Redesigned:
Life in the Genetically Engineered Society of the Near Future

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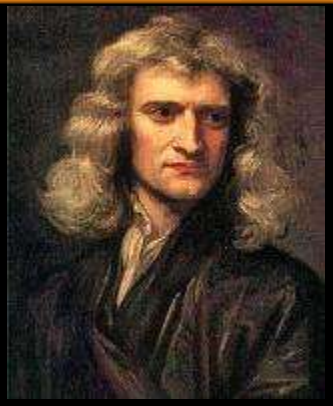
Presentation at Monthly Vi Lecture Series
Grayhawk, Scottsdale. 27 October 2016

The Journey to the Anthropocene: Mastery of Increasingly Sophisticated Intellectual Challenges and Technological Acceleration

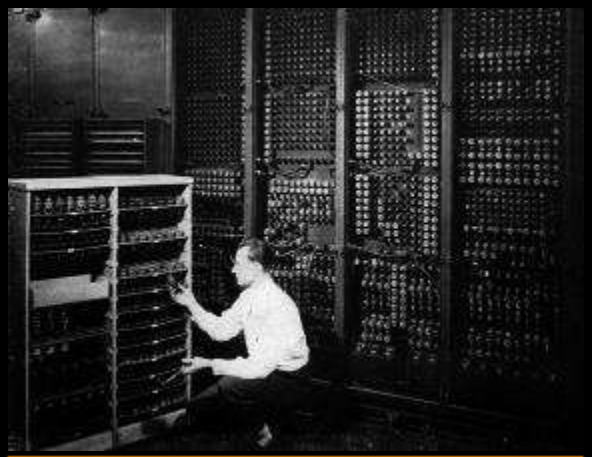
First Communication Revolution 70K YBP

Agrarian Revolution 11K YBP

Scientific Revolution 0.5K YBP



Industrial Revolution 0.25K YBP



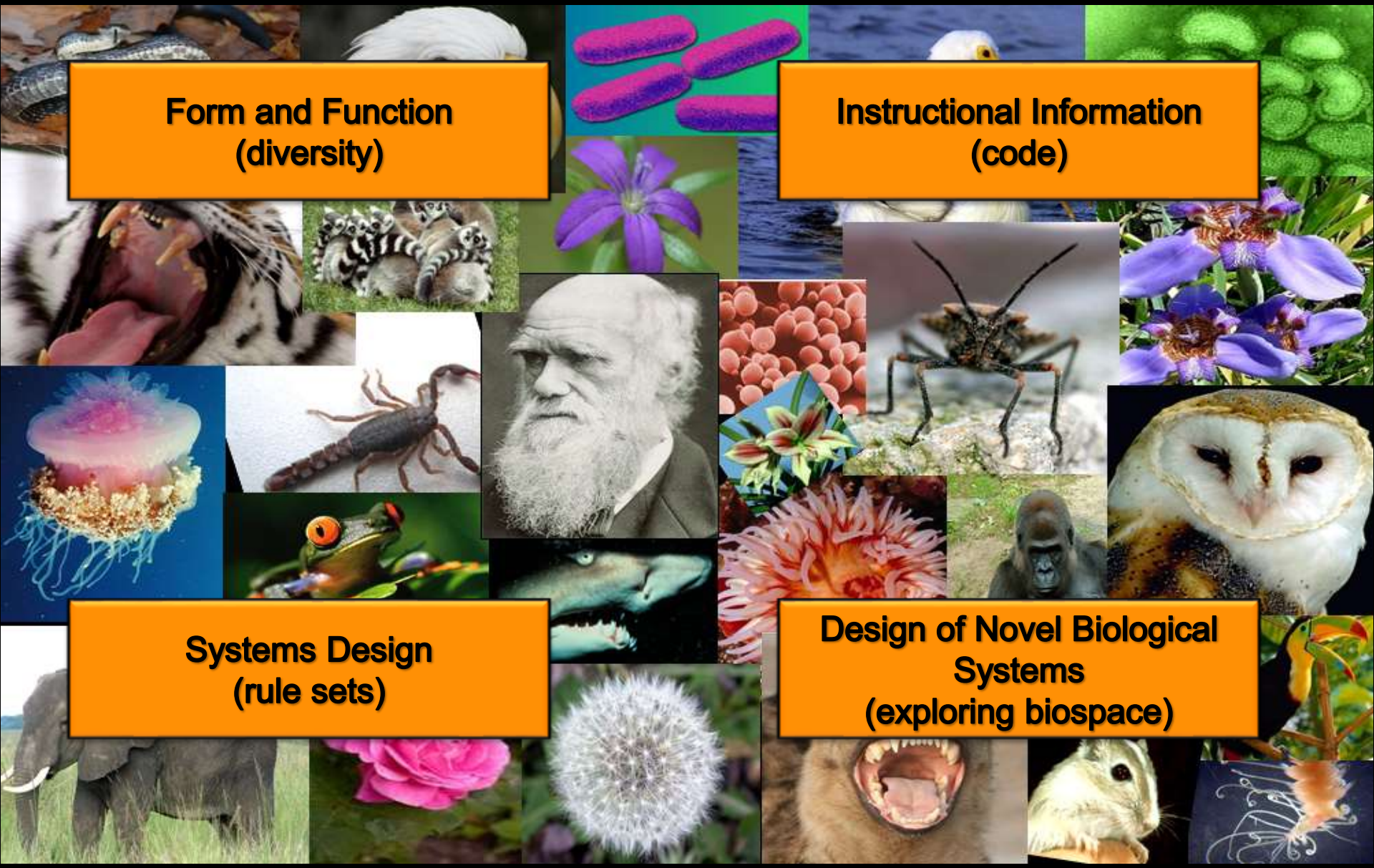
Digital Revolution 0.1K YBP

Molecular Biology Revolution 0.05K YBP

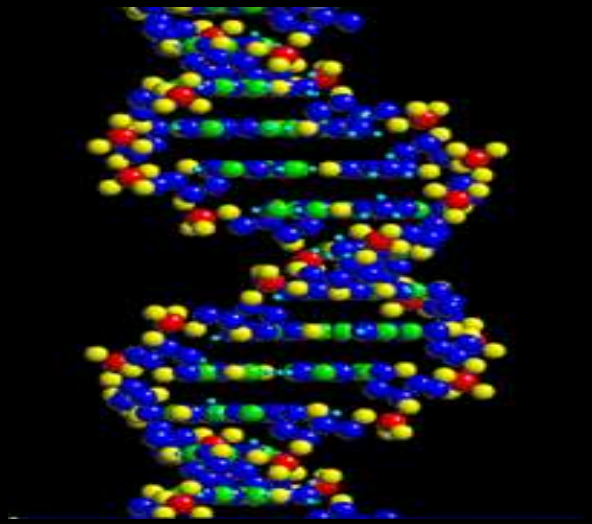
Synthetic Biology and Genome Design as the Next Major Wave of Technological Disruptions in the Anthropocene

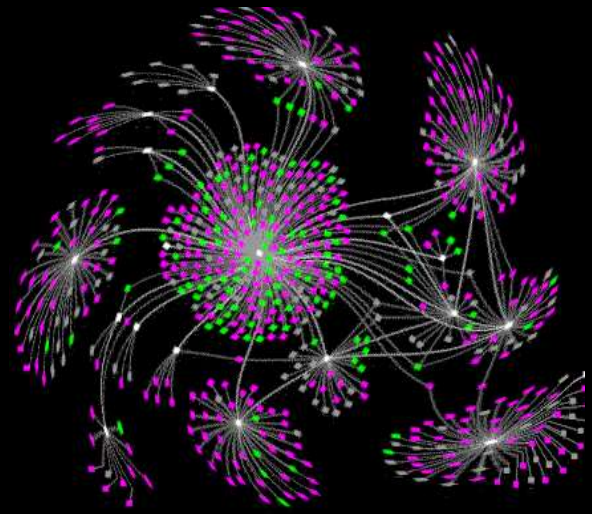
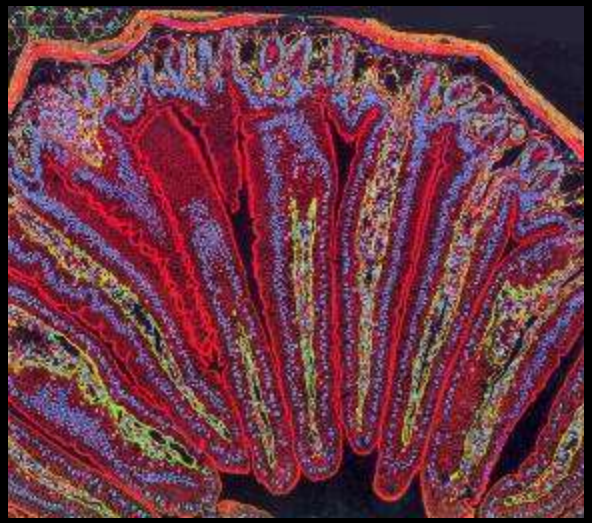
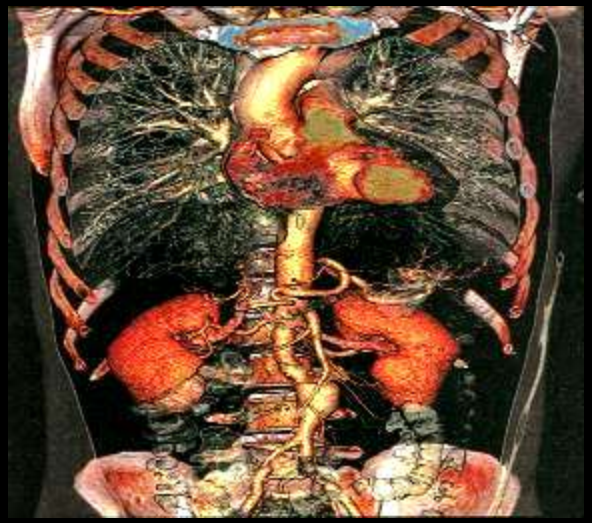
Biological Diversity and Variation: "Endless Forms Most Beautiful"

"Endless Forms Most Beautiful"
Systems and Synthetic Biology and Exploring Biospace



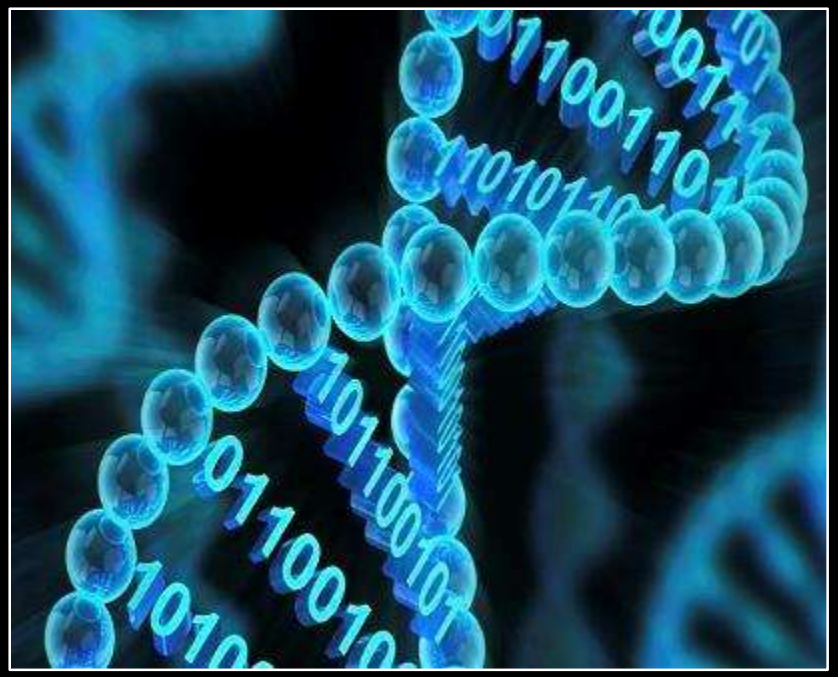
Comprehending Biological Organization: The Construction of Complex, Adaptive Networks of Increasingly Higher Structural Order




Digital Biology and Synthetic Biology
“It from Bits”

“It”
(hardware)
(wetware)



“Bits”
(software)

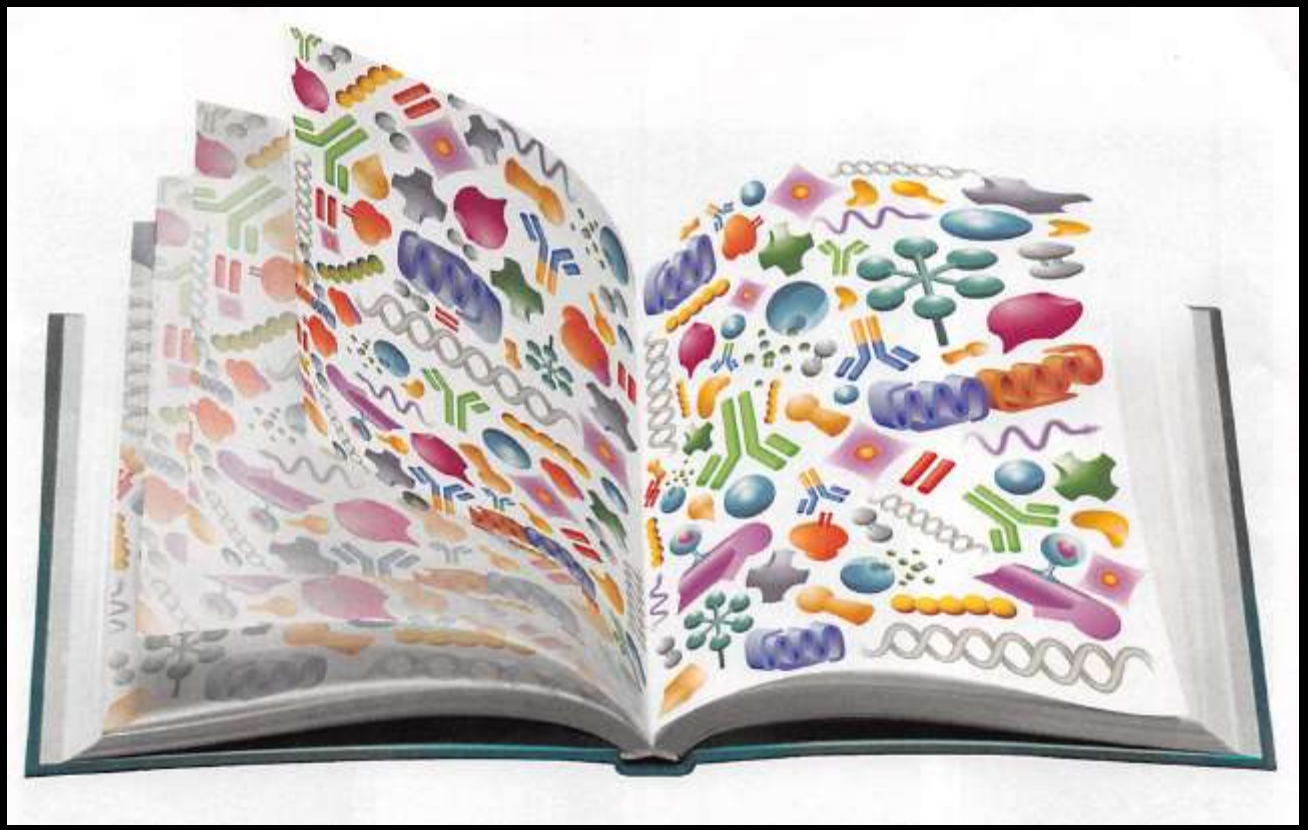
Synthetic Biology:
Accelerated and Directed Evolution

“Creating artificial life with DNA synthesis.
That’s sort of the equivalent
of machine-language programming.
If you want to change the world in some big way,
use biological molecules.”

Bill Gates
Wired 2010

Synthetic Biology

Biological Parts Catalog



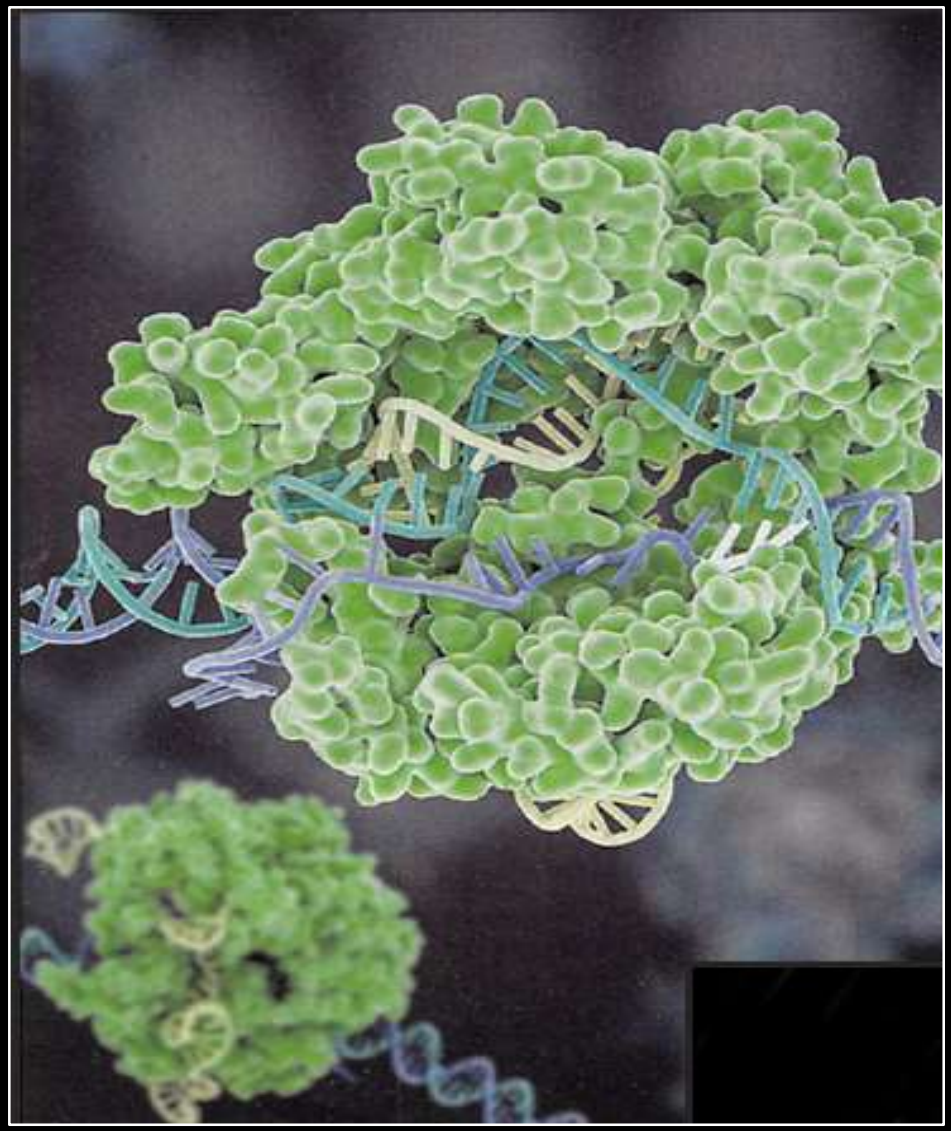
The Three Foundational Capabilities Required for Design and Assembly of New Biological Systems

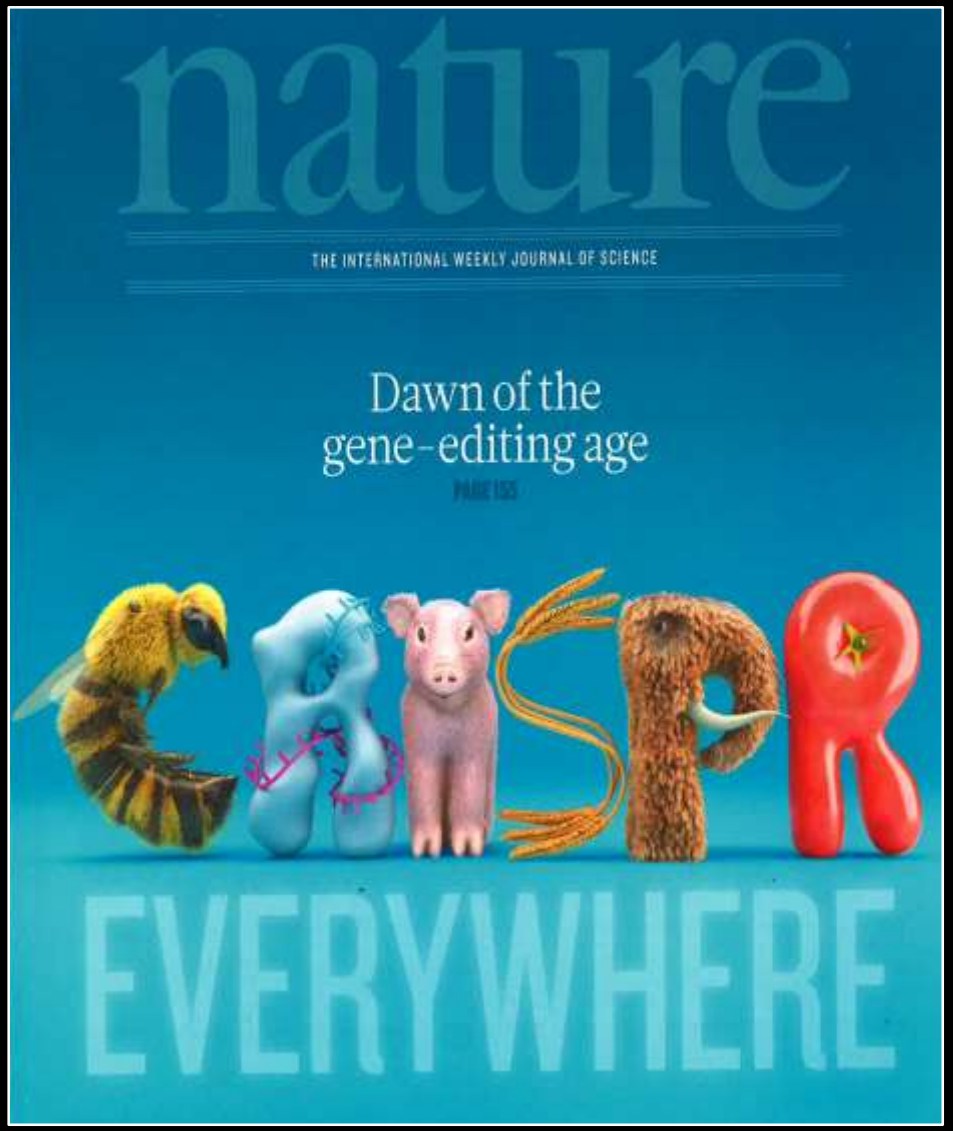
- ***Reading*** **genome codes (sequencing)**
- ***Writing*** **genome codes (synthesis)**
- ***Editing*** **genome codes (precision and assembly)**

Genome Editing

- targeted highly specific modification of genomes in any species
  - microorganisms, plants, animals, people
- single or multiple genes
- introduce entirel novel genes with no known natural (evolutionary) counterpart

CRISPR-cas9 and Precision Gene Editing



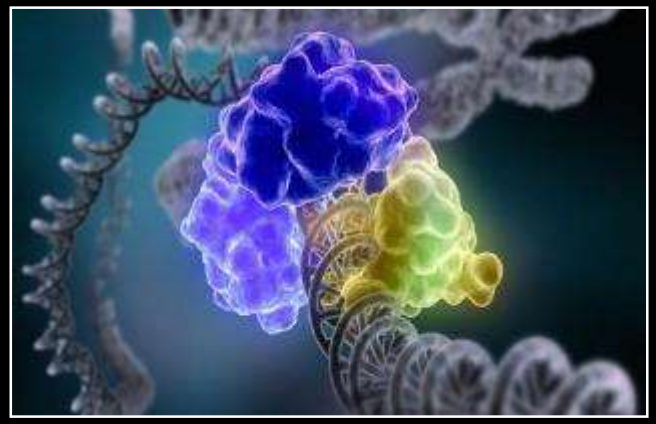


CRISPR-Cas and Precision Genome Editing

Using An Evolutionary Mechanism from 3-4 Billion Years Ago for 21st Century Genome Design

Change, Delete or Replace Genes in Any Living Species, Including Humans

CRISPRs: An Ancient Immune System



- **C**lustered, **R**egularly, **I**nterspersed, **S**hort, **P**alindromic **R**epeats

- role in protection of bacteria against viral (phage) attacks

Gene Editing

- ‘knockout’
  - delete or render non-functional
- ‘knock-in’
  - precision insertion of new gene(s) or control elements
- ‘silence’
  - switch off expression but DNA code unchanged
- ‘activate’
  - switch on gene expression by modification of regulatory proteins

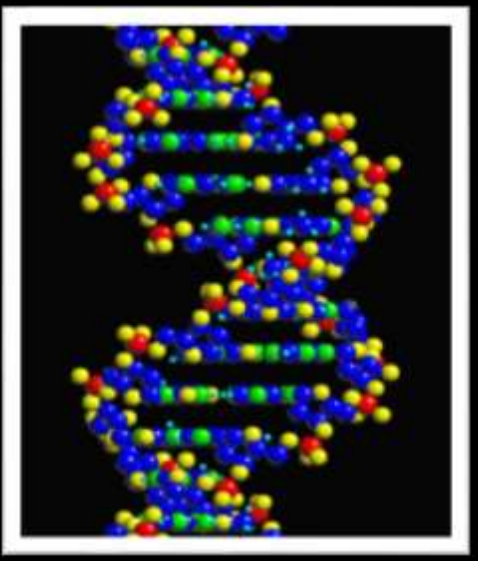
Gene Editing

- germ line modification
  - changes in gametes (sperm/egg) with inheritance by progeny
- somatic modification
  - changes in non-germ line cells with no inheritance by progeny

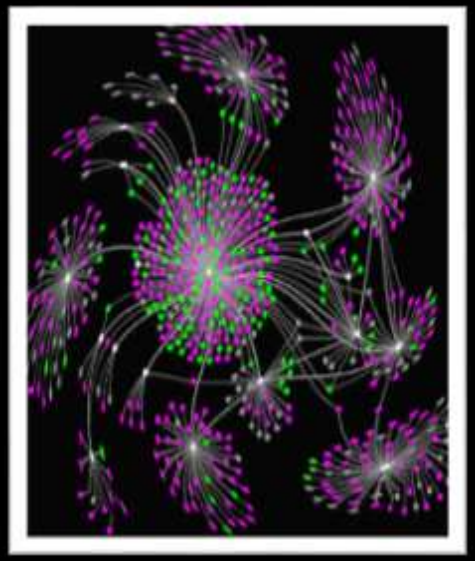
Fundamental Questions

- what does each gene do?
- how do alterations in genes and/or their control mechanisms lead to disease?
- how can this knowledge be used for productive applications in health, agriculture and sustainable ecosystems?
- how can the same information used for beneficent purposes be usurped for malignant applications?

Understanding Instructional Codes and the Disruption of Molecular Information Networks in Disease

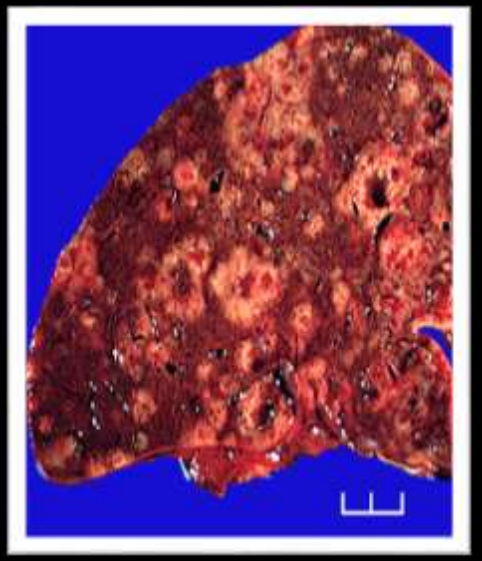


encoded information and expression as cell-specific signaling network



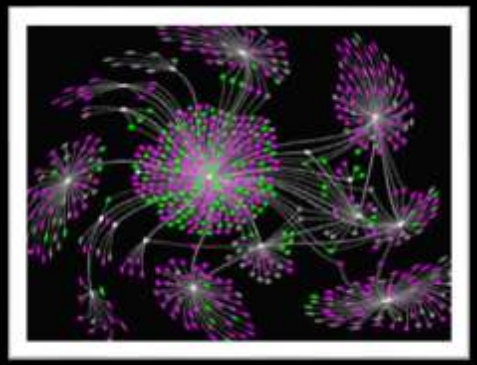
biological information and topology of signaling networks

stable networks and information fidelity (health)

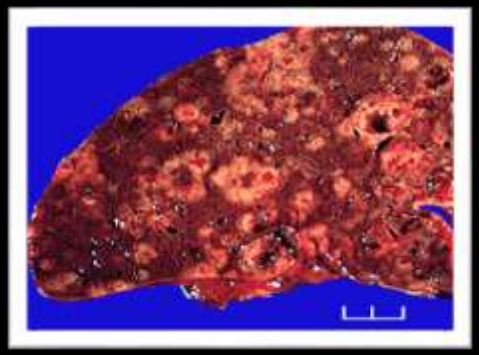


dysregulated networks and altered information patterns (disease)

Research Applications of Precision Gene Editing

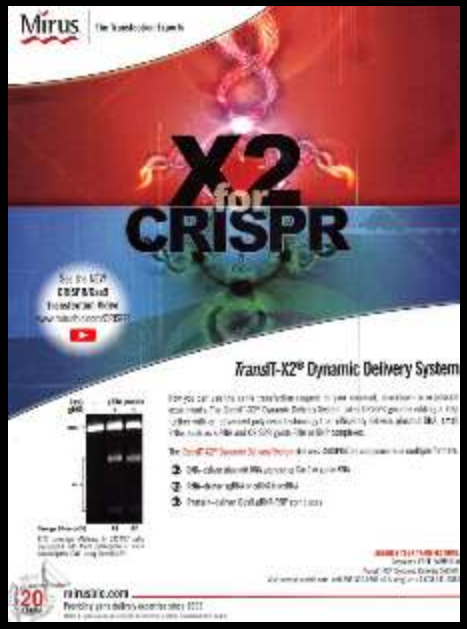


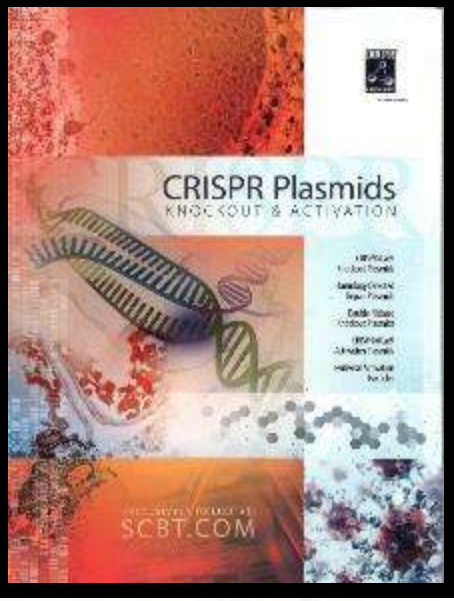
- understanding the function of specific genes
- mapping the genes for information signaling networks (circuit diagrams) responsible for diverse biological functions

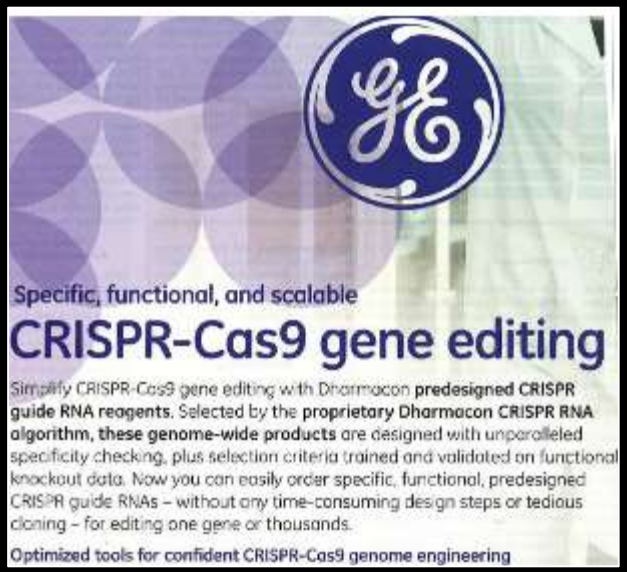


- characterization of how alterations in specific genes/circuit diagrams produce disease
- improved animal models of human diseases for selection of new drugs/vaccines for human trials

The Rapid Growth of a New Industry Supply Chain for CRISPR-Cas Gene Editing Services







Synthetic Biology and Engineering Enhanced Traits in Food, Feed and Fiber Products



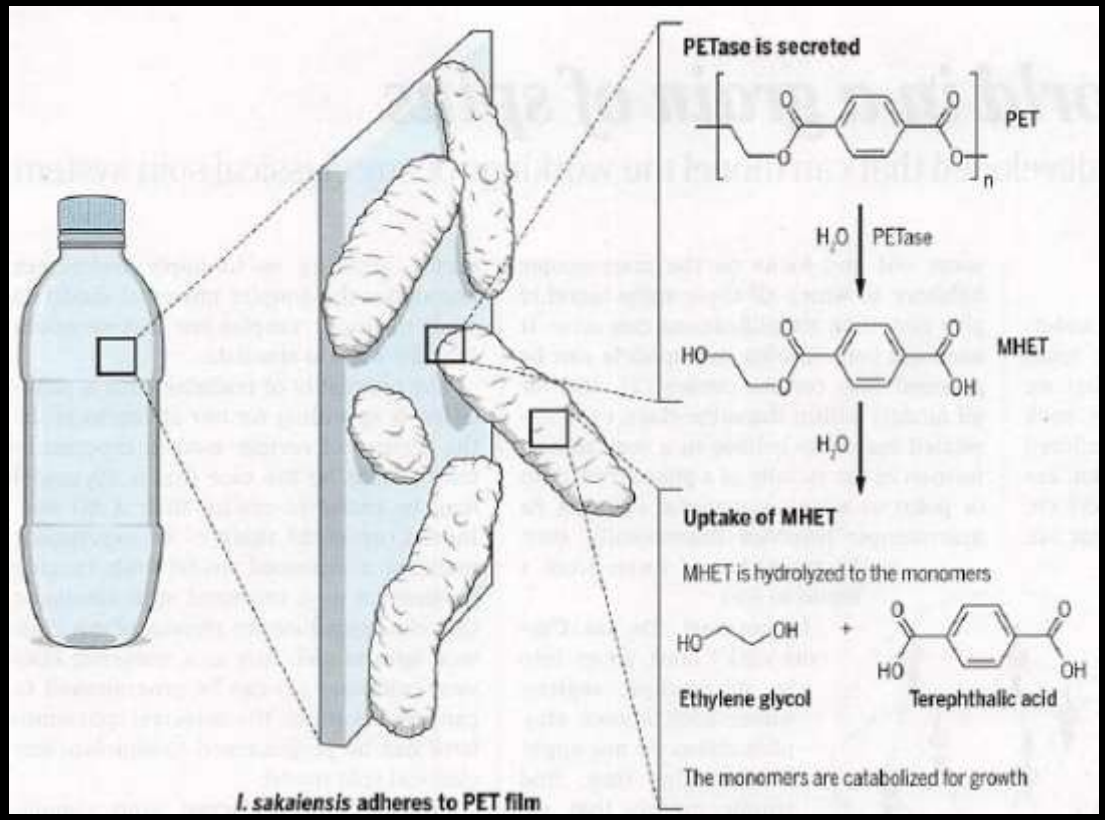





CRISPR-Cas and Engineering Wheat Resistance to Powdery Mildew

Extremophiles: Feeding on Toxics
Bacteria in Diverse Environments Adapt to Use ‘Niche’ Chemicals as Nutrients

Some Bacteria Think Plastic is Delicious: Science (2016) 351, 1155



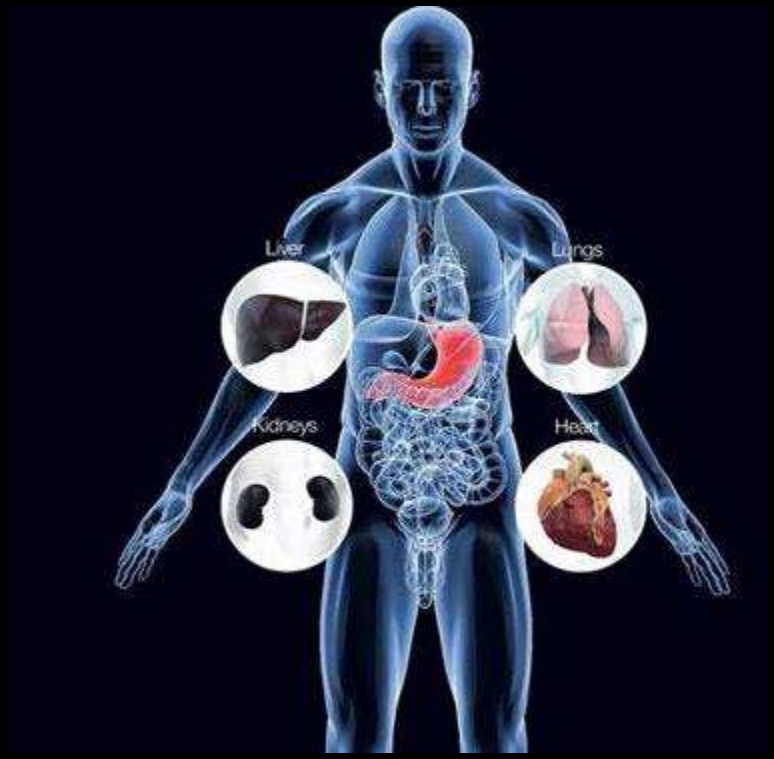
- **recovery and reuse of TPA**
- **major savings in plastic production**
- **eliminate need for gasoline-based starting materials**

CRISPR-Cas Precision Gene Editing and Engineered Resistance to Viral Diseases

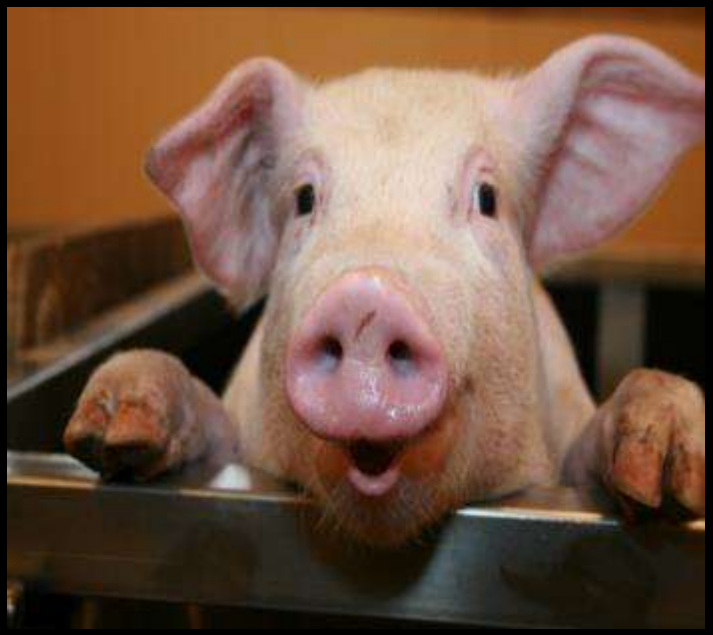
susceptible to African swine fever (ASV)

transfer ASV resistance genes to domestic pigs

CRISPR-Cas and Gene Editing to Design Pig Organs for Xenogeneic Transplantation to Humans



122K Americans on Waiting List for Organ Transplants



Elimination of Pig Genes That Trigger Transplant Rejection

Less Inspiring Commercial Applications of Gene Editing Techniques

Chinese Mini-Pigs

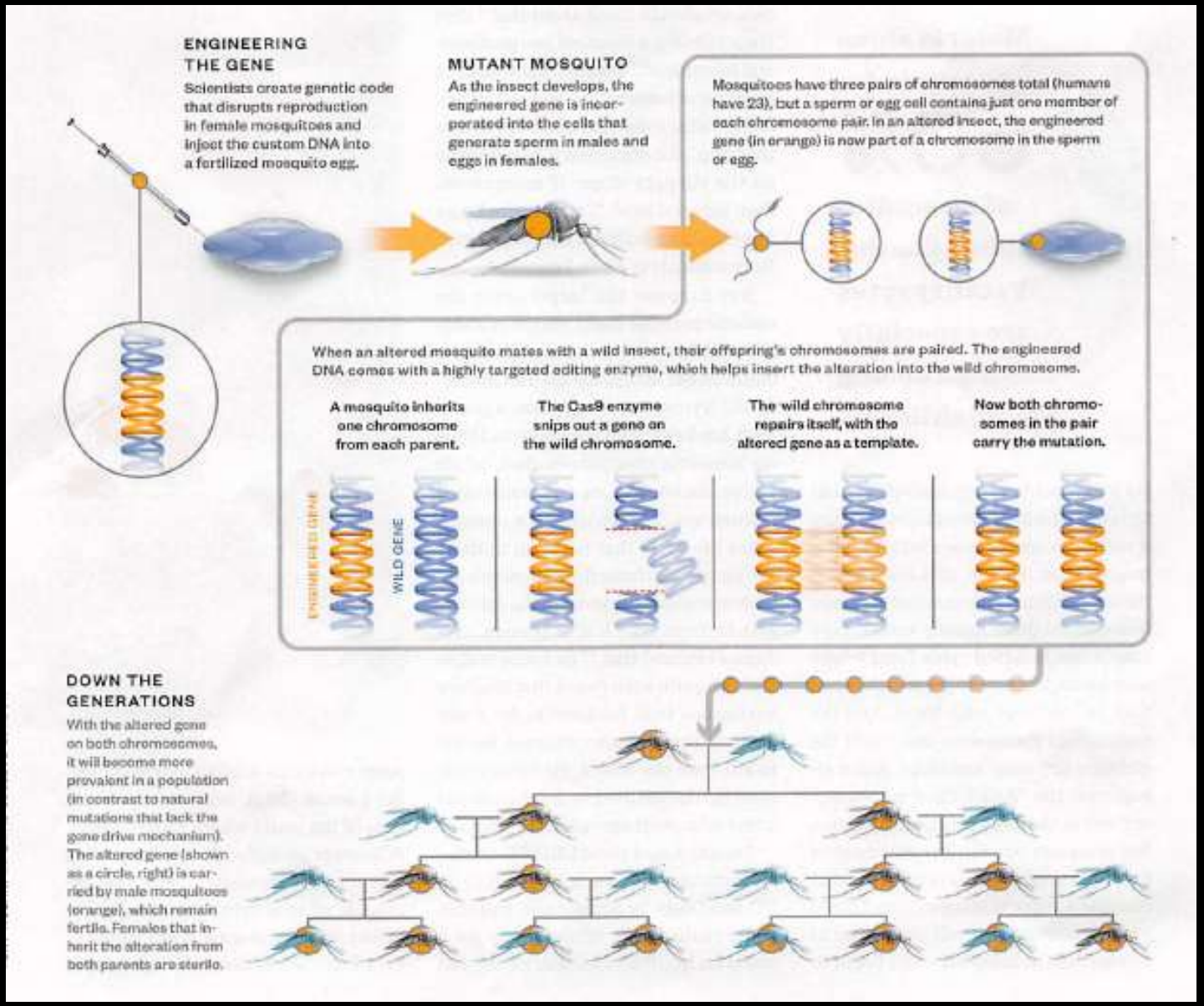
Desired Koi Coloration Patterns

The Toll of Vector-Borne Diseases

Zika virus microcephaly

Aedes aegypti vector

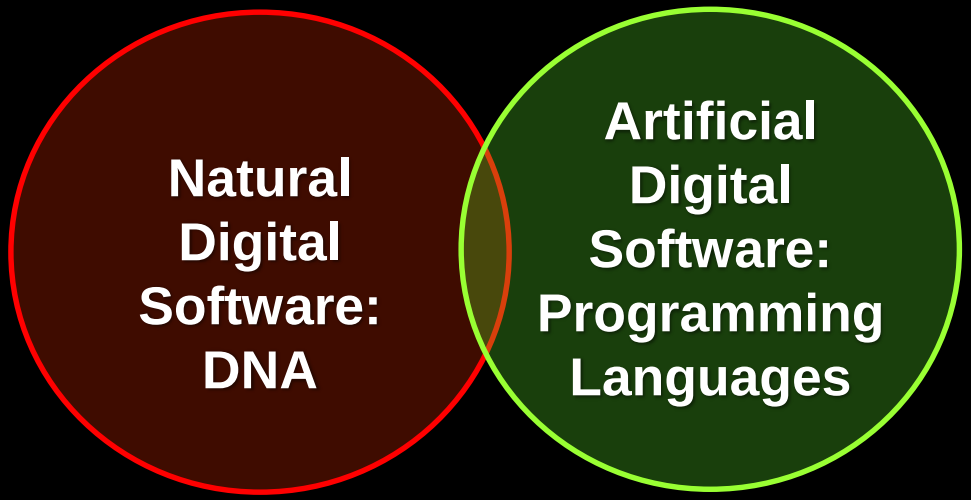
Gene Drives and Sterilization of Mosquitoes



From: Jerry Adler , SMITHSONIAN MAGAZINE June 2016

Gene Drives:
What are the Ecological Consequences of Eliminating a Species?

Digital Convergence



$3 – 4 \times 10^9$ years old

60 - 70 years old

Digital Biology

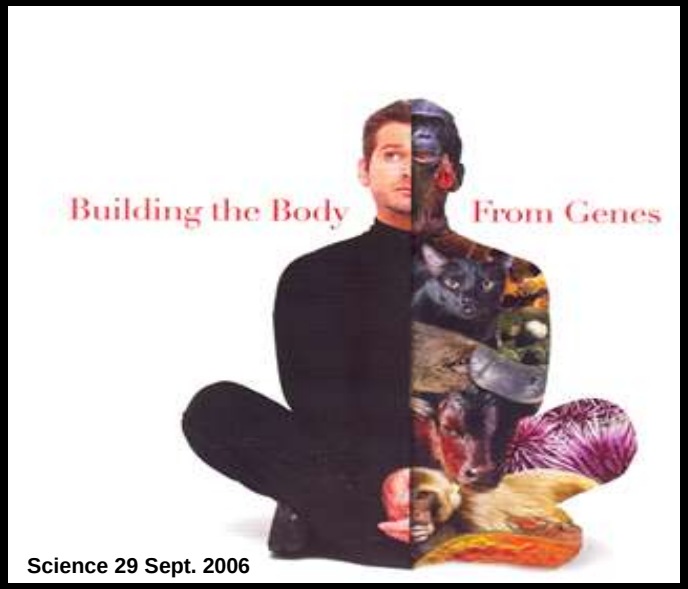
- DNA is a digital code
- biology at internet speed
  - transmission of digital instruction code to any location
  - geographic uncoupling of design (code) from manufacture (synthesis and assembly)

Reprogramming Body Cells to Express New Functions

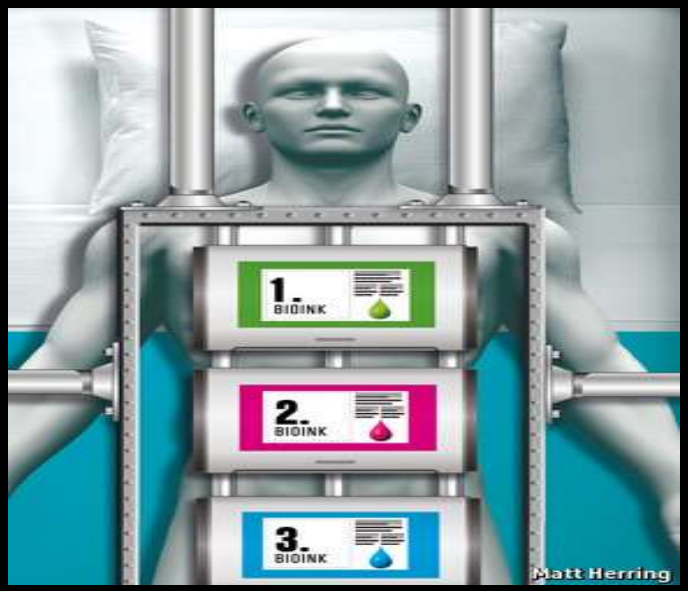
Reprogramming Body Cells to Express New Functions

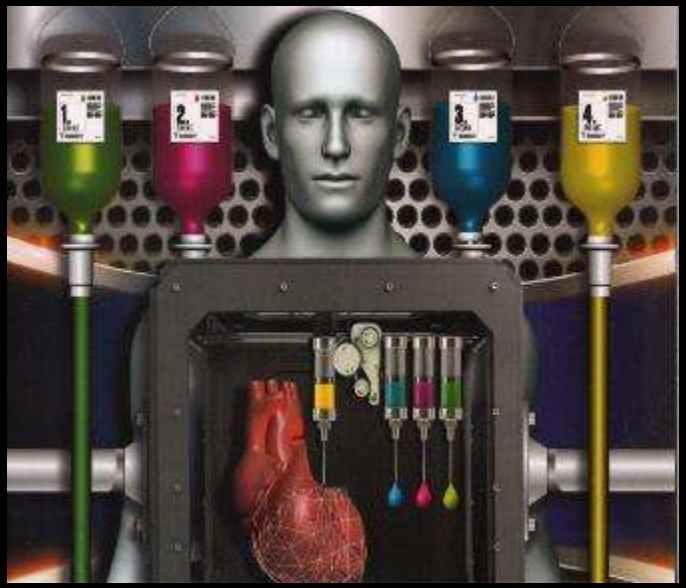
- gene therapy to introduce missing function into body cells (Rx)
- conversion of one cell type into another

Regenerative Medicine:
Synthetic Biology and Tissue Engineering



Science 29 Sept. 2006





Dual-Use Technologies

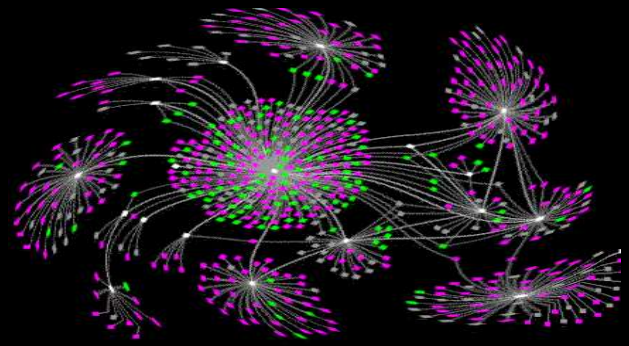
Beneficent and Maleficent Applications of the Same Knowledge

Synthetic Biology, Genome Editing and Engineering of Biological Circuits

digital biology: "it from bits"

de novo synthesis of organisms

engineered virulence



华大基因学院
BGI college
华大基因研究院
BGI research

targeted modification of any biological circuit in any organ

mapping neural circuitry brain – machine interfaces

accelerating technological diffusion

Synthetic Biology, Genome Editing and National Security: The Ultimate Dual-Use Technology for Modification of Biological Systems?

Statement for the Record

Worldwide Threat Assessment
of the
US Intelligence Community

Senate Select Committee on Intelligence

James R. Clapper

Director of National Intelligence

February 9, 2016

Technology Diffusion, Automation and Simplification

Outmoded CBW Treaty: New Oversight Mechanisms

Gene Editing of Humans

Augmentation (non-heritable)

Enhancement (heritable)

Genetic Modification of Somatic Cells Versus Germ Cells (Gametes)

Very Different Ethical, Legal and Social Complexities

Editing Humanity:
Moral and Legal Constraint or Hubris and Irresistible Inevitability?

- long standing science fiction scenarios and philosophical, religious, ethical, legal debates on the societal implications
- previous luxury of theoretical debate because the technology was not available

Editing Humanity:
No Longer An Abstract Question

Research article

CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes

Puping Liang[1], Yanwen Xu[1], Xiya Zhang[1], Chenhui Ding[1], Rui Huang[1], Zhen Zhang[1], Jie Lv[1], Xiaowei Xie[1], Yuxi Chen[1], Yujing Li[1], Ying Sun[1], Yaofu Bai[1], Zhou Songyang[1], Wen[illegible] Ma[1], Canquan Zhou[1] ✉ and Junjiu Huang[1] ✉

(1) Guangdong Province Key Laborato[illegible]eproductive Medicine, the First Affiliated Hospital, and Key Labora[illegible] Gene Engineering of the Ministry of Education, School of Life Sciences, [illegible] Yat-sen University, Guangzhou, 510275, China

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✉ **Junjiu Huang (Corresponding author)**
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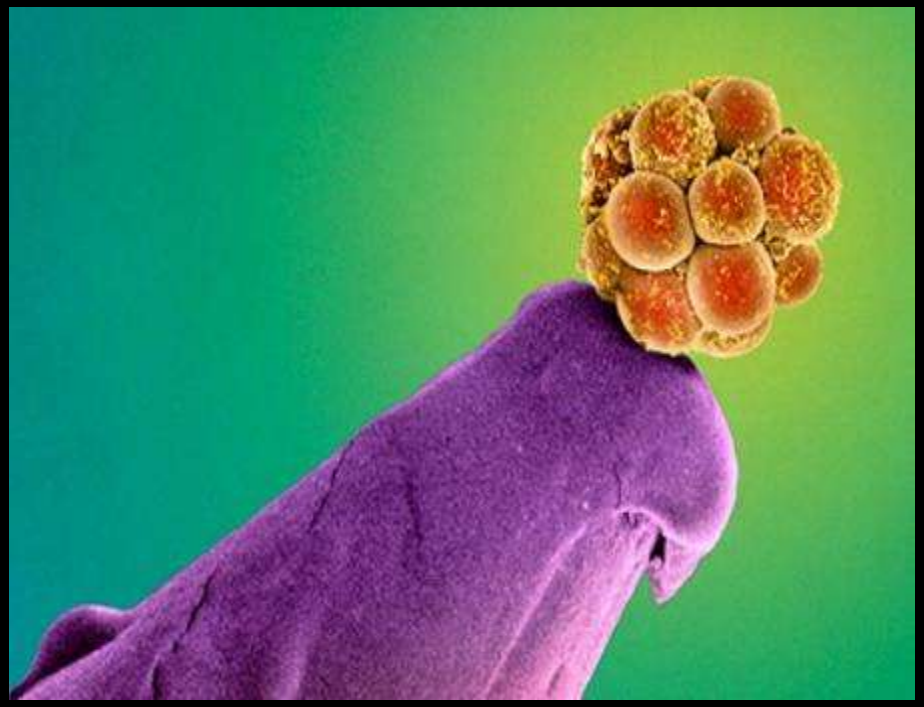


International Summit on Human Gene Editing: Washington, DC 1-3 December 2015

"Today, we sense that we are close
to being able to alter human heredity.
Now we must face the questions that arise.
How, if at all, do we as a society
want to use this capability?

Dr. David Baltimore

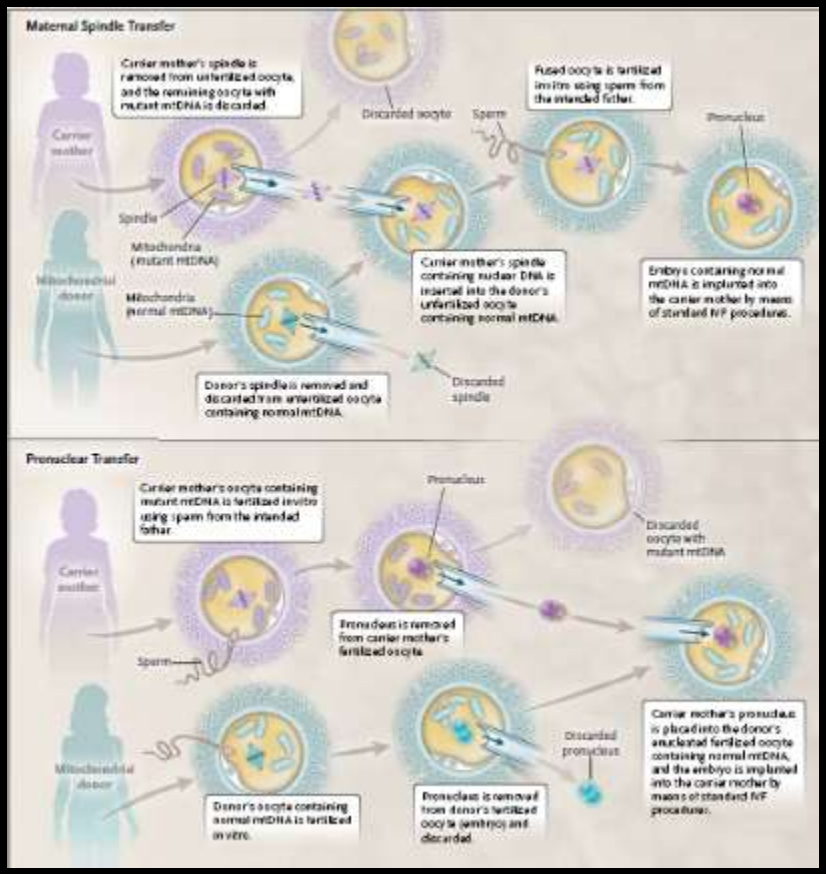
Germ Line Gene Editing and Heritable Genetic Modifications

- complex ethical, social and legal issues
  - impact on future generations
  - moral status and rights of the unconsented embryo
- varied responses of patient advocacy groups affected by inherited disorders
  - “hell yes, do it” versus “let’s wait to see the technology mature”
- the lurking spectre of eugenics
  - social justice, equity, coercion
  - economic forces
  - who decides?

Human Fertilisation & Embryology Authority

THE FRANCIS CRICK INSTITUTE

Mitochondrial Replacement Therapy



From: M.J. Falk et al. (2016) NEJM 374, 1103

Genome Engineering and Medical Tourism

Offshore Surrogate Mothers, Stem-Cell Treatments and Organ Transplants

Market Precursors for Next Phase of Customized Gene Edited Human Embryos?

Different Technical Challenges in Single Gene Versus Multi-gene Modifications

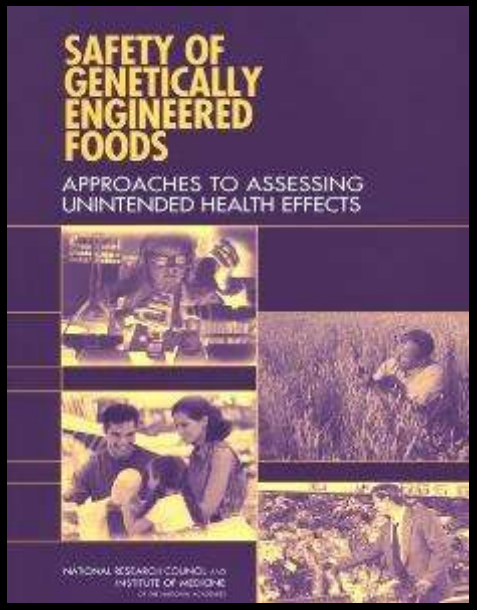
- inherited single gene disorders
  - Cystic Fibrosis
- currently unknown number of genes responsible for complex late onset diseases
  - Type 2 diabetes, cancer, neurodegeneration

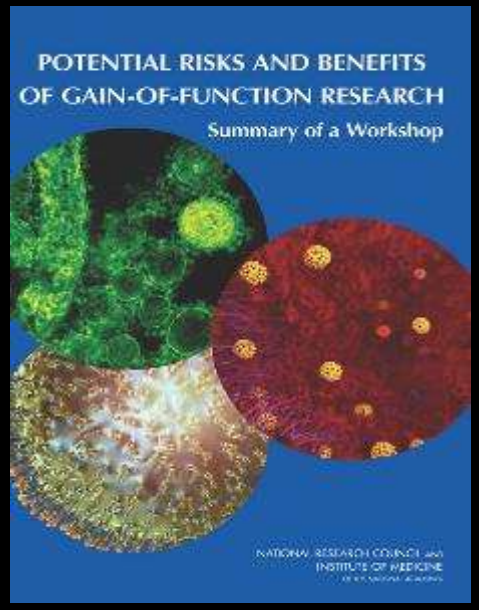
Reprogramming of Somatic Cells to Produce Totipotent Stem Cells, Spermatozoa and Ova

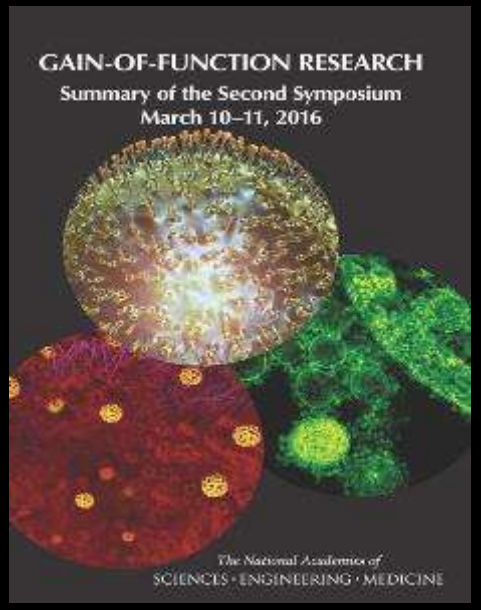
- convert easily accessible non-gamete cells (e.g. skin) into cells with reproductive potential (gametes)
- produce totipotent stem cells able to generate a complete organisms (cloning)

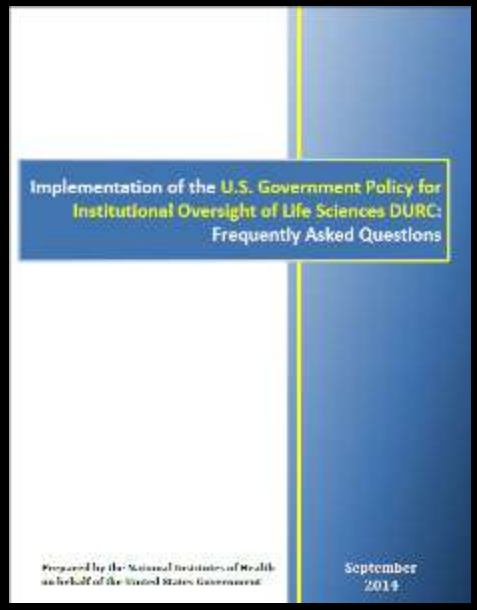
Reprogramming of Somatic Cells to Produce Spermatozoa and Ova

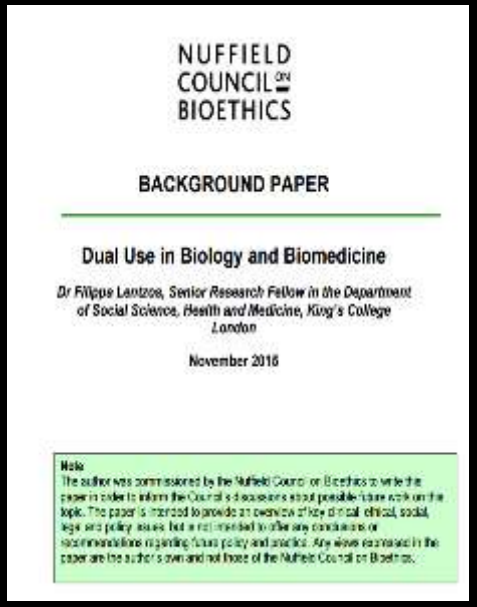
- convert skin cells into gametes
- transfer of genetic information from infertile donor to achieve pregnancy by IVF
- dual-use risks
  - mass production of sperm/eggs from single donor and large scale propagation of donor genes (animal husbandry versus human eugenics)
  - theoretical scenario of production of egg and sperm from same donor and IVF conception

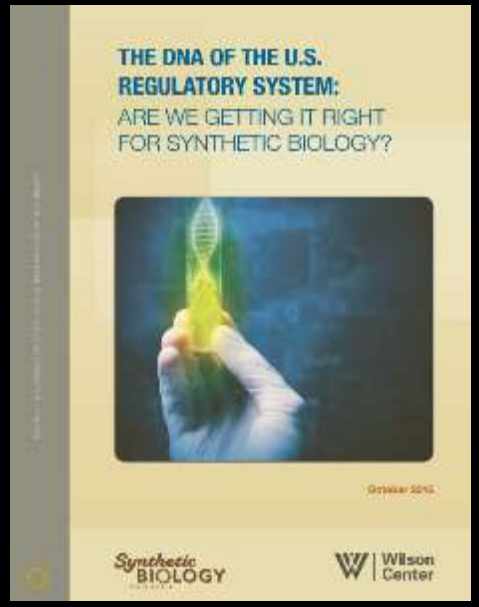

SAFETY OF GENETICALLY ENGINEERED FOODS
APPROACHES TO ASSESSING UNINTENDED HEALTH EFFECTS
NATIONAL RESEARCH COUNCIL AND INSTITUTE OF MEDICINE


POTENTIAL RISKS AND BENEFITS OF GAIN-OF-FUNCTION RESEARCH
Summary of a Workshop
NATIONAL RESEARCH COUNCIL AND INSTITUTE OF MEDICINE

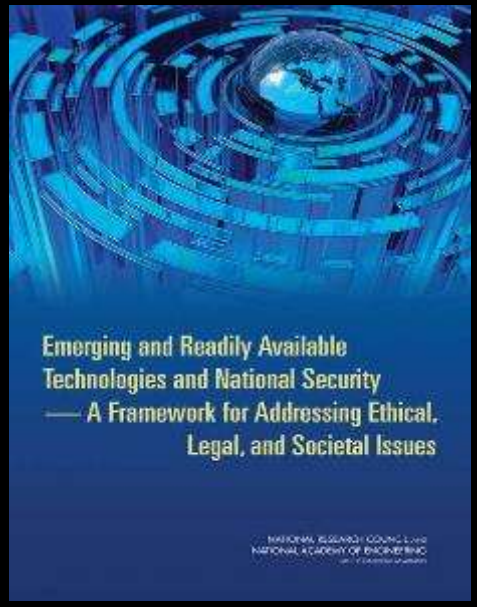

GAIN-OF-FUNCTION RESEARCH
Summary of the Second Symposium
March 10–11, 2016
The National Academies of
SCIENCES • ENGINEERING • MEDICINE


Implementation of the U.S. Government Policy for Institutional Oversight of Life Sciences DURC: Frequently Asked Questions
September 2014


NUFFIELD COUNCIL ON BIOETHICS
BACKGROUND PAPER
Dual Use in Biology and Biomedicine
Dr Filippa Lentzos, Senior Research Fellow in the Department of Social Science, Health and Medicine, King's College London
November 2016
Note
The author was commissioned by the Nuffield Council on Bioethics to write the paper in order to inform the Council's discussions about possible future work on the topic. The paper is intended to provide an overview of key ethical, social, legal and policy issues but is not intended to offer any conclusions or recommendations regarding future policy and practice. Any views expressed in the paper are the author's own and not those of the Nuffield Council on Bioethics.


THE DNA OF THE U.S. REGULATORY SYSTEM:
ARE WE GETTING IT RIGHT FOR SYNTHETIC BIOLOGY?
Synthetic BIOLOGY
Wilson Center

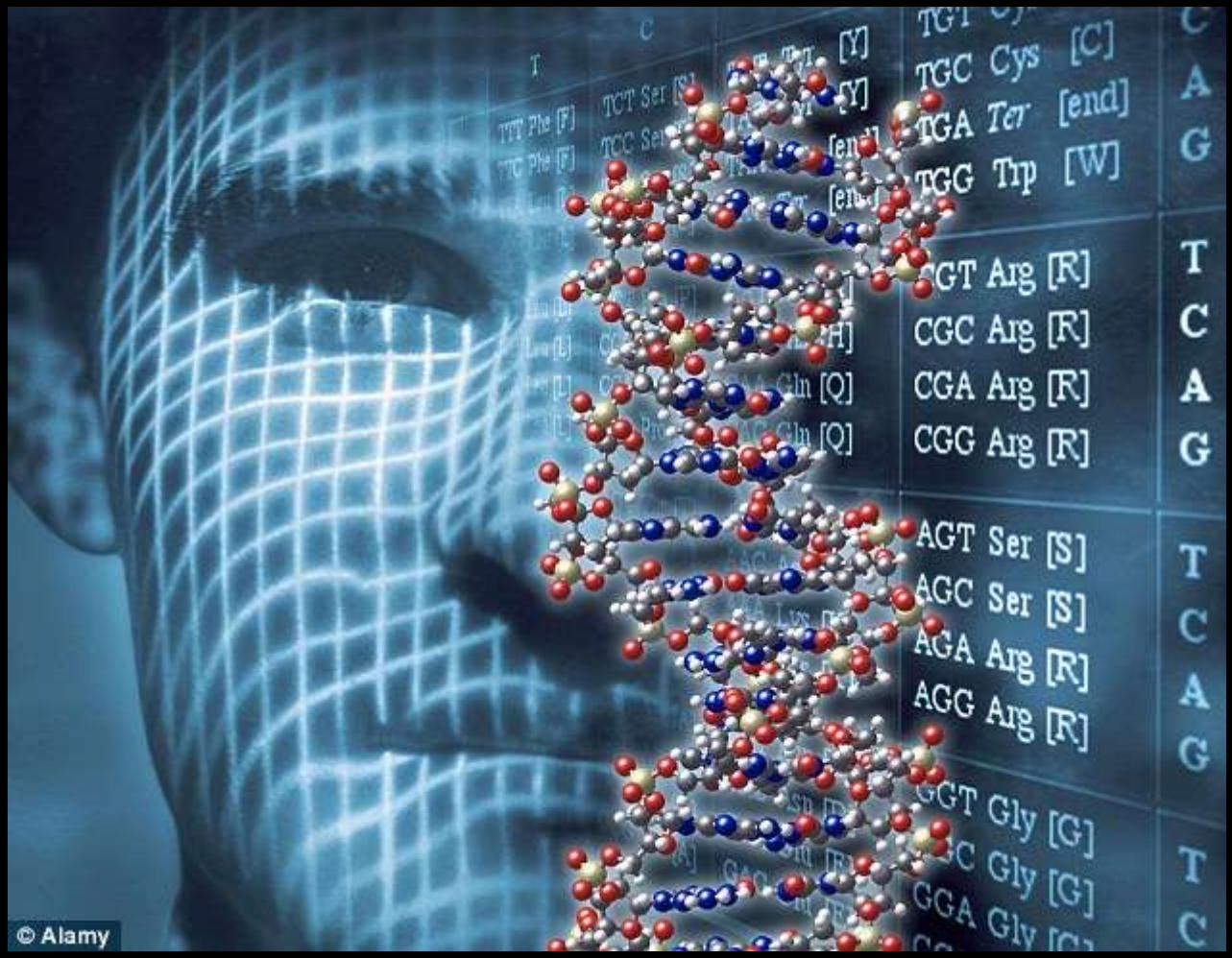

Opinion on
Synthetic Biology II
Risk assessment methodologies and safety aspects
Scientific Committees


Emerging and Readily Available Technologies and National Security
— A Framework for Addressing Ethical, Legal, and Societal Issues
NATIONAL RESEARCH COUNCIL AND NATIONAL ACADEMY OF ENGINEERING

The Human Condition:
Rights, Risks and Responsibilities

We hold these truths to be self-evident, that all men are created equal, that they are endowed by their Creator with certain unalienable Rights, that among these are Life, Liberty and the pursuit of Happiness.

The Human Condition:
Rights, Risks and Responsibilities



"What unalienable Rights do we now hold as self-evident in an era of new technologies for genetic modification?"

Arguments Against Bioenhancement

- religious objections of ‘Playing God’ and ‘Scientific Hubris’
- secular concern of ‘altering the natural balance of nature’
- subversion of human dignity by commodification of human traits and capabilities
- disruption/destruction of qualities that render us human
- eugenics
- inequitable access and distributive justice
- prejudice and fragmentation of the species
- unknown and unintended consequences

The Journey to the Anthropocene: The Long History of Technology-Enabled Human Augmentation

- improved health, shelter, labor, education
- improved nutrition, clean water, sanitation, infrastructure
- transportation
- public policies and protection of individual rights
- advances in clinical medicine and therapeutics
- devices, implants, prostheses
- computing, connectivity and communication
- in vitro fertilization
- somatic cell gene therapy

The Journey to the Anthropocene: The Long History of Technology-Enabled Human Augmentation

- improved health, shelter, labor, education

These ‘protections’ have shaped the gene pool of today’s population

- devices, implants, prostheses
- computing, connectivity and communication
- in vitro fertilization
- somatic cell gene therapy

Arguments in Favor of Bioenhancement

- limit human suffering
- intrinsic human drive in the Promethean quest for new knowledge, new capabilities and richer experiences
- next phase in the technological trajectory of human control of the natural world (the anthropocene)

Core Questions in the Bioenhancement Debate

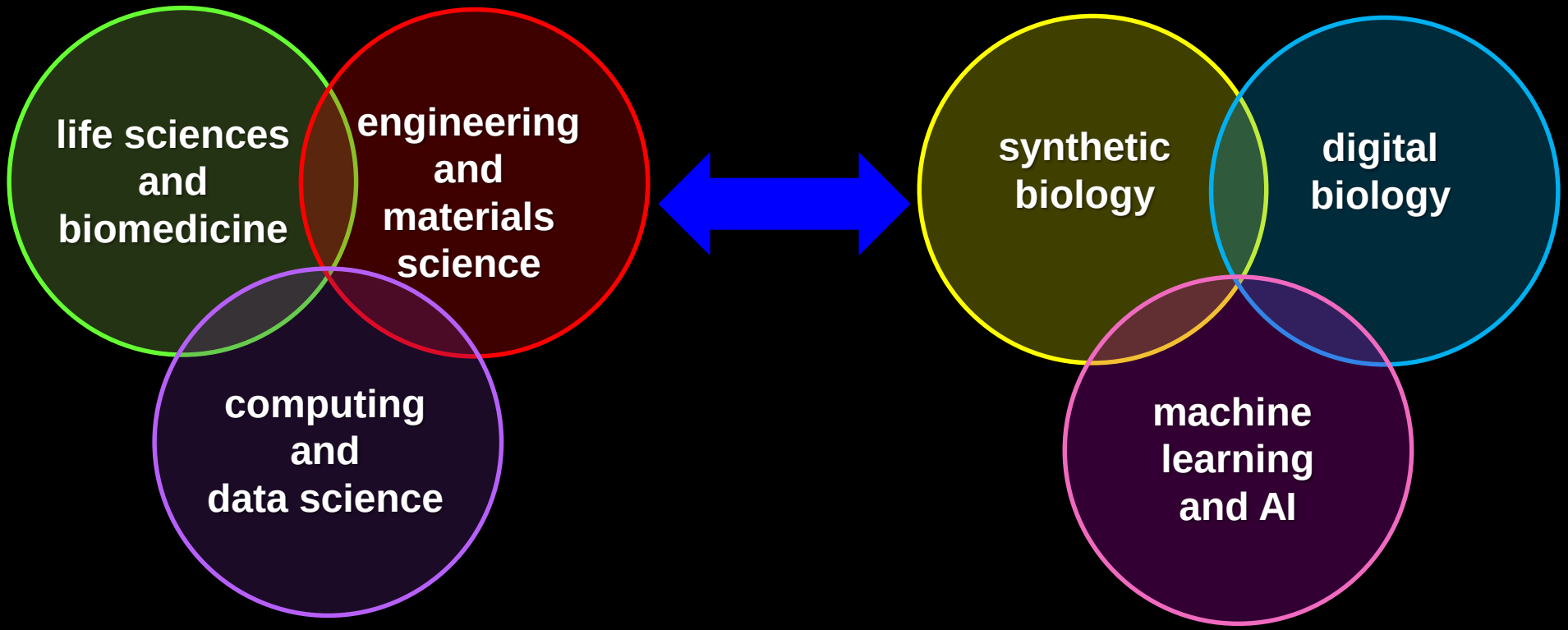
- future directed and accelerated evolution by purposeful design of desired of desired new biological systems
- what should be designed?
- who has access?
- who decides?

The Governance and Oversight of New Technologies

Technology Acceleration and Convergence

The Growing Gap Between Technological Change and Adaptive Public Policies

Technology Acceleration and Technology Convergence
"The Exponential of the Exponentials"



Societal Retreat from Complexity and The Dangers of Increasing Scientific Illiteracy

Societal Retreat from Complexity and the Dangers of Increasing Scientific Illiteracy

- shortcomings in K-12 STEM education
  - priority, resources, teaching methods, standards
- the cocoon of comfort and complacency
  - out-of-sight, out-of-mind
- “bread and circuses”
  - keeping society amused/diverted
  - media focus on the local and the superficial
  - reality TV, tweets
  - reduced attention spans
- legislative inertia and ignorance at national and international levels
  - “too-hard problem category”
  - “kick the can down the road”

Societal Retreat from Complexity and the Dangers of Increasing Scientific Illiteracy

- shortcomings in K-12 STEM education
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strategic implications for future national competitiveness, economic strength and national security

  - reduced attention spans
- legislative inertia and ignorance at national and international levels
  - “too-hard problem category”
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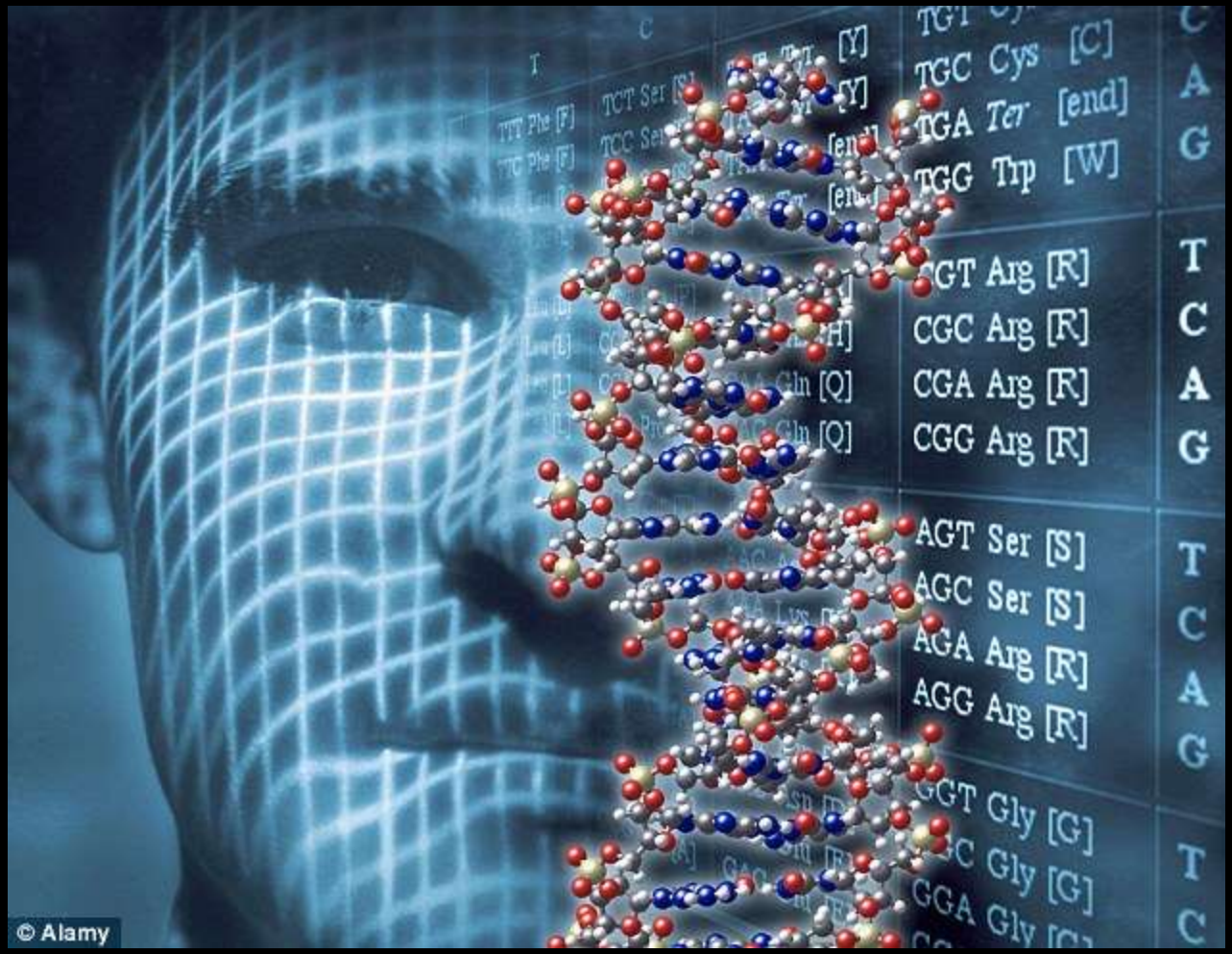
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A Philosophy for Robust Preparedness Against Complex and Existential Challenges

**"Politics is the art of the possible,
the calculated science of survival"**

Prince Otto von Bismarck

**"Survival owes little to the art of politics,
but everything to the calculated application
of science".**

**Professor Rudolph Virchow
(in reply)**