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Science & Society

Synthetic Biology R&D Risks: Social–Institutional Contexts Matter!

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Factors that shape actual research practices – 'social and institutional context' – typically are missing from considerations of synthetic biology R&D-related risk and containment. We argue that analyzing context is essential in identifying circumstances that create, amplify, or diminish risk, and in revealing new opportunities for avoiding or managing those risks.

Synthetic biology is among the suite of emerging technologies that offer the promise of transformative science and tremendous societal benefit. . .but also potential peril. Numerous publications address risk and containment issues associated with synthetic biology. This article focuses on synthetic biology R&D and suggests that there is a gap in the synthetic biology risk-related literature. That gap is behavioral. In R&D settings, research practices constitute behavioral translations of many factors into real-world actions. We argue that attention to factors that influence behavior, which we label 'social and institutional context,' augment current considerations of synthetic biology risk and containment in important ways.

Broadly, social and institutional context encompasses the settings in which people interact and how behavior is shaped by formal and informal rules and ways of operating. In synthetic biology R&D, rules and standard practices are influenced by such factors as scientists' research organizations, laboratory or field procedures, disciplinary training, roles and responsibilities, and professional ambitions. We highlight 'normal' research contexts, not deliberate attempts to use organisms for nefarious purposes. Analyzing social and institutional context offers the possibility of detecting otherwise overlooked circumstances that create, amplify, or diminish risk during R&D, and of avoiding research practices that inadvertently may increase risks.

Our arguments are germane to many emerging technologies; it is important to apply them to synthetic biology now for three main reasons. First, synthetic biology is evolving rapidly, and understanding inadvertent gaps can have a particularly strong impact at early phases of R&D [1]. Second, synthetic biology experimentation increasingly is being conducted outside traditional research organizations. Third, current renewed attention to biotechnology-related biosafety and regulation [2,3] may benefit from considerations of social and institutional factors that shape behavior.

Synthetic biology has multiple definitions and is viewed differently across disciplines (Box 1). These differences may influence perspectives about the degree to which synthetic biology is an extension of traditional genetic engineering versus something new and, perhaps, perspectives about potential human health and environmental risks. Regardless, synthetic biology is distinctive in: (i) its application of engineering principles such as standardization and modularity to design and compartmentalize biological processes [4]; (ii) the scale of modification, often involving the insertion or replacement of long strands of DNA or metabolic pathways; and (iii) large, explicit efforts to engage students and individuals who are not science professionals, most notably through the annual iGEM (International Genetically Engineered Machine) Competition (http://igem.org).

The summary of risk-related synthetic biology literature in this article demonstrates that the distinctive elements of synthetic biology already have spurred considerable attention to their potential human health and environmental consequences. Moreover, new gene editing techniques (e.g., clustered regularly interspaced short palindromic repeats, CRISPR), although not exclusive to synthetic biology R&D, seem to be catalyzing many pertinent considerations of human health and environmental risks

Box 1. What is Synthetic Biology?

'Synthetic biology' has multiple definitions. A widely used definition is:

'...the design and construction of new biological entities such as enzymes, genetic circuits, and cells or the redesign of existing biological systems.' (http://www.synberc.org/what-is-synbio)

However, synthetic biology is thought of differently from biological, chemical, and engineering perspectives [4,6]. The extent to which these perspectives are associated with differing risk- and containment-related conceptions and practices could be a topic of future empirical inquiry.

Biological

'for biologists, the ability to design and construct synthetic biological systems provides a direct and compelling method for testing our current understanding of natural biological systems.' [4]

Chemical

'synthetic biology is a tool for manufacturing novel molecules and molecular systems for various uses.' [6]

Engineering

'for engineers, biology is a technology; building upon past work in genetic engineering, synthetic biology seeks to combine a broad expansion of biotechnology applications with...an emphasis on the development of foundational technologies that make the design and construction of engineered biological systems easier.' [2]

[5]. The single gene changes associated with traditional genetic engineering seem dwarfed by the extensiveness of modification in (multiple) biological components and processes now possible, and by the potential perpetuation of modifications achieved through gene editing. The complexity, scale, and temporal reach of modifications may render existing risk- and containment-related assessments and practices inadequate.

We categorize the literature as taking one of three predominant orientations toward risk and containment – bioethical, governance, or technical. Differences in orientation are consequential; they embody different ways of thinking about synthetic biology-related risks and produce different types of recommendations (Table 1).

Literature Orientations

We see the three existing orientations – and the fourth that we propose – as complementing, not competing, with one another. Table 1 introduces how a behavior-focused social and institutional orientation could augment considerations of synthetic biology risk and containment. Note that much of the risk-related synthetic biology literature references social and institutional elements such as biosafety committees and formal rules or guidance, but typically not in terms of how those elements translate into practice.

Literature associated with a bioethics orientation [1,6,7] address social and ethical concerns and principles. For instance, the 2010 Presidential Commission for the Study of Bioethical Issues report espoused five ethical principles to understand the social implications of synthetic biology: public beneficence, responsible stewardship, intellectual freedom and responsibility, democratic deliberation, and justice and fairness [6]. However, recommendations for action in the bioethics literature are relatively broad-brush, for example, calling for risk assessments, and proper containment to prevent escape, but not specifying which elements should be assessed to prevent those risks. Authors discuss safeguards, but not how safeguards should be implemented in practice.

Governance-oriented literature focuses on policies and regulations for synthetic biology and contrasts among different

Table 1. Overview of Risk-Related Orientations Toward Synthetic Biology in the Literature

Orientation	Orientation is Characterized by a Focus on:	Literature Tends to Emphasize:	Illustrative Recommendations:	Illustrative Refs:
Bioethics	Normative, broad perspectives on synthetic biology risk and containment	• Underlying principles • Recommendations for action	• Conduct risk assessments prior to field releases • Review and identify reliable safeguards	[1,6,7]
Governance	Policies, regulations, and procedures	• Points of intervention; policy options; 'desirability criteria' • Structuring policies, regulations, procedures • Insufficient knowledge • Accidental/deliberate releases	• Develop standardized procedures and practices • Balance interests of relevant stakeholders	[8,9]
Technical	Types of harm that could result from synthetic or redesigned organisms	• Toxicological or ecological impacts • Commercial-scale production or use • Biosecurity or dual use	• Engineer biocontainment • Share best practices among research community	[10,11]
Social and Institutional[a]	Conditions that inadvertently create or increase risks in practice	Our proposed emphases: • Context elements • 'Normal' practices/behaviors • Alignment among formal/informal risk-related guidance	Could include: • Create guidelines tailored to different disciplines • Encourage consistent research practices across institutions	Literature gap

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