Challenges for the Governance of Synthetic Biology and Implications for UN Security Council resolution 1540 (2004)

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Global markets are the drivers of advances in S&T

The biotech market will grow at an average annual growth rate 11.6% (2012 to 2017) and reach a value worth USD 727.1 billion by 2025.

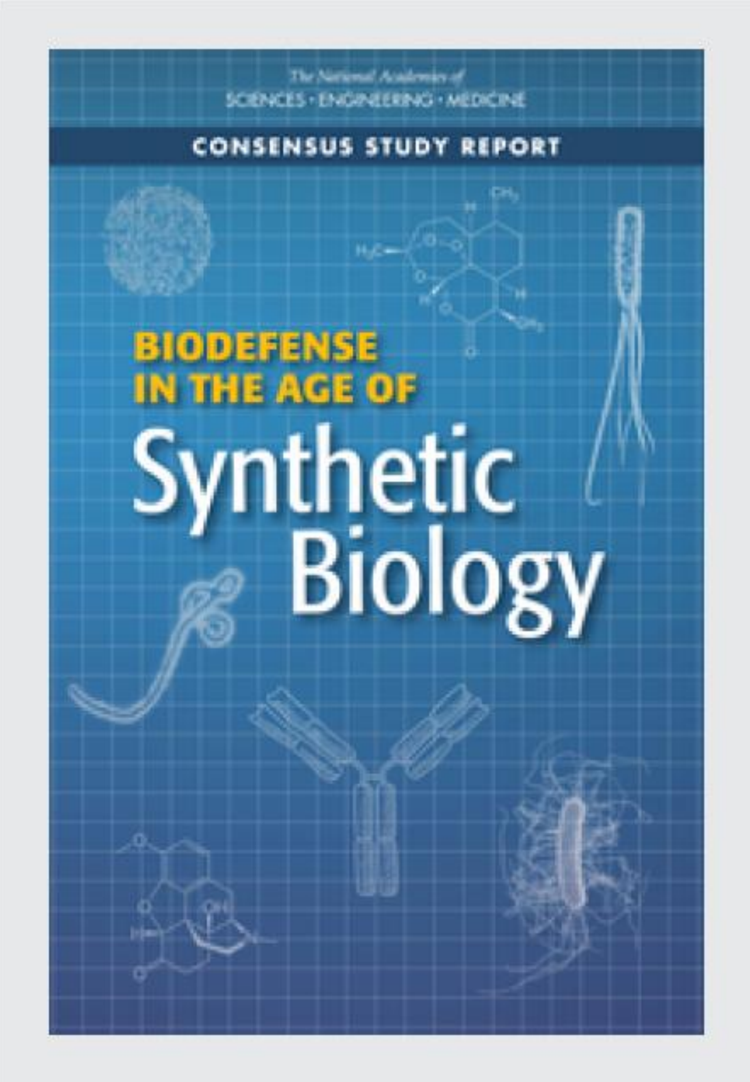
The synthetic biology market will grow at an average annual growth rate of 44.2 %(2017-2020) and reach a value worth USD 38.7 billion by 2020.

http://www.prnewswire.com/news-releases/
https://www.grandviewresearch.com/press-release/global-biotechnology-market
http://www.bio-itworld.com/

What is synthetic biology?

- SynBio collectively refers to concepts, approaches, and tools that enable the modification or creation of biological organisms.

- SynBio is being pursued overwhelmingly for beneficial purposes ranging from reducing the burden of disease to improving agricultural yields to remediating pollution.



However….

It is also possible to imagine malicious uses that could lead to events that might threaten the health and safety of citizens, destabilize governments, disrupt social enterprises, destroy agriculture and the global economy, and imperil the very survival of the planet.

Enabling technologies for synbio

- DNA/RNA/protein sequencing and synthesis
- Microfluidicis
- Nanotechnology
- Modularity
- Robotics
- Synthetic transcription factors
- Biosensors

Key SynBio approaches in use

Approach	Beneficial application
Re-creating known bacteria, viruses, algae	Vaccine design, other MCMs
Making existing pathogens more dangerous	Pathogenesis studies
Creating new bacteria or viruses	Biofuel production or cleanup
Manufacturing chemicals using metabolic pathways	Pharmaceuticals, biofuels
Modifying the human microbiome	Reprogramming the gut
Modifying the human immune system	Immunotherapeutics
Modifying the human genome	Somatic vs germ line

TABLE 7-3 A summary of the relative maturity of selected convergent technologies. For each column, darker shading indicates the technology is in routine use for that community, lighter shading indicates emerging use, and white background indicates little or no use. Adoption flows from left to right in most cases.

Technology	In development	In use by developers of the technology	In use by the synthetic biology community	In use by the molecular biology community	In use by amateur biologists
Gene therapy					
Nanotechnology					
Automation					
Additive manufacturing					
Health informatics					

Framework for assessing concern

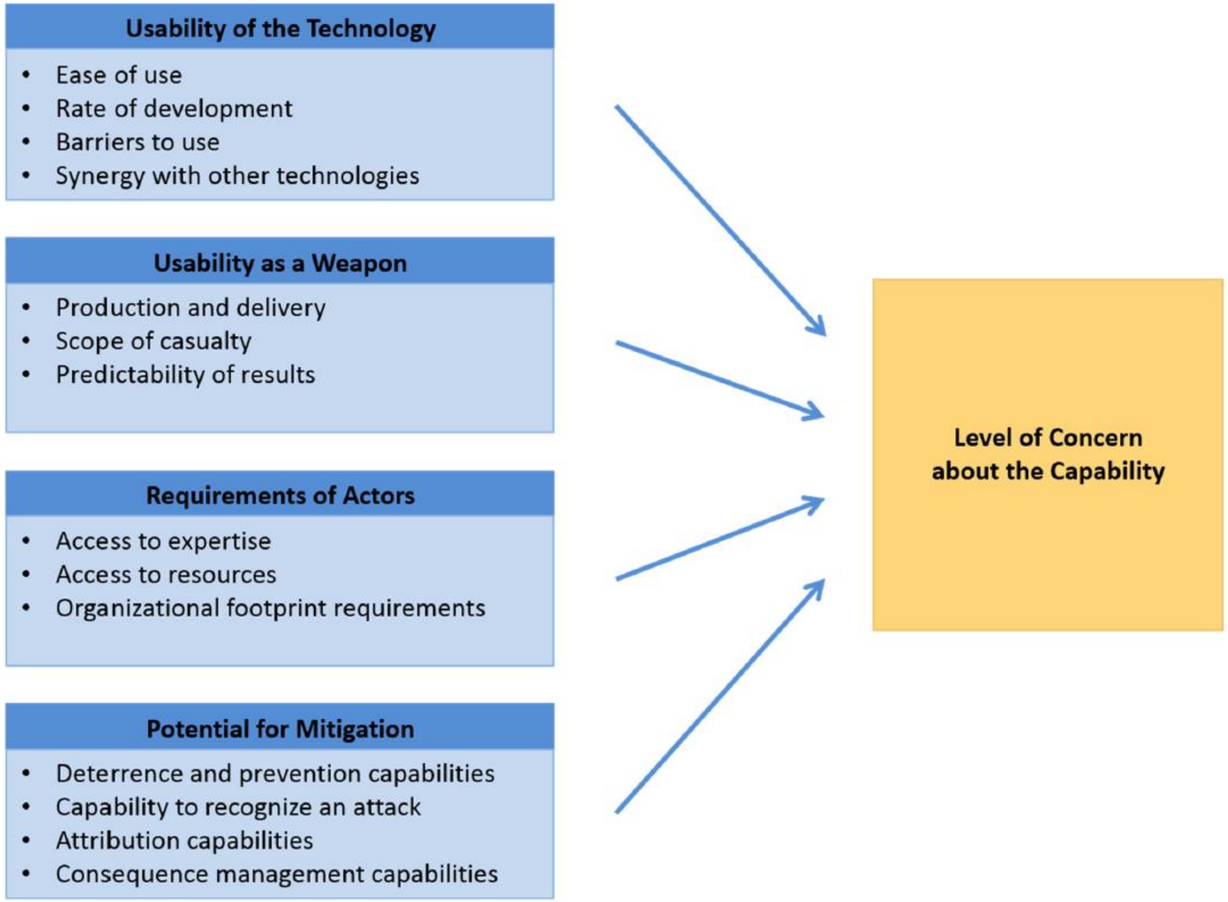


FIGURE S-1 Framework for assessing concern. The framework for assessing concern consists of four factors, along with descriptive elements within each factor. The factors are Usability of the Technology, Usability as a Weapon, Requirements of Actors, and Potential for Mitigation.

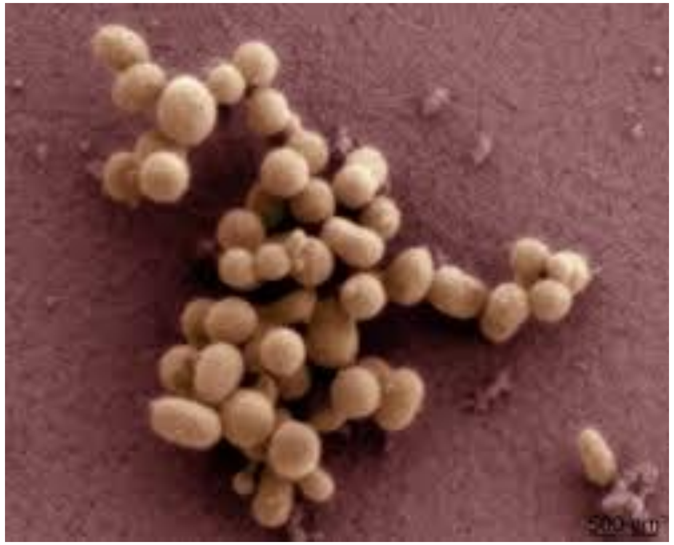
1. Usability of the technology
2. Usability as a weapon
3. Requirements of actors
4. Potential for mitigation

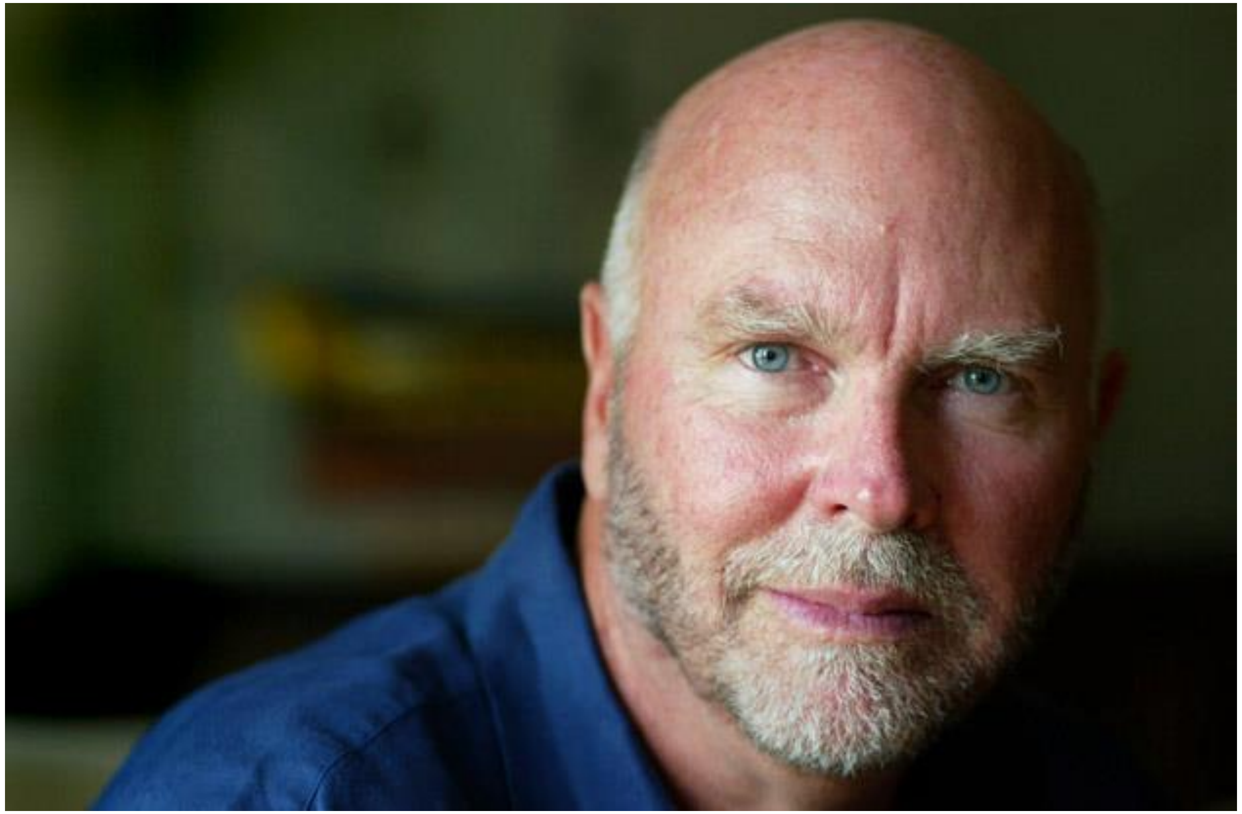
Biodefense in the age of synthetic biology, US-NASEM 2018

WIRED

Scientists Build First Man-Made Genome; Synthetic Life Comes Next

By Alexis Madrigal 01.24.08 | 11:00 AM





Science
AAAS

Lartigue et al. , pp. 632 - 638

Originally published in *Science* Express on 28 June 2007
Science 3 August 2007:
Vol. 317. no. 5838, pp. 632 - 638
DOI: 10.1126/science.1144622

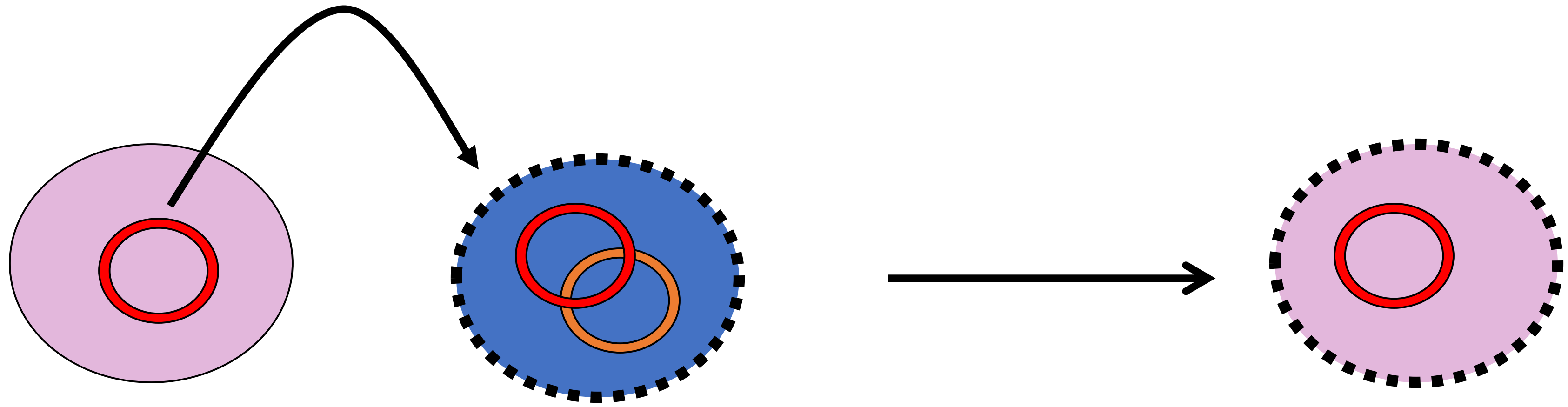
RESEARCH ARTICLES

Genome Transplantation in Bacteria: Changing One Species to Another

Carole Lartigue, John I. Glass,* Nina Alperovich, Rembert Pieper, Prashanth P. Parmar, Clyde A. Hutchison, III, Hamilton O. Smith, J. Craig Venter

The Venter Experiments

1.



RESEARCH ARTICLE

Complete Chemical Synthesis, Assembly, and Cloning of a *Mycoplasma genitalium* Genome

Daniel G. Gibson, Gwynedd A. Benders, Cynthia Andrews-Pfannkoch, Evgeniya A. Denisova, Holly Baden-Tillson, Jayshree Zaveri, Timothy B. Stockwell, Anushka Brownley, David W. Thomas, Mikkel A. Algire, Chuck Merryman, Lei Young, Vladimir N. Noskov, John I. Glass, J. Craig Venter, Clyde A. Hutchison III, Hamilton O. Smith*

We have synthesized a 582,970–base pair *Mycoplasma genitalium* genome. This synthetic genome, named *M. genitalium* JCVI-1.0, contains all the genes of wild-type *M. genitalium* G37 except MG408, which was disrupted by an antibiotic marker to block pathogenicity and to allow for selection. To identify the genome as synthetic, we inserted "watermarks" at intergenic sites known to tolerate transposon insertions. Overlapping "cassettes" of 5 to 7 kilobases (kb), assembled from chemically synthesized oligonucleotides, were joined by in vitro recombination to produce intermediate assemblies of approximately 24 kb, 72 kb ("1/8 genome"), and 144 kb ("1/4

genome, we needed to establish convenient and reliable methods for the assembly and cloning of much larger synthetic DNA molecules.

Strategy for synthesis and assembly. The native 580,076-bp *M. genitalium* genome sequence (*Mycoplasma genitalium* G37 ATCC 33530 genomic sequence; accession no. L43967) (*3*) was partitioned into 101 cassettes of approximately 5 to 7 kb in length (Fig. 1) that were individually synthesized, verified by sequencing, and then joined together in stages. In general, cassette boundaries were placed between genes so that each cassette contained one or several complete genes. This will simplify the future deletion or manipulation of the genes in individual cassettes. Most cassettes overlapped their adjacent neighbors by 80 bp; however, some segments overlapped by as much as 360 bp. Cassette 101 overlapped cassette 1, thus completing the circle.

Short "watermark" sequences were inserted in cassettes 14, 29, 39, 55 and 61. Watermarks are

The Venter Experiments

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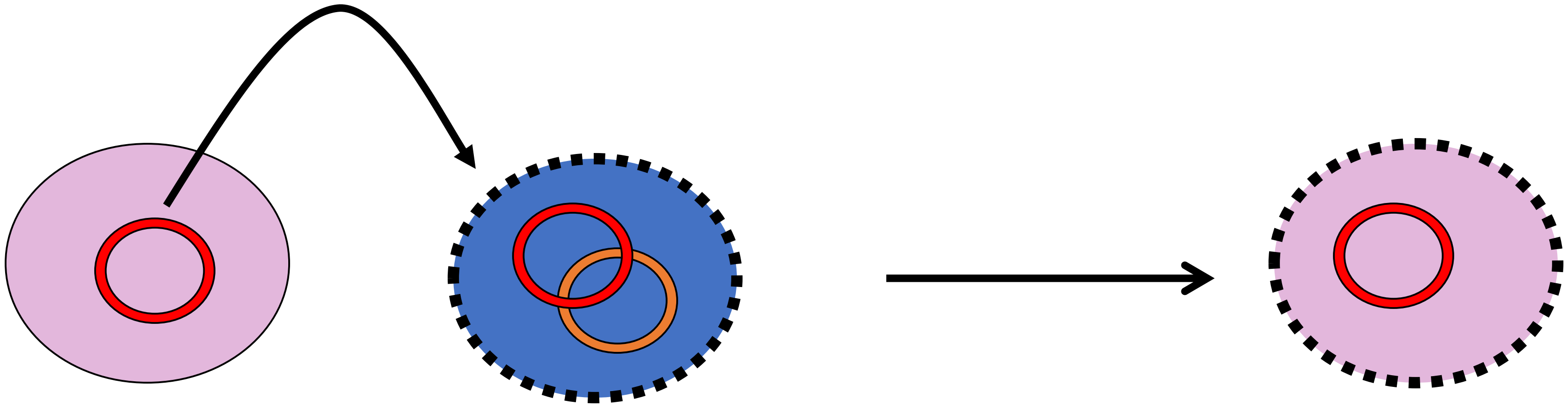

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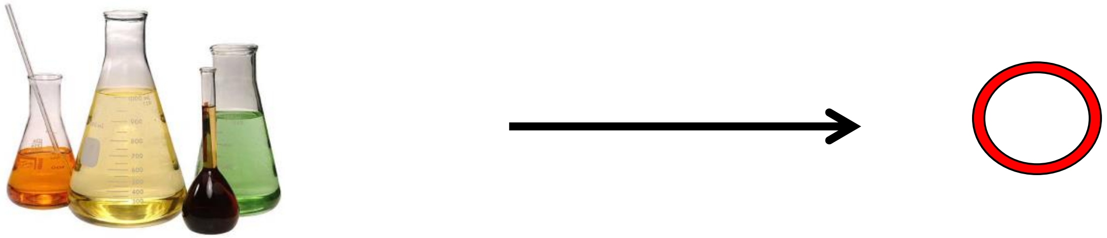

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Science 2 July 2010:
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DOI: 10.1126/science.1190719

RESEARCH ARTICLES

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,[1] John I. Glass,[1] Carole Lartigue,[1] Vladimir N. Noskov,[1] Ray-Yuan Chuang,[1] Mikkel A. Algire,[1] Gwynedd A. Benders,[2] Michael G. Montague,[1] Li Ma,[1] Monzia M. Moodie,[1] Chuck Merryman,[1] Sanjay Vashee,[1] Radha Krishnakumar,[1] Nacyra Assad-Garcia,[1] Cynthia Andrews-Pfannkoch,[1] Evgeniya A. Denisova,[1] Lei Young,[1] Zhi-Qing Qi,[1] Thomas H. Segall-Shapiro,[1] Christopher H. Calvey,[1] Prashanth P. Parmar,[1] Clyde A. Hutchison, III,[2] Hamilton O. Smith,[2] J. Craig Venter[1,2,*]

The Venter Experiments

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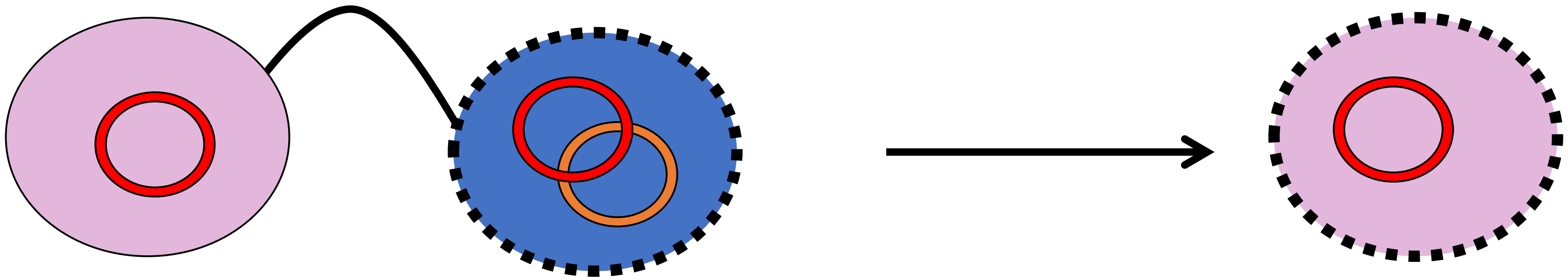

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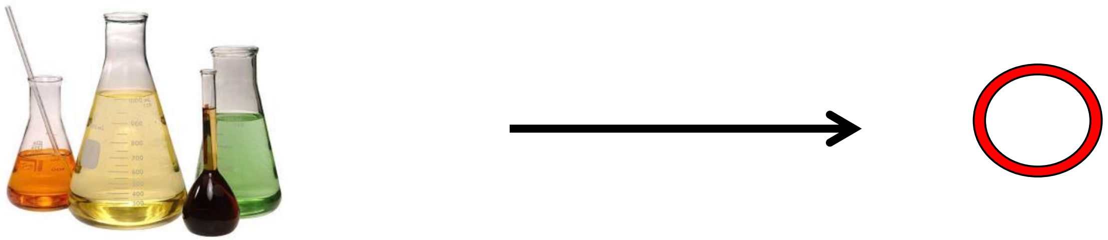

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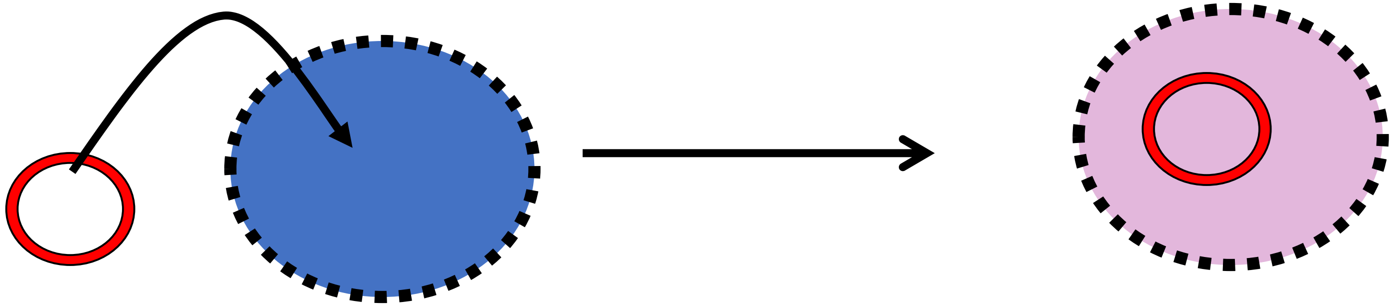
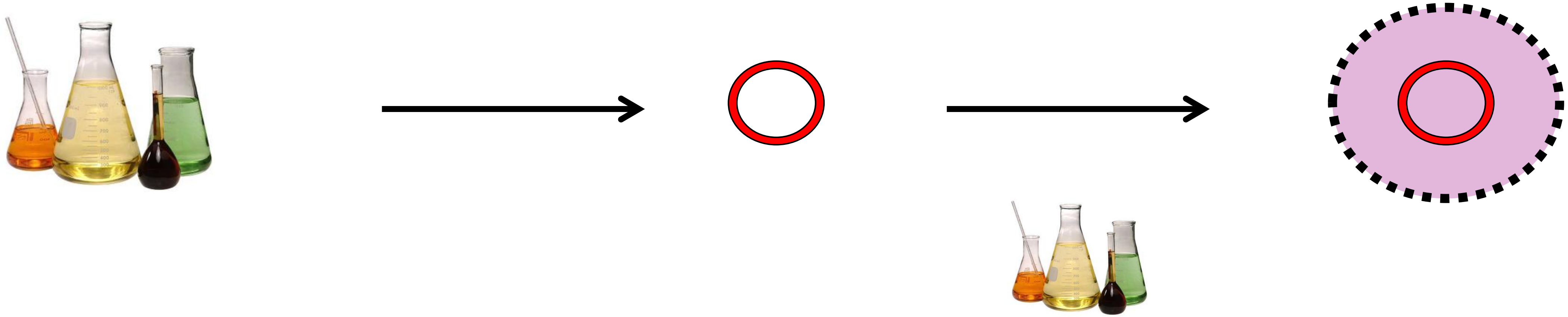




CRISPR-edited algae with high biofuel yield created by ExxonMobil, Craig Venter's Synthetic Genomics

Bradley Fikes | San Diego Union-Tribune | June 21, 2017

SUSTAINABILITY

Can Algae Feed the World and Fuel the Planet? A Q&A with Craig Venter

The geneticist and entrepreneur hopes to use synthetic biology to transform microscopic algae into cells that eat up carbon dioxide, spit out oil and provide meals

advance toward commercializing algae-based biofuels.

International Genetically Engineered Machine Competition

Join us at the iGEM 2018 Giant Jamboree !

October 24 - 28, 2018 - Hynes Convention Center in Boston, MA, USA

Registry of Standard Biological Parts

iGEM tools **catalog** repository assembly protocols help search BBa_

Browse Catalog
- Well Documented Parts
- Frequently Used Parts
- All The Parts

Browse by Type
- Promoters
- RBS
- Coding sequences
- Terminators
- Backbones
- Function

Collections
- All Curated Collections
- CRISPR
- Bioremediation
- Drug Delivery
- Hardware
- Reporter Proteins
- Freiburg TALE
- Anderson Promoters
- Genome Integration (miniTn7)

The Registry has many ways to find parts. The Catalog has been improved to allow you to browse our collection by part type, chassis, function or by several other ways. We made categories much more important in terms of classifying parts to form the basis of the catalog system.

- the plasmid backbone

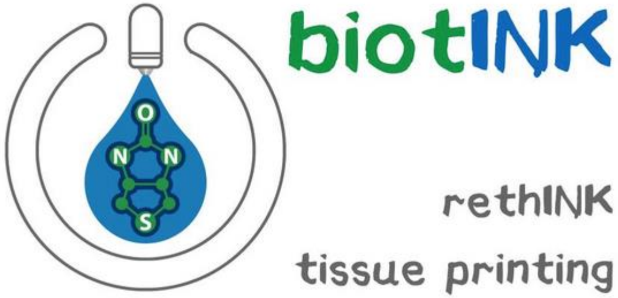
Why would you want to use more than one plasmid backbone?

One part can be used in several different plasmids backbones. It's easy to move a part from one plasmid backbone to another

International Genetically Engineered Machine Competition

Imperial College 2016

Grand Prize Undergraduate Section winners, Team Imperial, worked on developing a Genetically Engineered Artificial Ratio (GEAR) system to control population ratios in microbial consortia.



LMU-TUM_Munich 2016

Grand Prize Overergraduate Section winners, Team LMU-TUM_Munich, worked on creating a novel bioink that exploits the rapid and specific interaction of biotin and its tetrameric binding protein streptavidin.

HSiTAIWAN 2016

Grand Prize High School Section winners, Team HSiTAIWAN, worked to create a series of cheap, user-friendly E. coli biosensor that can detect the poison inside the Chinese Medicine by just examining the fluorescence intensity.

Manufacturing chemicals

- Medicines produced by plants and microbes have been used for centuries (infections, pain, hypertension, etc)
- Other chemicals include fuels, commodity and specialty chemicals, food ingredients
- Metabolic engineering of ever increasing complex pathways
- Harmful chemicals : toxins, anti-metabolites, controlled substances (opioids, explosives, chemical weapons)

Modifying the human microbiome

Why -

- Human health is highly dependent on the microbiome
- Active area of research – correction of metabolic disorders in clinic

Methods -

- Delivery of harmful cargo via the microbiome.
- Use of the microbiome to increase the impact of an attack.
- Engineered dysbiosis

Problems -

- Enormous variation across populations
- Homeostasis of the system – difficult to engineer

Modifying the human immune system

- Immune system is what defends us against infection; many pathogens attack by directly affecting the function of the immune system.
- Explosion in work on immunotherapy
- Engineering immune deficiency, hyperactivity, autoimmunity

- The current state of knowledge regarding immunity is such that it is likely far easier to craft an immunomodulatory weapon than an effective response to one (as we learned from HIV/AIDS)

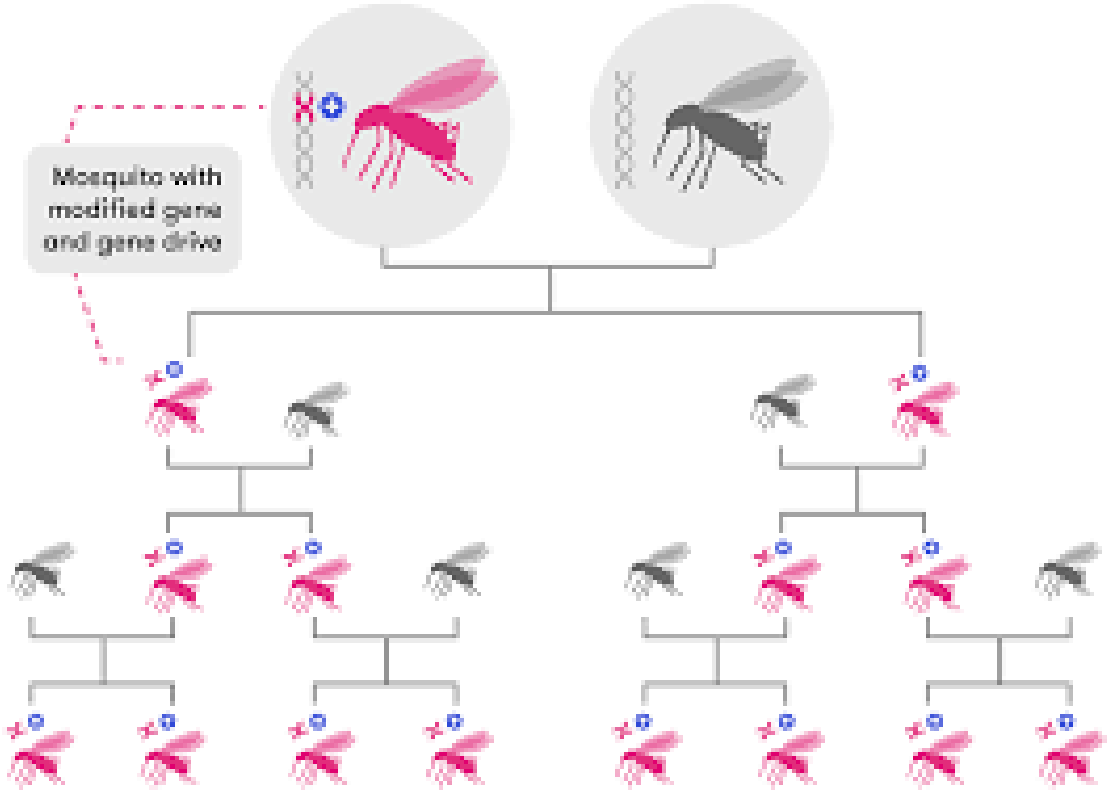
Modifying the human genome

- It may be possible to insert engineered genes directly into the human genome via horizontal transfer, using CRISPR or nano-lipid delivery. (vaccines, cellular reprogramming)
- Deletions or additions of genes, epigenetic modifications, small RNAs, CRISPR/Cas9, CRISPR-RNP.
- cause non-infectious disease, such as cancer or neurological debilitation, or to degrade immunity.

Digitization of biology

An example of how the digitization of biology accelerates vaccine development: The Novartis H7N9 influenza vaccine response – combining synthetic virus generation with flu cell culture platform

Genomics: gene drives



- Mosquitoes and malaria:
- engineer mosquito populations for infertility
- engineer mosquitoes to be unable to carry malaria

Genomics: gene drives

nature
International journal of science

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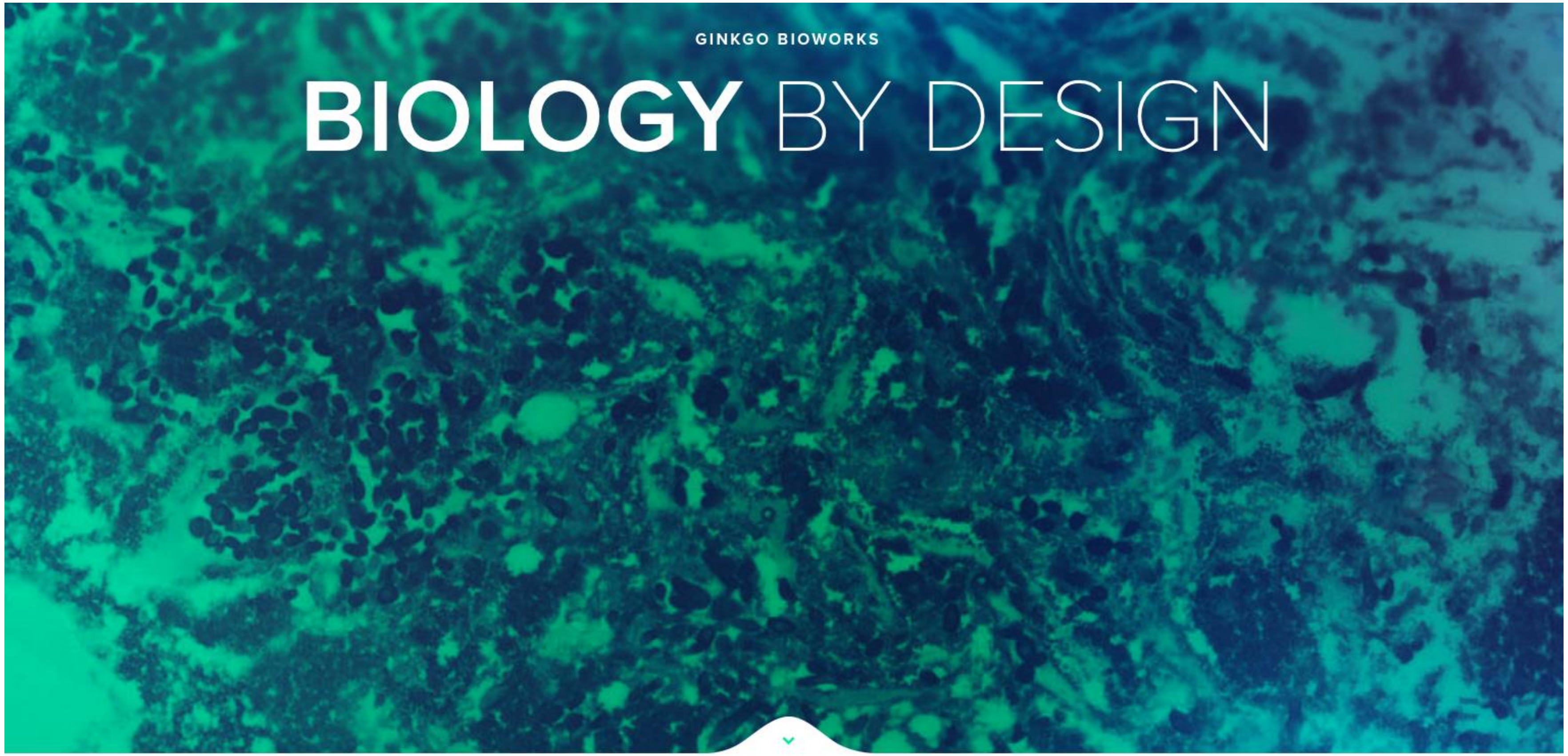
NEWS · 06 JULY 2018

Controversial CRISPR 'gene drives' tested in mammals for the first time

Experiments in mice suggest that the technology has a long way to go before being used for pest control in the wild.

Mice are the first mammals in which gene-drive technology has been tested. Credit: Stuart Wilson/Science Photo Library



Ginkgo Bioworks is the organism company. We design custom microbes for customers across multiple markets. We build our foundries to scale the process of organism engineering using software and hardware automation. Organism engineers at Ginkgo learn from nature to develop new organisms that replace technology with biology.

BUILDING WITH BIOLOGY

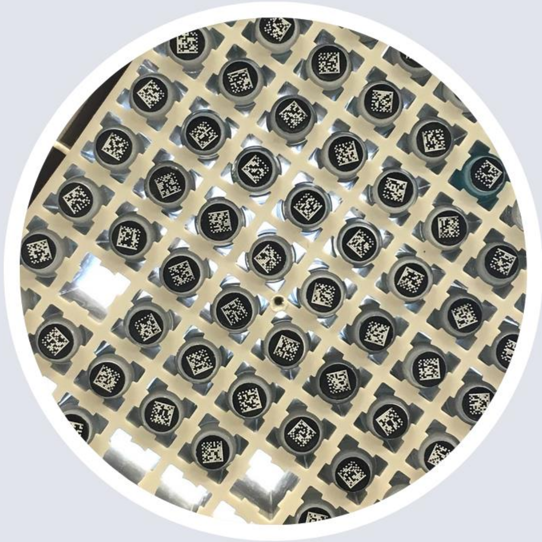
Biology is the most advanced manufacturing technology on the planet.

We're inspired by the power of biology and driven to build tools that make it possible to access that power in new ways. If you're passionate about engineering with biology, please join us!

Our Areas of Expertise

CULTURED INGREDIENTS

Producing valuable ingredients via fermentation with engineered yeasts for perfumes, foods, cosmetics, and more.



STRAIN IMPROVEMENT

Where fermentation is already used in bioindustrial applications, organism engineering can improve efficiency and sustainability.

ENZYMES

Enzymes are used in applications from cheesemaking to pharmaceuticals to stonewashed jeans. We're discovering better enzymes for more applications.

Rose oil from yeast
Plants that fix N

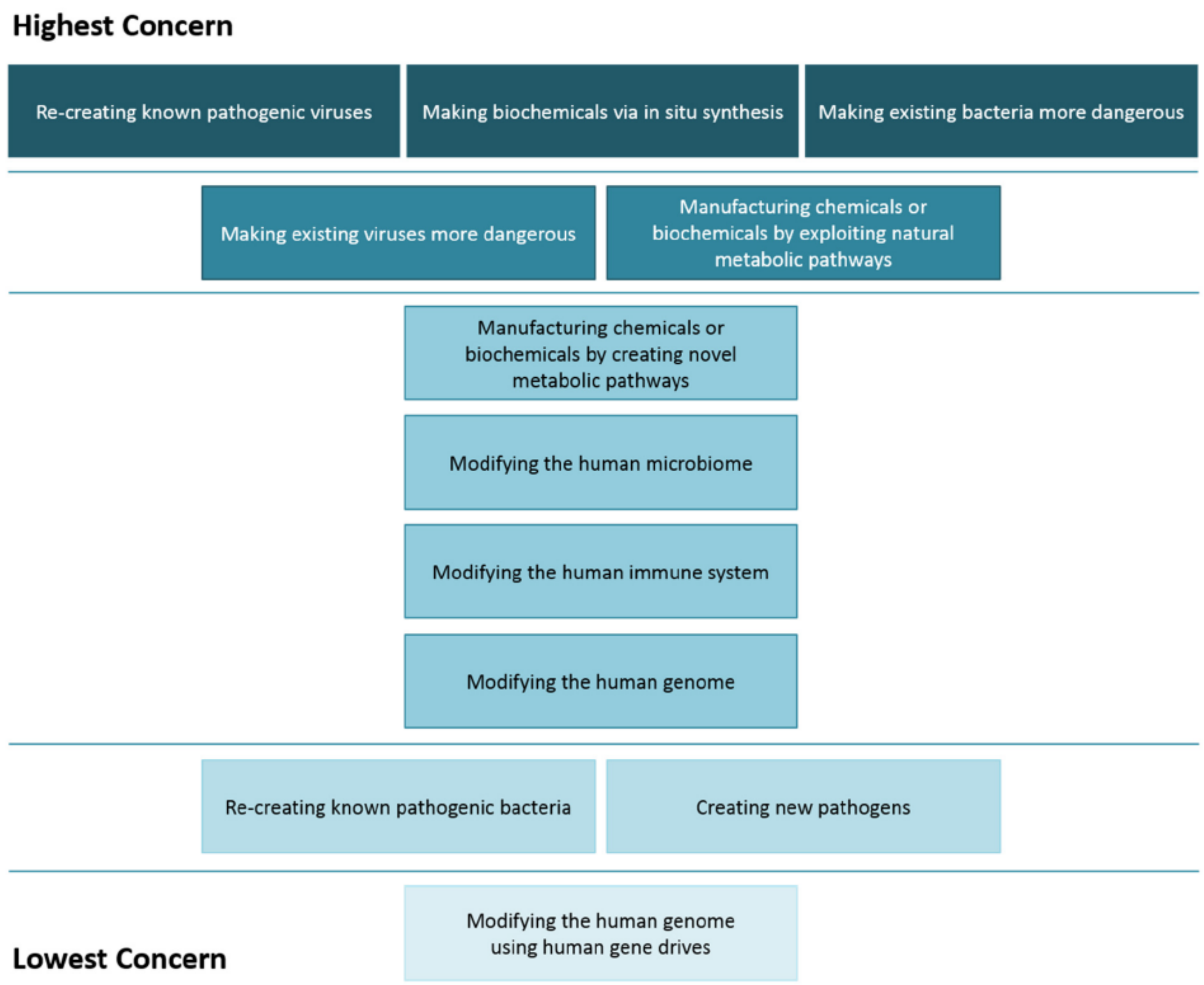


FIGURE 9-1 Relative ranking of concerns related to the synthetic biology–enabled capabilities analyzed. NOTE: At the present time, capabilities toward the top warrant a relatively high level of concern while capabilities toward the bottom warrant a relatively low level of concern.

NASEM 2018

Applications of SynBio

Malicious use

Consequence management

MCMs

Cures, solutions and improvements

detection

attribution

regulation

prevention