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Genomics:GTL

Systems Biology for Energy and Environment

John Houghton

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

Briefing for Biomass R&D
Technical Advisory Committee
Feb. 7, 2008

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http://genomicsgtl.energy.gov/index.shtml

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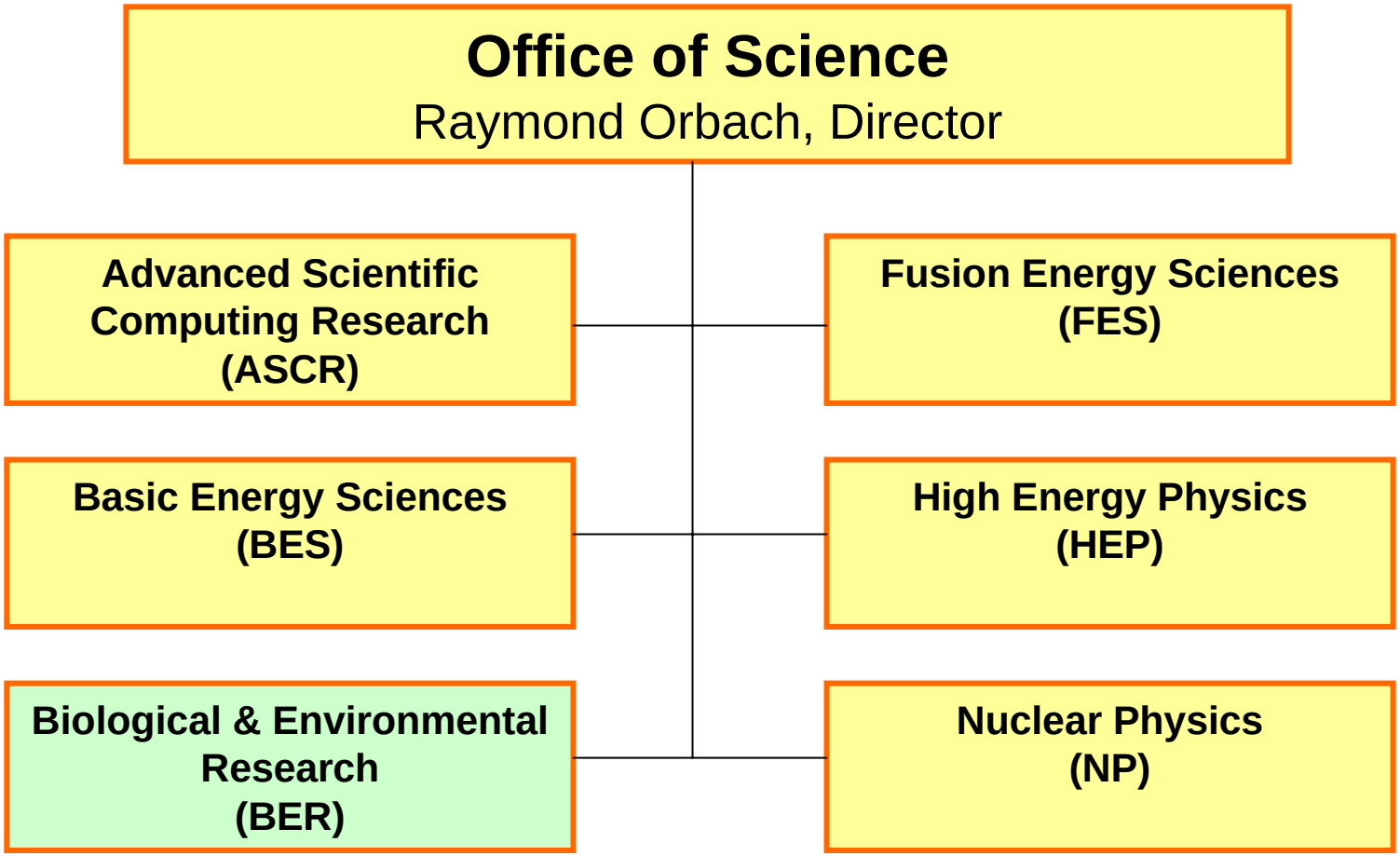

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Mission-Inspired Science

Just as DOE's mission to understand health impacts of energy inspired the Human Genome Program, GTL is a systems approach to understanding biology, built on genomics, inspired by DOE missions in Energy, Climate, and Environment.

- **Develop biofuels as a major secure national energy resource.**
- **Understand relationships between climate change and earth's ocean and terrestrial ecosystems and assess options for carbon sequestration in these systems.**
- **Develop biological solutions for difficult environmental problems.**

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Mission Challenges for Biology

Biofuels

Gain knowledge and tools for using microbes and plants to build a national biofuel capability to

- Develop sustainable energy crops.
- Develop biotechnologies for producing advanced biofuels

Cleanup

Understand microbial and plant impacts on subsurface contaminant fate to

- Develop better assessment tools.
- Design improved bioremediation methodologies.

Climate Stabilization

Determine ocean and terrestrial ecosystems' contributions to the global carbon cycle to

- Improve projections of climate change and its impacts.
- Create carbon-biosequestration strategies.

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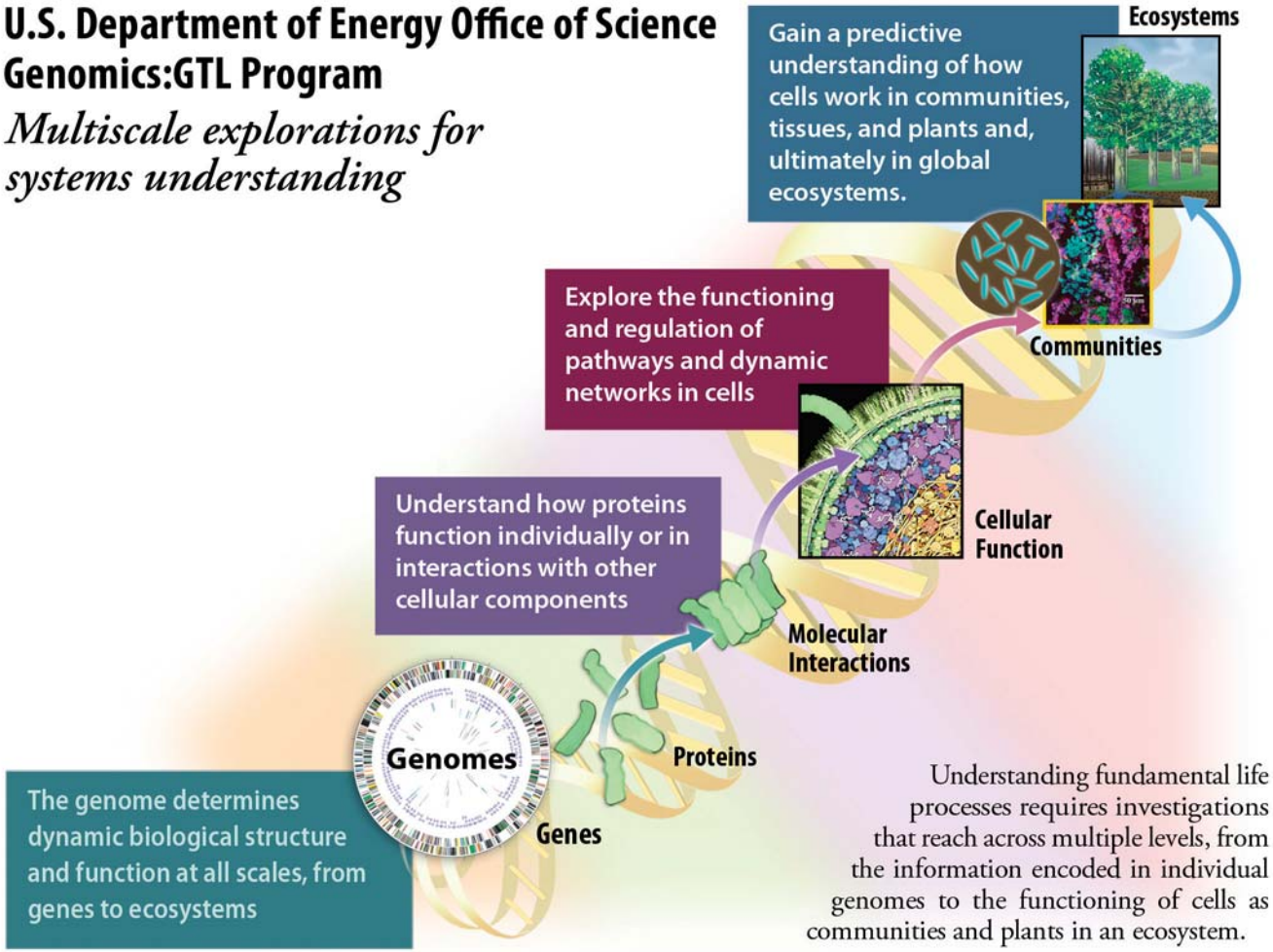
GTL Concept

U.S. Department of Energy Office of Science Genomics:GTL Program

Multiscale explorations for systems understanding



Understanding fundamental life processes requires investigations that reach across multiple levels, from the information encoded in individual genomes to the functioning of cells as communities and plants in an ecosystem.

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Science at Scales

- ***Molecular:*** Focusing on genes, proteins, multicomponent protein complexes, and other biomolecules that provide structure and perform the cell's functions -- to understand how the genome determines dynamic biological structure and function at all scales from genes to ecosystems, and to understand how proteins function individually or in interactions with other cellular components.

- ***Whole cell:*** Investigating how dynamic molecular processes, networks, and subsystems are controlled and coordinated to enable such complex cellular processes as growth and metabolism in cells.

- ***Microbial community and higher organisms:*** Exploring how diverse cellular systems interact to carry out coordinated complex processes and both respond to and alter their environments – how cells work in communities, tissues, and plants, and ultimately in global ecosystems.

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GTL Goal and Objectives

GTL's Ultimate Scientific Goal

Achieve a predictive, systems-level understanding of plants, microbes, and biological communities, via integration of fundamental science and technology development, to enable biological solutions to DOE mission challenges in energy, environment, and climate.

- ***Objective 1***

  Determine the genomic properties, molecular and regulatory mechanisms, and resulting functional potential of microbes, plants, and biological communities central to DOE missions.

- ***Objective 2***

  Develop the experimental capabilities and enabling technologies needed to achieve a genome-based, dynamic systems-level understanding of organism and community functions.

- ***Objective 3***

  Develop the knowledgebase, computational infrastructure, and modeling capabilities to advance the understanding, prediction, and manipulation of complex biological systems.

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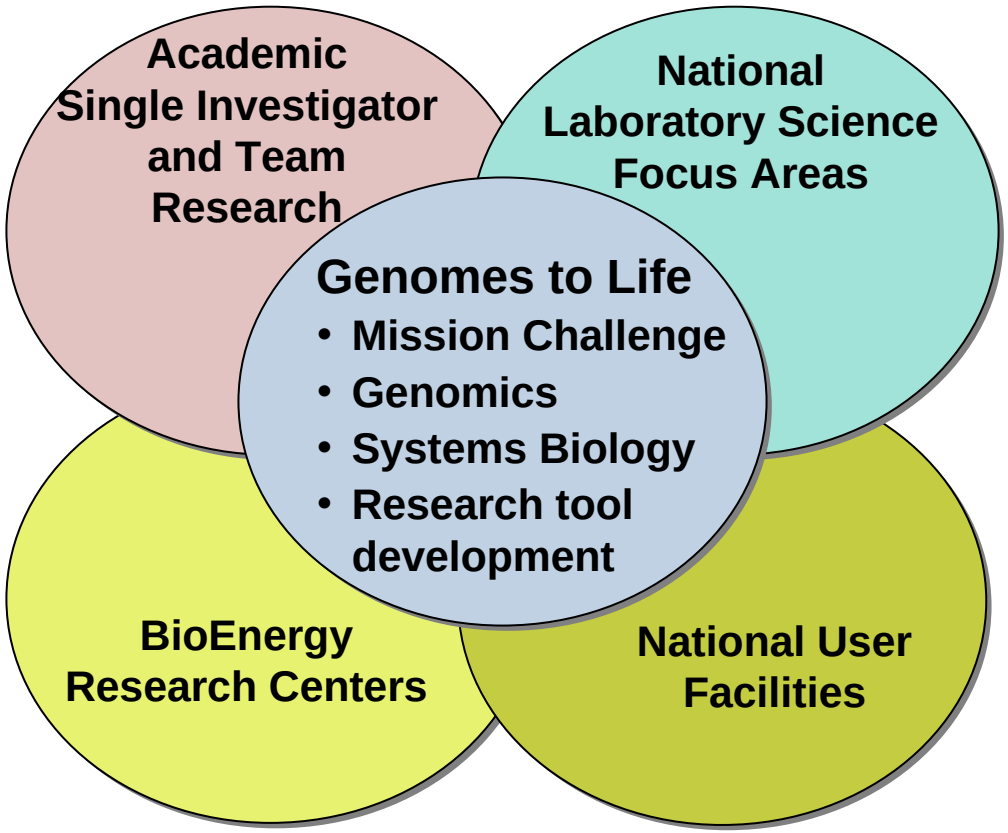
The GTL Research Enterprise



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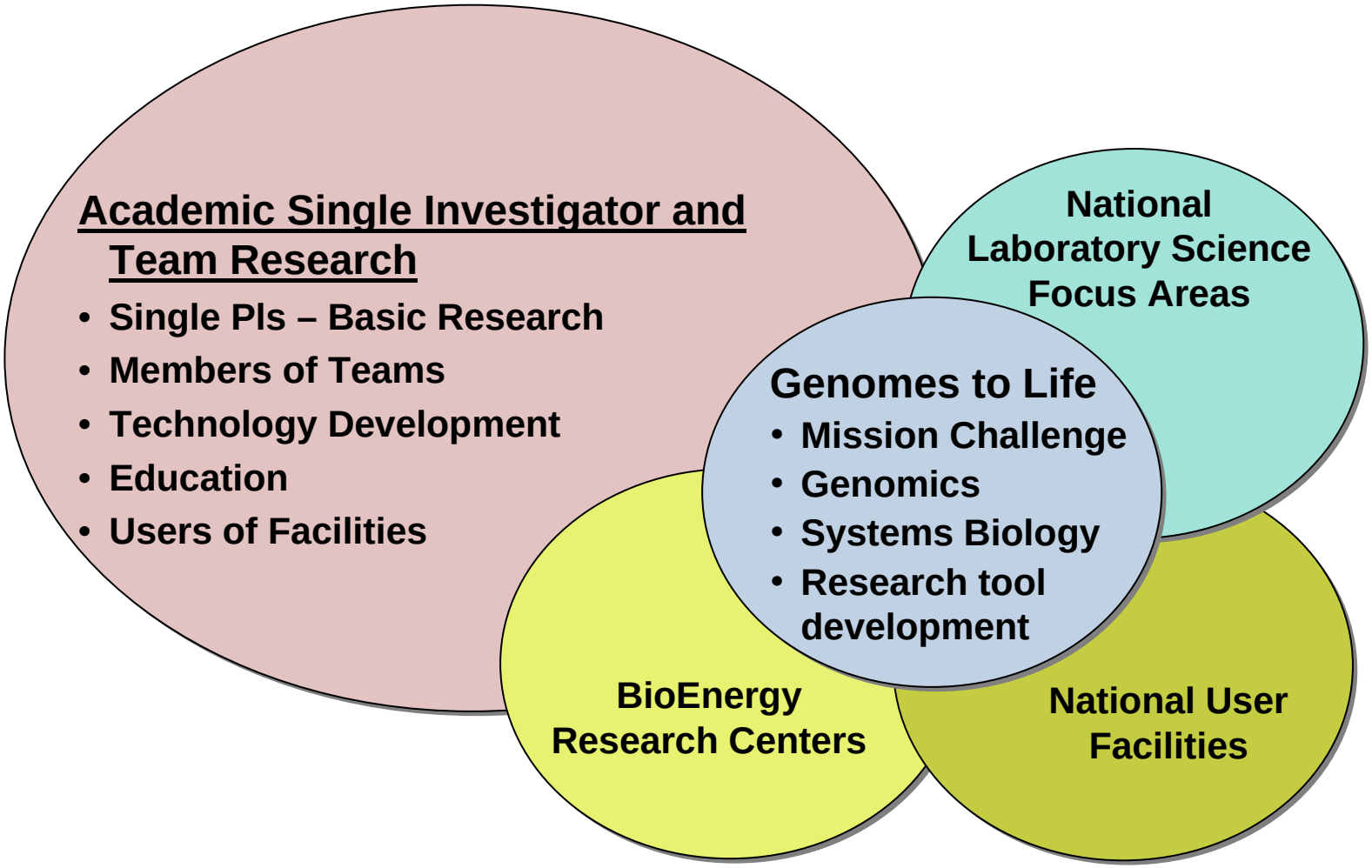

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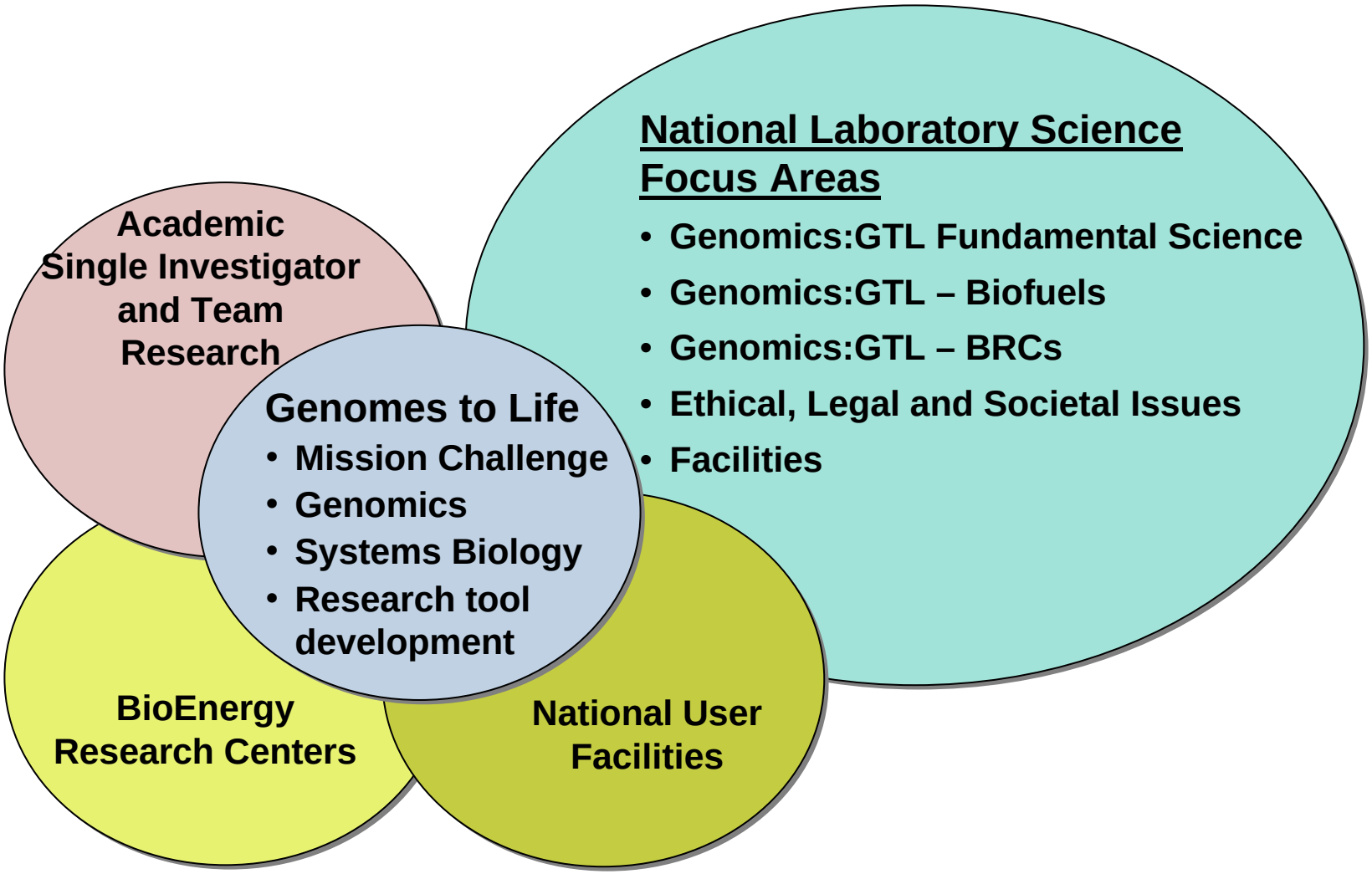

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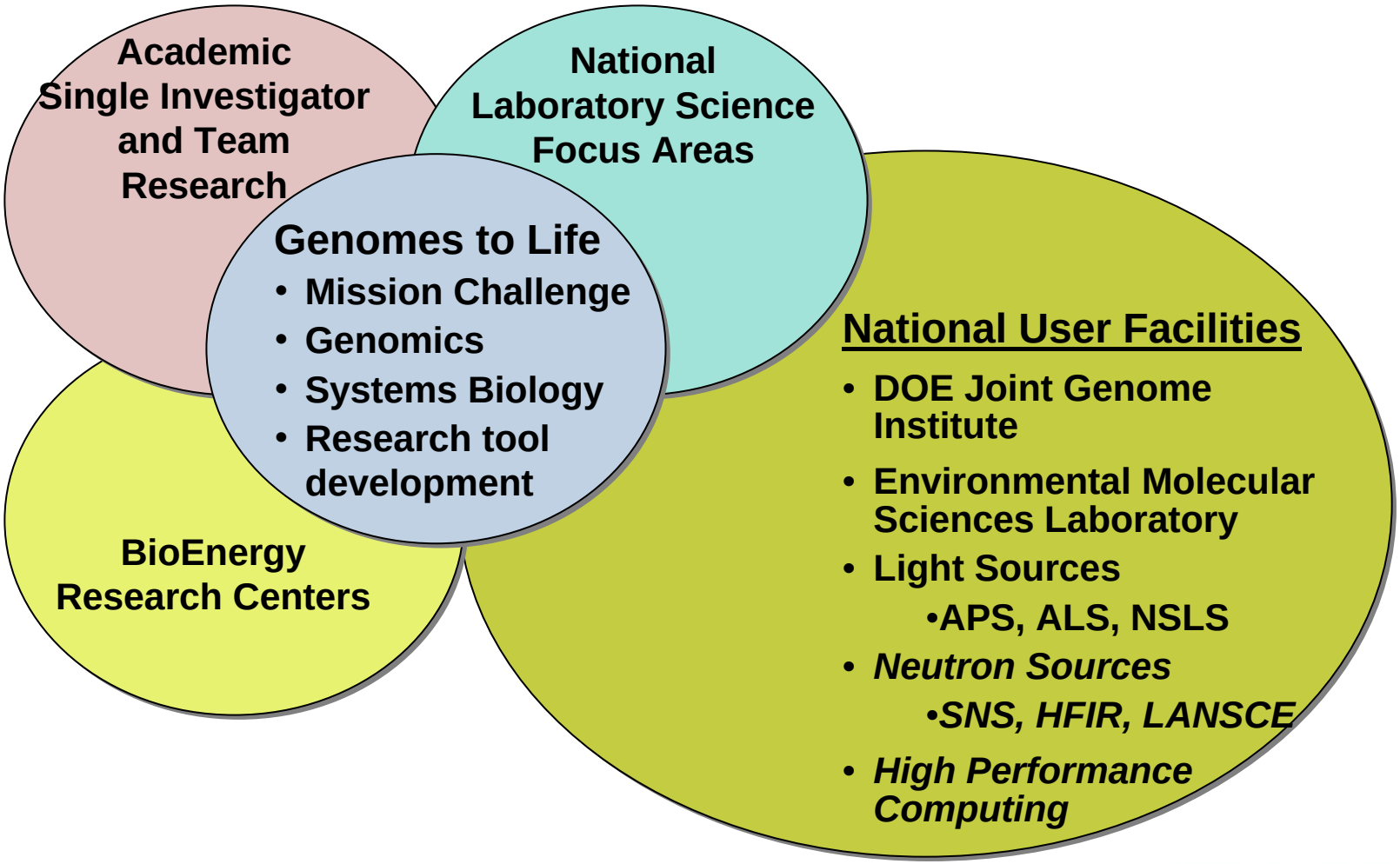

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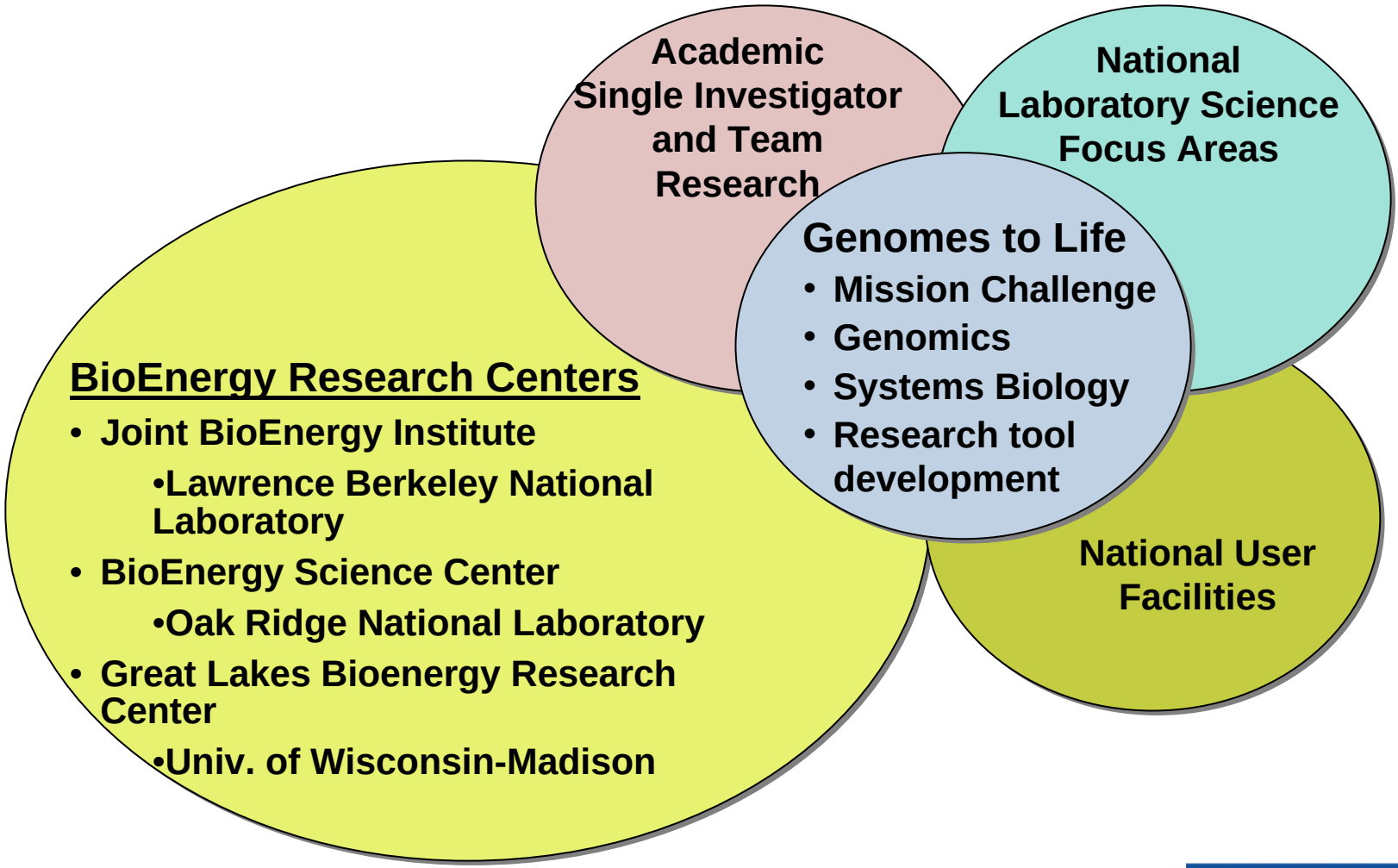

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GTL Operational Hallmarks

- Maintains a strategically-managed portfolio to respond to emerging national priorities and mission needs
- Selects research based on scientific merit and peer-review
- Has research conducted by individual investigators, collaborative teams, and research centers at DOE national laboratories, academic institutions, and industry
- Leverages capabilities and resources across BER programs and scientific user facilities
- Encourages communication across the scientific community through the annual GTL program meeting, workshops, symposia, and exhibits
- Fosters an atmosphere of open access to data and information
- Coordinates with other DOE programs and other federal agencies

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Biomass to Biofuels Workshop Plan 2006

GTL workshop with OBP created foundation for science to break barriers to cellulosic ethanol production on an industrial scale

DOE OBER GTL- & DOE Energy Efficiency and Renewable Energy - Sponsored workshop

Workshop research strategies influenced

- GTL Bioenergy Research Centers FOA
- Individual GTL investigator projects in bioenergy
- BP Center call for proposals
- Biofuels research agendas internationally
- Commercial planning including VC

Copies available at:
http://genomicsgtl.energy.gov/biofuels/b2bworkshop.shtml

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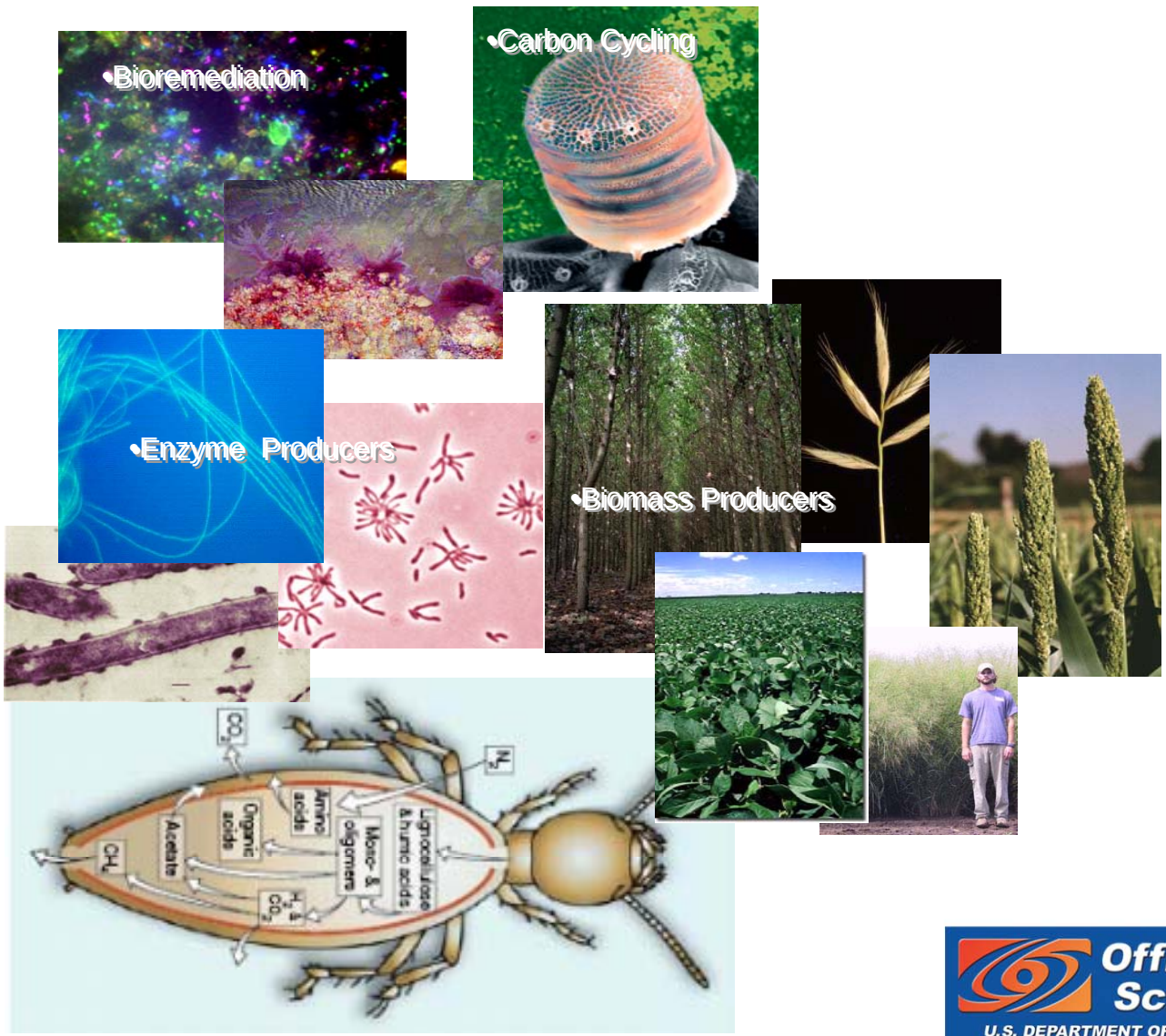
DOE Joint Genome Institute



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The Joint Genome Institute
A DOE User Facility

- **Expanding, fully-utilized genome sequencing capacity to sequence and analyze the genomes and metagenomes of a growing collection of organisms and communities**
  - **A first step toward whole biological systems understanding required for biological applications to DOE missions of critical national needs**
  - **State of the art capabilities, expert staff in an array of computing and biological research disciplines, workshops, and annotation jamborees are unique, value-added features critical to the broad biological user community and DOE mission science.**

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Biological and Environmental Research—The DOE Joint Genome Institute

JGI DOE JOINT GENOME INSTITUTE
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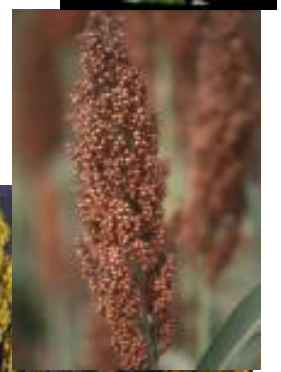
- **DOE user facility for genome sequencing**
- 3.6 billion bases per month

Community Sequencing Program (CSP)

- **60% of the capacity at the JGI**
- **a small-genome program for shotgun sequencing of genomes < 200 Mb and other smaller sequencing projects**
- **a large-genome program for shotgun sequencing of genomes > 200 Mb. Large-genome proposals must be supported by experimental evidence of the organism's genome size, polymorphism rate, and repeat content. Otherwise, submit a small-genome proposal to obtain this information.**
- **Selected by peer review -- scientific merit and mission relevance**

http://www.jgi.doe.gov/CSP/index.html



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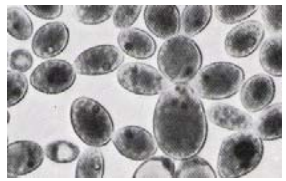
JGI and Bioenergy

Improved Feedstocks

Cellulosic Materials
- Poplar
- Maize/Corn Stover
- Switchgrass
- Brachypodium
- Sorghum



Saccharification → **Sugars** → Fermentation

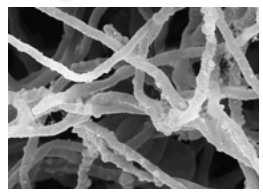


- *Saccharomyces cerevisiae*
- *Zymomonas mobilis*
- *Thermoanaerobacter ethanolicus*
- *Pichia stipitis*

Ethanol producing organisms

Improved cellulose & lignin degradation

- Termite hindgut microbiota
- White Rot Fungus
- *Clostridium thermocellum*
- *Saccharophagus degradans*
- *Acidothermus cellulolyticus*



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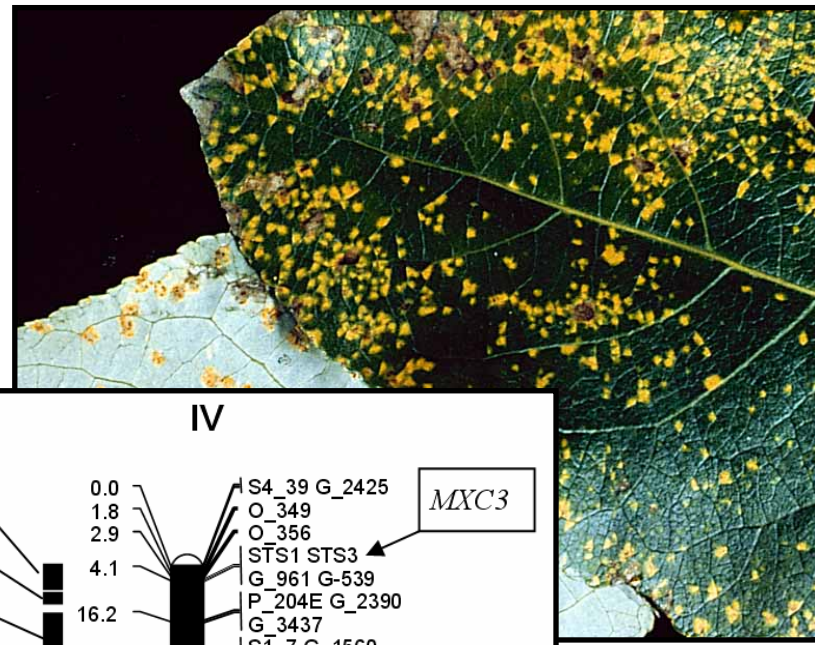
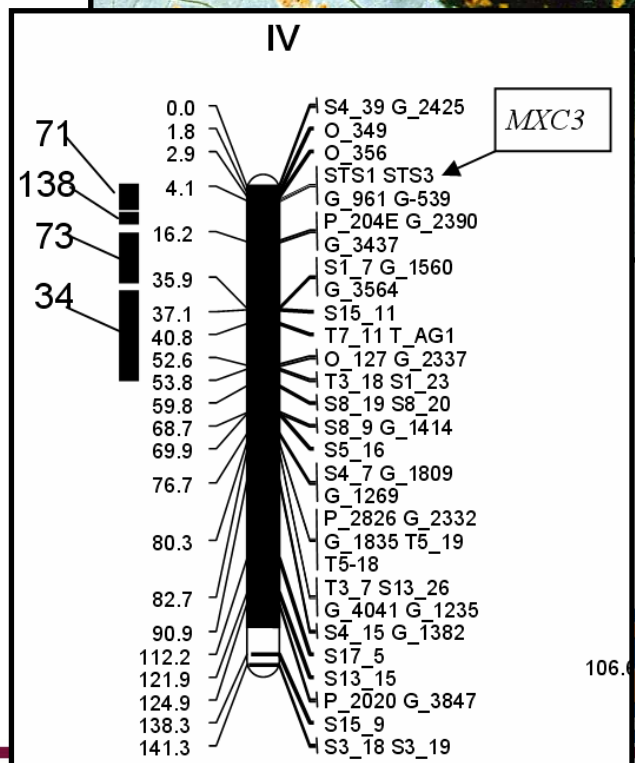
Poplar genome provided insight into disease resistance

- *Melampsora spp*. is a leaf rust of great commercial importance in *Populus* cultivation
- Disease resistance in *P. trichocarpa* mapped to MXC3 chromosome walking failed
- Examining the genomic scaffold in this region provided a candidate gene …. thaumatin-like domain protein





Stirling et al. 2001. TAG 103:1121

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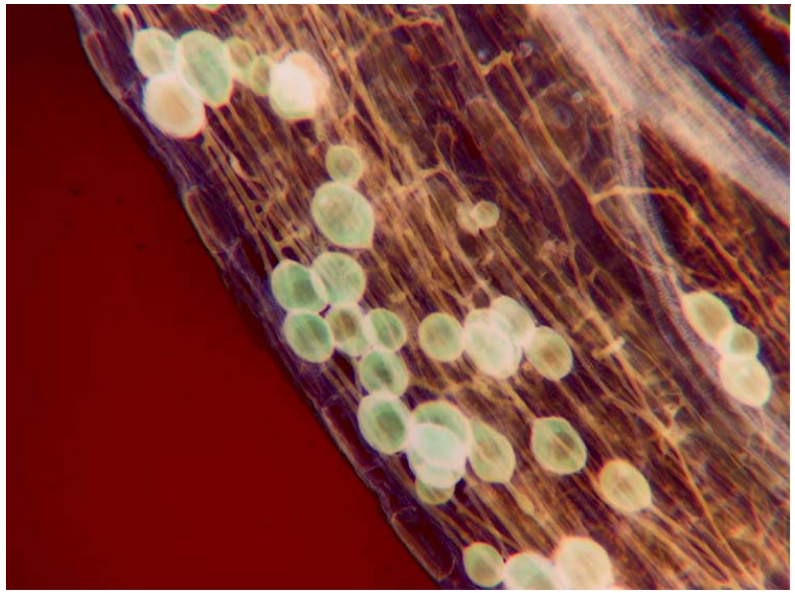
The *Poplar* "ecosystem" - sequencing in progress …

- ***Glomus intraradices*: endomycorrhizal (zygomycete) fungus, an (ancient) intracellular symbiont, aids in uptake of P, minerals; resistance to biotic/abiotic stresses.**
- ***Laccaria bicolor*: ectomycorrhizal (basidomycete) fungus, forms protective sheath around root tip and aids in uptake of water, mineral salts and metabolites.**



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Metamethods

Metagenomics and Metaproteomics

Genomic and molecular characterization of entire environmental communities has revolutionized Microbial Ecology

- **> 99% of microbes resist lab culture techniques**
- **Genomic metamethods are revealing genes encoding interactions in complex communities**
  - **Stunning gene diversity (millions of unique genes) discovered in marine and terrestrial metagenomics and metaproteomics studies**
  - **New mechanisms for survival and adaptation by massive genetic exchange and creation of new families of proteins within communities.**

These methods and discoveries have much fundamental and practical value

- **Opening a new era of scientific discovery resulting in entirely new**
  - **Industrial applications including biofuels**
  - **Understanding of planetary nutrient cycles important for bioenergy crop sustainability**

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Life at the Limits
Mining Acid Mine Drainage

Metagenomics and metaproteomics

- Dense microbial communities in extremely high acid and toxic metal concentrations
- Discovered that bacteria in these communities survive and adapt by exchanging large sections of their genomic DNA, resulting in the modular creation of new proteins.
- Metamethods for discovery of these robust and diverse capabilities opens a new era in microbial ecology and new paths to industrial processing and soil maintenance.

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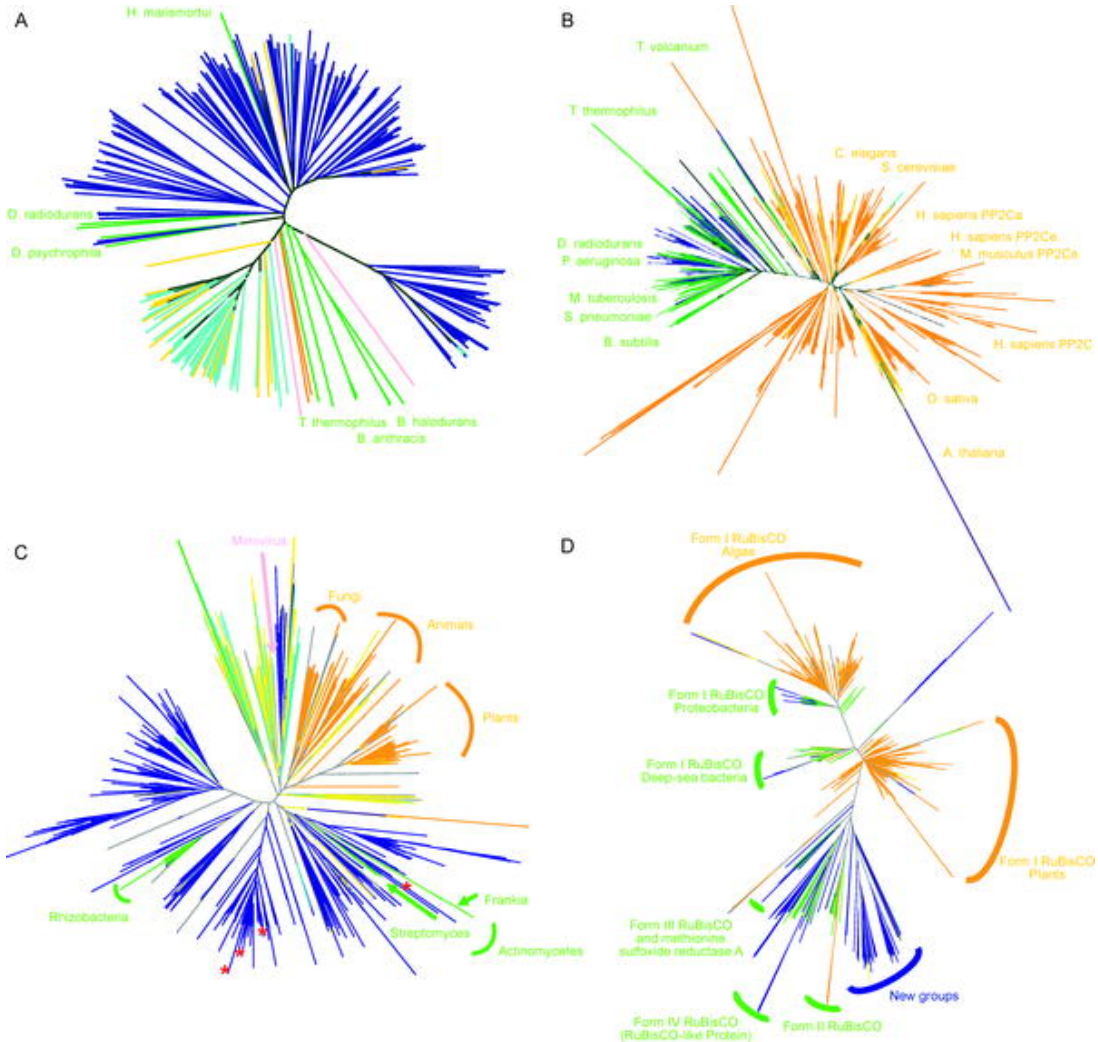
Global Ocean Survey (GOS)
A Sea of Proteins



Metagenomics of diverse global aquatic environments—6.3 billion base pairs

Led to powerful new computational tools to predict protein function and genetic adaptation from sequence

Astonishingly high number of new proteins – a new era in protein function discovery and industrial innovation.

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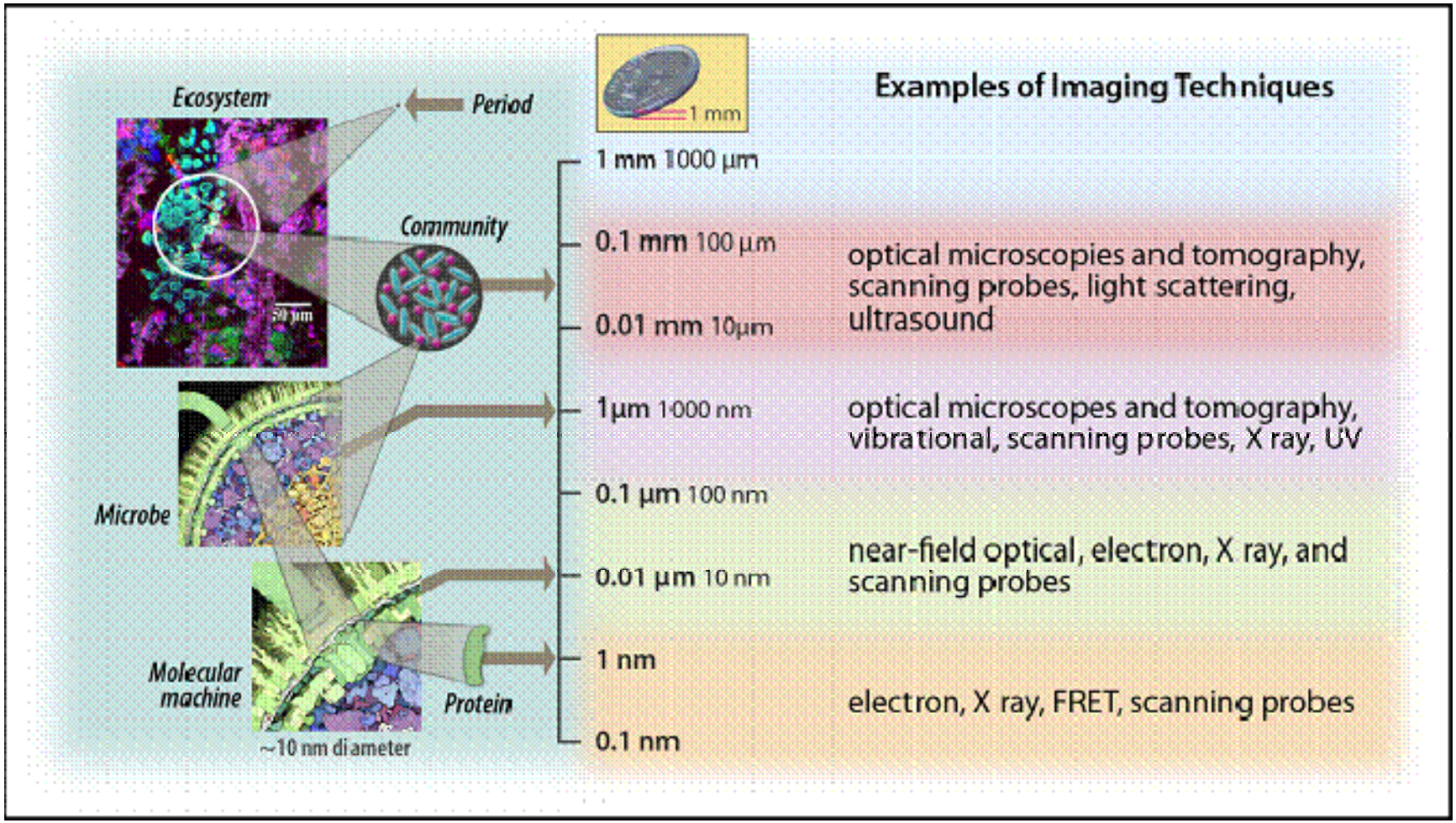
Imaging technologies



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Plant Feedstock Genomics for Bioenergy

USDA

- DOE/USDA Joint Research Program
- Supports research on plants for improvement of:
  - Biomass Characteristics
  - Biomass Yield
  - Degradability of Lignocellulose

http://genomicsgtl.energy.gov/research/DOEUSDA/index.shtml

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Other FY07 Genomics:GTL Solicitations

- **New Analytical and Imaging Technologies for Lignocellulosic Material Degradation, and for Multiplexed Screening for Plant Phenotypes**

- **Quantitative Microbial Biochemistry and Metabolic Engineering for Biological Hydrogen Production**

- **New Genomic Strategies and Technologies for Studying Complex Microbial Communities and Validating Genomic Annotations**

- **Ethical, Legal, and Societal Implications (ELSI) of Research on Alternative Bioenergy Technologies, Synthetic Genomics, or Nanotechnologies**

Thank you for your attention