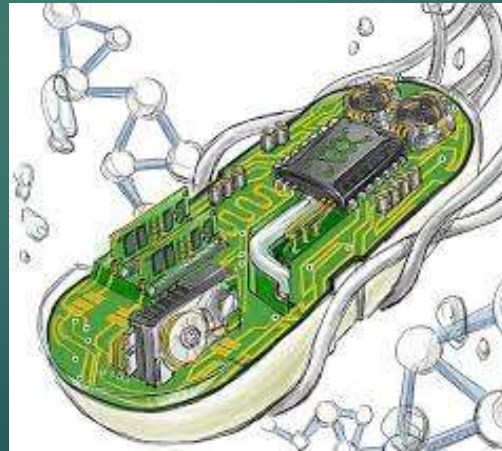




# Playing God or Just Playing:

SCIENTIFIC RESPONSIBILITY IN THE AGE OF SYNTHETIC  
BIOLOGY AND BIOHACKING

# Convergence of technological and social changes



# Social changes

- ▶ Decentralization
- ▶ De-institutionalization
- ▶ De-professionalization
- ▶ Democratization?



# Technological changes



- ▶ Synthetic biology

- ▶ “Synthetic biology is a maturing scientific discipline that combines science and engineering in order to design and build novel biological functions and systems.” (SynBERC)

- ▶ Minimal genome

- ▶ Metabolic pathway engineering for production of plastics through microbial fermentation of sugars instead of from petroleum products

# Technological changes



## ▶ Gene editing

- ▶ Insertion, deletion or replacement of one or more segments of DNA in a genome
  - ▶ Alteration of sexually reproducing populations of mosquitoes to eradicate disease-carrying species
- ▶ Clinical trials in China, US approved
  - ▶ US trial of zinc-finger nuclease editing of T cells in HIV (2014)
  - ▶ US trial of CRISPR/Cas9 editing of T cells in cancers (2016)
- ▶ Gene editing research using non-viable human embryos in China, viable human embryos in Sweden, UK

# But are these changes ethically significant?

## *These Foods Aren't Genetically Modified but They Are 'Edited'*

By KENNETH CHANG JAN. 9, 2017



Gene-edited soybeans will be made into cooking oil that will not need hydrogenation, which yields trans fats.  
Cofco Group

### RELATED COVERAGE



By 'Editing' Plant Genes, Companies Avoid Regulation  
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JULY 14, 2016



G.M.O.s in Food? Vermonters Will Know  
APRIL 20, 2016



A Lonely Quest for Facts on Genetically Modified Crops  
JAN. 4, 2014

# And are there any new ethical issues?

- ▶ Minimal genome – the smallest set of genes that allows for replication of the organism in a particular environment (*Mycoplasma genitalium* as a model with the smallest known genome of any free-living organism)
  - ▶ Reductionism
  - ▶ Re-defining life, playing God
  - ▶ Justice, benefits and ownership
  - ▶ Maleficence and dual use

The logo for Science magazine, featuring the word "Science" in white on a red rectangular background, with the word "magazine" in black on a white rectangular background below it. The logo is positioned to the right of a large light blue circle.

GENETICS:

## **Ethical Considerations in Synthesizing a Minimal Genome**

**Mildred K. Cho,\* David Magnus, Arthur L. Caplan,\* Daniel McGee, and the Ethics of Genomics Group\***


# And are there any new ethical issues?

- ▶ Ethical norms and regulatory regimes already developed for genetic manipulation are considered applicable to human gene editing in somatic cells
- ▶ For human gene editing in germline cells, additional concerns are:
  - ▶ Long-term risks to future generations and populations
  - ▶ Parental autonomy
  - ▶ Abusive and coercive eugenics
  - ▶ Use of human embryos
- ▶ But these concerns have been raised for other reproductive technologies



# General classes of concern



- ▶ Intrinsic morality of genetic modification and nature
  - ▶ Health, environmental and other risks and benefits
    - ▶ Including “informed consent” and transparency
  - ▶ Justice – distribution and representation
    - ▶ Regarding burdens, benefits, access and control
- 

# Lack of consensus remains



REVIEWS NEWS VIDEO HOW TO SMARTHOME CARES DEALS DOWNLOAD

## Gates foundation to promote synthetic biology

Most people associate E. coli with bad chicken, but researchers say the microbe can be used to produce new drugs.

WorldViews

## Bill Gates: Bioterrorism could kill more than nuclear war — but no one is ready to deal with it

By Avi Sella February 18



Speaking at the Munich Security Conference on Feb. 18, Microsoft cofounder and philanthropist Bill Gates said the new global epidemic has a "good chance" of originating on a computer screen. (AP)

# Lack of consensus remains

“Research on viruses is driven not only by an urgent need to understand, prevent, and cure viral disease. It is also fueled by a strong curiosity about the minute particles that we can view both as chemicals and as “living” entities.”

**Science** AAAS

Home News Journals Topics Careers

Science Science Advances Science Immunology Science Robotics Science Signaling Science Translational Medicine

**SHARE** REPORT

### Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template

Jerónimo Cello, Aniko V. Paul, Eckard Wimmer\*

\* See all authors and affiliations

Science 09 Aug 2002  
Vol. 297, Issue 5583, pp. 1016-1018  
DOI: 10.1126/science.1072206

## H5N1

### REPORT

## Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets

Sander Herfst,<sup>1</sup> Eefje J. A. Schrauwen,<sup>1</sup> Martin Linster,<sup>1</sup> Salin Chutinimitkul,<sup>1</sup> Emmie de Wit,<sup>1,\*</sup> Vincent J. Munster,<sup>1,\*</sup> Erin M. Sorrell,<sup>1</sup> Theo M. Bestebroer,<sup>1</sup> David F. Burke,<sup>2</sup> Derek J. Smith,<sup>1,2,3</sup> Guus F. Rimmelzwaan,<sup>1</sup> Albert D. M. E. Osterhaus,<sup>1</sup> Ron A. M. Fouchier<sup>1,†</sup>

**Science** AAAS

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**SHARE** RESEARCH ARTICLE

### Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus

Teresa M. Tumpey<sup>1,2</sup>, David J. Nisbet<sup>1</sup>, Patricia K. Aguirre<sup>1</sup>, Hai Song<sup>1</sup>, Alicia Salazar-Vizcarra<sup>1</sup>, David E. Swayne<sup>1,3</sup>, Ross H. Blackmore<sup>1,4</sup>, David M. M. Donnelly<sup>1,5</sup>, Robert G. Webster<sup>1,6</sup>, and Paul B. Kruger<sup>1,7</sup>

Made available first. This research was done by staff taking antiviral prophylaxis and using stringent biosafety procedures (BS) to protect the researchers, the environment, and the public. The fundamental purpose of this work was to provide information critical to protect public health and to develop measures effective against future influenza pandemics.

\* See all authors and affiliations

ISSN 0036-8075  
DOI: 10.1126/science.1120000  
PUBLISHED ONLINE 11 AUGUST 2009

# Lack of consensus remains



Pathogenic H5N1 avian influenza has led to the culling of hundreds of millions of birds. A human-transmissible form could have much worse consequences.

## Adaptations of avian flu virus are a cause for concern

Members of the US National Science Advisory Board for Biosecurity explain its recommendations on the communication of experimental work on H5N1 influenza.

“The NSABB was unanimous that communication of the results in the two manuscripts it reviewed should be greatly limited in terms of the experimental details and results.”

# Lack of consensus



## Don't edit the human germ line

Heritable human genetic modifications pose serious risks, and the therapeutic benefits are tenuous, warn **Edward Lanphier**, **Fyodor Urnov** and colleagues.



# How do we address ethical concerns about genetic manipulation?

- ▶ External regulation
- ▶ Professional and industrial standards
- ▶ Training

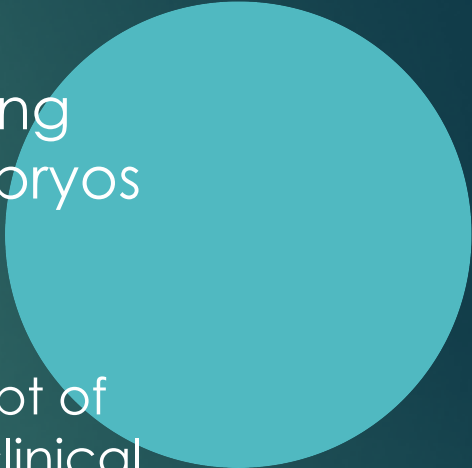



# Regulation in US



- ▶ IBC, IACUC, USDA
- ▶ IRB, FDA, NIH, ESCRO, RAC
  - ▶ Oversight largely limited to research at institutions that receive federal funding
  - ▶ FDA – oversight is not determined by source of funding, but limited to research on “products”
  - ▶ RAC – is advisory only and since 2016 only reviews protocols at request of IRBs, IBCs or NIH Director
  - ▶ Select Agents – oversight by institutions and limited to research of certain types on predetermined set of microbial and viral agents and toxins
  - ▶ DNA synthesis – regulation limited to federally funded research

# Regulation in US – human genome embryo editing



- ▶ NIH statement on funding of research using gene-editing technologies in human embryos (2015)
  - ▶ “NIH will not fund any use of gene editing technologies in human embryos. The concept of altering the human germline in embryos for clinical purposes has been debated over many years from many different perspectives, and has been viewed almost universally as a line that should not be crossed”



# Regulation in US – human genome embryo editing

## ▶ NIH statement, continued

- ▶ “The Dickey-Wicker amendment prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed (H.R. 2880, Sec. 128). Furthermore, the NIH Guidelines state that the Recombinant DNA Advisory Committee, “...will not at present entertain proposals for germ line alteration”. It is also important to note the role of the U.S. Food and Drug Administration (FDA) in this arena, which applies not only to federally funded research, but to any research in the U.S.”

## ▶ Consolidated Appropriations Act of 2016

- ▶ FDA may not acknowledge receipt of a submission for application for investigational use of human embryos with a heritable genetic modification

# Professional and industrial standards

- ▶ Industry standards and policy positions
  - ▶ Industry Association Synthetic Biology “Technical solutions for security in synthetic biology”
  - ▶ Lanphier *et al.* “Don’t edit the human germline” (Alliance for Regenerative Medicine)
- ▶ Professional society policy positions
  - ▶ Human genome germline editing - American Society of Human Genetics, National Society of Genetic Counselors, Canadian Association of Genetic Counsellors, International Genetic Epidemiology Society, Association of Genetic Nurses and Counsellors
  - ▶ Human genome germline editing - National Academy of Sciences

# NAS – human germline gene editing

- ▶ NAS – “Heritable germline genome editing trials must be approached with caution but caution does not mean they must be prohibited.” Should be permitted only:
  - ▶ Within a robust and effective regulatory framework
  - ▶ In the absence of reasonable alternatives
  - ▶ With restriction to preventing serious disease or condition with genes that strongly predispose to them
  - ▶ Based on credible data
  - ▶ With multigenerational follow-up
  - ▶ With maximum transparency consistent with patient privacy
  - ▶ With reassessment of benefits and risks, participation and input by the public
  - ▶ With reliable oversight to prevent other uses

# ASHG *et al.* – human germline gene editing

- ▶ Unacceptable to perform germline gene editing that culminates in human pregnancy
- ▶ Currently, there is no reason to prohibit *in vitro* genome editing on human embryos and gametes, with appropriate oversight and consent from donors, to facilitate research on the possible future clinical application of gene editing
- ▶ Future clinical application of human germline genome editing should not proceed unless, at a minimum, there is
  - ▶ a compelling medical rationale,
  - ▶ an evidence base that supports its clinical use,
  - ▶ an ethical justification, and
  - ▶ a transparent public process to solicit and incorporate stakeholder input.

# Training

- ▶ NSABB “culture of responsibility” (NRC, NSC)
  - ▶ Heightened consciousness of the implications of research
  - ▶ Consciously live and demonstrate beliefs, attitudes and values through day-to-day practices of mindful research
  - ▶ Accountability with a shared commitment to advancing science and maintaining public trust



## Guidance for Enhancing Personnel Reliability and Strengthening the Culture of Responsibility

A Report of the National Science Advisory Board for  
Biosecurity

# Ethical principles of scientific responsibility



- ▶ NIH mission statement - “to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science”
- ▶ NAS *On Being a Scientist* – “a responsibility to reflect on how their work and the knowledge they are generating might be used in the broader society”
  - ▶ But as long as the values of honesty, fairness, collegiality, and openness “are honored, science – and the society it serves – will prosper.”

# PCCSBI Ethics of Synthetic Biology and Emerging Technologies (2010)

- ▶ **Public beneficence** – to act to maximize public benefits and minimize public harm (by individuals and institutions), adopting a societal perspective in weighing risks and benefits
  - ▶ Based on duty of society to promote that which has potential to improve the public's well-being



# PCSB Ethics of Synthetic Biology and Emerging Technologies (2010)

- ▶ **Responsible stewardship** – obligation to act to demonstrate concern for those who are not in a position to represent themselves (eg children, future generations, their environment)
  - ▶ Calls for prudent vigilance, establishing processes for assessing likely benefits and risks before and after projects undertaken and mechanisms for limiting use of technologies when necessary
- ▶ **Intellectual freedom and responsibility** – to use creative potential in morally accountable ways, while acknowledging that the possibility of harm alone is generally insufficient to justify limits on intellectual freedom
  - ▶ Endorses principle of regulatory parsimony

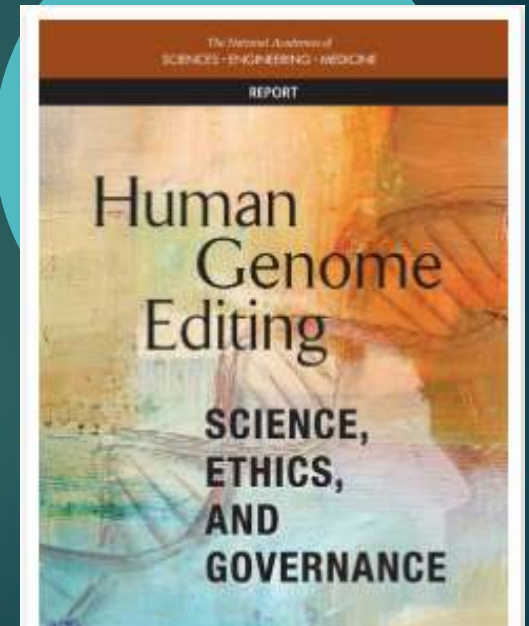


# PCRSBI Ethics of Synthetic Biology and Emerging Technologies (2010)

- ▶ **Democratic deliberation** – reflects approach to collaborative decision making that includes debate of opposing views
  - ▶ Encourages participants to adopt a societal perspective over individual interests
- ▶ **Justice and fairness** – of distribution of benefits and burdens across society

# Principles of governance of human genome editing (NAS report 2017)

- ▶ **Promoting well-being** – providing benefit and preventing harm to those affected
- ▶ **Transparency** – disclosing information and obtaining meaningful public input into policy-making process
- ▶ **Due care** – proceeding carefully and deliberately, and only when supported by sufficient and robust evidence
- ▶ **Responsible science** – high quality design and analysis with review, transparency and correction



# Principles of governance of human genome editing (NAS report 2017)

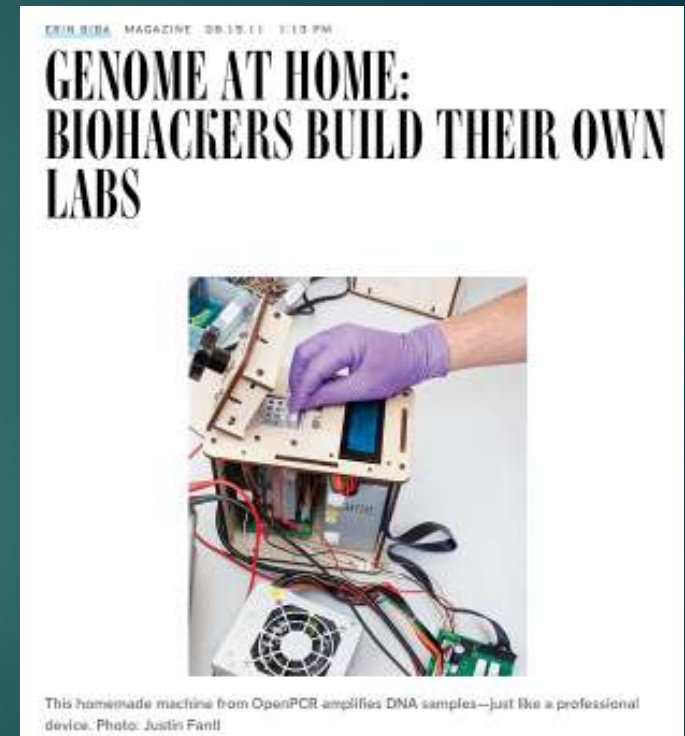
- ▶ **Respect for persons** – autonomy in decision-making, respect for equal value of individuals (preventing abusive forms of eugenics and commitment to destigmatizing disability)
- ▶ **Fairness** – equitable distribution of burdens and benefits of research and broad, equitable access to benefits
- ▶ **Transnational cooperation** – collaboration and data sharing and coordination of regulatory standards and procedures where possible, while respecting different cultural contexts

# Positive obligations - beyond minimizing risk

- ▶ Promoting well-being and public benefit
- ▶ Fairness in distribution of risk and benefit
- ▶ Due care, proceeding with awareness of implications
- ▶ Public participation and input


# The age of biohacking and DIYbio

- ▶ Biohacker as tinkerer
  - ▶ Focused on molecular biology and microbes
  - ▶ Generally uses tools of professional scientists
  - ▶ Values innovation and playfulness



# Biohacker as tinkerer

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BioCurious is the World's First Hackerspace for Bio. Built in the Heart of Silicon Valley.

We are a community of scientists, technologists, entrepreneurs, and amateurs who believe that innovations in biology should be accessible, affordable, and open to everyone.

located in Sunnyvale, CA, our co-working laboratory space and shared equipment is ideal for entrepreneurs, citizen scientists, hobbyists, and students.

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### About

We are Counter Culture Labs, a community of scientists, tinkerers, biotech professionals, hackers, and citizen scientists who have banded together to create an open community lab — a hackerspace for DIY biology and citizen science. Help us build a space for creative exploration and discovery: a place to innovate, learn, work on fun projects, and tinker with biology and other sciences. Help us build YOUR lab!



For far too long, science has been locked away in the "Ivory towers" of universities and research labs. Silicon valley was born out of garage workshops and hobby clubs, the precursor to today's hackerspaces. And much of tomorrow's innovation will be born out of the garage labs of today.

# Biohacker as tinkerer

## DIY CRISPR Kits, Learn Modern Science By Doing

San Francisco, United States

Technology

### Bay Area biologist's gene-editing kit lets do-it-yourselfers play God at the kitchen table

By Lisa M. Krieger | lkrieger@mercurynews.com (mailto:lkrieger@mercurynews.com)

UPDATED: N/A YEARS AGO



### DIY Bacteria CRISPR Genome Engineering Kit

Bacteria are a commonly used organism in Synthetic Biology because they grow quickly and have simple cellular structures, making them easy to engineer. This kit allows users to make specific edits to genes using CRISPR allowing the bacteria to survive on alternative growth media when it normally would not. Everything required to perform these experiments is included in the kit.



# The Tinkerer ethic



## DIYbio Code of Ethics - European

- ▶ **Transparency** Emphasize transparency and the sharing of ideas, knowledge, data and results.
- ▶ **Safety** Adopt safe practices.
- ▶ **Open Access** Promote citizen science and decentralized access to biotechnology.
- ▶ **Education** Help educate the public about biotechnology, its benefits and implications.
- ▶ **Modesty** Know you don't know everything.



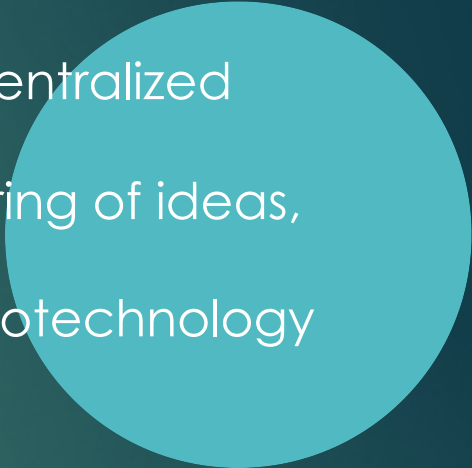
# The Tinkerer ethic

- ▶ **Community** Carefully listen to any concerns and questions and respond honestly.
- ▶ **Peaceful Purposes** Biotechnology must only be used for peaceful purposes.
- ▶ **Respect** Respect humans and all living systems.
- ▶ **Responsibility** Recognize the complexity and dynamics of living systems and our responsibility towards them.
- ▶ **Accountability** Remain accountable for your actions and for upholding this code.

# The Tinkerer ethic



## DIYbio Code of Ethics – North American

- ▶ **Open access** Promote citizen science and decentralized access to biotechnology.
  - ▶ **Transparency** Emphasize transparency, the sharing of ideas, knowledge and data.
  - ▶ **Education** Engage the public about biology, biotechnology and their possibilities.
  - ▶ **Safety** Adopt safe practices.
  - ▶ **Environment** Respect the environment.
  - ▶ **Peaceful purposes** Biotechnology should only be used for peaceful purposes.
  - ▶ **Tinkering** Tinkering with biology leads to insight; insight leads to innovation.
- 

# Just playing?

- ▶ Self-directed, with freedom to quit and to develop and accept rules
- ▶ Not goal-directed, means more valued than ends
- ▶ Imaginative, but imaginary - not real-life

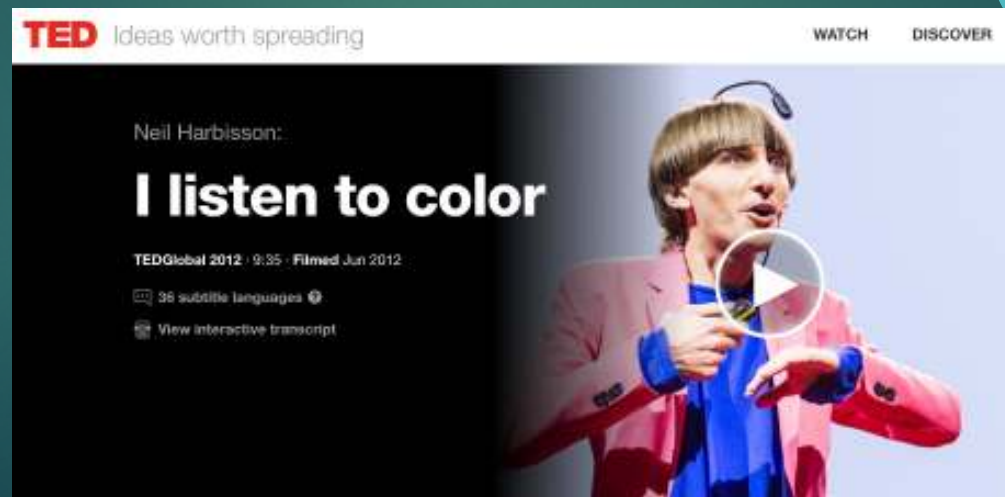
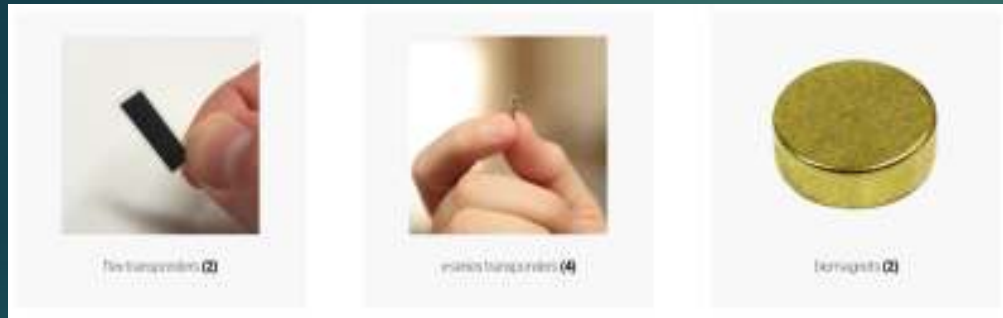


# Biohacker as upgrader

- ▶ Focused on self-experimentation and the “quantified self”
- ▶ Not limited to genetics
- ▶ Values self-improvement



# The biohacker - upgrader



# The Upgrader ethic

- ▶ “The ability to upgrade yourself now, with powerful new capabilities – this is the future of human evolution. The right to choose and implement our own futures. Our bodies are our own, to do what we want with. The ‘socially acceptable’ of tomorrow is formed by boundaries pushed today.”



# The Upgrader ethic

NOOTROBOX Home

## THE BIOHACKER GUIDE

The Biohacker Guide from Nootrobox is the definitive biohacking resource and guide. There's tremendously exciting research in the areas of cognitive modulation, biohacking, and human enhancement. With that excitement, however, comes misinterpretation and hype. The guide cuts through the noise and distills the latest data, results, and conclusions from peer-reviewed, statistically significant studies.

In this compendium, we seek to establish a resource for you to begin hacking your biology. We believe that optimization is an iterative process, so we have written protocols that are a good place to start your journey as a biohacker. In addition to our protocols, we list tools to quantify the domains you are trying to optimize, that we have found through research and personal experience to be the best in class. For example, macro-nutrient tracking options to optimize your diet or cognitive testing tools to optimize your brain function. Through these pages, you will also find in-depth explanations of each facet of the protocols, from descriptions of the nootropics to descriptions of the biological domains they modify.

### Hacking Cognition

What is optimal cognition? It depends on your state and goals, and to some degree, it is a highly personalized choice that may be most affected by your personal situation. For example, insufficient sleep, or a suboptimal diet can also interfere with peak cognitive performance. Read on, to see our biohacker protocol for optimizing cognition. ([Learn more](#))

NOOTROBOX Home

## ETHICS OF HUMAN ENHANCEMENT

"A good rule of thumb seems to be whether or not use of a substance or enhancement technique is harmful to the athlete's health in the long term. This serves to further underscore the need for rigorous scientific vetting and solid medical evidence before treatments or regimens are prescribed. Many of the same issues exist in the realm of cognitive enhancement and personal optimization, and these are drawing more attention than ever."

# The Upgrader ethic

**THE WALL STREET JOURNAL.**

ESSAY

## **The Ethics of Experimenting on Yourself**


Ethicists are pushing back against 'citizen scientists' who want to do medical research on themselves



# The Upgrader ethic



## **Transhumanist Values Bostrom 2003**

- ▶ Hubris rejected – nothing wrong with “tampering with nature”
  - ▶ Individual choice in use of enhancement technologies
  - ▶ Peace, international cooperation
  - ▶ Open-mindedness and inquiry
  - ▶ Individual and collective improvements in powers of understanding
  - ▶ Recognizing fallibility, epistemic tentativeness
  - ▶ Pragmatism, problem solving
  - ▶ Diversity
  - ▶ Caring about well-being of all sentience
  - ▶ Saving and extending lives
- 

# What are social responsibilities of biohackers? Of "professional" scientists"

- ▶ Are biohackers doing science? Are they scientists?
- ▶ Does role matter?
  - ▶ If you are the research subject and researcher?
  - ▶ If you are "just playing" can you be "playing God"?
- ▶ Do risks matter?
- ▶ Do goals matter?
- ▶ Do knowledge and skills matter?

# General obligations



- ▶ General duty of care:
- ▶ To not be reckless
  - ▶ Knowingly creating unreasonable risk to self or others
- ▶ To not be negligent
  - ▶ Unknowingly creating such a risk but with insufficient scrutiny or bad judgment
- ▶ To anticipate intended and unintended consequences of one's actions

# General obligations?

- ▶ Prudent vigilance
- ▶ Preventing and minimizing harm
- ▶ Due care, proceeding carefully and deliberately

## TINKERER

- ▶ Safety and peaceful purposes
- ▶ Listen to concerns
- ▶ Respect living systems
- ▶ Be accountable for actions

## UPGRADER

- ▶ Caring about well-being

# Role-related obligations

- ▶ Avoid bias and conflicts of interest
- ▶ Generate reliable, valid, reproducible data
- ▶ Report and critique honestly
- ▶ Share data and materials
- ▶ Train next generation of scientists
- ▶ Promoting well-being and public benefit
- ▶ Fairness in distribution of risk and benefit
- ▶ Public participation and input

# Role-related obligations?

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- ▶ Public participation and input

## TINKERER

- ▶ Share ideas, knowledge and data
- ▶ Promote citizen science and access to biotechnology
- ▶ Educate the public
- ▶ Tinker and innovate

## UPGRADER

- ▶ Open-mindedness
- ▶ Epistemic tentativeness
- ▶ Diversity
- ▶ Saving and extending lives

# Implications



- ▶ All moral agents have the general obligation to anticipate consequences of their actions and to prevent or mitigate negative consequences
- ▶ The more the purpose of the activity is to generate and apply generalizable knowledge, the more that role-related obligations attach
- ▶ The more specialized knowledge and skills an individual has, the more role-related obligations