“NSF Convergence Accelerator: Workshop for the Development of Infrastructure for Distributed Bio-Manufacturing and Bio-Readiness”

Workshop Report

March 2021

Introduction

This report is the result of the workshop series entitled **"NSF Convergence Accelerator: Workshop for the Development of Infrastructure for Distributed Bio-Manufacturing and Bio-Readiness".** These workshops were held virtually in five sessions on September 29th, 30th, October 1st, 6th, and 8th 2020. Over 250 people expressed interest and registered for one of the workshop sessions. The sessions were organized as a result of NSF Award #2035346 under the supervision of Prof. Douglas Densmore from Boston University. Infrastructure and additional support for the sessions was provided by SynBioBeta (https://synbiobeta.com/) led by Stephen Hubbard.

Report Contributors

Douglas Densmore (Boston University), Stephen Hubbard (SynBioBeta), Devin Strickland (University of Washington)

Workshop Overview

Details on the workshop can be found at - https://www.nonasoftware.org/nsf-conv-accel-workshop
The complete list of attendees is in the appendix. **There were over 240 total attendees over the 5 workshops.**
Here are the agendas from each of the five workshop sessions. The scope of this workshop remained broad during the first 3 days and was narrowed during the final 2 days.

Day 1: National BioFoundry and BioReadiness Infrastructure Needs – 45 min

- Convergence Accelerator Introduction – Linda Molnar, NSF – 5 min
- Introduction to the workshop process – Douglas Densmore, Boston University, 5 min
- Needs Overview Discussions – 16 min
    - Bioengineering Perspective (Technical) – 4 min
    - Infrastructure Engineering Perspective (Technical) – 4 min
    - Industry Perspective – 4 min
    - Law/Policy Perspective – 4 min
- Breakout discussions – 15 min
    - Bioengineering Breakout
    - Infrastructure Engineering Breakout
    - Industry Breakout
    - Law/Policy Breakout
- Wrap up – Douglas Densmore, Boston University, 4 min

Day 2: Challenges in setting up a National Biofoundry and BioReadiness Network – 45 min

- Recap of progress – Douglas Densmore, Boston University, 5 min
- Challenges Overview Discussions – 16 min
    - Bioengineering Perspective (Technical) – 4 min
    - Infrastructure Engineering Perspective (Technical) – 4 min
    - Industry Perspective – 4 min
    - Government/Policy Perspective – 4 min
- Breakout discussions – 20 min
    - Bioengineering Breakout
    - Infrastructure Engineering Breakout
    - Industry Breakout
    - Law/Policy Breakout
- Wrap up – Douglas Densmore, Boston University, 4 min

Day 3: Key Opportunities Stemming from a National Biofoundry and BioReadiness Ecosystem– 45 min

- Recap of progress – Douglas Densmore, Boston University, 5 min
- Opportunities Overview Discussions – 16 min
    - Bioengineering Perspective (Technical) – 4 min
    - Infrastructure Engineering Perspective (Technical) – 4 min
    - Industry Perspective – 4 min
    - Law/Policy Perspective – 4 min
- Breakout discussions – 17 min
    - Bioengineering Breakout
    - Infrastructure Engineering Breakout
    - Industry Breakout
    - Law/Policy Breakout
- Wrap up and discussion of Oct 6th and 8th – Douglas Densmore, Boston University, 7 min

Tuesday the 6th - "Formulate"

Ideas

- 11-11:30am - An organized recap of the 29th, 30th, and 1st SynBioBeta workshops
- 11:30am - Noon - Exercises to capture any additional ideas, approaches, etc.

Discussion Exercises

- North Stars
- Hills - https://www.ibm.com/design/thinking/page/framework/keys/hills - Devin Strickland (UW)

Educate

- Noon – 12:20pm - Review Convergence Accelerator Structure - Linda Molnar (NSF)
- 12:20-12:30pm - Quick recap of other resources and programs
    - DOE Agile Biofoundry
    - DARPA SD2
    - DoD MII
    - Global Biofoundries Alliance
- 12:30 - 1pm - Break

Breakout/Working Meeting

- 1 – 2:30pm - Working groups map Challenges, Needs, and Opportunities to:
    - Need for convergence research
    - Evidence of research community readiness
    - Scientific and societal needs
    - Stakeholders and Partnerships
    - Deliverables that could be expected within a two-year research effort
    - Expected impacts
    - Track Coherence
- 2:30 - 3:00pm - Report back on group work

Thursday the 8th - "Refine"

Review

- 11-11:30am – Review mapping exercise

Stakeholders

- 11:30 - Noon - Identify "Archetypes" (individuals and groups) for created efforts
- Noon - 12:30pm - Break

Breakout/Working Meeting

- 12:30 - 2:30pm - Working groups. TBD based on results from the 6th and previous discussion. Topics include:
    - "Vertical" integration of efforts
    - Further refine topics "horizontally"
    - "Build your own program" - what would you do (team, project, $$, deliverables, etc.)
- 2:30 - 3:00pm - Report back on group work - workshop ends - next steps

Workshop Leadership

Primary Organizers
Douglas Densmore, Boston University
Linda Molnar, NSF
Stephen Hubbard, SynBioBeta

Primary Support
Jacob Beal, Raytheon BBN Technologies
Nathan Hillson, Lawrence Berkeley National Lab
Ben Keller, University of Washington
Mike Koeris, BIIOME
Peter Lee, Strateos
Devin Strickland, University of Washington
Prashant Vaidyanathan, Microsoft Research

Report Structure

This report is intended to both summarize the discussions from the workshop as well as provide guidance to NSF related to how an NSF Convergence Accelerator Program could be organized around the topic of Bio-Manufacturing and Bio-Readiness. More globally this report illustrates which aspects of this topic are mature enough to become part of a funded program and those which still require development. To that end, the report is structured as follows:

1. Framework discussion
2. Challenges Overview
3. Needs Overview
4. Opportunities Overview
5. “Hills” Framework
6. Convergence Accelerator Framework
7. Recommendations
8. Conclusion

Framework

All participants understood the general thrust and goals of this workshop - there are significant benefits to our society having the ability to rapidly mobilize our knowledge, expertise, and creativity pertaining to the production of biological molecules (high-value drugs, medical countermeasures, useful materials, food, and commodity chemicals) and perform biological manipulations (testing, research, conversions). Additionally, participants understood that in order to realize these benefits,

there is immediate value to establishing a distributed network of bio-manufacturing capabilities in our country.

There was a level of divergence in the understanding of the range of operations that would be performed at these distributed facilities, the range of human participants using these capabilities, and the ways that the humans, the equipment and the pooled body of knowledge would interact. **A major challenge in this area and the first that would have to be addressed by NSF, is to appropriately define the scope, timeline, outcomes, and participants in any funded effort.**

Because the operations that would be included in this network are diverse (using robots to build new microbes with genetic constructs is very different from using large fermenters to brew production-level amounts of a small molecule), there was a wide range of expertise represented. Ultimately, the nation needs the input of all stakeholders - **connecting their input alone would be a successful program if implemented.**

A potential set of axis to think about approaches are as follows:
:

Operations to be performed:

- **Process** - Strain (or any biological material) specify, design, build, test, learn cycle
- **Automation** - Automation of molecular biology techniques (everything from transformation to sample testing and analysis)
- **Scale** - Scale up of production processes
- **Case Studies** - Large scale manufacture of bio-based solutions like therapeutics, materials, and bio-energy

Infrastructure involved:

- **Experimentation Space** - Wetlab facilities
- **Hardware Equipment** - Automation of protocols
- **Computation** - Servers, digital infrastructure
- **Small Capacity** - Small scale and pilot fermentation capacity
- **Large Capacity** - Production scale fermentation

Enabling technology, policy, and societal framework

- **Testing** - Automated biofabrication and small-scale testing
- **Cyber Infrastructure** - Organized registry databases of available capacity (equipment and human) within the network.
- **Legal** - frameworks for the promotion, dissemination, implementation, and security of large scale, distributed bio-manufacturing

Personnel to be involved:

- **Computational -** Computer scientists/engineers, bioinformaticians, mathematicians, and computational biologists (for example).

- **Experimental -** Molecular biologists, chemists, physicists, and process engineers
- **Legal/Policy** - Lawyers, policy advocates, anthropologists, and social scientists
- **Trainees -** Graduate students, post docs, early stage researchers

One observation would be that commercial entities have addressed many of these axes. While companies like Amyris, Ginkgo Bioworks, and Zymergen have a variety of engineering biology pipelines, **none of them is explicitly design to be made available to the nation during times of emergency**, standardized to allow for the modular introduction of new facilities or capabilities, or specifically tasked with curating the hardware, software, and wetware needed to respond to a bio-crisis or national challenge.

The general framework of this report ideally will help to identify the following areas related to bio-manufacturing and bio-readiness. The workshops solicited feedback on these areas and were used to organize the feedback to create a coherent narrative around each one.

[Note that each of these should be filtered with a high-level analysis of which are required for readiness and can be rapidly mobilized and distributed]

- **Products**- what technical developments will increase the USA's ability to develop new bio-manufactured products and services? Which products are needed? Which products exist? Which products have the greatest ability to be improved or modified by biology?
- **Process** - what processes must be developed to support the previously mentioned products and services? Which processes are currently most developed to date? Which processes are of interest but underdeveloped? Which processes have been tried unsuccessfully?
- **Network/Distribution** - how can the products be distributed? How will participants in the network collaborate? What "network effects" are possible with such an effort? What are the strengths of a network? What are the weaknesses of a network?
- **Security -** What security measures need to be put in place for an effort of this type? Which measures are unique to this effort? Which can be reused from other efforts? How much security risk is involved? Where are the risks located?
- **Standards** - what standards need to be involved? Which are in place? Which need to be improved? Standards involved data, material transfer, documentation, design, and regulatory (minimally).
- **Data** - how do we manage the data in such an effort? Storage? Distribution? Security? Validation? Lifetime? Reports? Analysis?
- **Society and Community** - to what extent does this effort impact the larger society and surrounding communities? How can we address potential societal impacts? Who are the stakeholders? Proponents? Opponents?

In the following sections, the general topics of "Challenges, Needs, and Opportunities" are viewed through these elements and we report on the general consensus of the workshop participants.

Challenges

Five of the framework concepts around challenges in this area can be summarized as follows:

1. **Network** - A robust and distributed network of facilities (and registry of capabilities) at all parts of the process scale up path
2. **Security** - Assess and protect the network
3. **Standards** - Encode our best practices
4. **Data** - Collecting and sharing knowledge
5. **Societal/Community** -

The following tables detail the workshop conversations in these areas.

Network Challenges	
Idea	**Description**
Capabilities Registry	Creating and maintaining a registry of current capabilities and capacity that exist throughout the distributed network (to enable better sharing of resources) will require novel cooperation from a vast array of stakeholders and a full assessment of the fungibility of differently sized and differently featured facilities.
Abstraction Layers	Abstraction layers (for equipment protocols, DNA designs, testing methods, fermentation production processes, etc.) will need development in order to share and compare.
Leadership Hierarchy	Determining the leadership hierarchy of a distributed network is non-trivial, but will be necessary to access economies of scale and facilitate rapid coordinated response to immediate national needs.
Scaling	"Getting beyond the molecule, to a cell or a larger organism" in order that a distributed bio-manufacturing network can address even more complex challenges will require advancing nascent technologies, methods, and equipment. It will also require a more systematic, standardized approach to the design of biological systems that expects to capture failure and use that failure in subsequent design iterations.

Security Challenges	
Idea	**Description**
Distributed Physical Security	Distributed bio-manufacturing capabilities may pose additional bio-security risks - creating creative and robust methods for preventing misuse is needed.
Distributed Virtual Security	Distributed networks with broad data sharing require robust security to prevent IP and strategic secret theft.

Standards Challenges	
Idea	**Description**
Regulatory	Regulatory streamlining will be necessary for full widespread network growth. Current regulatory frameworks (GxP) are a good starting point but need modification to allow for speed and rapid sharing of best practices. Automated tools to assess regulatory compliance of methods, protocols and supply chains and new copyright frameworks like Free Genes and Open MTA may need to be developed and implemented. Regulatory frameworks may need to shift focus from process to product, enabled by improved analytical technologies.
Best Practice Capture	Industry alignment requires openness to best-practice adoption consistently across industry segments of failure mode analysis, statistical process control, effects analysis, and technological readiness levels beyond what is currently the norm. How can we encourage all players to adopt methods that may be arduous at first but ultimately beneficial?

Data Challenges	
Idea	**Description**
Sharing Data	Realization of the full potential for learning from successes and failures requires new methods for and norms around widespread data sharing. Increased sharing will be adopted

	when benefits of participation can be demonstrated, differential incentives for academia and industry are articulated, and IP protection and bio-security concerns are addressed.
Storing Data	Public funds may be needed to purchase and open-source private data as a way of normalizing sharing.

Societal/Community Challenges	
Idea	**Description**
Environmental Footprint	The environmental footprint of biotechnology could increase significantly with distributed capabilities and should be monitored, assessed and mitigated.
Public Trust	The scale out of bio-manufacturing solutions to human problems relies critically on the increased public trust in, and access to, bioengineering/biotechnology and biological knowledge while maintaining democratic input on use.

The following table captures a series of discussions that attempt to map "Wants" to the "Challenges" facing them.

	Want	Challenges to overcome
1	Full physical facilities and hardware "stacks" locally available during all parts of a process-scale-up.	- Need to drop the cost of biofoundry equipment, reagents, infrastructure - Need to efficiently virtualize training of bioprocess expertise
2	Rapid access to scale up facilities.	
3	Consistent and committed sources of funding for development of a bio-manufacturing network	- Better defining ROI on any of the technologies that utilize these platforms so that investors understand why and how to fund.
4	Developed market incentives	

4 5	Significant regulatory streamlining in regards to distributed manufacturing Wise public policy informed by increasing biological expertise in government	- Need to increase public trust in bioengineering/biotechnology - Public needs to be able to interact with biotech tools+knowledge, have democratic input on use
6	Better understanding of security/resilience of next-gen (bio)manufacturing infrastructure (centralization vs decentralization)	- Some applications are better suited for distributed production (diagnostic testing, production of lower cost molecules). Some applications require centralized control (weapons, dangerous chemicals). Uncertainty about where this line will be drawn - and if we move toward decentralized, will we have enough resources
7 8	Meaningful regulatory standards across industry so we can regulate products, but not necessarily processes Benchmarking standards akin to semiconductor industry	- What apples are we looking to compare to other apples? Need to define a product
9 10	Parallel development and processing of new strains, tools, methods, and processes Top-down coordination toward urgent needs (RADx)	- Need to test how variability in development and processing from one parallel site to another actually affects the outcome
11 12	Standardized electronic communication of biological protocols Adoption of language or translation protocols	- Need an abstraction layer that ports protocols across diverse hardware - Adoption of some set of equipment?
13	Standardized libraries of genetics parts	- Getting everyone to use the same assembly standards - IP restrictions on parts in the libraries
14	Best-practice adoption of failure mode analysis, statistical process control, effects analysis, technological readiness levels	- Industry alignment on the utility of statistical process control, data analysis
15	Precise metrology of the cell	- Need NIST invest more (other top down bodies) How can bottom up entities contribute to this project?

16 17	An expanded worldview: Manufacturing US independence -life, liberty, and the pursuit of happiness Democratized usage of biology so communities can solve their unique problems	- Getting more young americans involved in biotechnology- 1. Collective decision making requires the enthused 2. Need for skilled workforce 3. Only with understanding will people accept new technologies that are ultimately helpfuL 4. Top-down control doesn't and can't actually know how to solve all the problems - Should NSF partner with garage biohackers?
18	The ability to learn from each other's failures and successes (sharing of data)	- No current incentive to publish mistakes - Can we get government to purchase data that illustrates failure? Is failure data cheaper to purchase?

Needs

A summary of five of the framework concepts around needs in this area can be summarized as follows:

1. **Network** - A robust and distributed network of facilities (and registry of capabilities) at all parts of the process scale up path
2. **Security** - Assess and protect the network
3. **Standards** - Encode our best practices
4. **Data** - learn from successes and failures through the network, encode and share positive and
5. **Societal** - Changing attitudes and norms of the general public, investors, policymakers

The following tables summarize in more detail the workshop conversations in these areas.

Network Needs	
Idea	**Description**
A robust and distributed range of physical facilities	A robust and distributed range of physical facilities and hardware stacks available at multiple parts of a process-scale-up path capable of demonstrating spatial reproducibility.
A Capabilities-Register	A Capabilities-Register of the facilities and equipment that currently exist and could be utilized for someone else's experiment (enabling a sharing economy of biotech infrastructure and data).
National public	National public pre-competitive test-beds to evaluate

pre-competitive test-beds	bio-manufacturing/bioprocess unit operation substitutability

Security Needs	
Idea	**Description**
Security/resilience trade-offs	Better understanding of security/resilience trade-offs of next-gen (bio)manufacturing infrastructure (centralization vs decentralization)
Clear IP protection framework	Clear IP protection framework allowing for honest and open collaboration within the network

Standards Needs	
Idea	**Description**
Failure Analysis	The ability to learn from each other's failures and successes via easy-access sharing of digitally encoded processes between facilities with different infrastructure/feedstocks. Sharing of positive and negative control data as a general measure of experimental success.
Widespread adoption	Meaningful standards across industry so we can regulate products which allows for significant regulatory streamlining regarding distributed manufacturing
Data transmission	Standardized electronic communication of biological protocols and processes
Cross experiment normalization	Standards - Development of biological platforms and understanding/modeling of those platforms.
Biological Platforms	Development of standards to allow for cross experiment normalization (measurement standards, cell state standards, context standards)

Data Needs	
Idea	**Description**
Best Practice Adoption	Best-practice adoption of failure mode analysis, statistical process control, effects analysis, technological readiness levels
Round Robin Transferability	Round robin bioprocess transferability studies between facilities.
Predictive Toolchains	Predictive toolchains to anticipate how well/the likelihood that a given bioprocess could be transferred (with minor variations as needed) between specific facilities.
Data Warehouse	Data warehouse for negative and positive data so that protocol performance, facilities/infrastructure performance, biological performance can be accurately studied and learned from.

Societal/Community Needs	
Idea	**Description**
Reinvention of current cultural attitudes	Reinvention of current cultural attitudes about biotechnology - ideally groups see biotechnological infrastructure in their communities as a critical part of the American pursuit of manufacturing independence, sustainable production, and local solutions to local problems.
Increased public trust	Consistent and committed sources of funding for development and maintenance of a bio-manufacturing network

Opportunities

Here is a summary of the opportunities discussed during the workshop.

1. **More innovative solutions.** With more distributed bio-manufacturing capabilities in place, the biotechnology community can propose more compelling and executable solutions for

pressing human problems such as food scarcity, regionalized effects of climate change, and emerging infectious disease.

2. **Significant cost reductions**. The cost for leveraging biotechnology may rapidly decrease. Frugal Science, (Bio)Fab-Labs, and Free Genes are all models for how traditional cost structures are not inevitable - distributing bio-manufacturing and bio-readiness capabilities will increase the amount of actors thinking creatively about finding low-cost solutions.

3. **Significant time savings**. Estimates of time-to-solution will be improved as many more products, solutions, and methods are deployed and analyzed. Currently, the length of a DBTL cycle can be unpredictable - much more data that is captured and shared thoughtfully will give us all better prediction power.

4. **Increased government coordination and cooperation.** Currently there are many branches of government working to accelerate biotechnology solutions - NSF developing infrastructure to focus on pre-competitive and TRL 1-3 and MRL 1-3 projects will help coordinate facilitation efforts across our government.

5. **New interdisciplinary efforts.** Creating teams that cross traditional domain boarders will set the stage for incredibly important future collaborations. Academia/industry/policy silos will particularly benefit from cross pollination but there are many others where increased collaboration will be beneficial and necessary.

6. **Additional R&D resources.** Nodes in the distributed network will effectively serve as R&D test beds for new capabilities that may be beneficial in response to new unmet needs. Local creative problem solving will benefit everyone more rapidly.

7. **"Future proofing" via standards.** Standardization of equipment, facilities, protocols and procedures can be highly synergistic for distributed networks - for production, workforce development, and regulatory considerations. Current systems have a fair amount of customization as a matter of inertia and previous uncoordinated development.

8. **Societal impacts.** Workforce development, community acceptance and investment , equitable distribution of resources and pursuit of all manner of STEM enterprises result from democratized technology

"Hills" Framework

The "Hills" method is part of IBMs Design Thinking methodology. This exercise communicates the intent for a project with clarity and flexibility. It frames problems as intended user outcomes, not

predetermined implementations, empowering teams to discover breakthrough solutions. They help keep a group's eye on the prize, even in spite of the many challenges.

Hills start with the user to serve, the outcome we are trying to enable them to achieve, and the differentiator that will make this solution exceed expectations. IBM refers to these elements as the **Who**, the **What**, and the **Wow.**

The Hill statements that proposed roughly fall into three broad categories of **Who**

1. **Non-experts in biology** who become capable of using the distributed bio-manufacturing infrastructure to accomplish things that are comparable with what they had previously been doing/making/accomplishing, but now with advanced bio-based tools.
2. **People experienced with biology using new infrastructure** and tools that only exist because of this network effort.
3. **Experts in biology who are already using bio-manufacturing tools** become connected to, invested in, and contributing to the distributed network in new ways that allow for new levels of collaboration and sharing.

Category 1 Examples:

Two people in a garage in farm country should be able to launch a new bio-manufactured product with two years and $50,000.

A **high schooler** should be able to teach themselves sophisticated biological engineering and complete what would today be a grand-prize-winning iGEM project, within one year and for less than $2,000 in equipment and reagents.

Category 2 Examples:

A startup of two scientists should be able to launch production of a high-value molecule in less than 1.5 years, with only their laptops

An early stage startup should be able to run experiments daily on a shared infrastructure without any need for their own experimental facilities.

Category 3 Examples:

Two geographically separated biomanufacturers should be able to transfer each other's bioprocesses with predictable, minimal adjustments; despite differences in feedstocks and facilities/instrumentation

A bioprocess/protocol developer should be able to access a network of geographically separated collaborators to attempt round-robin/transfer of a developed bioprocess/protocol to de-risk and increase commercialization potential.

Convergence Accelerator Framework

In this section the six general questions required of a Convergence Accelerator Program are described. We provide information in each that demonstrates that the proposed area would make a strong Convergence Accelerator Track Topic in 2022 and beyond.

1. **Description of the track topic and the need for convergence research**

Our nation's ability to rapidly manufacture bio-based solutions like therapeutics, materials, and bio-energy is crucial to our national economic advantage and national security. An agile national infrastructure to distribute the manufacturing of biological materials as well as provide the nation with a level of "bio-readiness" to address global pandemics and bio-threats is crucial in the 21st century.

The year 2020 was marked by multiple crises in the relationship between humans and their environment, from out-of-control fires to a global pandemic. A transformation of our national manufacturing infrastructure is necessary to address these problems in both highly-urgent and long-term timescales; consequently, our national economy and national security depend on our ability to harness biology to produce therapeutics, materials, and energy on demand.

This topic would help to create products, process, and a network to enable a national effort on bio-manufacturing and bio-readiness. This environment would be secure, enable and create standards, and carefully consider societal and community concerns and impact.

2. **Evidence of research community readiness (list of reports, other publications);**

Organizations
https://biofoundries.org/
https://sbolstandard.org/
https://www.nonasoftware.org/
https://synbiobeta.com/
https://www.nist.gov/programs-projects/nist-living-measurement-systems-foundry
https://agilebiofoundry.org/
https://www.biomade.org/
https://www.igb.illinois.edu/iBIOFAB
https://www.damplab.org/

http://web.mit.edu/foundry/

Efforts
https://github.com/OpenGene
https://www.protocols.io/

Reports
https://www.nap.edu/catalog/24890/biodefense-in-the-age-of-synthetic-biology
https://www.synthace.com/computer-aided-biology/

3. **Scientific and societal needs in the topic area;**

Our ability to rapidly manufacture bio-based solutions like therapeutics, materials, and bio-energy. This research area would also produce a distributed network of facilities to use those same applications and technology to respond to bio-threats such as global warming and international pandemics.

4. **Stakeholders in the ecosystem (including industry such as investors, start-ups, etc., IHEs, non-profits, government entities) and the potential for partnerships;**

The stakeholders are state and federal governments, research organizations, academic institutions and commercial businesses (both small and large.).

5. **Deliverables that could be expected within a two-year research effort by a cohort of teams (e.g., products, prototypes or proof-of-concepts); and**

Deliverables would include open source bio-manufacturing and readiness protocols and software for agile, rapidly deployed "bio-foundries". This would include training material for experimental and computational personnel.

6. **Expected impacts (including scientific and societal impacts) of the project looking forward 10 years.**

A distributed infrastructure of bio-based experimental facilities that can share data, protocols, expertise, and personnel to manufacture therapeutics, materials, and bio-sensors quickly, cheaply, and reliably. This network could also be configured quickly to address testing and research related to emerging bio-threats. Both of these efforts would create a new, highly trained workforce.

Synergistic Efforts

DOE Agile Biofoundry - As of the time of the completion of this report, there are ongoing active high-level (U.S. Federal Government) inter-agency discussions around supporting, accelerating, and increasing the international competitiveness of the U.S. bioeconomy, specifically around biomanufacturing. For example, the U.S. Department of Energy (DOE) and the National Science Foundation (NSF) are engaging towards the establishment of an inter-agency Memorandum of Understanding (MoU) that would further enable these DOE/NSF collaborations in the biomanufacturing space. One potential opportunity for a concrete realization of these prospective DOE/NSF collaborations would be for NSF Convergence Accelerator-supported teams to work together with the DOE-supported Agile BioFoundry (ABF). As a representative example of this, an NSF Convergence Accelerator sub-team with expertise and capabilities in microbial bioreactor fermentation could work together with analytical (proteomics, metabolomics) and machine-learning experts and infrastructure within the ABF, towards overcoming technical challenges and achieving mission goals that both projects share in common (e.g. making the fermentation scale-up and interfacility transfer process better understood and predictable). There are a number of mechanisms through which such collaborations could take place. Each year, the ABF has been setting aside $5M of its $20M/year operating budget for its Directed-Funding Opportunity collaborations, in which industry and academia can submit competitive proposals to collaborate with the ABF, with the ABF-efforts within successful/selected proposals supported with a portion of this $5M overall annual allocation. That is, the DOE supports the ABF efforts within these collaborations, and the industry/academic partners support their side of the collaboration through other means (i.e. project cost-share). The ABF could, for example, prioritize a portion of the $5M/year specifically for collaborations with NSF Convergence Accelerator grantees, who would submit collaboration proposals to the ABF's Directed-Funding Opportunity. In an NSF Convergence Accelerator Phase I project, these could be "seed" proposals, focusing on ideation and team building. For Phase II projects, these could be larger-scale multi-year projects in which the actual collaborative work takes place. Should such collaborations between the ABF and NSF Convergence Accelerator grantees be realized, this would be a great demonstration of the DOE and NSF working together in support of the U.S. bioeconomy and biomanufacturing.

BioMADE - BioMADE is working to build a sustainable, domestic end-to-end bioindustrial manufacturing ecosystem that will enable domestic bioindustrial manufacturing at all scales, develop technologies to enhance U.S. bioindustrial competitiveness, de-risk investment in relevant infrastructure, and expand the biomanufacturing workforce to realize the economic promise of industrial biotechnology. For more see - https://www.biomade.org/

Recommendations

Programs

1. *Sample Program 1:* **Infrastructure Development, Standards, Knowledge Curation** - Projects in this classification would develop various manufacturing workflows and identify the infrastructure needed to support them. In turn these would be developed, tested, promoted, refined, and sustained. They will work with partners to standardized appropriate aspects and promote these services.
2. *Sample Program 2:* **Brokering Service Development** - Projects in this classification would help to create workflows and processes that help to connect existing services and infrastructure to "customer" needs. It would work with service providers to help them expose their capabilities in such a way that a request can be decomposed into a collection of services in the network.
3. *Sample Program 3:* **Specific Manufacturing Challenges** - Projects in this classification would address specifica bio-manufacturing grand challenges to demonstrate the viability and effectiveness of particular approaches to the topics in this area.

Personnel

1. **Focused Teams, Smart Team Partnersing** - Interdisciplinary teaming of groups is encouraged. Teams themselves should be created to maximize the success of their individual effort. However, there should be strong inter-team relationships formed to create synergy.
2. **Archetypes** - Biological/Natural Science, Engineering, Manufacturing, Legal/Policy, Government, Social Science

Deliverables

1. Standards
2. Software Infrastructure
3. Policy
4. IP
5. Design Software
6. Biological Protocols
7. Biological Artifacts