

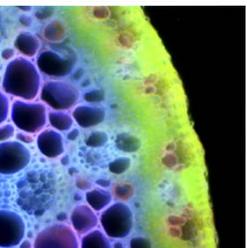
BERAC Meeting



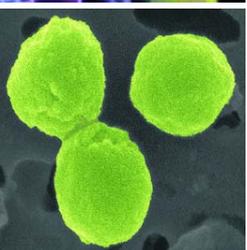
Biological Systems Science Division Update



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Biological Systems Science Division



March 9, 2011



Updates on Division Personnel

- **Marvin Stodolsky—retirement**



- **Pablo Rabinowicz—new IPA (plant molecular biology and bioinformatics)**

Updates on Division Solicitations

- **CURRENT SOLICITATIONS**
 - FOA-0000368 Genomic Science and Technology for Energy and Environment
 - Joint USDA-DOE Plant Feedstock Genomics for Bioenergy
 - Systems Biology Knowledgebase

DOE Switchgrass Workshop

January 18, 2011 at the Plant and Animal Genome Conference, San Diego, CA
CoChairs: Jeff Bennetzen (U Georgia) and Tom Juenger (U Texas)

Agenda/Goals:

- Discuss coordination of the switchgrass genome sequencing project
- Identify research needs and gaps

Participants:

- Switchgrass researchers from university and government labs including geneticists, breeders, molecular biologists, and genomicists
- Federal program managers as observers

Requirements noted:

- Screening for natural variation in desired traits
- Availability of protocols and vectors for high-efficiency genetic transformation
- Development of specific genome-based sequence markers to assist breeding

Action Items:

- Form a switchgrass executive committee
- Define the group's scope
- Develop processes for information sharing (wiki site, annual meeting)
- Follow-on discussions

Human Subjects Research Update

- **The DOE Human Subjects Protection Order has been updated to include: requirements set forth in the December 2009 Secretarial Policy Memo on “Military and Intelligence-related Research,” or Human Terrain Mapping.**
 - Human Terrain Mapping includes research and data gathering activities to understand the motivations and behavior patterns of the people among whom the U.S. Armed Forces are operating (i.e., Iraq, Afghanistan) and in other countries prone to political instability.
 - There are risks to participants and to researchers, with 3 U.S. researchers having been killed in Iraq and Afghanistan in recent years. The modifications to the Order prohibit DOE labs from sending researchers to these countries to do the data collection but allow them to contribute their computational and modeling capabilities and to analyze de-identified data.
- Other upcoming activities include:
 - Reviews of DOE Site Human Subjects Protection Programs (LANL, SRS, and INL in 2011 and LBNL, ANL, and PNNL in 2012).
 - Regular meetings of the Central DOE IRB, established in April 2010.

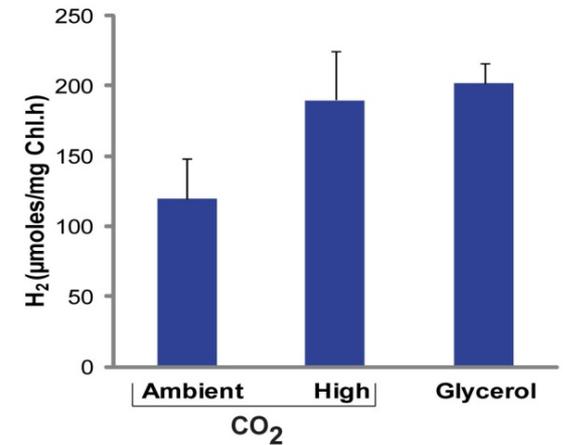
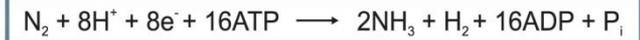
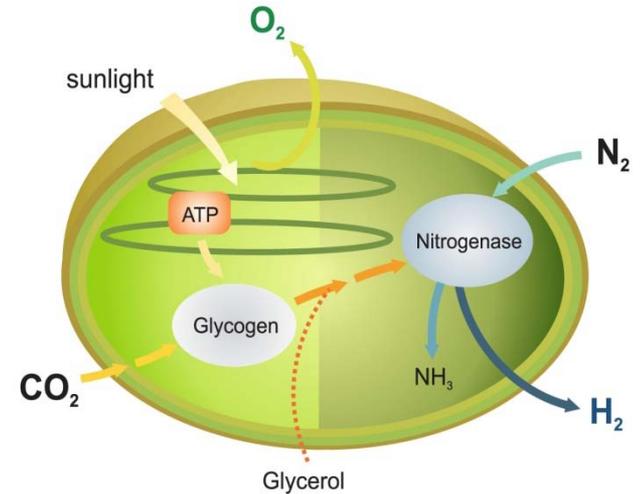
Cyanobacterial Hydrogen Production Under Aerobic Conditions

Objective:

Determine how *Cyanothece* 51142 achieves light driven hydrogen synthesis in the presence of air

Approach:

Incubate cultures under air with continuous lighting and elevated CO₂ or glycerol, measuring H₂ production and expression of relevant genes.



Bandyopadhyay et al. 2010. Nature Commun.
DOI:10.1038/ncomms1139

Understanding Structure-Function Relationships for Bioprocessing Enzymes

Objective:

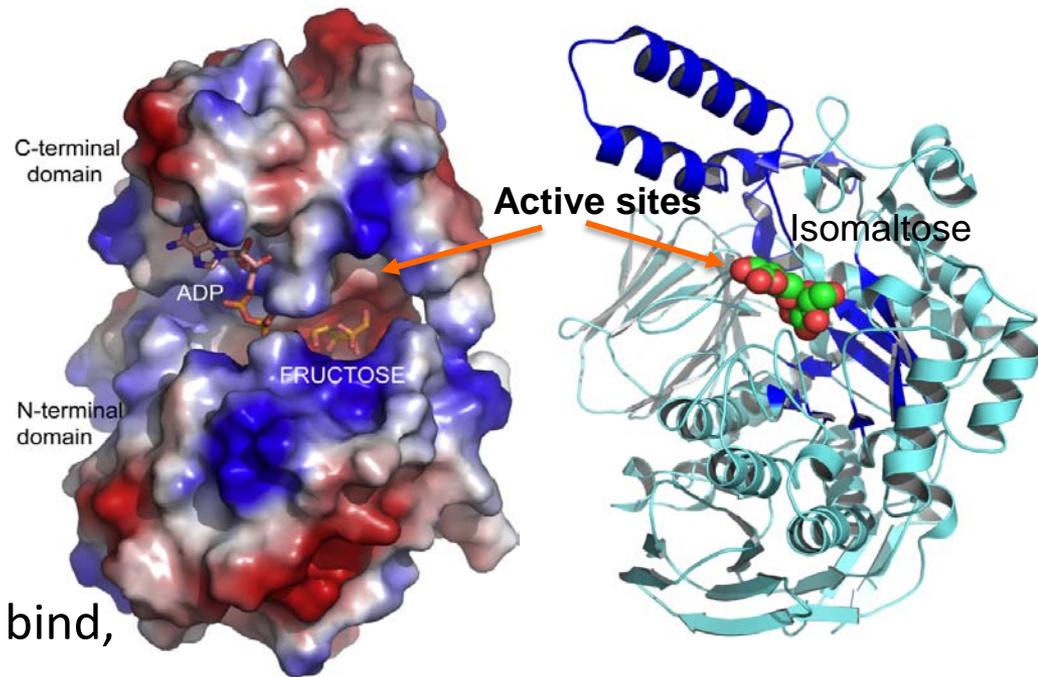
Improve conversion of biomass to fuels by using structural information to optimize enzymes for bioprocessing

Approach:

Use high-resolution synchrotron protein crystallography to discover how sugars are bound to enzymes

Results/Impact:

- New information about how enzymes bind, recognize and process carbohydrate substrates and how variations in enzyme structure impact enzyme function
- Demonstration of how structural biology can explain key steps in carbohydrate metabolism with atomic resolution



Fructose and ADP bound to ROK fructokinase from *B. subtilis*¹

Catalytic domain of α -glucosidase with bound isomaltose from *R. obeum*²

Research carried out the Structural Biology Center at the Advanced Photon Source, Argonne National Laboratory
Andrzej Joachimiak, Director and lead author

1. B. Nocek, et al., *J. Molecular Biology* (2011) **406**, 325–342
2. K. Tan, et al., *The FASEB Journal* (2010) **24**, 3939–3949

Semantic Indexing of Patent Literature

Objective

- Provide real-time microbial patent searching and indexing to the research and intellectual property communities.

Approach

- Based on semantic indexing techniques developed under a Phase II STTR.
- Produces “terminological fingerprints” of patents and scientific literature.
- No prior knowledge of patent indexing systems required.

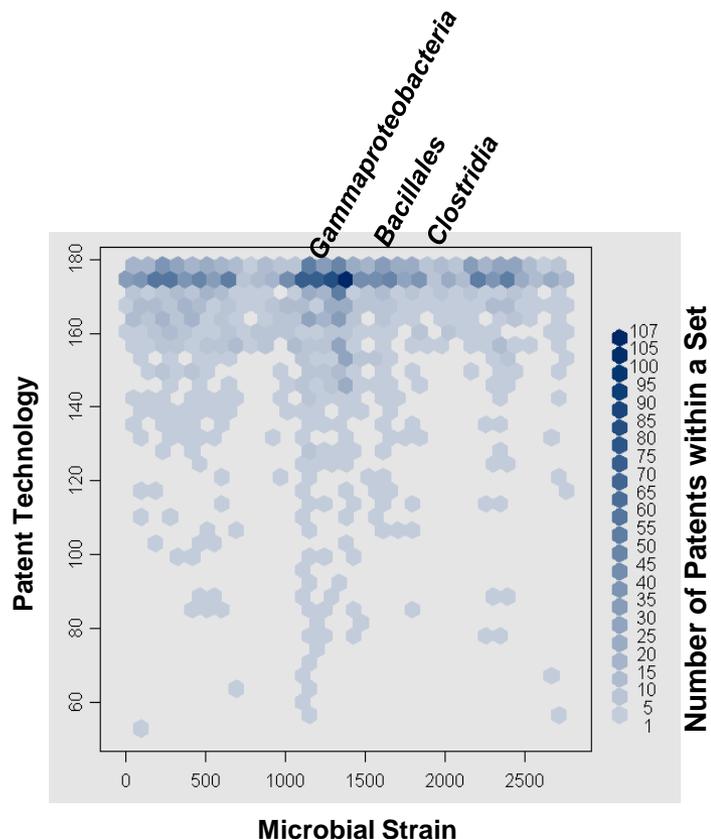
Results/Impacts

- Easy identification of key patents and publications based on organisms and technology of interest.
- Intuitive visualization allows users to refine results interactively.
- Technology integrates with existing commercial, academic, and USPTO data mining capabilities

Parker C, Lyons C, Roston G, Garrity G. US 20100198841, "Systems and methods for automatically identifying and linking names in digital resources", August 5, 2010.

Patent Clusters:

- Each contain related taxa (~ 50).
- Common technology based on patent classification
- Vectors represent all technologies



Computational Approaches to Simulate Microbial Ecosystems

Objective:

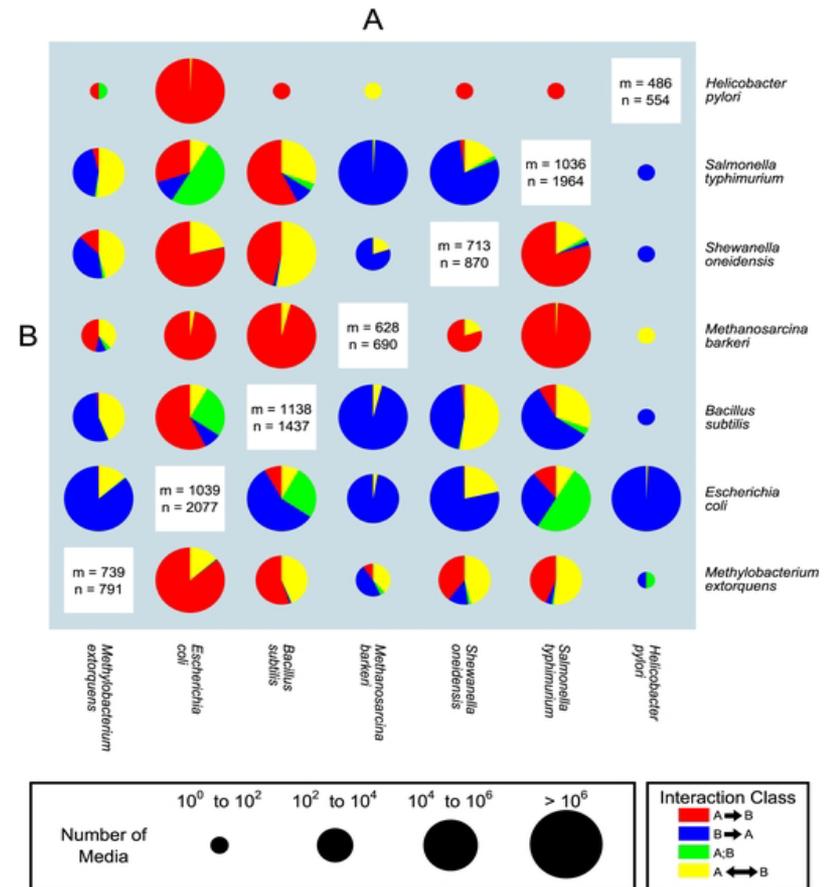
Simulate and test the obligatory mutualistic or commensal growth of microbial pairs.

Approach:

Novel constraint-based Flux Balance algorithms are applied to pairs of microbial genome-scale models (including complete sets of enzymatic and transport reactions). The algorithms search for growth media that force microbe pairs to cross-feed.

Results/Impacts:

- New ability to identify type of microbial interactions, nutrient exchange and media requirements for community growth.
- Findings also suggest that symbiotic (yellow) interactions may arise more readily through environmental fluctuations rather than genetic modifications.



The size of the pie chart reflects the number of media that allow growth of both organisms.

Niels Klitgord and Daniel Segre, Environments that Induce Synthetic Microbial Ecosystems, *PLoS Computational Biology*, volume 6 (Nov, 2010).

Biomass Degradation by *Cellvibrio japonicus*

Objective:

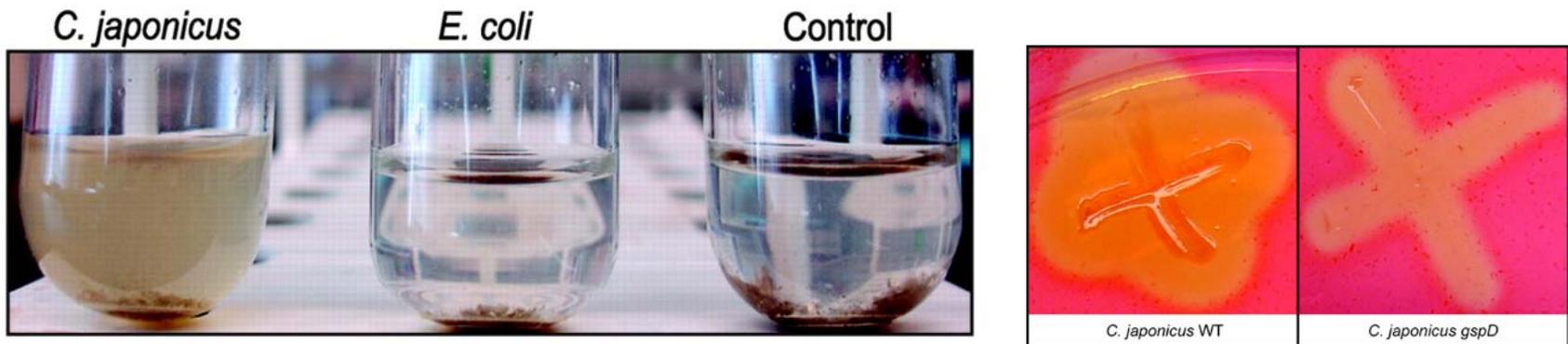
How does the gram negative bacterium *Cellvibrio japonicus* secrete its diverse complement of extracellular cellulases?

Approach:

Examine growth on cellulose or AFEX treated biomass (corn stover and switchgrass) and construct mutants lacking key secretory genes.

Results/Impact:

- Wild type *C. japonicus* effectively solubilized and consumed biomass, but mutants lacking the outer membrane secretin of the type II secretion system could not.
- Provides new targets for metabolic engineering of *C. japonicus*, as well as potential degradation systems to introduce into other gram negatives such as *E. coli*.



Gardner, J. & D. Keating 2010. *Appl. Environ. Microbiol.* 76(15):5079-5087

Microfluidic technology for the large scale screening of cellulases



Objective:

Need to rapidly and efficiently screen for candidate enzyme cellulases based on their ability to generate sugars from biomass hydrolysis.

Approach:

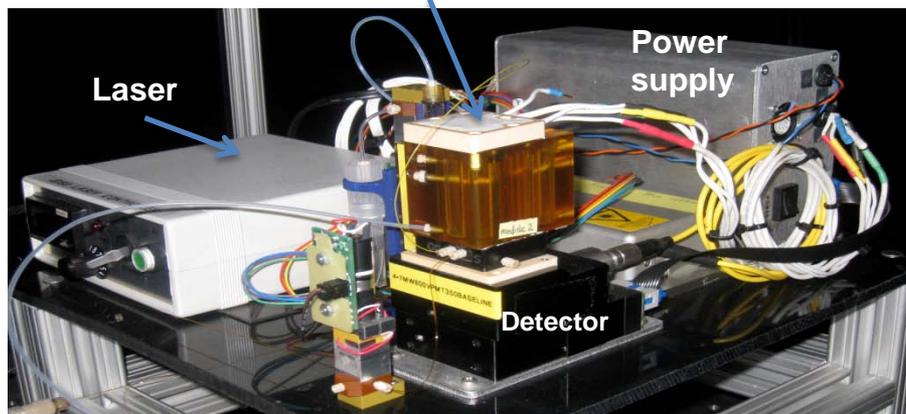
- JBEI has developed a new microfluidic chip-based assay for the rapid and precise characterization of biomass hydrolysis products, namely small sugars such as glycan and xylan.
- This system overcomes the difficulty in separating and identifying these closely related sugars by developing a mathematical model, based on molecular weight and separation parameters, to rationally select the system characteristics for optimized separation.

Results/Impacts:

JBEI researchers were able to rapidly screen for hydrolysis products on the order of one minute (~10-fold faster than HPLC methods)

Rajiv Bharadwaj, Zhiwei Chen, Supratim Data, Bradley M. Holmes, Rajat Sapra, Blake A. Simmons, Paul D. Adams and Anup K. Singh, *Anal Chem.* 2010 Nov 15;82(22):9513-20.

Microfluidic chip module
(2"x2"x 3")



Altered Gene Leads to Increased Biomass in Dicots

Objective:

Increase stem biomass by genetically activating ectopic secondary cell wall formation in pith cells of dicot plants.

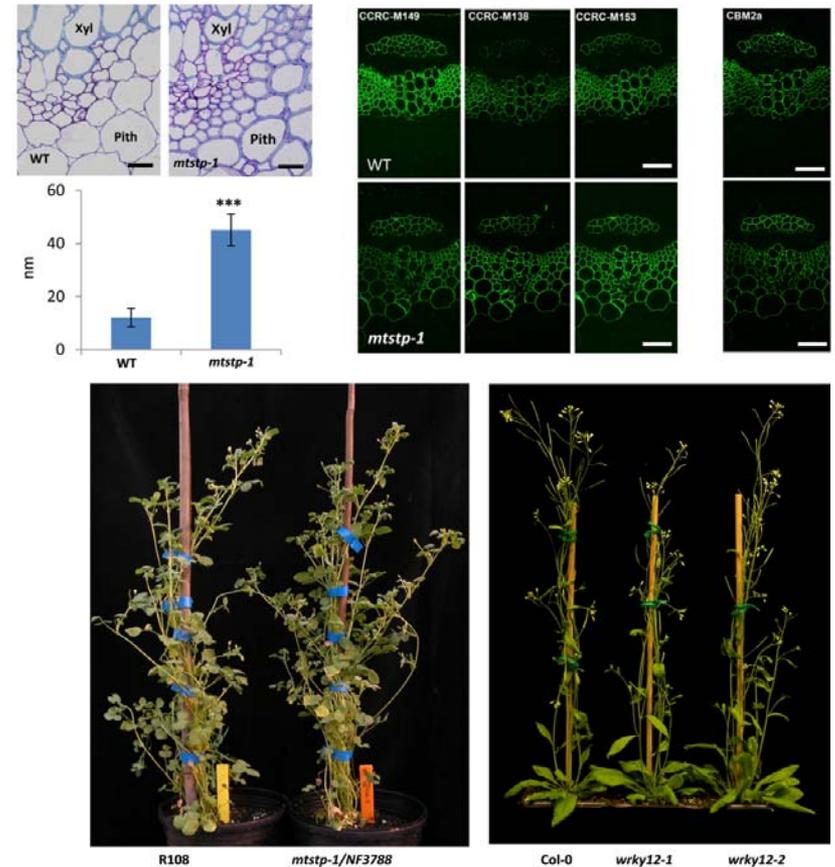
Approach:

-*Medicago truncatula* (alfalfa relative) and *Arabidopsis* plants with mutation in a specific regulatory gene have thickened, secondary cell wall formation in pith cells.

-Thickened pith cells are composed of xylan and cellulose as well as lignin

-Plants have ~50% increase in biomass density, no noticeable loss of vigor

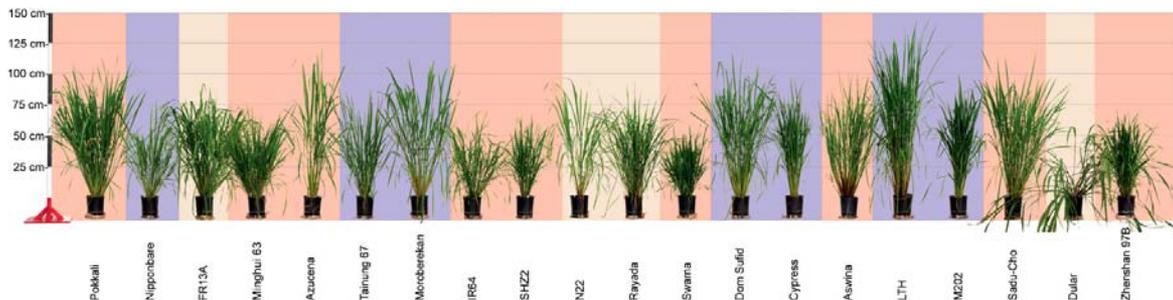
Results/Impacts: Loss of function in a single gene leads to a significant increase in stem biomass, suggesting a strategy to enhance biomass without adversely affecting the health and fitness of the plant.



Wang H, Avci U, Nakashima J, Hahn MG, Chen F, and Dixon RA. 2010. *Proc Natl Acad Sci* 107(51):22338-43.

Analyzing Rice Genetic Variation in Bioenergy Traits

Objective: Identify genetic variation and underlying genes that can be targeted for improving biomass production in perennial grass feedstocks.

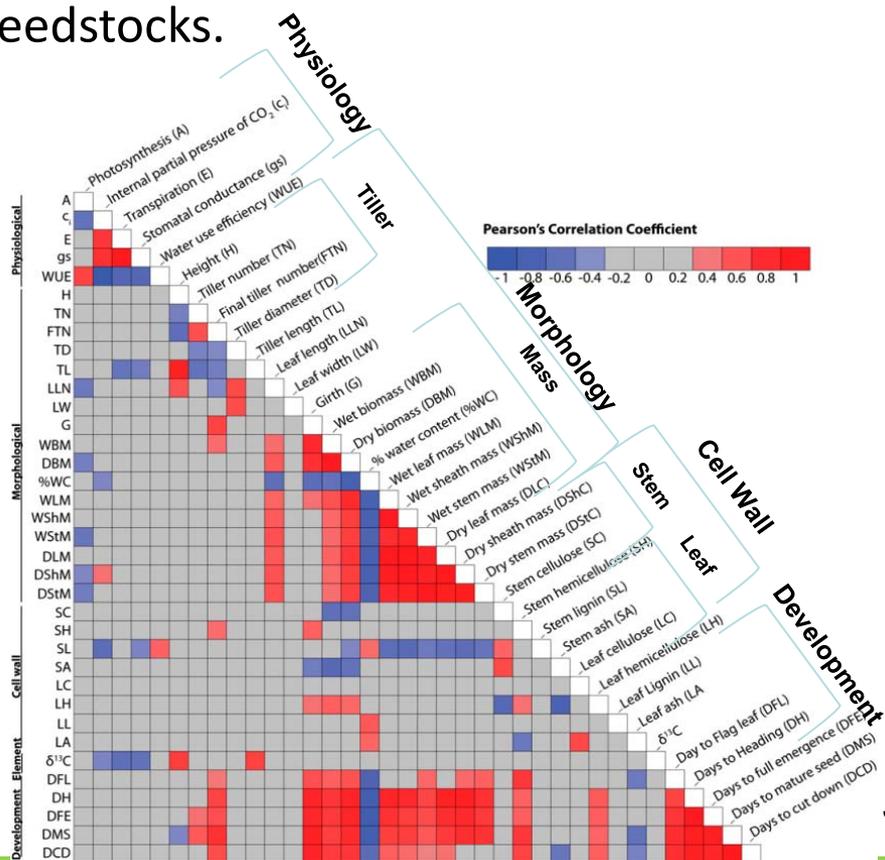


Approach: Exploit genomics and genetics resources by analyzing variation among 20 diverse rice varieties for bioenergy traits.

Results/Impact:

- Significant variation detected among all lines, morphological traits exhibited high heritabilities
- Variation explained largely by variety and breeding history, rather than varietal group
- Suggests existence of multiple targets for biomass improvement

Jahn et al. (2011) Plant Physiology 155(1):157-168.



New Tools for Re-Analysis of Radiation-exposed Tissues

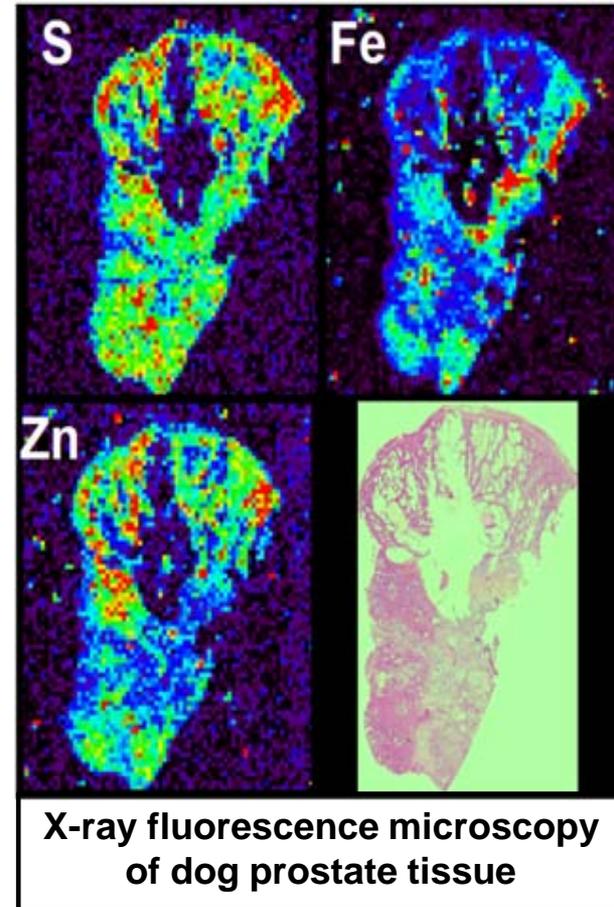
Objective: To measure elemental distributions in archived tissues and highlight applications of new molecular biology techniques in tissues from historic mega radiobiology studies

Approach:

- (1952-1991) Dog and mouse tissues from animals irradiated with external beam at Argonne National Laboratory and other labs were analyzed, then collected, processed, and archived for future re-analysis
- X-ray fluorescence microscopy (XFM) imaging was performed on sections of paraffin-embedded dog tissues to show the distributions of various elements (tin, iron, zinc,...)

Results/Impacts:

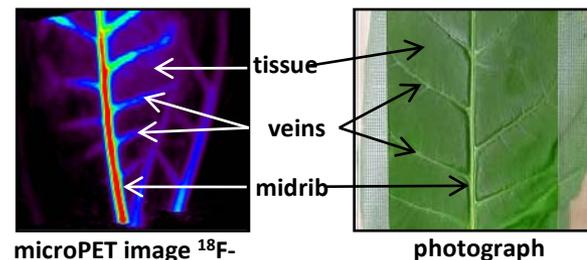
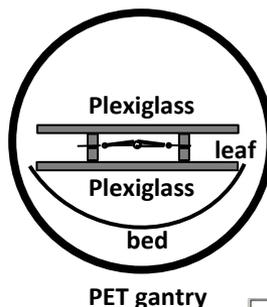
- In the case study, XFM imaging of zinc in dog prostate tissues measures disease progression
- Open access to these extensive archival materials provides a resource that can avoid or reduce the scope of new animal experiments while achieving a better understanding of radiation qualities, doses, and dose rates



Haley, et al., (2011) *Health Physics*, in press

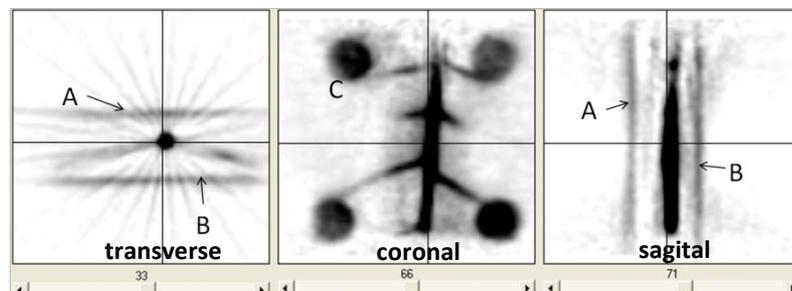
New Methods for Quantifying Positron Activity In Plants using PET

Objective: Develop quantitative methods for determining radiotracer concentration in plants.

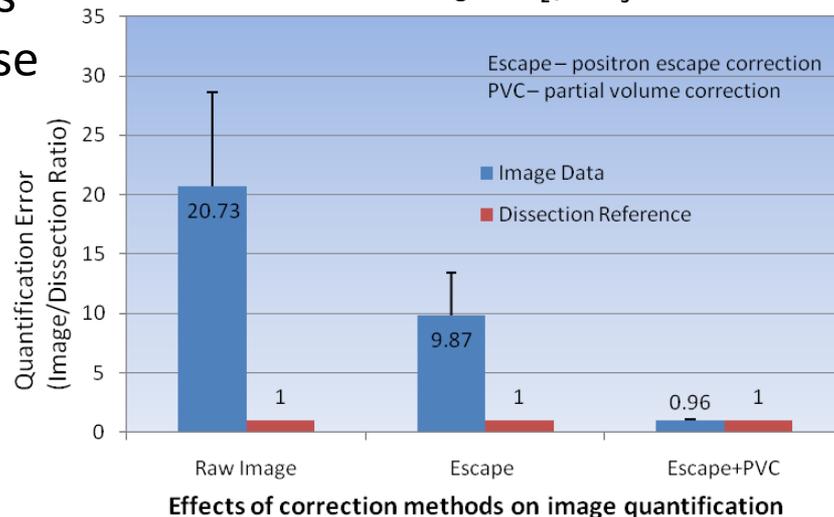


Approach:

- Characterize the two major sources of quantification error in PET imaging of leaves: escaping positrons from tissue and partial-volume averaging.
- Develop new image data correction methods for quantifying leaf activity and compare these results to “true” activity determinations derived using dissection.



microPET image $^{13}\text{NO}_2^- / ^{13}\text{NO}_3^-$



Impact:

Enables study of dynamic physiological processes in plants using PET to understand plant responses in active ecosystems.

Alexoff D et al, *S. Nuclear Medicine and Biology* Online publication 28 October 2010.

DOE JGI: Genomics for Environmental Response

- **Objective:**

Use whole genome-scale analysis to understand environmental response of complex biological systems

- **Approach:**

Sequence the genome of *Daphnia pulex* (the water flea), a keystone indicator species exquisitely sensitive to environmental contaminants

- **Results/Impacts:**

- Genome size ~ 200 Mb, > 30,000 predicted genes
- Many tandem gene clusters observed, with varying expression patterns under differing environments
- A solid basis for “ecogenomics”, the analysis of genetic contributions of environmental responsiveness



Left: Normal oxygenation
Right: Oxygen-deprived,
15x increase in
hemoglobin
concentration

Colbourne, et.al, (2011) *Science* 331:555-561

A look ahead for BSSD

- **Principal investigator meetings**
 - Radiochemistry and Instrumentation Research
 - Genomic Sciences
 - Low Dose
- **Future workshops**
 - Structural Biology
 - Synthetic Biology