Ethics in Synthetic Biology
RRI & emerging sciences
Synthetic Biology, Responsible Research and Innovation

- What is Synthetic Biology (examples)
- What is responsibility (network of relations)
  - What are ethical issues in Synthetic Biology?
  - How to spot an ethical issue (within the responsibility framework)
  - How to get answers on an ethical issue (where to look for help)
"We report the design, synthesis and assembly of the 1.08-Mbp *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *Mycoplasma capricolum* recipient cell to create new *Mycoplasma mycoides* cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including 'watermark' sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication." (Gibson et al 2010, 52)
Moreover, these findings, in combination with the recent de novo synthesis of the *M. genitalium* chromosome and successful genome transplantation of Mycoplasma genomes to produce a synthetic cell (Gibson et al., 2008, 2010; Lartigue et al., 2007, 2009), raise the exciting possibility of using whole-cell models to enable computer-aided rational design of novel microorganisms.”

→ “We conclude that comprehensive whole-cell models can be used to facilitate biological discovery.” (Karr et al 2012)
“Here we report on production of such petroleum-replica hydrocarbons in *Escherichia coli* [...] Rather than simply reconstituting existing metabolic routes to alkane production found in nature, these results demonstrate the ability to design and implement artificial molecular pathways for the production of renewable, industrially relevant fuel molecules.” (Howard et al 2013)
“All natural organisms store genetic information in a four-letter, two base-pair genetic alphabet. The expansion of the genetic alphabet with two synthetic unnatural nucleotides that selectively pair to form an unnatural base pair (UBP) would increase the information storage potential of DNA, and semisynthetic organisms (SSOs) that stably harbor this expanded alphabet would thereby have the potential to store and retrieve increased information. [...] This SSO is thus a form of life that can stably store genetic information using a six-letter, three-base-pair alphabet.” (Zhang et al 2017)
iGEM, Bielefeld 2010: Main construct of acetosyringone inducible luciferase expression system containing constitutive expression of the two component receptor system (virA+virG).

http://2010.igem.org/Team:Bielefeld-Germany/Project/Model
An early Definition

• „Synthetic Biology aims to engineer and study biological systems that do not exist as such in nature, and use this approach for achieving better understanding of life processes, generating and assembling functional modular components, developing novel applications or processes.” (TESSY 2008, 4)
Description of Syn. Bio research – 1. Venter

„The fundamental differences between what we do and what’s been done before and how we define synthetic genomics is: we start with digital information in the computer. From all our reading of the genetic code, my team sequenced the first genome of the living organism in 1995. And we went from having the “A,” “C,” “G” and “T’s” to 1’s and 0’s in the computer. Synthetic genomics as we defined it starts with those 1s and 0s and remakes the software of life and then activating that in cells.“ (Venter 2010, Presentation at the PCSBI)
Description of Syn. Bio research – 2. ETC Group

• “This is the quintessential Pandora’s box moment - like the splitting of the atom or the cloning of Dolly the sheep. We will all have to deal with the fall-out from this alarming experiment,” comments Jim Thomas of the ETC Group.” (ETC 2010)
• “J. Craig Venter Institute and Synthetic Genomics Inc announced the laboratory creation of the world's first self-reproducing organism whose entire genome was built from scratch by a machine (...) - a form of "extreme genetic engineering".” (ETC 2010)
A conflict surrounding Synthetic Biology

• Venter: „DNA software builds its own hardware”
  • → “make new vaccines” ... “get cells to capture CO2 and make basically a bio-crude that can go into refineries” (Venter 2010)

• ETC: „patenting pandoras bug“
  • → 111 NGOs demand a “moratorium on the release and commercial use of synthetic organisms and their products to prevent direct or indirect harm to people and the environment.” (FOE et al 2012, 1)
Any help from natural science in defining the field?

• The field is young and there is still debate on:
  • Is it a new field of research or a new kind of science? (Lam 2009)
  • Is it new in its own right or merely genetic engineering expanded? (Erickson 2011, 1254-1256; Engelhard 2011, 45)
  • “Do we need synthetic bioethics?” (Parens/Johnston/ Moses 2006, 1449):
    Whilst scientists still debate on a suitable definition on the scope and range of syn. Bio., the normative question is brought up, if the “value of life” is already being altered or even diminished by the emerging biotechnology (EKAH 2009, 65).
Die meisten schätzen den eigenen Wissensstand realistisch als gering ein

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<td>3</td>
<td>Nanotechnologie</td>
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Basis: Bundesrepublik Deutschland, Bevölkerung ab 16 Jahre
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### Spontane emotionale Reaktion auf Schlüsselbegriffe

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Problems

• New field of research with promising outlook, but, because its still emerging, ill defined
• No clear guidelines from official sources (EU)
• Conflict surrounding definition and use of Syn.Bio. ('creation’ of a cell vs. ‘pandoras box’)
• Uninformed, but nevertheless unsympathetic public perception

• How can these issues and upcoming ethical questions be addressed without any clear orientation available?
Classical Responsibility as a tool

Lat. re-spondere -> eng. to reply, to answer
→ answering for ones actions
→ Consequences of actions are attributed to an agent with regard to value statements (Kunzmann 2010)
  • Internally:
    • Conscience, virtues, fundamental beliefs; “acceptance of foreseeable consequences” (Weber 1946)
  • Externally:
    • Elements of the public sphere (political, legal, ethical, social and role-specific responsibility)

→ Responsibility is an at least three-dimensional relation:
  → Someone (X) is responsible for something (Y) according to an institution (Z)
Dimensions of responsibility

who
- Individuals
- corporation/institution
- society/state

for whom
- conscience
- other individuals
- groups
- court

what
- action
- omission
- result/product

what for
- foreseeable consequences
- unforeseeable consequences

why
- moral norms and values
- laws

when
- prospective
- current
- retrospective

how
- causation
- accountability
- liability

(Knoepfll 2010)
Responsibility as a general guideline

Generally, responsibility is aimed at the past. Something that has happened is attributed to an agent.

- But science is a societal endeavor supported and executed in a “sphere of trust” (EGE 2010, 37-38).
- The “sphere of trust” is trust, payed in advance, by society at large towards researchers, granting freedom of research.
- Responsibility towards the “sphere of trust” can be translated with Max Weber’s acceptance of foreseeable consequences (Max Weber 1946)
Responsibility and sphere of trust for general orientation

(Achatz/O’Malley/Kunzmann 2012)
One complex application of responsibility tools later
Use the general orientation to refine questions for each sphere

- Is it safe? Are regulations in place?
- Is it secure? Dual-use or misuse possible?
- Is it just? How are benefits and risks distributed?
- Does it promote further ethical or philosophical questions that might support their own research project?
- For researchers, shareholder, users and stakeholders
Ethics and Synthetic Biology

• Biosafety – Standards (laboratory guidelines)
• Biosecurity – Standards (dual-use, misuse)
• Justice – Law & societal consequences
  • participation – scientific, economic, political, educational
  • transparency
• Further philosophical questions: homo creator, artificial life (Achatz/O’Malley/Kunzmann 2012)
Responsibility and sphere of trust for general orientation

(Achatz/O’Malley/Kunzmann 2012)
Where to find help on ethical issues?

Your first source should always be at your institution. We would ask you to seek advice from colleagues with expertise in the ethics of research, such as:

• specialised ethics departments
• relevant managers in your university/research organisation
• hospital research ethics committees
• ethics advisers in your company
• data protection officer

(H2020 Programme, Guidance: How to complete your ethics self-assessment, Version 5.2, 12 July 2016)
Who can help answer those questions?

Local:
• Department
• University

Regional, national:
• research organizations
• National ethics councils

International, global:
• EU-regulations
• WHO
Official statements (if available) to identify conflicting issues

- DFG, Leopoldina, Acatech (Deutsche Forschungsgemeinschaft)
  - German 2009
- EKAH (Eidgenössische Ethikkommission für die Biotechnologie im Ausserhumanbereich)
  - Swiss 2010
- EGE (European group on ethics in science and new technologies)
  - European 2009
- PCSBI (Presidential Commission for the Study of Bioethical Issues)
  - American 2010 (after Venters publication in May 2010)

• SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), SCCS (Scientific Committee on Consumer Safety), SCHER (Scientific Committee on Health and Environmental Risks), Synthetic Biology I Definition, Opinion, 25 September, 2014.

• SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), SCHER (Scientific Committee on Health and Environmental Risks), SCCS (Scientific Committee on Consumer Safety), Synthetic Biology II Risk assessment methodologies and safety aspects, Opinion, May 2015.
Definition of the field

• „SynBio is the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms.“ EC Opinion 1, 2014

• „six novel SynBio developments: 1) Genetic part libraries and methods; 2) Minimal cells and designer chassis; 3) Protocells and artificial cells; 4) Xenobiology: 5) DNA synthesis and genome editing; and 6) Citizen science (Do-It-Yourself biology (DIYbio)).“ EC Opinion 2, 2015
Vielen Dank für Ihre Aufmerksamkeit!