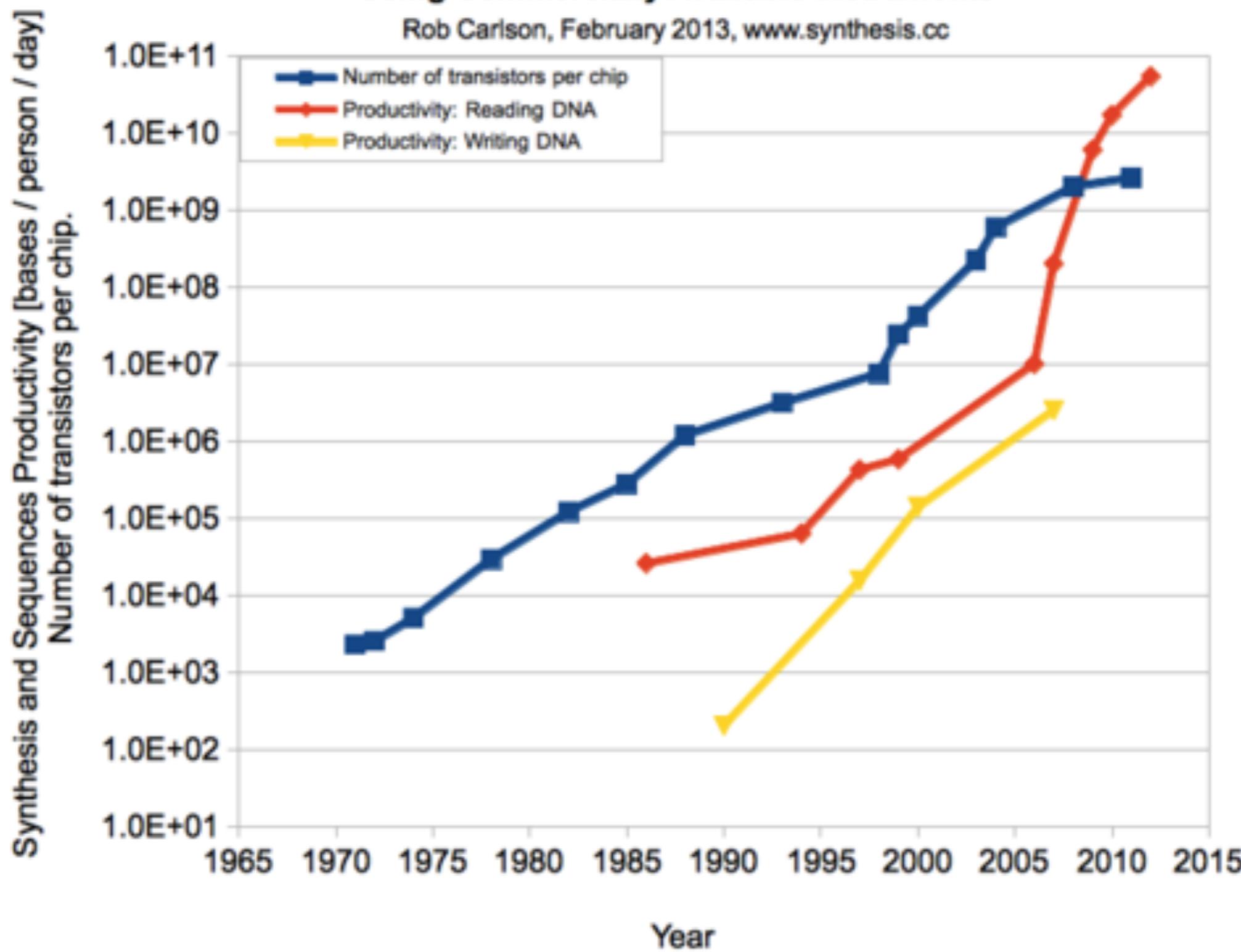


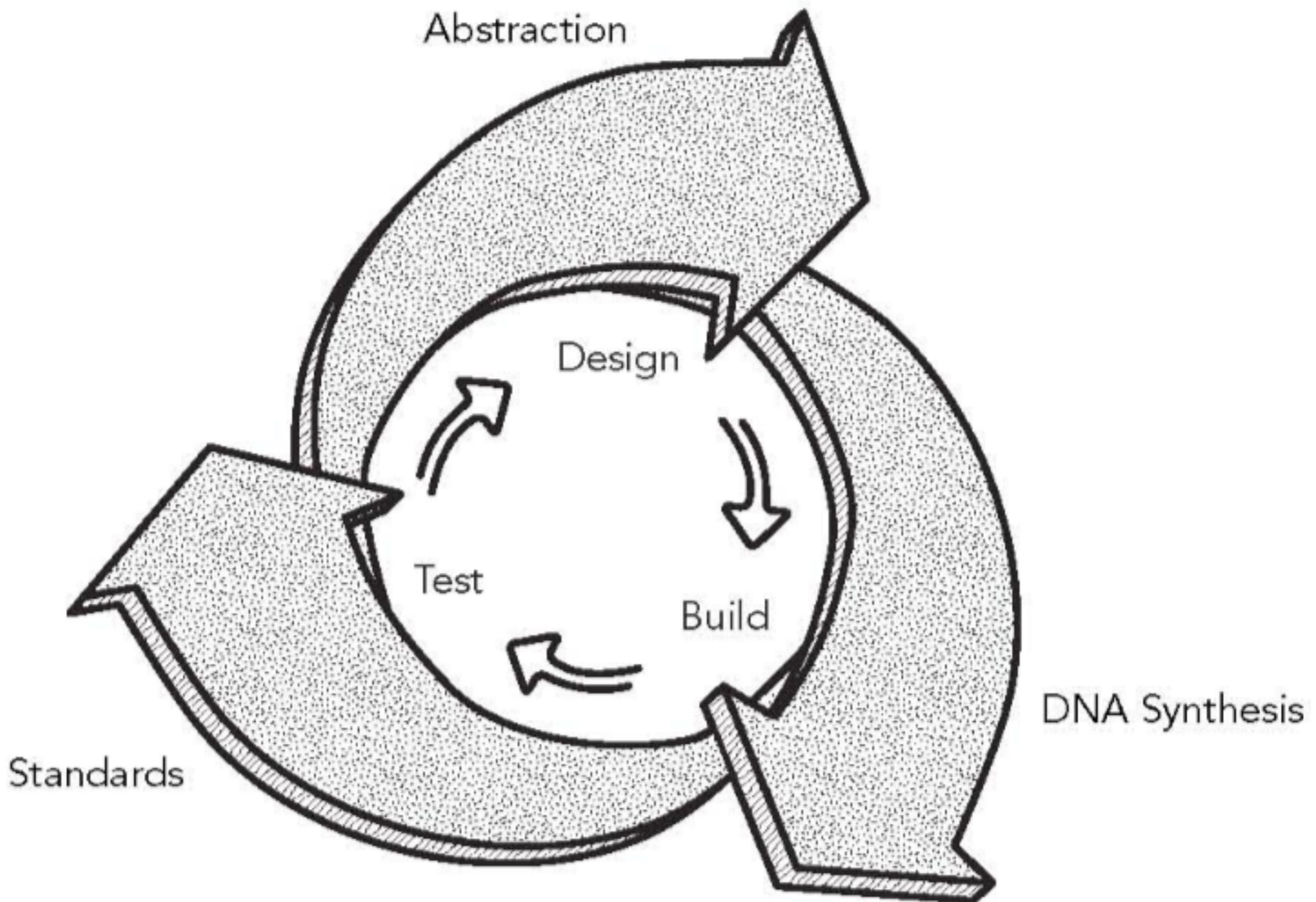
Productivity in DNA Synthesis and Sequencing Using Commercially Available Instruments

Rob Carlson, February 2013, www.synthesis.cc



<https://synbiobeta.com/time-new-dna-synthesis-sequencing-cost-curves-rob-carlson/>

https://en.wikipedia.org/wiki/Carlson_curve



Graphic from "Synthetic Aesthetics" MIT Press (2014)

Bioengineers should...

Cure diseases.

Save environments.

Understand & fix broken
biological systems.

Design & build useful organisms.

Make doing the above easier.



Il retourne chez les Egaux.
Voyez la Note 13. p. 259.

DISCOURS

SUR L'ORIGINE ET LES FONDEMENS
DE L'INÉGALITÉ PARMI LES HOMMES.

Par JEAN JAQUES ROUSSEAU
CITOTEN DE GENÈVE.

Non in depravatis, sed in his quæ bene secundum
naturam se habent, considerandum est quid sit na-
turale. ARISTOT. Politic. L. 2.



A AMSTERDAM,
Chez MARC MICHEL REY.

16° R M D C C L V.

6917

(P)

"The two fundamental principles of Rousseau's natural man are his natural, non-destructive love of self (amour de soi même), and pity/compassion for the suffering of others."

Bioengineers will inevitably or inadvertently..

Create diseases.

Destroy environments.

Misunderstand & abuse natural
biology & ecology.

Design & build harmful organisms.

Make doing the above easier.



“Hereby it is manifest that during the time men live without a common Power to keep them all in awe, they are in that condition which is called War; and such a war as is of every man against every man.

[...]

In such condition there is no place for Industry, because the fruit thereof is uncertain: and consequently no Culture of the Earth; no Navigation, nor use of the commodities that may be imported by Sea; no commodious Building; no Instruments of moving and removing such things as require much force; no Knowledge of the face of the Earth; no account of Time; no Arts; no Letters; no Society; and which is worst of all, continual Fear, and danger of violent death;

And the life of man solitary, poor, nasty, brutish, and short.”

— Hobbes, Leviathan

GOOGLE'S ORIGINAL X-MAN: A TALK WITH SEBASTIAN THRUN

FOREIGN AFFAIRS

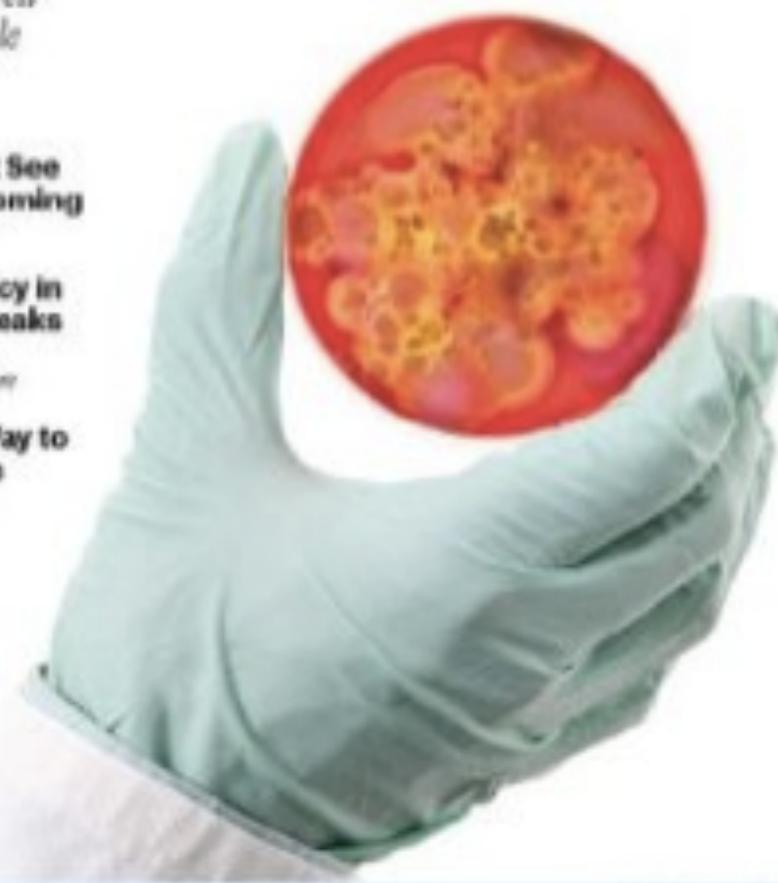
Biology's Brave New World Be Happy—and Worry

Laurie Garrett
Ronald Noble

Why I Didn't See
the Crisis Coming
Alan Greenspan

Foreign Policy in
the Age of Leaks
*Illiby Farrel &
Martha Finegan*

The Right Way to
Cut Defense
*Candy Williams
Malena Lefler*



FOREIGNAFFAIRS.COM

"In the new biology world, scientists can now create life themselves and learn about it from the inside," writes Garrett, CFR senior fellow for global health, in the cover story of the November/December issue.

She explains the scientific breakthroughs that have led to a revolution in synthetic biology. It is now possible to manufacture living organisms, including viruses and bacteria not yet seen in nature. Moreover, Garrett writes, such synthetic organisms can self-assemble and self-replicate, a process called 4-D printing.

"What begins as a human idea, hammered out intellectually on a computer, is then sent to a 3-D printer, resulting in a creation capable of making copies of and transforming itself."

Synthetic biology creates a "dual-use dilemma": it is a boon to both terrorists and scientists. "What all this means is that the dual-use dilemma that first hit chemistry a century ago, and then hit physics a generation later, is now emerging with special force in contemporary biology."

Are pathogen sequences online?

Should they be?

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OP-ED CONTRIBUTORS

Recipe for Destruction

By RAY KURZWEIL and BILL JOY

Published: October 17, 2005

AFTER a decade of painstaking research, federal and university scientists have reconstructed the 1918 influenza virus that killed 50 million people worldwide. Like the flu viruses now raising alarm bells in Asia, the 1918 virus was a bird flu that jumped directly to humans, the scientists reported. To shed light on how the virus evolved, the United States Department of Health and Human Services published the full genome of the 1918 influenza virus on the Internet in the GenBank database.



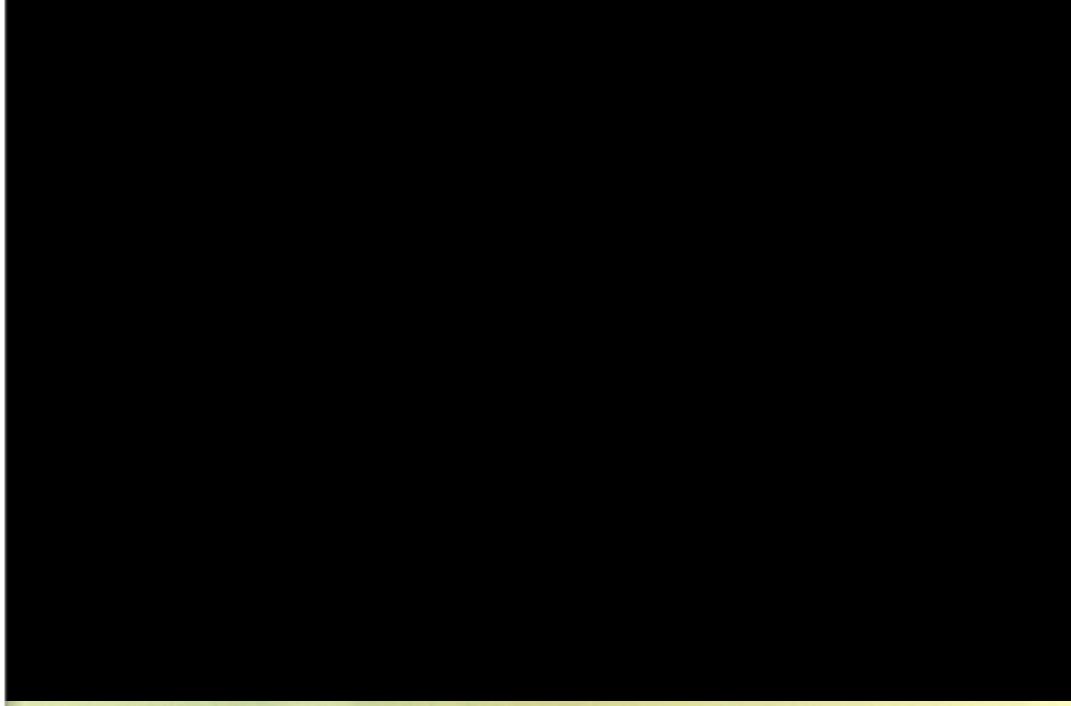
This is extremely foolish. The genome is essentially the design of a weapon of mass destruction. No responsible scientist would advocate publishing precise designs for an atomic bomb, and in two ways revealing the sequence for the flu virus is even more dangerous.

First, it would be easier to create and release this highly destructive virus from the genetic data than it would be to build and detonate an atomic bomb given only its design, as you don't need rare raw materials like plutonium or enriched

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ARTICLE TOOLS

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I THINK
I LOVE MY WIFE**1918 Flu and Responsible Science**

The influenza pandemic of 1918 is estimated to have caused 50 million deaths worldwide; 675,000 in the United States. The reconstruction of the 1918 virus by the synthesis of all eight subunits and the generation of infectious virus are described on p. 77 of this issue,* and the sequences of the final three gene segments of the virus are described in a concurrent *Nature* paper.† Predictably, but alarmingly, this virus is more lethal to mice than are other influenza strains, suggesting that this property of the 1918 virus has been recovered in the published sequence. The good news is that we now have the sequence of this virus, perhaps permitting the development of new therapies and vaccines to protect against another such pandemic. The concern is that a terrorist group or a careless investigator could convert this new knowledge into another pandemic.

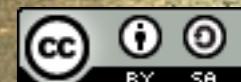
Should the sequence of the 1918 virus have been published, given its potential use by terrorists? The dual-use nature of biological information has been debated widely since September 11, 2001. In 2003, a committee of the U.S. National Academies chaired by Gerald Fink considered this issue, weighing the benefits against the risks of restricting the publication of such biological information. They outlined the tradeoff between erring on the side of prudence, thus potentially hindering the progress of critical science, and erring on the side of disclosure, thus potentially aiding terrorists. The U.S. National Science Advisory Board for Biosecurity (NSABB) was established to advise governmental agencies and the scientific community on policies relative to public disclosure. This board has begun to deliberate, but the questions are complex, as typified by these papers on the 1918 virus. It is reassuring that the NSABB was asked to consider these papers before publication and concluded that the scientific benefit of the future use of this information far outweighs the potential risk of misuse. People may be reassured that the system is working, because agencies representing the public, the scientific community, and the publishing journals were involved in the decision.

We firmly believe that allowing the publication of this information was the correct decision in terms of both national security and public health. It is impossible to forecast how scientific observations might stimulate others to create new treatments or procedures to control future pandemics. For example, in the *Nature* article, sequence comparisons suggest that the 1918 virus was generated not by incremental changes in the polymerase genes, but by the movement of these genes, in total, from an avian source into a human influenza virus. The availability of these sequences will permit identification of their avian origin and should show why this particular set of genes was selected. Similarly, the results in the *Science* article suggest that the cleavage of a protein on the surface of the 1918 virus, a step critical for virulent infection, may occur by a previously unknown mechanism—a hint that could lead to new drugs for inhibiting this step and thus preventing future pandemic eruptions.

Influenza is highly infectious, and a new strain could spread around the world in a matter of months, if not weeks. The public needs confidence that the 1918 virus will not escape from research labs. All of the described experiments were done in a Biosafety Level 3 laboratory, a high-containment environment recommended by the U.S. Centers for Disease Control and Prevention and the National Institutes of Health on an interim basis, whose use should become a permanent requirement for such experiments. Current evidence suggests that some available drugs and possible future vaccines could suppress infections by the 1918 virus. Given the prospect of another natural influenza pandemic, the recent decision by the U.S. administration to stockpile antivirals for influenza treatment seems wise. Finally, although a sequence of the 1918 virus has been determined and is highly virulent in mice, this may not be the specific form of the virus that caused the pandemic of 1918. An article in the same issue of *Nature*‡ reports the existence of sequence variation in a natural population of influenza virus; yet we have only one sequence for the 1918 pandemic strain, and the reconstructed virus described in the *Science* article was built into the backbone of a laboratory strain. Because a pandemic infection is dependent on many unknown properties, there is no certainty that the reconstructed 1918 virus is capable of causing a pandemic.

Phillip A. Sharp

Philip A. Sharp is Institute Professor at the Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA.



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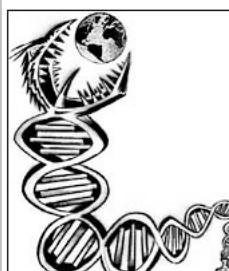
OP-ED CONTRIBUTORS

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VACCINES

Synthetic Generation of Influenza Vaccine Viruses for Rapid Response to Pandemics

Philip R. Dormitzer,^{1*} Pirada Supaphiphat,¹ Daniel G. Gibson,^{2,3,4} David E. Wentworth,² Timothy B. Stockwell,² Mikkel A. Algire,² Nina Alperovich,² Mario Barro,⁵ David M. Brown,² Stewart Craig,¹ Brian M. Dattilo,⁵ Evgeniya A. Denisova,² Ivna De Souza,¹ Markus Eickmann,⁶ Vivien G. Dugan,^{2†} Annette Ferrari,¹ Raul C. Gomila,^{1,7} Liqun Han,¹ Casey Judge,¹ Sarthak Mane,¹ Mikhail Matrosovich,⁶ Chuck Merryman,³ Giuseppe Palladino,¹ Gene A. Palmer,¹ Terika Spencer,^{1,8} Thomas Strecker,⁶ Heidi Trusheim,⁸ Jennifer Uhlandorff,⁶ Yingxia Wen,¹ Anthony C. Yee,² Jayshree Zaveri,² Bin Zhou,² Stephan Becker,⁶ Armen Donabedian,⁵ Peter W. Mason,¹ John I. Glass,² Rino Rappuoli,^{1,7} J. Craig Venter,^{2,3,4}

During the 2009 H1N1 influenza pandemic, vaccines for the virus became available in large quantities only after the virus had already spread across the globe. Synthetic influenza vaccine viruses could be generated rapidly in response to a new strain.

Virus Attenuation by Genome-Scale Changes in Codon Pair Bias

J. Robert Coleman,¹ Dimitris Papamichail,^{2,*} Steven Skiena,² Bruce Futcher,¹ Eckard Wimmer,^{1,†} Steffen Mueller¹

As a society, we must encode pair bias into our statistical understanding of the underlying contact patterns. This "kinds

DNA synthesis and biological security

Hans Bügl, John P. Danner, Robert J. Molinari, John T. Mulligan, Han-Oh Park, Bas Reichert, David A. Roth, Ralf Wagner, Bruce Budowle, Robert M. Scripp, Jenifer A. L. Smith, Scott J. Steele, George Church & Drew Endy

A group of academics, industry executives and security experts propose an oversight framework to address concerns over the security of research involving commercial DNA synthesis.

DNA synthesis allows the direct construction of genetic material starting from information and tools available on the Internet. This technology is accelerating innovation across many areas of research, from the development of renewable energy to the production of fine chemicals, from information processing to environmental monitoring, and from agricultural genetics to the design of pharmaceuticals and medicine. Like any powerful technology, DNA synthesis has the potential to be purposefully misappropriated. Misuse of DNA-synthesis technology could give rise to both known and unforeseen threats to our biological safety and security. Current government oversight of the use of synthetic biology falls short of addressing this unfortunate reality.

Here, we outline a practical plan for developing an effective oversight framework for the DNA-synthesis industry¹. The resulting framework serves three purposes. First, it provides a blueprint for international cooperation. It encourages the further responsible development of synthetic biology technologies and their continued, overwhelmingly constructive

application. And third, it is designed to be international in scope. Our plan is informed by the experience of the international security issues associated with DNA-synthesis technology^{2–6}, and represents the collective views of all founding members of the

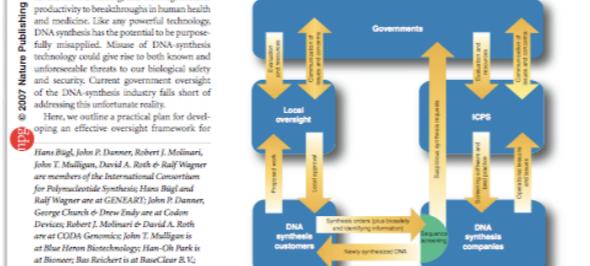


Figure 1. Our framework calls for the immediate and systematic implementation of a tiered DNA synthesis oversight process. To promote and establish accountability, individuals who place orders for DNA synthesis must provide relevant information about their work and the relevant biosafety information. Next, individual companies would use validated software tools to check synthesis orders against a set of agent or sequences to help ensure regulatory compliance and flag synthesis orders for further review. Finally, DNA synthesis and synthetic biology companies would work with the International Consortium for Polymers (ICPS) to develop a system capable of rapidly and continuously improve the underlying technologies used to screen orders and identify potentially dangerous sequences, as well as develop a clearly defined process to report behavior that falls outside of agreed-upon guidelines. ICPS, International Consortium for Polymers.

NATURE BIOTECHNOLOGY, VOLUME 25, NUMBER 6, JUNE 2007

627 © 2007 Nature Publishing Group http://www.nature.com/nature/biosafety

1918 Flu and Responsible Science

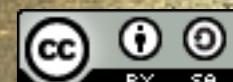
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Phillip A. Sharp



OK. All good, right?

No one will make a pathogen from scratch and cause harm...

Who would ever do such a thing?

RESEARCH ARTICLE

Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments

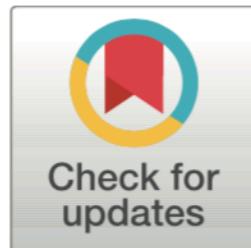
Ryan S. Noyce¹, Seth Lederman², David H. Evans^{1*}

1 Department of Medical Microbiology & Immunology and Li Ka Shing Institute of Virology, University of Alberta, Edmonton, Alberta, Canada, **2** Tonix Pharmaceuticals, Inc., New York, New York, United States of America

* devans@ualberta.ca

Abstract

Edward Jenner and his contemporaries believed that his *variolae vaccinae* originated in horses and molecular analyses show that modern vaccinia virus (VACV) strains share common ancestry with horsepox virus (HPXV). Given concerns relating to the toxicity of modern VACV vaccines, we asked whether an HPXV-based vaccine might provide a superior alternative. Since HPXV may be extinct and the only specimen of HPXV that has been identified is unavailable for investigation, we explored whether HPXV could be obtained by large-scale gene synthesis. Ten large (10–30 kb) fragments of DNA were synthesized based on the HPXV sequence along with two 157 nt VACV terminal sequences, and were recombined into a live synthetic chimeric HPXV (scHPXV) in cells infected with Shope fibroma virus (SFV). Sequencing of the 212 kbp scHPXV confirmed it encoded a faithful copy of the input DNA. We believe this is the first complete synthesis of a poxvirus using synthetic biology approaches. This scHPXV produced smaller plaques, produced less extracellular virus and exhibited less virulence in mice than VACV, but still provided vaccine protection against a lethal VACV challenge. Collectively, these findings support further development of scHPXV as a novel replication-proficient smallpox vaccine.



OPEN ACCESS

Citation: Noyce RS, Lederman S, Evans DH (2018) Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. PLoS ONE 13(1): e0188453. <https://doi.org/10.1371/journal.pone.0188453>

Editor: Volker Thiel, Universitat Bern, SWITZERLAND

Received: September 18, 2017

Accepted: November 7, 2017

Published: January 19, 2018

This paper should not have been published

drelman replied to PLOS_ONE_Group on 19 Jan 2018 at 20:15 GMT

I strongly disagree with the implication that an adequate assessment of the risks and benefits was undertaken, and strongly disagree with the statements made by your DURC committee. This paper should not have been published.

To suggest that poxviruses are no different from influenza or polio, and therefore that the details provided here "provided no new information" [about the synthesis of smallpox], is at best misleading, and better characterized as simply wrong. I could list for you the details provided in this paper that will substantively assist those with lesser degrees of experience to synthesize smallpox. The Committee mentioned compliance with relevant regulations. Which regulations are these, and how are they relevant and specific to this work at the University of Alberta? The so-called 'forthcoming' behavior in communications consisted of a presentation to the WHO Advisory Committee of a 'fait-accompli'. To my knowledge, there was no request for guidance before the work was undertaken. And the alleged benefits from this work simply do not hold water. This work was not needed or particularly helpful towards an improved vaccine.

What I find particularly inappropriate and frankly, unethical is that this paper with its obvious risks to public health was funded by and written by a for-profit, private entity (Tonix) that stands to gain money from this work and this paper. And the authors co-founded and consult for this entity and stand to make money from it. The conflicts of interest are obvious: the public health was put at risk by a private entity and a set of author-business partners who stand to gain financially from this work. This is wrong.

No competing interests declared.



Horsepox synthesis: A case of the unilateralist's curse?

By Gregory Lewis, February 19, 2018

	Horsepox synthesis is good	Horsepox synthesis is bad
Scientists do not synthesize horsepox	<i>All</i> scientists (incorrectly) see horsepox synthesis is bad	<i>All</i> scientists (correctly) see horsepox synthesis is bad
Scientists synthesize horsepox	At least one scientist (correctly) sees horsepox synthesis is good	At least one scientist (<i>incorrectly</i>) sees horsepox synthesis is good

Other factors can exacerbate the threat posed by the unilateralist's curse:

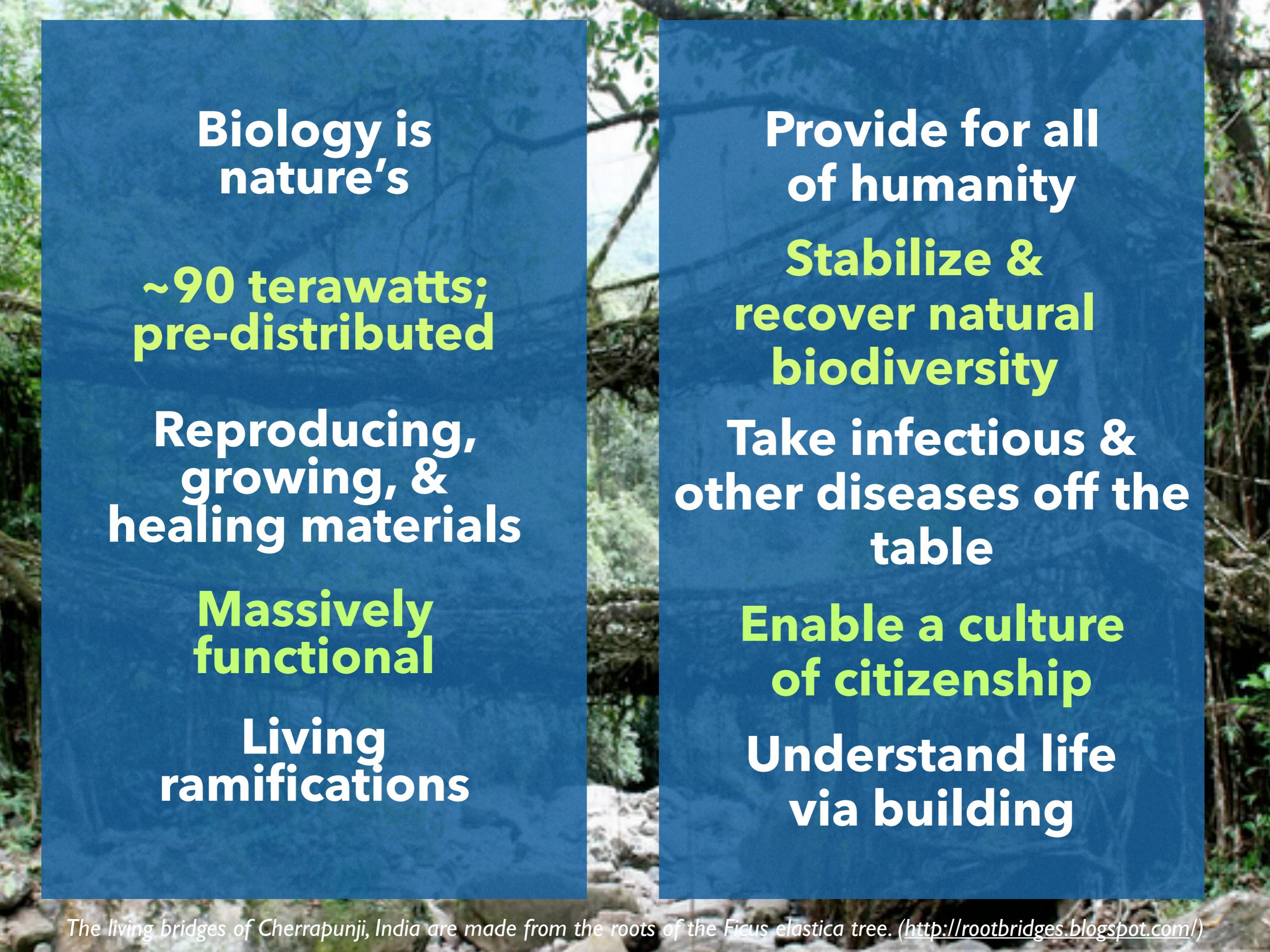
- 1. The number of potential actors who can act unilaterally:** If 10,000 scientists are wondering whether to conduct a piece of concerning research, the chance that one of them will mistakenly think it is a good idea is greater than if there were only 100 scientists (or 10, or one).
- 2. Time:** As time passes, the opportunity for a mistake to be made increases.
- 3. The difficulty of assessing a threat (or individuals' poor ability to assess a threat):** If scientists are more prone to committing errors in judgment where assessing benefit and risk are concerned—either because of the inherent difficulty of assessment, or their own poor ability to conduct accurate assessment—the chances increase that one scientist will greatly underestimate a danger.
- 4. Conflict of interest:** No matter how wide the spectrum of reasonable disagreement over a given piece of concerning research might be, the spectrum of *unreasonable* disagreement is still wider. Scientists may be motivated to pursue potentially dangerous work by the prospect of fame or monetary reward, inducements that may color their judgement about what is best for the common good. (The authors of the horsepox paper are listed as co-inventors on the patent relating to their work, and so stand to gain monetarily from any commercial applications.)
- 5. Tragedy of the commons:** If scientists suspect that another scientist might pursue dangerous work for personal gain, the implicit agreement among them not to perform such work is fragile. Scientists may think, “Well, if *someone* is going to do this work anyway, I might as well be the one who gets the benefit.”

Who should make decisions?

How should decisions be enforced?

Practically, can the right things happen in a networked tech world?

(questions to explore rest of week)



**Biology is
nature's**

**~90 terawatts;
pre-distributed**

**Reproducing,
growing, &
healing materials**

**Massively
functional**

**Living
ramifications**

The living bridges of Cherrapunji, India are made from the roots of the Ficus elastica tree. (<http://rootbridges.blogspot.com/>)

**Provide for all
of humanity**

**Stabilize &
recover natural
biodiversity**

**Take infectious &
other diseases off the
table**

**Enable a culture
of citizenship**

**Understand life
via building**

Keywords: text|lowercase-sort|unsorted
Laboratories
provide
time-sharing
UNIX
SAC | number|

*When the Tao is lost, there is goodness.
When goodness is lost, there is morality.
When morality is lost, there is ritual.
Ritual is the husk of true faith,
the beginning of chaos.*

--- Lao Tzu (Tao Te Ching, #38)

w/ thanks to Tim O'Reilly & Richard Matthews

What is our telos?
What will be our way?
Is “the way” engineerable?