Grand Challenges in Biology
Fundamental Research for the Bio-economy

AIBS Council Meeting
December 7, 2011

Charles D. Liarakos
Senior Policy Advisor & Director, Office of Emerging Frontiers
Directorate for Biological Sciences
National Science Foundation
<table>
<thead>
<tr>
<th></th>
<th>FY 2010 Actual</th>
<th>FY 2011 Current Plan</th>
<th>FY 2012 Request</th>
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</thead>
<tbody>
<tr>
<td>BIO</td>
<td>$714.77</td>
<td>$711.56</td>
<td>$794.49</td>
</tr>
<tr>
<td>CISE</td>
<td>618.71</td>
<td>635.10</td>
<td>728.42</td>
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<tr>
<td>ENG</td>
<td>775.92</td>
<td>762.71</td>
<td>908.30</td>
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<tr>
<td>GEO</td>
<td>891.87</td>
<td>884.77</td>
<td>979.16</td>
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<td>MPS</td>
<td>1367.95</td>
<td>1308.28</td>
<td>1432.73</td>
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<tr>
<td>SBE</td>
<td>255.31</td>
<td>247.23</td>
<td>301.13</td>
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<tr>
<td>OCI</td>
<td>214.72</td>
<td>209.94</td>
<td>236.02</td>
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<tr>
<td>OISE</td>
<td>47.84</td>
<td>49.04</td>
<td>58.03</td>
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<tr>
<td>OPP</td>
<td>451.77</td>
<td>439.51</td>
<td>477.41</td>
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<tr>
<td>OIA</td>
<td>274.89</td>
<td>260.26</td>
<td>336.25</td>
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<tr>
<td>US Artic Res. Comm.</td>
<td>1.58</td>
<td>1.58</td>
<td>1.60</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$5,615.33</strong></td>
<td><strong>$5,509.98</strong></td>
<td><strong>$6,253.54</strong></td>
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</tbody>
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Totals may not add due to rounding.
## BIO Funding
(Dollars in Millions)

<table>
<thead>
<tr>
<th></th>
<th>FY 2010 Omnibus Actual</th>
<th>FY 2011 Current Plan(^1)</th>
<th>FY 2012 Request(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular &amp; Cellular Biosciences</td>
<td>$125.90</td>
<td>$123.78</td>
<td>$145.72</td>
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<tr>
<td>Integrative Organismal Systems</td>
<td>216.32</td>
<td>212.79</td>
<td>231.65</td>
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<tr>
<td>Environmental Biology (DEB)</td>
<td>142.50</td>
<td>142.69</td>
<td>156.40</td>
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<tr>
<td>Biological Infrastructure (DBI)</td>
<td>127.19</td>
<td>129.48</td>
<td>135.95</td>
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<tr>
<td>Emerging Frontiers (EF)</td>
<td>102.85</td>
<td>102.81</td>
<td>124.77</td>
</tr>
<tr>
<td><strong>Total, BIO</strong></td>
<td><strong>$714.76</strong></td>
<td><strong>$711.56</strong></td>
<td><strong>$794.49</strong></td>
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</tbody>
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### NSF-wide Investments:

<table>
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<tr>
<th></th>
<th>FY 2010</th>
<th>FY 2011</th>
<th>FY 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAREER</td>
<td>30.60</td>
<td>29.06</td>
<td>33.01</td>
</tr>
<tr>
<td>BioMAPS</td>
<td>-</td>
<td>5.57</td>
<td>32.57</td>
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<tr>
<td>CIF21</td>
<td>-</td>
<td>-</td>
<td>6.00</td>
</tr>
<tr>
<td>SEES</td>
<td>121.00</td>
<td>25.85</td>
<td>27.25</td>
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</tbody>
</table>

Totals may not add due to rounding.

\(^1\)The FY 2011 and FY 2012 numbers shown above for SEES represent revised estimates rather than Current Plan and Request.
Major components of the bio-economy are summarized in the four strategic areas - Energy, Environment, Food and Health - identified in the 2009 NRC Report: A New Biology for the 21st Century.

Fundamental research relevant to the bio-economy is captured in ongoing investments throughout the Biology Directorate - in core research programs as well as special initiatives such as BioMaPS, SEES, and PGRP.

BIO also supports fundamental research in emerging areas such as “genomes to phenomes” and comparative neurosystems, which are foundational to the bio-economy and to the biomedical research supported by other federal agencies.
Five Grand Challenges

1. Synthesizing Life-Like Systems
2. Genomes to Phenomes
3. The Brain: NeuroSystems
4. Earth, Climate and Biosphere
5. Biological Diversity

NRC:2010

BioMaPS: Research at the Intersection of Biology, Math & Physical Sciences and Engineering

Collaborative partnership by the Directorates for Biological Sciences (BIO), Mathematical & Physical Sciences (MPS) and Engineering (ENG)
<table>
<thead>
<tr>
<th>Pure Basic Research <em>(Bohr)</em></th>
<th>Use-inspired Basic Research <em>(Pasteur)</em></th>
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<tbody>
<tr>
<td>Exploration &amp; Description</td>
<td>Pure Applied Research <em>(Edison)</em></td>
</tr>
<tr>
<td>Energy Environment</td>
<td></td>
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<tr>
<td>Biodiversity Biology Collections</td>
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Both Pure Basic and Use-inspired Basic Research are consistent with NSF core values and evolving practice.

Donald E. Stokes  
Brookings Institute
Synthetic Biology
Manufacturing Molecules Through Metabolic Engineering

Conversion of sugars to chemicals by means of microbial catalysts:

- Polyester intermediate 1,3-propanediol
- Malaria drug *artemisinin*

Genomes to Phenomes

Report of the 2011 NSF-USDA Phenomics Workshop

Phenomics research on reference and model organisms
Genomes to Phenomes
Synthetic Biology can create phenotypic diversity.

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome
J. Craig Venter, Science, 329:52 (July 2, 2010)

Synthetic chromosome arms function in yeast and generate phenotypic diversity by design (NSF, DOE, NIH, Microsoft)
J. Boeke, NATURE 477: 471 (Sept 22, 2011) (MCB 0718846)
Genomes to Phenomes

Comparative Neurosystems

Sensing the Environment
[Opsin-encoding genes]

Movement

Complex Behavior

Understanding Complex Behavior
Comparative Neurosystems

Creative breakthroughs at the intersection of neuro, cognitive, computer and physical sciences, and engineering.

- Cognitive, computer and physical sciences and engineering provide the tools and conceptual frameworks for new experimental approaches.

- Comparative neurosystems research offers potential biological solutions to otherwise intractable design and engineering problems.
Earth’s climate and life support systems are changing in novel and unexpected ways....
Genomes to Phenomes

Connecting genomes to ecosystems to identify possible sustainable futures

Community DNA

Ecophysiology

Ecosystem Metabolism

EVOLVING GENOMES

EVOLVING POPULATIONS

CHANGING ECOSYSTEMS
Integrating across drivers, responses, scales, and disciplines to reduce uncertainty about the future of life on Earth.
BIO Activities Relevant to SEES

Dynamics of Coupled Natural and Human Systems
[BIO, GEO, SBE, USFS]

Dimensions of Biodiversity
[BIO, GEO, OPP, Brazil, China]

Ecology and Evolution of Infections Disease (EEID)
[BIO, GEO, SBE, NIH]
SEES Research Coordination Networks

2011: 11 Awards for $8M

1. Build new links among existing projects and partners; add new participants in sustainability research
2. Develop workforce needed to understand and address complex issues of environmental sustainability

Pan American Biofuels
Fig. 1 An integrated science of climate-change biodiversity assessment will draw from multiple sources and approaches.
Dimensions of Biodiversity
[BIO, GEO, OPP]

10-year campaign to characterize the dimensions of biodiversity on Earth

1. Integrative approaches
2. Innovative concepts
3. Rapid advances

Initial focus on areas where three key dimensions overlap.

2010: 13 awards for $23.7M
   1 US-China joint I-RCN
2011: 11 awards for $19M

Plant Genome Research Program (PGRP)

- Leadership role in resource development for plant genomes of economic importance
- Supports basic research to address major challenges in fundamental plant biology
- Integrated project education and outreach activities
- Coordinates with USDA, DOE, NIH, USAID, and USGS through National Plant Genome Initiative
- $1.05 billion invested in 322 research awards between 1998 and 2010
New Projection Shows Global Food Demand Doubling by 2050

*Tilman et. al., PNAS 2011*

PGRP: Supports breeding for improved adaptation to biotic and abiotic stress - drought, heat, salinity, flood, disease and pests

iPlant Collaborative: national cyber-infrastructure center to address global plant biology questions that have implications for agriculture, energy, natural resources and the environment
Next Generation Biofuels

Cellulosic Feed Stocks

- Switchgrass
- Corn Stalks
- Wheat Straw
- Hybrid Poplar
- Mixed Prairie Grass

Cedar Creek LTER Site
Daphne Preuss, Co-Founder and CEO

6 NSF Awards (~ $3.8M) beginning with a Postdoctoral Fellowship in Plant Biology in 1991

10 Patents giving rights to National Science Foundation

7 of 10 Patents are held by Chromatin Inc.
* 9872641 – Plant Centromere Functions Defined by Tetrad Analysis and Artificial Chromosomes

Chromatin is developing and commercializing a portfolio of proprietary sorghum feed stocks targeted at the renewable energy sector, and plans to deploy and ultimately optimize sorghum as a purpose-designed feedstock for bioprocessing applications.
21st Century Biology
Crossing Borders

Basic Research to Enable Agricultural Development
[NSF, Bill & Melinda Gates Fdn]

Metabolomics
[IOS, MCB, DBI, JST]

Science Across Virtual Institutes (SAVI)
Creating international research partnerships around the globe…
Data Enabled Science

Integrating data from the biological, geological, physical and social sciences to address challenges to the future of life on Earth

An absence of life?

Atmosphere

Geosphere

The role of biodiversity?

Biosphere

Integrating data from the biological, geological, physical and social sciences to address challenges to the future of life on Earth
Advancing Digitization of Biological Collections (ADBC) – NSF 11-567

1. Enhance and expand the national resource of digital data document existing vouchered biological and paleontological collections

2. Improve access to digitized information (including images) residing in vouchered scientific collections across the United States.

National resource structured at three levels:

1. A central coordinating organization: National Resource for Digitization of Biological Collections: Integrated Digitized Biocollections at the University of Florida (iDigBio)

2. Series of thematic networks based on an important research theme

3. The physical collections
National Ecological Observatory Network (NEON)

- Hybrid operational and research platforms
- Long-term measurements
- Standardized infrastructure, procedures, quality control
- Free and open data access policy for near real time data
- Decision support tools
Dear Colleague Letter: Cyberinfrastructure in Support of Biological Sciences (NSF 12-019)

The Software Infrastructure for Sustained Innovation (SI2) program includes *Conceptualization Awards*, which are *planning awards* aimed at organizing an interdisciplinary community to examine and define their software requirements and challenges.

BIO is especially interested in conceptualization proposals that *focus on high priority research problems* and that will *significantly leverage existing investments* in ways that transform the infrastructure in support of BIO and BIO-related research.

Potential Grand Challenge Problems in Biology:
- Environmental research at macro scales
- Predicting phenotypes from genotypes
- Characterizing and understanding dimensions of biodiversity on the planet
- Understanding complexity in biological systems
- Research in science, engineering, and education for sustainability
The Bio-economy
A Biology Perspective

“The bio-based economy encompasses the full range of ecosystems – land and sea resources, biodiversity and biological materials (plant, animal and microbe), processing, and consumption. It includes the agriculture, forestry, fisheries, food, biotechnology and chemical industry sectors but also contributes to the sustainable growth and production of food, feed, energy and renewable materials and to the development of rural and coastal areas.”

European Commission, 2010
Sustainable Economy
“Shrimp on a Treadmill”

Louis Burnett, College of Charleston, SC
David Scholnick, Pacific University

BIO supported fundamental research to test whether activities that require high levels of oxygen, such as swimming, feeding or reproduction, are impaired by immune response to disease and exacerbated by environmental stress, such as low oxygen or acidic conditions.
Shrimp on a Treadmill
Potential Economic Impact

1. 95% decline in US wild shrimp harvest from 1992 (14,000 tons/yr) to 2009 (635 tons/yr).

2. World-wide shrimp aquaculture has increased to meet market demand; however, both US shrimp aquaculture and the natural shrimp fishery are in decline.

3. The US annually imports more than 90% of the shrimp it consumes (value ~ $400 million) mostly from SE Asia, China or Central America.

4. The shrimp studied here are the single most heavily cultured species for human consumption (2009 world-wide market of ~ $9 billion).

5. China invests heavily in research related to disease and disease resistance in marine organisms; the US invests almost nothing.
Diving Beetle Larva Bifocal Lens

Lenses of larval eyes 1 and 2 are bifocal, resulting in two distinct focal planes that are shifted dorsal-ventrally, which improves image separation and contrast.

1. First demonstration of a truly bifocal lens in the extant animal kingdom (*E. Buschbeck*, NSF/ IOS)
2. Interesting parallel to bifocal contact lenses, cataract replacement lenses and industrial bi- and multifocal lens systems (none of which use “image disparity”)
Bio-economy at the convergence of BIO-INFO-NANO TECH

An Engineering Perspective

Tom Kalil
OSTP
June 2010
Natural energy transduction systems can inspire biology-based technologies capable of delivering sustainable clean energy.

Integration of PS-I into a H₂ evolving nanoparticle

*Nature Nanotechnology: 2010; Barry Bruce, Univ. TN Knoxville*
Fig. 3 (A) Plot of the efficiency versus time for Co-OEC | 3jn-a-Si | NiMoZn PEC cell (left) in 1 M potassium borate (pH 9.2, black trace) and in 0.1 M KOH (pH 13, red trace) under AM 1.5 illumination.

Photoelectric Cell: Solar water-splitting semiconductor design inspired by PSI and PSII

S Y Reece et al. Science 2011;334:645-648
Working prototypes based on real organisms

Mark Cutkosky, an engineer at Stanford University, and Kellar Autumn, a biologist at Lewis and Clark College developed a gecko-like synthetic adhesive that functions like real gecko feet for climbing applications. [BIO/IOS]

*Stickybot* uses dry adhesion to climb walls.

Softbot robot with tobacco hornworm (*Manduca sexta*) that inspired it riding on its back. Inset images (clockwise from top left) show a telescoping caterpillar-like device (Telebot), a crawling/inching robot (InchBot), an autonomous inching/rolling robot (GoQBot), and a prototype rolling robot with its computer finite element simulation.

Barry Trimmer & team, Tufts Univ. [BIO/IOS]
NSF Innovation Corps (I-Corps)

• Determine readiness to transition technology developed by NSF-funded project

• $50,000 RAPID award to NSF-funded PI

• Mandatory attendance at grantee workshop by I-Corps award team:
  – NSF PI: overall award management
  – Entrepreneurial Lead: postdoc or grad student
  – I-Corps Mentor: experience in transitioning technology out of academic lab

• First Round (2011): 11 Awards; 1 BIO Team
RNA Interference (RNAi) - An ancient evolutionary mechanism for silencing gene expression

An innate and adaptive response that protects a cell from foreign genes by targeting invading gene messenger RNAs
The Bio-economy

...To Improving the Quality of Life

Practical application of RNAi in agricultural and medical biotechnology

Resistance to papaya virus

Therapeutic RNAi
macular degeneration

Fundamental biological research is creating the economic opportunities of the future.
21st Century Biology

Inspiring research, education and economic opportunity at the frontiers of the life sciences
Where discoveries begin