# SB 3.0 Biosecurity Presentation by G. Mukunda and S.C. Mohr (6/25/07)
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## Introduction

Synthetic Biology and DNA Synthesis have already been the subject of security concerns. **[Slide 2]** Focusing on the differentials over traditional genetic engineering introduced by Synthesis and those introduced by Synthetic Biology, we sought to analyze key security issues that might be raised by developments in both fields. We combined interviews with leading Synthetic Biologists and experts in biosecurity with the literature on biological weapons. Previous research on the impact of biotechnology on biological weapons has usually predicted a steady increase in the threat from state and non-state actors. **[Slide 3]** DNA synthesis and Synthetic Biology, however, because of their unique combination of rapid technological progress and radically new approaches to the manipulation of organisms, may invalidate these earlier analyses.

Defining short term as the next 5 years and medium term as the next 5 to 10, we found that Synthesis and Synthetic Biology are likely to have significant effects in the medium term, ranging from a rapid diffusion of capabilities, to a radical increase in the uncertainty and unpredictability of the threat environment, requiring new responses from the scientific and policy communities.

Interest in biological weapons is real. **[Slide 4]** At least ten countries are believed to have offensive programs, and many others have defensive ones. States have been unwilling to use biological weapons for reasons including the repugnance they inspire and governments' belief that conventional and nuclear weapons are more reliable. Terrorist groups have repeatedly attempted to acquire and use biological weapons, but so far without success.

Scott will now talk about examples of current benign Synthetic Biology research that potentially has mixed applications.

## Sample Multi-Use Syn Bio Research Projects

As a biochemist, I was reluctant to think about ways that life sciences could be misused. After a while, however, I realized that thinking about the unthinkable may be the only way to prevent it. Even Synthetic Biology research conducted for completely benign purposes may have significant security implications.

**[Slide 5]** For example, invasin, an outer-membrane protein of *Yersina pseudotuberculosis*, allows bacteria that express it to invade mammalian cells. By installing the *inv* gene in non-pathogenic *E. coli* strains under the control of quorum- and oxygen-sensing regulatory circuits, synthetic biologists have produced a vehicle to carry toxin-producing genes into tumor cells. **[Trigger animation]** Could minor modifications of this system produce a novel pathogen? Would presently existing surveillance systems detect it?

**[Slide 6]** Type III secretion systems employed by many pathogens can deliver toxic proteins to mammalian host cells. These devices have recently been used to facilitate export of genetically engineered proteins (*e.g.,* spider silk). **[Trigger animation]** Could they be used to create, from a harmless organism, engineered pathogens that would not elicit a strong immune response?

**[Slide 7]** Work about to be published demonstrates the separate transfer of several different genes into mammalian cells in culture and their controlled expression in response to external signals. In two cases these genes are toxic and kill the cells. The researchers are now testing the system in mice. **[Trigger animation]**

It's important to also consider the potential contributions of synthetic biology to biodefense. **[Slide 8]** A number of different defense-related projects are well-developed, including some carried out by iGEM teams over very short time frames. An arsenic sensor that can be applied under field conditions surely bodes well for designing systems to detect pathogens. Metabolic engineers have turned to drug production and their work should afford an opportunity to rapidly generate antibiotic variants. Finally, last year's winning iGEM project from Slovenia, presented here yesterday, demonstrated the potential feasibility of an engineered therapy for sepsis, a common component of bacterial infections. These are still preliminary results, but nevertheless they justify optimism that synthetic biology will lead to an era where powerful defensive tools can be developed much more rapidly than now.

Gautam will now speak about the implications of such research and suggest steps that we recommend to governments and the scientific community.

## Implications of DNA Synthesis and Synthetic Biology

We highlight 5 specific near and middle term impacts. **[Slide 9]** First, as in the Sloan Report, we believe that both synthesis and Synthetic Biology are unlikely to have short-term effects on security. At present it is still more difficult to synthesize a pathogen than to acquire it from nature. Once a genome has been synthesized, transforming it into a live agent requires considerable skill, with assessments on the difficulty of doing so varying widely. Similarly, there are currently relatively few well-characterized Synthetic Biology parts, and Synthetic Biology skills remain concentrated, making them less useful and less available to potential attackers.

Second, medium-term security implications are likely to be considerably larger. The overall impact is uncertain but, in the medium term, DNA synthesis and Synthetic Biology will probably help attackers more than defenders.

**[Slide 10] [Trigger Animation]** Synthetic Biology seems likely to help defenders build effective biosensors and produce difficult-to-manufacture therapeutics and vaccines. It may also help in their discovery and development. **[Trigger animation]** Defense against biological weapons is extremely time-critical and presents significant technical problems, however, so **[Trigger animation]** even the most optimistic proponents of Synthetic Biology doubt that it will, in the medium term, shorten new drug and vaccine development times enough to aid those defending against an attack.

**[Slide 11]** Attackers may benefit more in the medium term. **[Trigger animation]** DNA synthesis may make it possible to launch attacks with currently unobtainable agents. **[Trigger animation]** Synthetic Biology may make it easier for attackers to engineer agents from normally harmless viruses and bacteria, evading traditional defenses, or to modify already existing agents to make them more useful.

**[Slide 12]** Third, DNA synthesis and Synthetic Biology are likely to substantially increase two types of diffusion of capabilities. They may allow actors – like terrorists - currently unable to acquire biological weapons to do so, and they may decrease the differential in capabilities between leading practitioners and those who are trailing in the field. Both outcomes are enabled by Synthetic Biology's emphasis on the transformation of tacit to explicit knowledge. Traditional biotechnology, because of its high tacit knowledge component, requires extended “apprenticeships” and is thus characterized by slow diffusion of skills. Synthetic Biology, however, promises to make it easier for less skilled scientists and engineers to manipulate organisms, allowing trailing scientists to more easily duplicate the work of leaders in the field.

**[Slide 13]** Fourth, Synthetic Biology might weaken norms against biological weapons. **[Trigger animation]** The United States unilaterally ended its offensive bioweapons program in 1969 in part because it felt that such weapons were not useful. The USSR, disagreeing with this assessment, employed more than 50,000 people in its offensive bioweapons program despite signing the Biological Weapons Convention. **[Trigger animation]** If the utility of bioweapons improves, states will be increasingly tempted to research and use both them and defenses against them. Familiarity with such weapons, however, will weaken the taboo against them. American biodefense efforts, prompted in part by fears of the impact of progress in biotechnology, may already have had such an effect.

**[Slide 14]** Fifth, Synthetic Biology seems likely to substantially increase the uncertainties facing scientists and policymakers. Because of its focus on components and easily assembled parts, Synthetic Biology may foster interactions with discoveries from outside the field. For example: SynBERC proposes the creation of tumor-killing bacteria. To be effective, such bacteria must not trigger the immune system. Thus SynBERC must build a chassis invisible to human immune systems. Suppose that, at some time in the next 15 years, neurochemists identify a hormone which, when present in the brain at certain levels, puts people to sleep. Suppose additionally that pharmaceutical companies, while attempting to improve drug-delivery systems, discover reliable ways to penetrate the blood-brain barrier. Each of these developments is both plausible and laudable. Combined, they could make possible a non-lethal bioweapon that puts its targets to sleep. This sort of development is inherently unpredictable, because few if any people have sufficient expertise in all of the fields that might interact with Synthetic Biology to foresee such an outcome. Synthetic Biology might thus potentially enable rapid and unexpected changes in both offense and defense.

## Policy Proposals

We suggest three proposals to mitigate potential threats from advances in DNA synthesis and Synthetic Biology and enhance their contributions to defenses against both natural and artificial biothreats, beginning with a development of ideas in the Sloan report and building to proposals focused primarily on Synthetic Biology.

**[Slide 15]**First, future security regimes must adapt to the currently uncertain economies of scale in synthesis. **[Trigger animation]** If they are high synthesis is likely to be centralized. In that case an intensive surveillance system should be created, with synthesized genomes subject to software checks. A prize regime could encourage synthetic biologists to identify potential holes in the screening system. A buyer's cartel could refuse to purchase from companies that do not screen adequately. The creation of a central database tracking genome purchases would prevent buyers from assembling hazardous genomes by purchasing innocuous parts from several suppliers. **[Trigger animation]** If economies of scale are low we should expect distributed synthesis, which will be difficult to monitor through centralized surveillance. A garage biohacker culture may arise, making peer monitoring less effective and perhaps requiring a more intrusive inspection regime.

**[Slide 16]** Second, scientists and policymakers should strengthen community norms. **[Trigger animation]** We suggest the creation of an international Synthetic Biology Society with annual meetings and a code of conduct. Synthetic Biology should adopt the concept of a "safety hold" from aviation, in which any person involved in a project, no matter how junior, can freeze activity by expressing safety concerns. Despite the natural reluctance to be suspicious of fellow scientists, the Synthetic Biology community must also accept the fact that its innovations may be used maliciously and realize that it may even sometimes be necessary to alert authorities about suspicious behaviors. The society should seek to inculcate the norm that professors in the field keep track of the activities of both their current and former researchers, and these people should monitor each other's activities as well. A community will also provide scientists asked to work on offensive programs back channels through which they can alert the outside world.

**[Trigger animation]** Policymakers should return to the commitment the United States made during the 1970s to conduct as much biodefense research as possible in the open by declassifying as much research as possible and ensuring that all BL4 labs are on open campuses, even if the labs themselves are closed. Policymakers should also seek to make the production or use of biological weapons a crime under international criminal law.

**[Slide 17]** **[Trigger animation]** Third, Synthetic Biology's has the potential to revolutionize biodefense, but to do so it will need to be closely tied to its sister fields and better understand the obstacles to the development of treatments. **[Trigger animation]** We suggest the creation of a standing committee made up of leaders from synthetic biology, industry, government, and the international public health community that would award grants funded by the private and public sectors, with a mandate to invest in *highly speculative* defensive efforts – approaches with high potential payoffs that are too uncertain to get funding through traditional channels. **[Slide 18]**

(Final edit: 7/3/07)