Enabling the Bioeconmy: The Agile BioFoundry

Bioenergy 2016

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July 13, 2016

Ames Laboratory · Argonne National Laboratory · Idaho National Laboratory · Los Alamos National Laboratory · Berkeley Lab · NREL · Oak Ridge National Laboratory · Pacific Northwest National Laboratory · Sandia National Laboratories

The Opportunity Space

Agile BioFoundry

The U.S. has ~billion tons of renewable biomass available annually that is a strategic national resource for the bioeconomy

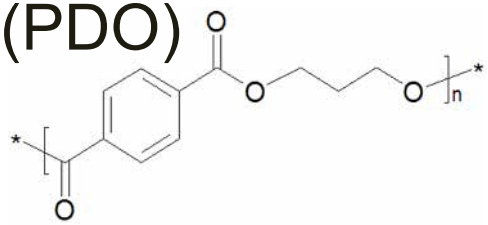
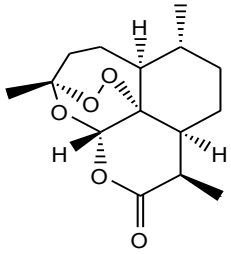
U.S. bioeconomy is estimated at ~$250B/yr and expected to grow significantly over the next decade

Mobilizing and valorizing this resource through biomanufacturing could rapidly expand the U.S. bioeconomy

Biomanufacturing remains nascent in terms of robustness, scale and standardization

The Challenge: Cost and Time to Market

Agile BioFoundry

Molecule	Company	Cost	Time
1,3-Propanediol (PDO) 	DuPont - Tate & Lyle	>$200M	15 years
Artemisinin 	UC Berkeley, Amyris, Sanofi	>$150M	10 years

Possible savings of *billions* of dollars by reducing development time of products, reducing energy intensity and increasing carbon efficiency

The Challenge:
Engineering Biology is Artisanal

Agile BioFoundry

Vision and Mission

Agile BioFoundry

Vision: Establish an Agile BioFoundry consortium that will leverage the unique and differentiated capabilities and skills at the labs

Impact: The National Lab consortium, in partnership with academia and industry, aims to achieve:

- 40% decrease in the energy intensity of current manufacturing processes
- 60% decrease in the carbon intensity of current manufacturing processes
- 50% increase in biomanufacturing cycle efficiency (cost, time)
- 10x improvement in Design-Build-Test-Learn cycle efficiency
- New manufacturing technologies, increase US industry competitiveness, and create new opportunities for private sector growth

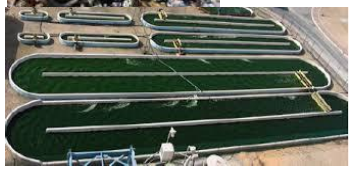
Agile BioFoundry Enables Sustainable Solutions for Multiple DOE Mission Areas and the Bioeconomy

Agile BioFoundry









Sugars

Lignin

Amino acids



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Breaking the Paradigm: The Agile BioFoundry Approach

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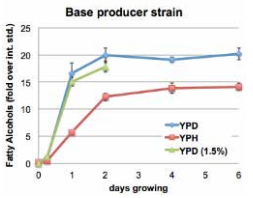

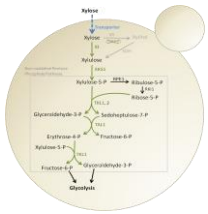

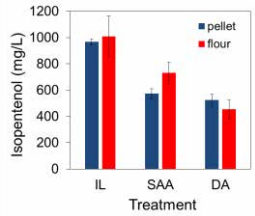

Targets

Selected Target

GenoCAD

iGEM

j5

Design

Build

Integration

Scheduler/LIMS

Learn

Test

Target Achieved

Scale-Up

1-1000L (ABPDU, NREL)

Predictive toolkits

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How Targets will be Identified

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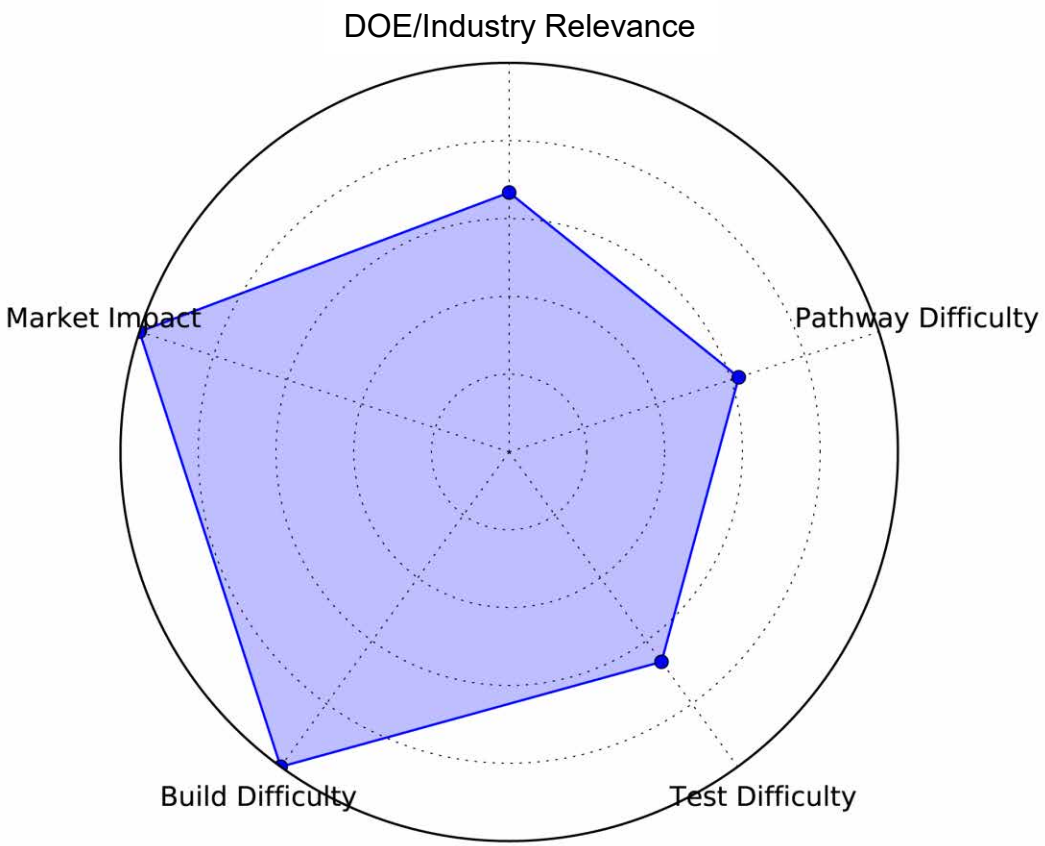
Scoring Functions

Pathway Difficulty:
- Gene confidence
- Intermediate toxicity
- Reaction energy
- Pathway length

Resource Usage:
- Synthesis requirements
- Difficulty to test

Value/Benefit:
- Downstream targets
- Economic value
- Institutional value
- GHG Emissions

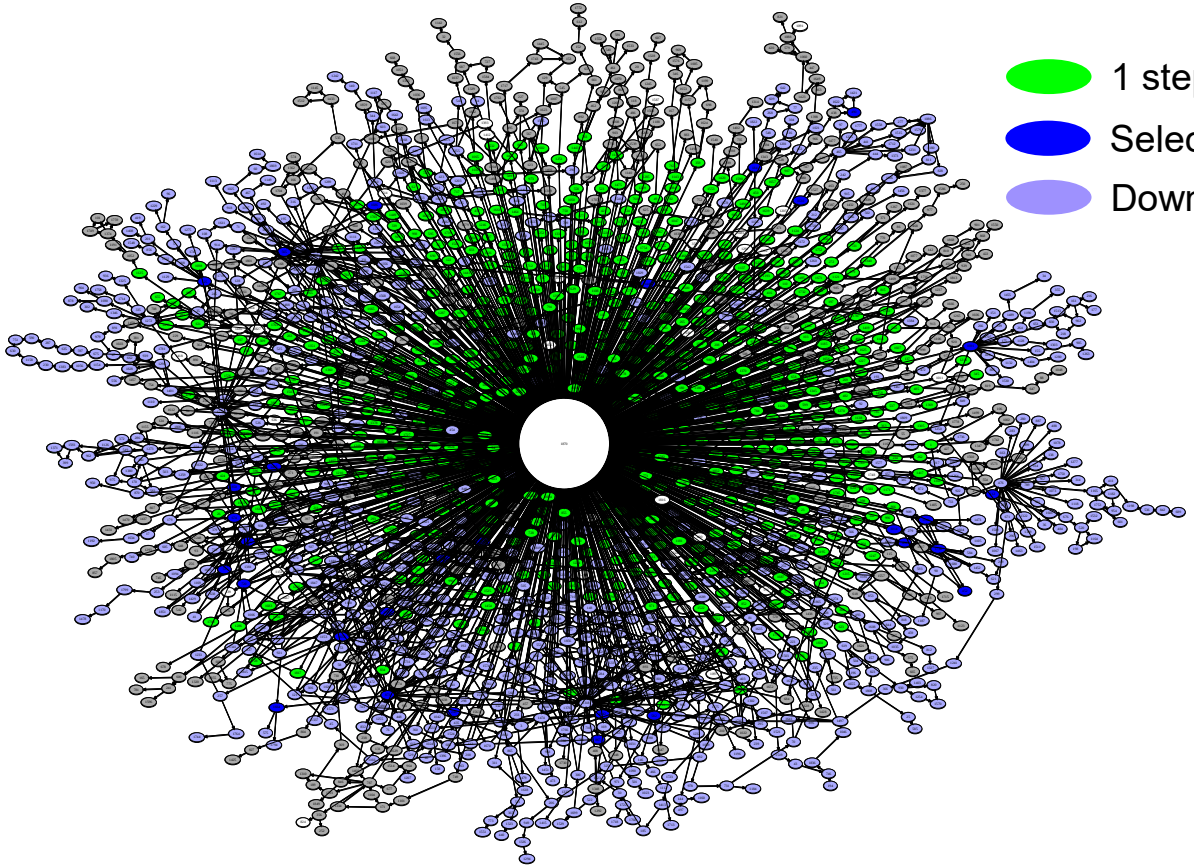
Multi-objective ranking from selected scoring functions



Reducing Development Costs using Targeted Key Molecules

Agile BioFoundry

Retrosynthetic Accessible Chemical Space

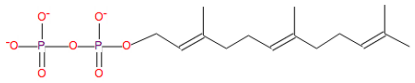


1 step from host organism

Selected targets

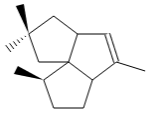
Downstream molecules

Example



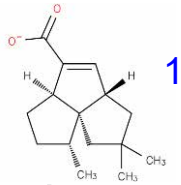
FPP (in host)

PtlA
(*S. avermilitis*)



pentalenene

PtlL (*S. arenae*)
+ NADPH + O_2



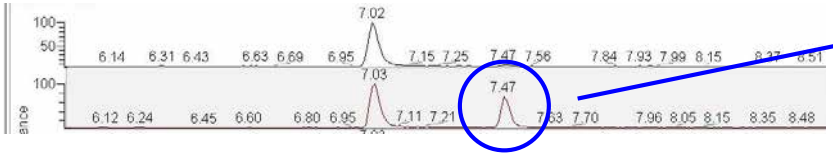
1-deoxypentalenate
[M-H]: 233.15

Proof-of-concept strain engineering success!

LC/MS

host (control)

host + pathway



(10 downstream molecules)

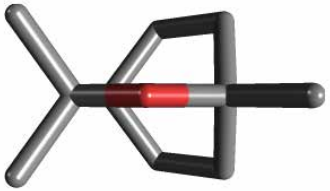
Agile BioFoundry Approach will Improve Cycle Times and Reduce Costs

Agile BioFoundry

1st Generation (Years 1-3)

Molecule X

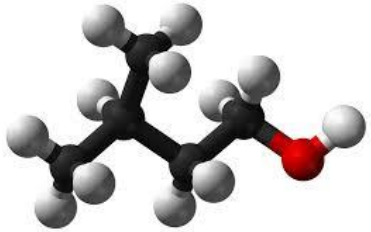
~10 years, $100M



2nd Generation (Year 5)

Molecule Y

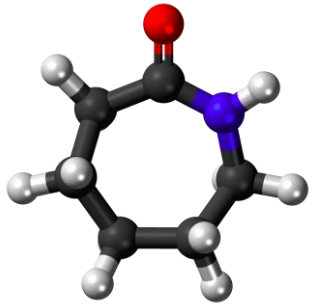
~8 years, $50M



3rd Generation (Year 10)

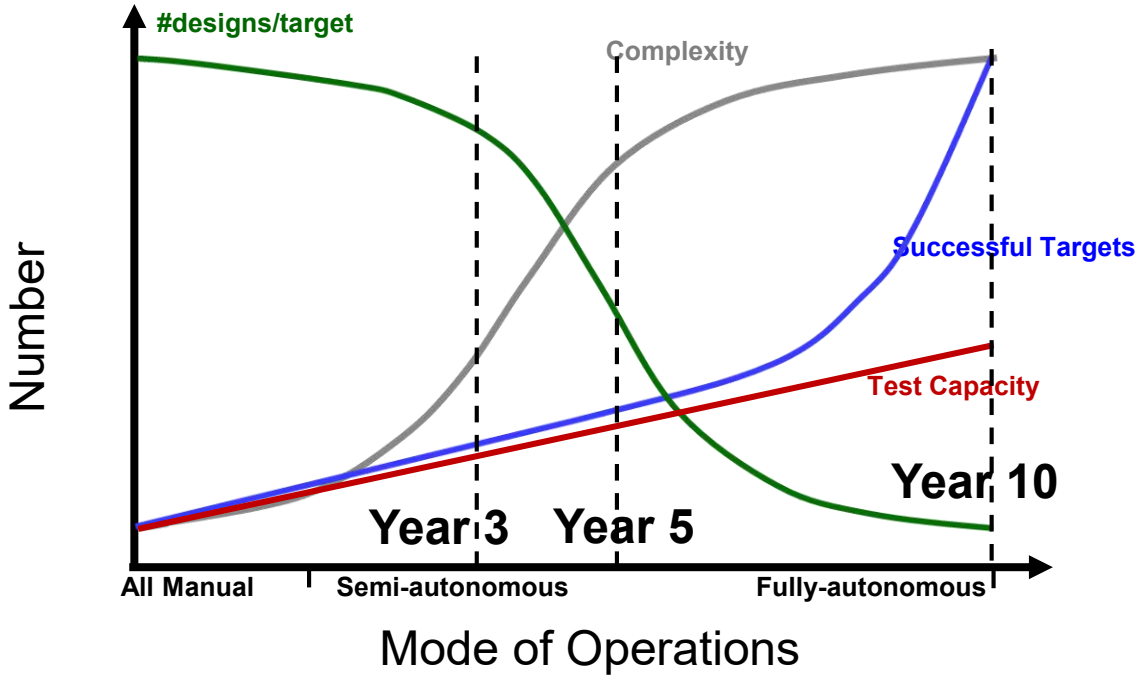
Molecule Z

~5 years, $25M



Time and cost for commercialization

Program Evolution and State of Operations



Year 3: Assemble and demonstrate distributed Agile BioFoundry capable of simultaneously screening/optimizing 100's of different molecules/pathways in multiple organisms, with key strategic collaborations with industry

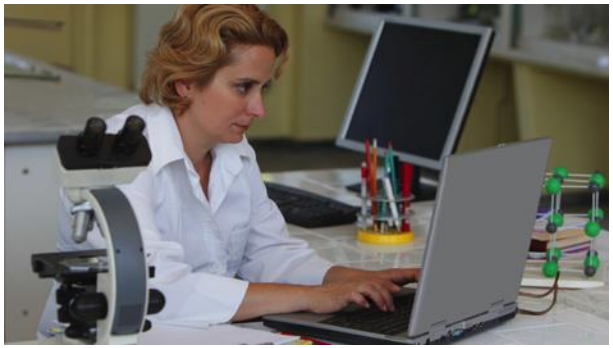
Year 5: Demonstrate full operational benefit of the Agile BioFoundry capable of simultaneously screening/optimizing 1000's of different molecules/pathways in multiple organisms relevant to internal and external customers, including industry and other federal agencies

Year 10: Agile BioFoundry Technology fully developed and deployed in the marketplace

Our Vision of the End State

Agile BioFoundry

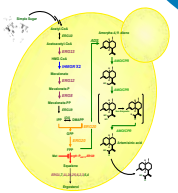
Biological designs

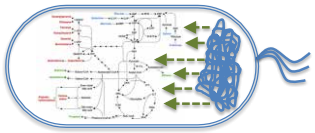


Scientists & Engineers

BioFoundry

Optimized organisms & pathways





Agile BioFoundry Crosscuts Across DOE and Intersects with Several Federal Agencies

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Why DOE? Why Now?

Agile BioFoundry

- Unique capabilities that are required to fully realize the entire Design, Build, Test, Learn, Integration, and Scale-up required for the SynBio Foundry
- Grand challenge that brings together multiple DOE programs and capabilities
- Use-inspired, mission driven program that enables achieving goals on renewable energy, biofuels, mission innovation, GHG emission reductions, and marketplace transformation

Systems and Synthetic Biology

KBase PREDICTIVE BIOLOGY
DOE Systems Biology Knowledgebase

DOE Bioenergy Research Centers

U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy
BIOENERGY TECHNOLOGIES OFFICE

arpa·e

High-performance computing

NERSC

U.S. DEPARTMENT OF ENERGY INCITE LEADERSHIP COMPUTING

Analytics

EMSL SCIENTIFIC INNOVATION THROUGH INTEGRATION

Sequencing

JGI JOINT GENOME INSTITUTE DEPARTMENT OF ENERGY

Feedstocks

INL Idaho National Laboratory

Scale-up

ABPDU ADVANCED BIOFUELS PROCESS DEMONSTRATION UNIT

NREL NATIONAL RENEWABLE ENERGY LABORATORY

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Public Infrastructure Investment Enables Private Industry

Agile BioFoundry

Public investment on biomanufacturing infrastructure

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

Adapted from PR campaign of Lyft

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Industry Engagement

- **iCORPS seed project completed Q4 FY15**
- **Initiated industry engagement in earnest Q1 FY16**
- **Held two industry listening days on March 15, 2016 in the Bay Area and June 14, 2016 in DC**
  - ❑ **All feedback collected in ThinkTank**
  - ❑ **Intended outcomes**
    - ➢ **Overall goal and objectives**
    - ➢ **BioFoundry concept**
    - ➢ **Management and IP considerations**
    - ➢ **Ideal mechanisms for industry collaborations and continued engagement**
  - ❑ **Identify potential members of an Industry Advisory Board to review visioning document**

Industry Interest in the Agile BioFoundry

Agile BioFoundry

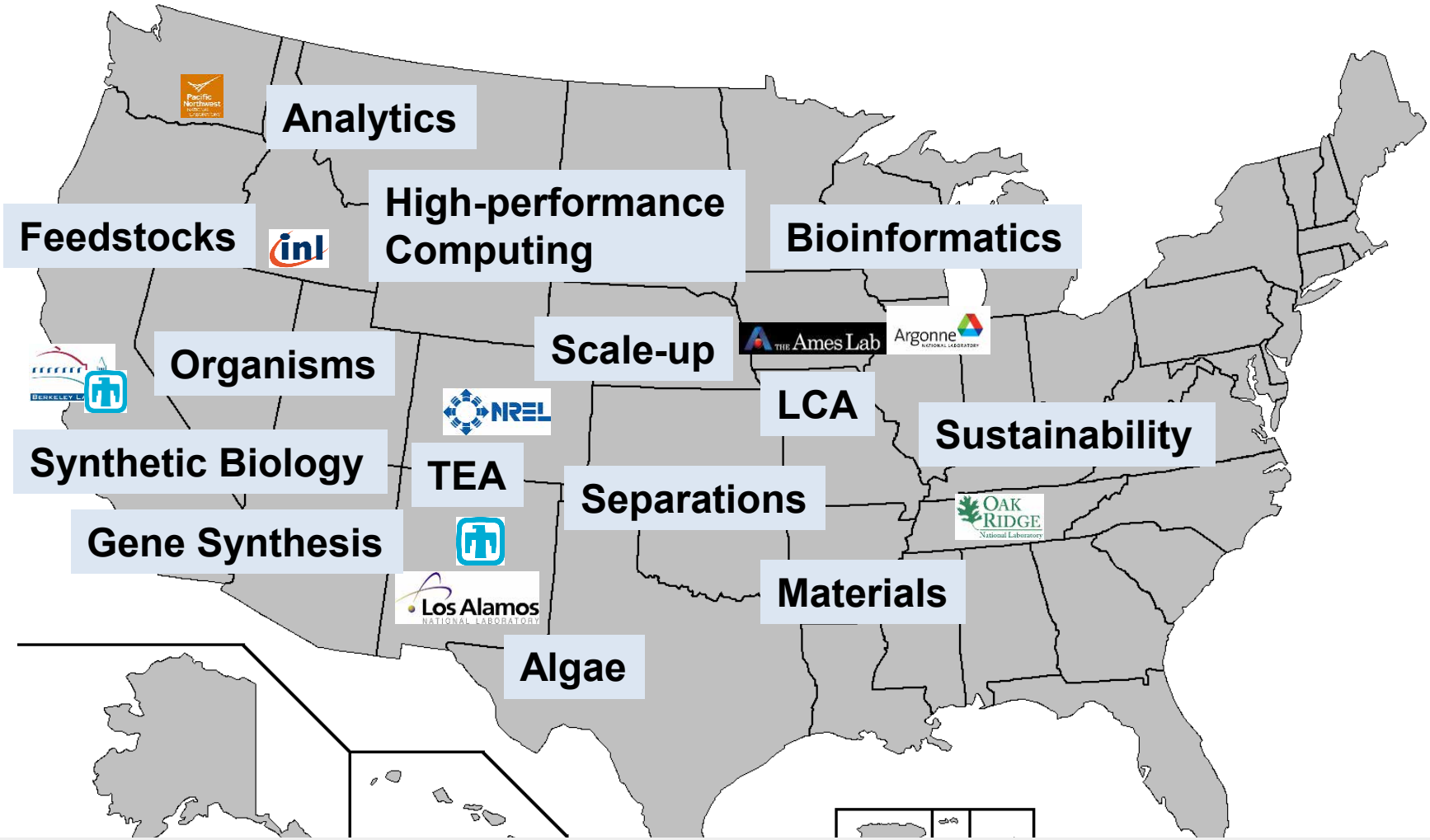
"I feel like your idea of a biotech foundry could be invaluable to [our company] and I'm looking forward to it."

"We are very interested in helping build the bio foundry and using it."

"The bio foundry would be of strategic benefit and help us in terms of open access tools and strain optimization."

The Agile BioFoundry: Enabling the Bioeconomy

Agile BioFoundry



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The Agile BioFoundry: Enabling the Bioeconomy

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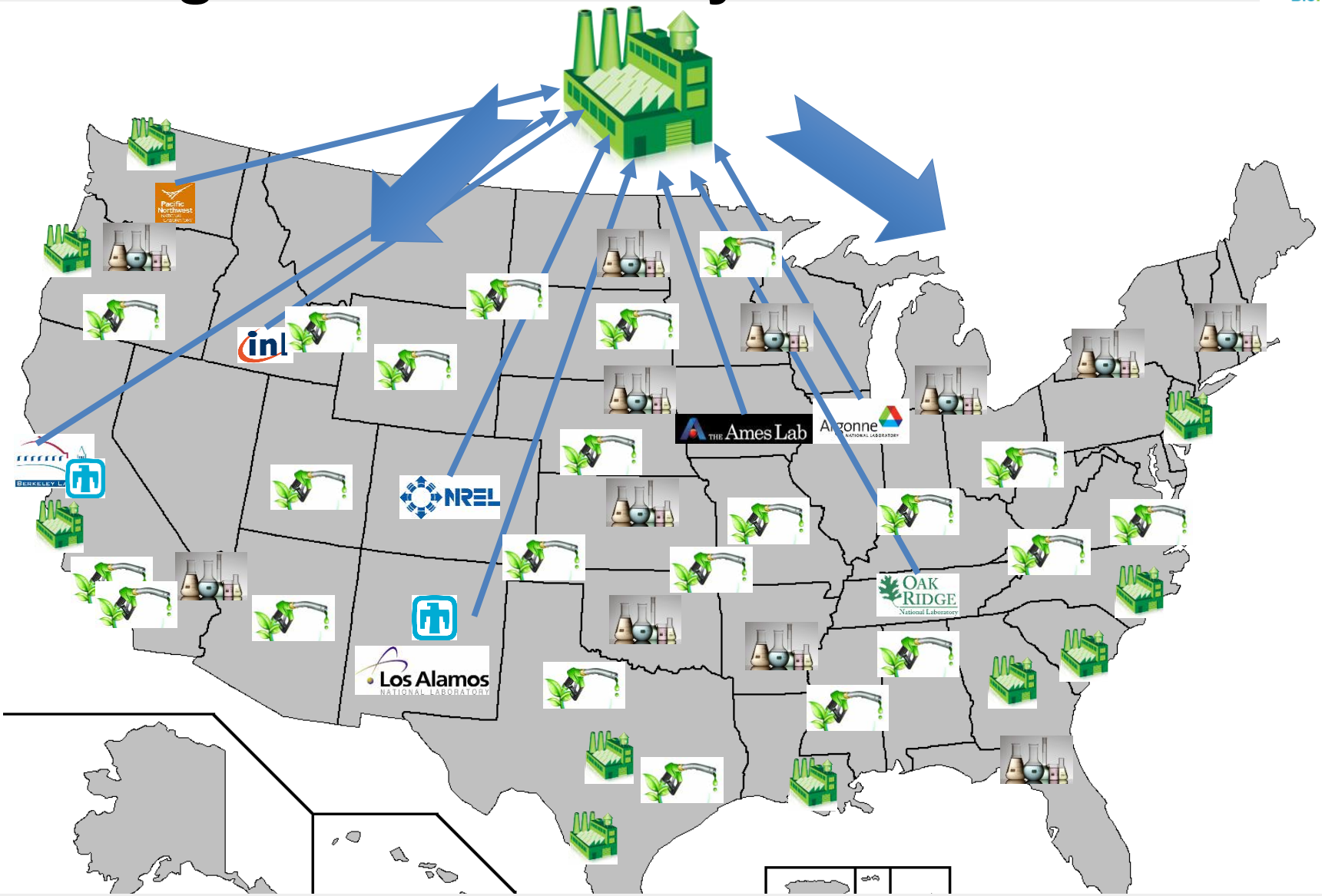

The Impact

Agile BioFoundry

- **Distributed, integrated capability operated as a collaboration facility with robust IP management and market transformation approaches**
- **Open approach to sharing data, pathways, organisms, tools, and technologies that enable the bioeconomy and biomanufacturing at the enterprise level**
- **Decrease the energy intensity by at least 40% and carbon intensity by 60%**
- **Increase biomanufacturing cycle efficiency by at least 50%**
- **10x improvement in Design-Build-Test-Learn cycle efficiency**
- **Increase US industry competitiveness, and create new opportunities for private sector growth and jobs**

The Lab Network

Agile BioFoundry

Ames Laboratory Igor Slowing, Marit Nilson-Hamilton, Cynthia Jenks	Argonne National Laboratory Jennifer Dunn, Phil Laible, Felix Odom	INL Idaho National Laboratory Dave Thompson, Erin Searcy, Chenlin Li, Rachel Emerson
Los Alamos National Laboratory Taraka Dale, Babs Marrone	Berkeley Lab Jay Keasling, Blake Simmons, Adam Arkin, Nathan Hillson, Mary Maxon, Katy Christiansen	NREL Adam Bratis, Gregg Beckham, Mary Biddy, Eric Payne
Oak Ridge National Laboratory Tony Palumbo, Adam Guss, Brian Davison	Pacific Northwest National Laboratory Malin Young, Jon Magnuson, Scott Baker, Mark Butcher	Sandia National Laboratories Anup Singh, John Gladden, Corey Hudson, Ryan Davis

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