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.
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
• Microfluidics
• Nanotechnology
• Modularity
• Robotics
• Synthetic transcription factors
• Biosensors
## Key SynBio approaches in use

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

<table>
<thead>
<tr>
<th>Technology</th>
<th>In development</th>
<th>In use by developers of the technology</th>
<th>In use by the synthetic biology community</th>
<th>In use by the molecular biology community</th>
<th>In use by amateur biologists</th>
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<tbody>
<tr>
<td>Gene therapy</td>
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<td>Nanotechnology</td>
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<td>Automation</td>
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<td>Additive manufacturing</td>
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<td>Health informatics</td>
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Framework for assessing concern

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

**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.

Biodefense in the age of synthetic biology, US-NASEM 2018
Scientists Build First Man-Made Genome; Synthetic Life Comes Next

By Alexis Madrigal 01.24.08 | 11:00 AM
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, Ill, Hamilton O. Smith, J. Craig Venter
The Venter Experiments

1.
Complete Chemical Synthesis, Assembly, and Cloning of a Mycoplasma genitalium Genome


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

1. [Diagram showing a process]

2. [Diagram showing a process]
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,2 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 Venter1,2*

1Department of Chemistry and Biochemistry, University of California, Santa Barbara, CA 93106, USA
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Received 20 May 2010; accepted 2 July 2010; published 16 July 2010

DOI: 10.1126/science.1190719
The Venter Experiments

1. 

2. 

3.
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
Join us at the iGEM 2018 Giant Jamboree!

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

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.
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 Undergraduate 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
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.
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.
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!
### Highest Concern

<table>
<thead>
<tr>
<th>Re-creating known pathogenic viruses</th>
<th>Making biochemicals via in situ synthesis</th>
<th>Making existing bacteria more dangerous</th>
<th>Manufacturing chemicals or biochemicals by exploiting natural metabolic pathways</th>
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<tr>
<td>Making existing viruses more dangerous</td>
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<tr>
<td>Manufacturing chemicals or biochemicals by creating novel metabolic pathways</td>
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</tbody>
</table>

### Lowest Concern

| Re-creating known pathogenic bacteria | Creating new pathogens | Modifying the human genome using human gene drives |

**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.
Applications of SynBio

Malicious use

Cures, solutions and improvements

Consequence management

MCMs
detection
prevention

attrition
regulation