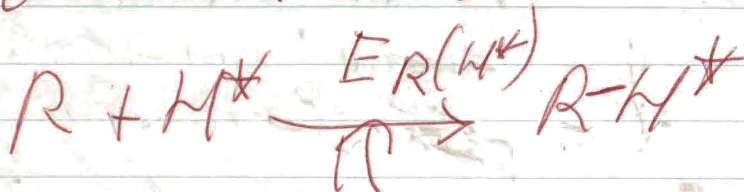
To Wollf:
Galactose inhibition [illegible]
of enzyme ~~[illegible]~~ must be overcome
with TMG! Is it true?

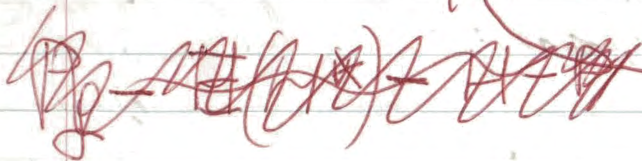
We are in trouble with [illegible]

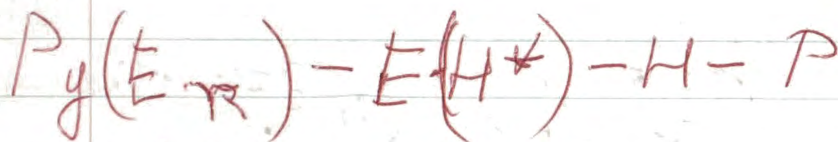
Inductivity is temp. sensitive
[Is the enzyme temp. sens.?] and
yet has suppressor (O.K.) Temp
sensitive only in sense that
it grows faster at higher
Temp and is inefficient.
Suppressor only increases amount!

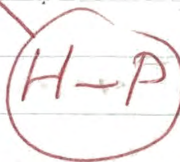
To Wollf:
If Lac_4^- can grow at all in the
absence of any Z, then wall must
be made also from Gal-1-PO_4
this is the escape ~~[illegible]~~ needed. —
I predict when (not leaky) [illegible] on Galactose
(inhibitory) ~~[illegible]~~ TPG must be

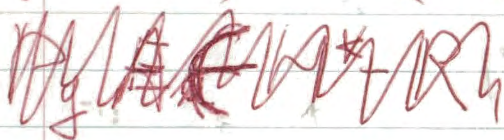



R + H* → R-H*
E_R(H*)




P_y(E_R) - E(H*) - H - P


H-P



the

paragen-this it can attach itself there to a protein or readily and form a H-P complex and combine ~~with P_g-E~~ to form a

$P_g - E_a - HP_r$ complex tying up paragen. —

Anamnestic Response mechanisms of H*

$P_g(H^*) - E_R - H-P_r$ tied up reduces ~~[illegible]~~ rate at which hence forth $E_r(H^*)$ is made. Hence anamnestic response! —

$E(H^*) \longrightarrow$ (H-R-H*)

H^*

(Pr-H) also

~~paragen E(H*)~~

~~paragen [E(H)] — A~~

E(H*) paragen — E(H*) — (H-Pr)

Good

(Pr-H) — E(H*) — Paragen for E(H*)

assume limiting factor is supply of H^*

~~E(H*) → (R-H*)~~

better! $R + H^* \xrightarrow{E(H^*)}$ (R-H*)

(Pr-H) also (Pr-H) — E(H*) - Paragen for E(H*)

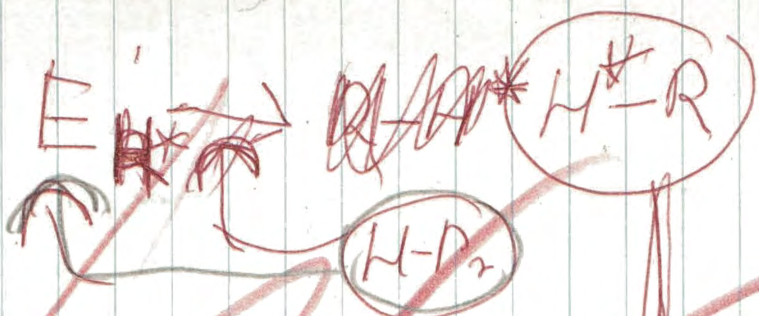
(R-H*) → E(H*) - P

(R-H*) ⟶ A(H) - Paragen for A(H)

Microsomes for E(H*) antigen can penetrate

Microsomes for A(H) <

6 weeks for secondary



Pg(A_H) — A_H

Pg(EH*) — (H-Pr)

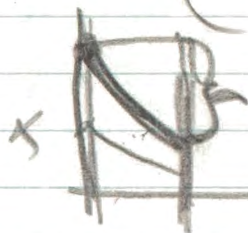
when a fixed low level is reached anti-
body ~~also~~ formation which was repressed by
R-H* begins.

Now antigen is administered and E is formed again
~~[illegible]~~ within weeks ~~[illegible]~~ the level of E again
approaches zero; now R-H* is then abundantly made and antibody
saturates ~~[illegible]~~ at a lower than the initial
level. — The corresponding ~~[illegible]~~ new level of R-H* is also lower than initially. If we
now inject antigen again the level of R-H*
falls again but since it starts from a lower
level it reaches quicker the dotted
line

However E

Degradation for (R-H*)

$$\frac{dX}{dt} = e\frac{K_S}{K_S + A} - \alpha X$$



free energy ~~potential~~

$$e^* = e\frac{K_S}{K_S + S}$$ (large small when time short light)

$S = A$

secondary 20–100 good
time is higher than
primary but ratio of
before and after is probably
much smaller for secondary
response —

E(H*) ~~remains~~ remains inhibited until antibody
appears. — When antibody
appears depends on rate of
decay of (R-H*)

Explain why ~~[illegible]~~ secondary
response comes faster.

adult

R-H*≠A-T(A)

(Prot-H) (Prot-H)

embryo

Prot-H = A = T

Tolerance

embedded within a structure

half life time of R-H* is days

halflife time of E is weeks

Phenomena

~~when~~ antigen is added for the first time after ~~some day~~ a certain number of days antibody appears and antigen is then eliminated. If weeks later antigen is injected again after a smaller number of days than before antibody appears and antibody is made at a 20 to 100 times higher rate than before.

P.T.O. Below

Before the first injection there was a certain level of R-H*; after the injection (if enough antigen is inj.) ~~rate of~~ production ~~[illegible]~~ stops and R-H* level decays exponentially

~~$R + H^* \xrightarrow{E} R\text{-}H^*$ — repressor~~

~~membrane (adult)~~

~~$R\text{-}H^* \sim A - T(A)$~~

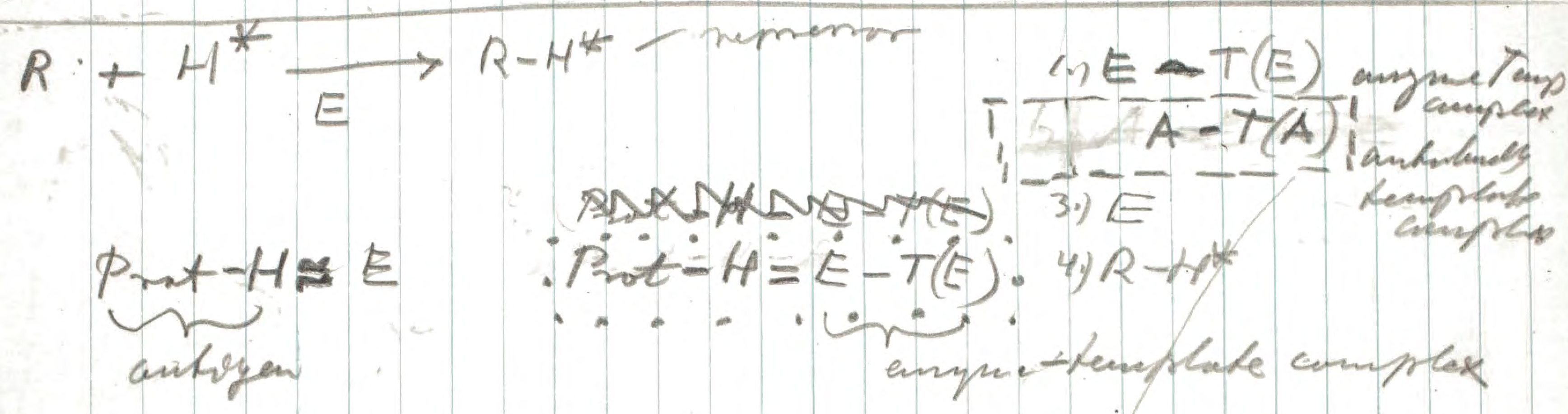
~~Prot-H~~

~~Prot-H = E — T(E)~~

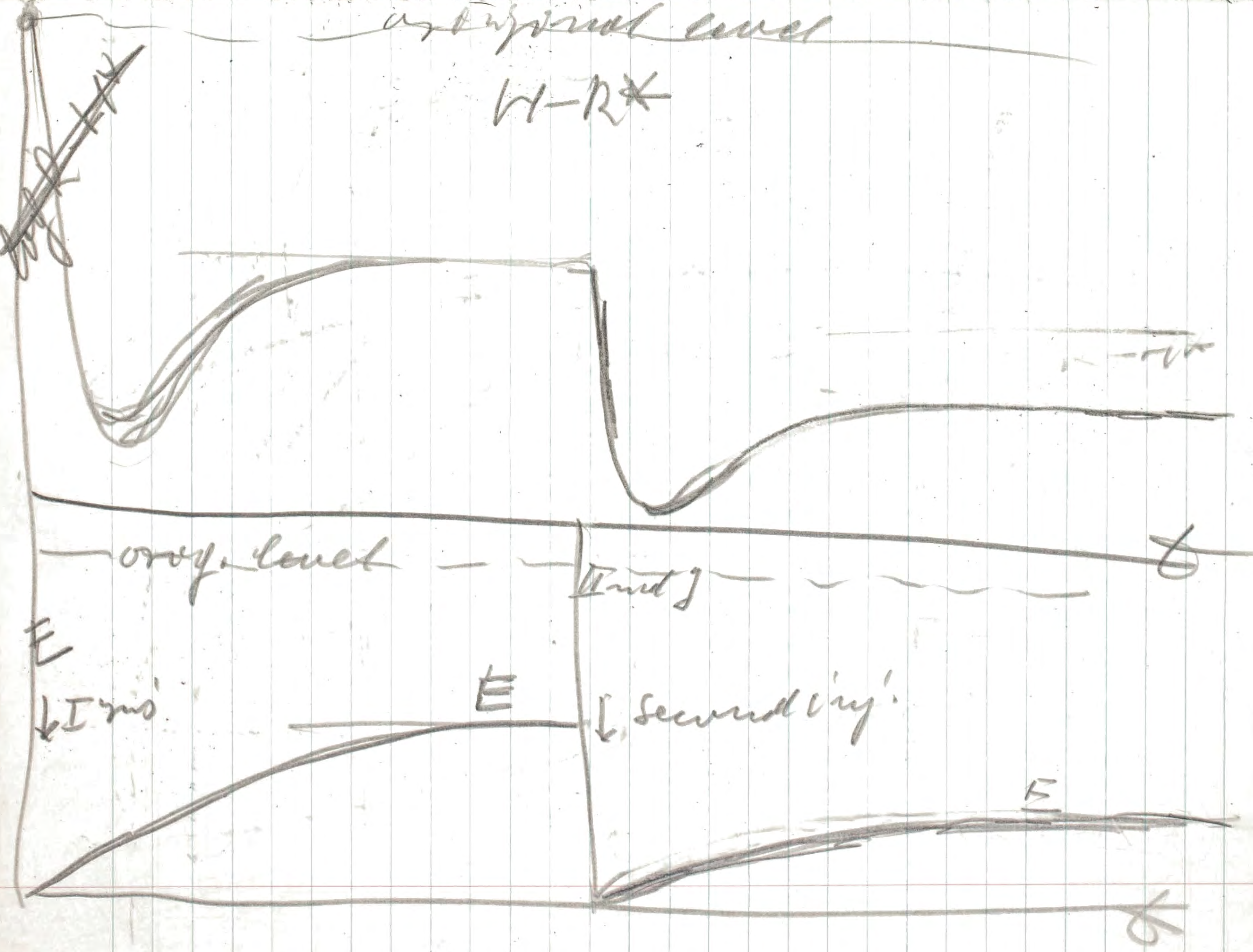
~~$R\text{-}H^* \sim E - T(E)$~~

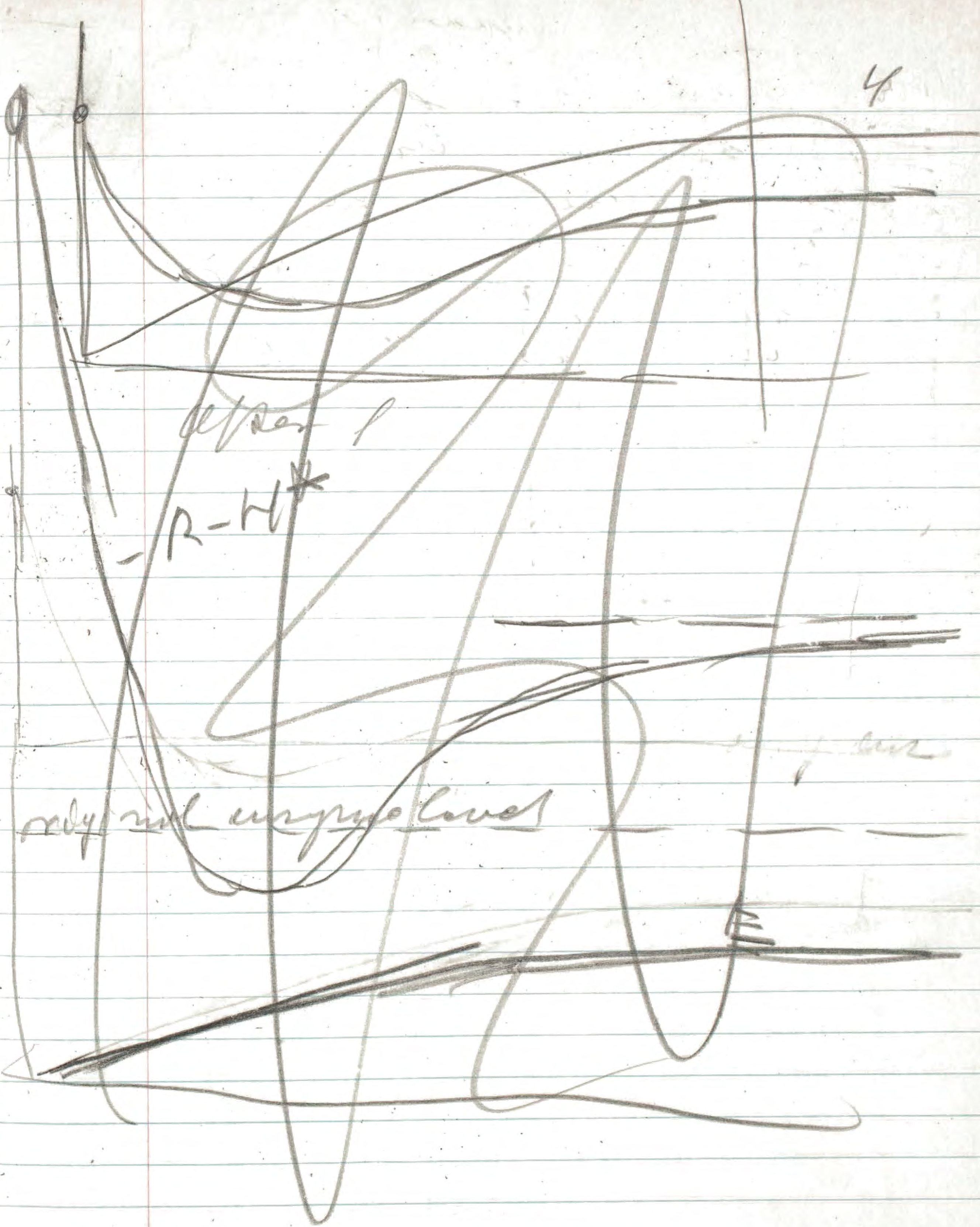
~~? (?)~~

~~antigen~~



unidentified structures in the cell or prot-ly membrane


H-R*
orig. level
E
E
E


-R-H*

(Quad?)

Now we understand why a hapten (i.e.) compound which is antigenic when coupled to a protein is in itself not an antigen. It must dissociate off from E and E-T(E)!

$\text{conc}(R - Rt) = X$

$$\begin{cases} \frac{dx}{dt} = -\alpha x + \lambda E \\ E = E_2 (1 - e^{-\beta t}) \end{cases}$$

$x = \frac{\lambda E_1}{\alpha}$ first $t = 0$

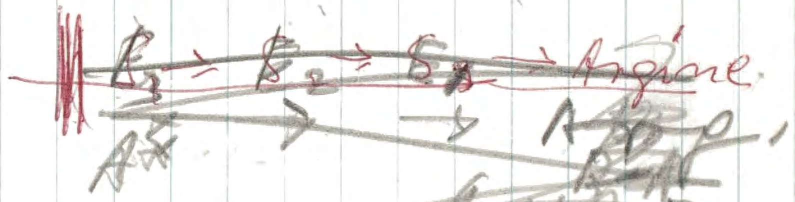
$\alpha = 10\beta$

$E_2 = \frac{1}{2} E_1$

General

Those which ~~hydrolyze~~ which react ~~to~~ together ~~complex~~ to any small proteins ~~or large polypeptides, or large~~ plus couple can penetrate the membrane or which can first penetrate the membrane and once inside can couple to ~~small~~ a protein forming an antigen inside the membrane.—

Question what is turnover number of Shorter enzymes? Ask Talbot



3.) $S_3 \rightarrow S_2^* \rightarrow S_0^*$ i
$E_2 \quad E_1$

$S_1 \xrightarrow{E_2} S_2$

E_1

$S_1^* + R \xrightarrow{E_R} S_0^* - R$ repressor

repressor because:

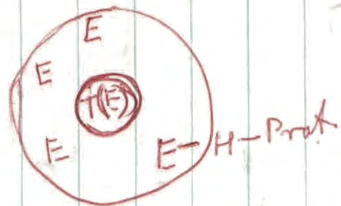
$T(E_2) - E_2 - S_0 - R$

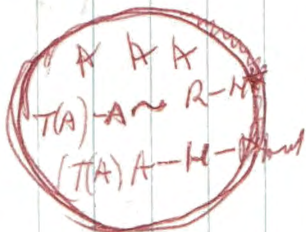
$S_3 \xrightarrow{E_2} S_2 \qquad S_2 \rightarrow E_1$

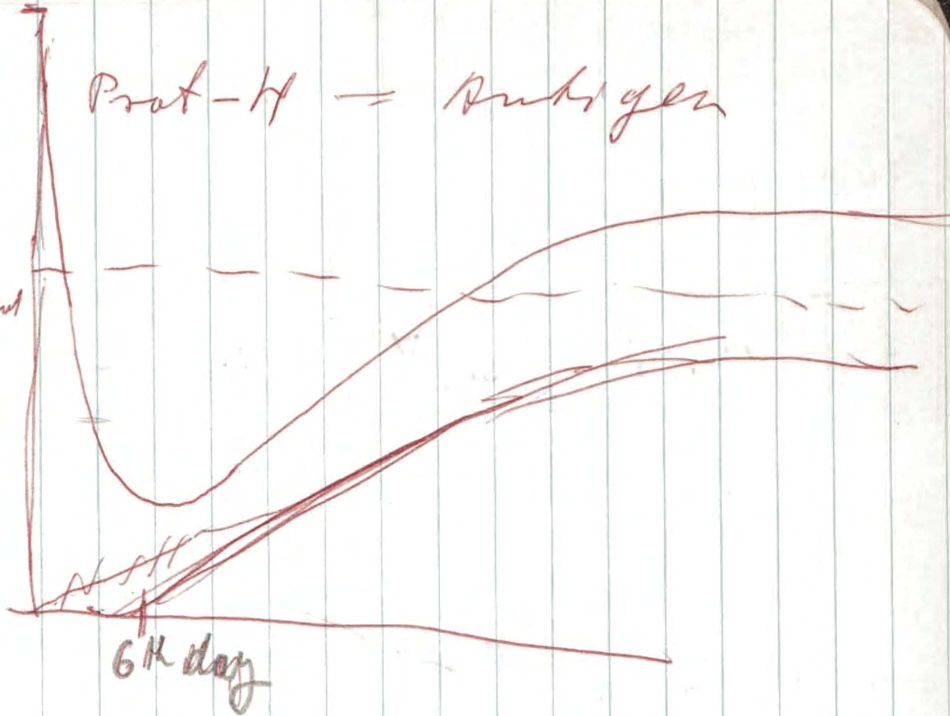
(3a) $S_2^* \xrightarrow{E_1} S_1^* \xrightarrow{E} S^*$ $\qquad S_2^* + R \xrightarrow{E_R} S^* - R \qquad T(E) - E \doteq S - R$

$S_2 \xrightarrow{E_1} S_1$

Mult R-H' —E→ R-H*

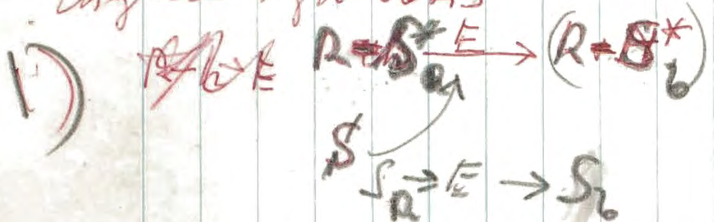






T(E)-E-H-R

Mult says Lac 4 — permease is induced by Lactose
understandable of UDPGal is inhibitor and 4
indicates E2. Proof in this strain repressor increase slows growth. —
Enzyme synthesis



R-S* repressor of enzyme E
T(E)-E-S*-R
supply of R-S* is limited

Adaptive Enzyme

favourable scheme

$R-S_1^* \xrightarrow{E} R-S^*$

~~[struck-out scheme]~~

$R-S^*-E-T(E)$

~~$T(E)-E-S$~~

$S_1 \xrightarrow{E} S'$

Strong affinity than turnover

Immunity Story

must have ~~[illegible]~~ too much repressed by S-R

unique

not adjacent

$S_1 \xrightarrow{E} S$ | $S+R \xrightarrow{E_R} S-R$

S^*

$T_E-E-(S-R)$

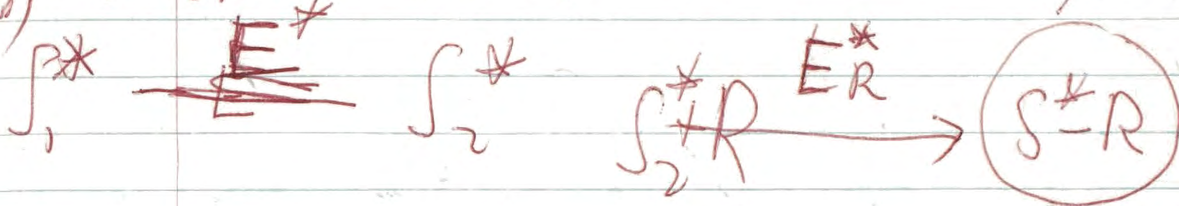
$T(E_R)-E_R-(S-R)$

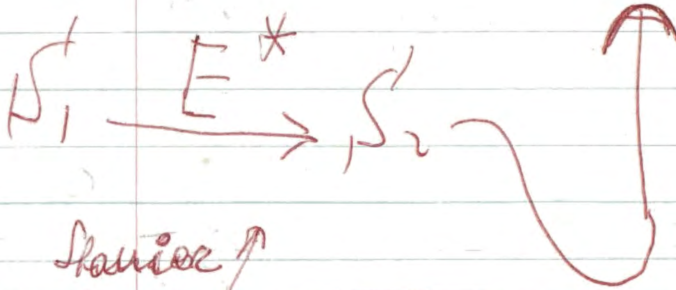
foreign gene makes S^* inhibitor of E_R

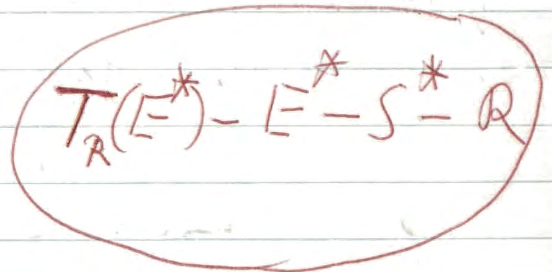
out of S'

Adaptive enzyme ?
continued

1°)

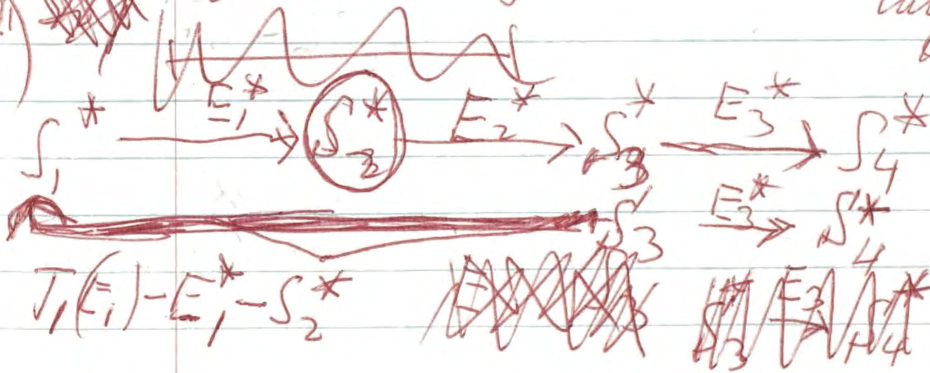






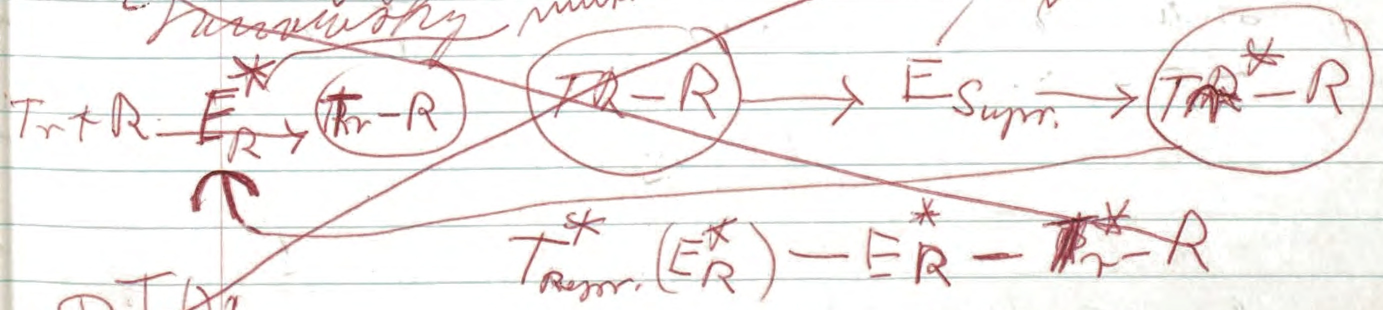
Slower ↑

2°)



Concept:
Dispensable meta-
bolite
(must slow
growth if
repressed

Vanovsky mutants



P.T.O.

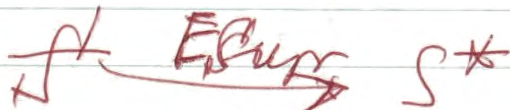
Adaptive enzymes || Jrancy
Ireproofosphy || $T_r^* = S^*$
$T_r \neq S'$

~~A A A*~~ Analog to S_1^{**} is substrate
Please note

E Supr. is controlled
~~by normal repressor~~
~~or mutated~~ Repressor metabolite

$$T(E^*_{Supr}) - E_{Supr} = (T_r - R)$$

~~[illegible]~~
assume now E_R^* back mutates to
E_R then E Supr becomes useless
but introduces
Good // Now: Adaptive Enzymes à
la Spanier
Substrate S analog to T_r or T_r^*

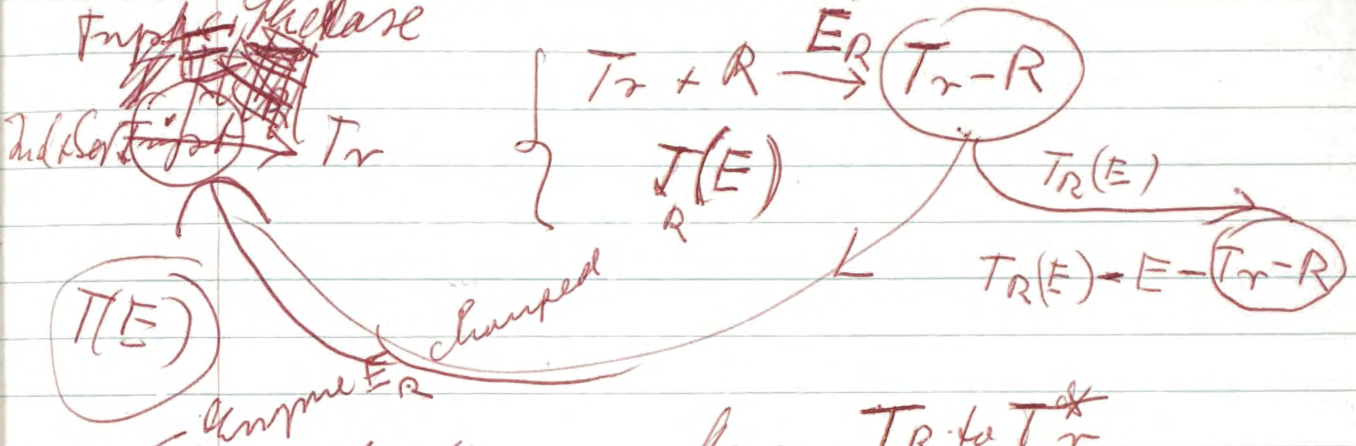


$$S \xrightarrow{E_{Supr}} S^*$$

and S will block E_R or E_R^*
thus reduce repressor and increase
conc. of E Supressor

Immunology continued; Good 41

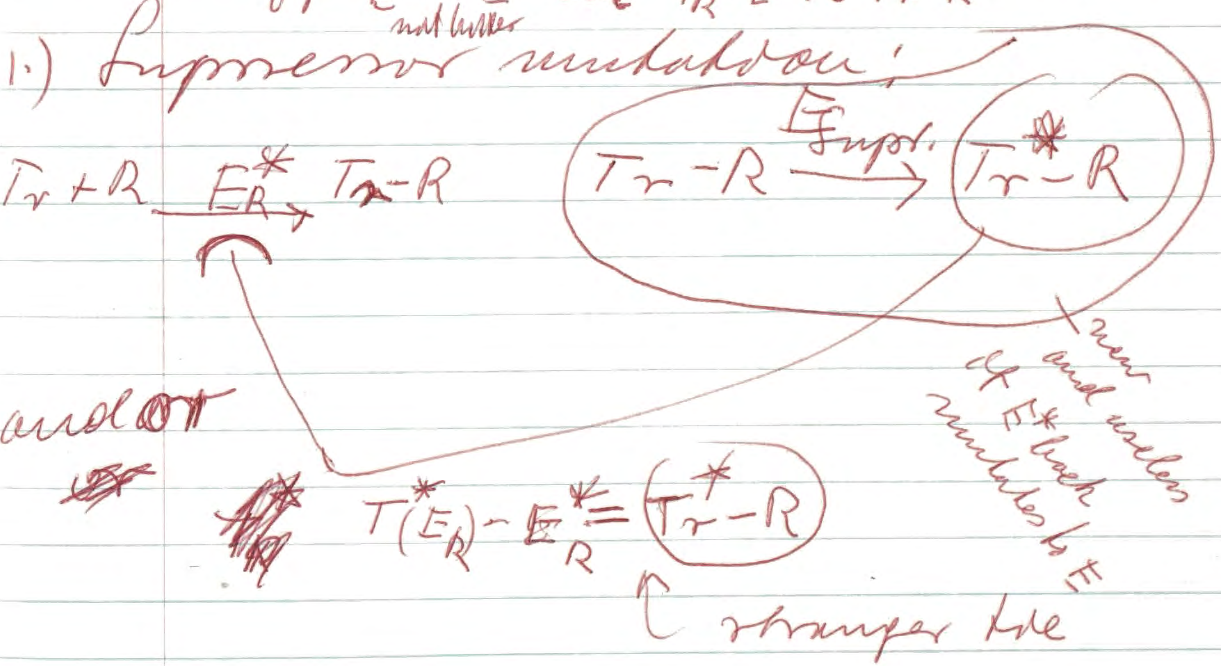
Prior to mutation:



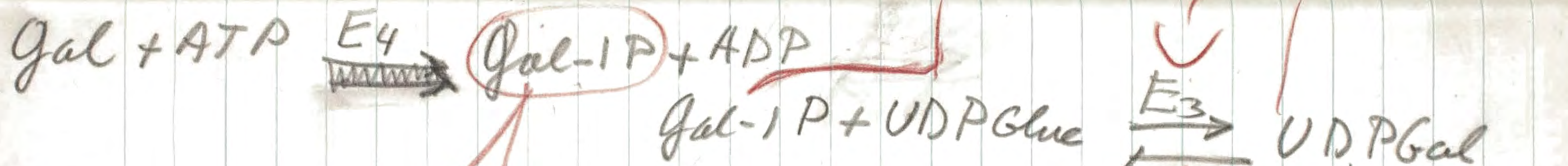
1.) Mutation: from T_R to T_r^*

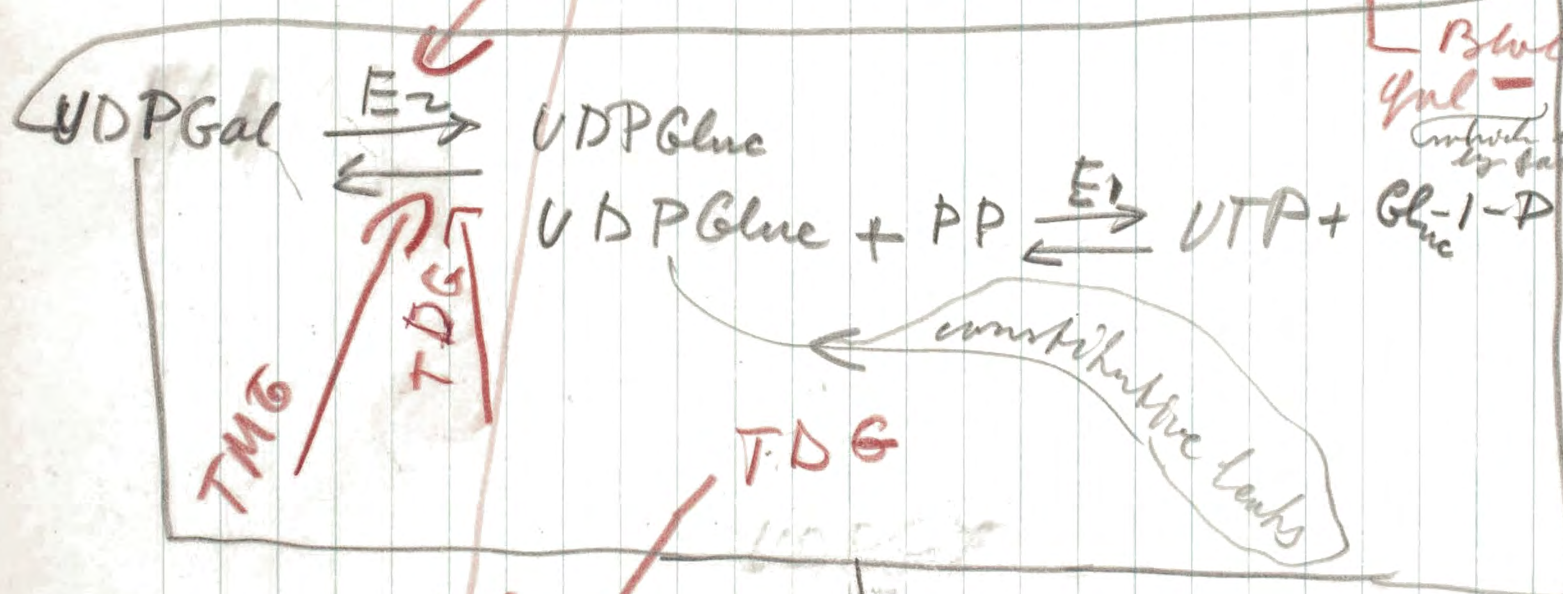
$E_R^* \geq E_R$ or more $T_r + R \xrightarrow{E_R^*} (T_r - R)$

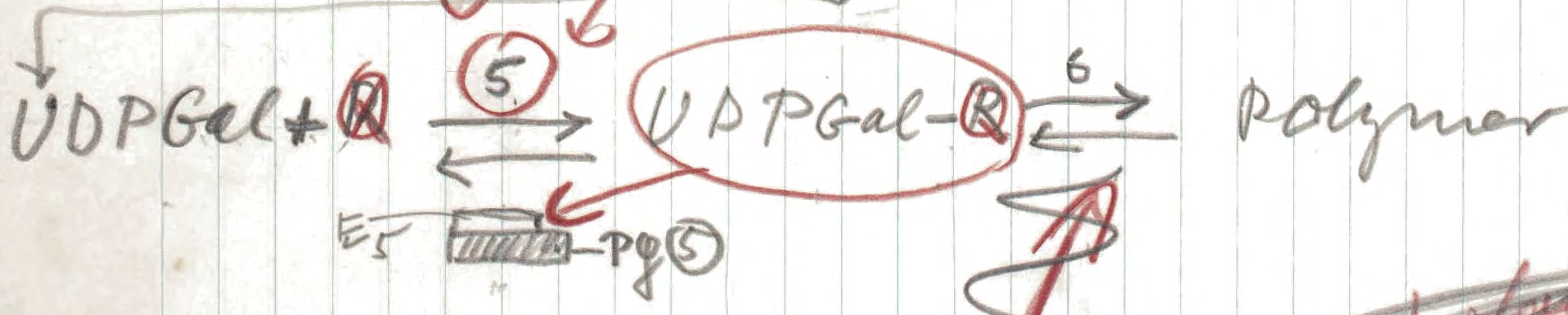
or $E^* \approx E$ (not better) but $T_R^* - E^* \sim T_r - R$



These could be of course for each different E^* different T^*







albert Dorfmann

Must ask how Lax places that galactose induces first two enzymes & induces E_3 even if E_4 defective. —

[Inducible constitution

Very strong constitution should be slow growers. In two chemostat mixture of const and wild type const should leak out

TPG Must does not enhance enzyme in apparatus induced by TMG

TPG must slow growth on galactose!

MK3 in background here

escape 2,TPG

Lou

Spiegelman

Mortimer

Ben - Rey 47902

253

253

Mabel Alexander
53555

53364

1130
VERNON ROYAL LINE
U. S. A