ETHICS FOR THE EDGE OF THE MAP OF THE WORLD:

Theories of Knowledge, Synthetic Biology, and The Questions of the Army Research and Development Board

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OUR SITUATION IS APORETIC

SYNTHETIC BIOLOGY IS A EPISTOMOLOGY

- Synthetic biology has captured the imagination and the anxieties of both the academic and popular imagination, for it seeks to rebuild and reengineer the world using the chemical pieces, or “biobricks” of DNA to make “useful” objects. While the project is intriguing at the basic science level, its power (and its danger) emerges from its claims to harness biology to make *de novo* creations. Synbio has a method and a pedagogy, and also a theory of knowledge, for it is heir to a tradition largely transmitted by engineering, and not biological science (which is itself a variant of natural philosophy).

- It is pragmatic in nature and phronetic in method, for its claim is that one learns what is true is by experimentation, intervention and alteration, by unmaking and making. The world is best understood as a sort of parts list and cells that are assembled in this way, it is imagined, are more stable, in a world more ordered than not. This idea—that the world can be understood by understanding its smallest ordered parts, is the first step in all industrial production. This sort of science has a telos suggested by the epistemic frame, yet, basic science at the limits of knowledge is far more aporetic that the theories of engineering suggest. By addressing the problem of unknowability in science, moral philosopher can raise inquiry about what ethical norms will be central to the next stage in the process of discovery in synthetic biology.

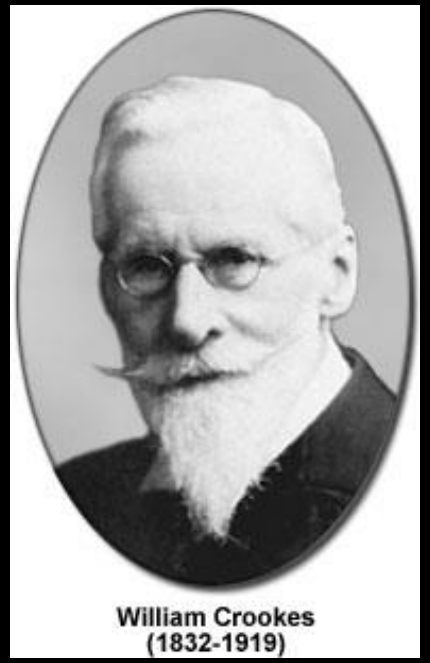
The claims are still largely speculative and the discuusion abouut what w
in a future still needs to proceed prior to discussions about products. Et
firsr about how a polity decides what is improtant about the future and th
of society we build.

TWO REAL STORIES WITHOUT ANY PROMISES OR WOOLY MAMMATHS

- What is the right act and what makes it so – the question of ethics– can be determined by norms and principles, or it can be surfaced by thoughtful consideration of canonical narratives.

- Three narratives of particular importance to the Army.

SIR CROOKE, INCOMING PRESIDENT BRITISH ACADEMY OF SCIENCE



1898, SIR WILLIAM CROOKES, FUTURE PRESIDENT OF BRITAIN'S ROYAL SOCIETY, WARNED:

- My chief subject is of interest to the whole world – to every race – to every human being. It is of urgent importance to-day, and it is a life and death question for generations to come. I mean the question of Food supply....England and all civilized nations are in deadly peril of not having enough to eat.

CROOKES IS A WORRIED MAN

- Believes in the catastrophe looming for the developed world because the naturally occurring nitrogen is depleted.
- But optimistic about Science!
- Sets in place an international competition to find an alternative- source for nitrogen.
- To a packed house.

THE ILLUSTRATED
LONDON NEWS.

The Wheat Problem: Based On Remarks Made In The Presidential Address To The British Association At Bristol, In 1898 (1899)

William Crookes
C. Wood Davis

IN 1898, SIR WILLIAM CROOKES

- Called on science to save Europe from impending starvation.
- “it is through the laboratory that starvation may ultimately be turned into plenty”
- British Association for the Advancement of Science calls for an international competition
- Basically: IGEM for nitrogen

FIREWORKS, FARMS AND GUNPOWDER

- Nitrogen (potassium nitrate– or saltpeter) is discovered first in China and used in fireworks and warfare and crop production

- Then vast amounts are discovered in Peruvian islands and deserts from sea bird waste, Chilian war→ supplies world– but now running out, in first global environmental crisis

CONSIDERING FRITZ HABER

FRITZ HABER

- Raised Prussia (now Poland) to town's most prominent Hasidic family
- Gets "firsts" in military exams, turned down because he is a Jew.

- Becomes "Lutheran" and gets into University of Berlin, job in Zurich becomes "thoroughly German."
- Fascinated by Crookes challenge
- Best friends with Einstein

SUPPLY LINES FROM CHILE TO THE WORLD

- Germany comes late to the nation building narrative, has no powerful navy to import chemicals– has to make them.

- So the idea: turn Nitrogen and Hydrogen into ammonia gas to “fix” it and make it usable for fertilizer

IN 1900 SUCCESSFULLY CHANGED THE BIOECONOMY

Haber-Bosch Process revolutionized food production

Huge city sized plants built in Germany, shifting production entirely to synthetic nitrogen (“saving 2 billion lives a year”)

Maddeners (diemakers) become extinct, chlorine created as a by product)Grain yields increase exponentially, (50% of all world’s food production, rats are also happy)

I.G. Faben becomes a city for chemistry

1918– won the Nobel Prize, was Germany most important scientist

Haber put in charge of Wilhelm Kaiser Institute

ACT 2: THE WORLD AT WAR.

- In WW I, he is urged by the German high command to use his genius to use gas as a weapon
- Main opponent was French chemist Victor Griegnard, Nobel Prize, 1912 who responded to the attacks using his expertise in mustard gas.
- Idea was the stop carnage of machine guns and trenches

“THE CHEMIST’S WAR”

- Haber and Griegnard are not the only ones
- In Britain, it is Chaim Weitzman
  - Born in Lithuania, educated in Berlin, job in Geneva
  - 1901 University of Manchester, 1910 British Citizen
  - 1914 David Lloyd George, head of new Ministry of Munitions, appoints him Head of British Admiralty Laboratory.

BEGINS THE GREAT WAR (FOLLOW UP FROM AMERICAN CIVIL WAR)

- Unprecedented use of “machine guns”
- Use of trenches
- End of the horse charge
- Equally matched armies (with experience in colonial wars)
- Deep pockets of both states and third parties
- And apparently an unlimited supply of Americans despite the influenza pandemic.

“CONKERS IN GREAT PILES”

- British run out of gunpowder, not able to import corn from the US.
- “shell crisis”, with guns only having enough black powder to fire 4 times a day.
- Conkers and acetone are used (synthentic chemistry) to make cordite

- Weitzman: solves powder crisis via synthetic chemistry

HABER'S DECISION

- Desperate to end the war using science
- Develops (with James Franke, Jewish Nobel Prize winner 1925) a way to use the chlorine byproducts and the masks. first developed gas mask filters in had used in the plant, and then he prepared small rockets to use ammonia as gas weapons.

- First use January 31, 1915, Next: Ypres. (Wipers) April, 1915, over 500, 000 killed

- War prolonged, French and British also use gas.

AFTERWARDS

- Shunned at meetings, it was widely understood that the chemists had prolonged the war and were fighting unfairly.
- His wife (only women chemist in generation) kills herself in protest when she failed to stop him.
- But given Iron Cross

THE WORLD ACTS TO STOP THE WEAPON

- First convention on international rules of war.
- Successfully stopped use of chemical warfare.
- There was no disagreement on this issue.


Fritz HABER
NOBEL 1918

AND BACK IN HIS LAB:

- Haber had turned back to agriculture to redeem his work after the war
- Working on pesticides for rats since grain was now so productive.
- Developed a product called Zyklcn B to kill rats.
- IG Faben becomes center of the new German chemical economy.

ACT 3: THE REST IS HISTORY

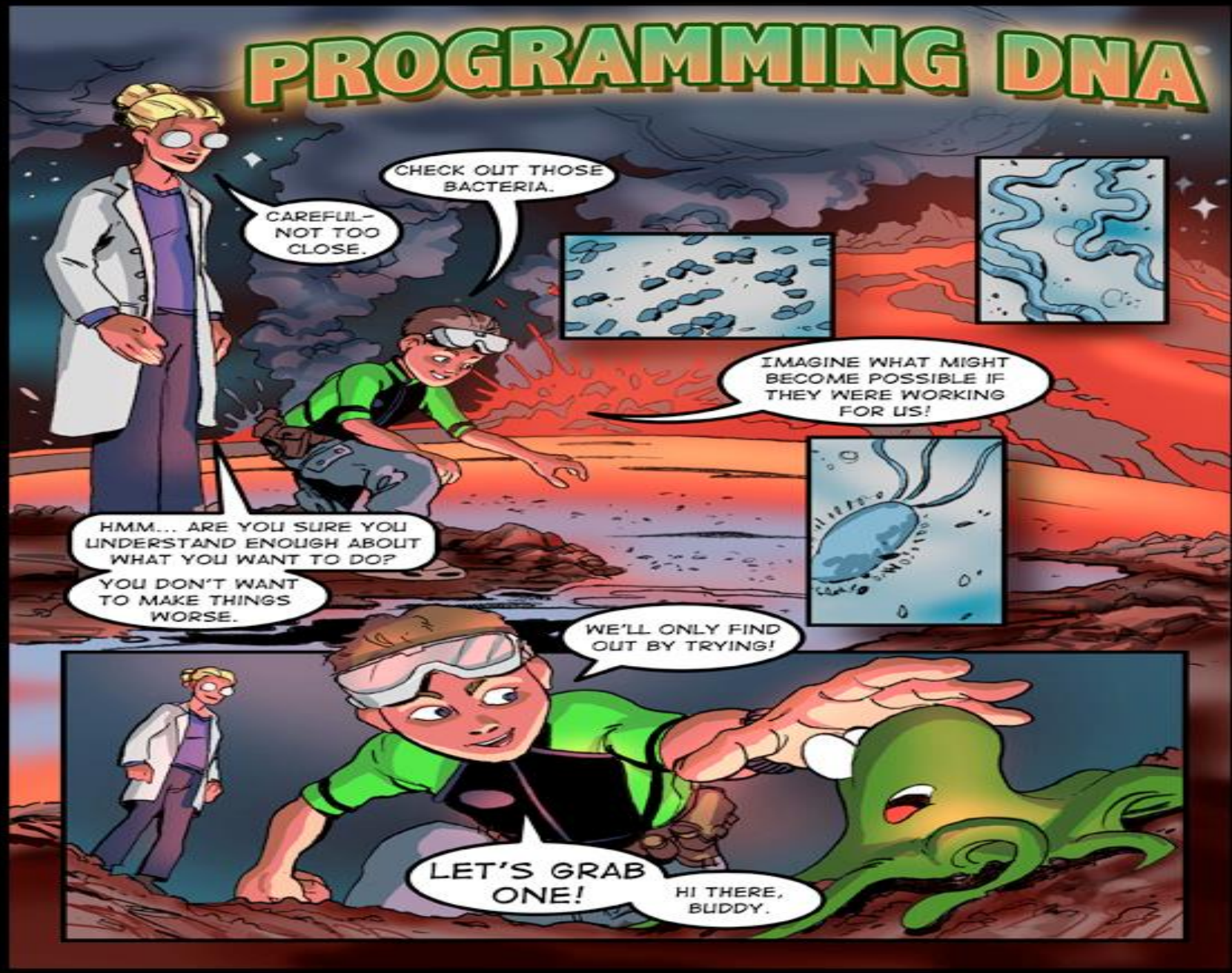
- Haber– now seen as “that Jew Haber” is asked to purge the KWI of all Jews (25% of all staff) by Nazi state, and refuses and resigns in disgrace.

- Flees Germany, goes to Cambridge, meets with Chaim Weitzmann, dies in route to Palestine.

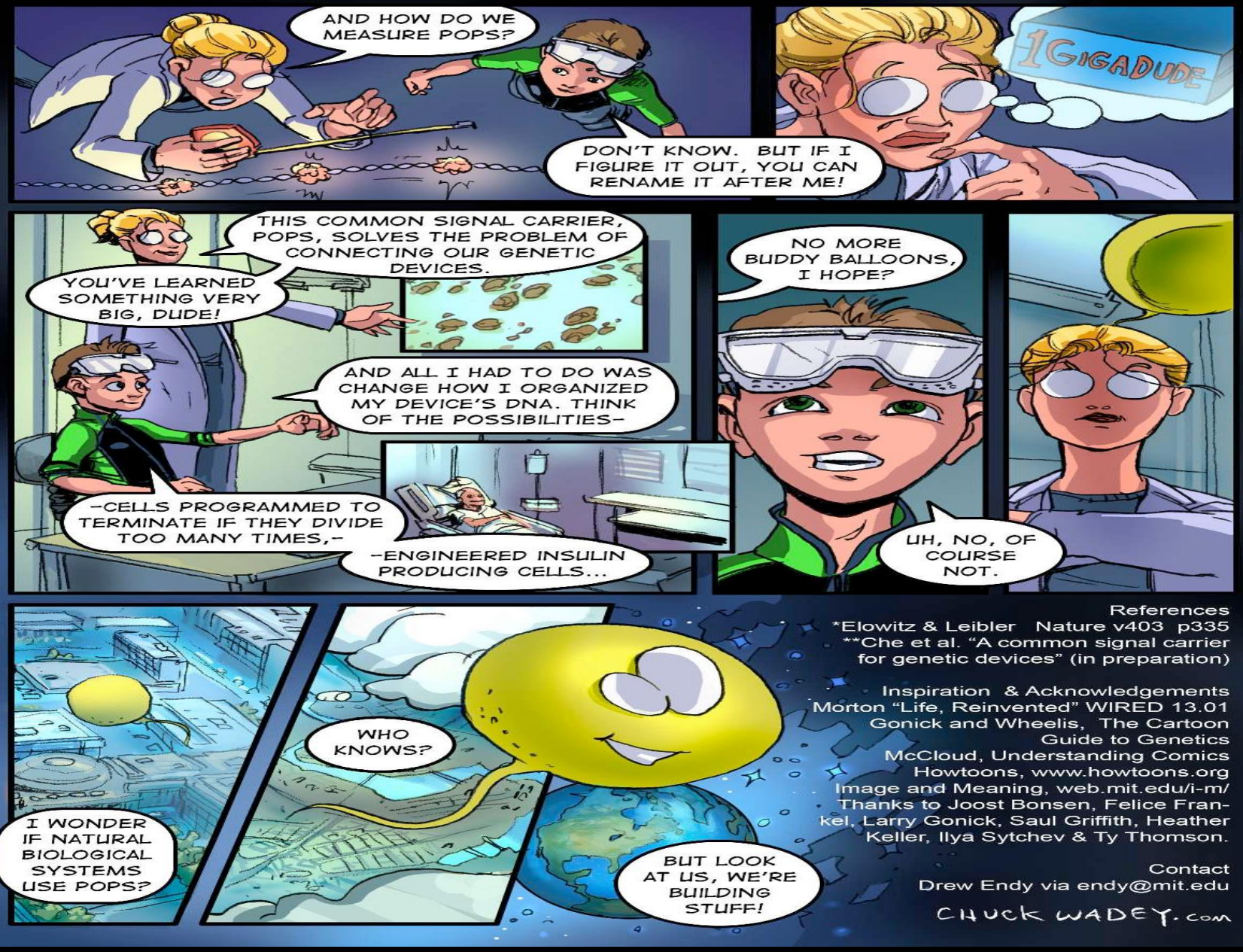
- Zyklon B put to a new use

NARRATIVE II

- Here is a quick review of slides from a meeting of synthetic biologists with NASA in 2012.
- The question: How to organize and how to govern synthetic biology
- One of several such events in the US, with parallels internationally
- SynBio 2.0, and IGEM begin annual meetings


PROGRAMMING DNA
CAREFUL- NOT TOO CLOSE.
CHECK OUT THOSE BACTERIA.
IMAGINE WHAT MIGHT BECOME POSSIBLE IF THEY WERE WORKING FOR US!
HMM... ARE YOU SURE YOU UNDERSTAND ENOUGH ABOUT WHAT YOU WANT TO DO?
YOU DON'T WANT TO MAKE THINGS WORSE.
WE'LL ONLY FIND OUT BY TRYING!
LET'S GRAB ONE!
HI THERE, BUDDY.


CHECK IT OUT! IT'S WORKING!!!
SWEET!
HMM. THAT DOESN'T LOOK RIGHT
BANG!
WHAAAT? WHAT WAS THAT?
YOU FORGOT TO TELL YOUR PROGRAM TO STOP!
BUDDY KEPT GOING UNTIL IT WAS TOO LATE.
HMM. I BETTER LEARN MORE ABOUT WHAT I'M DOING BEFORE I TRY ANYTHING ELSE.
GEE, YOU THINK?
TO BE CONTINUED...
CHUCK WADEY.com



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*Elowitz & Leibler Nature v403 p335
**Che et al. "A common signal carrier for genetic devices" (in preparation)

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Morton "Life, Reinvented" WIRED 13.01
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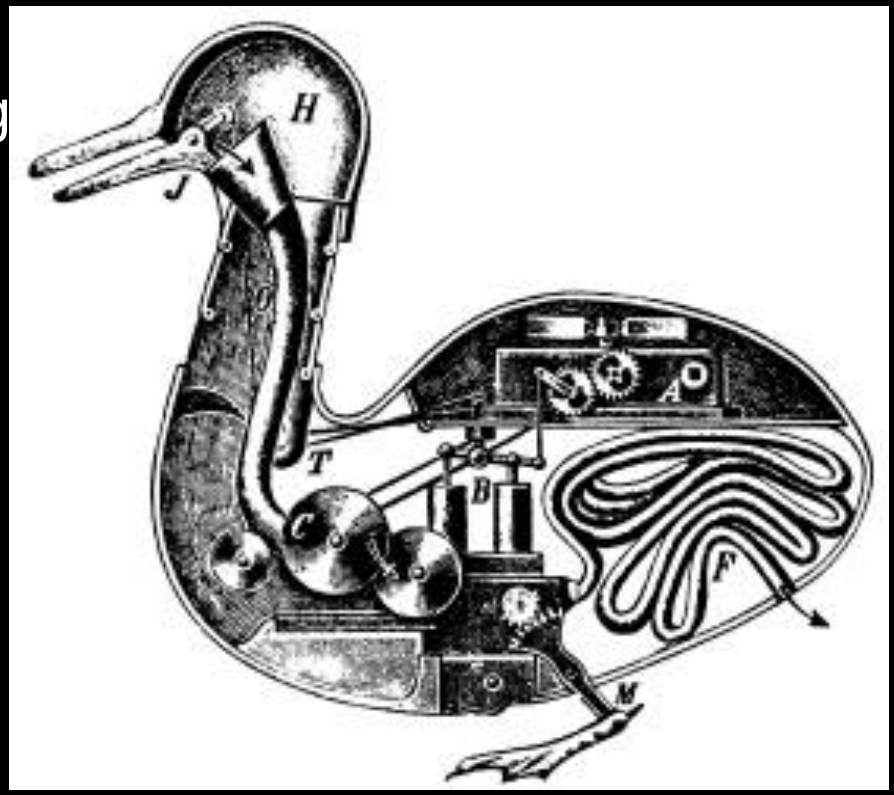
INSIDER KNOWLEDGE IS A PART OF ALL SCIENCE

The Digesting



QUICK HISTORICAL POINTS TO CONSIDER

- Ethical issues have long been a part of research on recombinant DNA
- 1972 Asilomar→ Recombinant DNA Advisory Committee or "RAC"→ **safety as main concern– viral vectors monitored**
- RAC lead to Appendix M "Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA Molecules into One or More Human Research Participants"
- RAC also led to Biosafety Committees and Guidelines for accidents in the lab

FEDERAL RULES WERE COMPLEX AND DETAILED—RAN ACROSS AGENCIES

- EPA modeling for release of microbes and studying TSCA implications
- Dept of Agriculture does inspection and certification of rDNA (foot to mouth virus, nematodes , plant germ plasm)
- FTC may regulate deceptive practices
- CDC has a 24 hour hotline for reports of leakages in shipping of agents if interstate
- NIOSH and OSHA funded for research on worker safety—no regulatory plans
- DOT may regulate rDNA as hazardous material
- Dept of Commerce and National Board of Standards may regulate by products in feedstocks. They also regulate patents, trade secrets
- State Department worked with UN
- DOE has regulations
- NSF committees suggested regulations (Law and Social Sciences and Ethics and Values in Science and Technology(EVIST)
- NAS grants and committees
- OTC studies

ALL CLINICAL GTR PROTOCOLS CONNECTED WITH INSTITUTIONS THAT RECEIVE FEDERAL FUNDING USE CASUISTIC MODEL AT LOCAL AND NATIONAL LEVEL

- What are potential harms and benefits to research subjects?
- How will potential harms and benefits be communicated so they can consent?
- How will selection among research subjects be made?
- How will privacy and confidential be preserved?

(Leroy Walters)

BUT WAIT--

- Altering DNA of existing organizims is one thing, but *making new DNA sequences?* Isn`t that tampering with creation itself?
- Even very smart and apparently nice scientists should not be trusted with creation itself, should they?

PRESIDENT OBAMA`S COMMITTEE REPORT ON SYNBIOLOGY 2011

- Synthetic Biology considered when Ventner Lab “created” new organism
- Marked within DNA with initials of scientists
- Used scaffolding of organisms, so not de nova creation

WHAT DID THE REPORT SAY?

- Not a new creation
- New really a new idea

  or process (looks like Asilomar…)
- Need national “monitoring” (but we have a lot…)
- Need stewardship and justice! (this last was the only new change since Asilomar
- However– RAC will now consider synbio and not just viral vectors.

BUT NEW EVENTS PUSH DISCOURSE

“SCIENTIST DELIBERATELY CREATED ARMAGEDDON BIRD FLU VIRUS! LAB SAYS ‘PUBLISH!’”

- “But others argue the virus should never have been created – and warn the potential if it escaped from the lab is ‘staggering’. There are also fears the recipe will be seized on by terrorists looking for a biological weapon.”

- “National Science Advisory Board for Biosecurity chairman Paul Kiem, an anthrax expert, said: ‘I can’t think of another pathogenic organism that is as scary as this one. I don’t think anthrax is scary at all compared to this.’

- One dramatic and troubling response– see next slide

THE PRINCIPLES FOR THE OVERSIGHT OF SYNTHETIC BIOLOGY MAY 2012

- *The undersigned, a broad coalition of civil society groups, social movements, local and indigenous communities, public interest, environmental, scientific, human rights, religious and labor organizations concerned about various aspects of synthetic biology's human health, environmental, social, economic, ethical and other impacts, offer the following declaration,*

UNTIL THIS IS DONE, A MORATORIUM ON ALL “RELEASE OR COMMERCIAL USE”

- I. Employ the Precautionary Principle
- II. Require mandatory synthetic biology-specific
- Regulations (no use to alter human or human microbiome)
- III. Protect public health and worker safety
- IV. Protect the environment
- V. Guarantee the right-to-know and democratic
- participation
- VI. Require corporate accountability and
- manufacturer liability
- VII. Protect economic and environmental justice

- This is to be enacted by international and nation state powers

ON THE BACK PAGE…..

- **“Synthetic biology, the next wave of genetic engineering, allows seed, pesticide and oil companies to redesign life so that they can make more money from it. These companies now want to take over the forests and land of the Global South to make so called biofuels for planes and boats of the military or to make new cosmetics for the rich. Using synthetic biology, a biofuels dictatorship joins the food dictatorship wrought by the first kind of genetic engineering. *The Principles for the Oversight of Synthetic Biology* is an important tool to help people reign (sic) in these new technologies.”**

- “Vandana Shiva is the founder of Navdanya International, which aims to defend and protect nature and the rights of people to access to food and water and dignified jobs and livelihoods.”

Opposition largely focus on two opposite views of the future (paradoxically held at the same time)

- That the technology will be a terrifying disaster!
  - Error (Japan)
  - Unintended consequences (mongoose)
  - Use as a weapon of mass destruction
- That the technology will be ***very good indeed*** and ordinary people will not get enough of it!
  - Two societies, enhanced and wild type
  - Oppression and marginalization of the poor

WHAT ARE THE ETHICAL CHALLENGES TO WORLD MAKING?

1. DNA as the really real self.

2. Nature is normative, good and fixed.

3.Suffering and mortality is the main thing that defines our humanity.

4. Slopes are slippery.

5. Dual Use is Inevitable

6. Error is Inevitable.

7. The marketplace will corrupt science

8. The world is already unfair and this will worsen injustice.

9. The world is already inauthentic and *umhiemlich* enough

10. Finitude and Contingency define us, not control– “mastery” is a mistakenness

ALL OF THESE CLAIMS HAVE SOME REAL VALIDITY

- First, all of them are more than trivially correct, and any sensible person could agree with many of these statements.
- Trouble begins here is their extremity when taken to their logical conclusion.
- These claims create new political alliances

ALL OF THESE CLAIMS ARE FAITH BASED

- Debates confuse expertise with authority
- They are statements of world view and eschatology, not of moral arguments. As such, they will not—cannot—be entirely agreed upon in a pluralistic democracy.
- Like many faith claims in our world, they are eschatological in nature (it is not now, it is Then)

SUCH CONCERNS REFLECT CORE CONCERNS

Classic ideas

a. that the world is terrifyingly mutable and unfixed in its borders and caprices and species

b. that Pandora is trouble

c. god-person boundary is at stake at all times

Modern anxieties

a. "What I cannot make I cannot understand"

b. That beings are really a sort of machine with a parts list, that we live in LegoLand and that we make not be able to put it back correctly

c. This sort of knowledge is partial and synthetic—what is lost to us is the pre-textual past where in the Real lies.

SCIENCE POLICY FOR A NEW IDEA IN SCIENCE IN A MUTABLE WORLD

- Naïve to think it is merely like all dual use issues– think about IGEM.
- Katrina, Korean Lab Scandal, JPMChase: Government, science and marketplace all seem less trustworthy
- Growing set of serious problems in need of solution (energy, environment, health)

- Future tense consent may be impossible for very long term (VLTR) research.
- New research may use unexpected routes and disciplines (nanotechnology, materials engineering, artificial life, computer science, chemistry)
- Limited public funds, more competition

WHY RISK BENEFIT DOESN'T WORK

- Unknowable risk
- Persons who benefit are not the same as persons at risk
- Anonymity and collectivity of decision making. (And this is true even if The Government or "The People" make the decision.
- We name certain endpoints as "risky" or "unsafe" based on what we value—what can we bear to lose? (People? Which People? Marketshare? Polar bears?)

WHY THE PRECAUTIONARY PRINCIPLE DOESN'T WORK

Every moral gesture leads to a future that is fundamentally unknowable

Especially in synbio, which begins with an acknowledgement of the brokenness of the world

We are creatures possessive of a "plight" which is that we cannot not act. (Korsgaard)

History is not linear in the Hegalian sense

RESEARCH FREEDOM AND CREATIVITY NEEDS TO BE PRESERVED

- New science is inherently subversive, in that it exists outside existing structures of knowledge
- It creates a open frontier that will need some way of ordering and limiting the power—either:
  - A sheriff with police power
  - A missionary with a strong rulebook
  - An outlaw gang with a strong peer to peer code
  - Individual moral agency

TWO IDEAS SO FAR: SCIENCE SELF REGULATION AND SERIOUS EDUCATION

Don’t focus on regulation of activities

Focus on the duties of people

- Scientists as moral agents
- The public as moral agents

(One may also turn to classic texts: Plato in The Republic in which philosophers had certain duties of citizenship) or many differing religious traditions)

Virtues at stake– courage and fidelity.

- ***Am I a good scientist/engineer and what does that mean?***

CORRELATIVE RELATIONSHIP BETWEEN RIGHTS AND DUTIES

- Meaning: society's trust in science's subversive activities means we allow (and pay) them to undermine the text and to "live outside the law."
- But: we have to trust that they are honest, careful, and sane.
- Right to free speech draws power and authority only from duty to "tell the truth and stand up for all humanity." (Sydney Brenner)

SO HOW DID THE NEXT DECADE WORK OUT?

- The NASA meeting decided that the risk was making a synthetic de novo entity that:
  - Was self-replicating
  - Was able to live in the real world not only a lab
  - was pathogenic.

ENTER SARS-COV-2 2019

- Regardless of origin issues, we now have answered one question: Can we contain an entity with these three characteristics?

- Answer: no.

HOW TO MAKE A DYI FACE MAKE AT HOME!!!

MILITARY TIMES

- Your Military
- **More troops are taking the COVID-19 vaccine, including those who rejected it before.** The Pentagon can’t say how many of those offered have turned down the vaccine because that information is not being tracked at higher than a local level.
- Later that month, the Joint Staff’s vice director for operations told lawmakers during a House Armed Services Committee hearing that about a third of troops did not get the vaccination. He added later he did not know why.
-

Decades after a tragic failure, gene therapy successfully treats a rare liver disease

•

Share on mailto

Josh McQuillin, shown in 2019, 1 year after being treated, says gene therapy has transformed his life.

By Jocelyn KaiserMay. 18, 2021 , 4:15 PM

Twenty-two years ago, one of scientists' first attempts at gene therapy ended in tragedy when a young man died. The story of Jesse Gelsinger, who had a rare liver disorder, became a textbook example of irresponsible medical research. For years, the case hobbled efforts to treat diseases by adding new DNA to a sick person's cells. Now, a fresh effort to cure Gelsinger's disease is bearing fruit, in the latest sign of the field's resurgence.

ON A UNCERTAIN SEA, YOU RELY ON A GOOD CREW

- Ethics means we debate difference moral arguments
- Each based on a choice of values we prioritize
- These stories tell us that values are in conflict– hence a dilemma

CORE VALUES FOR THE US ARMY

- Fidelity
- Courage
- Humility
- Veracity

SCIENCE IS APORETIC

- Synthetic biology has been at the end of the map for over a decade. Like other biotechnologies, (stem cells, nanotech) a lot needs to be understood about biology before it works.
- As a tool– DNA manipulation has become more refined but is still in its infancy.