

SYNTHETIC BIOLOGY APPLIED IN THE AGRIFOOD SECTOR: SOCIETAL PRIORITIES AND PITFALLS

Frewer, L.J.1*, Coles, D. 1,2, Dijkstra, A.M.3, Kuznesof, S.1, Kendall, H.1, and Kaptan, G4

*Author to whom correspondence should be addressed. Lynn.Frewer@newcastle.ac.uk +44(0)1912088272

¹ Food and Society Group, AFRD, Newcastle University, Newcastle, NE1 7RU, UK.

² Centre for Professional Ethics, UCLAN School of Health Brook 317, Preston, PR1 2HE, UK.

³ Faculty of Behavioural, Management and Social Sciences, University of Twente, PO Box 217, 7500 AE Enschede, Netherlands.

⁴ Leeds University Business School, Leeds University Business School, Maurice Keyworth Building, The University of Leeds, Leeds, LS2 9JT, UK.

Abstract: Synthetic biology offers potential for innovation in the agrifood sector, although concerns have been raised consumer rejection of applications will occur similar to that associated with the introduction of genetically modified foods. Risk-benefit assessment should address socio-economic, as well as health and environmental impacts. Ethical issues may be of particular relevance to the application synthetic biology, and may also resonate with societal concerns. A case-by-case analysis of relevant issues may be needed, and innovation must be driven by societal and consumer preferences as well as technological possibilities. Research into consumer and societal priorities is required early in the innovation trajectory.

Keywords: Consumer Perception; Synthetic Biology; Agrifood; Ethics; Research and Innovation Policy.

Introduction

There has been recent discussion regarding the potential for synthetic biology applications to deliver benefits across a range of application areas, including those within the agrifood sector (e.g. Moe-Behrens et al., 2013). At the same time, the evolving regulatory and governance environment is currently shifting from one that emphasises precautionary approaches and risk avoidance, to one that encourages socially responsible research and innovation, such that science and technology is steered towards societally approved and, indeed, preferred outcomes (Douglas & Stemerding, 2014). In common with regulatory relevant elements of other enabling technologies, such as nanotechnology, there is no standardised definition of the term “synthetic biology”, (Synthetic Biology Org, 2014; Cogem, 2013; Rerimassie & Stemerding, 2012), although there is consensus that it represents the convergence of biotechnology (in particular GM [genetic modification]) and systems engineering (Andrianantoandro et al., 2006; Purnick & Weiss, 2009). A defining element which unites various definitions is that synthetic biology represents “the design and construction of novel artificial biological pathways, organisms or devices, or the redesign of existing natural biological systems” (UK Royal Society, 2014). In other words, the goal of synthetic biology is to synthesis artificial and natural components to form new artificial living systems. The

inclusion of artificial DNA in the process, as well as broad claims, including within the media that synthetic biology is “creating life” (Gibson et al., 2008), has focused societal speculation on the ethical issues associated with the technology (e.g. BBC, 2010). In practice, however, it is important to note that the potential range of applications available for use in the short term remains more prosaic (Kitney & Freemont, 2012), and it is long term future developments which are the object of speculation (Kaiser, 2012; Vincent, 2013). Indeed, Bubela et al. (2012, p.132) have noted that “maintaining the trust of the public and policy regulators is paramount...Hype and exaggerated claims are counterproductive to developing adaptive and ethically sound regulatory models responsive to stakeholder concerns”. These authors argue that developing ethical frameworks is necessary to develop public trust in regulation and governance, as well as ensuring effective application and commercialisation of products, not least within the agrifood sector.

Examples of potential areas of application to the agrifood sector

The application of synthetic biology offers considerable potential for generating innovation in the area of agricultural production and food. Potential future applications include bioremediation (e.g. see Brenner et al., 2008; Lovely, 2003),

developments of healthier foods, (e.g. though increasing the lycopene and b-carotene contents of fruit and vegetables, Fraser et al., 2009), improving food safety (e.g. through bacterial detection (OECD 7 Royal Society, 2010), the production of metabolites and health-related products such as vitamins, nutraceuticals and probiotics (e.g. see Curran and Alpes, 2012; Fraser et al., 2009; OECD & Royal Society, 2010), production of improved preservatives (OECD & Royal Society, 2010), flavours and fragrance biosensors (e.g. see Urlacher & Eiben, 2006), and food waste processing (OECD & Royal Society, 2010). Synthetic biology in some ways can be described as representing an “evolution” of GM, albeit one which is described as a convergence with engineering applications, rather than a completely novel technology. This may not align with media representations of synthetic biology, where it is sometimes represented as novel, and separate from previous technological innovations (Bubela et al., 2012).

Potential drivers of societal responses to synthetic biology applied in the agri-food sector

Societal responses to the application of synthetic biology may distinguish between “top-down” and “bottom up” applications (e.g. see Bedau et al., 2009). As is the case for the definition of synthetic biology per se, a range of definitions of what constitutes “top down” and “bottom up” synthetic biology are available. Broadly, “top down” is generally regarded as being initiated from a pre-existing natural living system which is then re-engineered to obtain a specific goal (Ro et al., 2006), through genome synthesis (e.g. Gibson et al., 2008), or genome transplantation (Lartigue et al., 2007). “Bottom up” synthetic biology attempts to develop minimal chemical cellular life (or “protocells”) from inanimate raw ingredients (Rasmussen et al., 2008). The latter is less developed scientifically compared to the former. There has been speculation that it is “bottom-up” synthetic biology which will be the primary focus of societal risk perceptions, negativity and ethical concerns (Cranor, 2009). However, while the distinction between top-down and bottom-up synthetic biology is likely to represent a relevant distinction as far as regulation, governance and ethical debate are concerned, similar differentiation in societal debate and public acceptance may be less clear-cut, as many of the same issues (for example, the creation of “artificial life”) may be perceived to be relevant in both contexts (but see Bedau et al., 2009). It should be noted that a defining factor of the “protocell” is that the chemical system can adapt to changing environments and therefore has reproductive potential (Rasmussen et al., 2009b), which in turn implies that natural selection might result in unintended, and potentially uncontrollable, new life forms. The ability of an artificial living organism to reproduce and exist outside of contained facilities may be perceived to have irreversible impacts on human and animal health, and the environment. This perception, in turn, may be associated with negative affective (or emotional) responses on the part of the public, which will result in consumer rejection of specific products. Such an effect has been observed for various potential hazards

(Slovic et al., 2004). In addition, factors such as perceptions of unnaturalness, and in some cases religious concerns, may influence societal acceptance of synthetic biology and its applications. Research has shown that these factors have been drivers of societal negativity associated with GM foods (e.g. see Frewer et al., 2013a; Gaskell et al., 1999).

As a consequence of synthetic biology both having parallels with the application of GM technology in food and agriculture, and potentially raising additional issues of societal concern, there has been speculation that synthetic biology will be associated with a similar level of societal rejection to that associated with GM technologies (e.g. see Torgersen, 2009). Within the range of areas of application of GM technologies, GM applications linked to food production are judged by society to be the most controversial (e.g. see Costa-Font et al., 2006; Dannenberg, 2009; Frewer et al., 2013a). It might therefore be expected that, in discussions regarding the potential application of synthetic biology to different areas, its application to food and agriculture might be the area of application construed most negatively by the public (Philp et al., 2013; Torgersen & Schmidt, 2013). However, it can also be argued that the GM foods controversy should not necessarily automatically be regarded as a “normative” societal response to all agrifood innovations, as context and (perceived) product characteristics have, to a large extent, shaped societal responses to GM foods (e.g. see Frewer et al., 2011; Mehta, 2004). In addition, research into people’s risk perceptions has tended to focus on high profile and dramatic potential hazards at the expense of low profile and familiar ones (Hawkes & Rowe, 2008). In reality, consumer acceptance of novel products is likely to depend on the extent to which potential consumers perceive there is a benefit associated with the new product, and the extent to which perceived benefit is weighed against perceived risk (e.g. Brown & Ping, 2003; Frewer et al. 2003; Gupta et al., 2012; Poinhos et al., accepted; Ueland et al., 2012). Both the perceived risks and perceived benefits associated with different products produced using different emerging enabling technologies is likely to vary between individuals, and will be influenced by cultural and socio-demographic factors. Socio-economic impacts (for example, negative or positive effects on employment, industrial competitiveness, or national and regional competitiveness) also need to be assessed (see e.g. Frewer, 2013b; Mora et al., 2012)

As well as making comparisons between the agrifood application of Synthetic biology and the introduction of GM foods, it is also relevant to draw a parallel with societal responses to nanotechnology (including application to agri-food production), where the lack of negative societal response has characterised early commercial introductions, despite predictions that societal rejection of nanotechnology applications would occur (Torgersen; 2009). In this case, expert concerns about negative societal responses to agrifood nanotechnology (e.g. see Gupta et al., 2013) have not been matched, to date, by concern-based societal debate (Torgersen & Schmidt, 2013; Philp et al., 2013), despite NGO opposition to agri-food nanotechnology applications (e.g. Friends of the Earth, 2014), and requirements for more rigid regulation

associated with their application (AAAS, 2014). Frewer et al. (2014) have speculated that the lack of consumer opposition to nanotechnology as currently observed may be attributable to the following. First, innovative technological innovation applied to food production per se is not societally unacceptable. Rather (perceived) characteristics of specific technologies, or their application, or how these are regulated, may potentially be drivers of societal negativity (see also Frewer et al., 2011). Second, it may be too early in the implementation trajectory for societal negativity associated with specific applications of agrifood nanotechnology to have arisen, as consumers are not familiar with either nanotechnology or its application within the areas of agriculture or the human food chain. Third, lessons from the application of GM food technologies have been implemented by regulators and industry in the case of nanotechnology, which has resulted in increased acceptance of agrifood applications by consumers (see also Gupta, 2013). These issues will now be considered in the current analysis, and recommendations for the introduction and commercialisation of synthetic biology in agrifood sector will be developed.

First, if specific characteristics of technologies applied to agriculture and food production drive consumer responses, it is important to identify what consumers perceive to be associated with both risk and benefit of different applications of emerging technologies. Other values or attitudes will also shape peoples intention to adopt specific applications. For example, the extent to which people perceive a particular product, or the technology used to produce it, to be unnatural, or have ethical concerns about technology (see Costa-Font et al., 2008; Frewer et al., 2013a). Similar concerns have not arisen in association with agrifood applications of nanotechnology per se, but appear to focus on specific areas of application. For example, the acceptability of smart pesticides is focused on the issue of pesticide use rather than the issue of nanotechnology being used to develop pesticides (Gupta, 2013). The area of application should be considered when introducing the initial applications of agrifood synthetic biology, to ensure that these early applications deliver concrete and tangible benefits, in which the benefits perceived to be available to (at least some) consumers outweigh perceived risks. This raises the question of whether high levels of risk perception associated with GM was driven by concerns related to (for example) irreversibility of negative biological effects once released into the environment, such as the ability to confer “unnatural” traits on “descendant” organisms (Torgersen, 2009; Frewer et al., 2011). In comparison, nanotechnology may be perceived to be less uncontrollable and potentially amenable to mitigation strategies should problems occur. It might be predicted that synthetic biology will be perceived as being more similar to GM than to nanotechnology, given that living organisms are being manipulated (Bubela et al., 2012; Pauwels, 2013).

The second argument, that it is too early in the implementation trajectory for consumer attitudes towards specific applications of both agrifood nanotechnology and synthetic biology to have crystallized, is potentially

valid (Frewer et al., 2014). However, given that labelled nanotechnology consumer products are apparently accepted by many consumers who use them (e.g. in the cosmetics sector, DeLouise, 2012), it is reasonable to posit that societal rejection of nanotechnology per se will not occur. It is important to note that there has not been the same level of media coverage of either nanotechnology or synthetic biology applied to agrifood production when compared to the levels of media attention associated with GM foods (e.g. see Pidgeon et al., 2003; Frewer et al., 2002; Pauwels & Ifrim (2008), or even nanotechnology (Scheufele, et al., 2007). The occurrence of a negative, high profile media associated with a specific enabling technology might ignite societal controversy if it has extensive media coverage (Gupta et al., accepted). It is suggested that synthetic biology may be particularly prone to sensational media reporting, as previously discussed.

The third argument, that lessons learned from the commercialisation of agrifood GM have been applied to the introduction of nanotechnology, and may potentially be applied to synthetic biology, is also worthy of further consideration. The introduction of GM foods was not shaped by information about societal requirements for technological implementation, but rather driven by technological possibilities. However, the 21st century has witnessed the introduction of various policy changes associated with technological innovation which have built on, and attempted to remediate, the barriers to agrifood technology implementation associated with the latter part of the 20th century. For example, the need to assess socio-economic and ethical impacts associated with different applications of enabling technologies has been recognised by various researchers and is frequently embedded in policy (e.g. Rerimassie & Stemerding, 2012). The need for effective stakeholder, expert and public inputs into the research and development, commercialisation and policy process has also been identified as a factor facilitating acceptance of technology applications (e.g. Powell & Colin, 2008; Renn & Roco, 2006). More recently, there has been a greater likelihood of public engagement being applied prior to technological introductions, rather than subsequent to their application (MacNaghten, et al., 2005; Delgado et al., 2011). The consideration of a broader range of expertise in assessing different policy options might lead to better outcomes as more evidence (lay knowledge, perceptions, and preferences) is considered formally as part of decision-making (Reed 2008; Renn & Roco, 2006). For example, nanotechnology was successfully introduced to the public through a number of participatory events, which addressed concerns and problems raised by both experts and ordinary citizens (Torgersen & Schmidt 2013). Thus, public engagement can provide a route to enhance mutual understanding of technological issues, uncertainties associated with risk and benefit assessments, as well as value differences in different stakeholder constituencies (Dietz, 2012).

However, public engagement is unlikely to build societal trust in technology development and implementation if the outputs of such exercises do not make a discernable impact on policy in policy, regulation, and even product design. The lack

of policy impact associated with public engagement has indeed been recognised as problematic (Emery et al., , in press; PytlikZillig and Tomkins, 2011). Others (e.g. Kenyon, 2005) have noted the lack of generalizability of results from specific engagement exercises, which tend to focus on limited areas of application, across a broad policy issue. It is important to balance the interest and values of all relevant stakeholders (Hermans et al., 2012), and develop methods to assure timely incorporation of stakeholder perspectives into the decision-making process associated with synthetic biology policy development (OECD & Royal Society, 2010).

Ethical issues

As for other technologies, (see, for example, Coles & Frewer, 2013; Jensen et al., 2011), it is possible to identify generic and specific ethical issues which may influence both the technological development and commercialisation trajectories associated with synthetic biology. For example, the application of an Ethical Matrix analysis (Mepham, 2000) to synthetic biology applied to food production would enable a range of ethical issues to be assessed against the needs of different stakeholder groups, including basic scientists, technology developers, industry, consumers, and the environment. Very broadly, the ethical principles of autonomy (“self-determination”), non-maleficence (to “do no harm”), beneficence (“do good”) and justice (“fairness”) can be applied to different stakeholders. While this has limitations in analysing and weighing the ethical issues associated with a technology, it is helpful in identifying the types of issues that may need to be considered (Schroeder & Palmer, 2003). Synthetic biology may raise specific issues intrinsically related to the characteristics of synthetic biology (Deplazes-Zemp, 2012), insomuch as the design and synthesis of living organisms may lead to specific responsibilities on the part of scientists regarding the products they are developing. It may therefore be important to take these concerns into discussions regarding science and technology policies, possibly as a formal part of the analysis which precedes the enactment of regulation.

Regulatory issues

Synthetic biology, as for other areas of biotechnology, may have both positive and negative impacts, depending on how it is applied, and societal judgements of what constitutes positive or negative application. It has been argued that the current framework for regulation of laboratory research and development of commercial biotechnology products can serve as a basis for regulation of synthetic biology (see, *inter alia*, Erickson et al., 2011; Rerimassie & Stemerding, 2012). However, inter-regional differences in regulatory application have been associated with the regulation of biotechnology, in particular GM technologies (Vázquez-Salat et al., 2012), which have not facilitated societal trust in the regulatory process (Frewer et al., 2013b). In addition, some of the ethical issues associated with the development of artificial,

self-producing organisms may entail formal additional ethical assessment as part of the risk analysis process which informs regulatory decision-making and governance practices.

Consumer research

Published research in this area is sparse, which may reflect the fact that technological developments are comparatively recent. Given that biotechnology may represent an important benchmark against which synthetic biology is being evaluated by the public (Kronberger et al., 2009), one might predict similar societal concerns to arise in the agrifood sector. Pauwels (2009) notes that, the participants in their US study reported being unfamiliar with synthetic biology and its applications, their perceptions and related attitudes were framed by those they already held about existing biotechnologies such as GM and cloning (Pauwels, 2013). Furthermore, participants were positive about synthetic biology applications when these addressed societal, medical, and sustainability needs. Similarly, concerns arose if credible assessments of potential risks, uncertainties associated with these, and long-term implications were not made. Transparency and accountability through “tailored governance” (i.e. governance focused on specific issues associated with synthetic biology, in particular risks, benefits, and ethical issues) was required by participants. Ethical or moral impacts associated with the technology and its applications were reported as relevant in several studies. For example, research using Malaysian stakeholders (Amin et al., 2011) has identified ethical concerns to be associated with genetically modified (GM) rice which contains a synthetic mouse gene to increase its vitamin C content. At the same time, the loss of benefits from not developing the application were perceived to be inconsequential.

In summary, various questions need to be asked of synthetic biology prior to, and during, the commercialisation process associated with the agrifood sector. These are similar to those applied in other sectors although some issues specific to synthetic biology can be identified.

- Do the applications to the agrifood sector meet a recognised societal need? (see also Gupta et al., 2012)
- Can similarities between synthetic biology applied in the agrifood sector, and potentially societally controversial aspects of previously applied agrifood technologies be identified? (see also Frewer et al., 2011; 2014).
- Is agrifood application of the technology differently perceived by the public to other areas of application, such as pharmaceutical application? (Frewer et al., 2013a). In other words, is it the area of application, rather than the technology per se, which is associated with societal negativity? (Gupta et al., accepted).
- Are alternative, less controversial, technological approaches, which have potential to deliver the same benefits, identifiable? (Gupta et al., 2013).
- Are additional issues raised over and above those associated with other enabling technologies applied to food production? For example, are there specific ethical issues associated with synthetic biology which are not as-

sociated with the application of nanotechnology? (e.g. see Cranor, 2009).

- If the technology is, in itself, acceptable to society, what needs to be done to “fine tune” the development and implementation of agrifood applications of synthetic biology to align with consumer priorities for commercialisation of specific applications? (e.g. see Raley et al., submitted).
- Are there specific features of the regulatory framework which are required to ensure societal acceptance of specific applications (for example, formal and institutionalised ethical analysis and socioeconomic impact analysis)? (e.g. see Bubela et al., 2012).

An important part of implementing a societally acceptable development and commercialisation trajectory in particular in relation to synthetic biology applications which are potentially societally controversial (for example, application in the agrifood sector), will require inclusion of societal priorities and preferences for specific benefits to be included in the design of new applications. There are many ways to collate this information. Examples include public engagement regarding the development, implementation and governance of the technology during development, and qualitative and quantitative consumer research which can be applied to “fine-tuning the characteristics of specific applications. This will require closer engagement and communication between scientists, technologists and those with expertise in assessing societal and consumer preferences and priorities for technology and product design. In terms of regulation and governance, it is important to ensure that the outputs of public engagement are explicitly addressed in the development of regulatory and governance strategies if social trust in these is to be developed and maintained. In terms of the development of concrete products, research has suggested that the need to consider information regarding societal and consumer preferences would be most relevant prior to new product development and prior to any marketing activities being operationalized, as there is still time to alter the design and delivery of novel foods and processes. It may also be important to assess consumer responses to the first generation of synthetic biology products developed, in order to predict what features of second generation products are most likely to be successful. In other words, it is important to understand what applications are most wanted by consumers, and which are unacceptable. This could contribute to an application based risk(benefit) framework, The development of these principles is a consequence of lesson from the GM debate, and can be adapted to take account of specific characteristics of synthetic biology. This speaks to the third question identified in the introduction, namely that “lessons from the application of GM food technologies have been implemented in the case of nanotechnology, which can subsequently be applied to agrifood applications of synthetic biology”. Synthetic biology may be regarded as an acceptable technology by society, if appropriate societal benefits are delivered from its application, ethical issues are addressed, and transparent regulatory and governance structures are constructed. Rather than it being

“too early” in the process of synthetic biology development for public opinions and attitudes to crystallise, we suggest that this is the most appropriate point in the development trajectory to utilise public and consumer information in the development and design of agrifood synthetic biology applications.

Conclusions

The successful implementation of synthetic biology in the agrifood sector will be contingent on various factors. These include the development applications (in particular first generation consumer products) that society and consumers want, and regard as safe. Given the potentially diverse range of applications, assessment of societal and consumer priorities need to be on a case by case basis. Risk-benefit assessment should be an integral part of governance, and address socioeconomic impacts as well as health and environmental effects. Ethical issues may be of particular relevance to the application of synthetic biology, and may also resonate with societal concerns. Again a case-by-case analysis of relevant risk and ethical issues may be needed. Societal and consumer acceptance of agrifood applications of synthetic biology is likely to be driven by perceptions that applications are needed, but hindered by lack of public debate about risk, benefit and unintended effects, and the failure to establish and adequate regulatory framework to promote consumer and environmental protection.

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