Biodesic

hardware :: wetware :: mindware

The Pace and Diffusion of Synthetic Biology

Tsinghua University, Beijing, January 2013

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blog: www.synthesis.cc

The Past and ~~Future~~ Present of Biological Technologies

Photosynthetic Sea Slug
(*Elysia chlorotica*)
Evolved ~100 Myr BCE

PNAS

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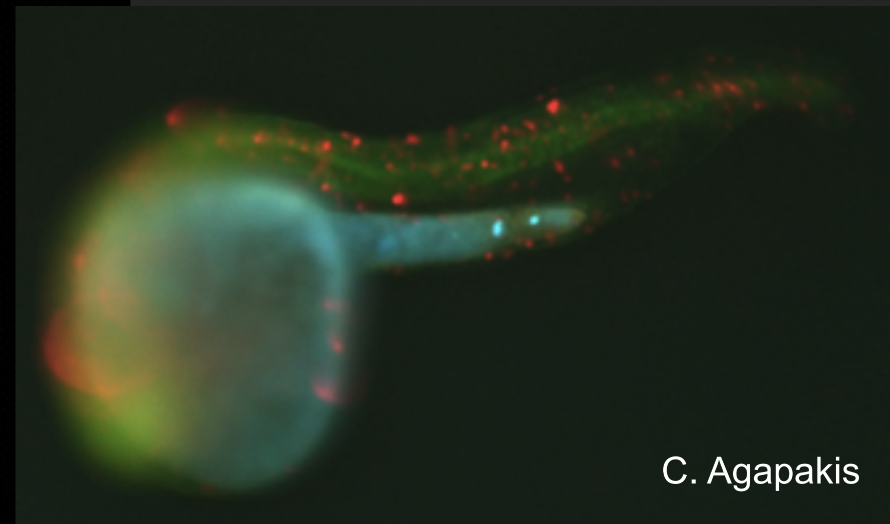


C. Agapakis

Photosynthetic Fish
(*Danio rerio*)
Engineered 2010 +5 (?) yrs
Pam Silver, Harvard Univ.

Parsing the Spread of Biological Technologies

Drivers

Economic Growth

Material and Energy Efficiencies

Carbon Load Reduction

Curiosity (It's cool, dude.)

FOOD,WATER, ENERGY!

Characteristics

1. International
2. Distributed (Beer Vs. Oil)
3. Increasing Capabilities
4. Decreasing Costs
5. "Open Source"?

Consequences

1. Widespread access to tools, skills, and materials.
2. Lower environmental impact (emissions).
3. Lower energy usage.
4. Reduction in foreign energy and materials dependency.
5. More diverse bio-economy that can withstand shocks.
6. More diverse technological development for rapid countermeasures.

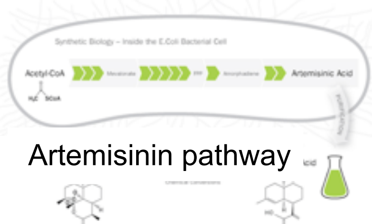
Major Uncertainties

Oil Price, Petroleum Production Investment, Gov't R&D Investment in Bio, National and Int'l Regulatory Policy, Threat Events, EU Carbon Labeling? US Electrification? Chinese Renewable Investment?

A Hierarchy of Engineering and Economic Complexities

Claudia Cadillo
Transplant Recipient

J.C. Venter



Artemisinin pathway

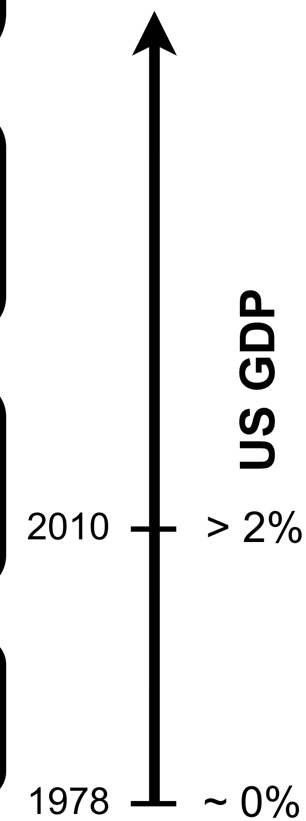
Expression in *E. coli*

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

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. **RFS.**

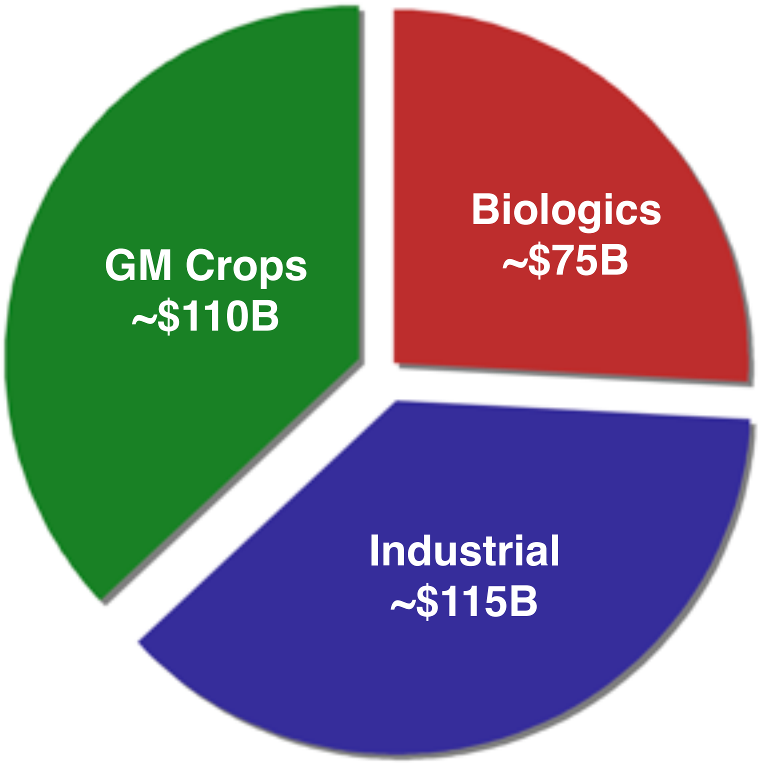
Single Gene in a Single Cell: Recombinant Proteins: Laundry Enzymes, HGH, EPO.



How Big is the Bioeconomy?

"Genetically Modified Stuff" in the US Bioeconomy (2010 est.): >$300B or Equivalent of >2% of GDP

U.S. Biotech Revenues (billions)



See: Robert Carlson, "Biodesic 2011 Bioeconomy Update", August 2011, www.biodesic.com

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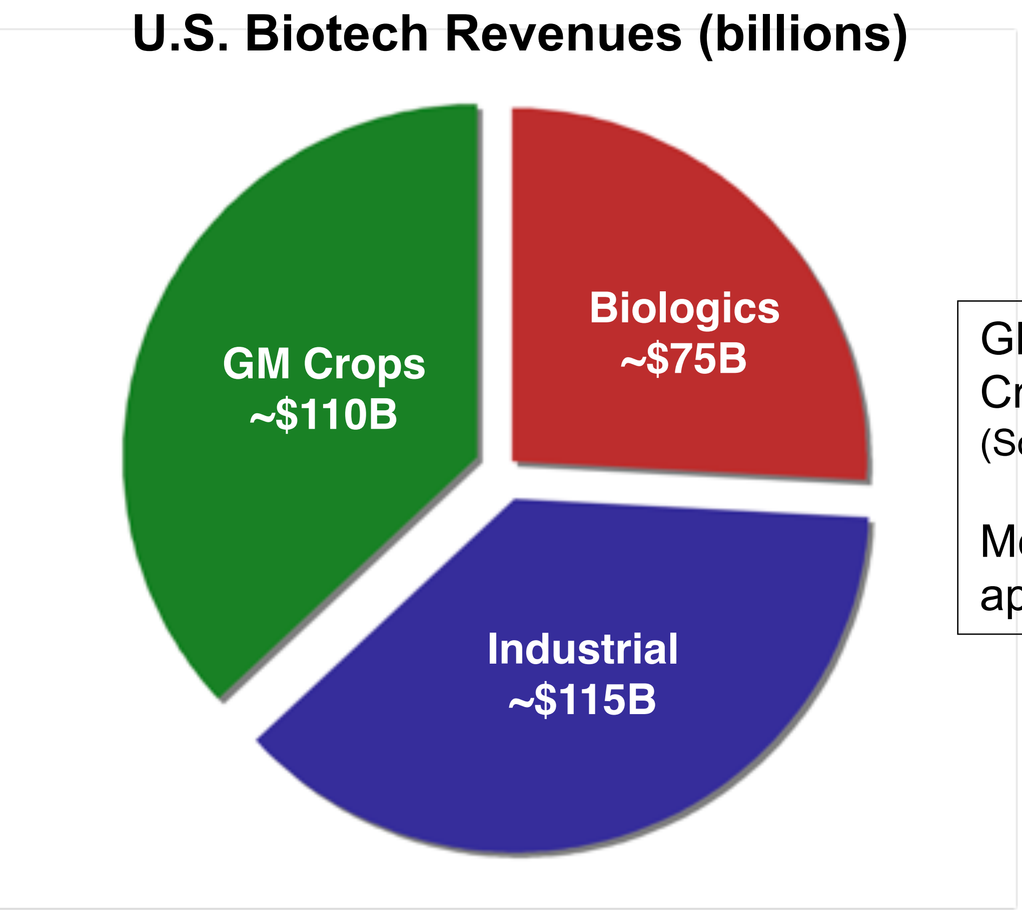


GM revenue growth:
Crops 10%, Biologics 10%, Industrial 20%.
(Sources: *Nat Biotech, Forbes*)

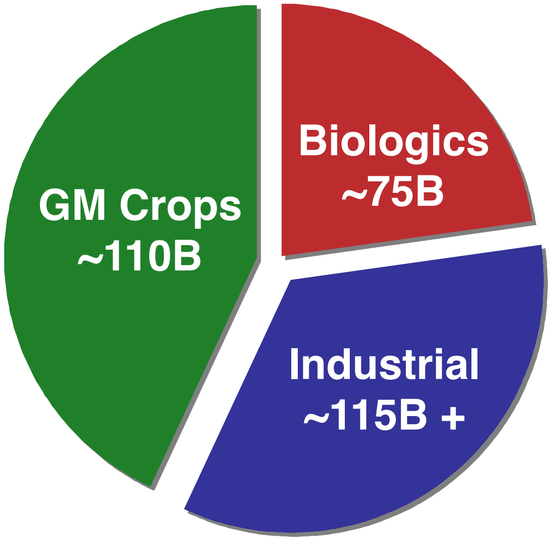
McKinsey and E&Y estimates for industrial apps range from $70B to $140B.

See: Robert Carlson, "Biodesic 2011 Bioeconomy Update", August 2011, www.biodesic.com

Scale and Regulation

U.S. Biotech Revenues in $ Billions

Medium regulation
Long lead times to market
~$100s millions

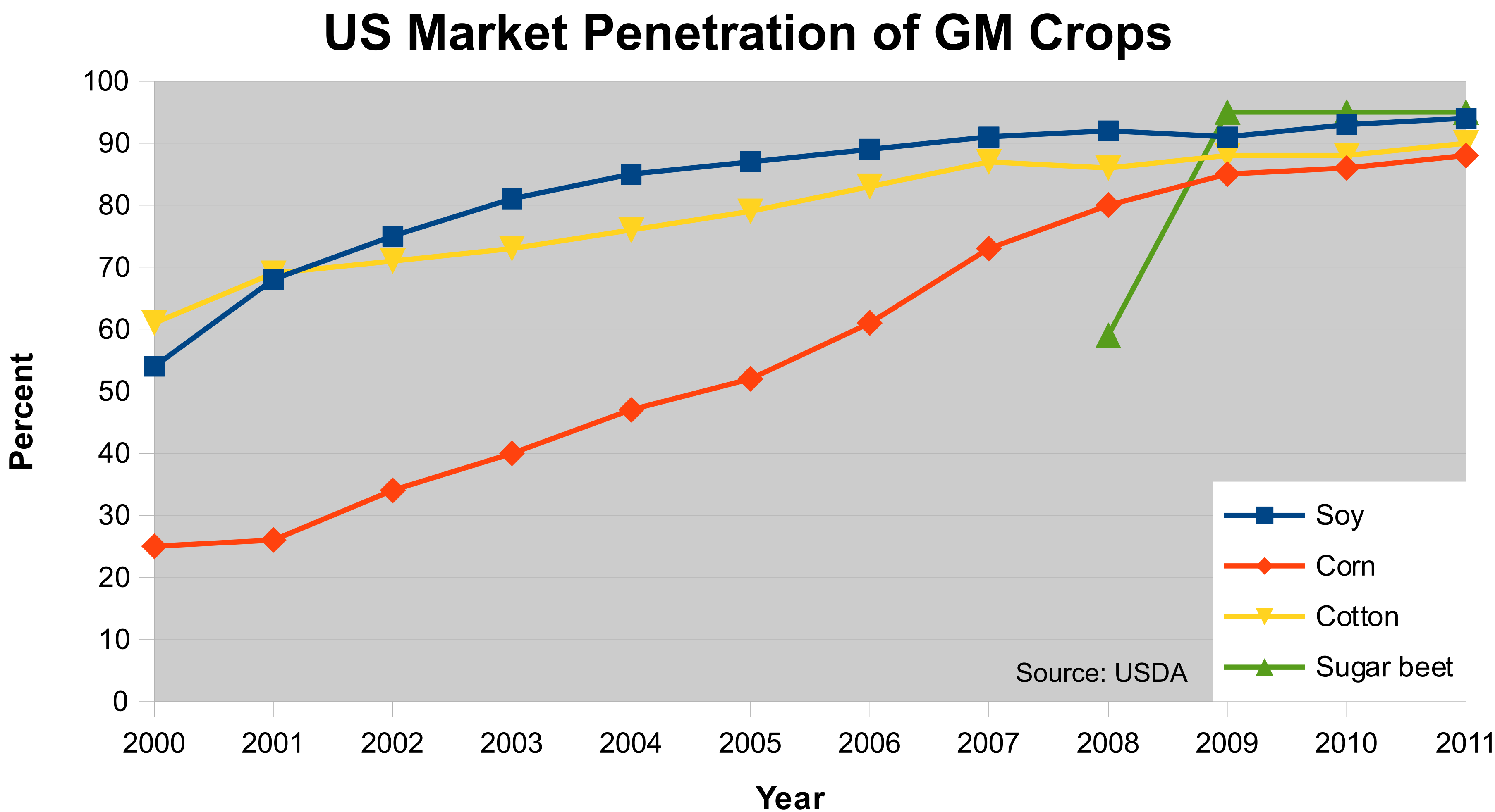


Highly regulated
Long lead times to market
~$1 billion

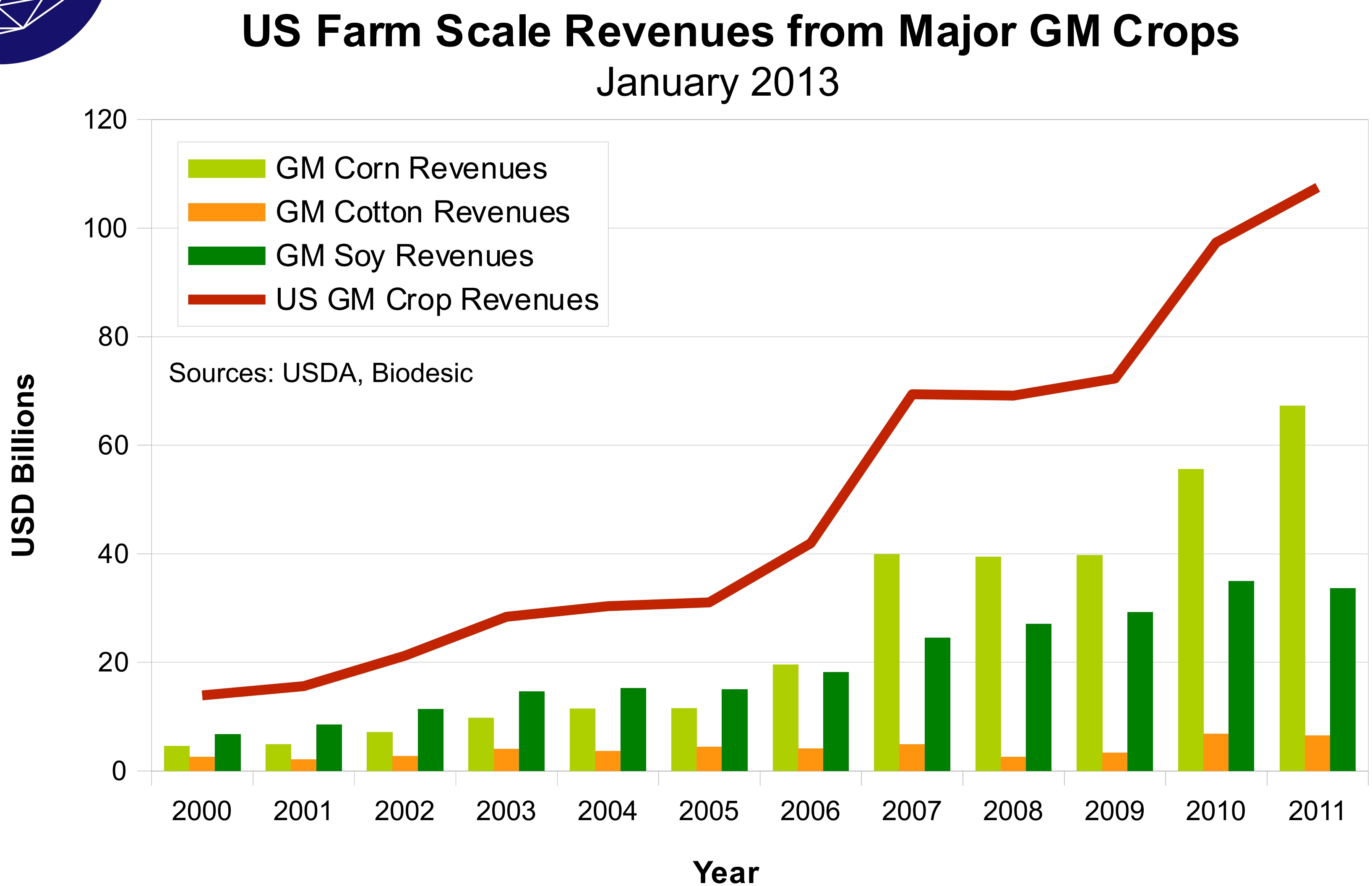
Market includes engineering tools
Operate closer to consumer
Could be much smaller, lower capital reqs.
As low as ~$10K-100K?

non-drug + non-food = not-so-regulated

U.S. Market Penetration and Pace of Major GM Crops

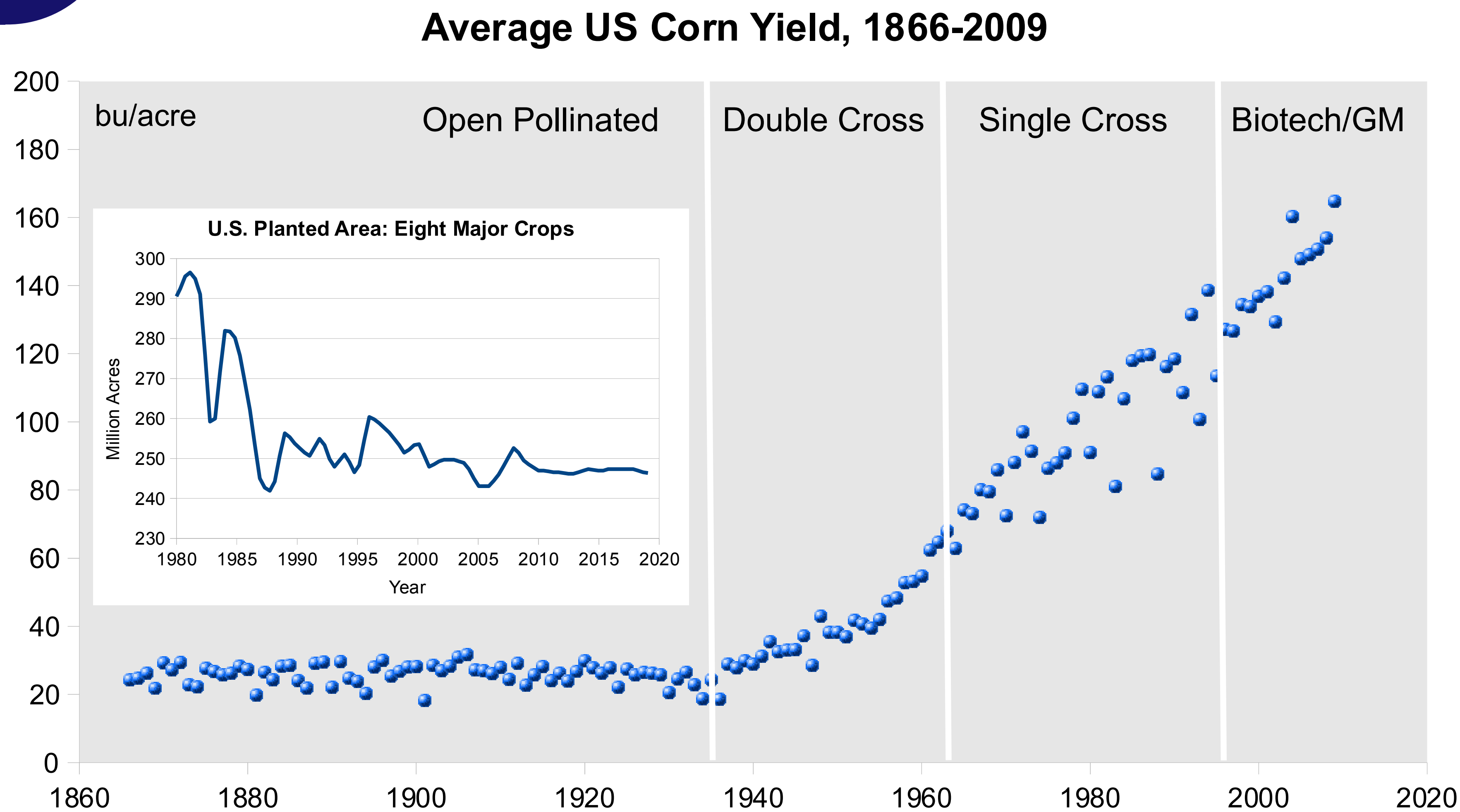


US Market Value of GM Crops



See: Robert Carlson, "The Market Value of GM Crops", *Nature Biotechnology*, **27**, 984, 2009.

Average US Corn Yields: No End in Sight



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

See: Robert Carlson, “Biodesic 2011 Bioeconomy Update”, August 2011, www.biodesic.com

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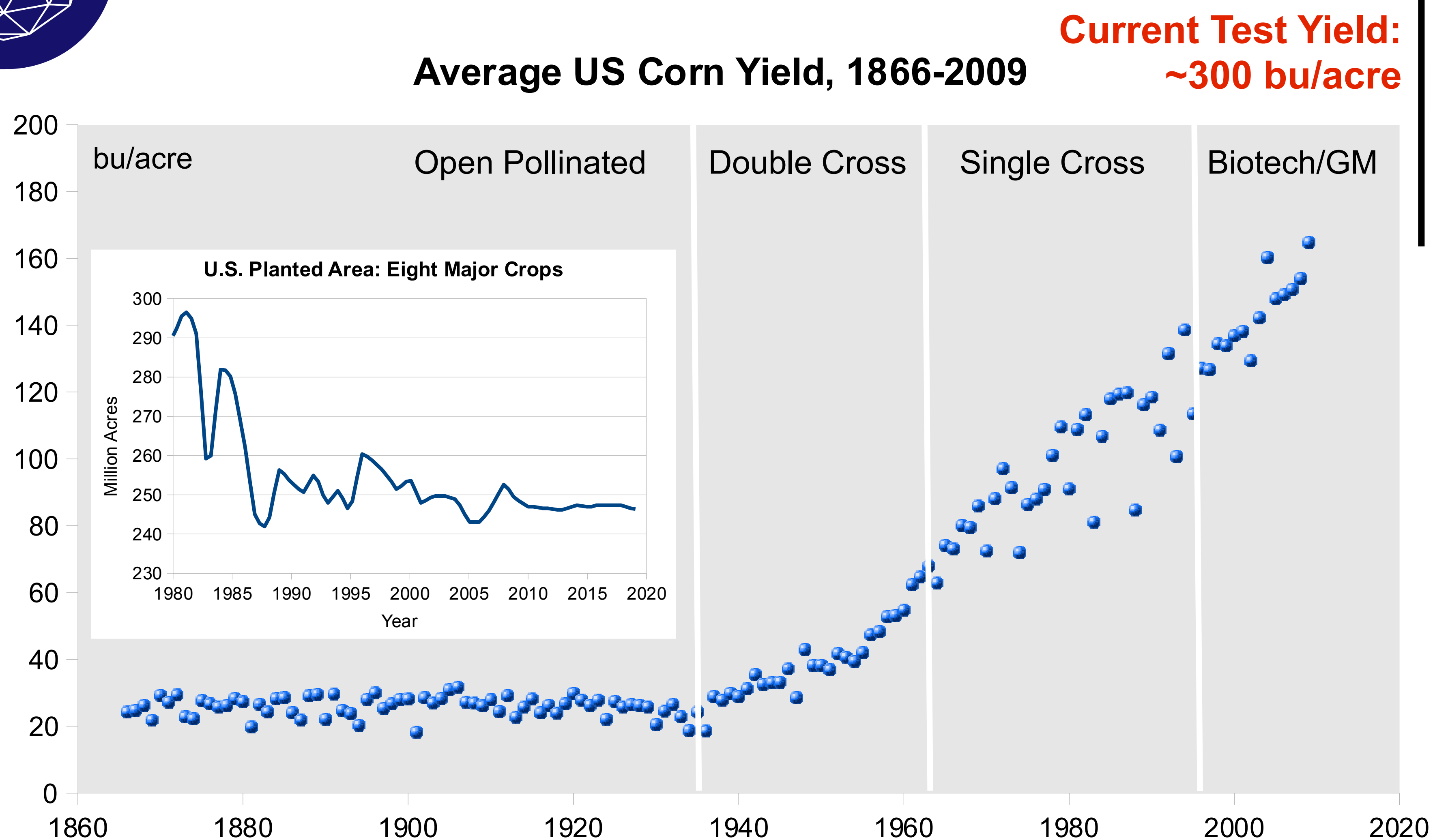

Sources: USDA-NASS; Troyer, *Crop Science* 46.2 (2006): 528; Pioneer (Rupert and Butzen, Crop Sci, 19(2))

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Economically Driven Global Adoption: Biotech Revenues as % of GDP

Country	2010 Biotech Revenues	2020 Target Biotech Revenues
United States	> 2%	NA
China	2.5% (?)	8%
Malaysia	2.5%	10%
India	0.24%	NA
Pakistan	1.4%	NA
Europe	~1%	NA

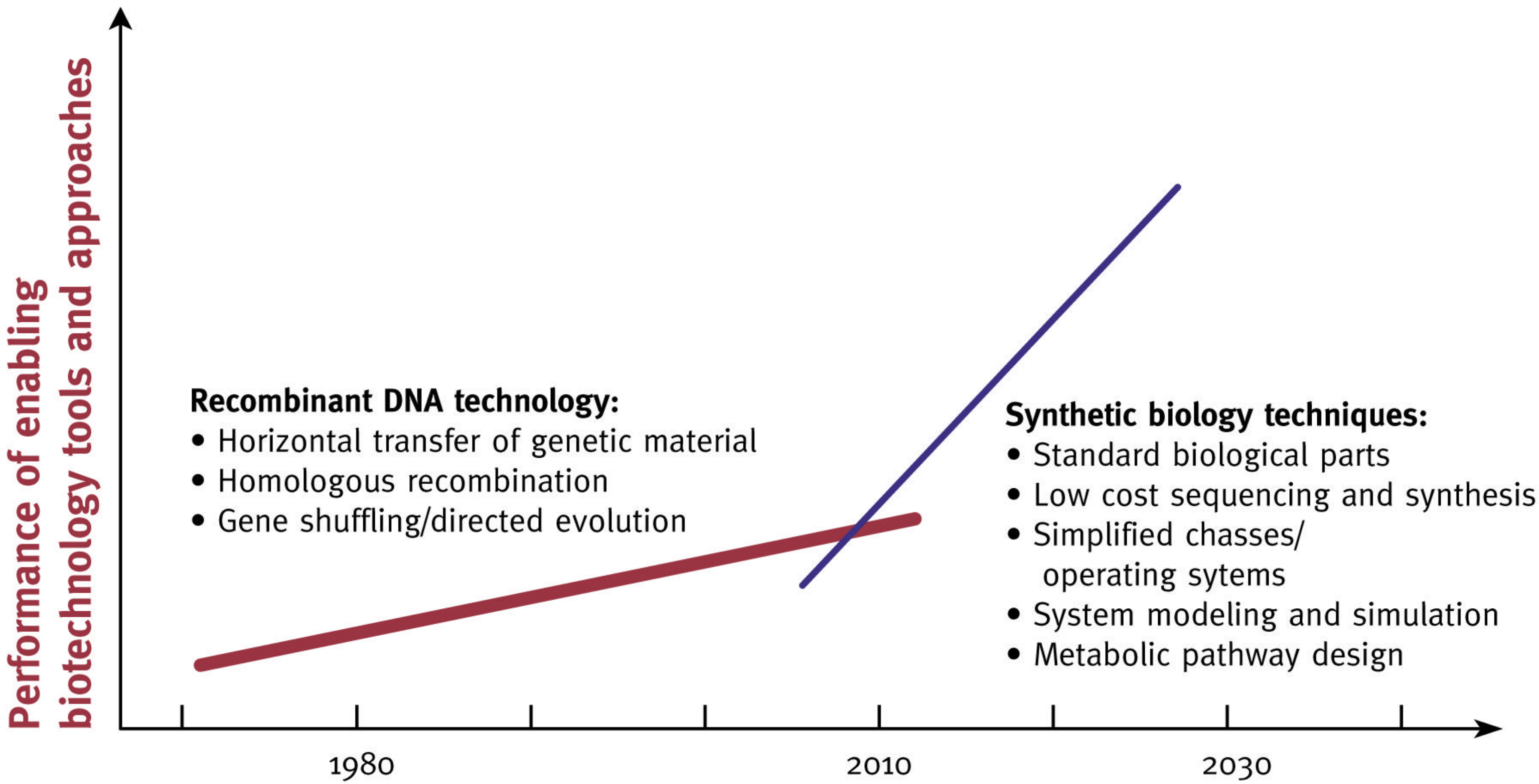
Source: Biodesic

Main source of uncertainty is definition of "biotechnology"; i.e., all biology or only products of genetic modification.

See: Robert Carlson, "Causes and Consequences of Bioeconomic Proliferation", 2012 Biodefense Net Assessment, Homeland Security Institute, http://bit.ly/Qm3fxi

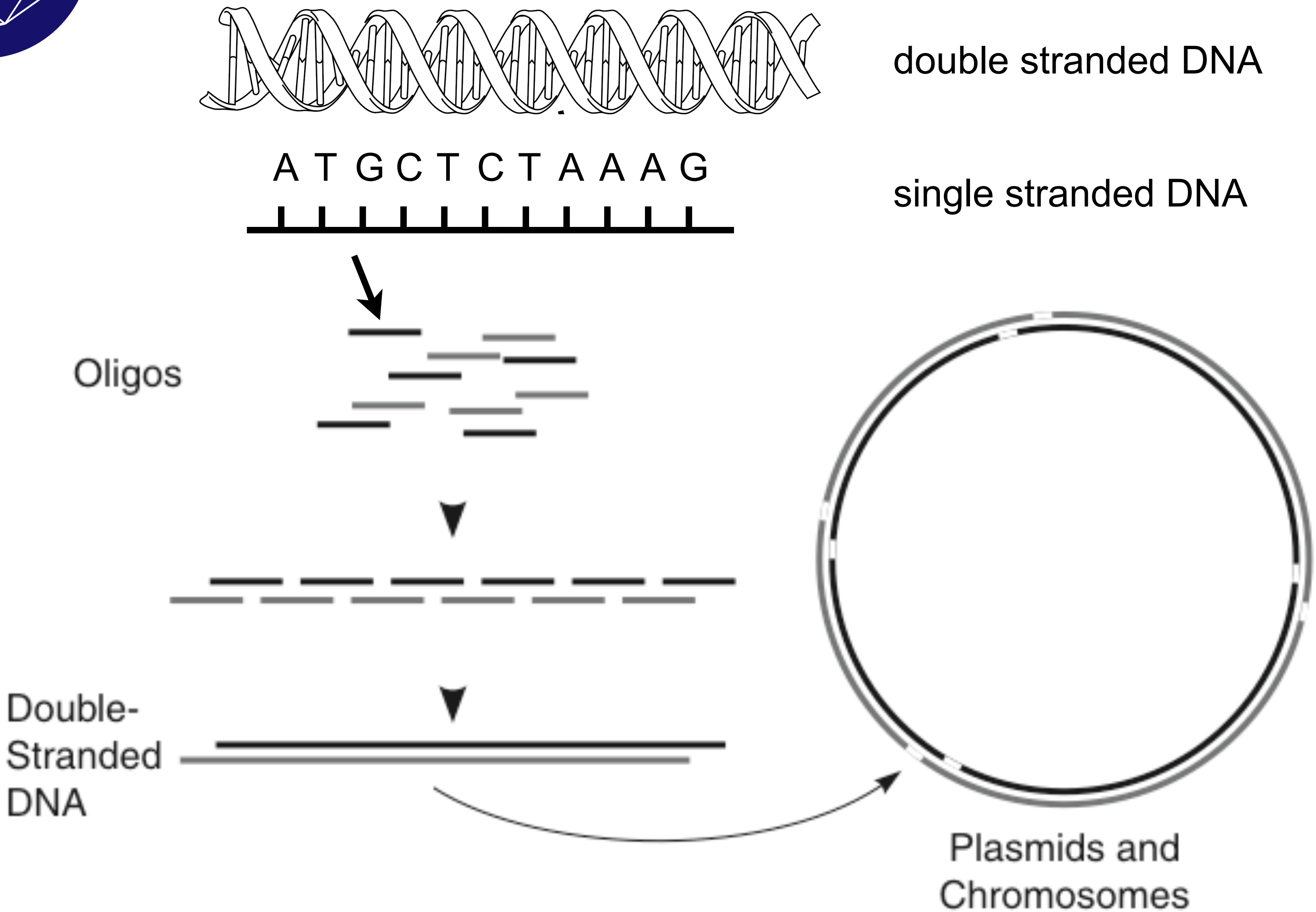
How Fast Is The World Changing?

An Inflection Point in Biotech Capabilities?

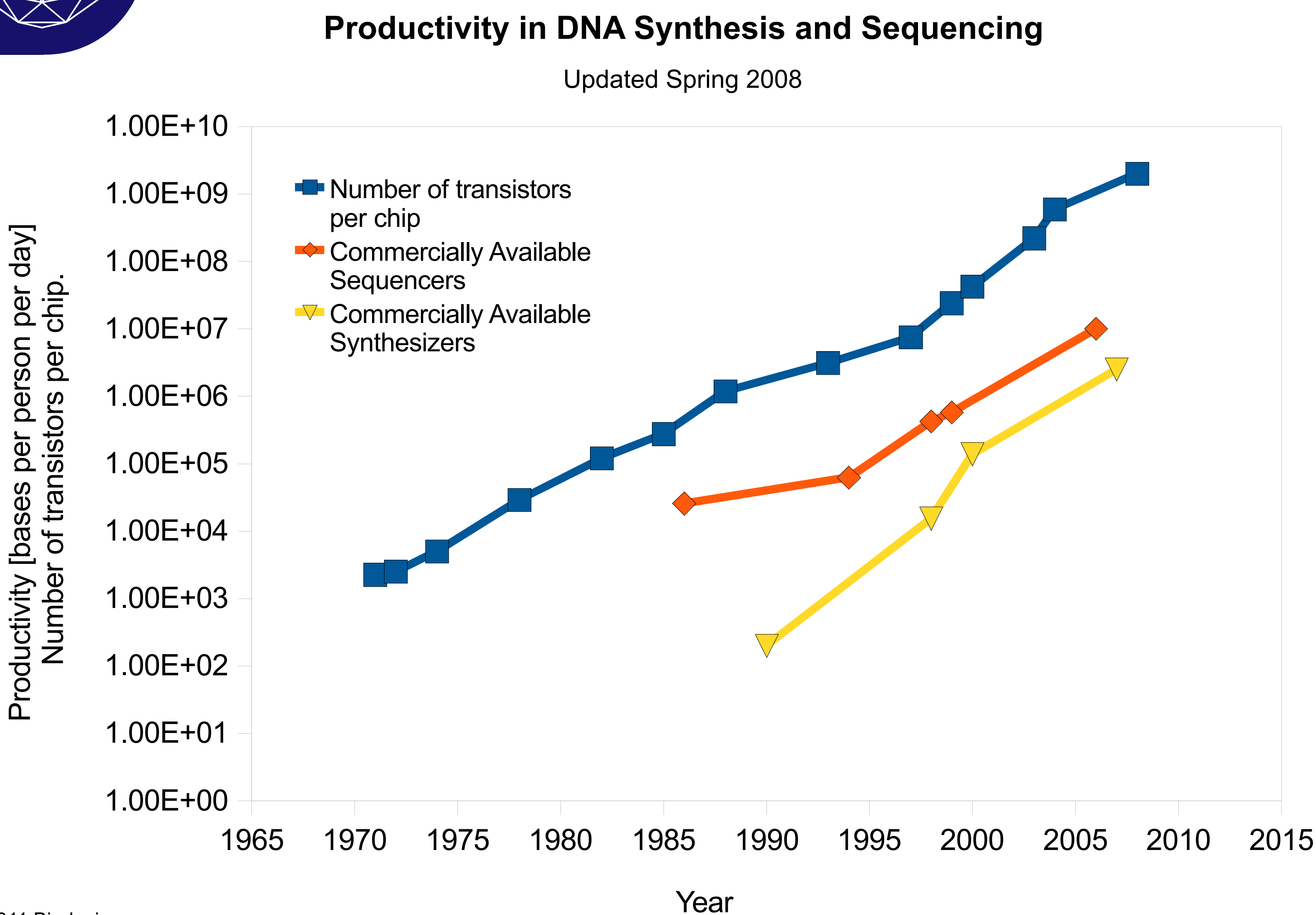


"Genome Synthesis and Design Futures: Implications for the U.S. Economy"
Bio Economic Research Associates, 2007. www.bio-era.net

Oligo Synthesis and Gene Assembly



Enabling Technologies Are Improving Rapidly



What is Moore’s Law?

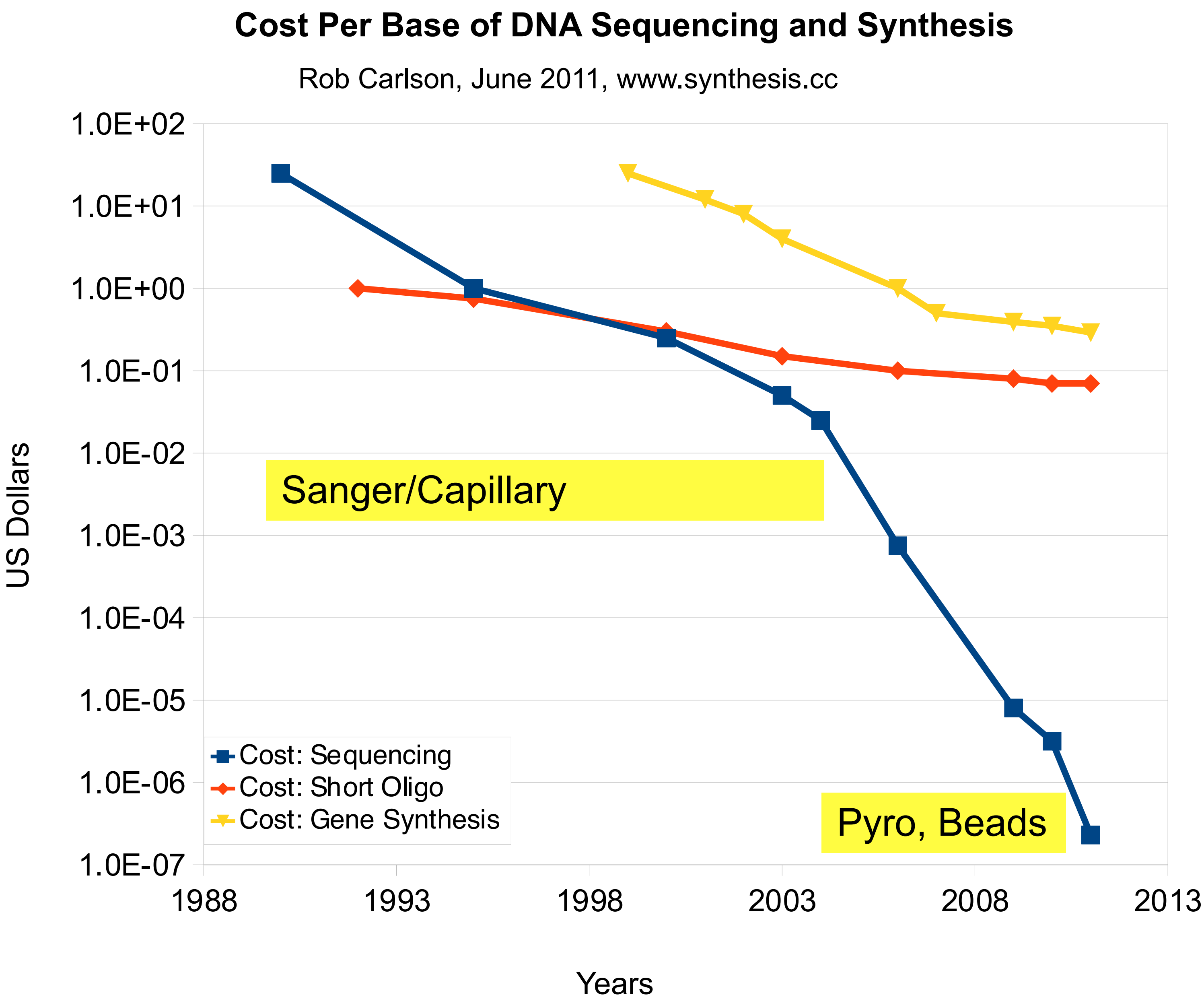
Moore’s Law is about vision, it's about what you're allowed to believe. Because people are really limited by their beliefs, they limit themselves by what they allow themselves to believe what is possible. So here's an example where Gordon [Moore], when he made this observation early on, he really gave us permission to believe that it would keep going. - Carver Mead

Also about finance and **planning** in a multi-billion dollar industry.

Finally, Moore’s Law is about *exponential markets* that, for some time period, grow faster than transistor costs fall.

Potentially *very different* than biology.

Cost c. 2011

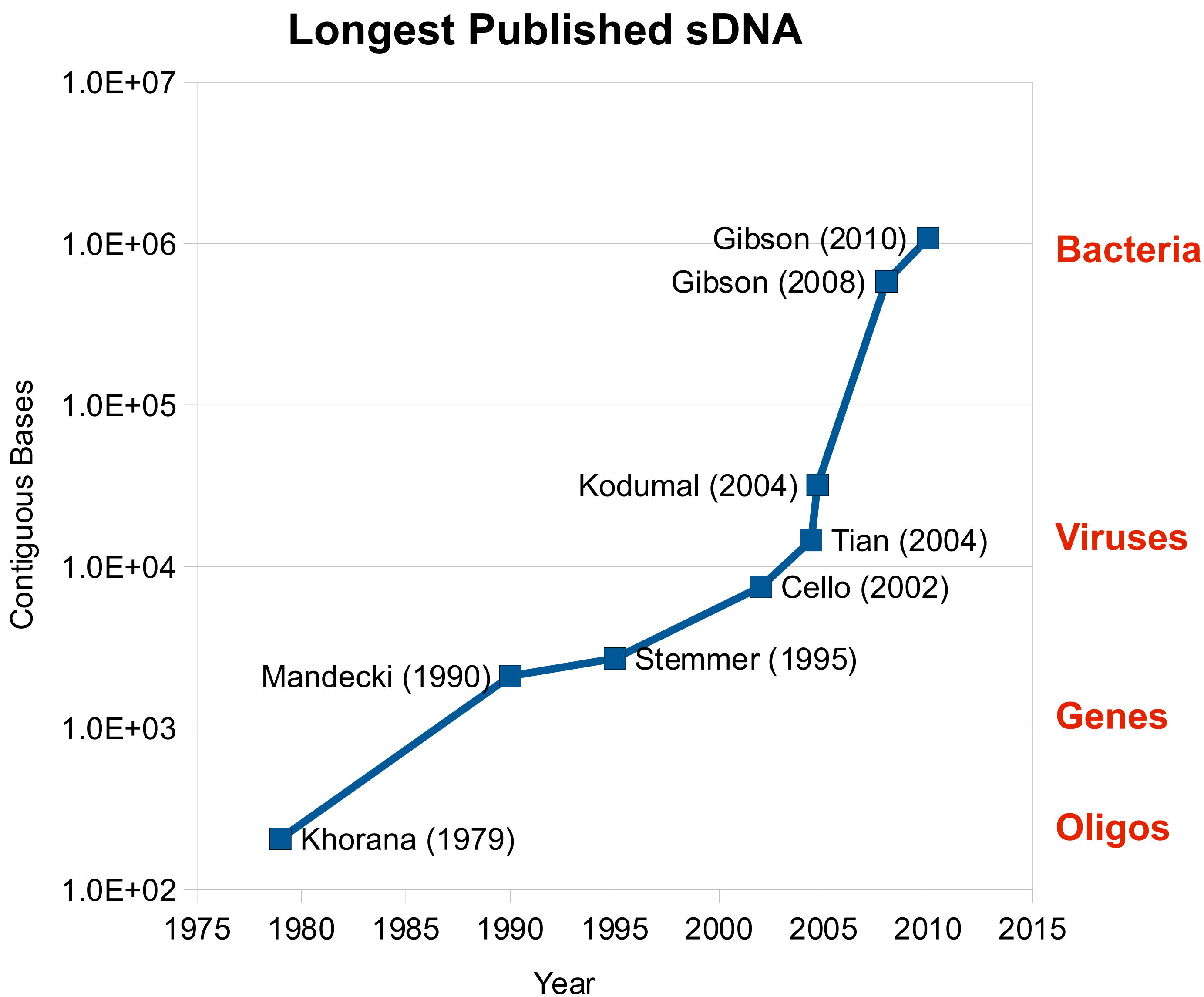


Cost Per Base of DNA Sequencing and Synthesis
Rob Carlson, June 2011, www.synthesis.cc
1.0E+02
1.0E+01
1.0E+00
1.0E-01
1.0E-02
1.0E-03
1.0E-04
1.0E-05
1.0E-06
1.0E-07
US Dollars
1988
1993
1998
2003
2008
2013
Years
Sanger/Capillary
Pyro, Beads
Cost: Sequencing
Cost: Short Oligo
Cost: Gene Synthesis

The Future?

Oxford Nanopore

Constructing Genes and Genomes



Sources: see http://www.synthesis.cc/2010/05/booting-up-a-synthetic-genome-1.html

“Synthetic Cells”

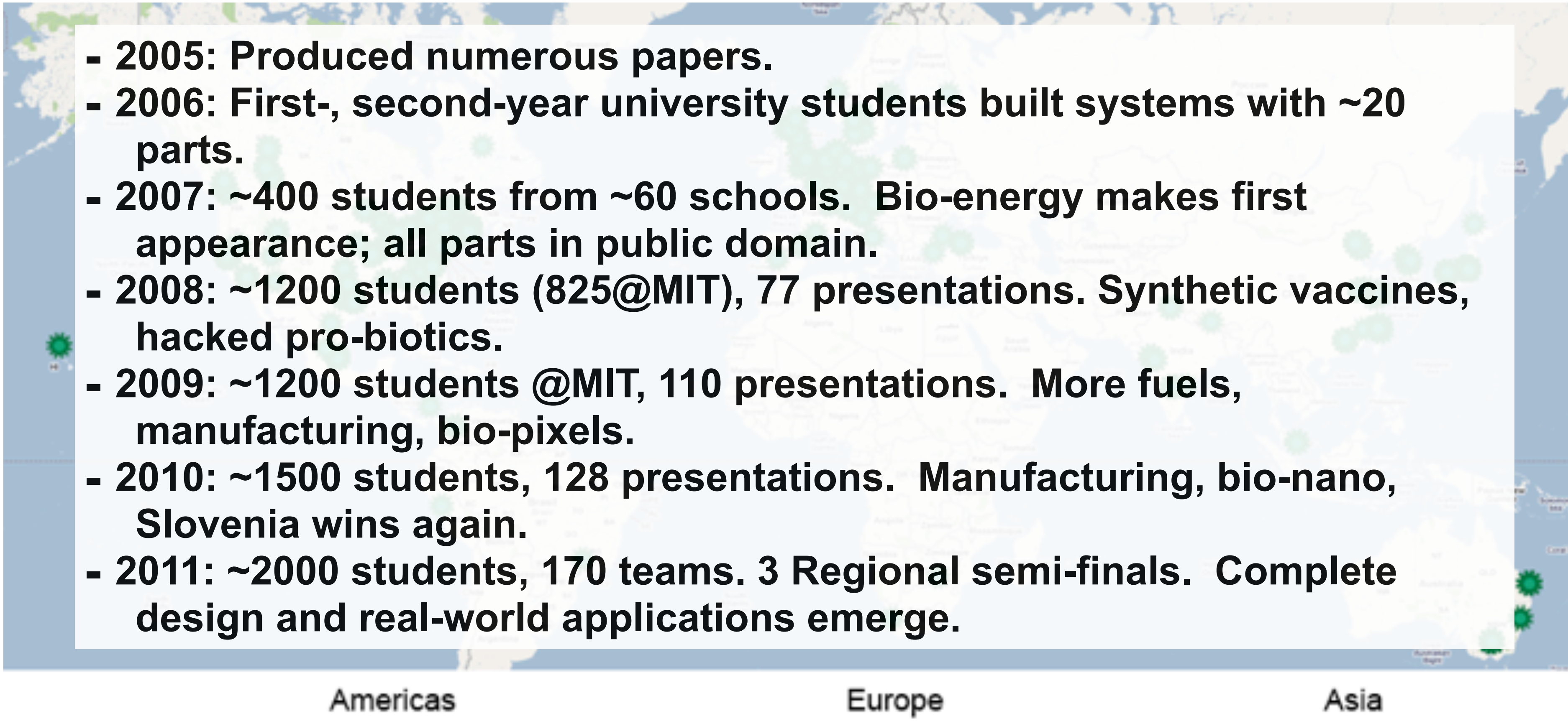
“What we are doing with the synthetic chromosome is going to be the design process of the future.”

J. Craig Venter
New York Times, 24 January 2008.

Synthetic Biology: Geographic Distribution iGEM 2011 Competitors

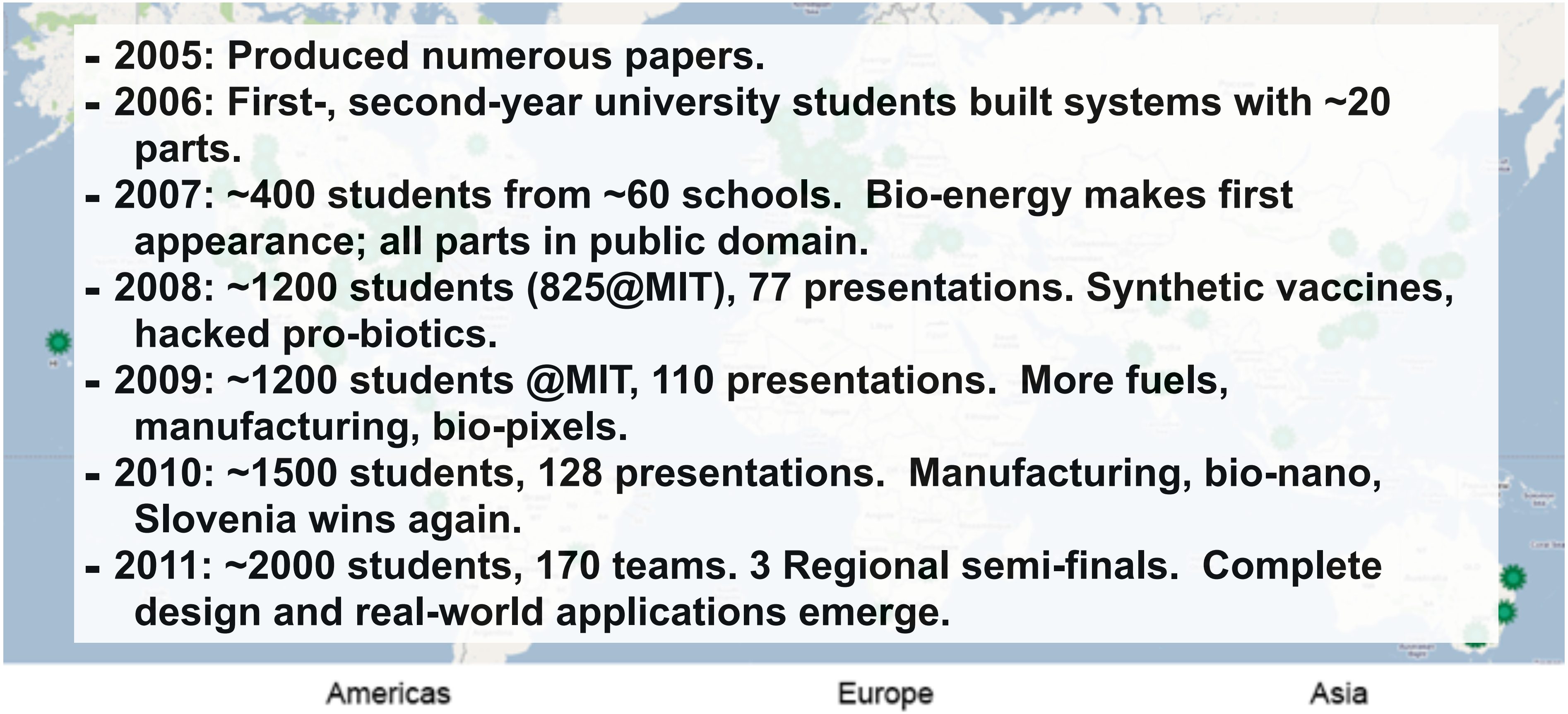
Americas Europe Asia

Synthetic Biology: Geographic Distribution iGEM 2011 Competitors



- 2005: Produced numerous papers.
- 2006: First-, second-year university students built systems with ~20 parts.
- 2007: ~400 students from ~60 schools. Bio-energy makes first appearance; all parts in public domain.
- 2008: ~1200 students (825@MIT), 77 presentations. Synthetic vaccines, hacked pro-biotics.
- 2009: ~1200 students @MIT, 110 presentations. More fuels, manufacturing, bio-pixels.
- 2010: ~1500 students, 128 presentations. Manufacturing, bio-nano, Slovenia wins again.
- 2011: ~2000 students, 170 teams. 3 Regional semi-finals. Complete design and real-world applications emerge.

Synthetic Biology: Geographic Distribution iGEM 2011 Competitors



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- 2011 Grand Prize Winning team from University of Washington used FoldIt to design gluten dehydrogenase that works **~800X better** than an enzyme currently in clinical trials.
- Also demonstrated first even and odd chain alkane synthesis in E. coli; direct diesel synthesis .

Where Should We Look For Innovation?

Examples of Small Organization Inventions: This is Where the Economy Starts

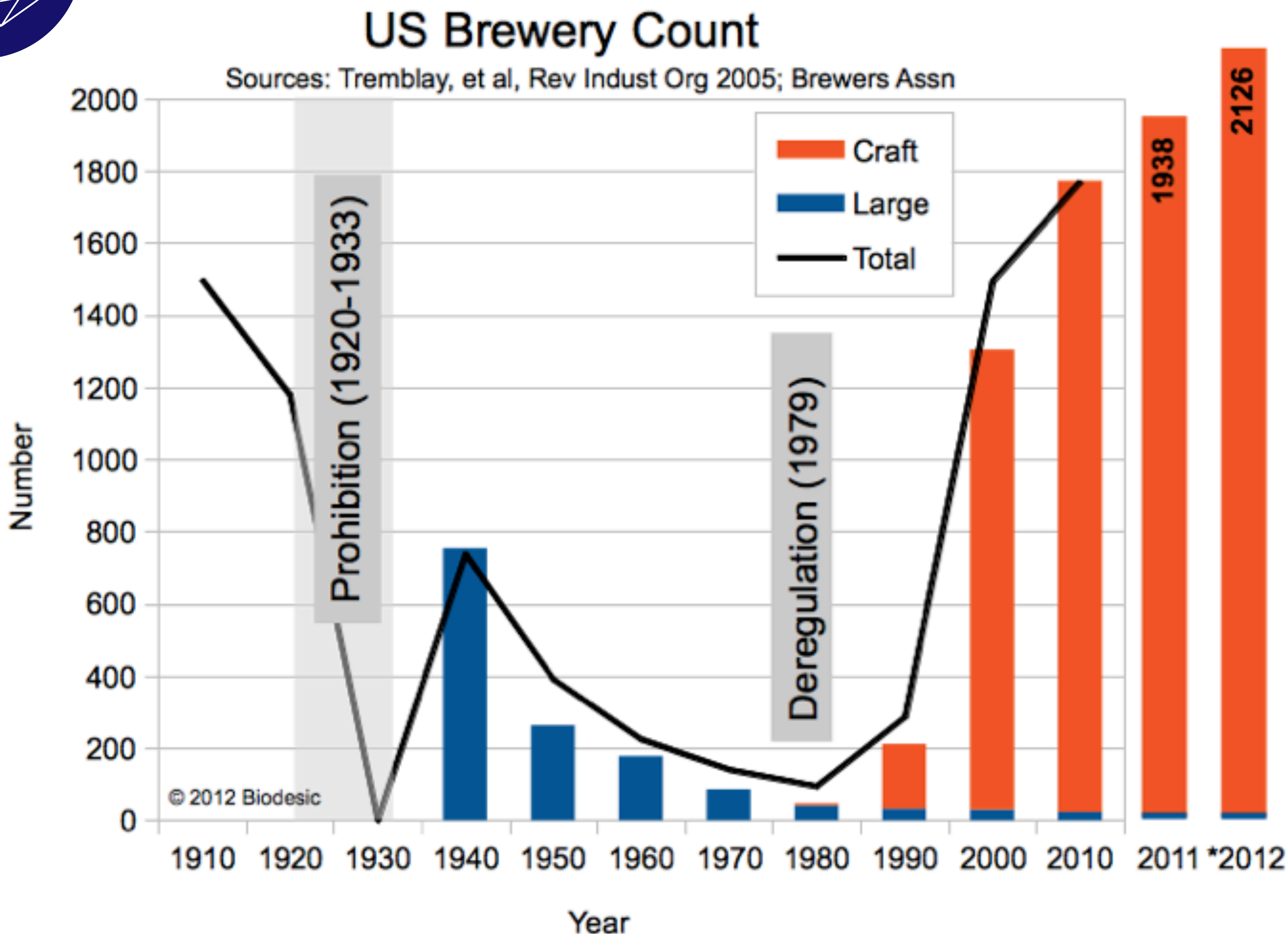
Source: Small Business Administration

- Air Conditioning
- Air Passenger Service
- Airplane
- Articulated Tractor Chassis
- Assembly Line
- Audio Tape Recorder
- Bakelite
- Biomagnetic Imaging
- Biosynthetic Insulin
- Catalytic Petroleum Cracking
- Cellophane
- Artificial Skin
- Computerized Blood Pressure Controller
- Continuous Casting
- Cotton Picker
- Defibrillator
- DNA Fingerprinting
- Double-Knit Fabric
- Electronic Spreadsheet
- Freewing Aircraft
- FM Radio
- Front-End Loader

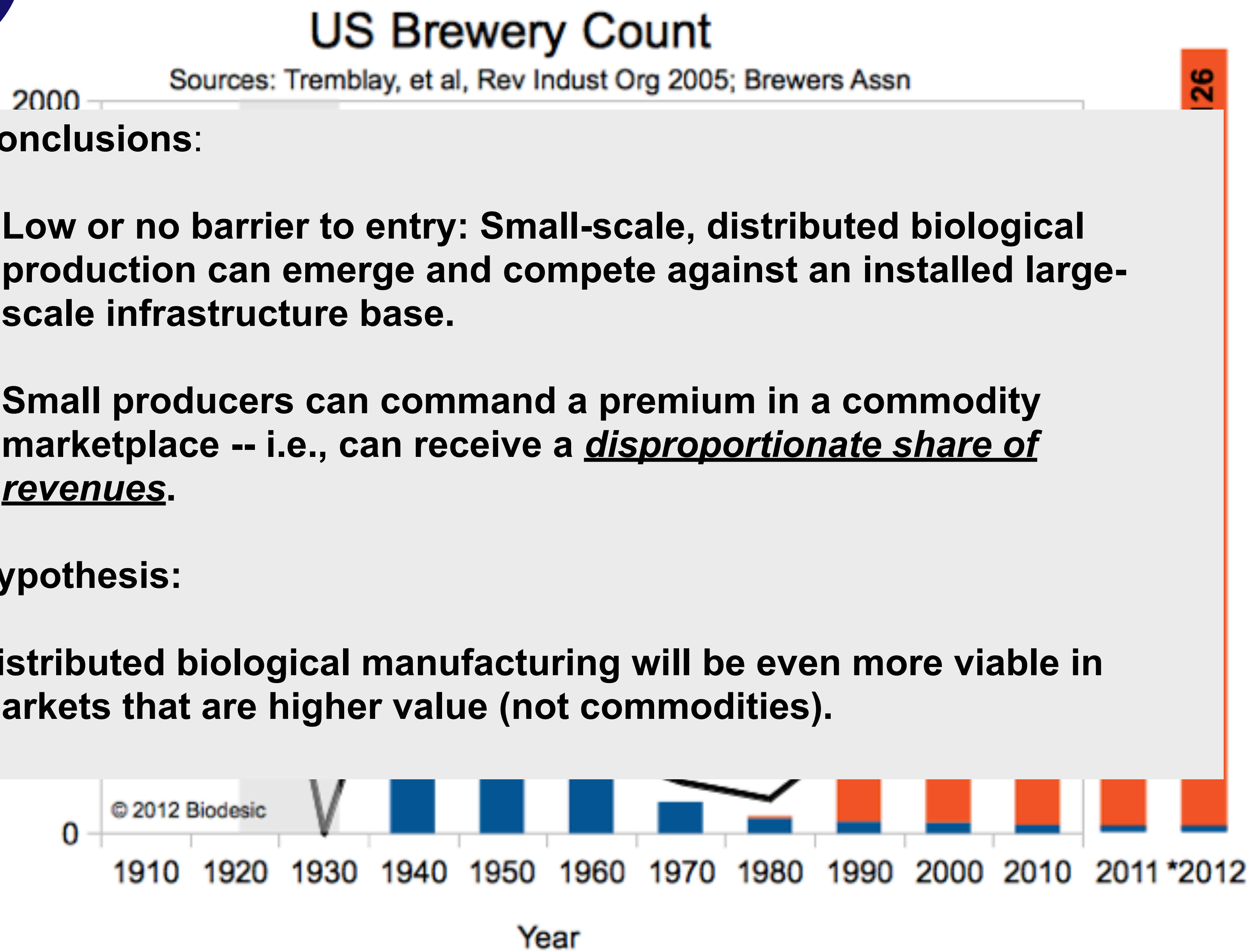
- Geodesic Dome
- Gyrocompass
- Heart Valve
- Heat Sensor
- Helicopter
- High Resolution CAT Scanner
- High Resolution Digital X-Ray
- Human Growth Hormone
- Hydraulic Brake
- Integrated Circuit
- Kidney Stone Laser
- Large Computer
- Link Trainer
- Microprocessor
- Microscope
- NMR Scanner
- Optical Scanner
- Oral Contraceptives
- Outboard Engine
- Overnight National Delivery
- Pacemaker
- Personal Computer
- Photo Typesetting

- Polaroid Camera
- Portable Computer
- Prestressed Concrete
- Prefabricated Housing
- Pressure Sensitive Tape
- Programmable Computer
- Quick-Frozen Food
- Reading Machine
- Rotary Oil Drilling Bit
- Safety Razor
- Six-Axis Robot Arm
- Soft Contact Lens
- Solid Fuel Rocket Engine
- Stereoscopic Map Scanner
- Strain Gauge
- Strobe Lights
- Supercomputer
- Two-Armed Mobile Robot
- Vacuum Tube
- Variable Output Transformer
- Vascular Lesion Laser
- Xerography
- X-Ray
- X-Ray Telescope
- Zipper

Micro-Brewing the Bioeconomy



Micro-Brewing the Bioeconomy



Conclusions:

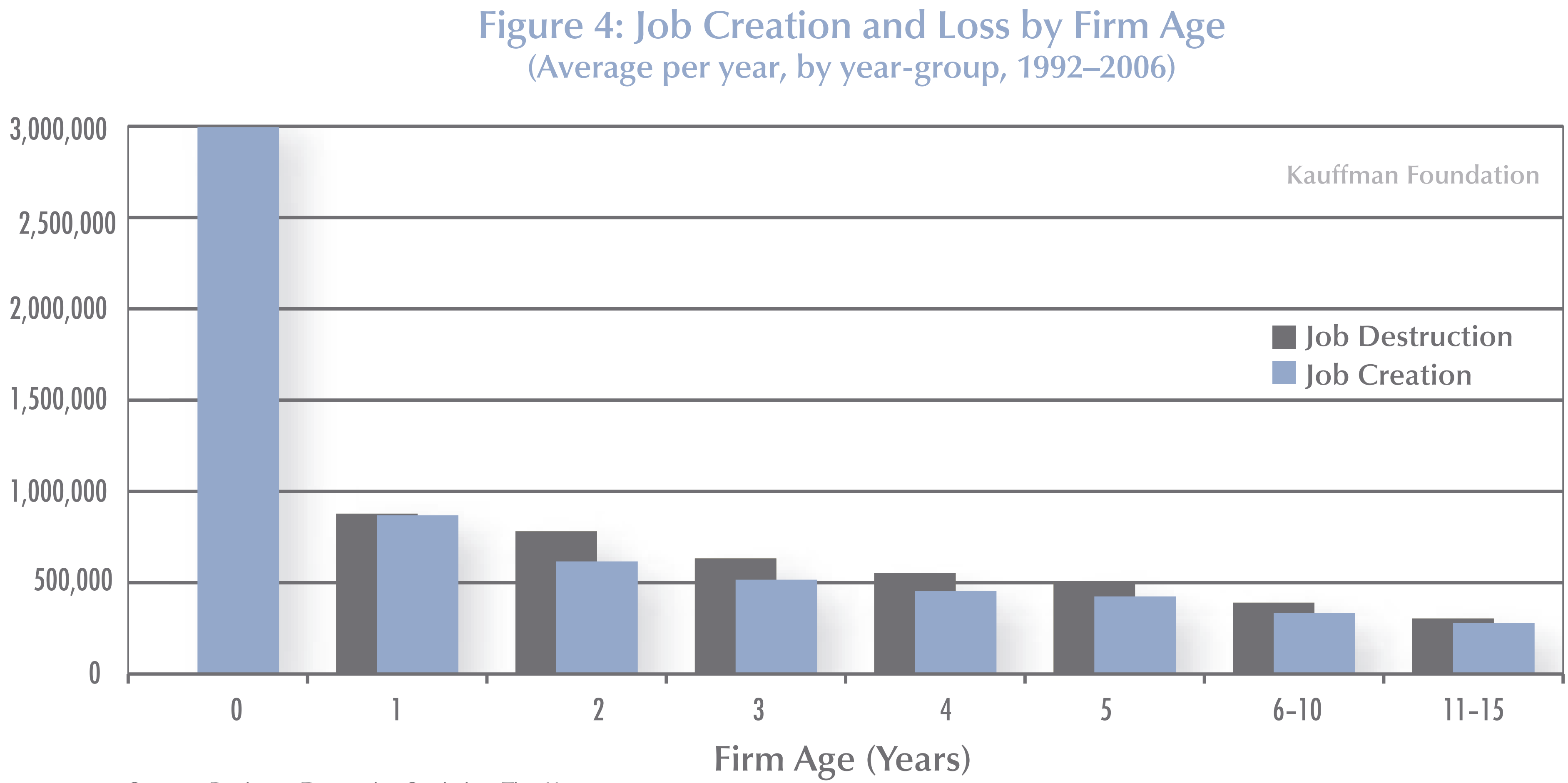
1. **Low or no barrier to entry: Small-scale, distributed biological production can emerge and compete against an installed large-scale infrastructure base.**

2. **Small producers can command a premium in a commodity marketplace -- i.e., can receive a *<u>disproportionate share of revenues</u>*.**

Hypothesis:

Distributed biological manufacturing will be even more viable in markets that are higher value (not commodities).

Start-Ups Are Responsible for 100% of Net U.S. Job Creation



Source: Business Dynamics Statistics, Tim Kane

(Synthetic) Biology@Home

WIRED MAGAZINE

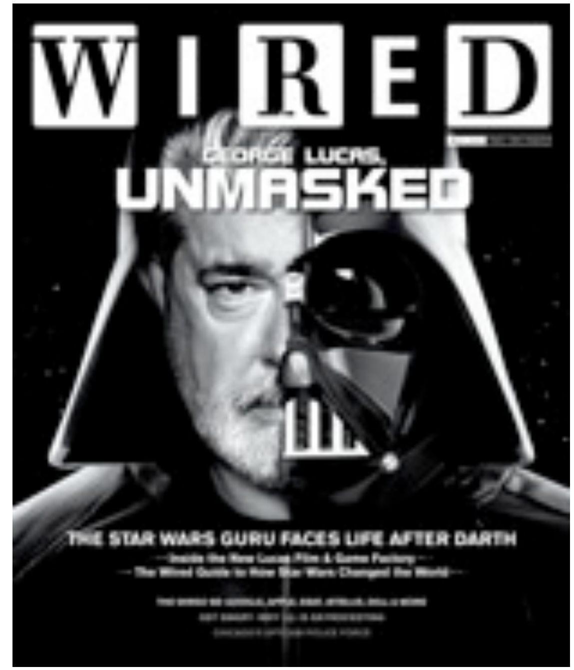
Issue 13.05 - May 2005

Splice It Yourself

Who needs a geneticist? Build your own DNA lab

By Rob Carlson

The era of garage biology is upon us. Want to participate? Take a moment to buy yourself a molecular biology lab on eBay...



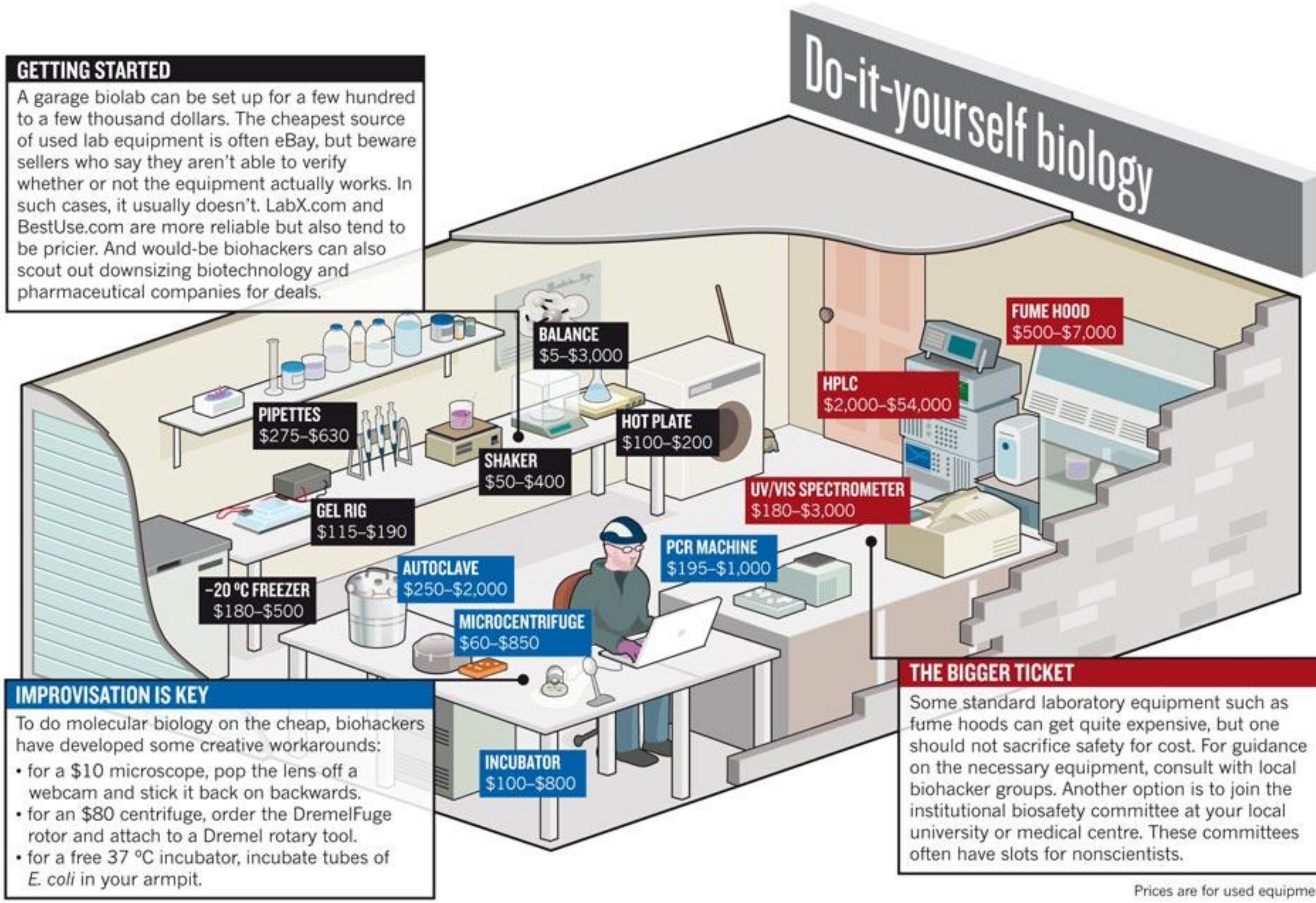
We can think of this as a <u>threat</u>, an <u>opportunity</u>, or even as a <u>*necessity*</u>.

My Garage Lab (c.2005)
(Fashion is Important)

Credit: S.L. Keller

The Sims: Garage Biology

NATURE | VOL 467 | 7 OCTOBER 2010



Garage Biology is Somewhere, Anywhere

Garage lab, undisclosed location, CA (c.2010).
Cell culture and anti-cancer compound screening.

Europe Joins the Garage Bio Party

Cathal Garvey
@onetruecathal

Follow

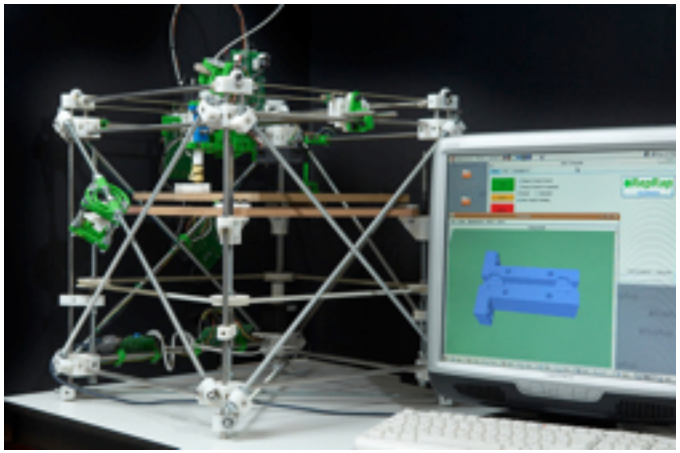
You can grow 20mg of recombinant protein in a 50ml reaction with some effort, overnight. That's $1.1M worth of EcoRI. #what #synbio

4 RETWEETS | **1** FAVORITE

6:55 AM - 28 Feb 12 via Hotot · Embed this Tweet

Reply Retweet Favorite

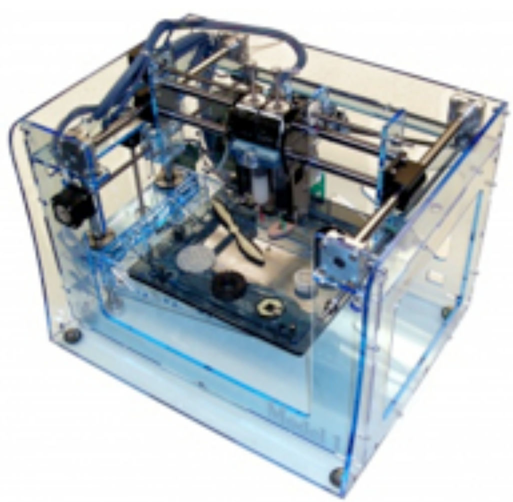
Distributed Innovation: "Innovation has gone public" - Bruce Perens



RepRap

http://ng.cba.mit.edu/dist/fab.pdf

Fab Lab



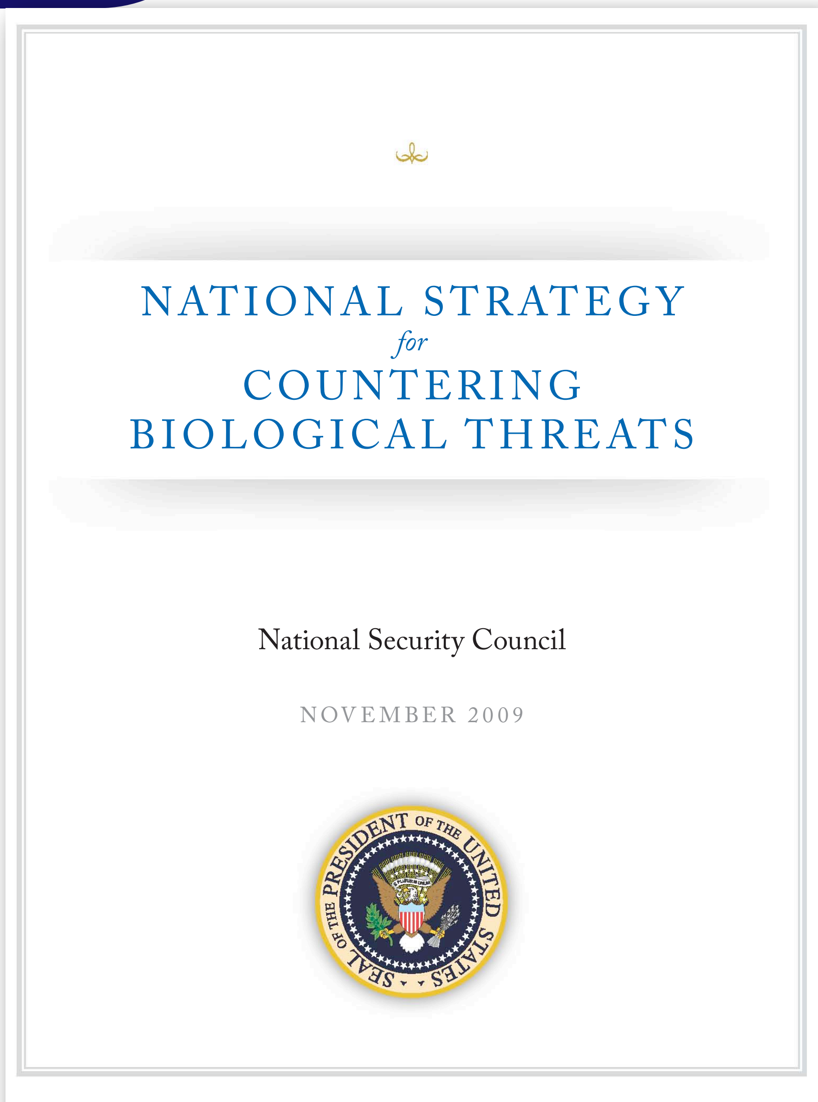
Fab@Home

Objet **Alaris™30**

Graphtec CE5000

What About Safety and Security?

President of the United States: "Garage biology is good."


NATIONAL STRATEGY
for
COUNTERING
BIOLOGICAL THREATS

National Security Council

NOVEMBER 2009

"The beneficial nature of life science research is reflected in the widespread manner in which it occurs. From cutting-edge academic institutes, to industrial research centers, **to private laboratories in basements and garages, progress is increasingly driven by innovation and open access to the insights and materials needed to advance individual initiatives."**

Unexpected Impacts of Policy on Proliferation

Cocaine:

http://blog.wired.com/27bstroke6/2009/01/new-law-harpoon.html

Restricting access to commodities can create dedicated technology development efforts to meet supply:

- ➡ "Narco-subs"
  - Cost of Construction:$.5-2 million.
  - Cargo: ~$1 billion in cocaine.
  - Now moved on to <u>fully submersible</u>

Meth:

"…<u>Marked success in decreasing domestic</u> methamphetamine production through law enforcement pressure and strong precursor chemical sales restrictions <u>has enabled Mexican DTOs to rapidly expand their control</u> over methamphetamine distribution."

http://www.usdoj.gov/dea/concern/18862/meth.htm

<u>Increased enforcement efforts have created a larger, blacker market</u> that is *"[M]ore difficult for local law enforcement agencies to identify, investigate, and dismantle because [it is] typically much more organized and experienced than local independent producers and distributors."*

"Methamphetamine Strategic Findings": http://www.usdoj.gov/dea/concern/18862

Safety in the stalls of Akihabara: Maximize Knowledge, Skills, Awareness

Reading and Thanks

Biology is Technology:

The Promise, Peril, and New Business of Engineering Life

Robert Carlson

Harvard University Press, 2010.

PROSE Award for Best Engineering and Technology Book of 2010

Best Books of 2010, *The Economist*

Best Books of 2010, *Foreign Policy*

Thanks to: Rik Wehbring, James Newcomb, Stephen Aldrich, Jay Keasling, Drew Endy, Roger Brent, Sydney Brenner, Freeman Dyson, Stewart Brand, Kevin Kelly, John Mulligan, Richard Danzig, Dave Franz, Sarah Keller and Pascale Carlson.

Fin