Ubiquitous Biological Manufacturing

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November, 2016

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What Do We Mean By Engineering?
"Our experiments, methodically conducted, will permit us, little by little, to learn completely ‘the art of the bird’.” – Octave Chanute (c.1900)

Source: NASA
How Big is the Bioeconomy?
A Hierarchy of Engineering and Economic Complexities

**Multiple Cells**: Control of growth and differentiation; products are cells and structures that cells make (Tissues, Organs, Animals, Houses). *3D Printing?*

**Synthetic Single Cells**: Looks initially like Metabolic Engineering; products are chemicals and biologicals made by cells.

**Multiple Genes in a Single Cell Type**: Metabolic Engineering: Fuels, Plastics, Terpenoids for Drugs, Flavors, and Fragrances.

**“Single” Gene in a “Single” Cell**: Recombinant Proteins: Laundry Enzymes, HGH, Bt, EPO.
2012 total U.S. biotech revenues were at least $324 billion; 2% of GDP.

For comparison, 2012 worldwide semiconductor revenues were $303 billion. (IHS iSuppli)

Biochemical revenues now far exceed that of biofuels.
Consistent Growth

Estimated U.S. Biotech Revenues 1980-2012
(bars = data, shaded area = interpolation)

Sub-sector Annual Growth Rates
(computed from interpolation)

Sources: Nature Biotech, March, 2016; Biodesic

Estimated Biotech Revenue Contribution to U.S. GDP and GDP Growth

Contribution of annual biotech growth to annual GDP growth
Contribution of biotech revenues to GDP

Annual Growth in U.S. GDP and U.S. Biotech Revenues

Crop Prices Can Go Up...And Down

- **Total U.S. Revenues from GM Crops and Seeds and Farm Scale Revenues of Major GM Crops**

- **U.S. Market Penetration of Five GM Crops**
Economics Driving Adoption from Top to Bottom

GM sugar beets save Idaho, Oregon growers millions

- cost for herbicides to control weeds has dropped from $66 per acre to $11 per acre
- herbicide application costs have dropped from $42 to $21 per acre
- cost of hand labor has fallen from $60 per acre to $0
- no longer “working all night long, spraying ineffective herbicides and then ultimately getting to harvest with a field full of weeds”

- Bt Cotton: incidence of pesticide-associated diseases in India, SE Asia falling dramatically
Average US Corn Yields: No End in Sight?

Average US Corn Yield, 1866-2009

Where Do We Get Our Stuff?
What is in a Barrel of Oil and How Much is it Worth?

Products Made from a Barrel of Crude Oil (Gallons) (2010)

- Other Distillates (heating oil) — 1
- Heavy Fuel Oil (Residual) — 2
- Liquefied Petroleum Gases (LPG) — 2
- Diesel — 10
- Jet Fuel — 4
- Other Products — 7
- Gasoline — 19

15% of volume
$10-1000/L
Biology Can Make Just About Anything

Source: 20n
Company X: Biological Synthesis of Fluoropolymers

• ~10 enzyme pathway.
• CAPEX is 40% of existing industrial chemistry process.
• OPEX is ? less.
• More importantly, bio pathway skips steps with intermediates stabilized in storage and transport by phosgene. Will result in massive increases in safety and security, lower capital and compliance costs.
The Future Of The Economy Looks Like Beer And Cows
Biological Production Is Higher Quality and Lower Cost.

GSK says of bio-production:

1. Replaces man-made organic solvents with water so almost 80% of the chemical waste associated with older processes has been removed.
2. It has helped to reduce the amoxicillin value chain carbon footprint by up to 12%.
3. It improves industry leading product quality standards.

GSK replaced chemical synthesis of amoxicillin in Singapore plant with biological production using enzymes. (collaboration with Codexis)
GE/JHL collaboration, for example, is driven by diverse needs:

- To develop resilience and flexibility as responses to infectious diseases drove the need to “stockpile capacity rather than stockpile a particular vaccine” near the point of use.

- “Chinese government requires that we manufacture products in China, even for IND [investigational new drug] submissions. If you want to be in the Chinese market and if you want to be treated as a domestic company, you have to be in China,”

- Control cost and quality when communicating processes across the planet; demonstrates a novel market for systems that allow the control manufacturing across borders.
Micro-Brewing the Bioeconomy (Existence Proof for Distrib. Biol. Manufac.)

Now at 11% of volume but 20% of $$$!
Micro-Brewing the Bioeconomy (Existence Proof for Distrib. Biol. Manufac.)

US Brewery Count
Sources: Tremblay, et al, Rev Indust Org 2005; Brewers Assn

- Craft
- Large
- Total
- 6X 200,000L
- Can directly process up to 1M tons of raw sugarcane annually.
- Building a portfolio of mid-value, mid-volume chemicals.

- **Impact**: farnesene-based tire rubber additive reduces rolling resistance, improves MPG up to 10%.

- Now up to $1.4B in development costs. (J. Melo, SBBSF 2016)
Just what is a “Biofactory”?  

Most organisms are small.

Animals larger than ~1m are relatively rare.

If production starts to lean heavily on biology, do individual production lines start to look more like biology?

Does the economy start to look more like an ecology?

Costs of Scaling Up

Industrial Chemistry

Port Arthur, TX: 300 kb/d, 2007

600 kb/d expansion, 2010

~$7 billion

- 61,175 piles for a total of 4,500,000 linear feet
- 285,000 cubic yards of concrete
- 3,100,000 linear feet of pipe (600 miles)
- 5,600,000 linear feet of cable
- 78,000 tons of structural steel (156,000,000 pounds)

Shell

Biology
Costs of Scaling Up

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Distributed Biological Manufacturing vs. ‘Oil’
### Distributed Biological Manufacturing vs. ‘Oil’

#### Advanced Cellulosic Biofuels Industry Requirements:

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Value</th>
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<tbody>
<tr>
<td>Production Units Required by 2022</td>
<td>527</td>
</tr>
<tr>
<td>Capital Cost of a Production Unit (100 mg/y)</td>
<td>$320 million</td>
</tr>
<tr>
<td>Replacement Cost of Productive Capacity</td>
<td>$168 billion</td>
</tr>
<tr>
<td>Volume of Annual Productive Capacity</td>
<td>22 billion gallons</td>
</tr>
<tr>
<td>Annual Retail Value of Fuel (at today’s prices)</td>
<td>~$66 billion</td>
</tr>
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#### US Dairy Industry Snapshot:

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Production Units</td>
<td>about 9.25M animals in 2012</td>
</tr>
<tr>
<td>Average cost of a production unit</td>
<td>between $1,500 - $3,000</td>
</tr>
<tr>
<td>Total replacement value of the herd</td>
<td>under $28 billion</td>
</tr>
<tr>
<td>Total volume of milk produced</td>
<td>about 23 billion gallons in 2012</td>
</tr>
<tr>
<td>Annual retail value of the milk</td>
<td>around $100 billion</td>
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