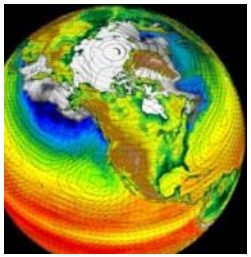
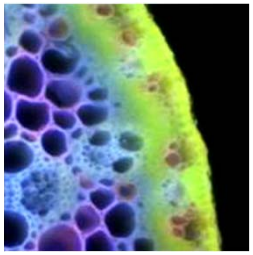
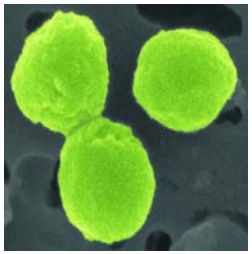


Biological Systems Science Division Update

Todd Anderson, Ph.D.
Director, Biological Systems Science Division,
Department of Energy, Office of Biological &
Environmental Research

June 27, 2013

Update Outline

- *Completed Programmatic Actions*
- *Division Components*
- *Core Philosophy*
- *Significant Activities*
- *Division Science Highlights*

Completed Programmatic Activities

FY2013 Reviews of DOE National Laboratory programs – Completed

- **Genomic Science: Biofuels Research**
  - Pacific Northwest National Laboratory – reverse site visit - Feb 27
- **Radiochemistry & Imaging**
  - Lawrence Berkeley National Laboratory – reverse site -June 5
  - Oak Ridge National Laboratory – reviews completed June 10

Upcoming Reviews

- **Science Focus Area competition – Program plans due in September**
- **Annual Bioenergy Research Center Reviews**
  - BioEnergy Science Center (BESC) – Oak Ridge, TN – Oct 23-24
  - Great Lakes Bioenergy Center (GLBRC) – East Lansing, MI – Nov 12-13
  - Joint Bioenergy Institute (JBEI) – Emeryville, CA – Dec 11-12

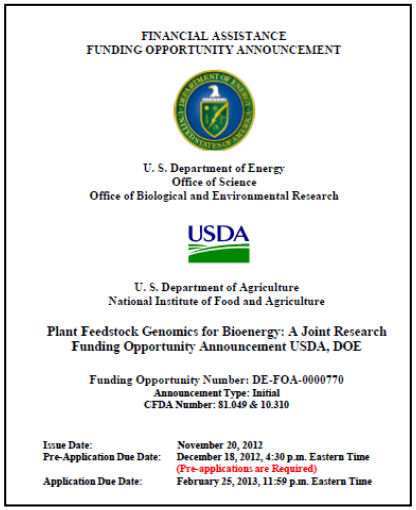
..And Busy FY2014 Ahead!

Completed Programmatic Activities Cont'd

Plant Feedstocks Genomics for Bioenergy: A Joint Research Funding Opportunity Announcement USDA, DOE (DE-FOA-0000770)

NATIONAL INSTITUTE OF FOOD AND AGRICULTURE
U.S. DEPARTMENT OF AGRICULTURE

Panel met on April 24-25
A total of 54 proposals reviewed
Selections are in progress
Joint announcement (with USDA) of awards later this Summer.


FINANCIAL ASSISTANCE
FUNDING OPPORTUNITY ANNOUNCEMENT

U. S. Department of Energy
Office of Science
Office of Biological and Environmental Research

U. S. Department of Agriculture
National Institute of Food and Agriculture

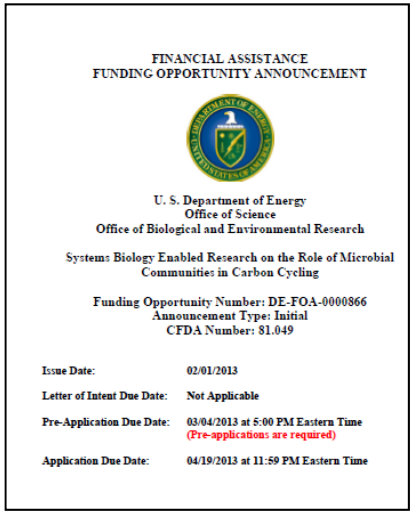
Plant Feedstock Genomics for Bioenergy: A Joint Research Funding Opportunity Announcement USDA, DOE

Funding Opportunity Number: DE-FOA-0000770
Announcement Type: Initial
CFDA Number: 81.049 & 10.310

Issue Date:	November 20, 2012
Pre-Application Due Date:	December 18, 2012, 4:30 p.m. Eastern Time (Pre-applications are Required)
Application Due Date:	February 25, 2013, 11:59 p.m. Eastern Time

Systems Biology Enabled Research on the Role of Microbial Communities in Carbon Cycling (DE-FOA-0000866)

Panel met on June 5-6
A total of 67 proposals reviewed
Selections are in progress


FINANCIAL ASSISTANCE
FUNDING OPPORTUNITY ANNOUNCEMENT

U. S. Department of Energy
Office of Science
Office of Biological and Environmental Research

Systems Biology Enabled Research on the Role of Microbial Communities in Carbon Cycling

Funding Opportunity Number: DE-FOA-0000866
Announcement Type: Initial
CFDA Number: 81.049

Issue Date:	02/01/2013
Letter of Intent Due Date:	Not Applicable
Pre-Application Due Date:	03/04/2013 at 5:00 PM Eastern Time (Pre-applications are required)
Application Due Date:	04/19/2013 at 11:59 PM Eastern Time

Several proposals in each Notice with linkages to KBase

Division Components

Genomic Science: Foundational

- Argonne National Laboratory
- Los Alamos National Laboratory
- Lawrence Berkeley National Laboratory
- Oak Ridge National Laboratory
- Pacific Northwest National Laboratory

Genomic Science: Biofuels

- Lawrence Livermore National Laboratory
- National Renewable Energy Laboratory
- Oak Ridge National Laboratory
- Pacific Northwest National Laboratory

Genomic Science: Systems Biology Knowledgebase

- Lawrence Berkeley National Laboratory (ANL, BNL and ORNL)

Radiobiology : Low Dose Radiation Research

- Pacific Northwest National Laboratory
- Lawrence Berkeley National Laboratory

Radiochemistry and Imaging

- Brookhaven National Laboratory
- Lawrence Berkeley National Laboratory
- Oak Ridge National Laboratory
- Thomas Jefferson National Laboratory

16 Science Focus Areas (SFAs)

3 Bioenergy Research Centers

- BESC
- GLBRC
- JBEI

1 User Facility

- Joint Genome Institute (JGI)

20 Beamlines at DOE Synchrotron Light and Neutron Sources

- Some joint with NIH

~100 Academic Lead PIs

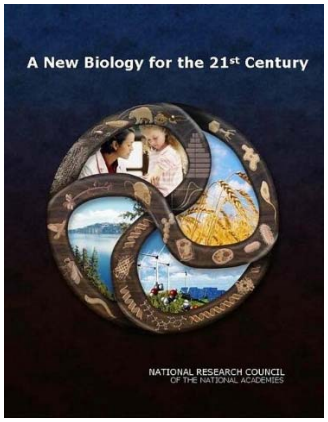
How to Coordinate Research Efforts Towards DOE Mission areas?

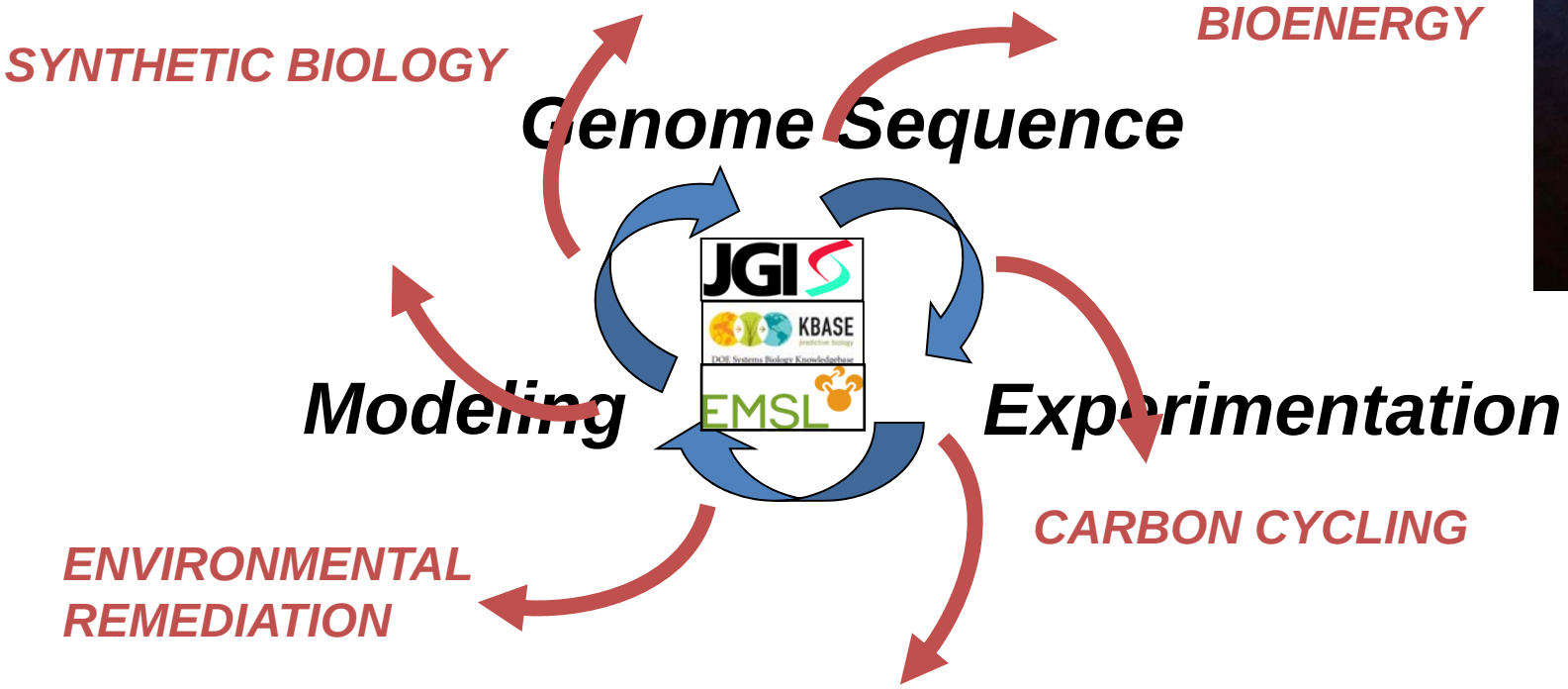
Core Philosophy

Advancing Systems Biology Research

Resources:
Researchers (National Labs, Academic Centers)
Technological capabilities (DOE User Facilities)
Computational systems

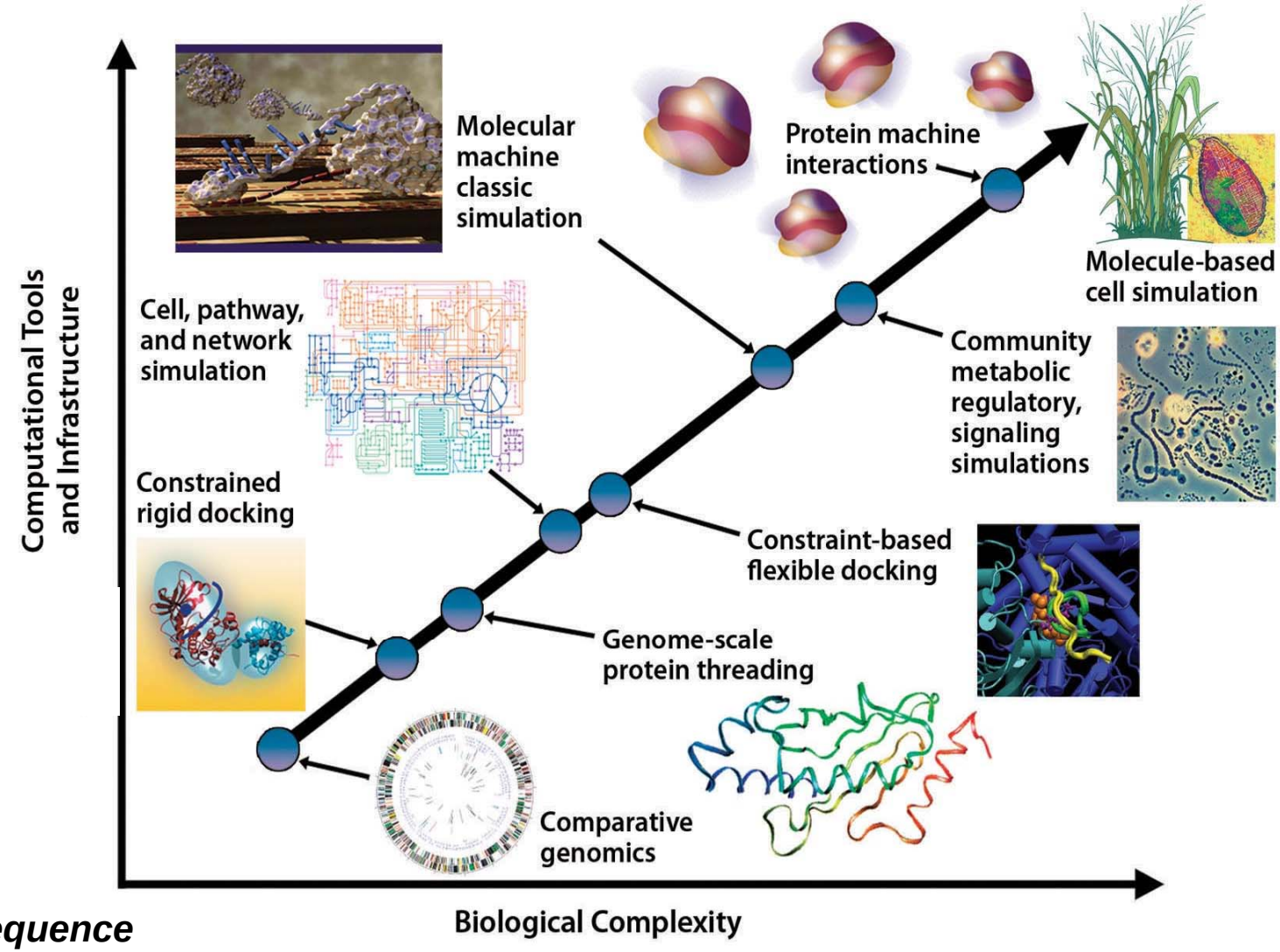
Integrative Research





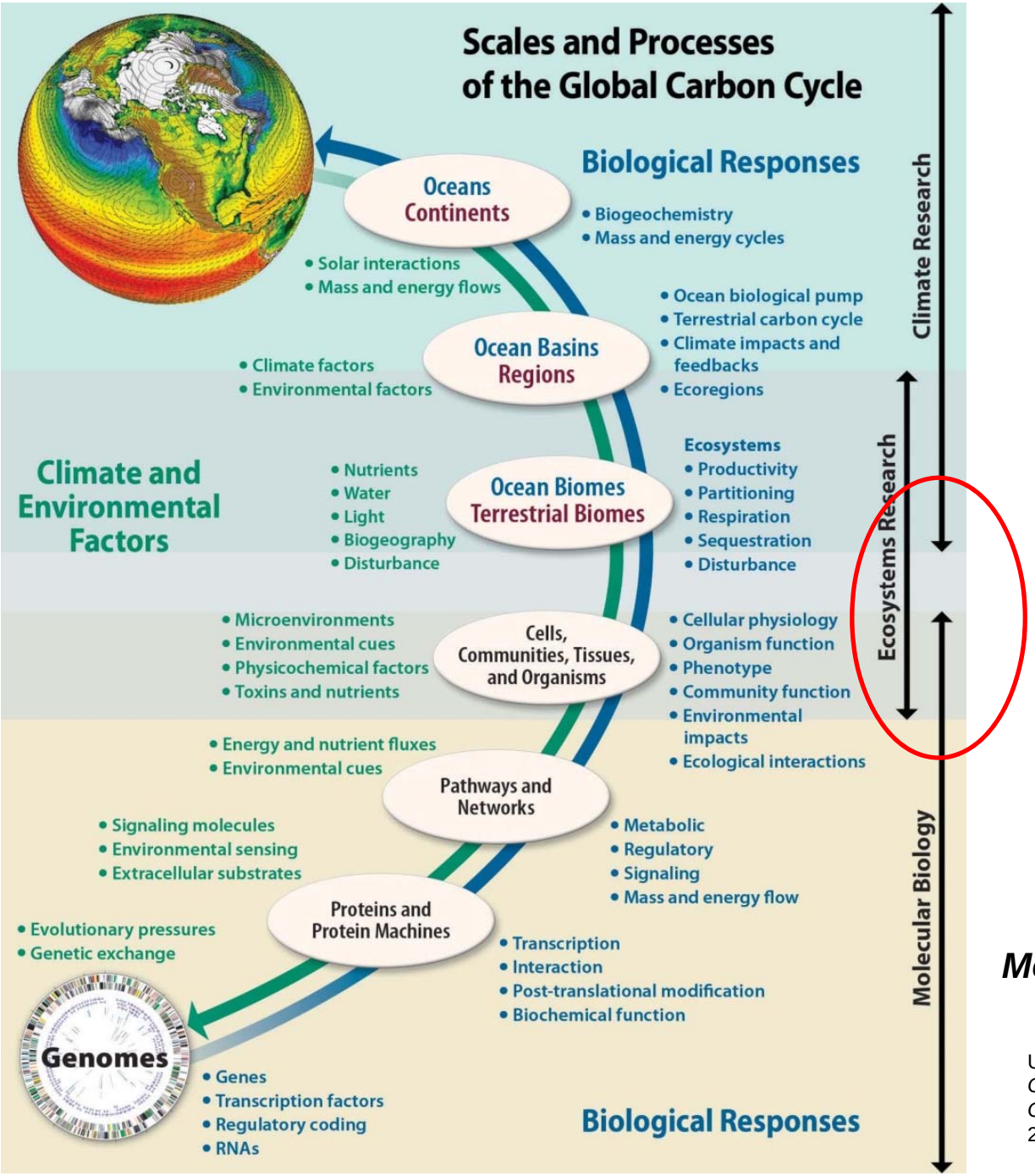
Hypothesis Generation Efficiency Systems Biology Programs

Core Approach is Applicable Across Observations Scales



Genome Sequence

Modeling ***Experimentation***



Resolving Biological Systems at Multiple Scales

Understanding & Model development facilitates science across larger scales relevant to BER Science

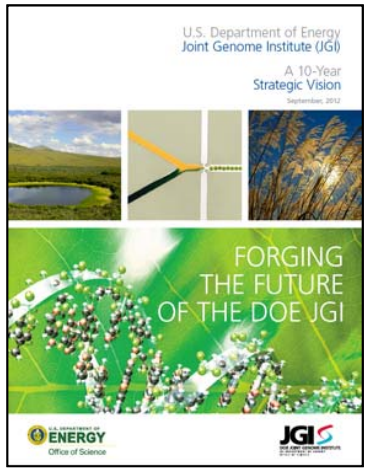
- Creates opportunities for interdivisional collaboration where programs meet.

U.S. DOE. 2008. U.S. Department of Energy, *Carbon Cycling and Biosequestration: Integrating Biology and Climate through Systems Science* Report from the March 2008 Workshop, DOE/SC-108

Emerging Technologies Opportunity Program

Six New Projects Awarded

- ***New technologies & capabilities for JGI***
  - *Single cell Raman spectroscopy (Stocker, MIT)*
  - *Microfluidics for single cells (Quake Stanford)*
  - *New metagenome assembly approaches (Banfield, UC Berkeley)*
  - *Advanced DNA synthesis strategies (Shendure, U. Washington)*
- ***Services enabling JGI user programs***
  - *Specialized plant genomic libraries (Wing, U Ariz.)*
  - *High-throughput fungal DNA prep & phenotyping (Magnuson, PNNL)*



http://www.jgi.doe.gov/programs/ETOP/

KBase Launch: Continuing

New Biological Capabilities:

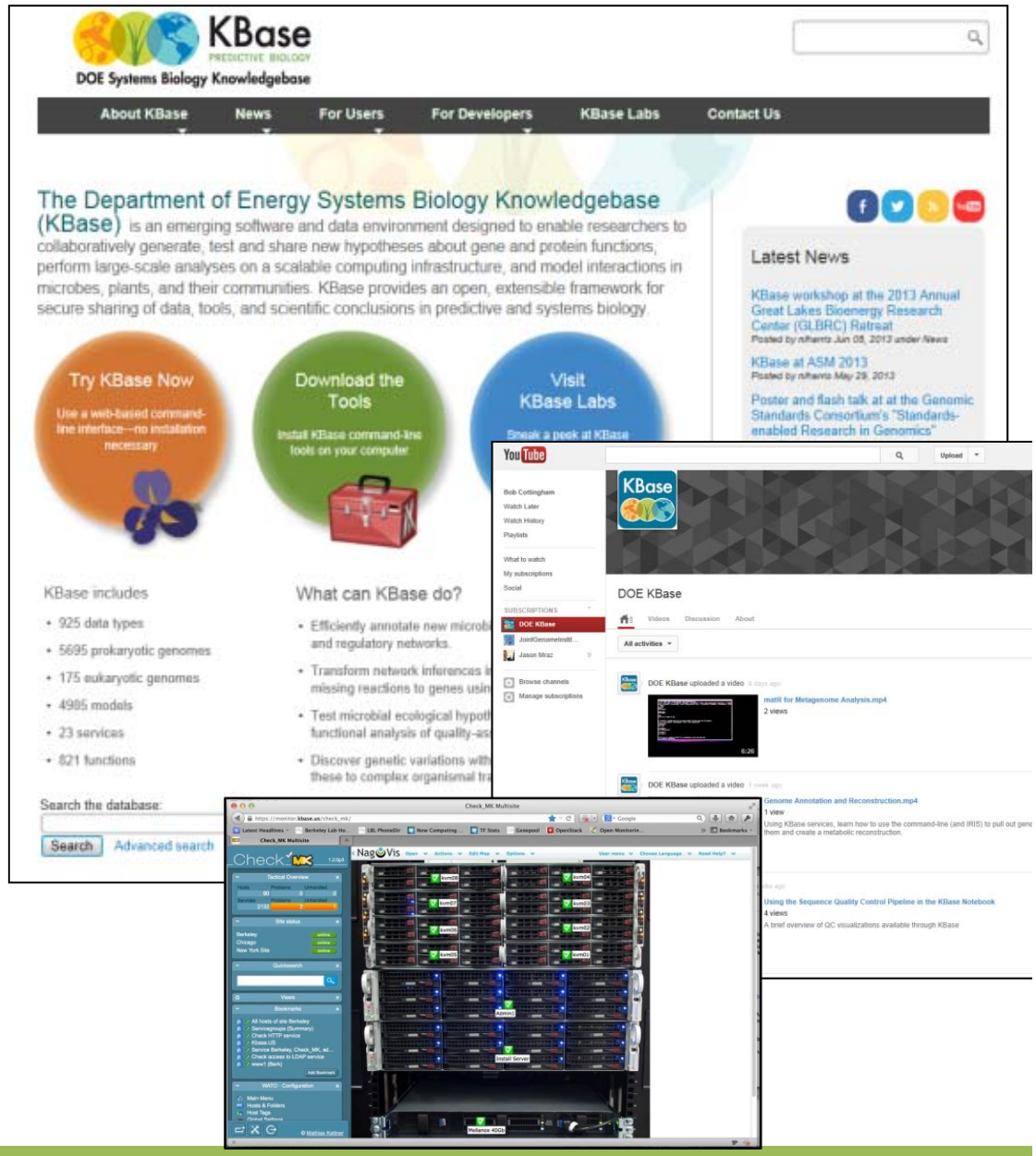
- Increased metabolic, regulatory and functional associations
- New capabilities to understand protein interactions
- Added functional abundance data

Outreach:

- Launched KBase YouTube channel with webinars and tutorials
- Launched Help Desk
- Ongoing Bootcamps and Tutorials

Infrastructure:

- Deployed redundant infrastructure at all sites
- Launched a monitoring system with visualization of computing system operations across all 4 sites



Joint Call for Exploratory Collaborations

- ***First-ever call between EMSL and DOE-JGI***
- ***Focused on plant, fungal, soil and microbial interactions and physiology related to***
  - *Biofuel production*
  - *Carbon cycling*
- ***Must require capabilities from both facilities***
- ***Schedule:***
  - ***27 Proposals Submitted!***
  - *Approved proposals start October 1, 2013*

EMSL

JGIS
DOE JOINT GENOME INSTITUTE
US DEPARTMENT OF ENERGY
OFFICE OF SCIENCE

BRC Science Highlight

BioEnergy Science Center

Thermophile simultaneously solubilizes lignin and carbohydrate in non-pretreated switchgrass biomass

Objective

➢ Determine the extent of untreated biomass solubilzation by the anaerobic thermophile, *Caldicellulosiruptor bescii*

Approach

➢ Incubate *C. bescii* with untreated switchgrass at 78 C

➢Analyze remaining biomass

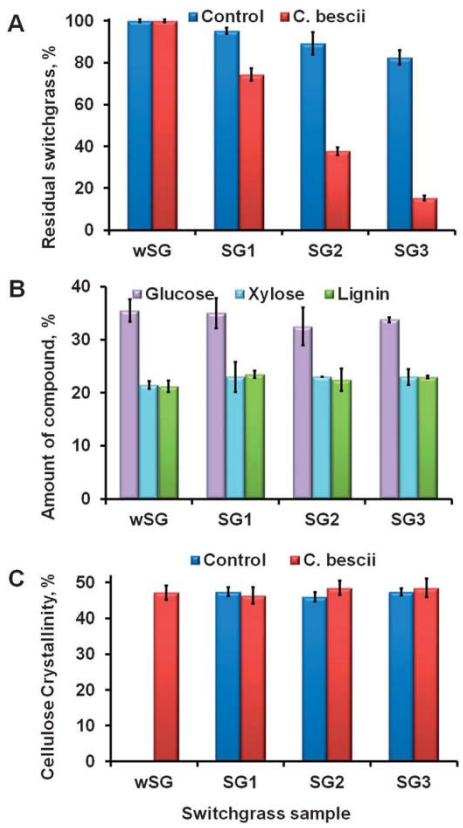
Results/Impacts

➢ The composition of remaining biomass was not significantly different from starting biomass indicating carbohydrates and lignin were solubilized at similar rates

➢Lignin monomers were found free in solution so they were not incorporated into microbial biomass

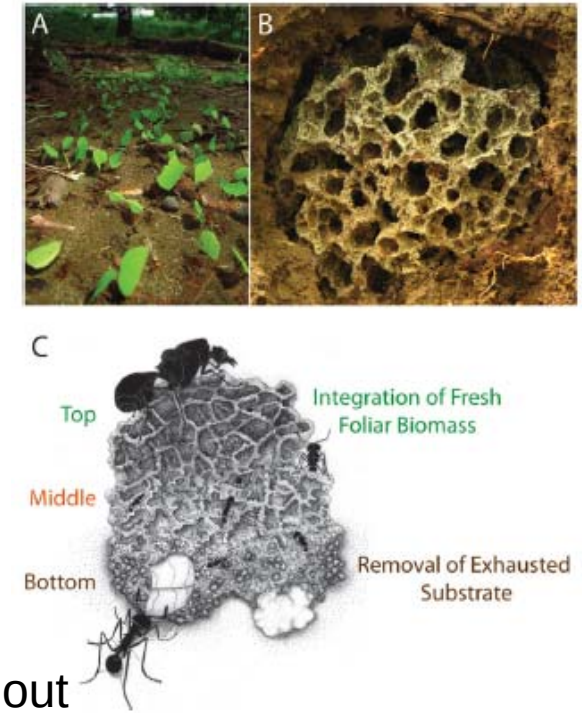
➢First anaerobe to solubilize cellulose, hemicelluloase and lignin!

➢Microbial solubilization of biomass without pretreatment is more efficient and economical



Kataeve et al., Carbohydrate and lignin are simultaneously solubilized from unpretreated switchgrass by microbial action at high temperature. EES DOI: 10.1039/c3ee40932e

Degradation of Recalcitrant Plant Polymers in Leaf-Cutter Ant Fungus



Objective:

- Understand the role of *Leucoagaricus gongylophorus* enzymes in digestion of plant material in the leaf-cutter ants fungus garden

Approach:

- Generate draft genomic sequence of *L. gongylophorus*
- Metaproteomics of fungus garden

Results/Impact:

- Fungus produces distinct sets of lignocellulases throughout the different stages of biomass degradation, including numerous cellulases and laccases
- Provides a detailed analysis of plant biomass degradation in leaf-cutter ant fungus gardens
- Adds to the set of lignocellulases to be mined for improved deconstruction

Alyward et al., 2013. *Leucoagaricus gongylophorus* Produces Diverse Enzymes for the Degradation of Recalcitrant Plant Polymers in Leaf-Cutter Ant Fungus Gardens. Appl. Environ. Microbiol. **79**:3770 doi:10.1128/AEM.03833-12

BRC Science Highlight

jbei Joint BioEnergy Institute

Genetically engineering plant results in decreased ferulic acid and increased saccharification

Objective

- To understand the role of BAHD acetyltransferases in synthesis of plant secondary wall and lignin

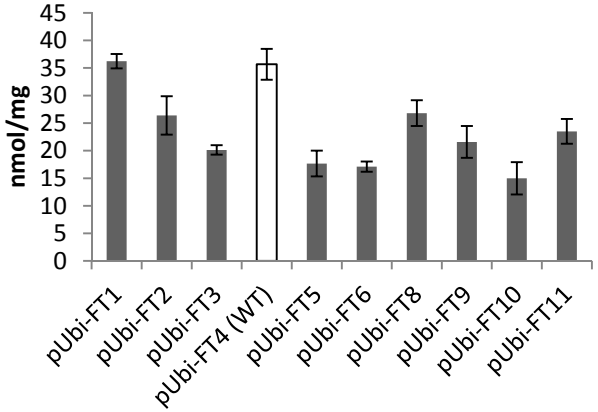
Approach

- Identify a clade of acyltransferase genes expanded in grasses
- Identify an activation mutant of OsAT10 with altered distribution of hydroxycinnamic acids

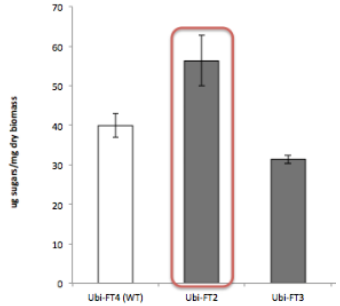
Results/Impacts

- OsAT10 plants had no discernible difference in growth or vitality
- Biochemical analyses reveal reduced FA and increased *p*-CA in matrix polysaccharides
- OsAT10 is a *p*-coumaroyl coenzyme A transferase involved in glucuronoarabinoxylan modification
- Thus, OsAt10 is an attractive target for improving grass cell wall quality for fuel and animal feed

Ferulic acid content green leaves



Enzymatic saccharification



40% increase in sugar release (following hot water pre-treatment)

Bartley et al., 2013 Overexpression of a BAHD Acyltransferase, OsAt10, Alters Rice Cell Wall Hydroxycinnamic Acid Content and Saccharification. **Plant Physiol** 161:1615-1633

BER Structural Biology Facilities Access: Enabling rapid solution of SAXS and SANS protein experimental data

Objective:

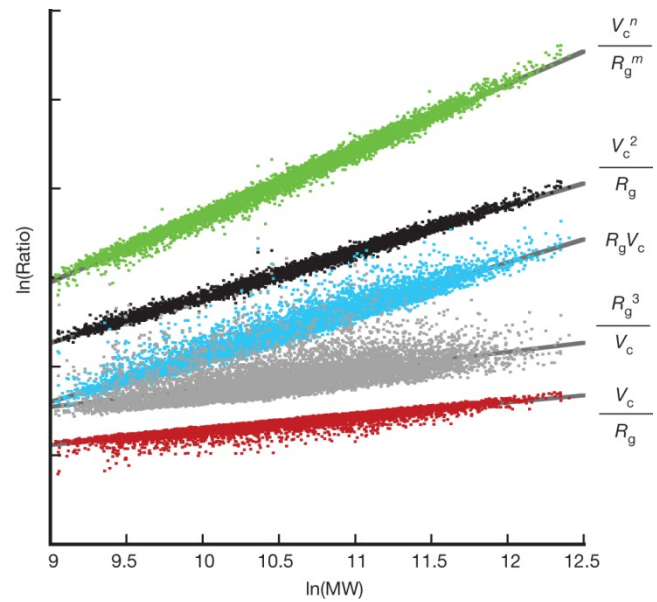
- Rapidly obtain shapes of proteins in solution under a wide range of experimental conditions.

Approach:

- Define a new invariant parameter, the volume of correlation (Vc), that can be calculated from a single scattering dataset.
- Employ and test Vc to define metrics for conformation, mass, and model accuracy from parameters measured experimentally. Test several proteins with known structures, using SAXS

Results/Impacts

- Vc predicts changes in shape when solution conditions change. Ex. smaller Vc when a metal ion is added that tightly binds to the macromolecule, causing it to become more compact.
- Enables the application of SAXS and SANS to many new types of biological systems and requires 1/100 the amount of time for experimental data collection.



Defining the power-law relationship between Vc, the radius of gyration (Rg) and protein mass. Fitting the linear power-law relationship (black) produces an average mass error of $4.0 \pm 3.6\%$. The other ratios display asymmetric nonlinear relationships.

Robert A. Rambo and John A. Tainer, "Accurate assessment of mass, models and resolution by small-angle scattering", **Nature** 496, 477–481(25 April 2013) doi:10.1038/nature12070

Structural Systems Biology Illustrates a New Method to Predict Heat Tolerance in *E. coli*

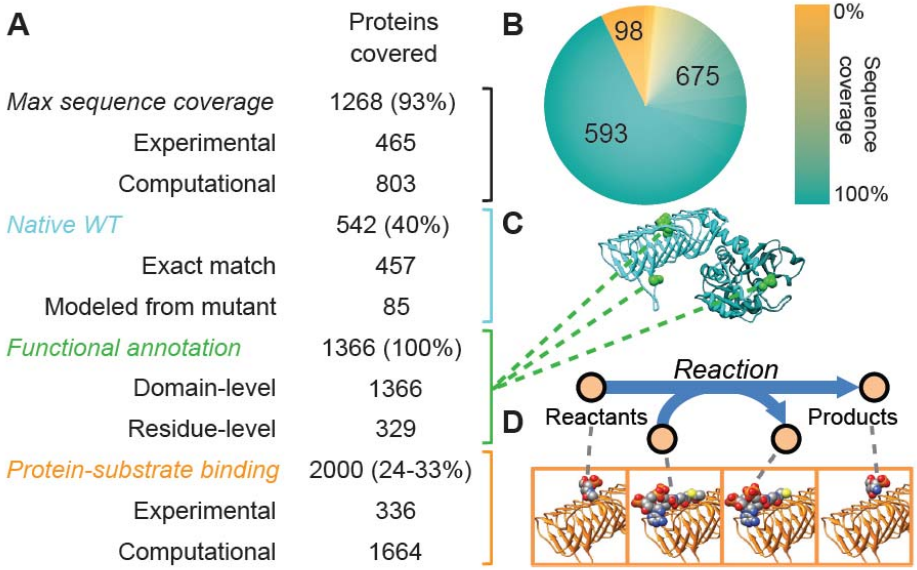
Objective:

Simulate growth of microbial species under various temperature conditions and provide mechanistic interpretations of mutations that conferred greater thermostability

Approach:

Integrate together the metabolic reactions of *E. coli* with the protein three dimensional structures of each catalytic enzyme

- 93% of Sequence Covered with functional annotations and 3-D protein structures
- 24% of protein-substrate binding reactions covered with 3-D structures
- Simulate temperature-dependent growth by imposing protein activity constraints on the metabolic models



Results/Impact:

- Simulation of growth of *E. coli* under various temperature conditions consistent with experimental growth data
- implications for development of industrial microbes for biocatalysts.

Roger L. Chang, Kathleen Andrews, Donghyuk Kim, Zhanwen Li, Adam Godzik and Bernhard O. Palsson, "Structural Systems Biology Evaluation of Metabolic Thermotolerance in *Escherichia coli*", ***Science***, 2013, 1220-1223 doi:10.1126/science/1234012

Fungi Significantly Modify the Soil Bacterial Community and Nitrogen Cycling During Litter Decomposition

Objective

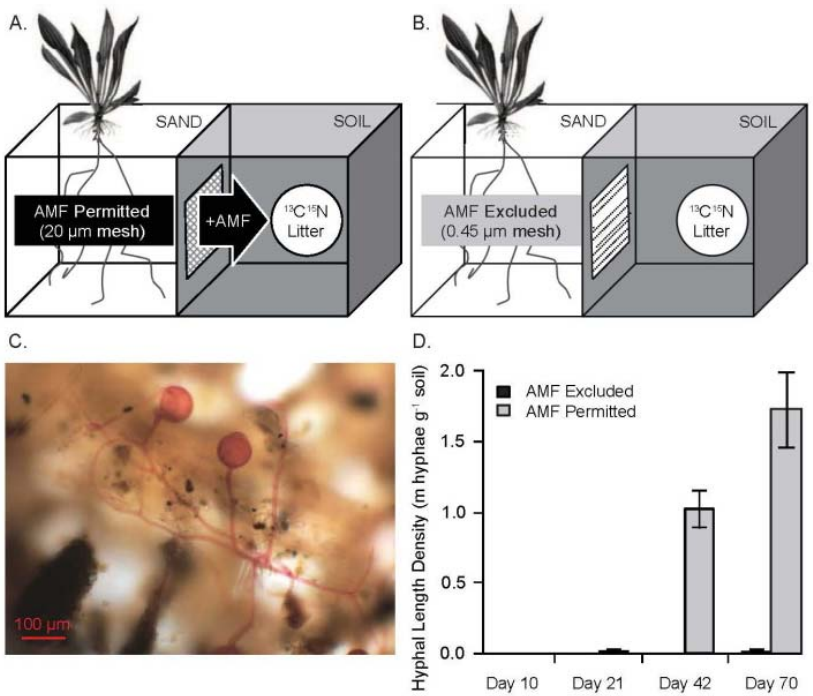
- Investigate how arbuscular mycorrhizal fungi (AMF) influence soil microbial communities during nutrient uptake. Do AMF modify the soil microbial community and N cycling during litter decomposition?

Approach

- Two-chamber system with ^{13}C- and ^{15}N-labeled litter in root-free soil; AMF either allowed access to or excluded from litter.
- Significant uptake of microbially-released N, but not C, by the AMF.

Results/Impact

- AMF may modify community and decomposition process through N export, part of a complex process by which C and N flow through ecosystems.



Nuccio EE, Hodge A, Pett-Ridge J, Herman DJ, Weber PK, and Firestone MK. 2013. An Arbuscular Mycorrhizal Fungus Significantly Modifies the Soil Bacterial Community and Nitrogen Cycling During Litter Decomposition. ***Environmental Microbiology***, DOI: 10.1111/1462-2920.12081.

Objectives

Develop agents for assessing sucrose transport in higher plants using PET.

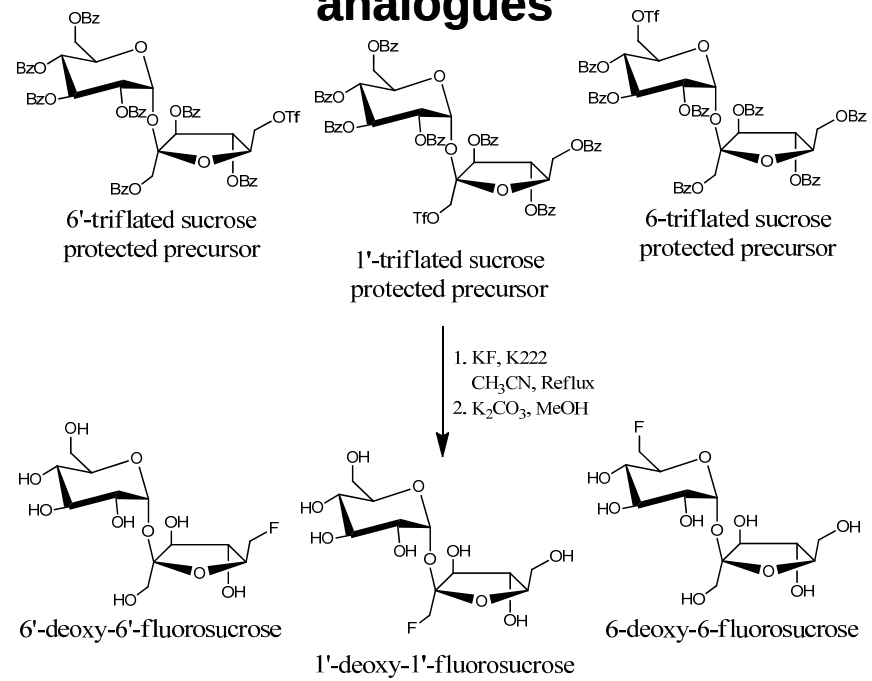
Approach

Develop syntheses of 3 isomers of deoxy-fluorosucrose suitable for incorporation of ^{18}F. Perform the hot syntheses and study the transport of the molecules in plants.

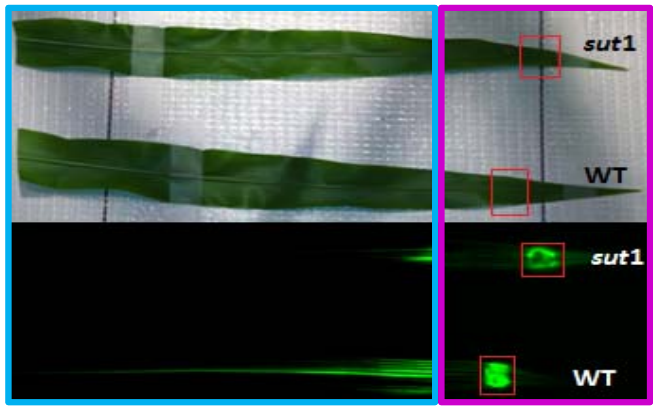
Results and Impact

- 6'-[F-18]fluoro-6'-deoxy-sucrose (FDS) has been synthesized to study sucrose transport in living plants.
- Automated synthesis of FDS has been developed to make it widely available for plant metabolic imaging studies.
- Positional isomers of [F-18]fluoro-deoxy-sucrose will allow probing of plant utilization of sucrose and its mechanism of transport.

Synthesis of 3 fluorosucrose analogues



Gaddam, V; Harmata, M *Carbohydrate Research* **2013**, *369*, 38-41.



Actual leaves used for imaging after excision from plant

Enhanced image to show distribution; less transport in *sut*1.

Rotsch, D; Brossard, T; Vikram, G; Harmata, M; Cutler, C; Robertson, JD, Jurisson, SS; Braun, D ***J. Labelled Compds Radiopharm***. **2013**, *56*, S118

Combining Predictive Models with Experiments to Understand Radiation Effects in Skin Tissue

Objective

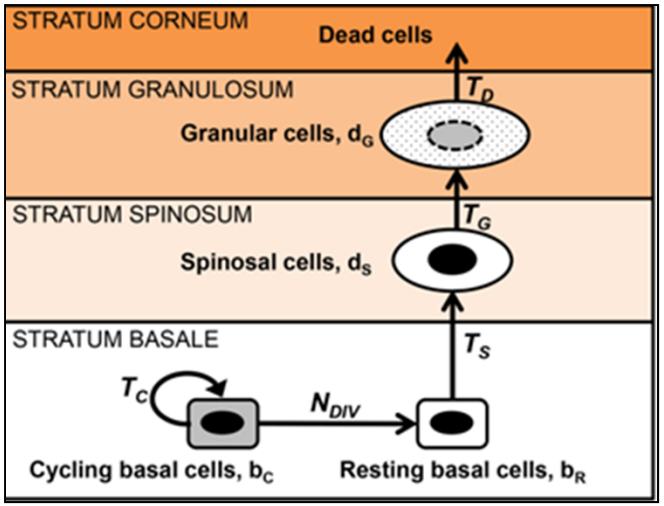
- To understand and predict risks from heavy ion radiation by studying effects on molecular, cellular and tissue-level processes in relevant experimental systems

Approach

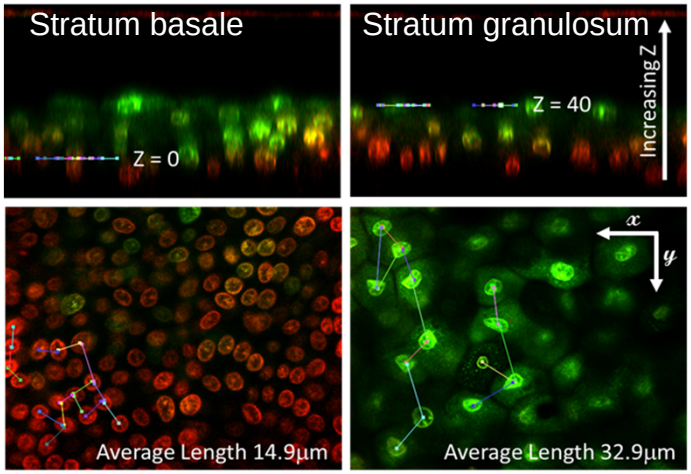
- Engineered 3D human skin tissues were exposed to neon ion irradiation, then several tissue-level properties were measured
- A mathematical model was developed to simulate the complex homeostatic changes in cell division, differentiation, and proliferation that were induced by the neon ion exposures

Impact

- Integrated approach provides a framework to understand responses of multicellular systems and can be adapted to other epithelial tissues and radiation exposure scenarios



Schematic descriptions of the mathematical models for unirradiated and neon irradiated skin tissue



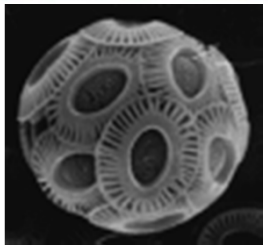
Confocal images to spatially characterize cell density in the tissue

von Neubeck C, H Shankaran, MJ Geniza, PM Kauer, RJ Robinson, WB Chrisler, and MB Sowa, "Integrated Experimental and Computational Approach to Understand the Effects of Heavy Ion Radiation on Skin Homeostasis." ***Integrative Biology*** (Accepted).

JGI Highlight

Pan genome of the phytoplankton *Emiliania* drives its global distribution

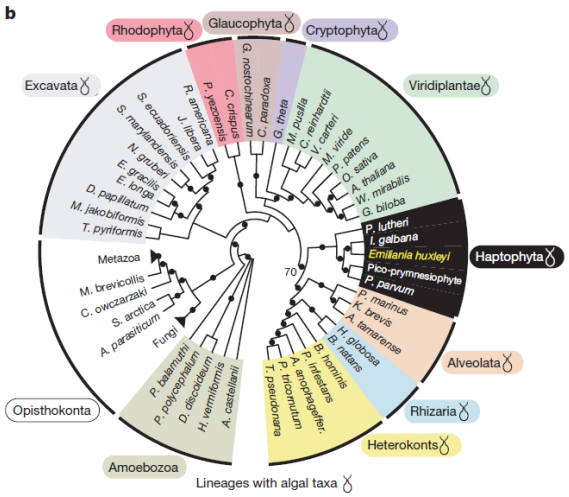
nature



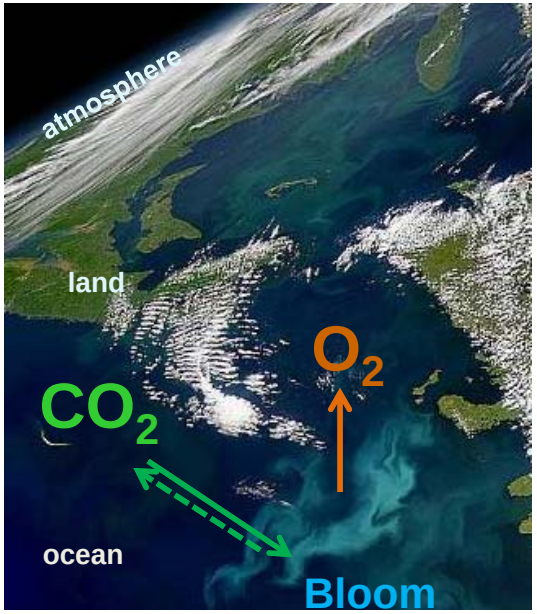
Betsy Reed, *et al.* (published on June 18 2013)

Emiliania huxlei, a single cell marine alga;

- Model for biomineralization (calcium carbonate exoskeleton);
- Balance of CO2 fixed during photosynthesis and released during calcification;
- The first sequenced haptophyte Ref Genome of (*E hux)* and 13 additional isolates.



Evolutionary significance:
fills a gap (Haptophytes) in the Tree of Life

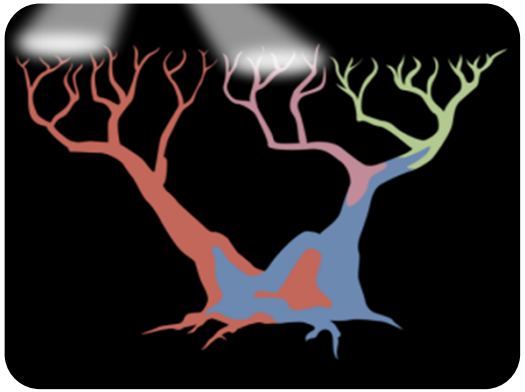


Ecological significance:
large blooms seen from satellites

Geological significance:
Cocoliths sediments - global fossil archive (200Myrs)

JGI Highlight

Insights into the Phylogeny and Coding Potential of Microbial Dark Matter



Objective

- Analyze genomes of Microbial Dark Matter (lineages/phyla without cultured representatives).

Approach

- Sample nine broadly distributed sites across the globe
- Recovered 201 genomes belonging to 29 uncharted branches of the tree of life

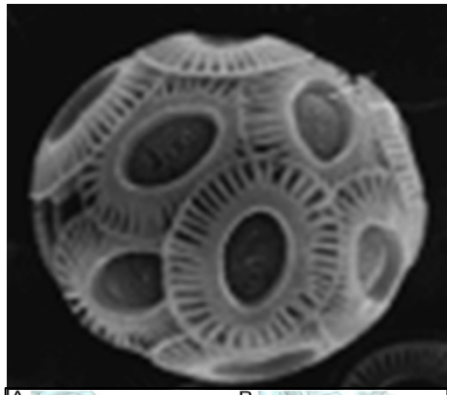
Results/Impacts

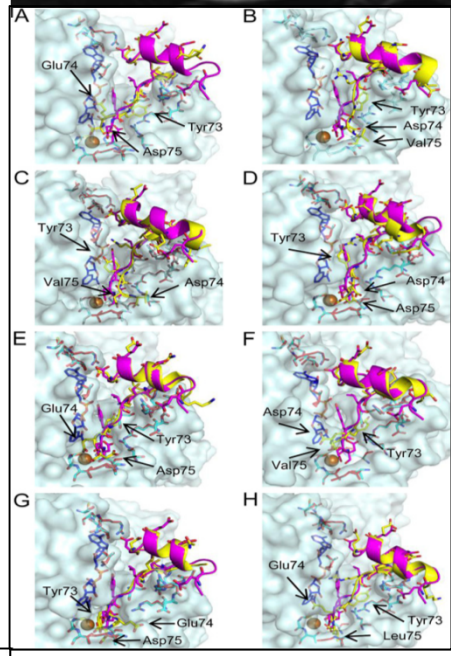
- Two recovered genomes exhibit evidence of recoding suggesting that the canonical genetic code may not be all that is out there in the wild

	# contigs	Length, Mb	Evidence that reassignment pipeline works (Positive controls)
Opal UGA->aa	290,064	1390.4	***Mycoplasma*,GN02 taxa.**
Ochre UAA->aa	20,357	480.3	***Tetrahymena*, ciliated protists**
Amber UAG->aa	10,314	130.1	

*Rinke, et al. (2013 **Nature**, in press)*

Selected JGI Publications





Read B et al. Pan genome of the phytoplankton *Emiliania* underpins its global distribution. ***Nature.*** 2013 June 12. doi: 10.1038/nature12221.

Stanley DN et al. Comparative Analysis of 126 Cyanobacterial Genomes Reveals Evidence of Functional Diversity Among Homologs of the Redox-Regulated CP12 Protein. ***Plant Physiol***. 2013 Feb;161(2):824-35. doi: 10.1104/pp.112.210542. Epub 2012 Nov 26.

Sutter M et al. Crystal structure of the FRP and identification of the active site for modulation of OCP-mediated photoprotection in cyanobacteria**.** ***Proc Natl Acad Sci*** *U S A*. 2013 May 28. [Epub ahead of print]

Zhang JY et al. Development of an integrated transcript sequence database and a gene expression atlas for gene discovery and analysis in switchgrass (*Panicum virgatum* L.). ***Plant J.*** 2013 Apr;74(1):160-73. doi: 10.1111/tpj.12104. Epub 2013 Feb 18.

Aylward FO et al. Comparison of 26 Sphingomonad Genomes Reveals Diverse Environmental Adaptations and Biodegradative Capabilities. ***Appl Environ Microbiol***. 2013 Jun;79(12):3724-33. doi: 10.1128/AEM.00518-13. Epub 2013 Apr5.

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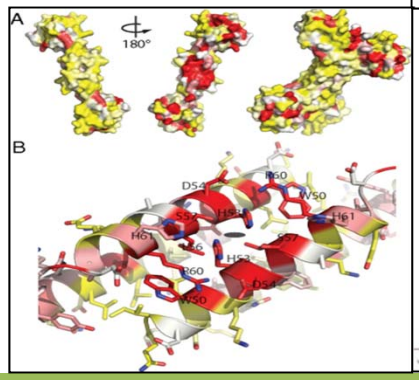

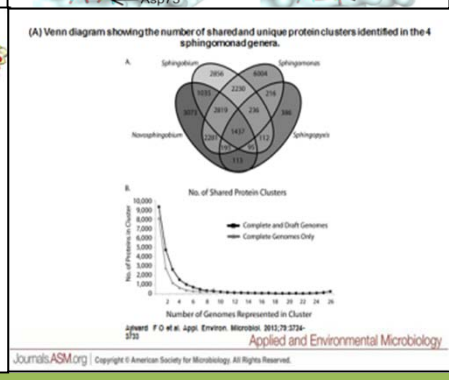

54 other publications since the last BERAC meeting

JGI Publication Highlights:
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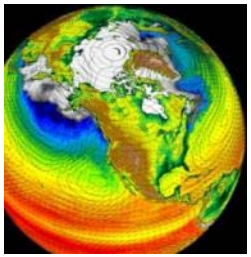

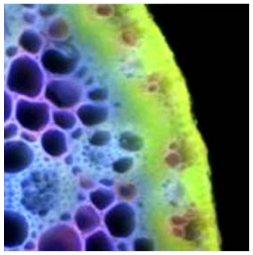

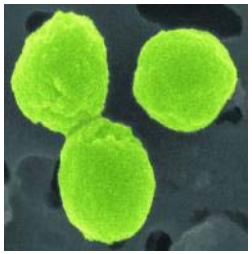

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Dissecting laccase regulatory network in poplar using miRNA

Objective:

- Understand role of the microRNA, ptr-miR397a, in the regulation of laccase genes in *Populus trichocarpa*

Approach:

- BLAST of *Arabidopsis* laccase genes against *P. trichocarpa* genome identified 49 laccase gene models in 6 clades
- Clone the full length ptr-miR397 and overexpress in *P. trichocarpa*
- Overexpression of a microRNA targets four clades of laccase gene models

Results/Impact:

- Overexpression of ptr-miR397a results in overall 40% less laccase activity and 12%-20% reduction in lignin content
- Transcripts for monolignol biosynthesis genes remain unchanged
- Lignin structure the same as determined by NMR
- Developed a regulatory network model based on differentially expressed genes between wt and the microRNA overproducing strain
- Illustrates importance of microRNAs in regulation of gene sets in lignin biosynthesis

Lu et al. 2013, Ptr-miR397a is a negative regulator of laccase genes affecting lignin content in *Populus trichocarpa*, **PNAS**