Review wheel of science and pathway of discovery in light of my own history. (How questions arise? Resources to answer.) 8/4/89

T/9

bacterial sex.

B+T → FSR idea of biochemistry

Avery — cure as a chemical. bacteria as tool.

! Transform Neurospora. Convergence of ideas

(a) opportunity of technique ⟷ 1) answer an outst. question

! Δ prior 2) open a field

Didn't work — reversions.

— validate method

Discover new question

Try it!

Worked.

Exploitation! Conjugal mechanisms

map + linkage — ie "genes in bacteria"

physiol genetics. genes → enzymes.

Get a lot of mutants.

What's wrong.

Salmonella.

Theoretical background. prior to expt.
E coli × ; K-W schema.
Salmonella ~ Enterobact., medically important
had developed mutants.
Idea of heterothallism: ∴ different strains. Lilleengen

Rigid cancer of a b × cd.
eventually worked.
FA! L-form side track. (Dienes ...)
Question: What was FA. conditions of prod: reduced by phage.
? HT-E first to suggest it?
(? Boyd's phages
re lysogens?

It's phage! ⟶ Idea of transduction.

□ - verify gene transfer.
- preferred crossing for genetic analyses.

Exploit. Understood K-W. / collab. c Edwards.
analyze H_1-H_2

accidental. - trails - BADS noted & guessed.
meticulous pedigrees (? Demerec ab. transd.
dates?
∘ details from BADS.

Exploitation. (p 21) Extract + characterize enzyme. Canonical.

Discoveries - found Cryptic - Hyps - [permeability ? to substrate ? to ions ? or internal organiz.

→ Na^+/K^+ any doc. why find?

Did I Tostoney other metal regs?

Baseline! — [internal indum

Needed better assay. NO2 & phosph. hydrolase assay.
mobilize KPLink; Siedmus - where?
Rosemon. — "

Other lac work. method Intersection of mutants (+ reversions)
indurus
substrates.

many other projects.
chemistry bounded
small group; no facilities
cadged samples - Pigeon, Stodola.
read all possible on sugar chemistry.

Needed mutants → EMB medium. (knew Salmonella = lac⁻ EMB used in)
TZ. surprise pH - sens.

observed sectoring → indirect effect? (Auerbach).

Exobiol.

All theory, but...

Mars since < 1938. Astronomy + cosmology >> most biologists

1957 - Sputnik + Haldane. (model of nuclear energy for war or peace).

Social-scientific nexus

few other scientists would forecast such prompt t'l expansion. Planets < US tried launched a satellite?

Political threat is that vacuum.

quarantine policy. + positive planning to include science instrumentation. → our lab

→ computers

theoretical planning for Mars missions

microhabitat theory of Mars

Dendral. computer as a tool. How exploit it.

(a) Discovery that molecules
are graphs
no developed theory

?? How apply computers in novel way to science. What they're good for.

mol. compositions → mol. graphs
(I'd known of Wiswesser. when?)
Heuze + Blau.

Designing algorithms for mol. comp.
"Immersion" — can I improve on that description?

graph theory development? ← learn published out.
(computer impl.)

Skepticism about AI.

° Can these retrospective models be substantiated?
fraction

Biography.

Still learning method. Contra Jacob
collecting data.

Discomfort was a problem. | ~1973 – Reply to Stent, Wyatt
re Avery.
1974 – CASBS
1975 – Tatum

began to see how unique archival resources
+ own memory.

Bio Hy.

half hearted. Pete Farley turned me off.
I didn't want to be swallowed by my own company.

More precisions that nit-grit.

and in all of above (and more) spread too thin for max impact in any 1 area. But that may still be best marginal value (as long as I can take the heat).

Repl-pt / Ind. sel.

Methodol need for gamening mutants.
Introspection of closed models. → use velvet.

→ indirect solution

→ do it in tubes!

- interest in application of science.
- Science as way of life — religious intensity — curiosity
- Method: abstraction or quantization: ~~[illegible]~~ wire bunch → velvet → tubes
- Ring all the changes (E.G. what other styles are possible? of AHK F Jacob.
- The systematic scan. — see Syrics of life.
- Go for broke. No inhibitions about silly or offbeat or prophetic extrapolation. Start things. Ask what questions are important? Then feasible?
- Learn everything possible about (a) new fields → spread too thin
- Intrudes planning convergence. post 1959 more behav. sci
- "formal proofs" see style of { p80, p79, p60
- self-referential effect: applying method to this case
- revelation of method, not nec. planned
  Ask "what am I doing"
- Use of mnemonics — let problems summer. So many brewsatance
- ex tempore delivery. Discipline Stimulation of an audience. can't evade at here and now
- Combination of circumstance → what comes to my attention (Constant foraging) But rarely drop anything! plane trip; (cabin) ltd. distrax
- Introspection on method as method. Not always transparent to me how others differ
- what am I most uniquely qualified for. "Self" as instrument. { values: social ⋮

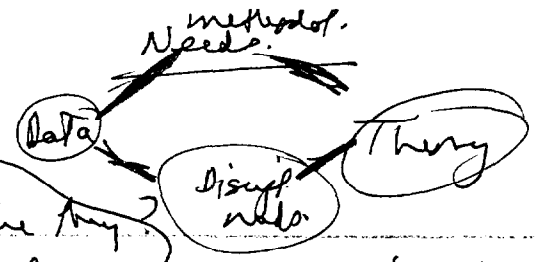
~~[illegible]~~

- who else has introspected on method? oo Bevridge → Altman
- How else could I write this? How would HAZ, Larry Holmes. ← who else is there?

and communication

E/K

penicillin



) L-forms – what are they?
generated by penicillin.

Social + Instrum. setting
Facilities
breadth + distr. of interests

) Penicillin lyses growing cells

) Weibull – sucrose stabilizes protoplasts.

~~Sy. penicillin method.~~

Needed selective method for anxotrophs
How do it?... Recall Gladys Hobby.

Are L-forms protoplasts?

(citations to Dienes
implications for w/o penicillin

Then methodical study (limited chemistry).

---

review what methods

involved much more chemical theory than used in lab.
No radioisotopes or chromatogr.
(Exptl. ingenuity – e.g. μ manip
V. limited lab chemistry

~~Limited managerial dim (sic!)~~

Strong theory, argument, broad knowledge
intuitions about organisms
Very strong theoretical background in biology, chemistry.
Moderate – – in physics, math.

EPM more than most biol + many chemists!

F, λ accidental discoveries
prompt analogies. → plasmid compts.

λgal. combo? of Morse. λdef. →.

outside
Field suddenly changed. Became competitive & crowded
special collaborations. (here, a few students). Still v. limited facilities*
Accumulation of knowledge – infinity of genetics
Broadening of interests: genetics as a mission.
→ somatic cells + immunology. (theor.)
→ exobiology
→ A.I.
→ algebra.

as part of method

→ Stanford. Mistake (?) to organize a dept: layer amis rather than focus my own lab.
*I didn't know to demand. Still very young! No role model for a lab head past brief experience c FJR. and not dominate a group.

v
all this
with HAZ

Socio historical circumstances.

Generational. b. 1925
precocious autodidact 1935 - 1941
Columbia College, Med School
V-12.

Jew 1st b. son orthodox rabbi.
immigrant from Israel. NYC advantages, Ryan
"objective" valuation of talent → opp'y to work
self-confidence
+ T'l optimism 1925-45. Power of science. Value of omniscience
Hitler + WW2
- escaped CP; most antisemitism: before reverse discrimination
+ 1948 - 1960. NIH, expansion of science, (e.g. Stanford)
+ Genesis of chemical biology: HG Wells reductionism.

why such a generalist? ① Science as a "religion" → scientific vocabulary. ② author of phrase
(Whitehead? Wells? Russell?)
② curiosity → integration
③ responsibility/guilt ... Jew, survivor. → applix.
④ self-confidence. Early success, parental + teacher esteem
No early trauma. Stresses only 1950's; 1961;
⑤ autodidact. Too "easy"