MYCOSYNVAC

WP8 - Risk assessment, Ethics,

and Public Perception

MycoSynVac

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Summary of empirical and ethical studies in existing research

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1. Introduction

To provide a comprehensive overview of potential ethical concerns about the methods and goals of the MycoSynVac project we have, as a first approach, conducted a systematic search in relevant databases for studies relating to the project. However, it has not been possible to identify any scientific publications reporting specifically on the ethics of applying synthetic biology to develop vaccines for farm animals. To develop a solid knowledge basis for the project we have instead identified key ethical concerns raised by synthetic biology in the literature through a literature search in relevant databases (see note 1). This corpus of literature has further been supplemented with relevant papers that are referred to in these texts. As the field of synthetic biology is still young, the number of papers reporting ethical issues and empirical studies of public concerns is limited. Therefore we have chosen to draw on the considerable research experience within the research group at the University of Copenhagen in the fields of biotechnology and ethics, public perception of biotechnology and animal ethics to qualify our preliminary assessment of the public concerns and ethical issues.

Issues discussed in the literature on the ethics of synthetic biology are often divided into two main categories (Coenen 2009, Federal Ethics Committee on Non-Human Biotechnology 2010, Rheeder 2014). The first, and narrower, category relates to the balancing of the benefits and risks of the technology. The second focuses on broader issues, including the integrity of organisms modified or constructed with synthetic biology (Federal Ethics Committee on Non-Human Biotechnology 2010), the issue of the perceived “unnaturalness” or “artificialness” of the technology (Heyd 2012, Heavey 2013, Dragojlovic and Einsiedel E 2013A), and the issue of whether synthetic biology raises religious questions such as whether synthetic biology can be considered in some way to be “playing God”? (Glick 2012, Dragojlovic and Einsiedel E 2013A, Rheeder 2014). There is also some literature on the way modern biotechnology is discussed within society. Finally, and in relation to this, there is discussion of what should be considered a fair division of the benefits and risks when it comes to the development and use of synthetic biology and other forms of modern biotechnology.

Accordingly, the review is divided into four main parts.

1. Section 2) Consequences of synthetic biology, in where it is discussed the consequences of the technology, following the above mentioned distinction between narrow and broad concerns.
2. Section 3) Deliberative processes, includes a discussion of deliberative/participatory issues, identifying views on how democratic processes that relate to the development and implementation of synthetic biology should be designed to achieve social robustness and democratic legitimacy.
3. Section 4) A fair distribution of benefits and risks, addresses issues of justice and fair access to the possibilities presented by synthetic biology, and the economic context of the development and implementation of the technology.

4. Finally, in section 5) Public perceptions, a brief review of empirical studies investigating public perceptions of synthetic biology is provided.

2. Consequences of synthetic biology

This section describes the ethical issues discussed in the literature on consequences of the technology's use. These, following the literature, are divided into narrower consequences as regards risks to human health and broader consequences relating to naturalness, integrity and the question of whether synthetic biology is a case of humans "playing God".

2.1 Narrow consequences

There is general agreement that various applications of synthetic biology entail both opportunities to address problems across a range of areas and risks to humans, either directly through adverse health effects or indirectly through effects on, for example, ecosystems that are damaging to human interests. Synthetic biology allows scientists and genetic engineers to replicate and modify complex genetic pathways rather than be limited to one or a few genes. For example, some plants produce extremely desirable biomolecules that cannot be duplicated by even the most sophisticated organic chemists. By introducing the gene pathways from plants into bacteria or yeast, these biomolecules can be produced in contained fermenters. A notable success story, funded by the Gates Foundation, has enabled the production of the antimalarial drug artemisinin, using modified yeast.

Much attention is currently being devoted to finding biological alternatives to fossil fuels (especially transportation fuels) to help alleviate global climate change. Useful building blocks (complex mixes of enzymes that break down cellulose, oil-producing gene pathways) are found in nature, but first-generation genetic engineering has not been up to the task. The hope and vision is that, for example, algae that can be grown in brackish water can be used to produce biofuels usable in today's vehicles. An inventory of other proposed applications of synthetic biology can be found here: http://www.synbioproject.org/cpi/.

Microorganisms developed synthetically and designed to be released in the environment to help, for example, to clear up oil spills are at the center of one ongoing discussion of the risks and benefits of synthetic biology. In this discussion it is asked how we can combine the necessary "robustness" of the engineered organism that is necessary to sustain it long enough to achieve the desired goals with an accompanying "fragility" that ensures the organism will not continue to spread after the goal has been reached (Anderson et al., 2012).

Another issue that is often discussed is the procedural novelty of the technology. Yearley (2009) compares synthetic biology to the world of Information Technologies, where the possibility of developing and engineering new hardware and software systems outside labs or big companies, gives rise both to fruitful innovation and new problems in the shape, for example, of computer viruses. Over time the ability to develop new biological systems could extend down to the “garage” level, bringing risks not only of bioterrorism (Seumas and Selgelid 2007, Douglas and Savulescu 2010, Rager-Zisman 2012; see also Deliverable 8.4), but also of purposeful or accidental release into the environment of organisms with unwanted consequences. The latter seems to be possible at all levels of development, from the garage to the governmental lab (Balmer and Martin 2008, De Vriend 2009, Yearley 2009, The European Group on Ethics of Science and New Technologies 2009, Presidential Commission on Bioethics, 2010, Anderson et al. 2012).

This combination of risks and opportunities leads to a discussion of how to regulate an area to achieve a continued development while adhering to a cautious approach which avoids mistakes. Synthetic biology is often heralded as a technology bringing huge opportunities in a wide range of areas, from human health, to the environment, energy production, and industrial applications. Yearley (2009) points out that the more powerful a novel technology is, the more promise it holds, but at the same time the higher the risks and therefore the need for safety and regulatory standards. It is generally agreed in the literature that these standards should be based not only on expert advice, but also on broader consultations covering social and ethical issues (Balmer and Martin 2008, De Vriend 2009, Yearley 2009, The European Group on Ethics of Science and New Technologies 2009, Presidential Commission on Bioethics 2010, Anderson et al. 2012). We will return to this in section 3, but before this we want to summarize some of the broader ethical issues raised by the potential consequences of synthetic biology.

Summary

Synthetic biology – opportunities:

- Designing biological systems, e.g. plants, to produce biomolecules
- Developing alternatives to fossil fuels
- Developing bacteria to clean up oil spills
- For more, see: http://www.synbioproject.org/cpi/

Synthetic biology – risks:

- Losing control of released microorganisms
- Accidental release of microorganisms

- Biohacking
- Bioterrorism

Synthetic biology – challenges

- The greater the promise, the larger the potential risks

2.2 Broader consequences

Discussion in these areas of the literature is dominated by publications addressing the ethics of producing novel life forms – and to a lesser extent by papers asking whether synthetic biology can be said to do this. The latter question is very much a matter of how one interprets the status of the results of synthetic biology. In its 2010 report the Swiss Federal Ethics Committee on Non-Human Biotechnology distinguishes between several positions. One is the “monist” position. This sees life as a purely material thing consisting of biological mechanisms that can be re-shuffled or constructed to perform certain services. This perspective, according to the report, views life in the perspective of a “LEGO-model” and sees no reasons why it should not be possible to construct new life forms through synthetic biology. Two other perspectives that are considered are labeled “vitalism” and “dualism”. In both, life cannot be solely explained by its material components, but comprises at least one essentially unknown, non-material property, and the proponents of these views are therefore doubtful as to whether it is possible to assemble living beings from non-living biological material. The last position described in the report is the “skeptical” position. Essentially, this involves the idea that we should withhold judgment on the ability of synthetic biology to produce living organisms until more is known (Federal Ethics Committee on Non-Human Biotechnology 2010).

This discussion links to another debate in the literature regarding “artificial life”. When is something “artificial” and when it is “living”? This discussion of the status of the products of synthetic biology does not in itself entail any particular ethical judgments. Its purpose is to clarify the potential of the technology and to explain how to classify and understand the different kinds of entity. Often, however, differing views on the status of the created entities will lead to a certain view of the ethics of “creating life”. As Coenen and colleagues have pointed out, it opens up an ethical discussion of whether it is right to do this – if it is possible – and further consideration of whether there is an ethical difference between “naturally” occurring life and “artificial life” (Coenen et. al 2009).

To some observers synthetic biology is just more of the same old stuff. In this perspective synthetic biology is seen as another step along a continuing path leading from controlled breeding, to biotechnology, and on to synthetic biology. Synthetic biology is merely another tool we can use to control the biological world and utilize it for human purposes. Heyd (2012) argues that synthetic biology raises no ethical issues that have not already been raised by various kinds of biotechnology and hence should not be treated any differently, especially as the claim of synthetic biology to be able to produce “synthetic” life is not in itself an ethical issue. He argues that the distinction between “natural” and “artificial” is not in itself ethically problematic; because humans have always created things that nature could not have created (he gives, as an example, a Shakespearian sonnet). It is only from what he sees as a religious perspective that the production of life forms that nature has not itself generated, or perhaps could not even in principle generate, comes to be regarded as an ethically questionable act of “playing God” (Heyd 2012).

Discussion of the “natural” versus the “artificial” or “synthetic” resonates through the literature. As we have just mentioned, Heyd (2012) rejects the notion that the distinction is ethically relevant: the interference in natural processes might run deeper with the tools of synthetic biology, but it does not differ qualitatively from other human interventions in nature. This view is shared by others (Glick 2012, Smith 2013, Rheeder 2014B). Others, such as Preston (2008), are more critical of the aspirations of synthetic biology, seeing it as something that transgresses evolutionary borders in bringing forth new life forms. Few, however, believe that synthetic biology introduces radical new opportunities that raise unique ethical questions we have not asked before. Heavey (2013) discusses this at length and concludes, on the basis of an ethical approach focusing on how human intention matters ethically, that although synthetic biology does not raise unique questions, there is still good reason to reflect on how the aspirations of the technology touch upon questions of human dignity, the integrity of nature, and the question whether synthetic biology does in some sense involve “playing God”.

There seem to be two main concerns if one accepts that synthetic biology in some ethically relevant way interferes with the boundary between the artificial and the natural. One is based on the religious perspective that we should not “play God”. However, this term seems to be mostly used by those arguing that this complaint makes little or no sense. The religious scholars who have discussed the subject do not support such an argument. Thus from a Christian viewpoint Rheeder (2014B) invokes the image of humans as beings created in the image of God who are therefore called upon to continuously develop and create new things, while Glick (2012), arguing from a Jewish perspective, states that although in the Jewish tradition humans are bestowed with stewardship of nature, which we should preserve and nurture, not exploit and destroy, there is nothing wrong in principle with utilizing synthetic biology as long as it happens in a “weighed balance between the precautionary and the ‘proactionary’ approaches” (Glick 2012).

The other kind of concern is based on the distinction between the “natural” and the “artificial”. As already stated there seems to be agreement among most participants in the discussion that synthetic biology is not unique in this respect, but simply moves the borders a bit further than earlier technologies, such as genetic modification, have done. Whether this raises hitherto unconsidered ethical issues is, as mentioned above, a highly debatable subject.

On the critical side, Cooper (1998) states that although a novel technology may just be another straw in the bale, from the perspective of the camel with the broken back it is a crucial straw. It is in that light that discussions of whether synthetic biology constitutes a novel issue in the area of “unnaturalness” are best understood. In this vein several scholars assert that synthetic biology risks blurring the difference between the “natural” and the “artificial” (Balmer and Martin 2008, Coenen 2009, Heavey 2013). The danger pointed out concerns a change in social and cultural understandings of what “life” and “living organisms” are: there may be a move towards a more reductionist view where life simply becomes a series of building blocks that can be put together to serve human ends.

These perspectives on the technology give rise to two discussions that have already been extensively played out in the biotechnology debate. One focuses on the definition of what can be seen as “natural”, the other examines the extent to which the distinction matters ethically. In other words, if some entities or technologies can be seen as more unnatural than others, how does this constitute an ethical relevant difference? Is that which is “unnatural” ethically problematic in itself, and why?

A final ethical issue with relevance to MycoSynVac is whether the development and implementation of the technology can be said to infringe upon, or damage, the integrity or dignity of the beings involved. Whether a certain use of synthetic biology compromises the integrity or dignity of the being that the technology alters or produces, obviously hinges on whether that kind of organism is considered to have a kind of integrity. With regard to the MycoSynVac project, the question here relates first and foremost to the vaccine designed and built, and secondarily to the animals that are to be vaccinated. The words “integrity” and “dignity” are used in this context to describe a certain moral quality, or inherent value, which renders it ethically wrong or problematic to modify organisms with that value to serve human purposes. When we speak of an organism’s integrity (from the Latin integer meaning “entire”) we signify that the organism in question is whole, or complete, before humans begin tampering with it, and corresponding the worry is that the tampering, although it may enable us to add new abilities and potentials to the organism, alters something that should not be changed (Röcklinsberg et al. 2014, Cooper 1998).

In its 2010 report the Federal Ethics Committee on Non-Human Biotechnology discusses this issue briefly. The authors point out that the issue can be framed in religious terms (a theocentric position). Microorganisms can either be seen a created beings bestowed with inherent value through their createdness or as created entities that are placed at the disposal of humans as a kind of biological service and resource to be utilized for human purposes. Alternatively the issue can be framed in secular terms and seen as part of the discussion of what kinds of being that possess ethical importance in themselves (Federal Ethics Committee on Non-Human Biotechnology 2010). The positions within this discussion are typically divided into those that are anthropocentric, sentientistic, biocentric and ecocentric. Only the ecocentric position will typically see inherent value in microorganisms (Heavey 2013, Gjerris et al. 2013, chapter 4).

A further issue to analyze here is whether the animals that the vaccine developed by MycoSynVac would be inoculated with can be said to have an inherent value, and whether that value would be infringed when the vaccine is used on them. It has not been possible to find literature on this subject, but wider discussions of biotechnology used on animals serve as a starting point for such an analysis – even though most of the literature discusses this in the light of animals being directly genetically modified and/or cloned (see e.g. Coles et al. 2015, Chan 2009 and Bovenkerk et al. 2002). The UNICPH group has undertaken research into this subject before (see e.g. Gjerris et al. 2013, Gjerris 2012, Gjerris et. al 2009) and on that basis the group will develop an analysis of possible ethical issues in this area.

The debate here outlined between those who see no problem in principle in changing life and utilizing new life-forms and those who wish to develop an ethical dividing line based on notions of “naturalness” or “integrity” is ongoing. So far the former, more liberal, view has been dominant in regulation of the field.

Summary

Synthetic biology – ethical questions raised and discussed:

- Are artificial life forms genuine forms of life?
- Is there an ethically relevant difference between natural and artificial/synthetic organisms?
- Is synthetic biology transgressing ethical borders?
    - Religiously: Is the creation/production of artificial life forms a way of “playing God”?

- o Philosophically: Does the creation/production of artificial life change our understanding of the difference between the natural and the artificial?
- Does the application of synthetic biology violate the integrity of the organisms involved?
  - o Microorganisms
  - o Animals
  - o Humans

3. Deliberative processes

The US Presidential Commission on Bioethics' suggestion that five principles should guide the development of new technologies, including synthetic biology, can be seen as a summary of the many calls for a development of the technology which balances the benefits against risks and avoids mistakes. The five principles are:

1) Public beneficence
2) Responsible stewardship
3) Intellectual freedom and responsibility
4) Democratic deliberation
5) Justice and fairness

(Presidential Commission on Bioethics, 2010, pp. 4-5)

Used as guidelines for the application of new technology, these principles should enable a judgment to be reached that ensures that advantages and disadvantages of the technology are properly balanced.

The weighing of pro and cons typically takes place within a broadly utilitarian framework where the goal is to maximize what is considered "the societal good". Whereas classical utilitarianism seeks to maximize either overall welfare or (in preference-utilitarianism) the number of satisfied, informed preferences, the principles of the Presidential Committee on Bioethics have a broader aim. Thus they also refer, for example, to democratic processes and the concepts of justice and fairness (see section 4).

In this, the Presidential principles mirror principles laid down for the development of biotechnologies in general by the Universal Declaration on Bioethics and Human Rights adopted by UNESCO's General Conference in 2005 (UNESCO 2005), the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine adopted by The Council of Europe in 1997 (Council of Europe 1997), and suggestions of the European Group on Ethics expressed in 2009 (European Group of Ethics 2009).

The question of how benefits and risks posed by a technology can be balanced is one of two central questions to address in a thorough ethical evaluation. We will address it in the next section. The other question, to be addressed in this section, concerns the process through which decisions concerning new technology are made. Here there is generally a call for a deliberative process involving not just scientists with suitable expertise but also the broader public. This, it is argued, will ensure not only the democratic legitimacy of the process, but also that less quantifiable issues involving notions such as integrity, naturalness/artificiality and religious concerns are included.

What is being stressed here is that discussions of policies to guide and/or regulate the development and implementation of emerging technologies like synthetic biology should not be left to scientists and/or financial interests alone. Instead the political process should include a much wider circle of stakeholders to ensure societal legitimacy – not only because the consequences of implementing the technologies and related risks will be better understood in this way, but also because the process will be shown to be legitimate and therefore be more likely to meet with wide approval.

To some, this simply means educating the public to prevent what are seen as uninformed and exaggerated fears dominating public perceptions (Glick 2012). To others, it means developing transparent policies and including the public in the deliberation process through, for example, Citizens' Juries, public meetings and similar forums (e.g. see Presidential Commission on Bioethics 2010, European Group on Ethics of Science and New Technologies 2009 and Yearley 2009). For an example of such a process, see the report from The Royal Academy of Engineering (2008).

The demand for public inclusion in the deliberation process is not specific to synthetic biology and is often made in connection with emerging biotechnologies (e.g. see the Universal Declaration on Bioethics and Human Rights adopted by UNESCO's General Conference in 2005 (UNESCO 2005), and the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine adopted by The Council of Europe in 1997 (Council of Europe 1997)).

To date, we have been provided mainly with quantitative and qualitative studies on public perceptions of synthetic biology and some studies of stakeholder perceptions. These are more fully described in section 5. The UNICPH group has for many years worked on public perceptions of biotechnology and has analyzed different models for the inclusion of stakeholders and the public in deliberation on emerging technologies (see e.g. Nielsen et al. 2011; Nielsen et al. 2007).

On the basis of that work, together with published work on public perceptions of synthetic biology and studies of public perceptions of the MycoSynVac project, we propose both to analyze the ethical issues that are most pertinent from a societal point of view and to describe different models of a broad deliberative process.

Summary

Synthetic biology – The deliberative process

- Goal:
    - Public beneficence
    - Democratic legitimacy
- Methods
    - Include non-experts in the development of policies to ensure social legitimacy
    - Include concerns of the public in the debate
    - Suggestions for methods of inclusion, e.g. supplying information to the public and Citizens' Juries

4. A fair distribution of benefits and risks

The final area of ethical debate to be addressed in this review is the question of how the potential benefits and risks of synthetic biology should be distributed. The European Group on Ethics mentions this explicitly in its opinion on the issues of patenting, trade and global justice (The European Group on Ethics). The Presidential Commission on Bioethics discusses it at length in its 2010 report, recommending a fair distribution of risks posed by synthetic biology research so that no individuals or groups carry a heavier burden than others. The same principle should be applied to commercial use of the developed technologies, but in this area: *"Manufacturers and others seeking to use synthetic biology for commercial activities should ensure … that the important advances that may result from this research reach those individuals and populations who could most benefit from them".* (Presidential Commission on Bioethics, 2010, p. 17).

Concern about the distribution of risks and benefits can also be found in other international policy documents on emerging technologies (e.g. see UNESCO 2005 and Council of Europe 1997).

In relation to MycoSynVac, an analysis must be undertaken which evaluates the distribution of potential risks and benefits of the developed vaccines. It has been shown that the degree of public acceptance of biotechnology depends to some extent not only on the technology itself, but also on the wider context surrounding the development and introduction of the technology (Lassen & Jamison 2006).

To expand on this, it may matter who is developing and/or introducing the technology and whether the technology is perceived to be something that is being developed to benefit corporate economic interests or, for example, low-income people in the developing world. This also connects with a broader discussion of whether "special rules" should apply to emerging technologies to ensure public acceptance – the idea being that less controversial projects such as developing and selling kitchen hardware do not seem to meet with the same demands for fairness and justice and can be left to develop in accord with market imperatives.

Summary

Synthetic biology – Distribution of risks and benefits

- Many suggest that principles of justice and fairness should be included in policies on the distribution of technological advances in synthetic biology
- Should limits on the distribution of products developed through synthetic biology differ from those governing more conventional products where such distributive demands are seldom raised?
- Analysis is needed to discover how distribution issues can be integrated into the MycoSynVac project

5. Public perceptions

While no empirical studies address public perceptions of the combination of animal vaccine and synthetic biology, a few studies disclose public concerns about synthetic biology. A Eurobarometer study published in 2010 (Gaskell et al. 2010) concluded that, by and large at the time, synthetic biology was unfamiliar to non-specialist Europeans. Only 17% had heard about synthetic biology. The figures, however, varied dramatically between countries, with 30% of the Swiss population having heard about it compared to just 10% in Turkey. A later longitudinal study of the US public (Pauwels E 2013) showed increasing levels of awareness, with figures tripling from 9% who were aware of the subject in 2008 to 26% in 2010.

The Eurobarometer study further concluded that Europeans consider synthetic biology a sensitive technology calling for precaution. This is illustrated by the fact that, after they had been given a short introduction of the technology, only 3% of respondents across the European countries fully approved of it, while about 38% either disapproved or only approved under very special circumstances. Levels of approval were found to be higher in Portugal, Ireland, Spain, Romania, Estonia and Hungary, and lower in countries including Germany, Iceland, Slovenia and Austria.

Interestingly, a study based on data from this Eurobarometer survey demonstrated that there is a correlation between belief in God and a more skeptical perception of synthetic biology (Dragojlovic N and Einsiedel E 2013A). By comparison, a combined qualitative and quantitative 2010 study of the US public's view of synthetic biology (Pauwels E 2013) showed that 33% supported a ban on synthetic biology until its risks and implications are better understood. This study also demonstrated that perceptions depend on the area of application. Applications addressing societal, medicinal or sustainability issues were regarded more acceptable – a phenomenon that is well known from studies of public perceptions of genetic technologies in general (e.g. see Lassen & Jamison, 2006).

Summary

Synthetic biology – Public perceptions

- There are no specific studies on synthetic biology used to develop farm animal vaccines
- A few studies have examined general perceptions of synthetic biology
    - Technology not well known to European public
    - Only a few fully approve of technology – many call for a precautionary approach
    - Religious respondents tend to be more skeptical than those with no declared religion
    - Approval of technology is dependent on its perceived usefulness
        - applications addressing societal, medicinal or sustainability issues are regarded as more acceptable

6. Conclusion

Synthetic biology can be seen to raise a number of ethical issues. These relate both narrowly to its risks and benefits and more broadly to the uniqueness of the technology, to the difference between the artificial and the natural, and to whether the technology threatens the dignity and integrity of the entities changed/produced by it or affected by it. The deliberative process and the distribution of the technology also need further analysis.

The goal of the ethical reflections coming out of the MycoSynVac project is not to present definite answers to these difficult questions, but, through careful analysis, to show the complexity of the issues, to highlight the ethical values at stake and – through sociological research – to explain how various stakeholders perceive the issues.

Note 1. Studies reporting ethical aspects and empirical studies of public perceptions, all published between 2000 and 2015, were identified in a search in the following databases: Web of Science, Scopus and Cab Abstracts. Each search used a search string combining synonyms for animals, meat, synthetic biology, vaccine, areas of concern/consequences and perceptions. Papers disclosed by the searches were screened following examination of their abstracts. Relevant papers were then read and formed the basis of this review.

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