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Biosafety and Public Outreach in Synthetic Biology

synbiosafe

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CI·SYN·BIO

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SynbioSafety EU-China

国家自然科学基金委员会 National Natural Science Foundation of China

FWF Der Wissenschaftsfonds.

Markus Schmidt, IDC,
Biosafety Working Group
DG Sanco, Brussels
18-19th March, 2010

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„What I cannot create, I do not understand“

Richard Feynman

but...

Do I understand what I can create?

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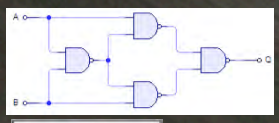
Subfields of contemporary SB

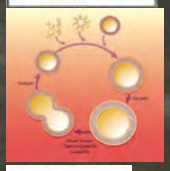
1. DNA Synthesis

2. DNA based bio-circuits

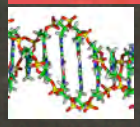


3. Minimal genome

4. Protocells



5. Chemical SB



http://www.synbiosafe.eu/uploads/pdf/Schmidt_etal-2009-SSBJ.pdf

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3 main biosafety challenges

- Can we (still) assess the risks from new SB products, functions and systems?
- How can we improve safety through SB biosafety engineering?
- What happens if non-professionals start using SB?

http://www.synbiosafe.eu/uploads/pdf/Schmidt_etal-2009-SSBJ.pdf

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Case-by-case

	DNA synthesis	DNA-based biocircuits	Minimal genome	Proto-cells	Chemical SB
Risk assessment					
Biosafety engineering					
DIYBio - diffusion					

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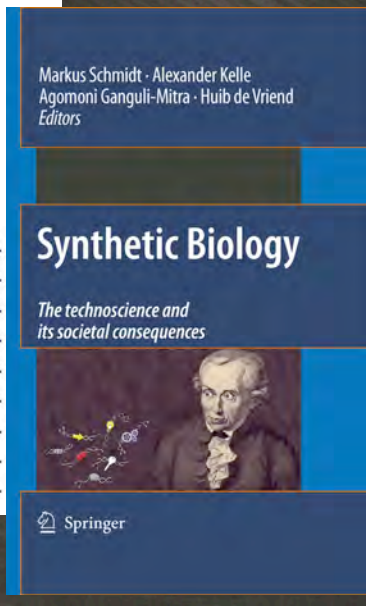
Chapter 6
Do I Understand What I Can Create?

Biosafety Issues in Synthetic Biology

Markus Schmidt

Contents



http://www.springer.com/biomed/book/978-90-481-2677-4

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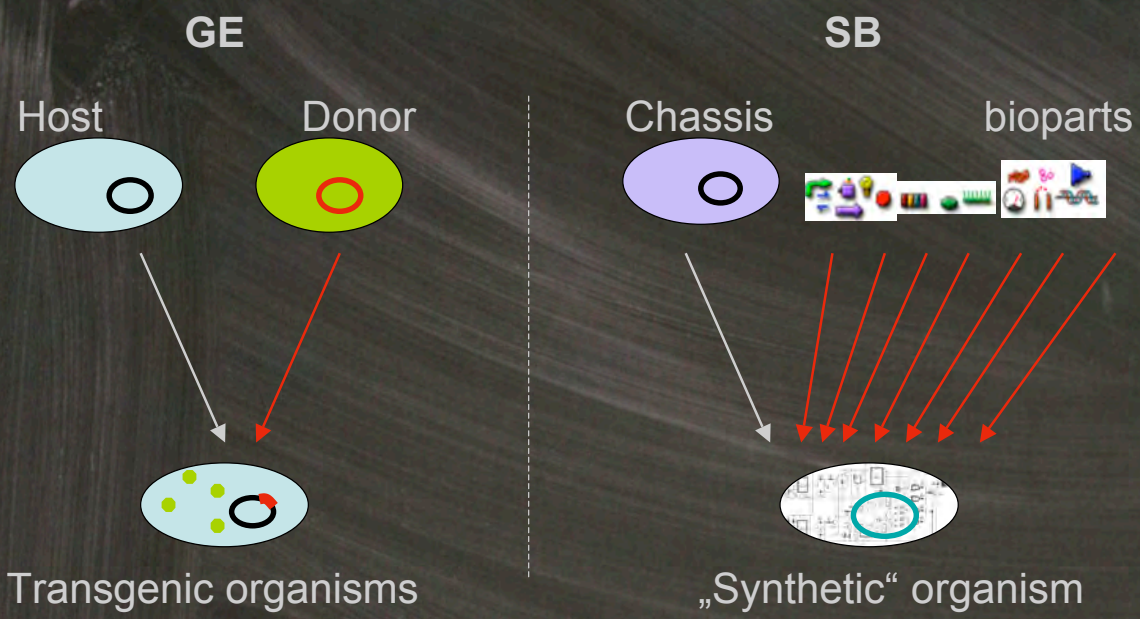
Risk assessment



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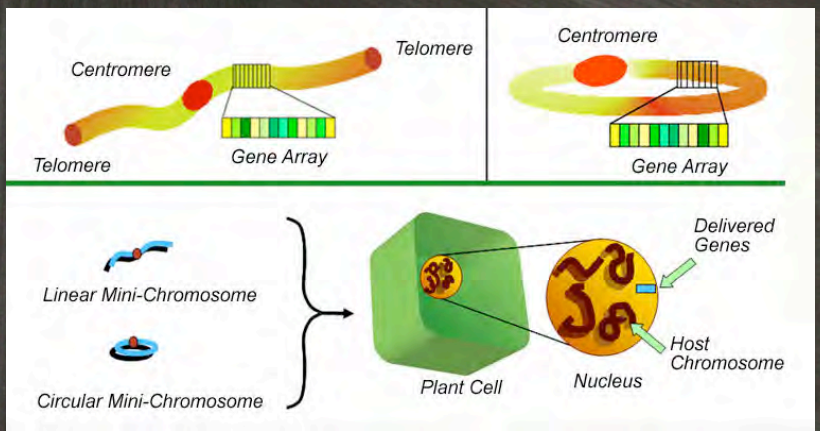
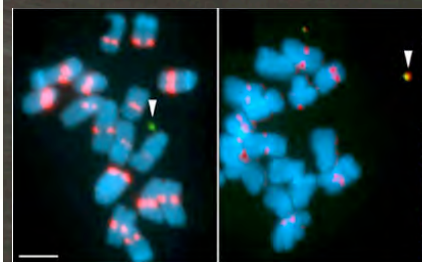
Mini-chromosomes in crop plants

- Chromatin Inc. developed a mini-chromosome
- Has centromer and telomer, up to 200kbp
- In corn and sugarcane
- Licensed to Bayer CropScience and Syngenta





www.chromatininc.com

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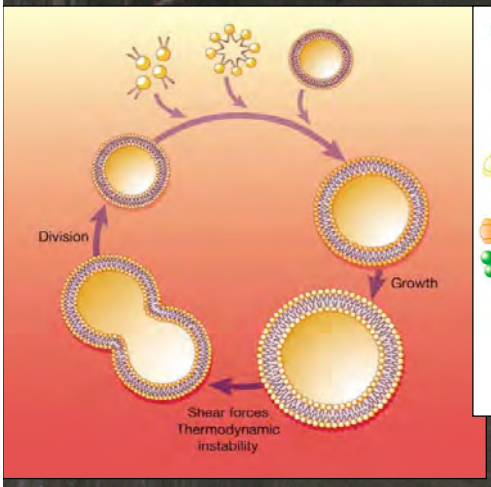
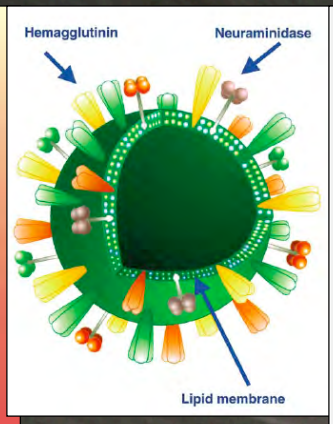
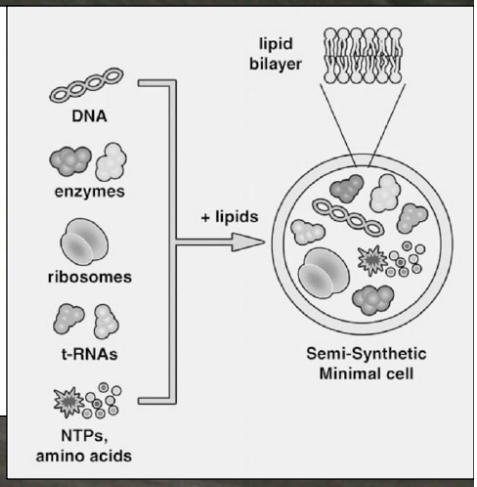
Protocells: life from the bottom up





Virosome



Liposome, made from phospholipids, grows and divides.

Semi-synthetic cell

Szostak et al. 2001, Nature Zurbriggen 2003. Vaccine Chiarabelli et al. 2009 Curr Opinion Biotech

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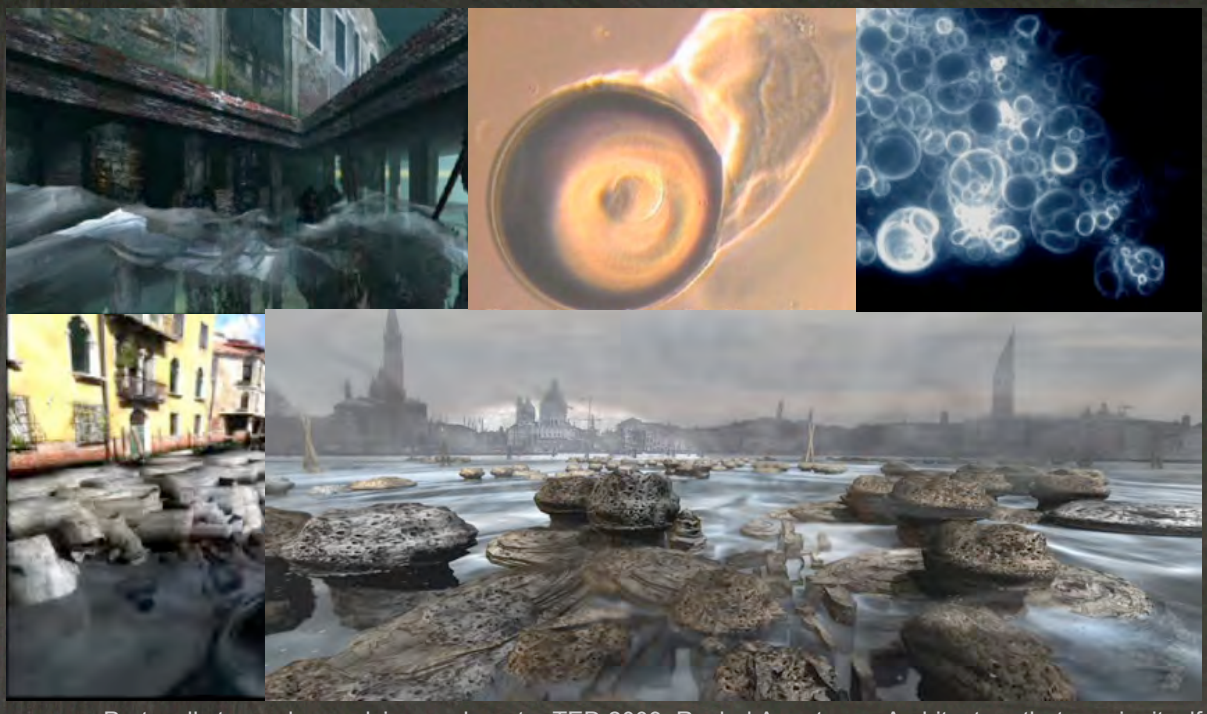
Artificial reefs under Venice



Protocells to produce calcium carbonate: TED 2009. Rachel Armstrong: Architecture that repairs itself

Syst Synth Biol (2009) 3:65–75
DOI 10.1007/s11693-009-9039-2

RESEARCH ARTICLE

Social and ethical checkpoints for bottom-up synthetic biology, or protocells

Mark A. Bedau · Emily C. Parke · Uwe Tangen · Brigitte Hantsche-Tangen

Critical Reviews in Toxicology, 38:1–11, 2008

ISSN: 1040-8444 print / 1547-6898 online
DOI: 10.1080/10408440701524519

informa
healthcare

Lipid Vesicles as Membrane Models for Toxicological Assessment of Xenobiotics

Helmut H. Zepik and Peter Walde
Department of Materials, ETH Zürich, Zürich, Switzerland
Elisabet L. Kostoryz, Jim Code, and David M. You
University of Missouri, Kansas City, Missouri, USA

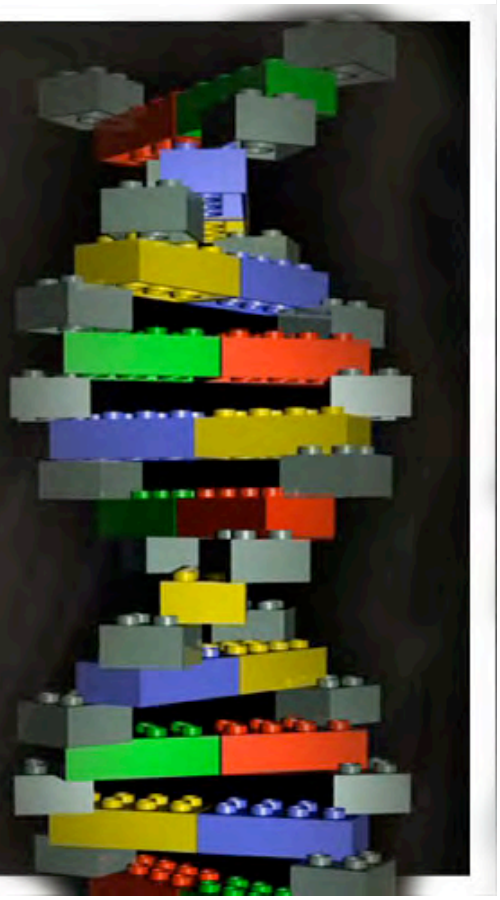
RECENT ADVANCES WITH LIPOSOMES AS PHARMACEUTICAL CARRIERS

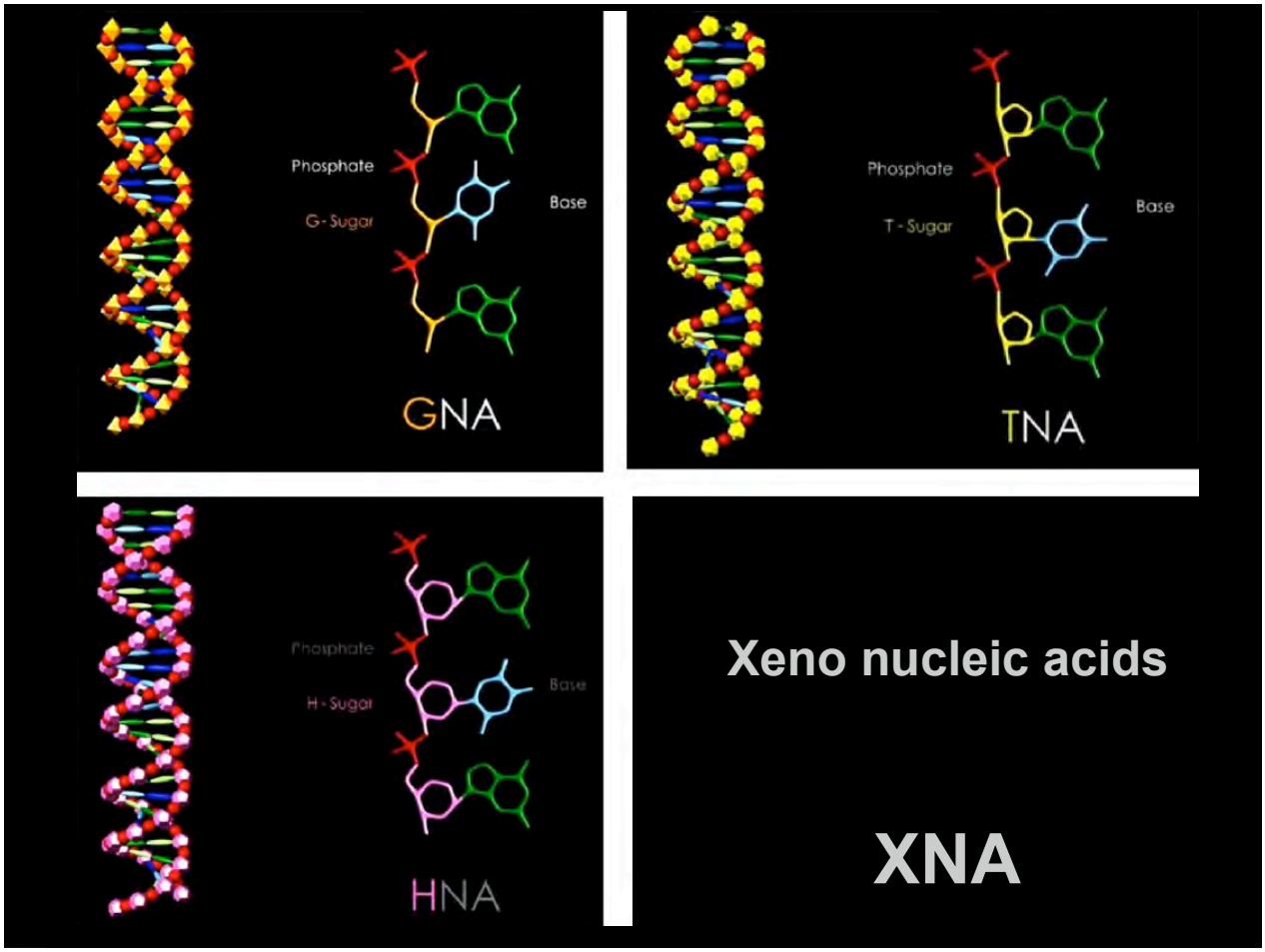
Vladimir P. Torchilin

Abstract | Liposomes — microscopic phospholipid bubbles with a bilayered membrane structure — have received a lot of attention during the past 30 years as pharmaceutical carriers of great potential. More recently, many new developments have been seen in the area of liposomal drugs — from clinically approved products to new experimental applications, with gene delivery and cancer therapy still being the principal areas of interest. For further successful development of this field, promising trends must be identified and exploited, albeit with a clear understanding of the limitations of these approaches.

Biosafety engineering with Chemical SB

chemical monopoly





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Forms of orthogonality

- XNA (Herdewijn, Marliere)
- Enlarged genetic alphabet (Benner, Romesberg)
- Reassigning triplet codons (Chin, Budisa)
- Quadruplet codons (Schultz, Chin)
- Non-canonical aminoacids in proteins (Luisi, Budisa, Marliere)
- Mirror life (Church)

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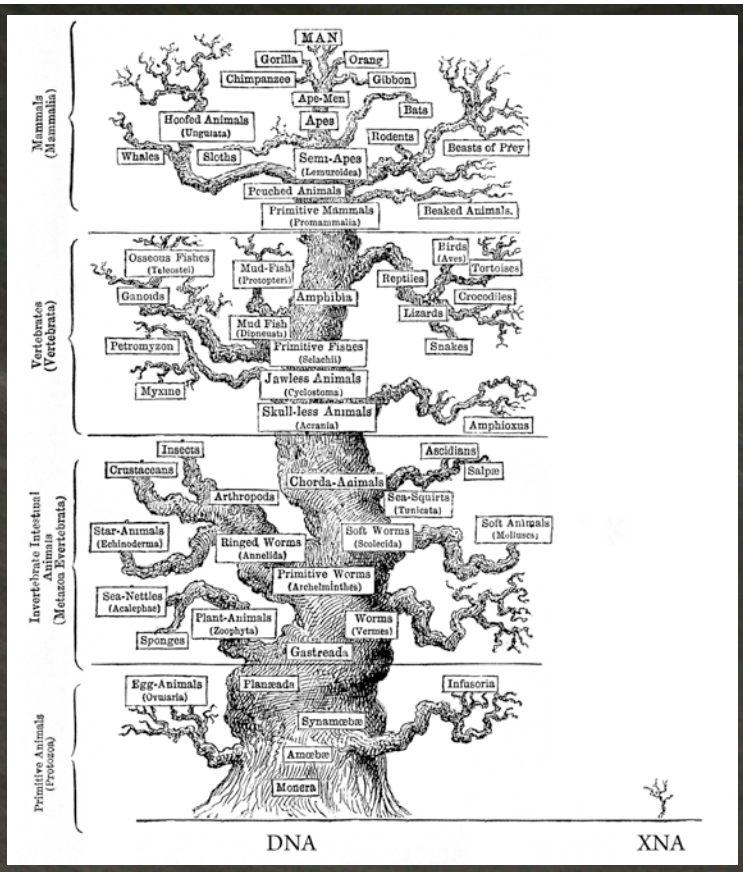
Parallel world



Schmidt 2010. Xenobiology: a new form of life as the ultimate biosafety tool. BioEssays

http://www.markusschmidt.eu/pdf/Xenobiology-Schmidt_Bioessays_201004.pdf

Xenobiology: A new form of life as the ultimate biosafety tool

*Markus Schmidt**

Organisation for International Dialogue and Conflict Management, Kaiserstr.

Synthetic biologists try to engineer useful biological search for

nature biotechnology

Genome engineering

hurch[2]

ngineering genetic material have pursued increasingly challeng
he genetic engineer have grown to encompass new extremes o
engineering. Today, our capacity to generate larger *de novo* as
decreases in manufacturing cost). We are also witnessing poter
on with engineering approaches targeting large numbers of spe
ngineering with unprecedented levels of design originality and
cal world and the diversity of applications for societal benefit.

Syst Synth Biol (2009) 3:77–84
DOI 10.1007/s11693-009-9040-9

The farther, the safer: a manifesto for securely navigating synthetic species away from the old living world

Philippe Marliere

009) 791

Toward Safe Genetically Modified Organisms through the Chemical Diversification of Nucleic Acids

by **Piet Herdewijn**[a]) and **Philippe Marlière**[b])

[a]) Laboratory for Medicinal Chemistry, Rega Institute for Medical Research, Minderbroedersstraat 10, B-3000 Leuven

[b]) Isthmus Sarl, 31 rue Saint Amand, F-75015 Paris

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DIYbio

FRIDAY, AUGUST 22, 2008

Science without Scientists

As molecular tools get cheaper, and the know-how for using them more widely distributed, I think we're going to see a renaissance in science. The peculiar feature of this renaissance is that its going to take place outside of "science proper", away from the universities which dominate now, and funded out-of-pocket by enthusiasts without PhDs.

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Foto credits: Rob Carlson. See: http://www.synthesis.cc/2010/03/garage-biology-in-silicon-valley.html

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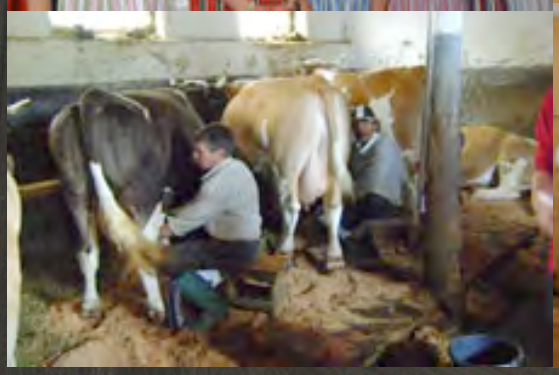
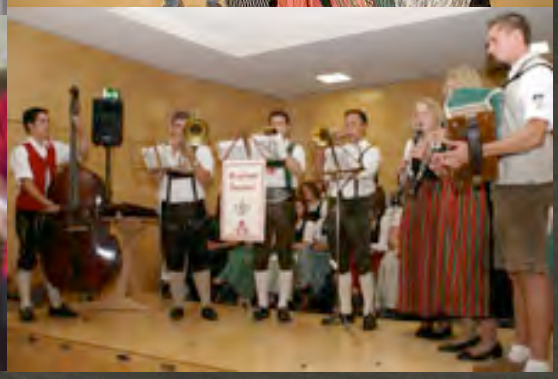
Austrian highschool





http://hlfs.ursprung.at/

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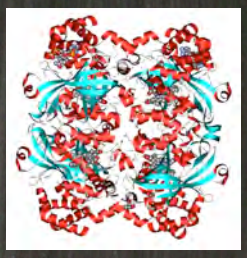
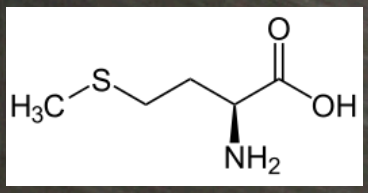
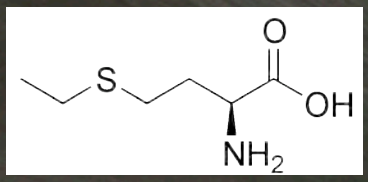
Catalase with non-canonical amino acids



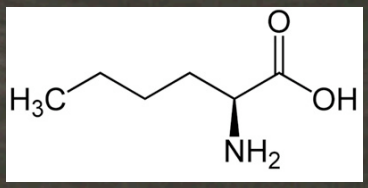
Catalase
Bacillus subtilis 1A55



Methionine



Ethionine



Norleucine

https://gbtpilot.plus.sbg.ac.at/tiki-index.php?page=Synthetische+Biologie+am+Prüfstand+der+Schule&structure=SynBio

International dialogue

www.idialog.eu/fwf/

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Science and Society

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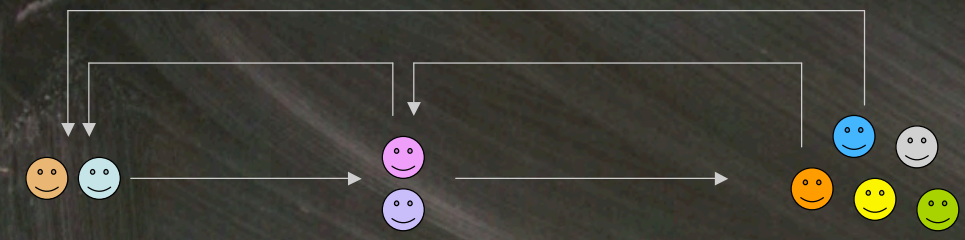
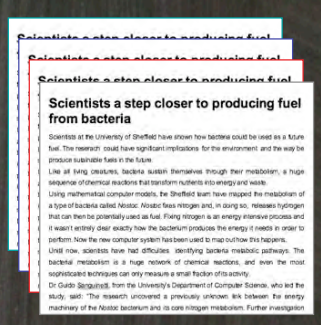
COSY

COSY: Communicating Synbio



scientists journalist „publics“



www.synbio.at

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Results COSY

- Synbio specifics get lost in communication process: „old wine in new bottles“
- First neutral, then polarized opinions
- Risk the same for everybody
- Sceptics don‘t „buy“ promised benefits

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Syst Synth Biol (2009) 3:19–26
DOI 10.1007/s11693-009-9031-x

ORIGINAL RESEARCH ARTICLE

Communicating Synthetic Biology: from the lab via the media to the broader public

Nicole Kronberger · Peter Holtz · Wolfgang Kerbe · Ewald Strasser · Wolfgang Wagner

Received: 30 April 2009 / Revised: 18 June 2009 / Accepted: 29 June 2009

Abstract We present insights from a study on commu- new technology will be met with similar pu

Documentary film

www.synbiosafe.eu/DVD

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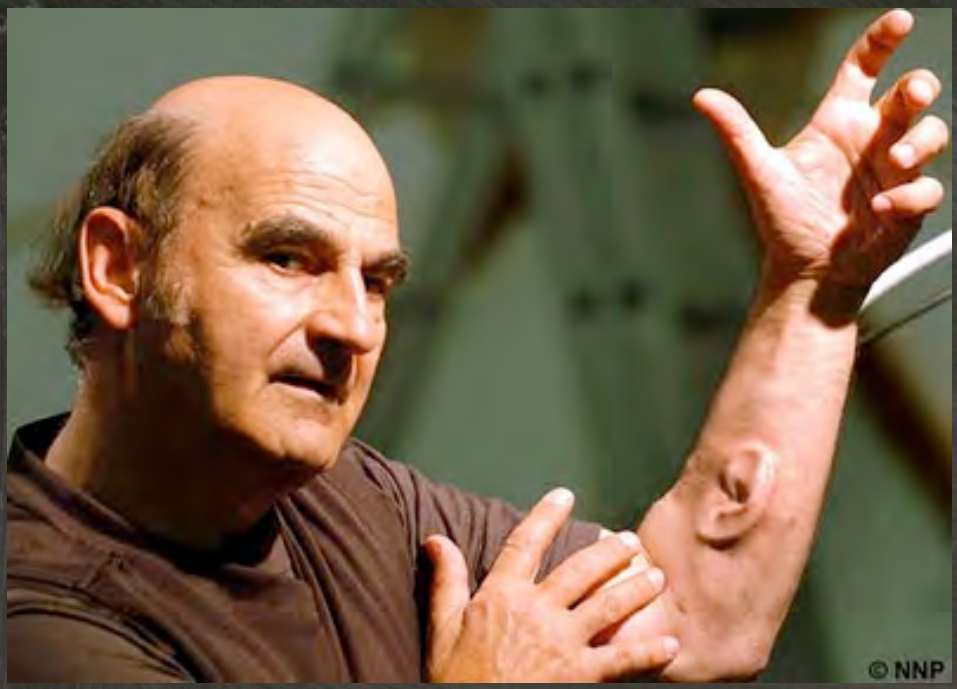
Science, Fiction, and Science Fiction



Stellarc

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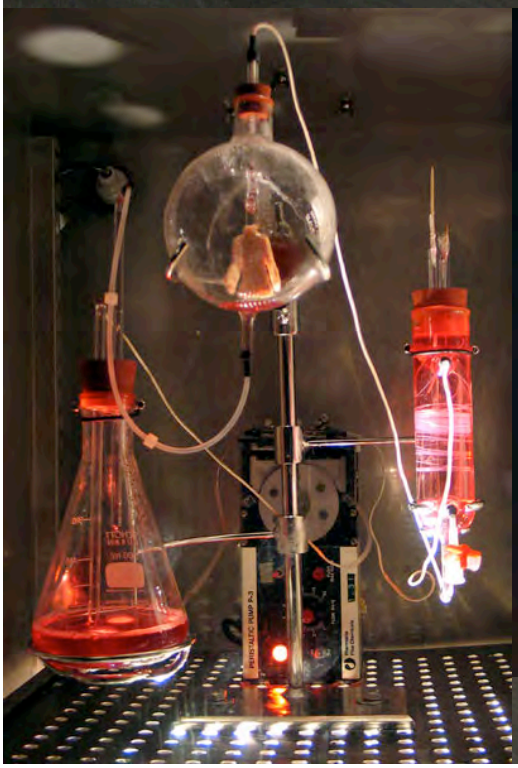
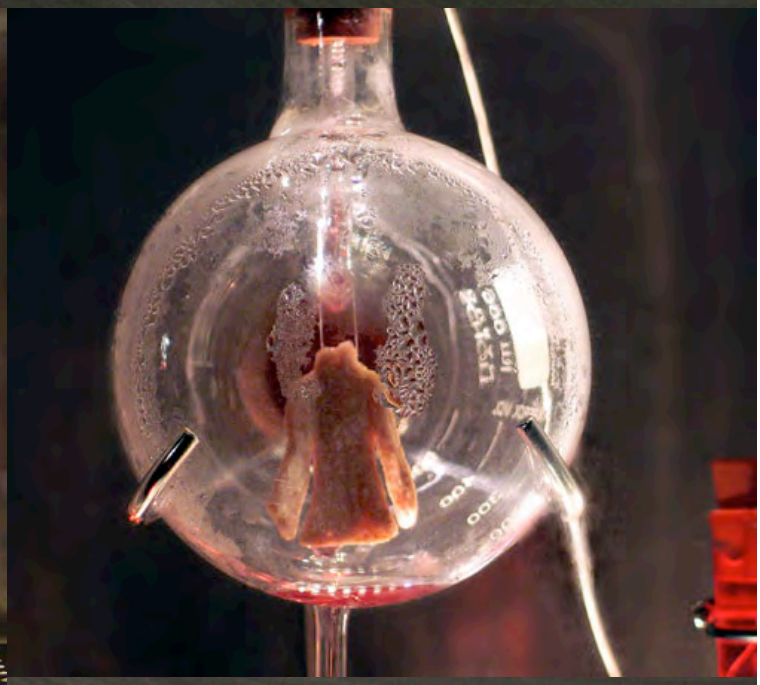
Victimless leather





SymbioticA

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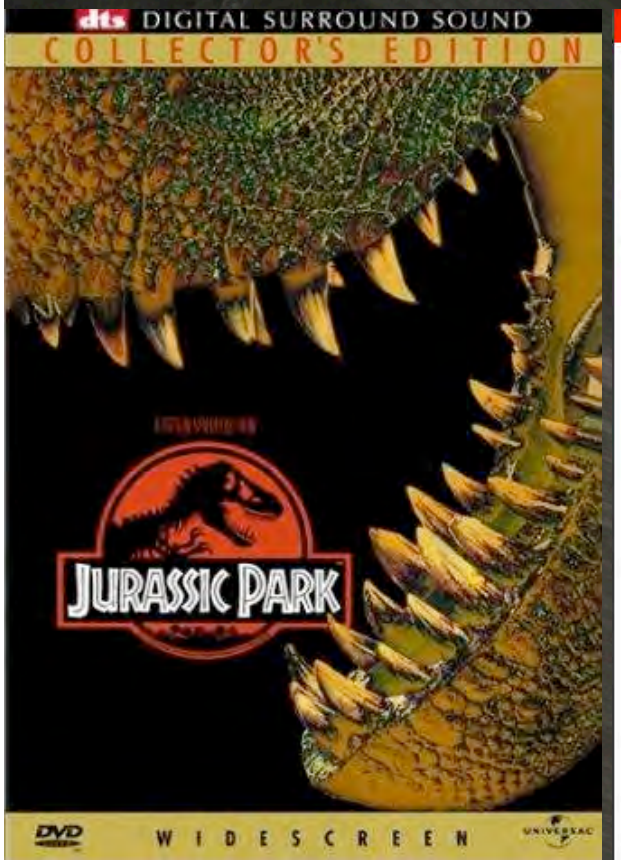
Cinema and Synthetic Biology

www.cisynbio.com



The order of the reference list and citations have been corrected in this PDF.

LET'S MAKE A MAMMOTH

Evolution assumes that extinction is forever. Maybe not. **Henry Nicholls** asks what it would take to bring the woolly mammoth back from the dead.

In 1990 the late Michael Crichton gave the idea of reviving extinct species a slickly plausible and enormously entertaining workout in his novel *Jurassic Park*. At that time the longest genome that had ever been sequenced was that of a virus. The best part of 20 years on, hundreds of animal genome sequences have been published. This week, for the first time, the genome of something undoubtedly charismatic and definitively extinct joins the list: the mammoth (*Mammuthus primigenius*)[1]. If you want to bring a species back to life, the mammoth would be almost as dramatic as a dinosaur. And unlike *Tyrannosaurus rex*, the mammoth has close living relatives to lend a hand.

It is a fair bet that a complete genome and closely related species would make it easier to pull a Crichton on a mammoth than on a dinosaur. But easier is far from easy. To put flesh on the bones of the draft sequence — to go from a genome to a living, breathing beast — would require you to master, at the very least, the following steps: defining exactly the sequence or sequences you want for your creature; synthesizing a full set of chromosomes from these sequences; engulfing them in a nuclear envelope; transferring that nucleus into an egg that would support it; and getting that egg into a womb that would carry it to term. None of those steps is currently possible. From getting a definitive sequence to harvesting eggs from an elephant there are all-but-insurmountable obstacles at every stage, and no evidence that anyone is going to work very hard to solve them. But do any of them actually make the dream impossible?

The sequence

The first stop in this mammoth challenge is to obtain a sequence good enough for us to contemplate using it as the basis for a living being. The sequencing of long-dead DNA such as that of mammoths uses fragments at various levels of degradation. To detect and correct the base-pair changes that can occur after death and to avoid the inevitable errors involved in assembling millions of these tiny fragments into a coherent sequence, it is necessary to sequence much more than a single genome's worth of DNA. "If we want fewer than 1 error in 10,000 base pairs — a reasonable quality genome — we would need to sample in the order of 12-fold coverage," says Svante Pääbo, director of the genetics department at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, who has worked on Neanderthal genomes[2]. The genome published today has roughly 0.7-fold coverage. 'Reasonable quality' for science does not mean the sort of genome you would want to live with: in a human genome that error rate would mean 300,000 mutations.

"Genome synthesis is further developed today than genome sequencing was when Crichton wrote *Jurassic Park*."

Coverage can be improved as long as there's the money to do it, but old samples offer particular challenges: a lot of contamination by bacterial, fungal and other species' DNA. Thirty-five-fold coverage, which Pääbo says is as good as it gets, would be "extremely costly and extremely time-consuming", according to Eske Willerslev, head of the Ancient DNA and Evolution Group at the University of Copenhagen. Ever-cheaper sequencing, however, and the possibility of better preserved and prepared samples, mean that those expenses of cost and time will shrink. Willerslev sees nothing to stop researchers from producing a mammoth genome as good as any genome today at some point in the future. Whether such a genome would be good enough for a living being remains a somewhat open question — but with time and effort, it's plausible that a sufficiently error-free genome can be arrived at.

A sequence on its own, though, is not enough: researchers will need to work out exactly how it divides up into chromosomes. The obvious solution would be to tot up the number of chromosomes in an intact mammoth cell and sift through the genomic data looking for their beginnings and endings. But even the very best mammoth material falls short of this kind of preservation (see 'You need to do more than thaw'). "We have no idea — yet — how many chromosomes mammoths had," says Hendrik Poinar, a geneticist at McMaster University in Ontario, Canada. Kerstin Lindblad-Toh, co-director of the genome sequencing and analysis programme at the Broad Institute in Cambridge, Massachusetts, says that the institute will release a sequence of the African elephant (*Loxodonta africana*) to seven-fold coverage some time in 2009. When they do, the mammoth geneticists

www.bio-fiction.com

BIO:FICTION

SCIENCE, FILM & ART FESTIVAL, VIENNA, MAY 2011