

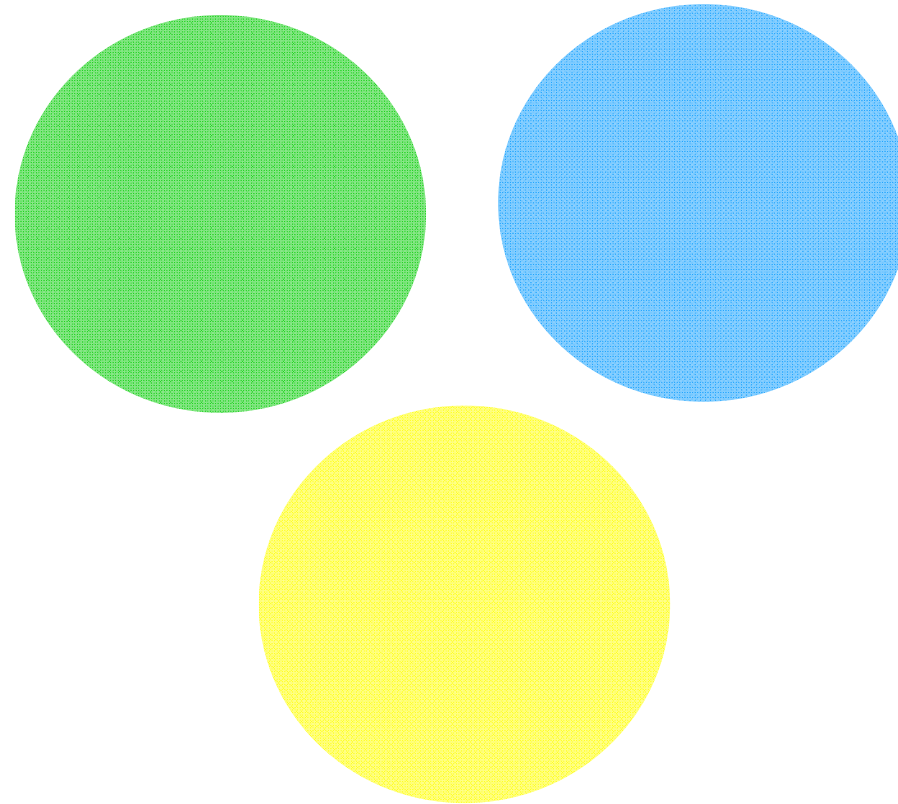
Biology as engineering: concepts, cultures and collaborations

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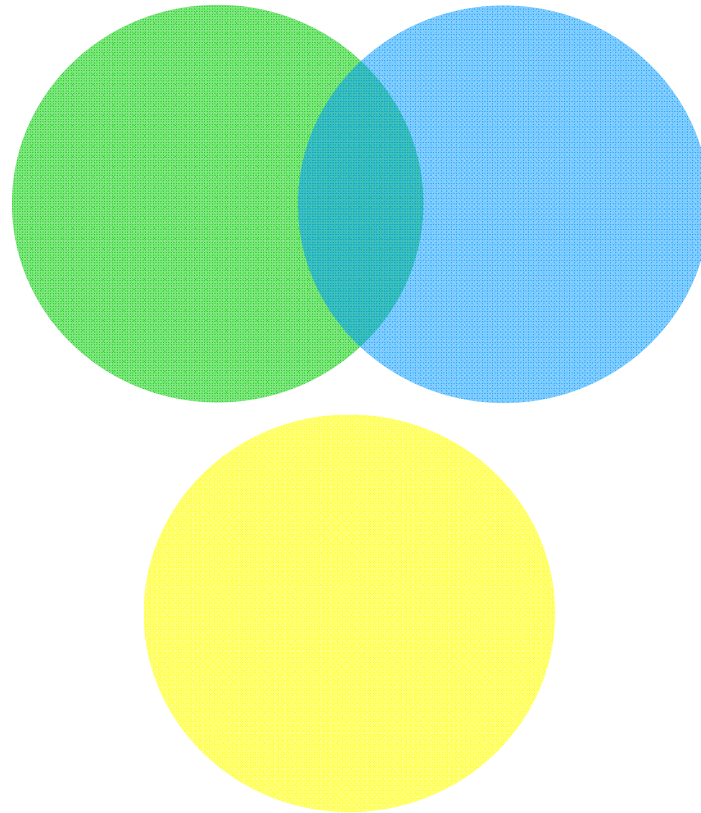
RoSBN Net Synthetic Biology Workshop 2009
St Anne's College, University of Oxford
14th-16th September 2009



Biology as engineering



Biology as engineering

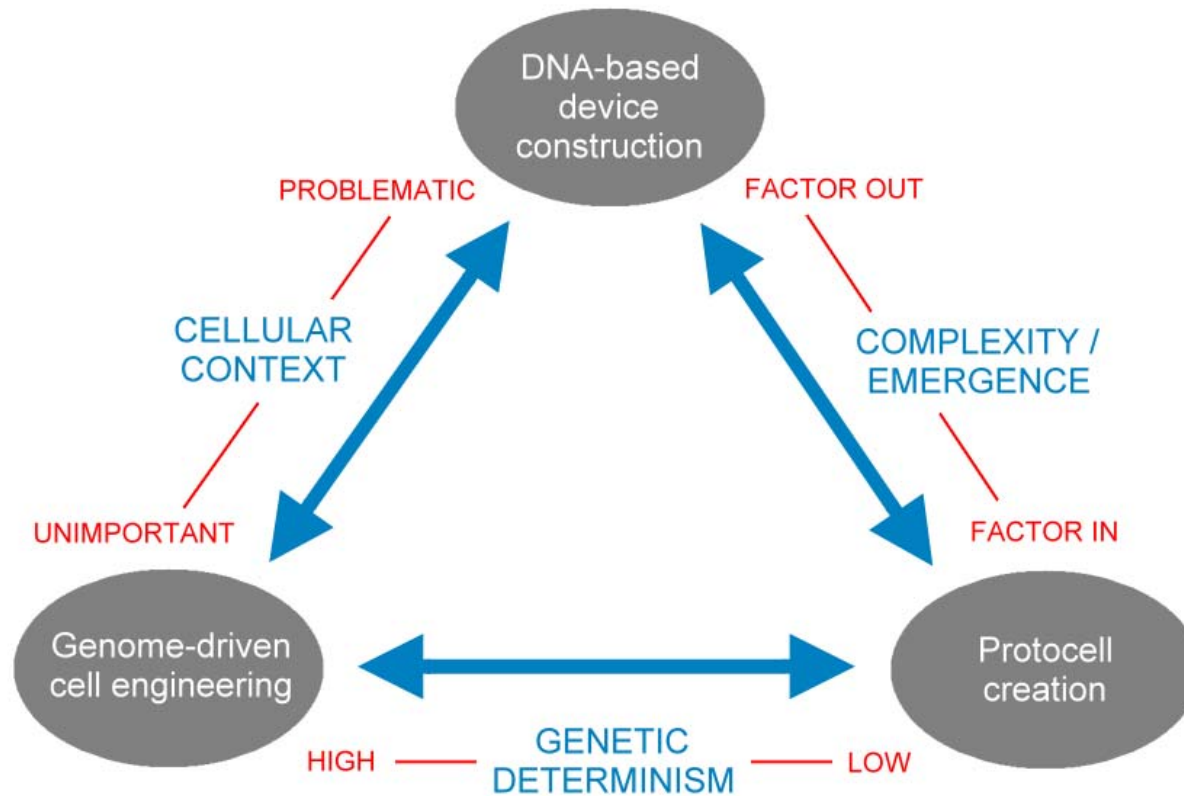


Outline

- Concepts
 - Biology as engineering
 - Engineering principles: modularity
 - Engineering analogies
- Cultures
 - Interdisciplinarity and disciplinary tensions
- Collaborations

Concepts

Schools of synthetic biology



O'Malley, M, Powell, A, Davies, J & Calvert, J (2008)
'Knowledge-making distinctions in synthetic biology' *BioEssays* 30:57-65

“Biology is as important as the lifeless sciences of matter, and biotechnology will in the long run be more important than mechanical or chemical engineering” (Julian Huxley, 1936)

Making biology into an engineering discipline

Synthetic biology: new engineering rules for an emerging discipline

Ernesto Andrianantoandro^{1,3}, Subhayu Basu^{1,3},
David K Kariq^{1,3} and Ron Weiss^{1,2,*}

A partnership between biology and engineering

Roger Brent

Systems biology

Synthetic biology—putting engineering into biology

Matthias Heinemann^{1,†} and Sven Panke^{1,*}

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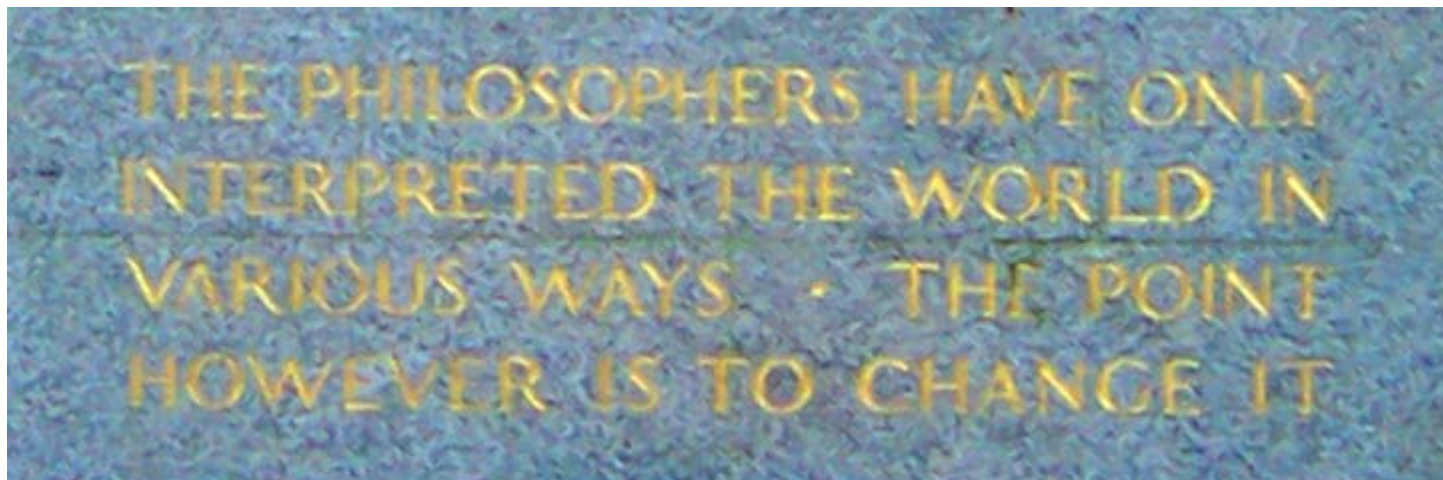
Making biology into an engineering discipline



- One of the often-expressed aims of synthetic biology
- Not new...(Leduc 1912, Loeb 1912, Jacob and Monod 1961)
- But what exactly is meant by this objective?
- What assumptions underlie it?

Differences between biology and engineering

- “A scientist discovers that which exists. An Engineer creates that which never was” (Theodore von Karman)
- Biologists want to understand
- Engineers want to construct



Differences between biology and engineering

Science	Engineering
Discovery Understanding Comprehension	Creation Construction Design

- Driven by different *intentions*

Differences between biology and engineering

- But synthetic biology can increase understanding of natural biological systems
- The acid test of systems biology
- Measure of success of synthetic biology: how well the creation of artificial systems “drives new discoveries and new theories” (Benner and Sismour 2005)



What I cannot create,
I do not understand.

Why can't I solve it. Po

TO LEARN:

Bethe Ansatz Probs.

Kondo

3-D Hall

well Temp

Non linear Chiral Hydro

Know how to solve every
problem that has been solved

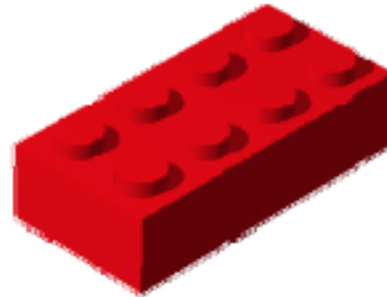
$$\textcircled{A} f = U(r, a)$$

$$g = 4(r \cdot z) u(r, z)$$

$$\textcircled{B} f = 2|K \cdot a| (u \cdot a)$$

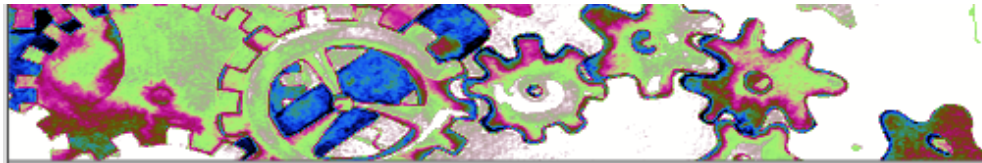


Engineering principles



Engineering principles: modularity





Registry of Standard Biological Parts

Go Search

page discussion view source history

Log in / create account

Welcome to the Registry of Standard Biological Parts.

The Registry is a collection of ~3200 genetic parts that can be mixed and matched to build synthetic biology devices and systems. Founded in 2003 at MIT, the Registry is part of the Synthetic Biology community's efforts to make biology easier to engineer. It provides a resource of available genetic parts to iGEM teams and academic labs.

The Registry is based on the principle of "get some, give some". Registry users benefit from using the parts and information available from the Registry in designing their engineered biological systems. In exchange, the expectation is that Registry users will, in turn, contribute back information and data on existing parts and new parts that they make to grow and improve this community resource.



Catalog of parts & devices



Help



Users & groups
(Apply for an account)



DNA repositories

Registry tools

- [Search parts \(?\)](#)
- [Add a part](#)
- [Request a part](#)
- [Send parts to the Registry](#)
- [Sequence analysis](#)



You'll notice some significant changes to the Registry recently. In particular, the Registry [catalog of parts](#) has been entirely redesigned to allow for easier browsing of the available parts and devices. You can now browse parts and devices by type, by function, by chassis and by standard. You'll also notice that the documentation and help pages for each class of parts have been greatly enhanced.

The Registry of Standard Biological Parts is **always** a work in progress. Please browse the new catalog and let us know what you think, or feel free to edit and improve the pages further.

Registry news

- **June 22, 2009:** You can now link to part pages directly from the iGEM wiki by typing the following `<partinfo>BBa_B0015</partinfo>`.
- **June 11, 2009:** We are considering changing the license terms of the Registry so that we can share our information with other databases. Go [here](#) to read the proposal or add your comments.
- **June 2, 2009:** Most of the hard information about a part is now presented in the header and footer of the part's Main Page. In particular, the functional parameters and the categories for a part are presented in the footer. All of this information may be edited using the Edit button near the footer.
- **May 30, 2009:** For the convenience of software developers, the sequences and basic information about every part is available in FASTA format. Learn more [here](#).

Engineering principles: modularity

- Is modularity a characteristic of natural systems?
- Or are they are simply best understood as modular by the engineering approaches adopted in synthetic biology?
- No consensus on this issue!
- Arkin and Fletcher (2006): “The key observation that biological systems exhibit **some degree of modularity** underlies the current belief that useful and ‘engineerable’ design principles exist”

What constitutes a module?

- What you think of as a 'module' might depend on your disciplinary perspective
- And what a scientist regards as a functional module might be different from what a cell regards as one
- It may be that we are carving out modules in nature to satisfy with our desire for biological understanding
- Can we separate our conceptual activities of understanding the world from the world itself?

Scepticism about modules

- Are modules “a human invention designed to assist people in engineering very complex systems by ignoring unnecessary details” (www.openwetware.org)?
- But even if natural systems aren't modular, synthetic biology will allow us to make them modular
- The engineering principles that have been so useful in other areas might become incorporated into new biological systems (laziness?)

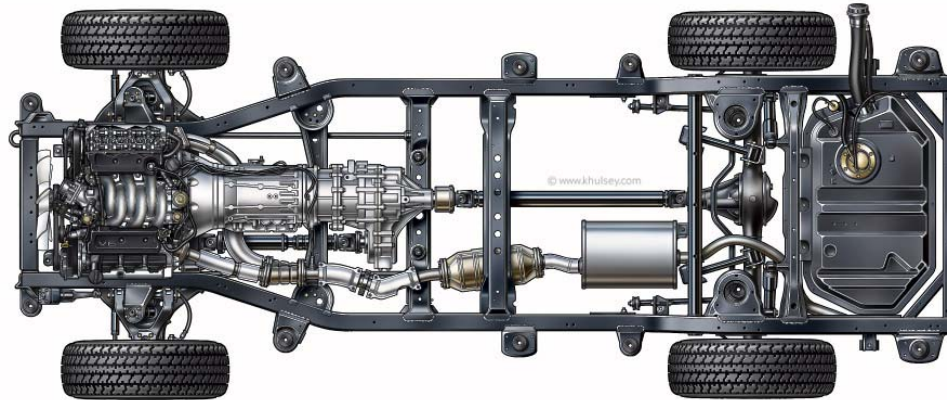


Engineering principles: modularity

- Engineering principles have social dimensions: modularity is favoured by an engineering approach
- Modular systems are not only easier to engineer, they are also well suited to particular types of intellectual property regimes
- The technical is political



Engineering analogies



Engineering analogies

- Will these analogies affect the biological systems that are produced?
- Is there the potential for the imposition of engineering ideals on new living things?
- Are we seeing an “overly simplistic projection of electronic engineering concepts into supposedly biological counterparts”? (de Lorenzo and Danchin 2008)

The reduction of complexity

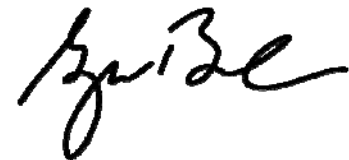
- Tensions also revolve around the attempt to reduce biological complexity
“A biologist is delighted with complexity. The engineer’s response is: ‘How can I get rid of this?’” (Tom Knight)
- E.g. of the reduction of complexity: ‘Refactoring Bacteriophage T7’ (Chan et al. 2005)

```
A Wild-type T7
-----2.8----->
acgcaaagggaggcgacatggcaggttacggcgctaa;
      <--3-RBS--><-----3-->
```

```
B T7.1
acgcaaGgggagAcgacaCggcaggttacggcgctaa;
-----2.8----->
```

Biology becomes a product of design choices

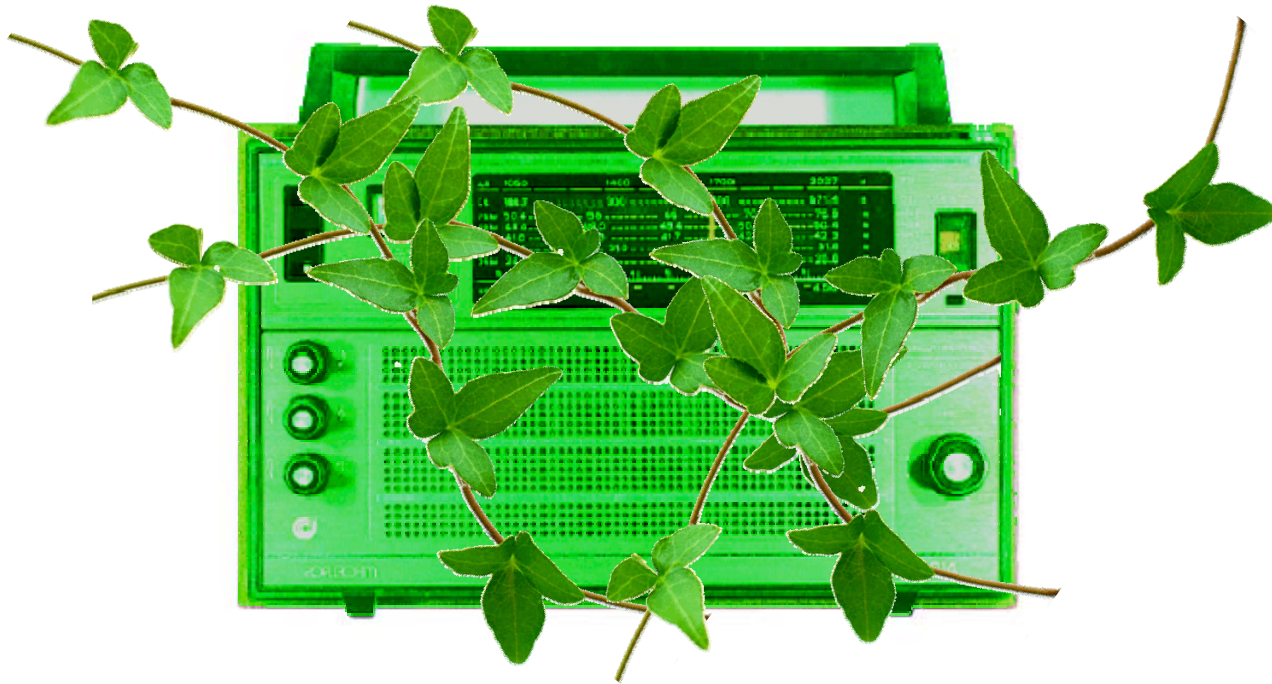
- If we can eliminate biological complexity, biology becomes a product of design choices, rather than evolutionary pressures
- Can include industrial and political imperatives (e.g. safety)
- The integration of social concerns into synthetic biological products
- Familiar to engineers
- Synthetic biologists should sign their work

A handwritten signature in black ink, appearing to read 'G. J. B.', located in the bottom right area of the slide.

What makes biology different?

- Question of this conference...
- Can we eliminate the messiness of biology?
- Will synthetic biology will be continually eluded in its aspiration to reduce biological complexity?
- Does the idea of 'engineering' work when natural selection is involved?

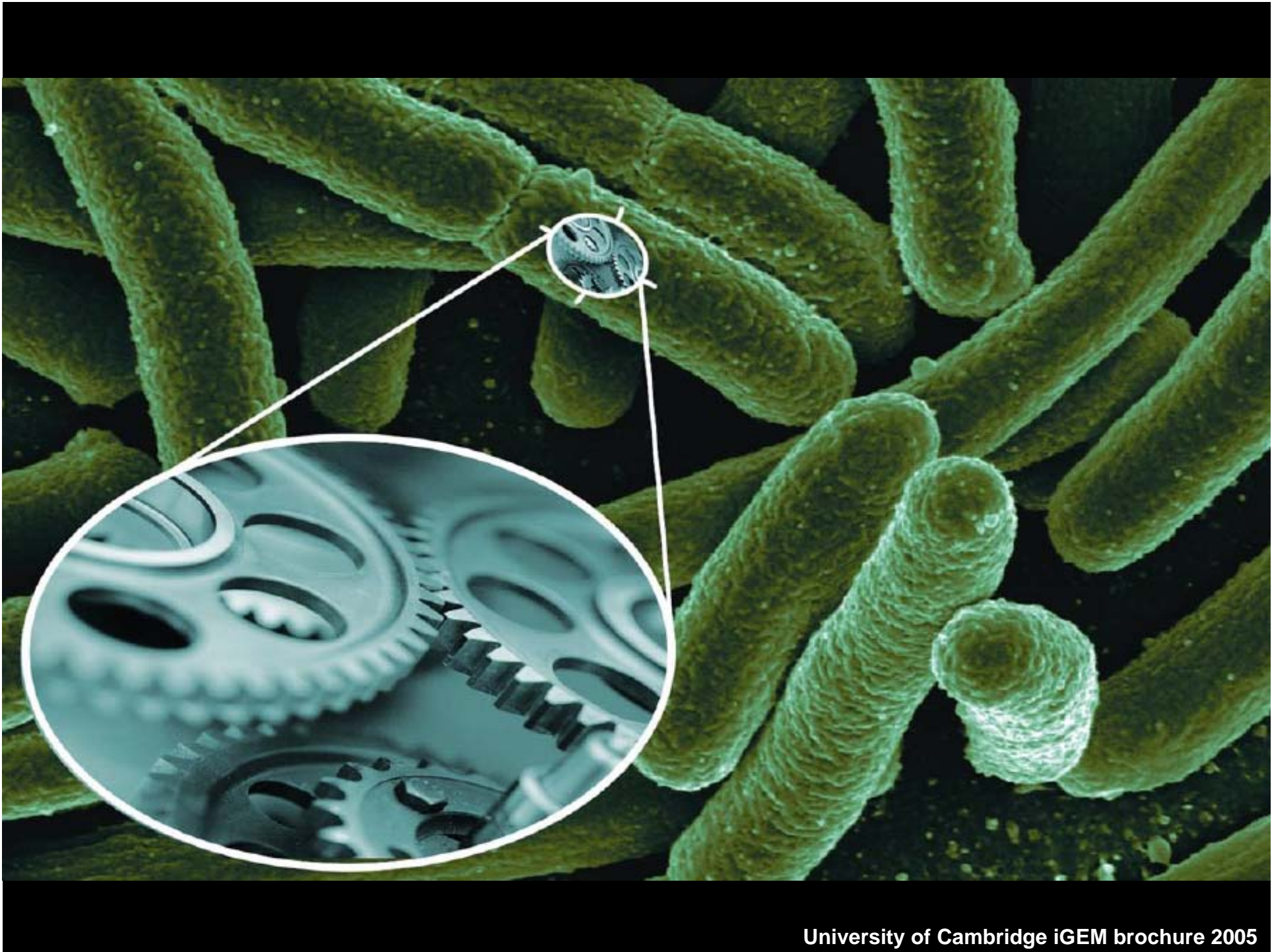
Can an engineer fix an evolved radio?

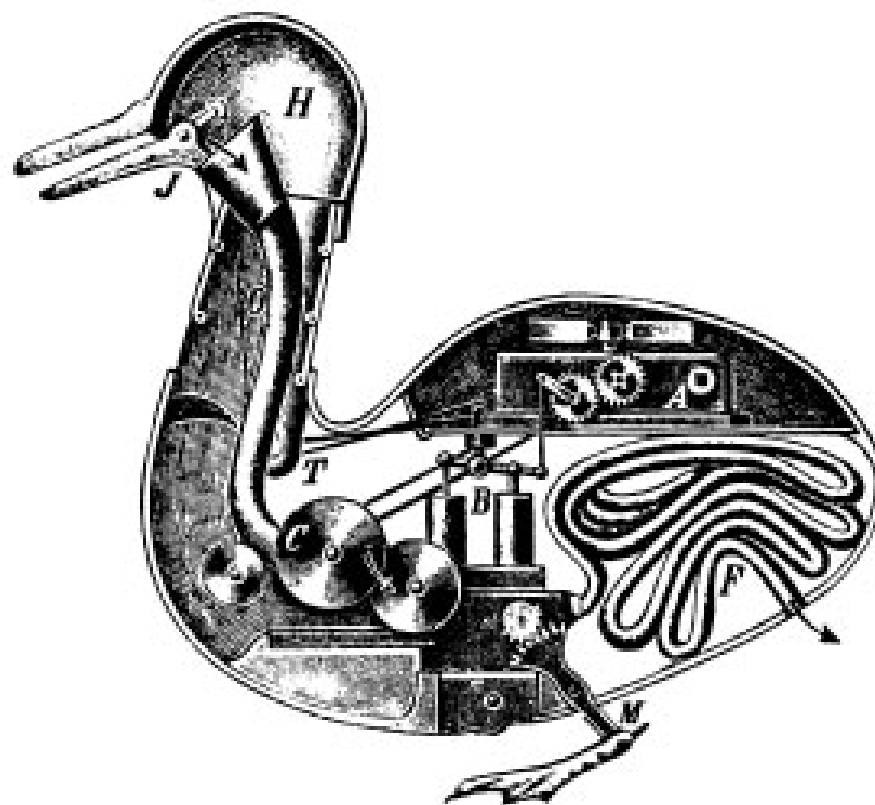


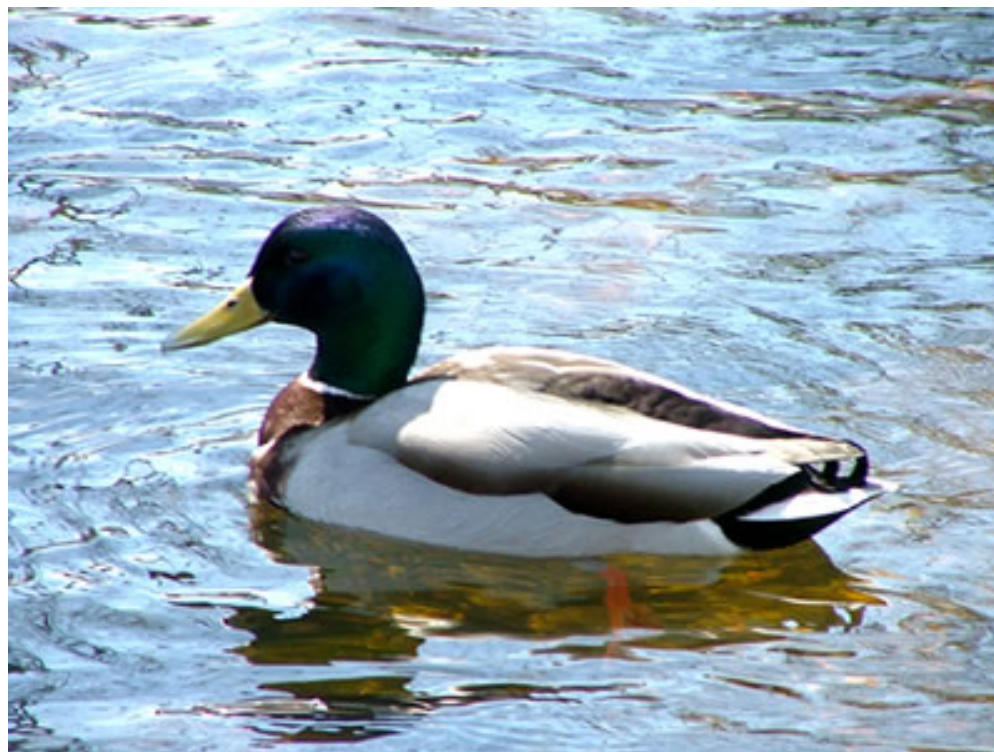
Engineer or tinkerer?

- François Jacob (1977) criticises the idea that evolution acts like an engineer
- An engineer works from a design, but evolution does not
- We should think of evolution as the product of “a tinkerer who uses everything at his disposal to produce some kind of workable object”
- A tinkerer just works with whatever is available e.g. from a bike wheel he might make a roulette wheel
- Is this contingency an important part of biological systems?
- Pam Sliver argues that the organism is “a long series of kludges...not necessarily a well-oiled machine”



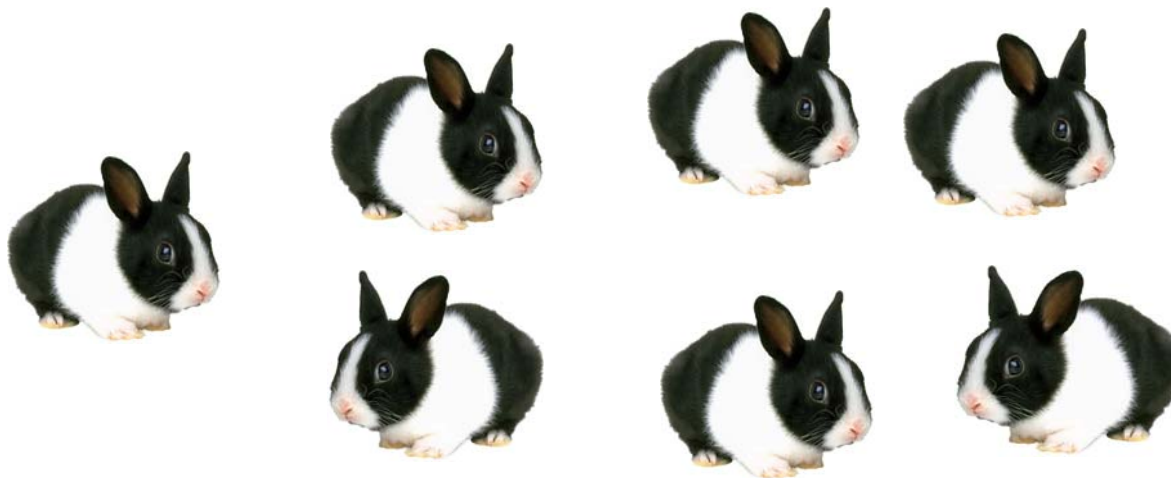






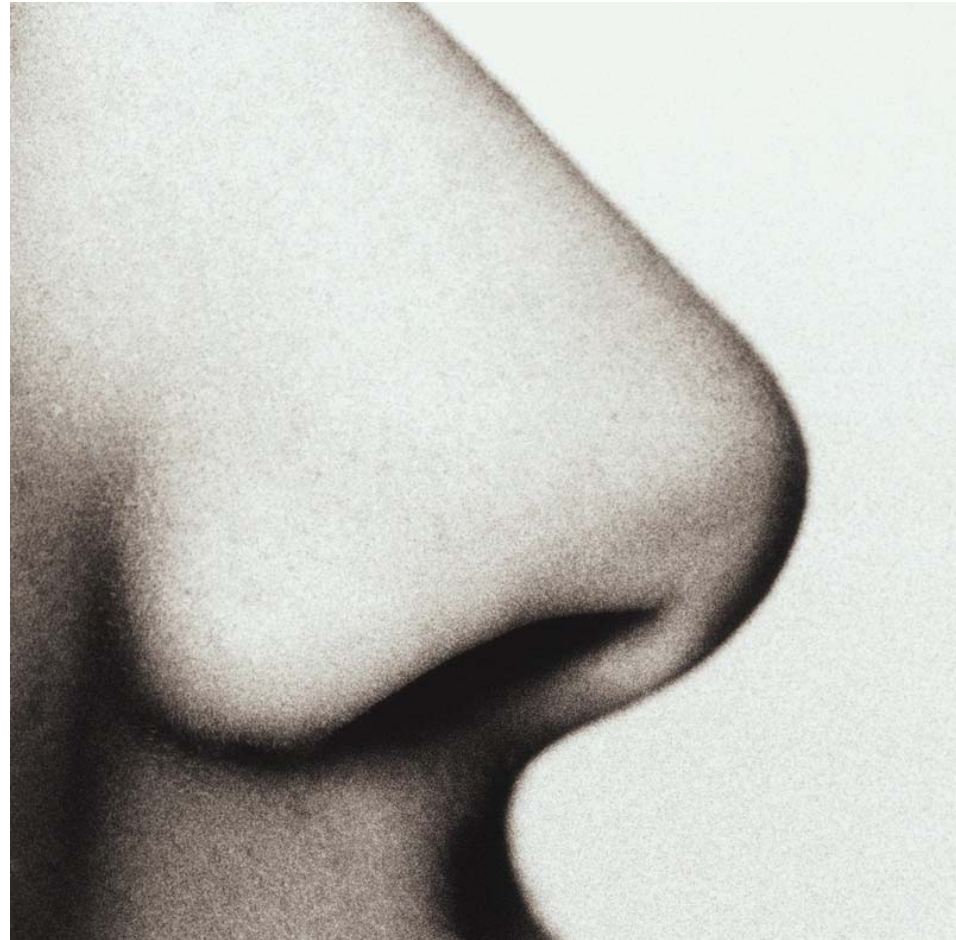
Different engineering principles?

- Heard how synthetic biology can make use of the natural propensities of organisms (e.g. to replicate)
"Fundamentally, biology is a manufacturing technology. The things it builds are more copies of itself" (Tom Knight)



Biology can be better than engineering

The exquisite
sensitivity of
biology



Cultures

Disciplinary tensions

- Many leading synthetic biologists think of themselves as engineers (e.g. Jay Keasling “I’m an engineer at heart”)
- Problems engaging the biological community?
- Leduc, Loeb etc. who had an engineering approach to life were accused of not doing *real* biology (Campos 2008)
- Lazebnik (2002) tries to explain this:
Biologists think that engineering approaches aren’t applicable to cells
“because these little wonders are fundamentally different from objects studied by engineers. What is so special about cells is not usually specified, but it is implied that *real biologists feel the difference*”
- Can synthetic biology be real biology?

Engineering cultures



- A different mentality?
- It's "way more cool" to do biology than computers
- Important that you learn how to play "like kids in the playground"
- Competitions not seen previously in biology
- iGEM: brings young people into the field
- Aim is to build a community which shares certain values about safety, security and open access
- A new community and a new way of doing science are being created simultaneously



2009.igem.org is now up! Head there to find out more information about iGEM 2009.

at a glance:

1925 minutes of talks 77 presentations
1200 participants 24 awards
825 jamboree attendees 22 weeks of work
84 teams 21 countries

News:

- Join the Institute of Biological Engineering and publish your iGEM work. Find out more about the [offer from IBE](#).
- **iGEM 2008 teams**, remember to add your project publications to the [Publication](#) page!
- Check out the [iGEM 2008 Jamboree Results](#).
- Share any publicity that your team has received on the [Publicity](#) page.



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- [GENEART and Mathworks Offers](#)
- [Using the wiki](#)
- [Registry of Standard Parts](#)
- [Main page archive](#)

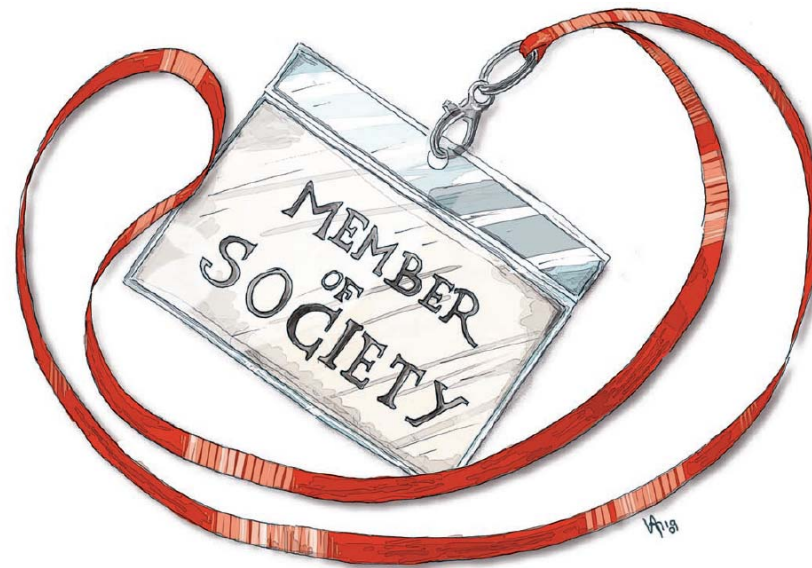
Collaborations

New organisational arrangements

- We are seeing new organisational arrangements in synthetic biology: early stage attention to social and ethical concerns
- Social scientists are becoming a required component of research programmes and networks
- What kind of role should social scientists play in these new situations?

Possible roles

- Wait for the scientists and engineers to do the work, and then deal with the social and ethical consequences
(Assumes that the technical and the social can be easily separated)
- Represent the public



Possible roles

- Can 'translate' or 'facilitate' between different groups (e.g. scientists and the public)
- Can contribute to specialised discussions of safety, security, regulation or intellectual property

Possible roles

- Topics for the sociology of science:
 - The relationship between *construction* and *comprehension* in synthetic biology
 - Questions about the *modularity* of biological systems
 - How engineering *analogies* may affect the biological systems that are produced
 - Whether biology will become a product of *design choices*
 - Whether we need *different engineering principles* when it comes to engineering biology
 - Whether synthetic biology is '*proper biology*'



New objects

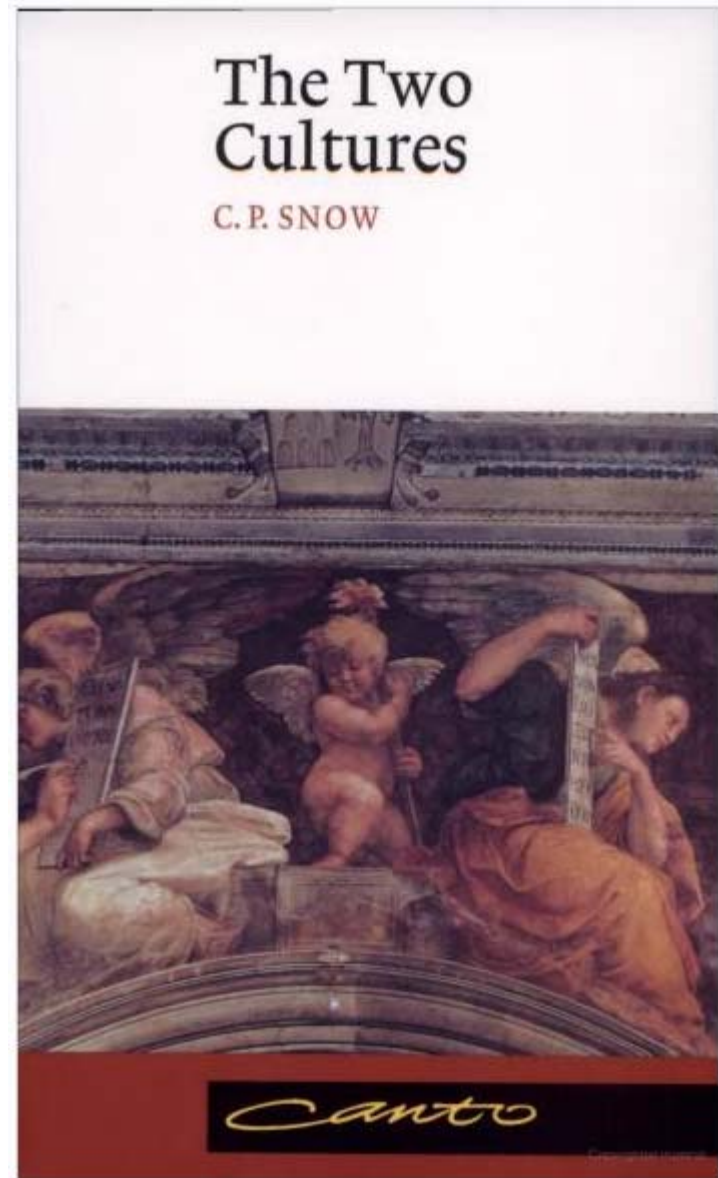
- New objects are being brought into the world in synthetic biology
- Can't apply the same engineering principles
- Can't apply the same sociological principles to synthetic biology
- New kinds of engineering and new kinds of social science
- Biological systems are interconnected and complex; social and political systems are worse



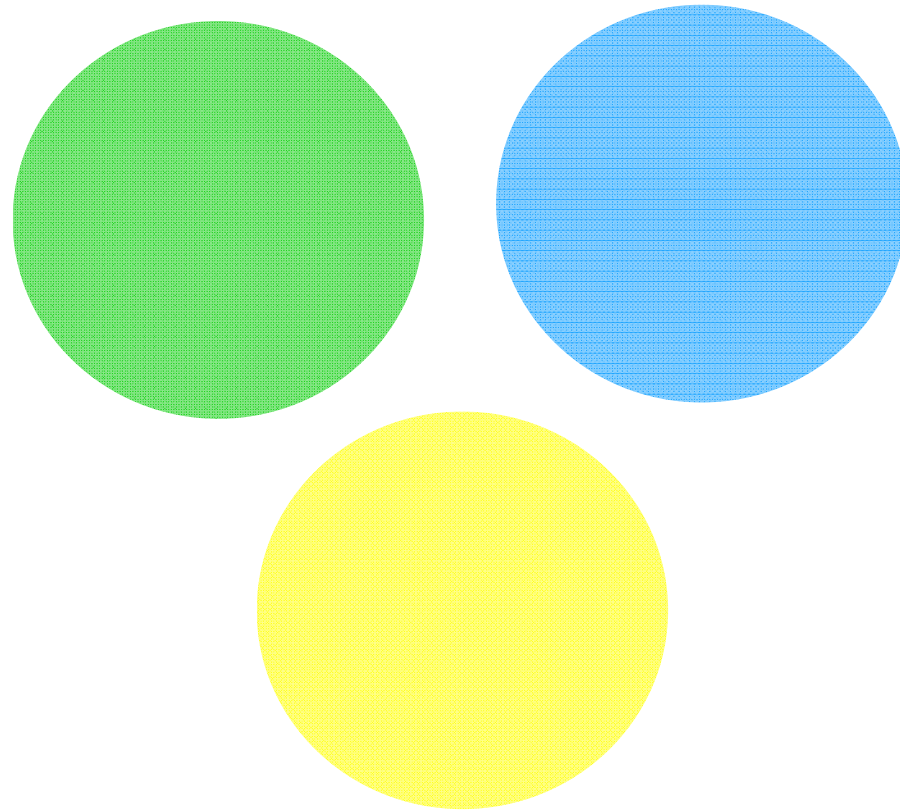
ELSI = Ethical,
Legal and Social
Issues

New collaborations

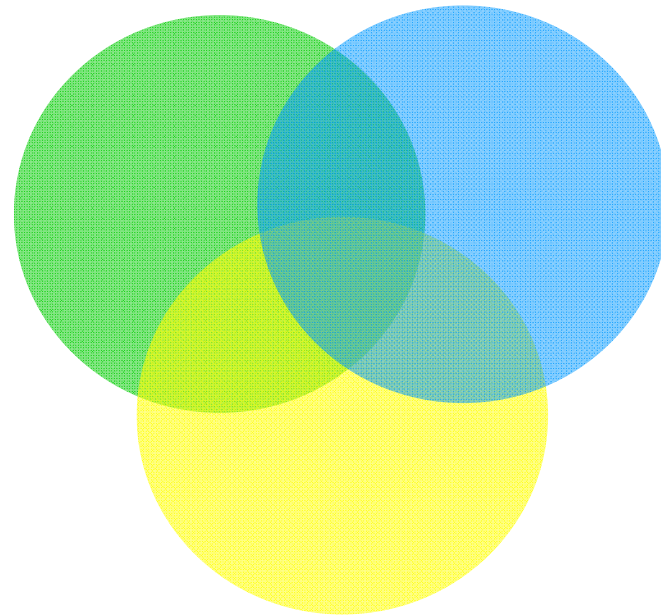
- Potential for new forms of collaborative work
- Doesn't just follow the science, but interacts with it
- “We can engage in interdisciplinary conversation about what science is, what it does, and what it should do. In this way science and the social study of science merge” (Hamlin 1992)



New collaborations



New collaborations



Positive signs

- This community is remarkably open to collaboration
- Keen to discuss the broader implications of synthetic biology
- Involved in iGEM teams
- This conference!
- Possibilities for genuine collaboration

The support of the Economic and Social Research Council (ESRC) is gratefully acknowledged. The work presented forms part of the programme of the ESRC Genomics Network at Innogen.

