Agile BioFoundry Overview

Nathan J. Hillson
njhillson@lbl.gov

Lead PI, DOE Agile BioFoundry

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Goal

• **Goal**: Enable biorefineries to achieve 50% reductions in time to bioprocess scale-up as compared to the current average of around 10 years by establishing a distributed Agile BioFoundry to productionize synthetic biology.

• **Outcomes**: Development and deployment of technologies enabling commercially relevant biomanufacturing of a wide range of bioproducts by both new and established industrial hosts.

• **Relevance**: $30M/year public infrastructure investment that increases U.S. industrial competitiveness and enables opportunities for private sector growth and jobs.
Public infrastructure investment enables private industry

Public investment in biomanufacturing infrastructure

Private investment in product development, scaling, and tailoring to unique pathways and products

Adapted from Lyft and BART
Metabolic beachheads and targets

**Beachheads** are strategic metabolic intermediates that can be converted into several bioproducts

**Targets** are molecules to be produced

- Beachhead
- Target
- New Beachhead
Hosts and exemplar molecules

Metabolic engineering strategies developed for a given target can be applied to targets associated with the same beachhead.

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**Exemplars** are representative target molecules downstream of a given beachhead.

- **C. glutamicum**
- **P. putida**
- **New Host**
- **Muonic Acid**
- **Protocatechuate**

**Beachhead**
**Exemplar**
**New Beachhead**
ABF metabolic cartography

01 Xylose
02 Glycerol
03 Protocatechuic acid
04 L-Tyrosine
05 Prephenic acid
06 Chorismate
07 Acetolactate
08 2-Ketoisovalerate
09 Pyruvate
10 Acetoacetyl-CoA
11 Malonyl-CoA
12 Acetyl-CoA
13 L-Aspartate
14 Citrate
15 Geranyl diphosphate
16 Farnesyl diphosphate
17 Geranylgeranyl diphosphate
18 2-ketobutyric acid
19 Propionyl-CoA
20 L-Lysine
21 Succinyl-CoA
22 L-Glutamate
23 L-Proline
24 L-Arginine
25 Glutaric acid

Current ABF target molecules
Current ABF beachhead molecules
Potential beachhead molecules

ABF hosts and tier system

Six Hosts Onboarded to Tier 1:
Bacteria - *Cupriavidus nector*,
*Rhodobacter sphaeroides*, *Clostridium ljungdahlii*

Fungi - *Lipomyces starkeyi*,
*Aspergillus pseudoterreus*,
*Zymomonas mobilis*

Four Hosts Elevated to Tier 2:
Bacteria - *Pseudomonas putida*,
*Corynebacterium glutamicum*

Fungi - *Rhodosporidium toruloides*,
*Aspergillus niger*

Tier 1 represents the fundamental tools & information needed for any rational DBTL cycle; these basics must be achieved to be “onboarded”.

Tier 2 criteria consist of the tools and knowledge needed for rapid and robust DBTL cycles.
Exemplar TechnoEconomic Analyses and Life Cycle Assessments

2,3-butanediol (BDO) converted to butadiene (BD)

- Lowest possible MSP: $1.85/kg
- Current market price: $1.06/kg
- Reduction in GHG emissions for any case

Malic acid

- Lowest possible MSP: $0.75/kg
- Current market price: $2.00/kg
- Reduction in GHG emissions for yields higher than 42% of the theoretical maximum
The Agile BioFoundry approach

- **Design**: Putative Targets
- **Build**: Integration
- **Learn**: Target Metrics Achieved
- **Test**: Scale-up
- **Host Onboarding & Development**: TEA/LCA
Agile BioFoundry will reduce time-to-scale up

**Years 1-3 (5 hosts)**
- Molecule X
- ~10 years, $100M

**Years 4-6 (15 hosts)**
- Molecule Y
- ~8 years, $50M

**Years 7-9 (50 hosts)**
- Molecule Z
- ~5 years, $25M

Time and cost for commercialization
Six Tasks

- **Task 1: Design-Build-Test-Learn** *(Nathan Hillson - lead)*
  - **Infrastructure:** Integrate design-build-test-learn cycle with process automation
  - **Demonstration Projects and Strategic Beachheads:** Demonstrate uses of DBTL infrastructure and establish and improve routes in microbial hosts to beachhead molecules of high strategic interest

- **Task 2: Integrated Analysis** *(Bruno Klein / Thathiana Benavides – co-leads)*
  - Analyze proposed target and beachhead molecules with TEA and LCA methodologies

- **Task 3: Host Onboarding & Development** *(Taraka Dale / Adam Guss – co-leads)*
  - Onboard additional microbial host organisms and further develop them to higher capability tiers through tool development and data collection

- **Task 4: Process Integration & Scale-up** *(Violeta Sanchez i Nogue / Deepti Tanjore – co-leads)*
  - Provide DMR-EH hydrolysates, and test and scale fermentation to improve titer, rate, and yield

- **Task 5: Industry Engagement & Outreach** *(Chris Johnson / Phil Laible / Emily Scott / Amanda Barry – co-leads)*
  - Identify barriers to industry adoption of ABF technologies, expand number and diversity of industry partnerships, and establish a set of metrics for determining impact of ABF technologies on industry

- **Task 6: Management** *(Blake Simmons - lead)*
  - Manage project management, develop internal and external communications, provide deliverables to BETO, and make capital equipment purchases
A distributed Agile BioFoundry
ABF 2022 budget / resource planning

• **Budget**: $30M
  - $23M internal projects
  - $7 collaborations (e.g. Directed-Funding Opportunities)
    • $3M Open
    • $2M BioMADE
    • $1M NSF
    • $1M MSRDC

• **AI/ML related resource allocation**: $10M
  - $6M internal projects
  - $4M collaborations