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# Commentary on Synthetic Biology: Policy, Society & Systems

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## Introduction

Beyond the technical challenges associated with synthetic biology, there are a number of associated challenges ranging from societal acceptance and coherent policy design, to legal and ethical issues [1,2]. Although synthetic biology holds tremendous promise, these areas merit proactive consideration given the potential risks and uncertainties posed by an emerging technology with such broad impact on society. The objective of this short report is to highlight primary social and policy domains that should be part of the early focus. Frameworks and recommendations for pursuing solutions in these areas have been proposed. The underlying theme of this commentary is to draw attention to a co-evolutionary approach that would enable policy institutions to evolve in step with increasing complexity and penetration of synthetic biology products. The primary message is based on the following thrusts:

1. Understanding the Technology Evolution Framework: *technical hierarchy*.
2. Adopting a Flexible Policy Design approach: *proactively keeping pace with technology.*
3. Promoting a Systems Innovation Perspective: *including social elements.*

Each of these is discussed below.

## Understanding the Technology Evolution Framework

The technology evolution framework can be analyzed based on a progressive classification hierarchy proposed for synthetic biology products [1]. In addition to the increasing complexity in this hierarchy, there is also an element of time (evolutionary aspect) as each of these layers builds upon underlying layers (Figure 1). This framework can be considered to be complementary to other approaches that address the increasing complexity of Synthetic Biology creations (for example, http://parts.mit.edu).

*Synthetic Elements*: "At the most basic level, synthetic elements are the fundamental building-blocks that provide primitive functionality. Analogous to switches, oscillators, flip-flops etc. in the electronics world, these would represent the equivalent of off-the-shelf components. The level of integration would vary somewhat (switch versus flip-flop). However, the basic attribute is a primitive function with a modular implementation. An example of a synthetic element would be the genetic toggle switch or genetic oscillator mentioned earlier in this article. Other entities of this classification system would be composed of such elements at the basic modular level." [1]. Additionally, synthetic sequence construction can be classified to belong to this level.

*Synthetic Networks*: "Synthetic networks are composed of interacting components that are individual synthetic elements. The added complexity is achieved via mechanisms to enable communications between these elements. An example of a synthetic network would be a regulatory network of synthetic genes and promoters designed to induce transcription under certain deterministic external stimulus." [1]

*Synthetic Organisms*: "Synthetic organisms are the result of synthetic assembly of complete or minimal genomes (set of genes critical for survival) of an organism. These genomes would most likely be substituted in place of an existing genome in a favorable cellular environment. In addition to the artificial genome, the synthetic organism could contain synthetic networks and synthetic elements. Examples of success in creating synthetic genomes include creation of an artificial genome of the Polio virus (which can infect living tissue) and the artificial minimal genome of a bacteriophage." [1]

*Synthetic Systems*: "The ultimate goal of synthetic biology would be to design synthetic systems composed of multiple synthetic organisms working synchronously to achieve a complex objective. One of the major hurdles to this task would be to design a robust communication system between component organisms." [1]

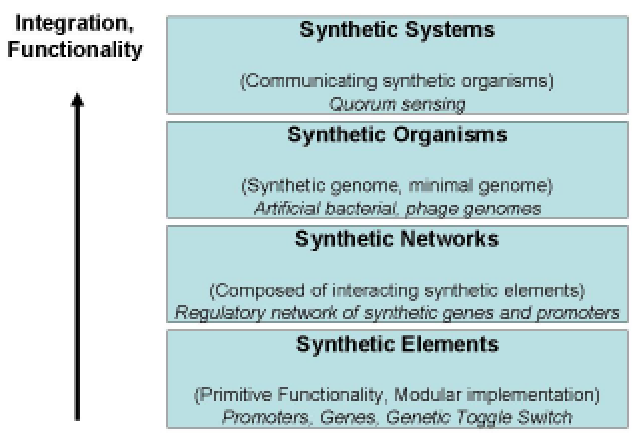


**Figure 1**: Classification hierarchy for the evolution of Synthetic Biology products. Increasing time and complexity results in greater integration and functionality upwards in the hierarchy. (the reader is referred to [1] for a detailed discussion).

## Adopting a Flexible Policy Design approach

In contrast to static policy recommendations for emerging technologies, a flexible approach in step with technological advances is proposed. In the context of the synthetic biology technology evolution framework (Figure 1), this means adapting policy instruments to suit the specific needs of various levels of the hierarchy. Three areas relevant to policy design and social acceptance were analyzed in detail in [1]: *Patentability*, *Ethics*, and *Regulation* (the reader is referred to [1] for a detailed discussion of the challenges, proposed frameworks, and recommendations for each area). Figure 2 shows how these policy recommendations relate to various levels of the technology hierarchy. Some, for example regulatory requirements of a "defined lifespan outside controlled conditions", are applicable to the third and fourth levels in the hierarchy (synthetic organisms and systems) while others like a well-characterized "disable signal" might dominate at lower levels (ensuring a built-in feature at the most elementary level). This is but a peek into the different policy dimensions. The primary message is to promote a flexible approach to synthetic biology policy design that adapts to evolving needs of the technology.

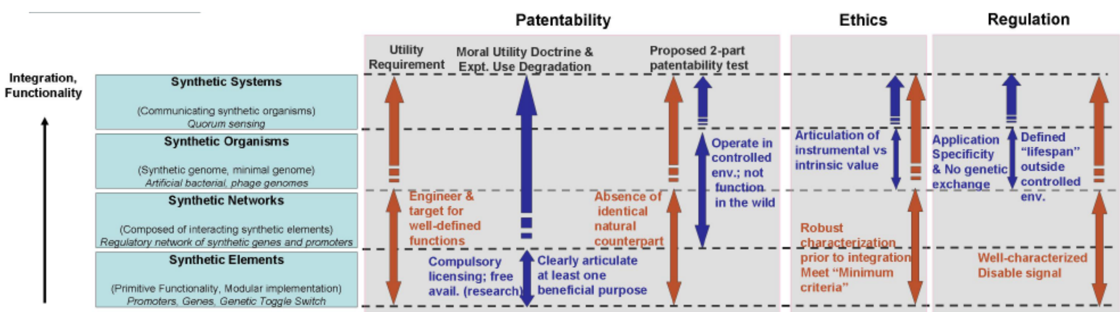


**Figure 2**: Exploring the impact of flexible policy design in the context of the Synthetic Biology product classification hierarchy (the reader is referred to [1] for a detailed discussion).

## Promoting a Systems Innovation Perspective

An "innovation systems map" [3-6] identifies the primary actors and networks (or simply put, influence pathways) in a specific innovation system. For technologies such as synthetic biology, such a map can be constructed (Figure 3) to initiate a systems based discussion (the reader is referred to [7] for a more thorough discussion). This map includes *policy making entities, technical advancement entities, market elements and* *societal connections*. Additionally, vectors related to public perception, market stimulation and global coordination can be studied in the context of such a framework.

Primary entities include policy making bodies (International governments, EU, their regulatory arms and Intellectual Property Rights management bodies), research and commercial entities involved in pushing the technology to new heights, market entities responsible for overall market pull, funding entities (other than the government) that act as facilitators in the process, and the *society at large which influences constraints placed on the types of research and the kinds of products developed*.

The links between these entities represent a network which tracks the key channels of influence between these entities. Some of the annotation in figure 3 highlights issues and success factors important in the context of Synthetic Biology. Various points of systems failure and risk can be identified in this network.

For Synthetic Biology, environmental risk and safety risks are primary considerations that should be studied in the context of this systems framework [7]. Primary bio-safety risks were identified in [1]:

- Risk of negative environmental impact
- Risk of natural genome pool contamination
- Run-off risk

Each of these deserves a detailed analysis within such a systems framework to understand the control levers and failure points, in order to tune policy instruments.

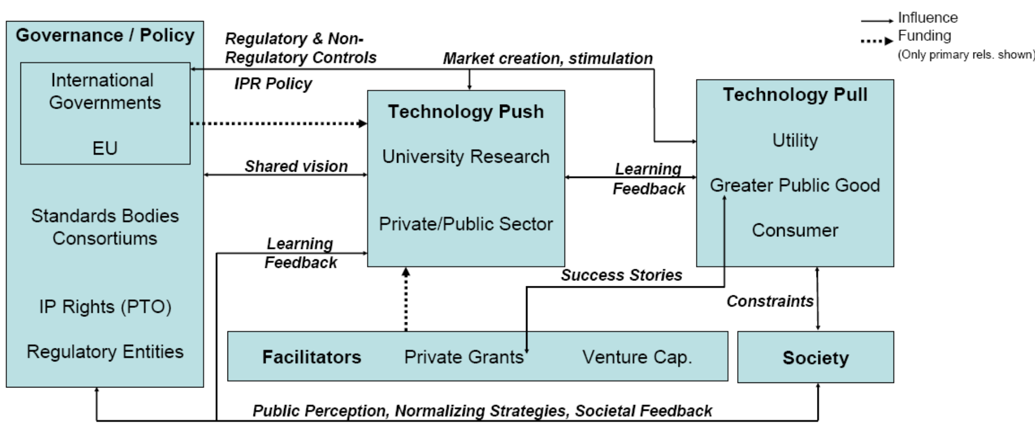


**Figure 3**: A *preliminary* “innovation systems map” showing primary entities and networks (channels of influence) important in the context of technologies like Synthetic Biology (the reader is referred to [7] for a detailed discussion). Comments along network arrows highlight some of the important issues and success factors in this context. Key elements of risk and points of systems failure can also be identified at various locations along this network. Appropriate mitigation strategies can then be proposed.

## Conclusion

Social and policy dimensions of synthetic biology deserve early attention to keep pace with rapid advances in technology. There is a unique opportunity to be realized by early engagement in order to promote rapid diffusion of the technology. It is proposed that flexibility and adaptability of policy instruments in the social and technical contexts be desirable characteristics of any such endeavor.

## References

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