

Ubiquitous Biological Manufacturing

Rob Carlson

November, 2016

Bioeconomy Capital
Biodesic
Seattle, WA

www.bioeconomycapital.com

@rob_carlson

blog :: www.synthesis.cc

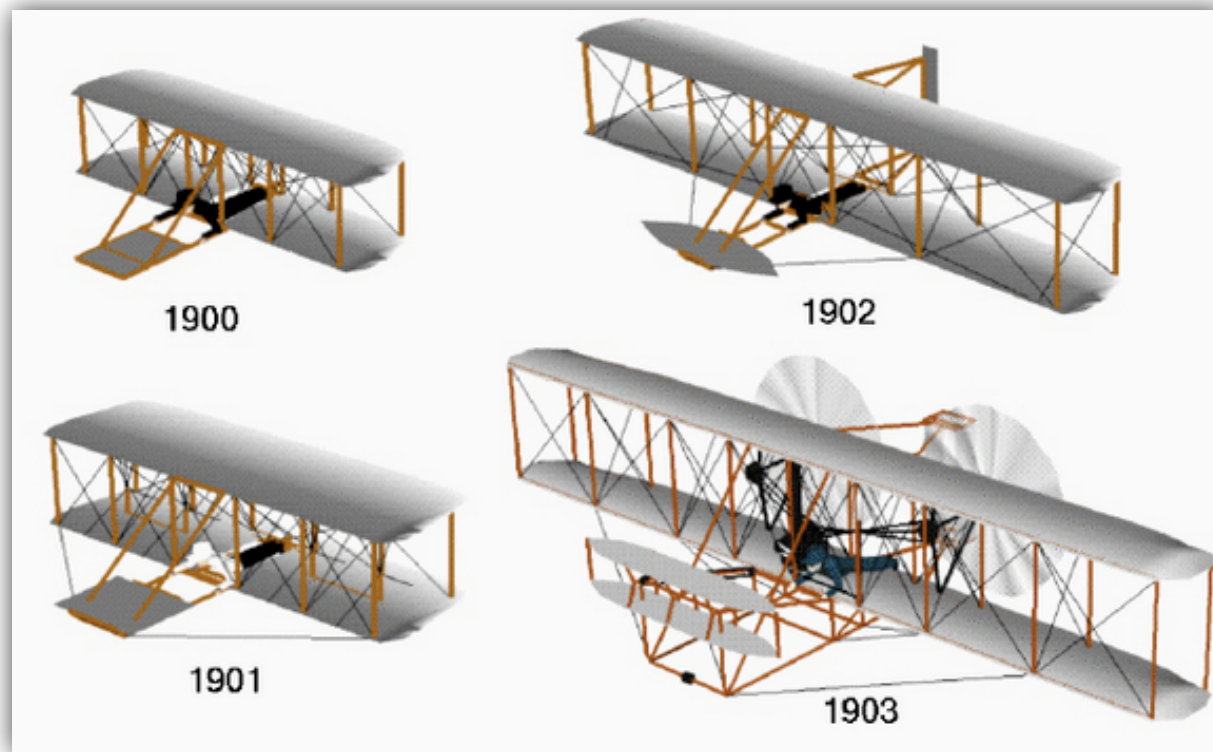
Disclaimer

This presentation is neither an offer to sell nor a solicitation of an offer to buy any securities. You should not rely on any information in this presentation in purchasing any securities. The specific terms of any proposed investment would be set forth in the Fund's Limited Partnership Agreement to be entered between the Fund and each investor. The information contained herein speaks only as of the date hereof and the information may change after that date. Such information also includes "forward-looking statements". There are many factors that could cause an investor to lose the investor's entire investment. You should rely on your own investigation and the terms of the Limited Partnership Agreement before making any decision to purchase the Fund's securities. The information contained in this presentation is not legal, tax, business or financial advice. You should consult your legal, tax, business or financial advisor with respect to your particular circumstances.

What Do We Mean By Engineering?

Understanding Through Construction

“Our experiments, methodically conducted, will permit us, little by little, to learn completely ‘the art of the bird’.” – Octave Chanute (c.1900)



Source: NASA

Pinnacle Of Forward Engineering



How Big is the Bioeconomy?

A Hierarchy of Engineering and Economic Complexities



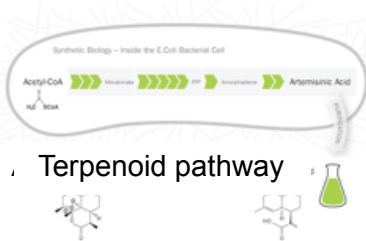
Claudia Cadillo
Transplant Recipient

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

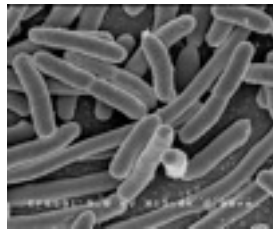


J.C. Venter

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



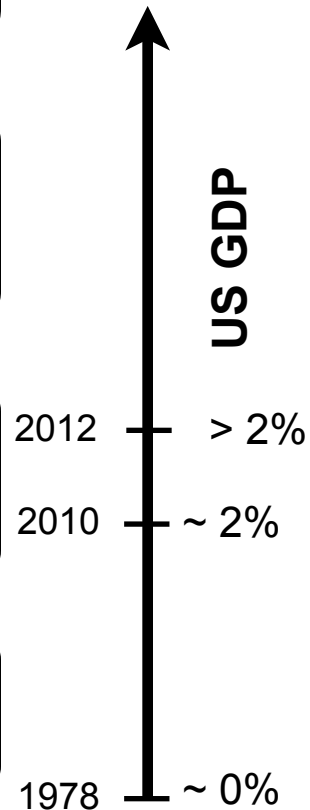
Terpenoid pathway



Expression in *E. coli*

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.



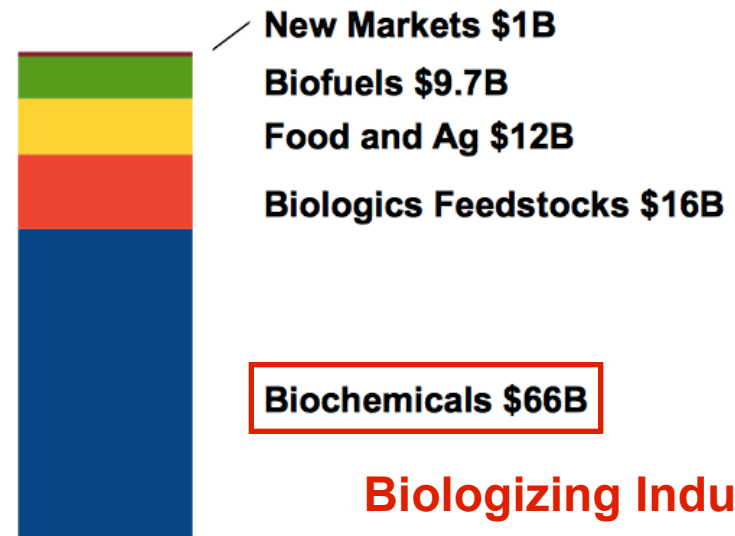
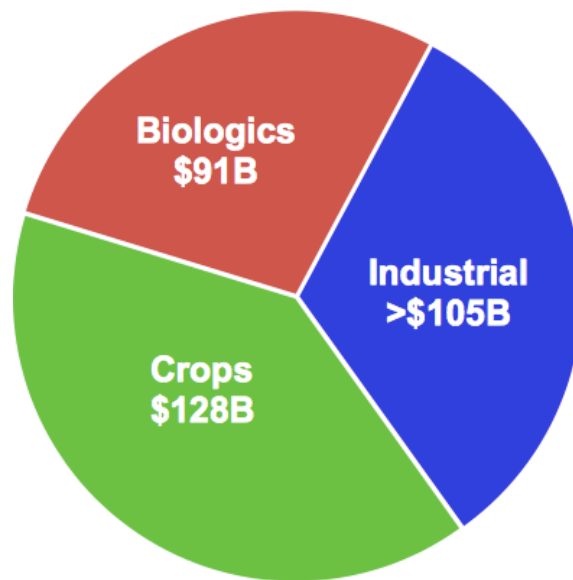
2012 US Biotechnology Revenues: \$324 Billion; 2% of GDP

2012 total U.S. biotech revenues were at least \$324 billion;
2% of GDP.

R. Carlson, *Nature Biotech*, In Press

B2B Industrial Revenues

(D. Solomon [Agilent], U.S. Senate Briefing, 5 Nov 2013)



Biologizing Industry

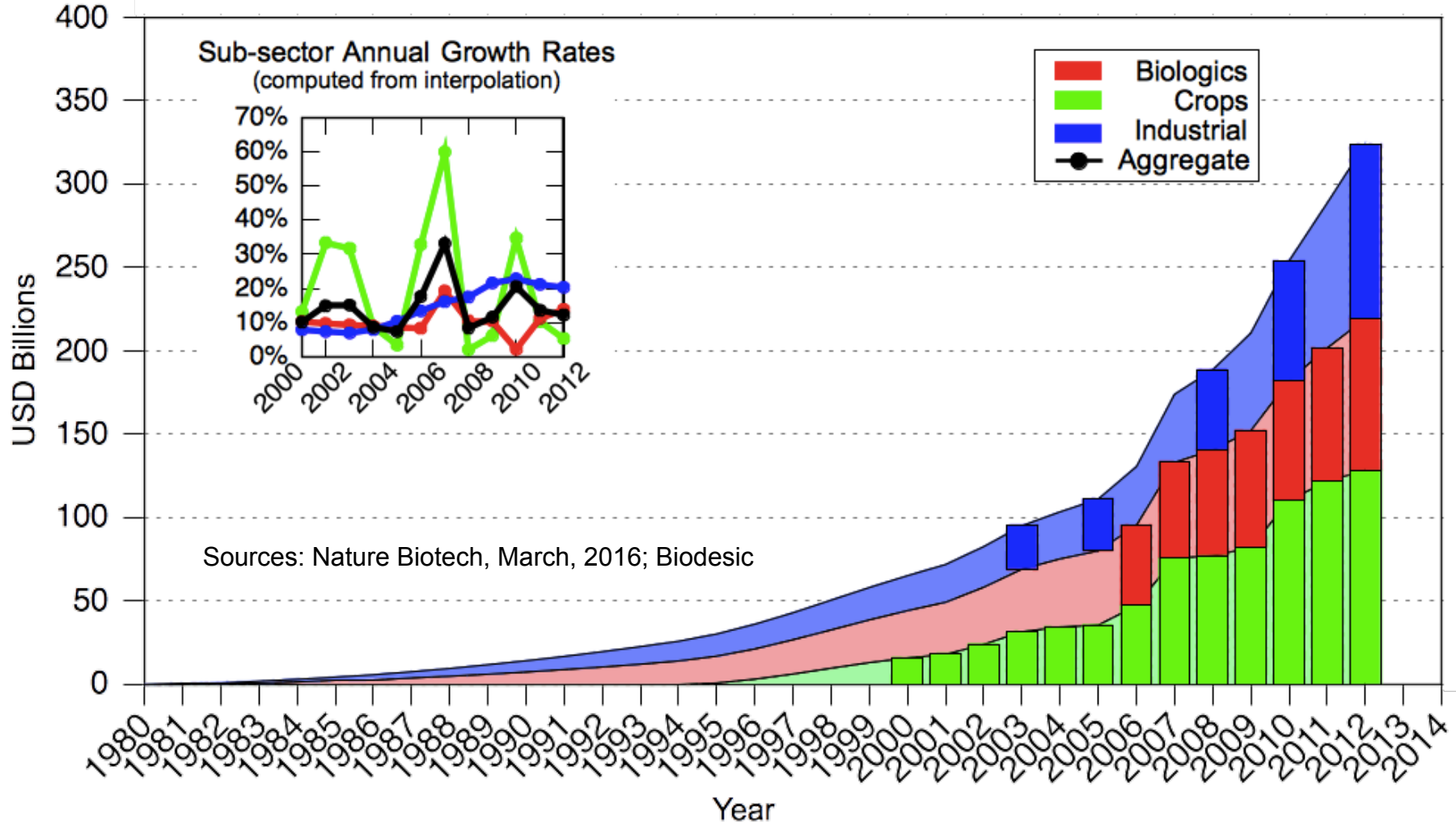
For comparison, 2012 worldwide semiconductor revenues were \$303 billion. (IHS iSuppli)

Biochemical revenues now far exceed that of biofuels.

Consistent Growth

Estimated U.S. Biotech Revenues 1980-2012

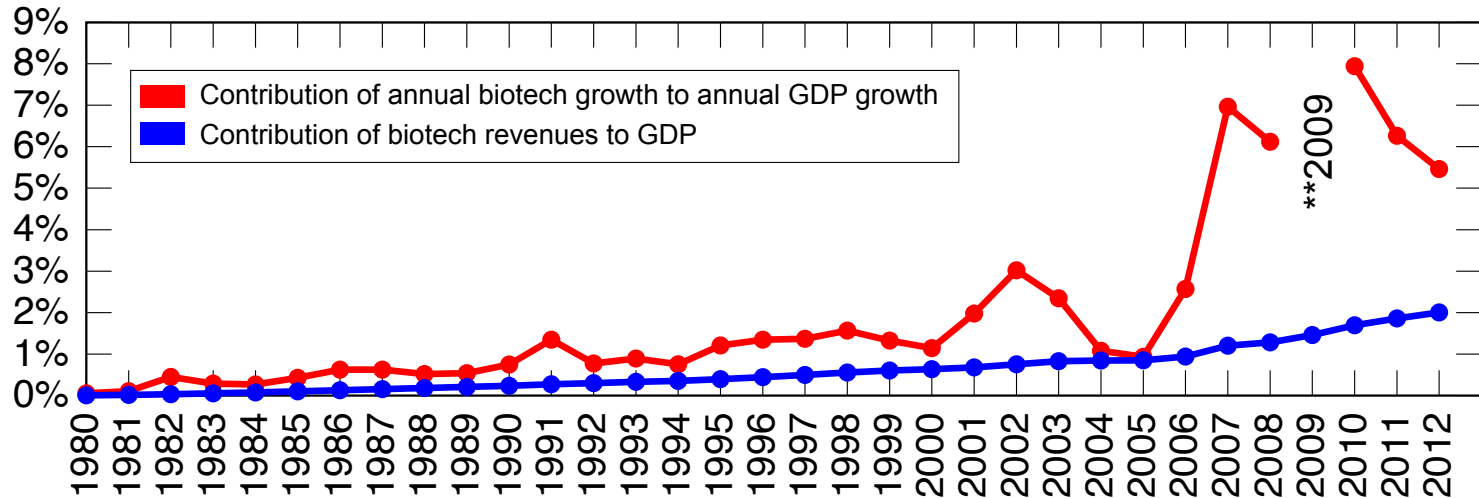
(bars = data, shaded area = interpolation)



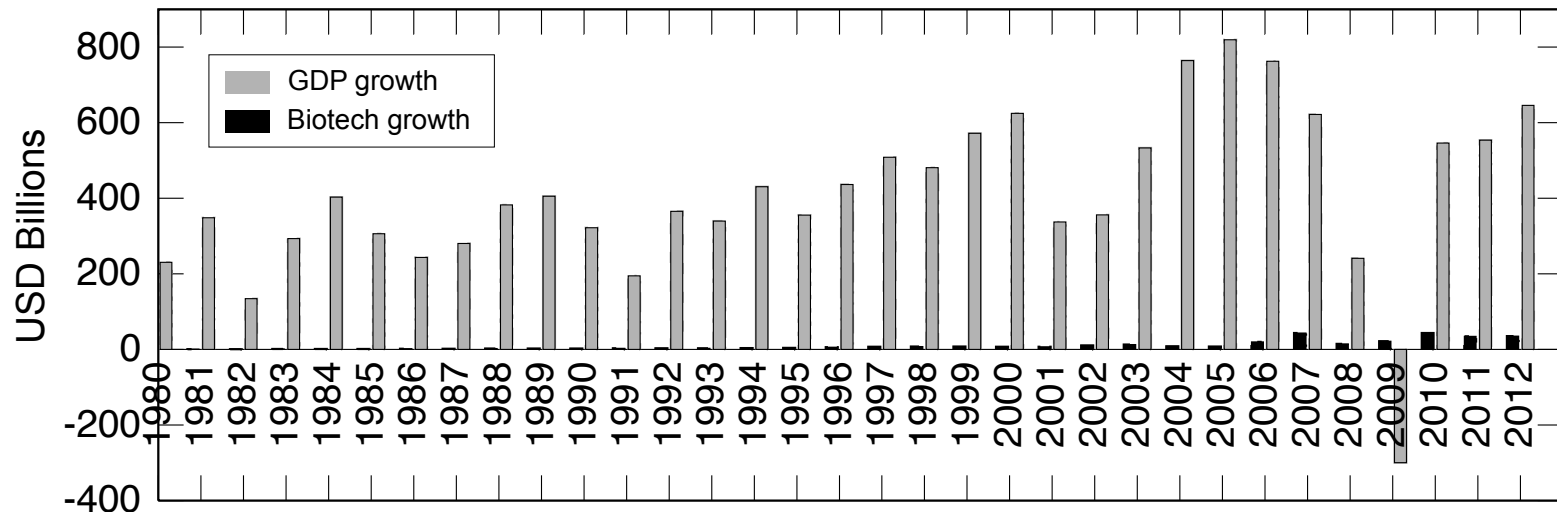
R. Carlson, *Nature Biotech*, March 2016.

Share of GDP and GDP Growth

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



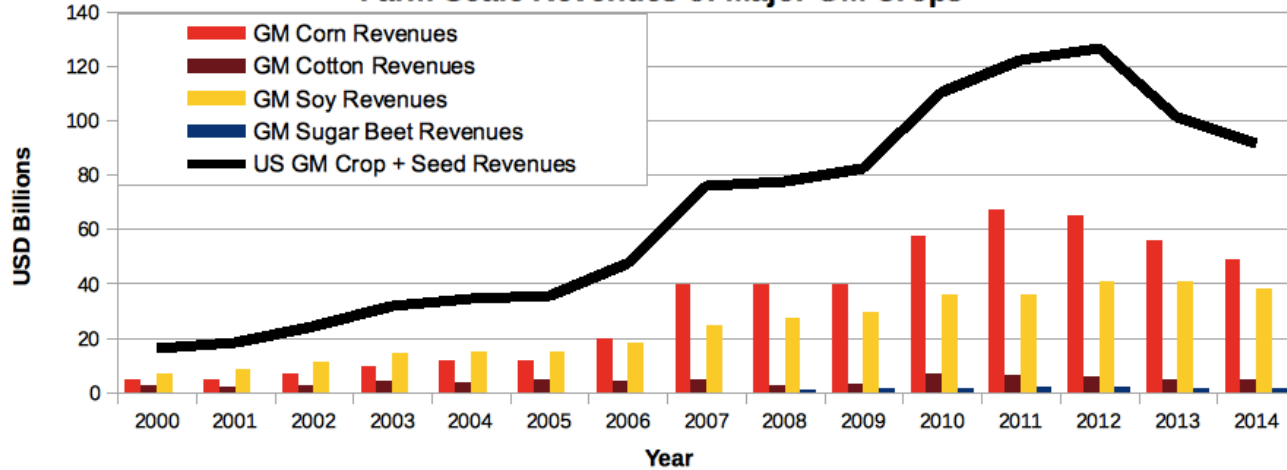
Annual Growth in U.S. GDP and U.S. Biotech Revenues



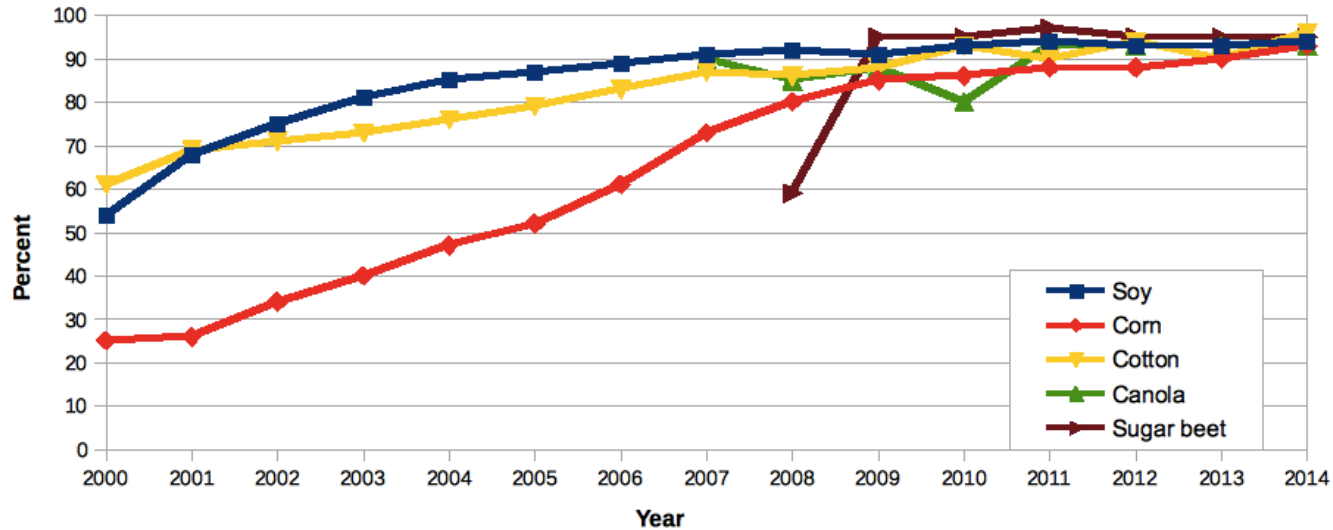
R. Carlson, *Nature Biotech*, March, 2016.

Crop Prices Can Go Up...And Down

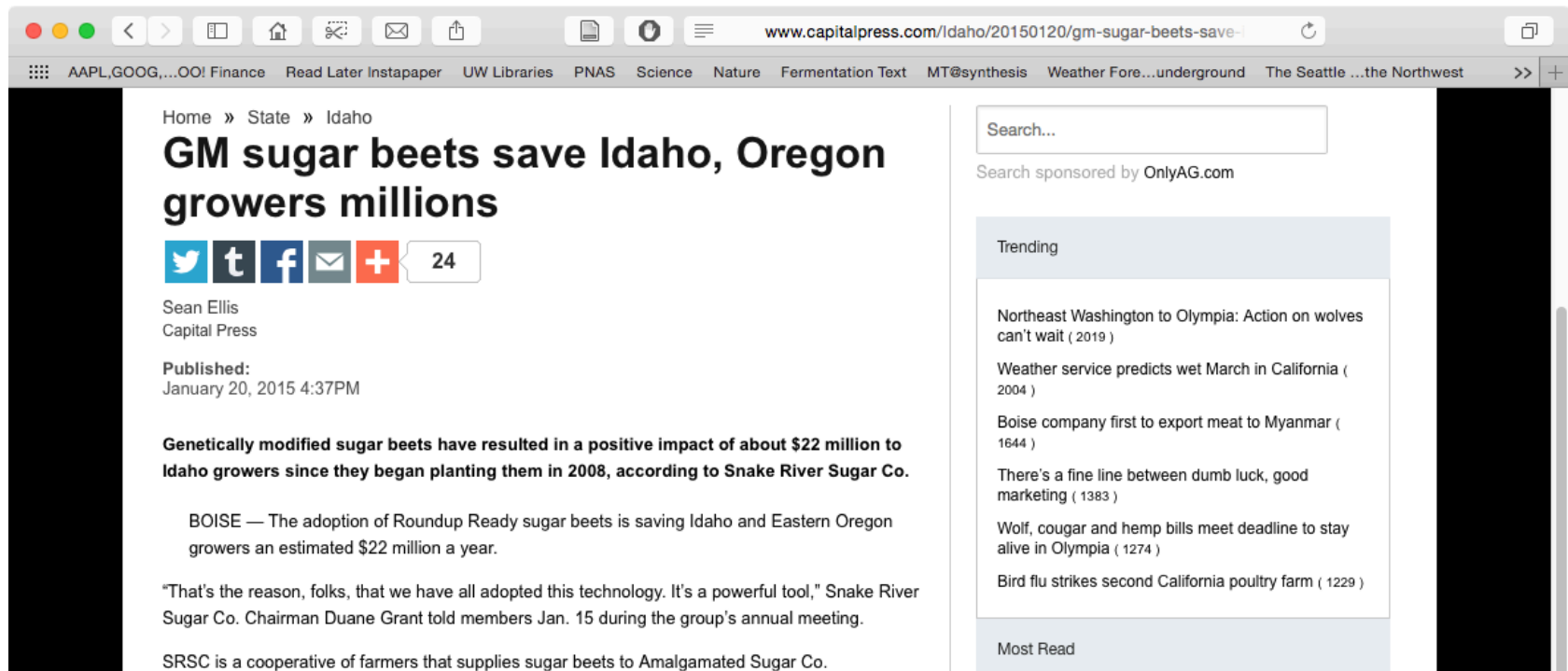
Total U.S. Revenues from GM Crops and Seeds and Farm Scale Revenues of Major GM Crops



U.S. Market Penetration of Five GM Crops



Economics Driving Adoption from Top to Bottom



The screenshot shows a web browser window with the URL www.capitalpress.com/Idaho/20150120/gm-sugar-beets-save-. The article title is "GM sugar beets save Idaho, Oregon growers millions" by Sean Ellis, published on January 20, 2015. The article text states that genetically modified sugar beets have resulted in a positive impact of about \$22 million to Idaho growers since they began planting them in 2008, according to Snake River Sugar Co. It also mentions that the adoption of Roundup Ready sugar beets is saving Idaho and Eastern Oregon growers an estimated \$22 million a year. A quote from Snake River Sugar Co. Chairman Duane Grant is included, along with information about SRSC as a cooperative of farmers.

Home » State » Idaho

GM sugar beets save Idaho, Oregon growers millions

24

Sean Ellis
Capital Press

Published:
January 20, 2015 4:37PM

Genetically modified sugar beets have resulted in a positive impact of about \$22 million to Idaho growers since they began planting them in 2008, according to Snake River Sugar Co.

BOISE — The adoption of Roundup Ready sugar beets is saving Idaho and Eastern Oregon growers an estimated \$22 million a year.

"That's the reason, folks, that we have all adopted this technology. It's a powerful tool," Snake River Sugar Co. Chairman Duane Grant told members Jan. 15 during the group's annual meeting.

SRSC is a cooperative of farmers that supplies sugar beets to Amalgamated Sugar Co.

Search...

Search sponsored by OnlyAG.com

Trending

- Northeast Washington to Olympia: Action on wolves can't wait (2019)
- Weather service predicts wet March in California (2004)
- Boise company first to export meat to Myanmar (1644)
- There's a fine line between dumb luck, good marketing (1383)
- Wolf, cougar and hemp bills meet deadline to stay alive in Olympia (1274)
- Bird flu strikes second California poultry farm (1229)

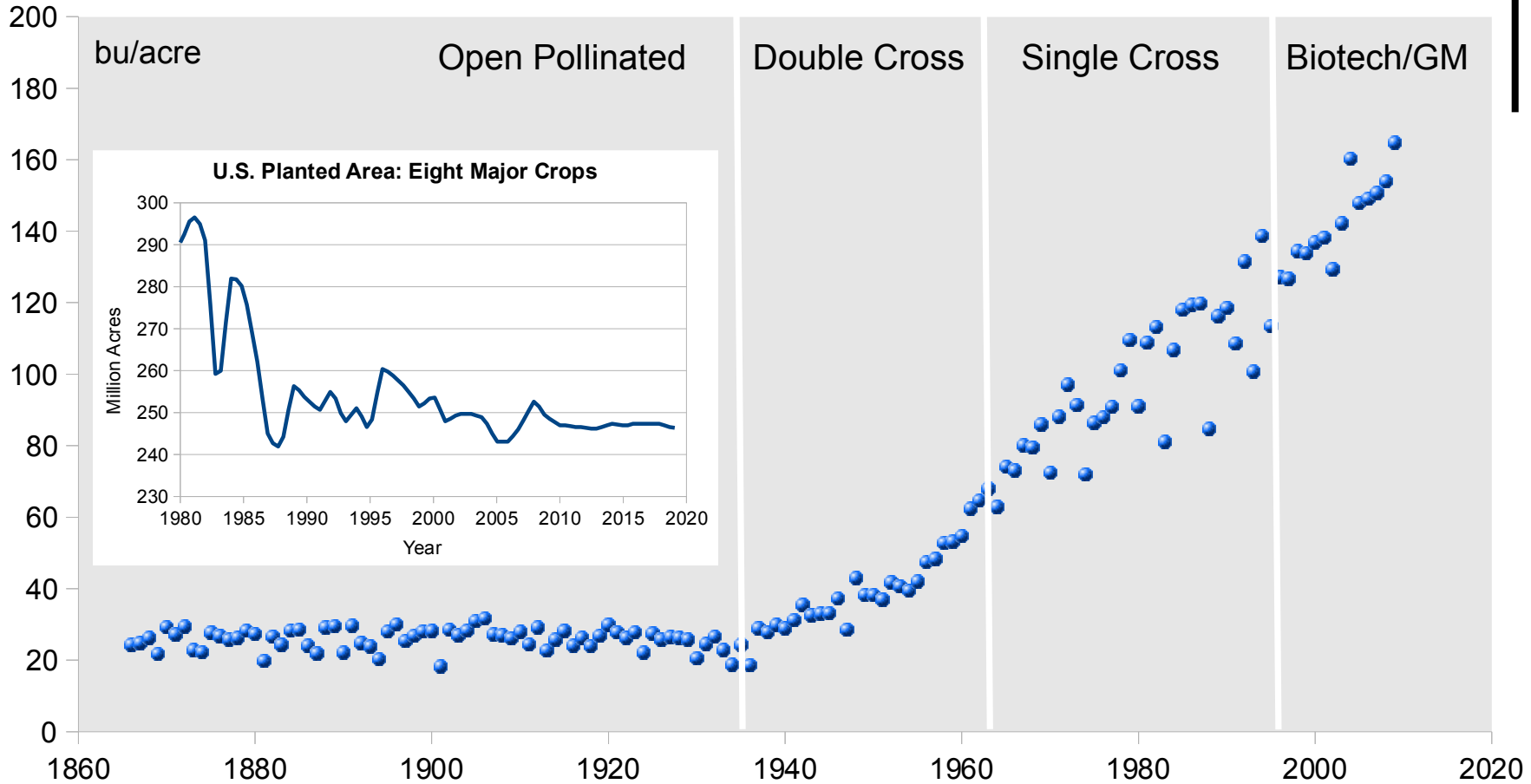
Most Read

- 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?

Current Test Yield:
~535 bu/acre

Average US Corn Yield, 1866-2009

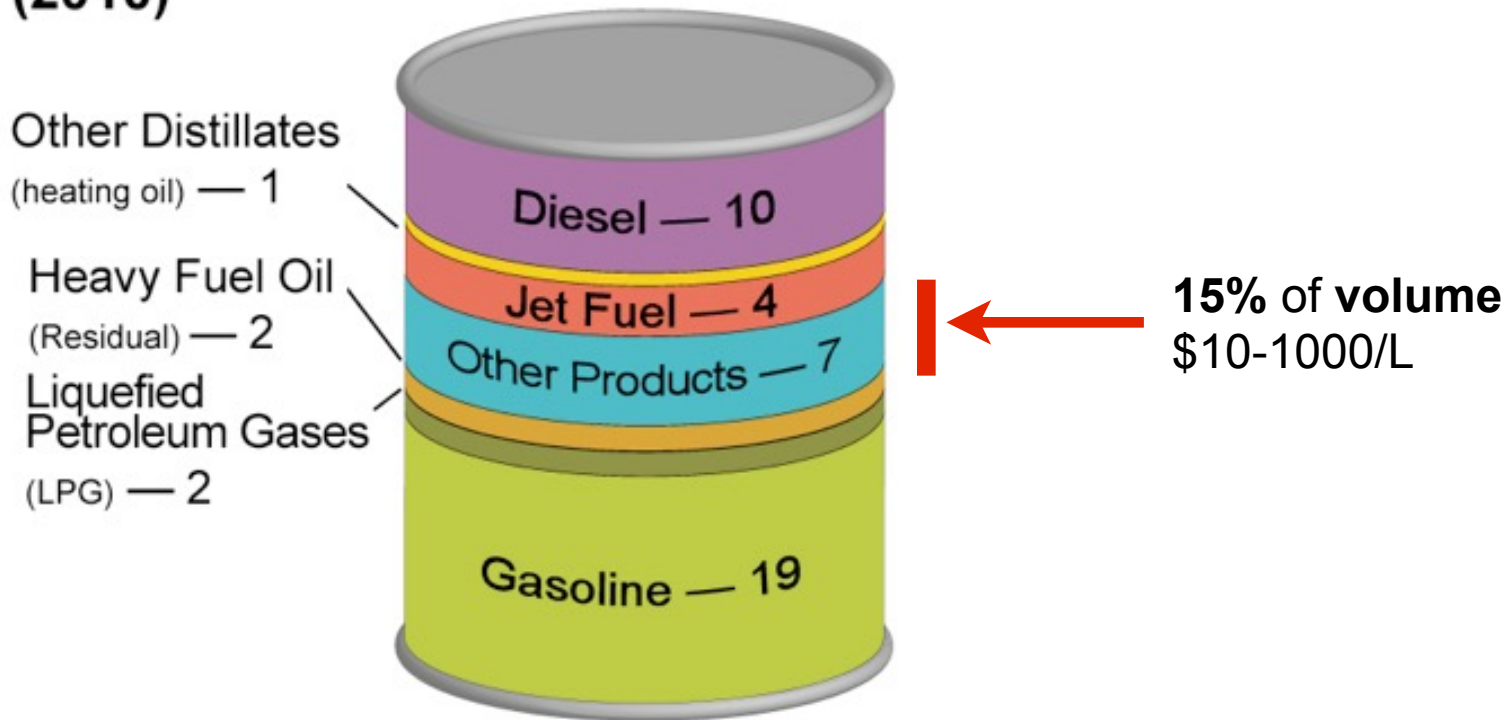


Sources: USDA-NASS; Troyer, *Crop Science* 46.2 (2006): 528; Pioneer (Rupert and Butzen, *Crop Sci*, 19(2))

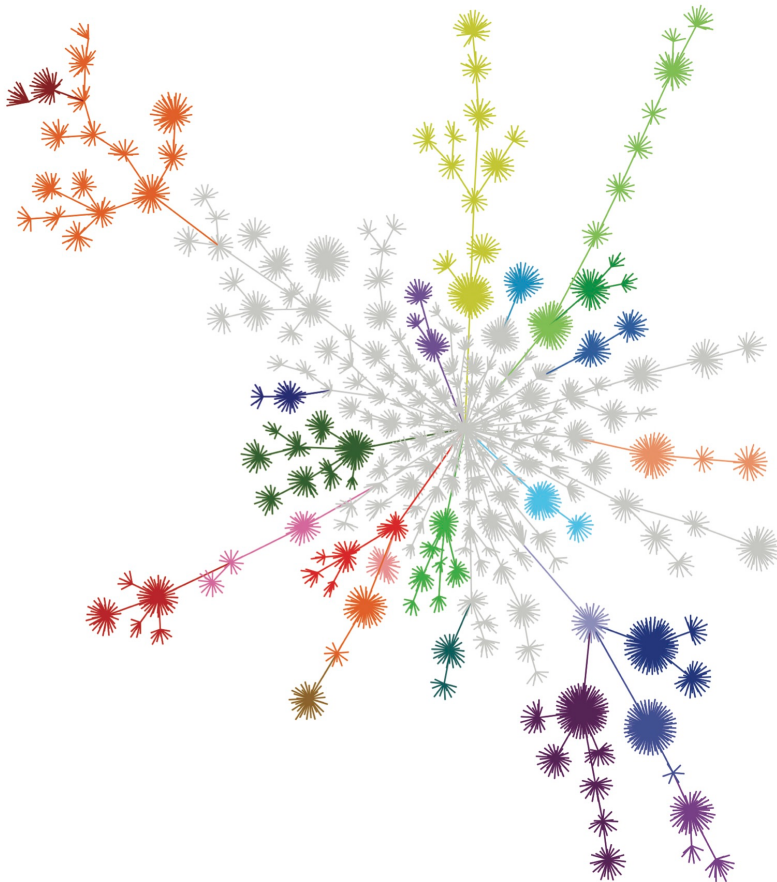
Where Do We Get Our Stuff?

What is in a Barrel of Oil and How Much is it Worth?

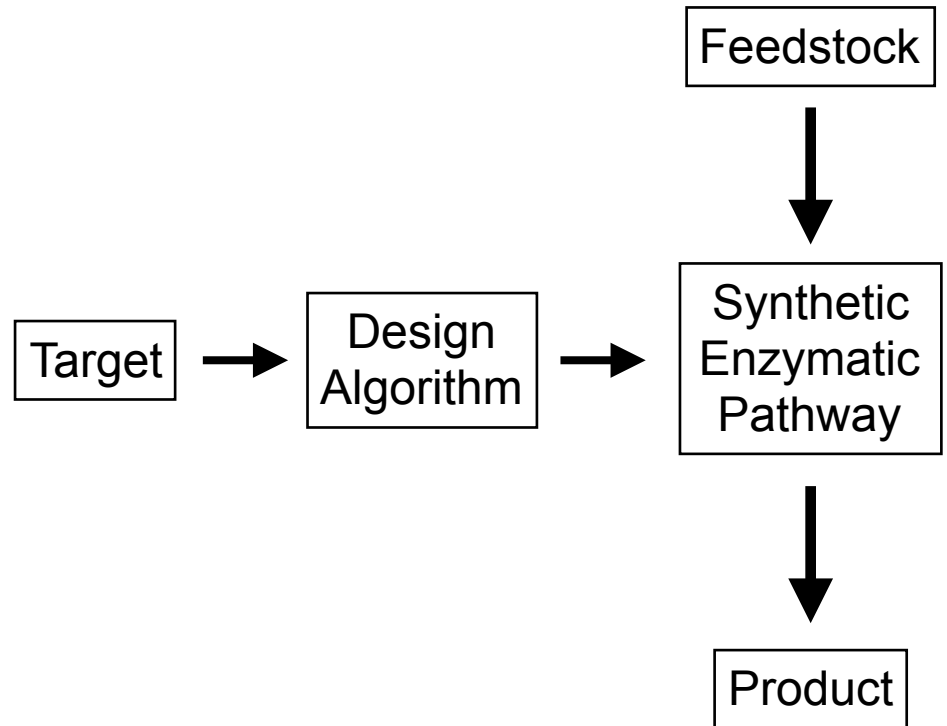
Products Made from a Barrel of Crude Oil (Gallons) (2010)



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 replaced chemical synthesis of amoxicillin in Singapore plant with biological production using enzymes. (collaboration with Codexis)

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.

Pre-Fab Production Systems

GE/JHL collaboration, for example, is driven by diverse needs:

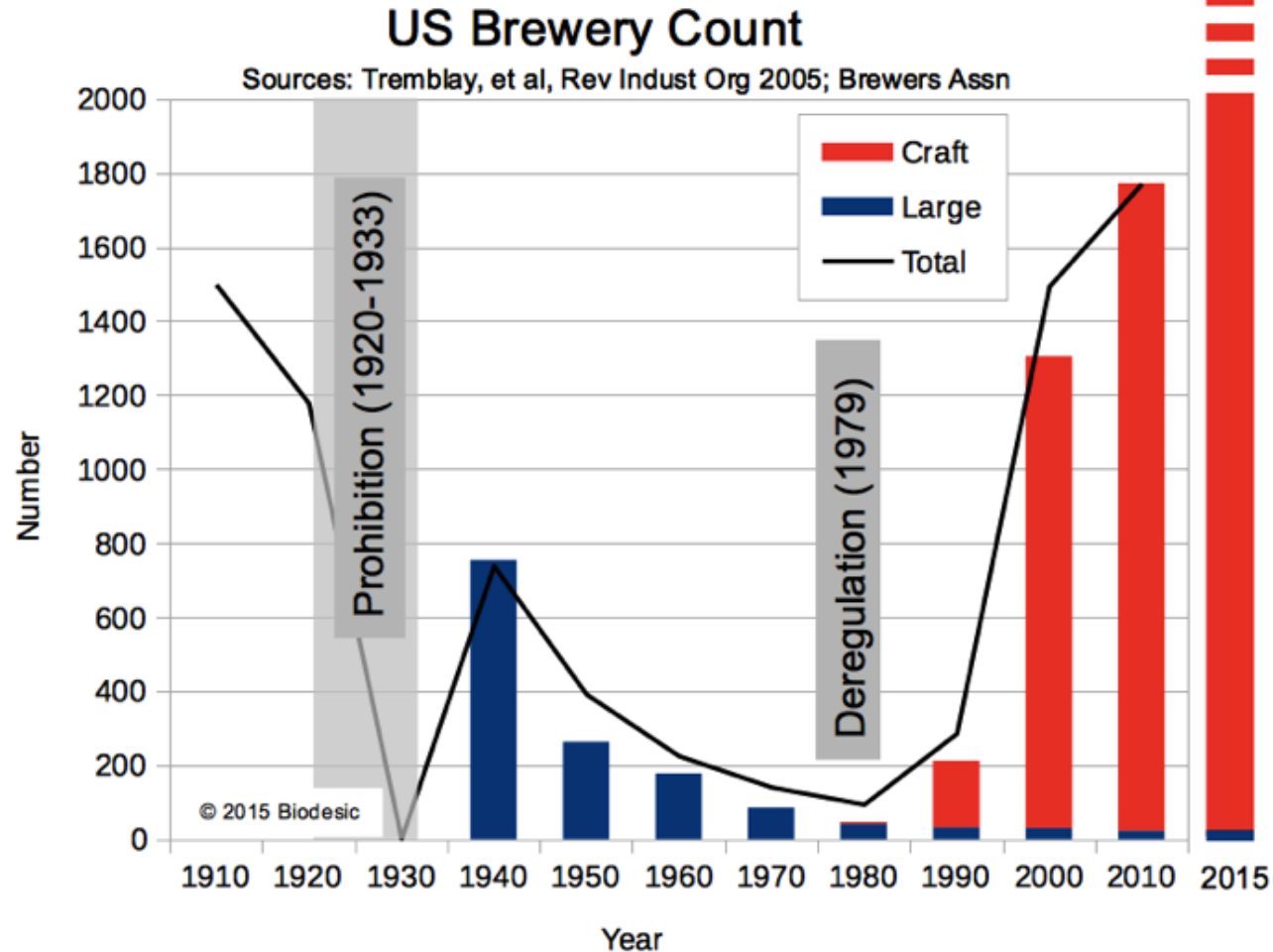


- To develop resilience and flexibility as responses to infectious diseases drove the need to “stockpile capacity rather than stockpile a particular vaccine” near the point of use.
- “Chinese government requires that we manufacture products in China, even for IND [investigational new drug] submissions. 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.

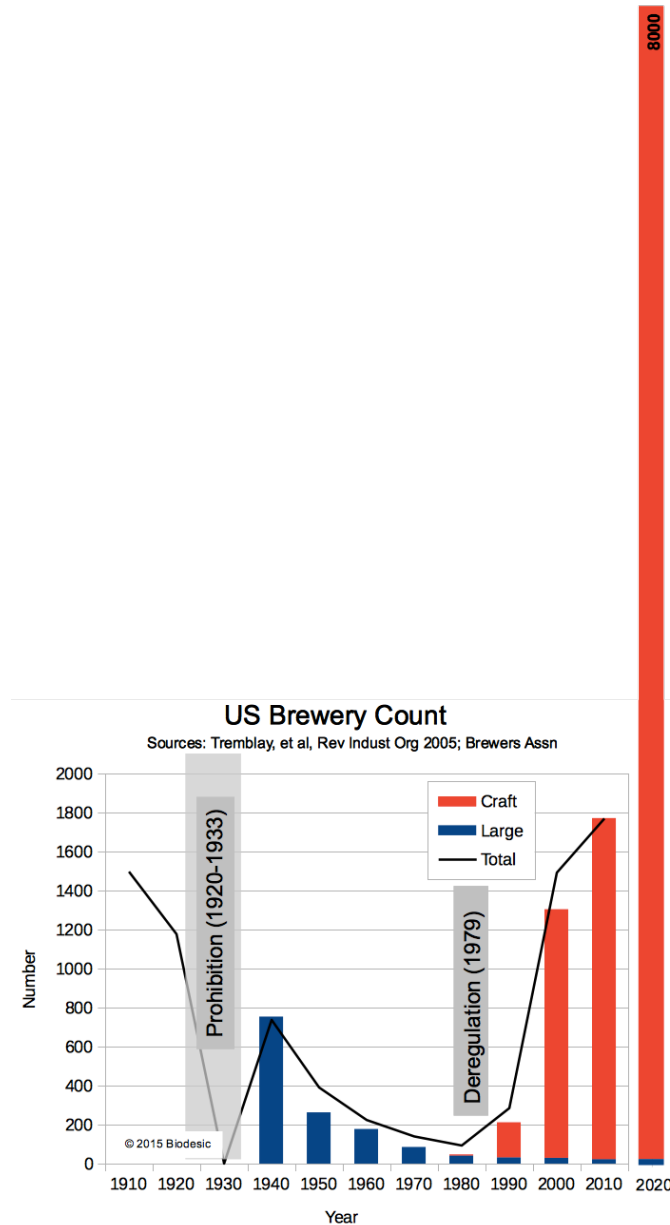
<http://www.biopharma-reporter.com/Upstream-Processing/GE-ships-pre-built-plant-to-China-as-Asia-pursues-homemade-production>

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.)

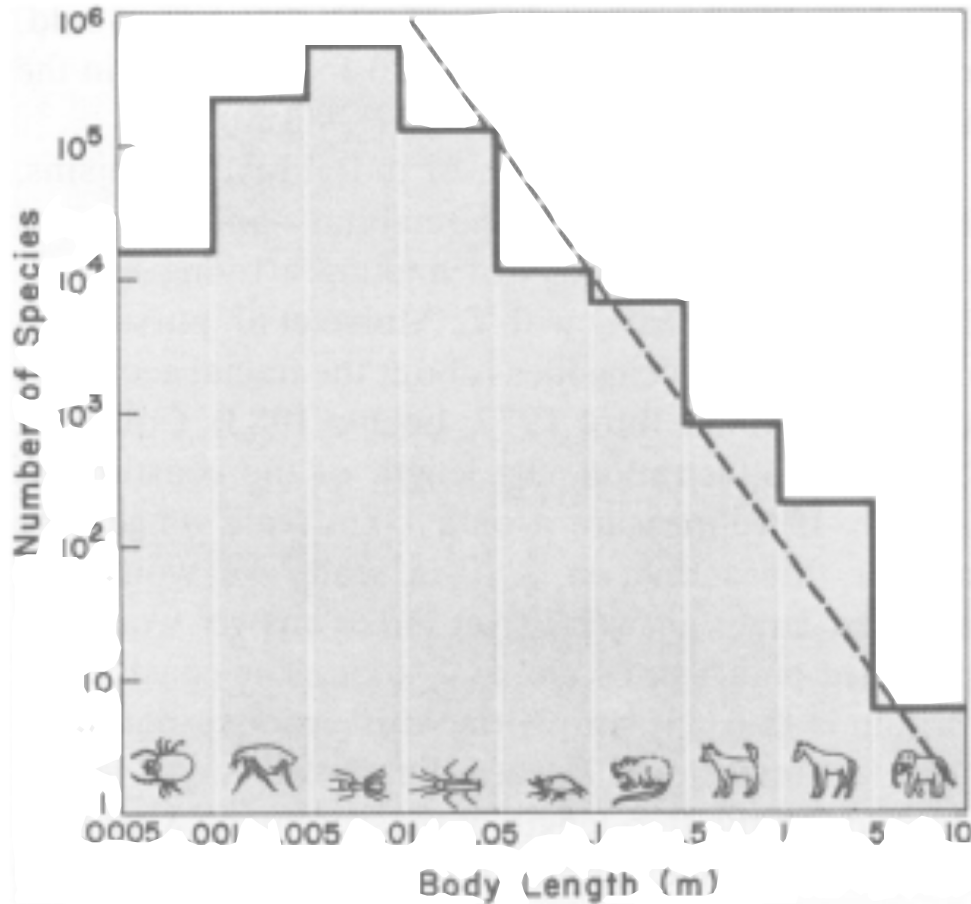




Source: Amyris

- 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?

Robert M. May, “The Search for Patterns in the Balance of Nature”,
Ecology, Vol. 67, No. 5 (Oct., 1986), pp. 1116-1126

Costs of Scaling Up

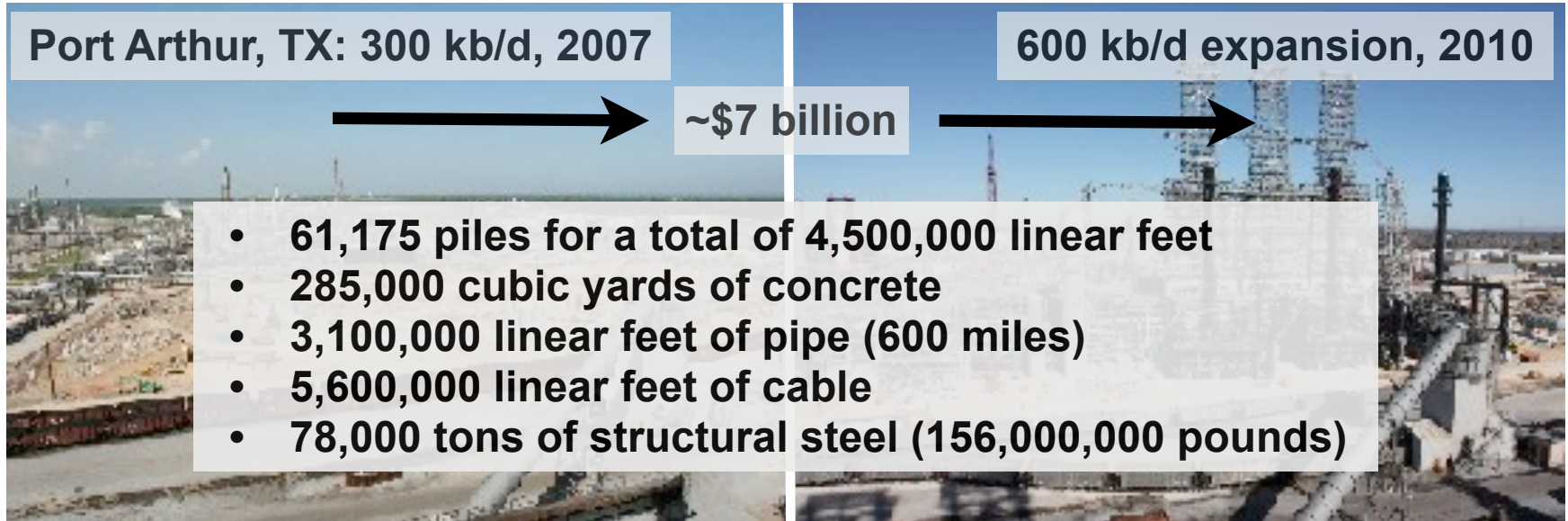
Industrial Chemistry

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

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



Distributed Biological Manufacturing vs. 'Oil'



Distributed Biological Manufacturing vs. 'Oil'

Advanced Cellulosic Biofuels Industry Requirements:

Production Units Required by 2022:	527
Capital Cost of a Production Unit (100 mg/y):	\$320 million
Replacement Cost of Productive Capacity:	\$168 billion
Volume of Annual Productive Capacity:	22 billion gallons
Annual Retail Value of Fuel (at today's prices):	~\$66 billion



US Dairy Industry Snapshot:

Production Units:	about 9.25M animals in 2012
Average cost of a production unit:	between \$1,500 - \$3,000
Total replacement value of the herd:	under \$28 billion
Total volume of milk produced:	about 23 billion gallons in 2012
Annual retail value of the milk:	around \$100 billion