Synthetic Biology and Biosecurity

Yin Li
li_y@tib.cas.cn
Tianjin Institute of Industrial Biotechnology
Chinese Academy of Sciences
Sept. 2016, Wuxi
### Public conception on synthetic biology

**What Do You Think Synthetic Biology Is?**

*(Volunteered Comments)*

<table>
<thead>
<tr>
<th>Description</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unnatural, man-made, something that isn’t real, artificial</td>
<td>31%</td>
</tr>
<tr>
<td>Reproducing/recreating life, cloning, genetic/DNA manipulation</td>
<td>15%</td>
</tr>
<tr>
<td>Prosthetics, artificial limbs/organs/tissues</td>
<td>10%</td>
</tr>
<tr>
<td>Synthetic oils/composites/materials</td>
<td>9%</td>
</tr>
<tr>
<td>Development of medicines/treatments for diseases</td>
<td>6%</td>
</tr>
<tr>
<td>Agricultural applications, weather-resistant plants/crops</td>
<td>6%</td>
</tr>
<tr>
<td>Based in science/scientific experimentation/research</td>
<td>5%</td>
</tr>
<tr>
<td>Don’t know; no response</td>
<td>24%</td>
</tr>
</tbody>
</table>

*Awareness & Impressions of Synthetic Biology, 2013*
From molecular biology to synthetic biology
SynBio: from discovery to innovation

Core of Molecular Biology

- DNA → mRNA → Protein → Metabolites
- Genome, Transcriptome, Proteome, Metabolome

Initiation: 1990 - Forward engineering (Top-down strategy)

- DNA → mRNA → Protein → Metabolites

2000 - Reverse engineering (Bottom-up strategy)

- Systems Biology
  - Parts, Devices, Modules
  - Synthetic Biology

Pathway Regulation
Synthetic biology: new frontiers of biology

- Synthetic biology aims to design and engineer novel biologically based parts, devices and systems, as well as redesign existing natural biological systems for useful purposes.

- It incorporates the principles of engineering e.g. modularity, abstraction and orthogonality into classical biotechnology.
Understanding the minimal number of parts needed for life, to serve as a basis for engineering minimal cell factories for new functions

- Expanding genetic information storage and adding coding capacity

- Designing synthetic gene circuits that may be based on standard biological parts

- Engineering biosynthetic pathways to yield useful products and overcoming/removing elements that block production

- Bottom-up chemical design approaches to create new cells

- Utilising and exploiting synthetic molecular machines based on cellular systems
The *de novo* engineering of genetic circuits, biological modules, and synthetic pathways is beginning to address these critical problems and is being used in related practical applications.
Synthetic biology: disruptive technology

2004
MIT Technology Review:
Synthetic biology is one of “10 emerging technologies that will change your world”.

2010
Science magazine:
The Breakthroughs of 2010 include synthetic biology

2013
McKinsey & Company:
Synthetic biology is one of disruptive technologies that will change life, business, and the global economy

2014
United States Department of Defense:
Synthetic biology is one of six disruptive basic research areas
“The third revolution in biology”

- From “Read life” to “Design life”, indicating new revolution in biology
- Synthetic biology will open a novel way to understand the principle of life and develop a new paradigm for biological research

“The third revolution: The Convergence of the Life Sciences, Physical Sciences, and Engineering” (2011) --- Massachusetts Institute of Technology
Importance of synthetic biology recognized

2014 OECD: Emerging Policy Issues in Synthetic Biology
Now more than 40 countries and 500 organizations have supported the research of synthetic biology in the world
Synthetic biology is breaking life boundary

The successful developments of artificial DNA, artificial genetic codes, non-natural amino acids indicate life design is possible

The first “artificial DNA” *Science* 2010

Synthesize artificial genetic material XNA *Science* 2012

Non-natural amino acids in *E. coli* *Nature* 2015

Creating novel functions for ribosome *Nature* 2015
The potential of application of synthetic biology is unlimited

New breakthroughs in synthesis of natural products, biofuel and disease detection provide huge potential for the application of synthetic biology

Synthesis of *Artemisinin* by yeast will decrease the cost 90%
*Nature 2013*

Synthesis of taxol will open a new way to protect rare plants resource
*Science 2010*

Biosynthesis of alkane to produce diesel and gasoline
*Science 2010*

Biosynthesis of chemicals from CO$_2$ by electric energy
*Science 2012*

Changing traditional treatment of hyperuricemia
*Nature Biotech 2010*
The progress in synthetic biology technologies indicate that it is possible to make biological systems logical, programmable, controllable and predictable.

**Synthetic biology techniques**:
- Standard biological parts
- Low-cost sequencing and synthesis
- Simplified chassis, operating system
- System modeling and simulation
- Metabolic pathway design

**Recombinant DNA technology**:
- Horizontal transfer of genetic material
- Homologous recombination
- Gene shuffling; directed evolution
Synthetic biology has disruptive capabilities in materials, therapeutics, sensors and manufacturing paradigms

- Multi-cellular constructs
- Self-repairing systems
- Sentinel Organisms
- Polymers
- Catalysts
- Heterogeneous, functional materials
- Chemicals
- Fuels
- Pharma
- Multi-cellular constructs
- Self-repairing systems
- Sentinel Organisms
Synthetic Biology in China

- Synthesis of artificial human insulin
- Joined human genome project
- Start 973 project in synthetic biology
- Joined Yeast Sc2.0 project
- Chinese synthetic biology roadmap
- Preparing synthetic biology initiative

**Number 2 in patent application**

**Number 2 in publications**

<table>
<thead>
<tr>
<th>Year</th>
<th>US</th>
<th>CN</th>
<th>CA</th>
<th>JP</th>
<th>KR</th>
<th>EP</th>
<th>AU</th>
<th>DE</th>
<th>RU</th>
<th>GB</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td></td>
<td>7405</td>
<td></td>
<td></td>
<td>5341</td>
<td></td>
<td>2723</td>
<td></td>
<td>1417</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1201</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>966</td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Patent application statistics
- Publication trends
Synthetic Biology Research in China

- National needs driven; government-investment driven
- Design, engineer, and synthesis cells of industrial relevance/importance
- Design cellular systems for production of antibiotics, vaccines, proteins, anti-tumor drugs
- Design of energy-efficient plants and crops
- Design of microbial populations
- Enabling technologies/tools/methods
Synthetic Biology for Industrial Biotech

- Genome minimized design
- Artificial synthesize and join genome
- Chemical synthesis of genome
  - Natural and un-natural pathway
  - Synthesize and assemble un-natural components
- Construct in vitro synthesis system
- Major bio-products tested in pilot scale

- Photosynthesized carbon fixation module
- Optimization of chassis cell
- Construction of non-natural pathway
- Re-construction of natural pathway
- Modification of natural pathway
- Pilot of bio-butanediol
- Pilot of bio-isopropanol
- Industrialization experiment of bio-succinic acid

- Slight modification of artificial cell
- Moderate modification of artificial cell
- Deep modification of artificial cell
- Artificial cell and artificial life
Convergence of new elements from synthetic biology, nano-science, electronic engineering will provide novel biotechnologies for biosecurity, biological terrorism, and biological weapon.
Synthetic biology raises a number of policy issues around biosecurity, ethics, regulation and public engagement.
The UK has now become the first country to approve laws to allow the creation of babies from three people. (1/6500)

In the coming future “life” would be designed and synthesized by human

Synthetic biology brings life ethic thinking
Synthetic biology and bioweapon

Possible to make bioweapon by synthesis of (super) virus
Challenge of synthetic biology
——Public engagement

What is synthetic biology

Synthetic biology will provide a huge shock to public because it changed the common sense of natural life.

• What is life?
• What is boundary between nature and artificial?
• Can we play as “God”? 
• Who are parents?
• Can we make monster?
• How can we control the risk and benefit?
Security management of synthetic biology - Global views

- May 2006, 38 environmental and social organizations: assess and control risks raised by synthetic organisms.

- March 2012, 111 supervisory organizations: synthetic biology is an extreme form of genetic engineering, and synthetic organism and its subsequent products release and commercial applications should be temporarily stopped.

- July 2012, WHO: guidance on security and safeguard of H5N1 avian influenza virus, people engaged must be approved by the government and comply with this guidance.

- December 2012, BWC annual meeting: some countries/organizations are possible to construct causative agent through malicious use of new technology, and thus a threat.
Security management of synthetic biology - USA


- 2010 the Ministry of Health “a guide of filter frame for double-stranded DNA synthesis suppliers”.

- 2012 “US Government policy for oversight of life sciences dual use research of concern”.

- 2013 “US Government policy for institutional oversight of life sciences dual use research of concern”.

- 2013 NIH revised the “guideline for research involving recombinant DNA” to “Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules”.
Security management of synthetic biology - EU

- June 2009, RAE: synthetic biology social and moral issues, synthetic biology research must be carried out with social scientists and philosophers, to raise awareness of ethical and social issues.

- December 2010, the European Academy of Sciences Advisory Council: synthetic biology belongs to rDNA technology, the existing laws and regulations are totally able to regulate it, self-discipline rules are still needed in scientific community.

- May 2014, the German Ethics Committee: German government should intervene in the legislation to regulate the so-called dual use research, it should be set up a national committee to judge the plan of life sciences dual use research
Security management of synthetic biology - China

- In 2008, NSFC special joint-projects with NSF of Austria on biological safety of synthetic biology.
- In January 2010 and October 2011, two workshops were held on biological safety and risk management of synthetic biology.
- CAS, CAE, CAST series workshops for biological safety supervision.
Strategic, prospective, critical scientific questions

Synthetic Biology Initiative

Organizations:
China Academy of Sciences,
Ministry of Education,
Ministry of Science and technology
Biosecurity Research in SynBio initiative

- The orthogonal life, consisted of non-natural components, will not exchange genetic materials with natural life.
- Potential applications in biosecurity research.

- Biological parts of natural life, e.g. promoter, enzyme, etc. can be designed and synthesized through synthetic biology technology.
- New parts will have similar function but not crosstalk with natural parts.

Natural cell | unnatural cell
---|---
ATGC | XYZW

Without genetic communication

Without functional crosstalk
Biosecurity Evaluation in SynBio initiative

• produce toxic and harmful substances to destroy the natural environment?

• Biological interactions with the natural environment will produce harmful substances?

• Artificial life will affect the balance of species in the natural environment?

• Artificial life will have genetic exchange with natural life, resulting in a serious ecological crisis?
Strategy of biosecurity management in SynBio initiative

- Top-level design, relevant laws and regulations
- Biological safety education, awareness self prevention
- Register system of synthetic biological manipulation, strictly control the outflow of the artificial life
- Relevant research, national security defense, deal with possible biological terrorist attacks
- Synthetic biology education, public awareness of life science, unnecessary panic to artificial life
- International cooperation, global anti-bioterrorism system
Biological scientist code of conduct: Views from China

- Dual-use bio-science and technology research may pose challenge to global bio-safety and security governance
- Bio-scientists: primary defense to prevent the unpredictable negative impact and the misuse of dual-use biotechnology
- Importance of codes of conduct and self-regulatory mechanisms and their development, promulgation, adoption
- Strengthen the guidance and specification on bio-scientific and technological research
- Timely evaluate risk of bio-research, consciously avoid and properly tackle possible negative impact, prevent the occurrence of technological misuse
Thanks!