LEAP
Synthetic Biology
Leadership Excellence Accelerator Program

Coherent Block Funding for Microbial Environmental Risk Assessment and Mitigation Strategy Development

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Synthetic Biology LeAP Strategic Action Plan
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Synopsis

Coherent Block Funding is a mechanism for government, industry, and institutional agencies to support and coordinate the assessment of environmental risks posed by genetically engineered microbes, and the development of strategies to mitigate these risks. In short, a single block of funding would support several testing facilities in addition to multiple individual investigators developing mitigation strategies. Unlike current funding mechanisms which distribute funding piecemeal at 5% or less of larger science projects, do not align the incentives of separate investigators, and make it difficult to accomplish meaningful outcomes, Coherent Block Funding can sustain real-world test-bed infrastructure and provide return on investment through establishing which mitigation strategies are actually effective. This strategic action plan aims to garner high-level support within federal and institutional agencies to prioritize Coherent Block Funding as the support mechanism for genetically engineered microbe environmental risk assessment and mitigation strategy development.

Addressing the possibility of environmental exposure to engineered microbes

Political leaders and citizens alike are increasingly concerned about the possibility of genetically engineered organisms, such as biofuel-producing microbes, being unintentionally exposed to the environment. The overall sensitivity of the public to the possibility of environmental exposure is perhaps not surprising, given the inclusion of California Proposition 37 (label genetically engineered foods) on the November 2012 ballot, and the emergence of anti genetic engineering community events organized by groups such as SynBioWatch. Concerns range in sophistication from how long an engineered microbe would survive in the environment, to

[1] This paper is a working version. Please contact the author at njhillson@lbl.gov to provide feedback.
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whether the debilitating modifications deliberately introduced into the microbes would actually be effective in reducing their capacity to survive and transfer genetic information. While it is not yet readily possible to directly answer all questions concerning the survival of engineered microbes in the environment and their potential to transfer genetic information, organizations including Berkeley Lab and the EPA are actively investigating these issues. In late 2010, the U.S. Department of Energy (DOE) Office of Science began to fund Berkeley Lab to investigate the most likely environmental exposure scenario for biofuel-producing microbes, namely engineered microbes surviving downstream to a wastewater treatment plant. After two years of infrastructure development efforts, Berkeley Lab is now approaching the point where survival and genetic transfer measurements can be made. Complementing the development and maintenance of environmental exposure test-bed infrastructure, individual investigator laboratories are independently developing mitigation strategies. These mitigation strategies include pursuing "kill switches" that aim to prevent microbes from surviving outside of the laboratory, and "orthogonal biologies" that aim to encipher genetic information so as be nonsensical if transferred to an environmental microbe. However, since maintaining real-world test-bed infrastructure is far beyond the scope of individual academic laboratories, mitigation strategy development generally concludes with proof-of-concept experiments that may not be representative of real-world testing conditions. While it would be greatly productive to ascertain if the developed mitigation strategies are actually effective leveraging real-world test-bed facilities, funding is rarely allocated to do so and the incentives for test-bed facilities and the mitigation strategy developers are not necessarily aligned.

Current practices: funding mechanisms and inter-agency opportunities

The DOE Office of Science currently distributes research funds for environmental risk assessment and mitigation strategy development piecemeal across multiple Biological Design grants (up to a 5% maximum per award). This support for environmental risk assessment and mitigation strategy development is bundled together with ELSI (ethical, legal and societal implications) research in this capped 5% allocation. While this funding mechanism is very well intentioned (*e.g.*, promoting ELSI considerations as an important component of the Biological Design process, while concurrently capping the ELSI component at 5% to assuage scientific advisory criticism that ELSI efforts unduly divert funding from scientific research), it fails in several respects. First, bundling ELSI together with environmental risk assessment and mitigation strategy development is unwarranted and unnecessary, since the latter fall squarely within the domain of scientific research that is demonstrably important to the public, government, industrial, and institutional interests. Second, this funding mechanism makes it unfeasible to maintain environmental risk assessment test-bed infrastructure. For example, more than the entire ELSI allotment of five independent $1M/year Biological Design awards would be required to minimally support the operation of the Berkeley Lab sewage reactor test-bed. Third, this funding mechanism precludes meaningful outcomes and outputs for mitigation strategy development efforts, since 5% of a $1M/year Biological Design award supports less than half the effort of a single postdoctoral research fellow.

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Government agencies, industry, private foundations, and the academic research community all have vested interests in ensuring that microbial environmental risk assessment and mitigation strategy development is pursued in a highly effective manner. When (not if) unintentional engineered microbial environmental exposure occurs, all entities will want to know the likely consequences and have confidence that the instituted mitigation strategies will actually attenuate undesirable outcomes. Several agencies are currently independently supporting microbial environmental risk assessment and mitigation strategy development research. Depending on the agency, however, the semantics of "exposure" may differ. For example, corporate entities and the Department of Defense may be especially interested in preempting industrial espionage (*i.e.*, exposure to a thief, rather than exposure to the soil). Despite the fact that all agencies are aligned in the general ambition that engineered microbes should not survive or transfer genetic information beyond their home facilities, there is little formal inter-agency coordination to synergize related risk assessment and mitigation strategy development efforts.

Coherent Block Funding

Coherent Block Funding will coordinate and consolidate existing research funds to effectively support the maintenance and continued development of several test-beds (*e.g.*, sewage reactors, soil containment systems) along with the innovation and testing of diverse sets of mitigation strategies (*e.g.*, microbial "kill switches", orthogonal biology). Unlike current uncoordinated funding mechanisms that exclusively focus on either risk assessment test-beds or mitigation strategy development, coherent block funding would align the interests of test-bed facilities and individual mitigation strategy investigators by holding all parties accountable for the assessment of mitigation strategy performance. Integral to the approach is an annual awardees workshop (modeled upon the JCVI/SynBERC Biocontainment Workshop slated for February 2013) to disseminate collective knowledge and strengthen interpersonal relationships. Beyond the immediate focus on environmental risk assessment and mitigation strategy efforts, coherent block funding could be extended support ELSI and regulatory science efforts, or fruitfully applied to promote other research endeavors and agendas.

Desired Outcomes

- Maintenance and continued development of test-bed facilities and infrastructure
- Real-world testing and assessment of mitigation strategies
- Increased confidence in mitigation strategy performance
- De-prioritization of ineffective mitigation strategies

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- Tangible quantitative results communicated to the public and policy makers, potentially supported by standards consortia and institutes such as NIST
- Demonstrated effectiveness of coherent block funding as measured by differentials in the above listed outcomes against current funding mechanisms

Strategy

1. Leverage a broad-base of investigator endorsement
2. Project the resulting unified vision to funding program managers
3. Garner high-level support of research priority-setting personnel within OSTP and other federal and institutional agencies to enable and prioritize plan execution

Tactics

- Iterate and refine this action plan in collaboration with established test-bed and mitigation strategy investigators and program managers
- Bolster support through presentations of the plan at risk assessment and biocontainment workshops
- Leverage interpersonal connections of plan supporters to place the plan in front of research priority-setting personnel.

Risks

Investigators who perceive that their funding may be threatened could prove antagonistic. Funding that supports ineffective mitigation strategies would be threatened, and the political inertia of those currently funded to do ELSI and related risk assessment research could be too much to overcome. Critics may identify Coherent Block Funding as an attempt to secure additional funding from already tight research budgets.

Plan implementation may be challenging even with the full support of all stakeholders. Many government agencies (*e.g.*, DOE/EPA/DoD/USDA/NSF/FBI/NIST/NASA) as well as industrial and private organizations have overlapping interests and jurisdictions in this space. It is important to note, however, that the overall success of this strategic plan will not depend on buy-in from more than a few key agencies.

Timeline

November 2012 – Initial version of the strategic action plan/whitepaper complete

December 2012 – Iterative feedback/revision process with stakeholders initiated

January 2013 – Initial revision of the strategic action plan/whitepaper complete

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March 2013 – Plan/whitepaper presented at JCVI/SynBERC Biocontainment Workshop

April 2013 – Revised whitepaper/support letters circulated to OSTP/program managers

June 2013 – Coherent Block Funding Opportunity Announcement

August 2013 – Coherent Block Funding proposals due

October 2013 – Coherent Block Funding begins

February/March 2014 – First Annual Coherent Block Funding Awardees Workshop

Budget

Coherent Block Funding will either be budget neutral (adjusting only the mechanism for existing research support), or will require additional funds to further support test-bed facilities and mitigation strategy assessment. The awardees workshop would require additional private foundational support (*e.g.*, from the Sloan Foundation).

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