Industrial or "White" Biotechnology Policy Trends: an OECD Perspective

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Theme

- ***Industrial or "White" Biotechnology increasingly is viewed as a key driver for developing the Bioeconomy, the "Next Production Revolution", and Green Growth by advancing:***
  - *Sustainable economic growth, innovation, advanced manufacturing, and competitiveness;*
  - *Solutions to societal grand challenges in multiple domains (energy, environment, food, health);*
  - *Security, including economic, energy, and geopolitical security; and*
  - *Jobs, education, and skills for 21st Century society and economy*

National Academy of Sciences 2010, 2012; 2014; 2015
U.S. National Science Foundation 2010, 2015

Benefits: Responding to Urgent Needs

L. Clarke, Co-Chair, UK SB Leadership Council, 2013

White Biotechnology as a Robust Set of Transformative Technologies for Innovating the Bioeconomy and Addressing Societal Grand Challenges

- "A bioeconomy is one based on the use of research and innovation in the biological sciences to create economic activity and public benefit"
- Leveraging advances in biology, engineering, and information sciences to drive and reshape biotechnology and advanced production for technological advantage and broad societal benefits

Building a Bioeconomy as Core Foundation for 21st Century Competitiveness, Grand Challenges, and Growth in Next Production Revolution (NPR)

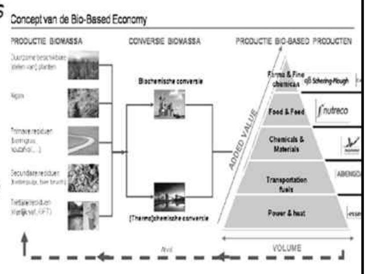
OECD Daejeon Ministerial Mandate for NPR - October 2015

OECD Capacity Building and Co-ordination for National Bioeconomy and Bio-Innovation Strategies

White Biotechnology – a new source of competitive advantage, domestically and globally

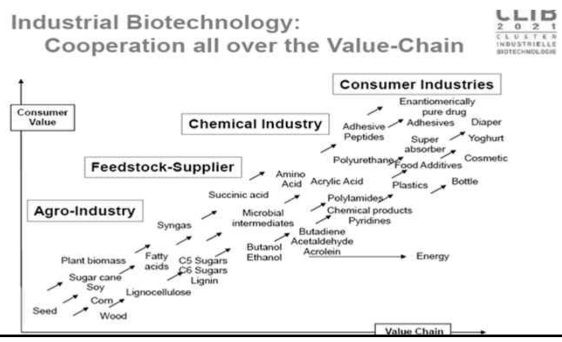
- Green chemistry, materials
- Water
- Agro-food
- Logistic sector
- Energy: Biofuels, Biogas
- Plantbreeding, horticulture

Biobased Economy as cross-sectoral theme

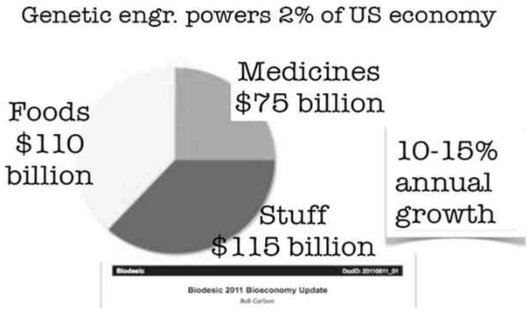


Dutch Ministry of Economic Affairs - 2012

Phase II Industrial Biotech Markets Beyond Biofuels – Shifts to Specialty Chemicals, Consumer Goods, New Materials, and Industrial Intermediates



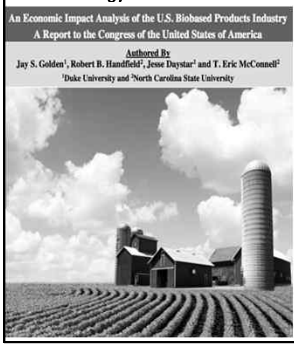
Biotech-based Markets Already Significant: Powers more than 2.5% of US Economy – perhaps as high as 8% if include Health-related Biotechnology



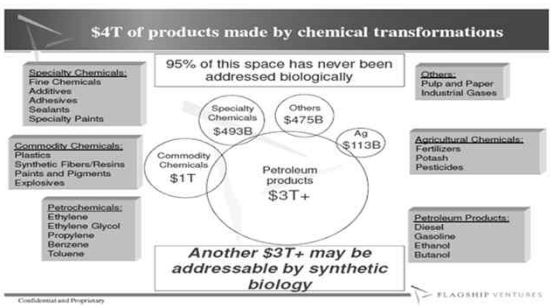
Industrial Biotechnology Continues to Grow Rapidly

USDA 2015 Report to Congress = *$369 billion* in Industrial Biotechnology in 2013

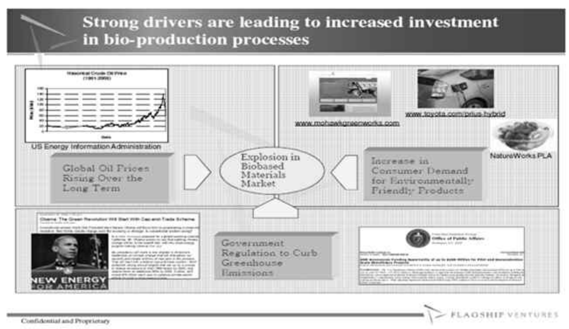
EU = *€50 billion from core industrial biotech*



-- But the Biggest Bioeconomy Market Opportunities Remain, Plus Creation of New Ones (Berry 2011)



Industrial Biotech as a Key Driver for Sustainable Growth and Grand Challenges -- Environment/Climate Change, Energy Security, and Resource Productivity (Berry 2011)



21st Century Solutions to a Wide-range of Key Global Challenges – Linking White Biotech, Sustainability, Climate Change and Green Growth

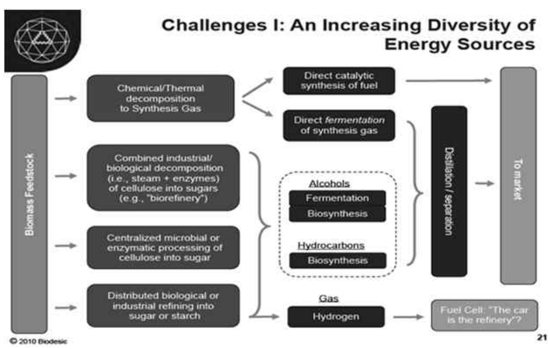
Key sustainability challenges

- Eradicating extreme poverty
- Defeating preventable diseases
- Providing the energy our economies need without wrecking the climate our environment needs
- Adapting to the degree of climate change that can no longer be avoided
- Managing the intensifying competition for the planet's land, water, & biomass
- Stemming the toxification of terrestrial ecosystems
- Maintaining the productivity & ecological integrity of the oceans

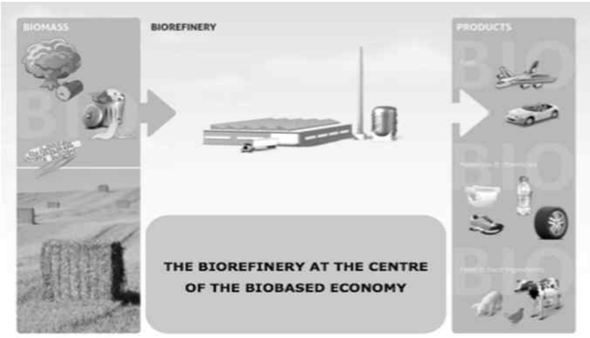
Industrial Biotechnology as an OECD Thematic Policy Priority (2014-2019)

10 Key Drivers Shaping Policy in the OECD for Industrial Biotechnology

1. Emerging White Biotech as a Disruptive Game Changer: Policies for the new Bio-based Production Platforms and Value Chains that Challenge Former Methods of Production (Carlson 2010)

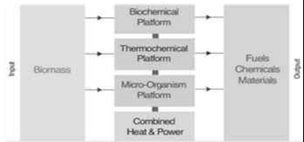


OECD Biomass Sustainability Platform



OECD Biorefineries Infrastructure Policy and Models

Biorefinery Concept – WEF 2010

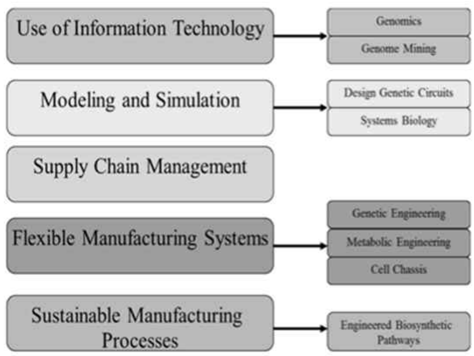


Next-generation Manufacturing (and Services/Data) Likely to be the Real "Killer App" and Innovation Frontier for Industrial Biotechnology

DARPA – Living Foundries: US$250M investment in next-generation bio-based manufacturing

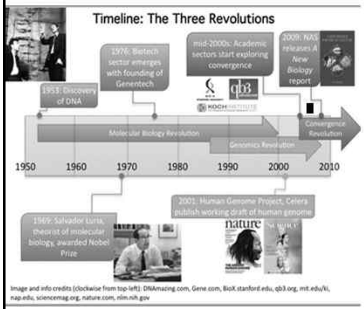
"The biological world is displacing the machine as a general world of design."

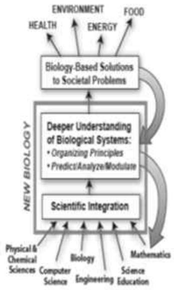
Neri Oxman, MIT Media Lab



IDA, Emerging Global Trends in Advanced Manufacturing (2012)

2. **CONVERGENCE** of Biology with Physical Sciences (including Green Chemistry) & Engineering = the Third Revolution in the Life Sciences. One of the foundational trends in STI for next 20 years MIT (2011)

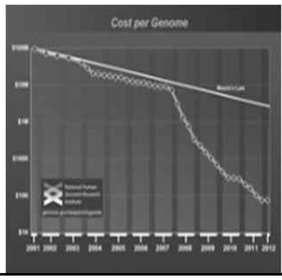




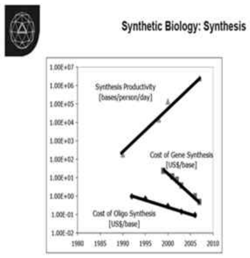
3. EXPONENTIALS: Industrial Biotech as a Tools Revolution

(1) Sequencing + (2) Synthesis + (3) Reading AND Writing DNA + (4) Genome Scale Engineering Tools + (5) High Throughput Technologies + (6) Code Refactoring + (7) Biological Parts and Circuits + (8) Genome Editing (CRISPR/Cas9)

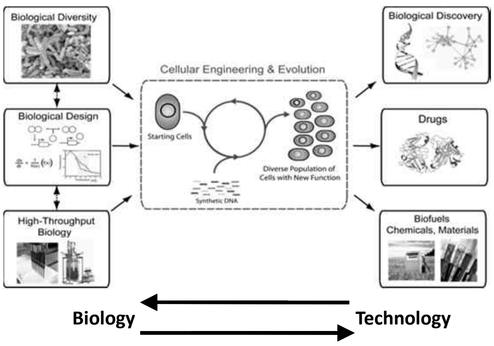
Tools in the Life Sciences: Moore's Law on Steroids



Synthesis and Carlson Curves



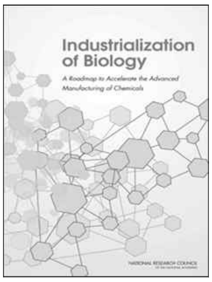
Summary: Set of Enabling Technologies to design, engineer and evolve biologically based parts, novel devices and systems, and to redesign naturally occurring biological systems and cells (Isaacs 2011)



4. Industrialization of Biology:

A Roadmap to Accelerate the Advanced Manufacturing of Chemicals

(*National Academy of Sciences May 2015)*



Thomas Connelly, Jr. (Chair), E.I. du Pont de Nemours & Company (ret.), Committee Chair

Douglas Friedman, Study Director

Richard A. Johnson, NAS Board on Life Sciences

Committee on the Industrialization Of Biology: A Roadmap To Accelerate Advanced Manufacturing Of Chemicals

Board on Chemical Sciences and Technology

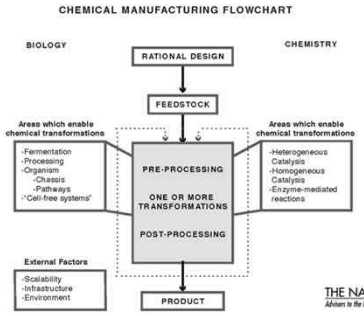
Board on Life Sciences

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

A Vision of the Future

- **Chemical Manufacturing**: The visions is one where biological synthesis and engineering and chemical synthesis and engineering are *on par with one another* for chemical manufacturing.



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Why Now?

- **Science is Advancing**: The past decade has seen an explosion in the technologies to compose, read, write, and debug DNA. This has rapidly increased the scale and sophistication of genetic engineering projects, and in the near term this will lead to more complex chemical structures and composite nanomaterials, which require precise control over dozens of genes.
- **Industry is Ready**: Increasing use of biology to produce high-valued chemical products that cannot be produced at high purity and high yield through traditional chemical synthesis, as well as increased production of high-volume chemicals in cases where biology represents a better synthetic pathway (cheaper and greener) than the conventional chemical synthesis.

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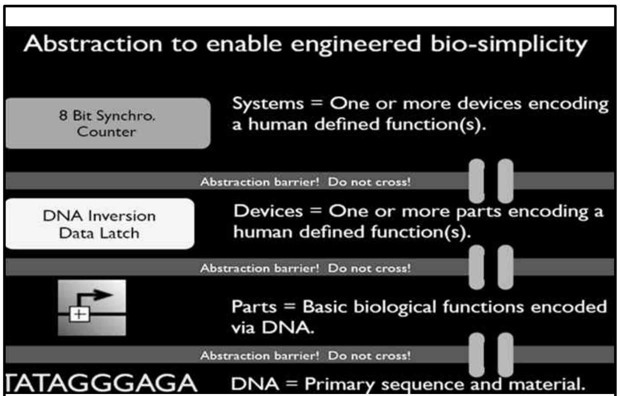
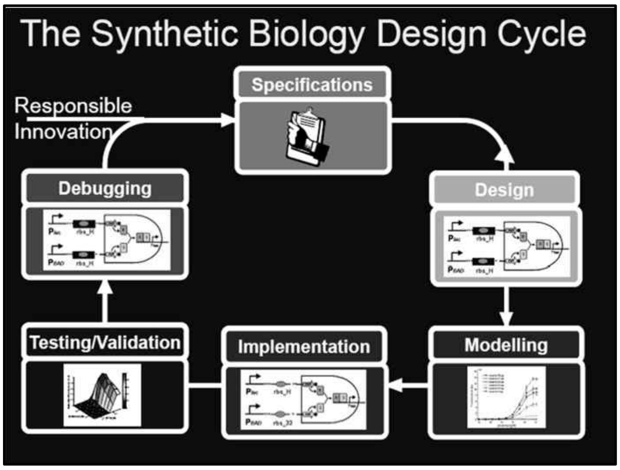
5. Synthetic Biology or Engineering Biology as the Core Driver and "New Normal" for Industrial Biotechnology



Endy, Stanford - 2012



Synthetic Biology Increasingly is a Foundational Technology for Industrial Biotechnology: Combines Economic Value Creation and Meeting Global Grand Challenges

World Economic Forum ranks SynBio as #2 key technology for 21st C. – after Big Data/ICT

Fidelity Investments – SynBio "is the defining technology of next century" for global investments (June 2013)

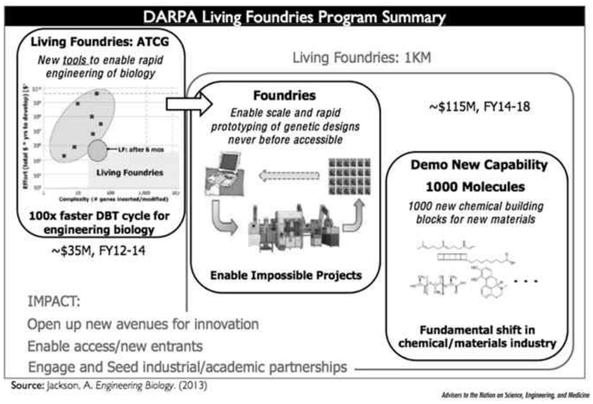
6. BIOLOGY as TECHNOLOGY –

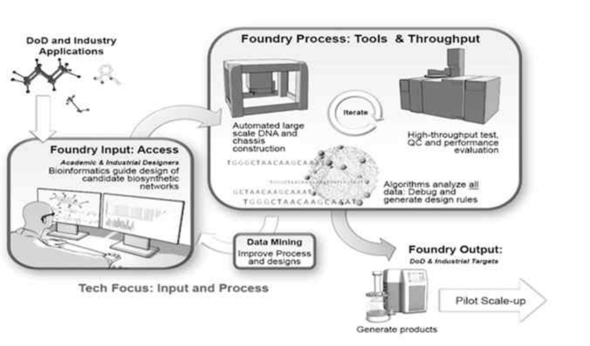
Leverage Biology as a Technology Platform for Multiple, Transformative Applications

DARPA

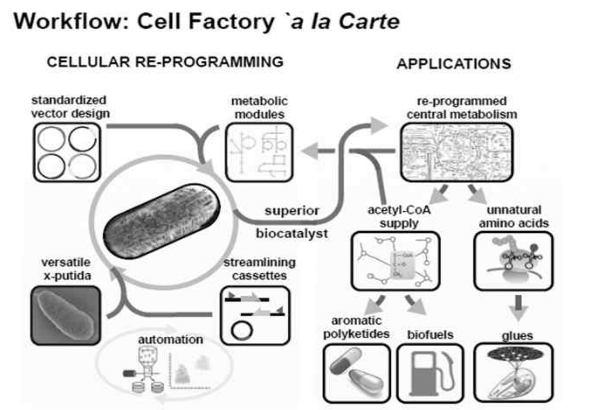
Engineering Biology

Design and construct genetic pathways, networks and systems to harness the powerful synthetic and functional capabilities of biology.



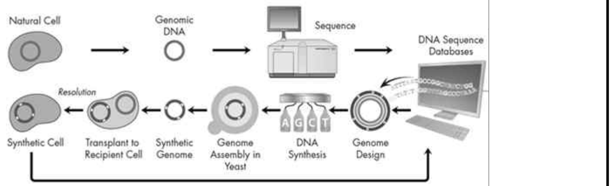


Develop Next-Generation Life Sciences Infrastructure



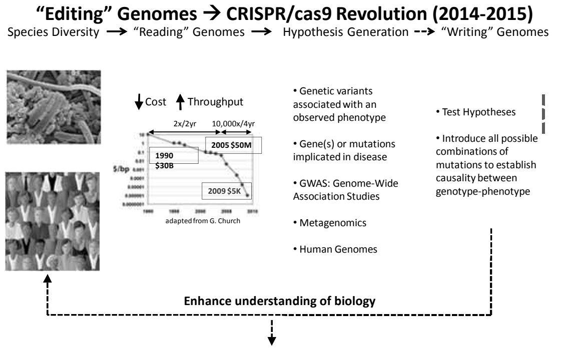
V. Dos Santos, Wageningen University, 2013

7. Digitalization of Biology and Making Life Programmable: Moving biological systems into the digital world (and back)



Our capacity to build microbes capable of solving human problems is limited only by our imagination (JCVI 2011)

"Reading" Genomes → Infer Function
"Writing" Genomes → Program New Biological Function (Isaacs 2013)
"Editing" Genomes → CRISPR/cas9 Revolution (2014-2015)

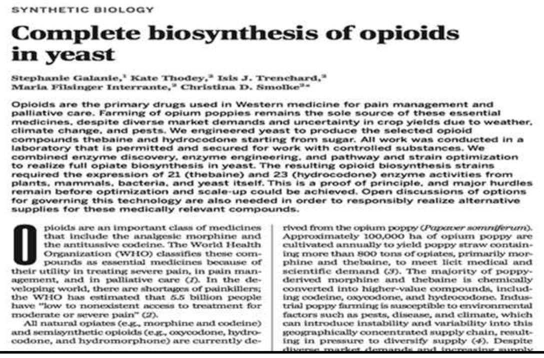


Use genetic information to program new biological function

Bioeconomy (and Policy) Increasingly Driven by Biology as an Information Science and Engineering Approaches

7. Control & dyn. systems
6. Reverse engineering
5. Fab, CAD & EDA
4. Standards & abstraction
3. Languages & grammars
2. Device design
1. Info. theory & signal proc.

8. **Bioeconomy – Will Disrupt Today's Global Value Chains and Farm-to Factory Supply Chains (*Smolke, July 2015)***



SYNTHETIC BIOLOGY

Complete biosynthesis of opioids in yeast

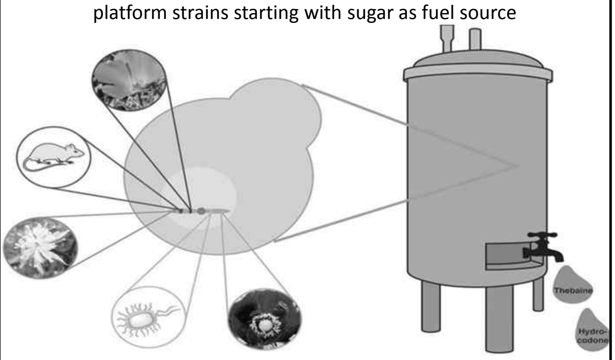
Stephanie Galanie,[1] Kate Thodey,[2] Isis J. Trenchard,[2] Maria Filsinger Interrante,[2] Christina D. Smolke[2*]

Opioids are the primary drugs used in Western medicine for pain management and palliative care. Farming of opium poppies remains the sole source of these essential medicines, despite diverse market demands and uncertainty in crop yields due to weather, climate change, and pests. We engineered yeast to produce the selected opioid compounds thebaine and hydrocodone starting from sugar. All work was conducted in a laboratory that is permitted and secured for work with controlled substances. We combined enzyme discovery, enzyme engineering, and pathway and strain optimization to realize full opiate biosynthesis in yeast. The resulting opioid biosynthesis strains required the expression of 21 (thebaine) and 23 (hydrocodone) enzyme activities from plants, mammals, bacteria, and yeast itself. This is a proof of principle, and major hurdles remain before optimization and scale-up could be achieved. Open discussions of options for governing this technology are also needed in order to responsibly realize alternative supplies for these medically relevant compounds.

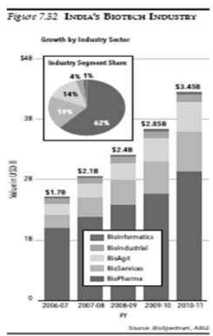
Opioids are an important class of medicines that include the analgesic morphine and the antitussive codeine. The World Health Organization (WHO) classifies these compounds as essential medicines because of their utility in treating severe pain, in pain management, and in palliative care (*1*). In the developing world, there are shortages of painkillers; the WHO has estimated that 5.5 billion people have "low to nonexistent access to treatment for moderate or severe pain" (*2*).

All natural opiates (e.g., morphine and codeine) and semisynthetic opioids (e.g., oxycodone, hydrocodone, and hydromorphone) are currently derived from the opium poppy (*Papaver somniferum*). Approximately 100,000 ha of opium poppy are cultivated annually to yield poppy straw containing more than 800 tons of opiates, primarily morphine and thebaine, to meet licit medical and scientific demand (*3*). The majority of poppy-derived morphine and thebaine is chemically converted into higher-value compounds, including codeine, oxycodone, and hydrocodone. Industrial poppy farming is susceptible to environmental factors such as pests, disease, and climate, which can introduce instability and variability into this geographically concentrated supply chain, resulting in pressure to diversify supply (*4*). Despite diverse market demands and increasing supply

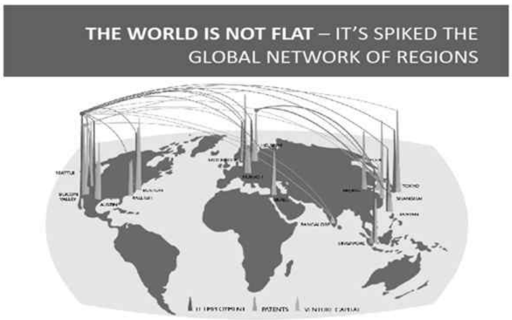
Future Revolution in BioManufacturing: Example - Smolke engineered complex, complete biosynthetic pathway in yeast for de-novo production of opioids and optimization of platform strains starting with sugar as fuel source



9. The Globalization of Industrial Biotech and Bioeconomy in National Innovation and Economic Growth Strategies



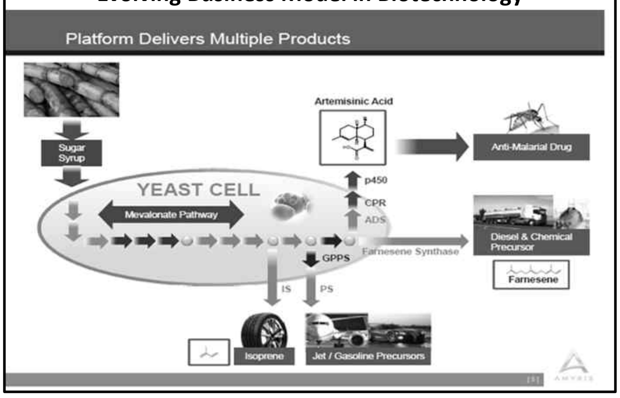
Globalization – an emerging era in the Bioeconomy with dispersed industrial biotech capacity, new value chains, new players, and new risks



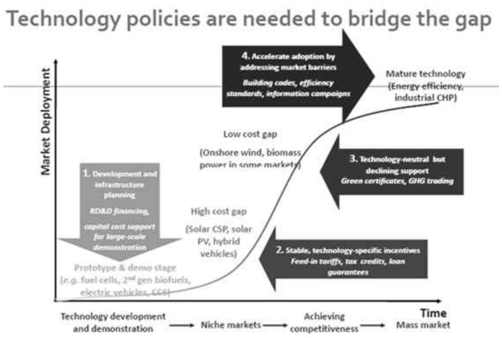
10. **Transformational New Business Models and Non-Technological Innovation are Driving Industrial Biotechnology**

Increased Focus on Disruptive Innovation to Change the Cost Curves, Technology Frontiers and Scaling Options

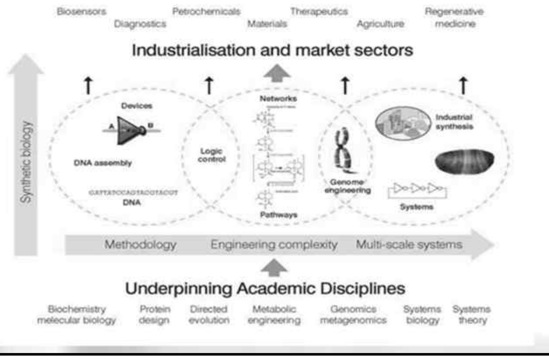
Multi-use Core Platforms and Infrastructure as Evolving Business Model in Biotechnology



Accelerating Transition to Low Carbon Economy Creates Huge New Innovation Opportunities for White Biotechnology (IEA Roadmap 2011)

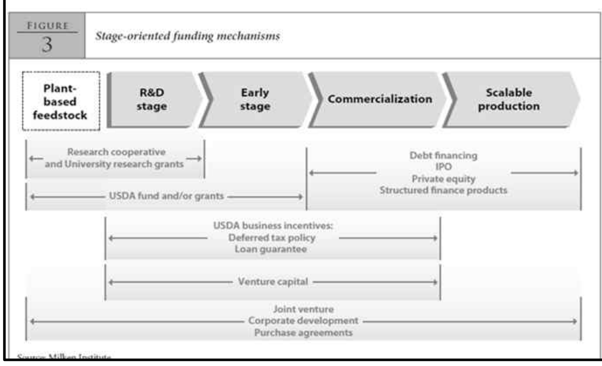


Economic Competitiveness, New Export Markets, and Trade Policy – Broad Range of Applications, Markets, and Business Models (estimates of $1-2 trillion)



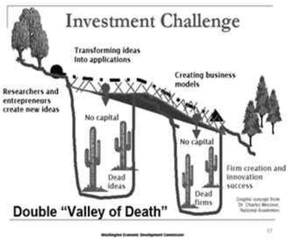
10 Key Policy Challenges in the OECD for Realizing Industrial Biotechnology's Economic and Social Benefit Potential

1. Need for More Robust Financing, Investment, and "De-Risking" Toolkit: Public, Private, and Philanthropic

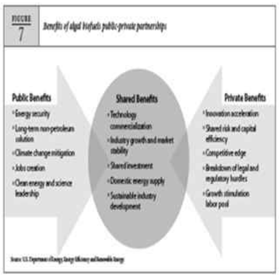


New Types of Research and Investment Funding Challenges in an Era of Fiscal Constraint – Scaling and Prototyping Industrial Biotechnology to Commercially Competitive Levels

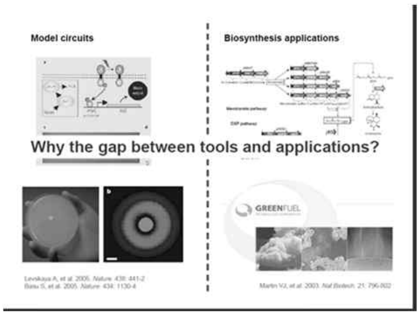
Aligning Investments, Lab-to-Market Policies, and Entrepreneurship Policy Frameworks



Global and National Public-Private Partnerships to "De-Risk" Biotech Investments



Leveraging Government Research Funding Policies by Investing in Shared, Open, and Accessible Infrastructure for 21st C Research and Pre-competitive Uses for the Industrialization of Biology



2. **Global and Domestic Governance Issues: Growing Regulatory Conflicts, Uncertainty, and "Disconnects"**

Regulatory Conflicts and Uncertainty … Within OECD Countries…
Magnified by Growing International Regulatory Divergence

Comprehensive Review of U.S. National Biotechnology Regulatory Framework and Biotech Policy Ordered by Pres. Obama – the "Coordinated Framework" (2015-2016)

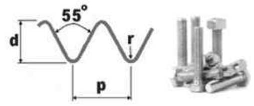
- "While the current regulatory system for biotechnology products effectively protects health and the environment, advances in science and technology since 1992 have been altering the product landscape. That's why today the White House is issuing a memorandum directing the three Federal agencies that have oversight responsibilities for these products— EPA, FDA, and USDA—to develop a long-term strategy to ensure that the system is prepared for the future products of biotechnology, and commission an expert analysis of the future landscape of biotechnology products to support this effort."

White House -- July 2015

Bioeconomy Complexity, Uncertainty & Multidisciplinary Nature Pose Problems for Traditional Regulatory Regimes

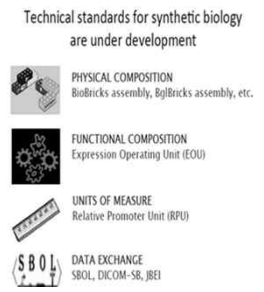
- Regulatory Science in all countries lags cutting-edge bioeconomy science, engineering, and innovative activities
- Trade Policy: WTO rules and the growing risks of "Techno-protectionism" in White Biotechnology trade (products/services/data) because the economic stakes are high
- Precautionary Principle v. Science or Risk-based Approaches
- Risks of technology "exceptionalism" – efforts to regulate the technologies rather than specific products or situations

3. International Standards and Metrology Policies are Key Enablers for the Bioeconomy



- Engineering and computer science influence
  - Standards setting, interoperability, and interchangeability
- Ethos of open innovation
  - Prominent concerns about intellectual property (primarily patents)
- Roles of standards
  - "[T]he definition, description and characterization of the basic biological parts, as well as standard conditions that support the use of parts in combination and overall system operation." (Endy 2005)
  - Structure, function, description, measurement, data, information exchange, software, biosafety and biosecurity, and even law

Standardization (Kahl 2013)



Science & Measurement Are Inextricably Linked

- Metrology, Tools, Platforms, Metrics, and Advanced Modeling

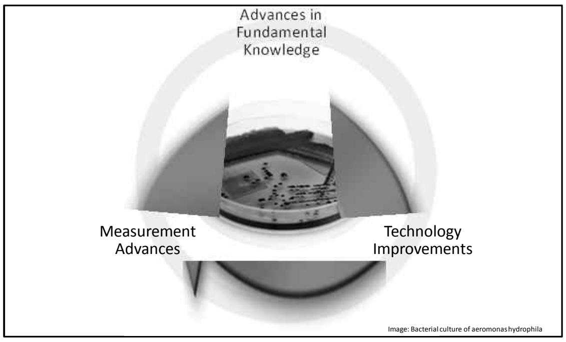


Image: Bacterial culture of aeromonas hydrophila

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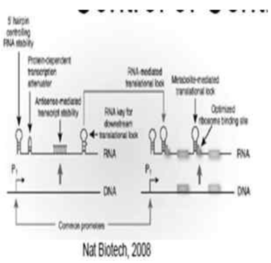
4. Open Science, Open Data, and Data-driven Innovation – OECD Mandates and Policy Recommendations (2015)

Creating a Bioeconomy "Production Commons" – e.g., BioFABS: Standardized Industrial-scale Platforms Sharing Biological Parts and Libraries of DNA Code

STANFOD BioFAB as a Model for Developing a Global BioFAB Network – Open, Shared, Accessible

Mapping Model Organisms and Producing Standardized Biological Parts in the Public Domain



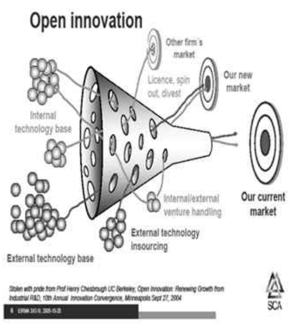
Nat Biotech, 2008

5. Getting the Balance Right is Hard, but Necessary – Intellectual Property Rights and Freedom-to-Operate

White biotech needs public policies and collaborative mechanisms that promote broad and robust pre-competitive openness, sharing, and access

But strong and robust IPR needed to enable later-stage economic value creation, IPR-enabled commercialization, open innovation, and market-based investments

Competing Visions of "Openness" Abound: Aligning Industrial Biotech with new "Open" Science and Innovation Models



Open source

Open science

Community Norms of Openness

Open Access

6. Policies for Safeguarding the Bioeconomy

Responsible Innovation

Beyond Traditional Biosecurity and Biosafety: Bio-CyberSecurity + new Global Value and Supply Chains + Resilience + Methods

7. Bioeconomy Workforce: Education, Training, and Skills as *Social Benefit Infrastructure* - e.g., iGEM Foundation and iGEM Global Competition

"*THE*" Engineering Biology Global Competition for students: 16,000+ Global, Connected Alumni in 10 years

2015 iGEM Jamboree in Boston: 50+ countries, 280 university teams, and 4,500+ participants

National Strategies for Skills: *e.g.*, U.S. Emphasizing Human Capital Ecosystem and Creative Talent for the Bioeconomy - "Soft Infrastructure", Connected Networks, "Knowledge Triangles", and Future Leaders

iGEM 2015

BioBricks FOUNDATION

synberc

LEAP Synthetic Biology Leadership Excellence Accelerator

Engineering Biology Research Consortium

8. Industrial Biotech: Direct Links to Development and Inclusive Growth Policies - Problem-oriented/Solutions-driven

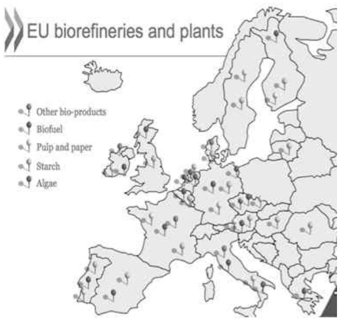
Ex. - CORE TECHNOLOGICAL PLATFORM for the Next GREEN REVOLUTION in AGRICULTURE and FOOD SECURITY

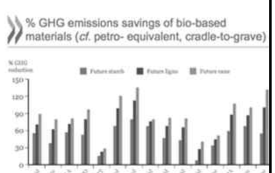
- **SUSTAINABLE INTENSIFICATION for Small Holder Farmers**
  - Yield Increases Sustainably Produced
  - Returning marginal lands to non-production
  - SB-produced DNA Sensors to monitor soil nutrients or detect food spoilage
- **CROP RESILIENCE and STABLE YIELDS**
  - Disease-resistant SB Plant Feedstocks, that can be supplemented with SB environmentally –friendly microorganisms to save water and other inputs
- **NITROGEN FIXATION/PHOSPHATE USE**
  - Engineer a Cereal Crop that can Fix its Own Nitrogen
  - Reduce Fertilizers/Ammonia

George Church (*Nature* 2010)

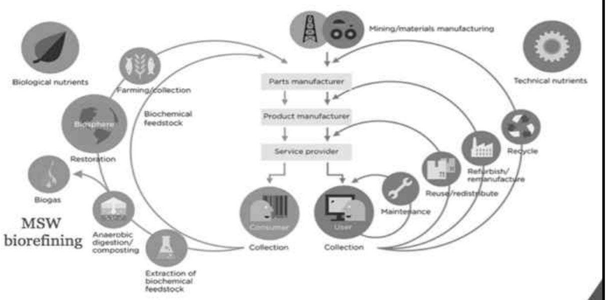
- ***Synthetic biology "will allow developing nations to leapfrog fertilizer-wasting, fossil-fuel-intensive and disease-rife farming for cleaner, more efficient systems, just as they are leapfrogging costly landlines in favor of mobile-phone networks."***

9. Decision Support for Bioeconomy Policymaking





Policy alignment: Circular Economy

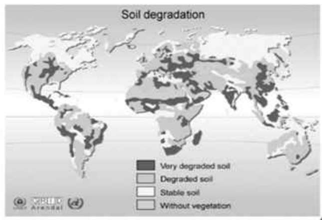


http://www.ellenmacarthurfoundation.org

OECD, BNCT - 2015

Food, water, soil security – reconciling agricultural and industrial needs of biomass

- Food production to increase 50-70% by 2050
- Models predict severe future droughts (e.g. 10 years in US Midwest)
- 70% of all fresh water use is for agriculture
- 1 in 4 may suffer water shortages by 2050
- Soil being destroyed at unprecedented rates
- **RESULT**: make more food with less water on less soil AND provide industrial biomass



http://greenfieldgeography.wikispaces.com/Soil+and+change

OECD, BNCT - 2015

10. Public Engagement – GENOME EDITING Case Study

http://www.frontlinegenomics.com/943/nih-will-not-fund-genome-ed... human-embryos/

정말 감사합니다
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