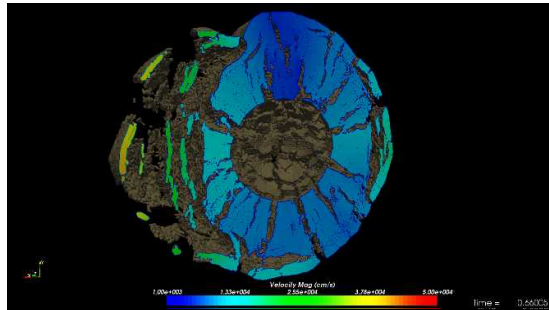


# **Sandia Biotechnology Overview**

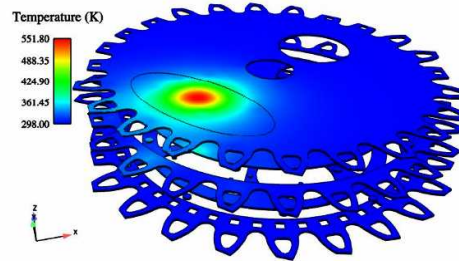
**Advanced Technologies for Biological Research**

**Anthony Martino, Ph.D.  
Manager, Biomolecular Analysis & Imaging**

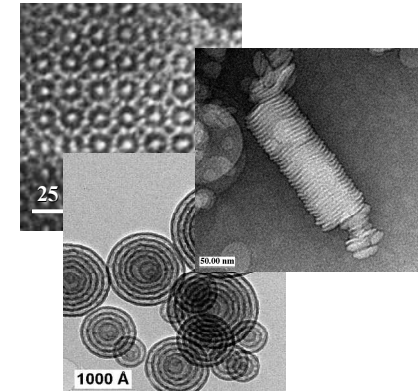
# Bioscience is a Sandia Research Foundation for National Security.



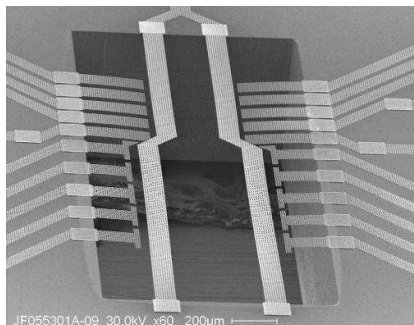
**Computational and  
Information sciences**



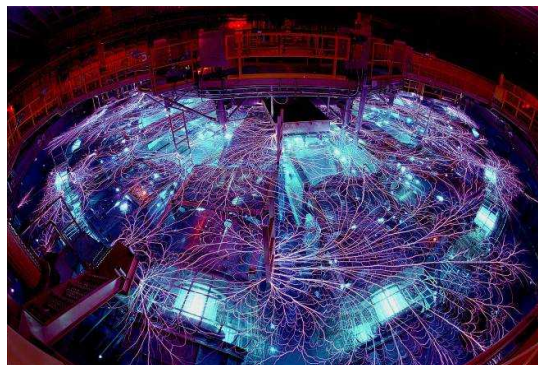
**Engineering Sciences**



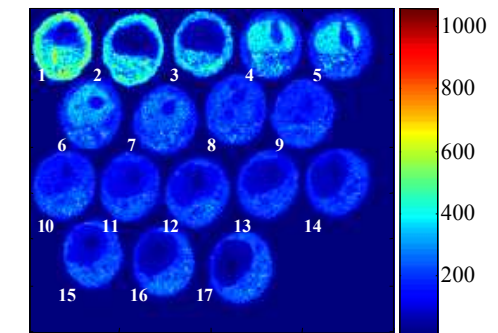
**Materials Science and  
Technology**



**Microelectronics  
and Photonics**



**Pulsed Power**

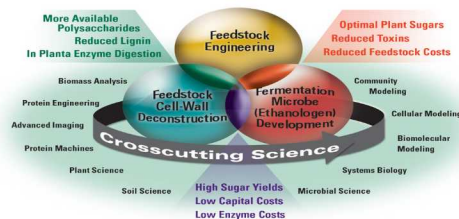


**Bioscience**

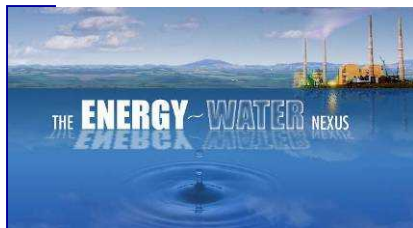
# ***Biosciences play a key role in many National Security challenges.***

## **Energy, Resources, and Nonproliferation**

### **•Biofuels**



### **•Water**



### **•BW proliferation**



## **Homeland Security and Defense**

### **•Pathogen Detection**



### **•Decontamination**



### **•Early Detection of Infectious Outbreak**





# ***Our Flagship Capabilities Define Laboratory Directions.***

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## **Red Storm Computing**



## **Microtechnology**



## **Chemical Imaging**

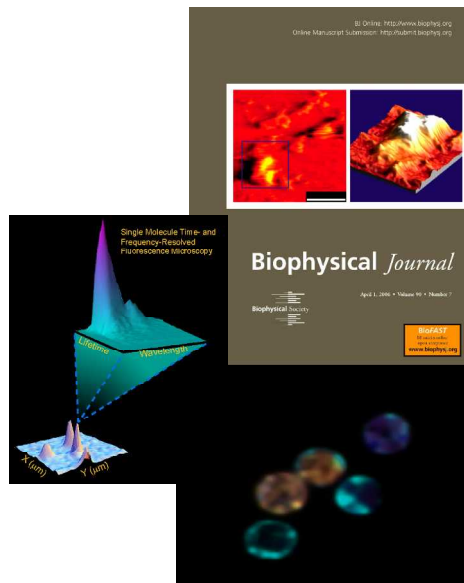


## **Nanoscience**

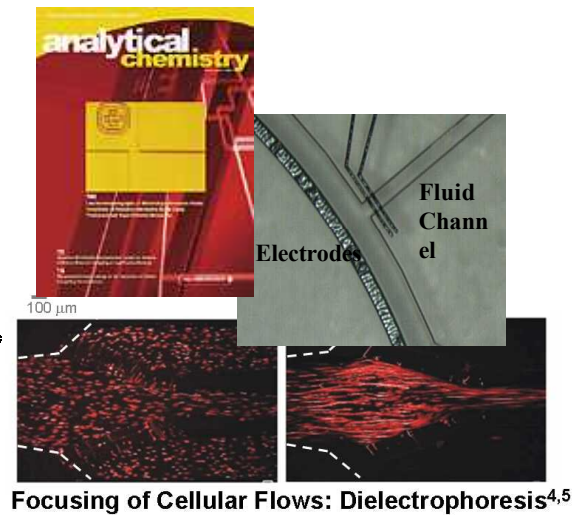


# Technology is providing new tools to address systems biology.

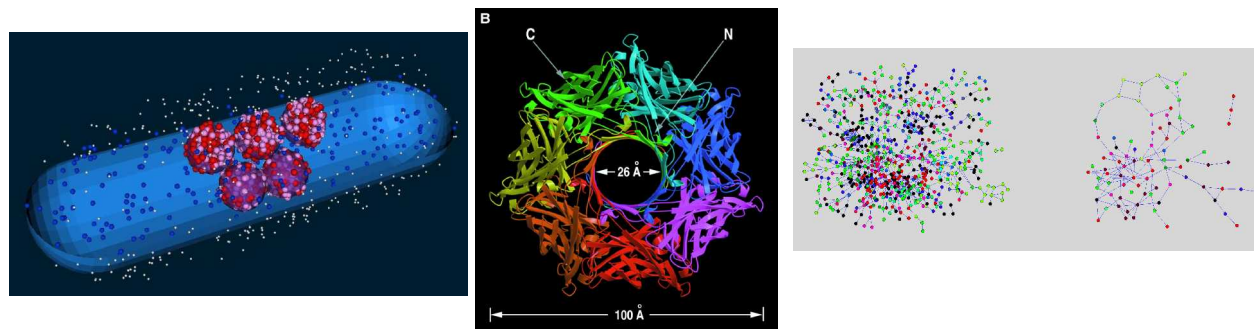
## Quantitative Chemical Imaging



## High Through-Put Experimental Platforms



## Predictive Modeling and Simulation





# ***Strategic Directions***

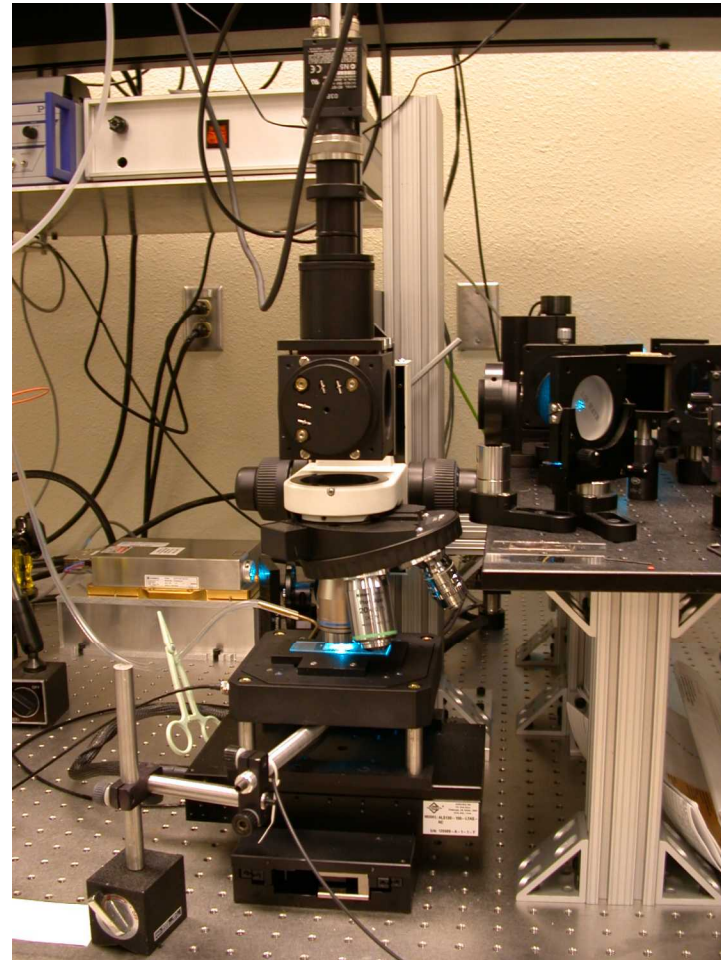
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- **Biodefense and Emerging Infectious Disease**
  - Detection, diagnostics, therapeutics
  - Single-cell immune response
  - MISL Grand Challenge
  - UTMB & UCSF Partnership
- **Biofuels**
  - Cellulosic fuels & algal bio-diesel
  - DOE/GTL Bioenergy Center (JBEI)
  - LBL, LLNL, Corporate Partnerships



# 3D Hyperspectral Confocal Fluorescence Microscope

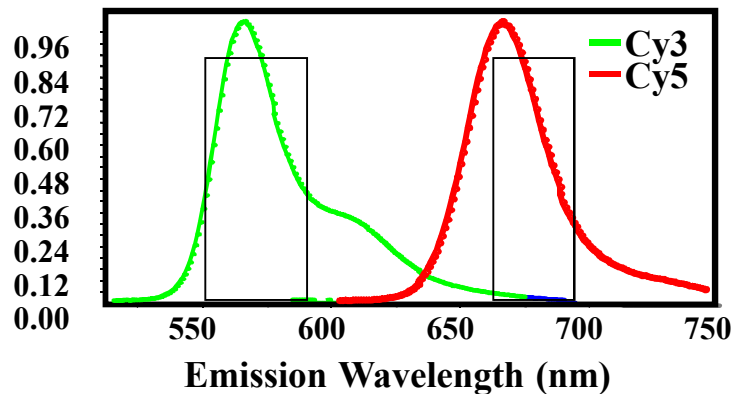
- Fully confocal design
  - high spatial resolution
  - optical sectioning
- High optical throughput
  - prism spectrometer
  - electron multiplying CCD
- Performance Specifications:
  - 488 nm laser excitation
  - 10x, 20x, 60x, 100x objectives
  - Lateral Resolution =  $0.25\ \mu\text{m}$
  - Axial Resolution =  $0.60\ \mu\text{m}$
  - Spectral range 490-800 nm
  - Spectral resolution = 1-3 nm
  - Acquisition rate = 8300 spectra/s



Sinclair, MB., et al. (2006). Applied Optics 45(24): 3283-3291.

# *Hyperspectral Imaging identifies all species in a single experiment.*

## Filter-based Microscope

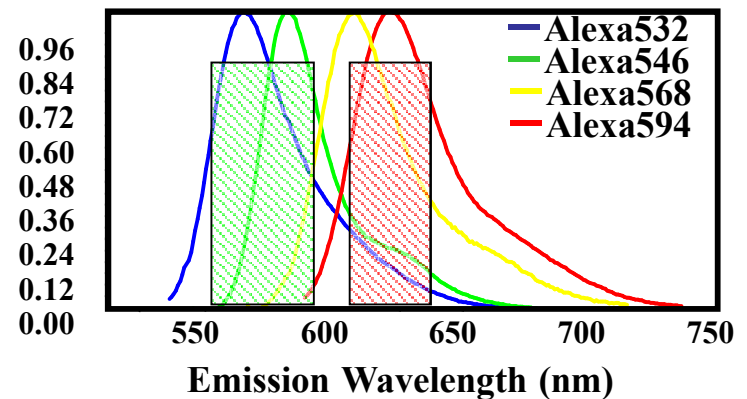


### Univariate

Collect all photons within a wavelength region

Require well-separated emissions and ONE laser per label

## Hyperspectral Microscope



### Multivariate

Collects an entire emission spectrum at each voxel

Excites multiple, overlapping dyes with ONE laser

**Multivariate data analysis is the key to information extraction from HS Images**



# DOE Bioenergy Research Centers Announced

Department of Energy - Energy Department Selects Three Bioenergy Research Centers for \$375 Million in Federal Funding

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June 26, 2007

## Energy Department Selects Three Bioenergy Research Centers for \$375 Million in Federal Funding

*Basic Genomics Research Furthers President Bush's Plan to Reduce  
Gasoline Usage 20 Percent in Ten Year*

**WASHINGTON, DC** – U. S. Department of Energy (DOE) Secretary Samuel W. Bodman today announced that DOE will invest up to \$375 million in three new Bioenergy Research Centers that will be located in Oak Ridge, Tennessee; Madison, Wisconsin; and near Berkeley, California. The Centers are intended to accelerate basic research in the development of cellulosic ethanol and other biofuels, advancing President Bush's Twenty in Ten Initiative, which seeks to reduce U.S. gasoline consumption by 20 percent within ten years through increased efficiency and diversification of clean energy sources. The Department plans to fund the Centers for the first five years of operation (Fiscal Years 2008-2013).

### News

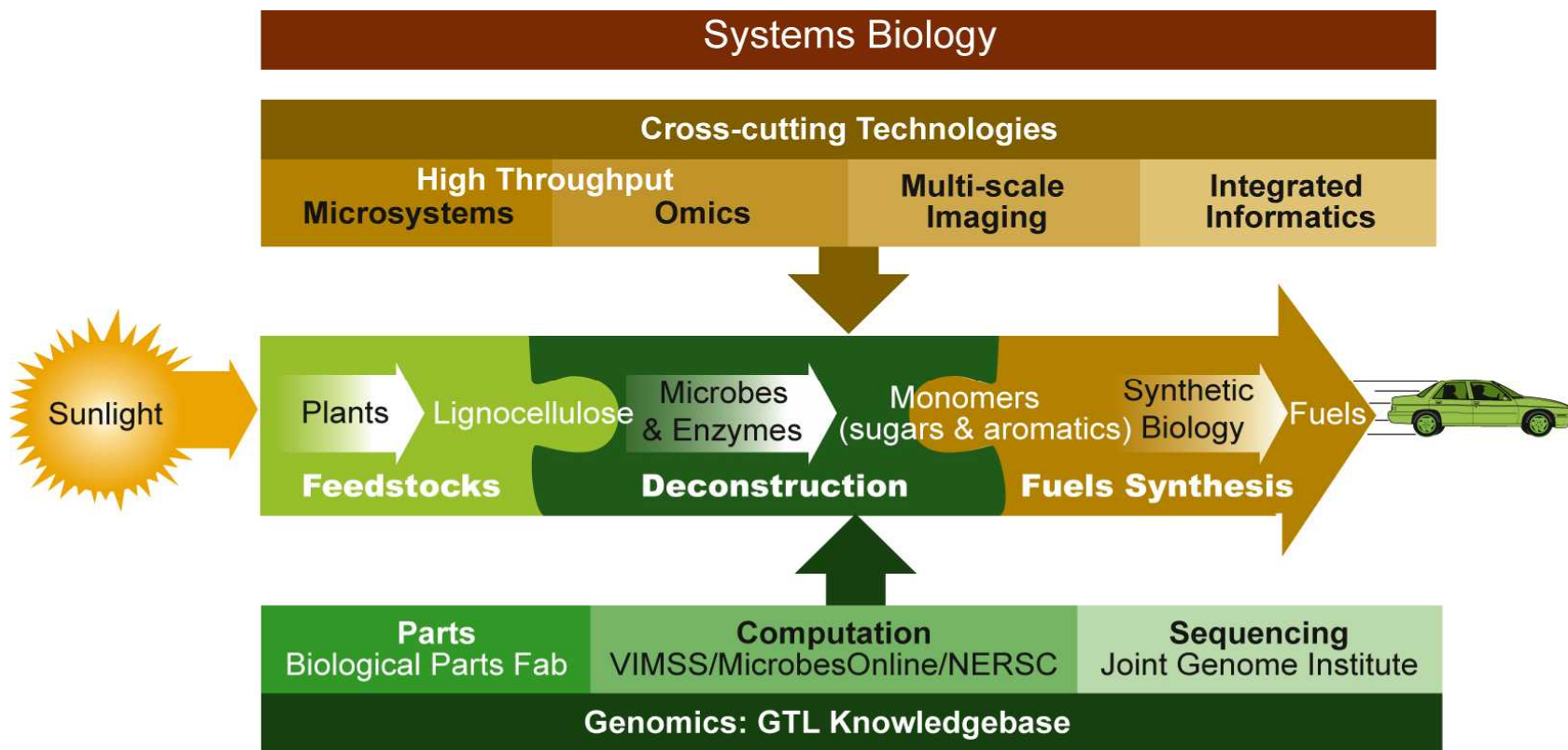
University of M  
Communication  
Department of  
2007 Solar Dec

German Univer  
Architecture Co  
Department of  
Third Solar Dec

Opening Ceren  
Solar Decathlo

DOE Office of S  
Publishes Upda  
Landmark Plan  
for the Future  
Twenty-Year O

# JBEI Research Strategy



# Biomass to Bioenergy: Protein & Metabolic Engineering

## Making a Superior Enzyme

- Enzymes are highly specialized.
- Absent their normal working environment, they typically suffer in terms of activity and durability
- Some of chemical and physical prerequisites for full enzyme activity may be deleterious for our process goals

**Our goal:** Modifying enzymes at the genetic level to improve performance for glucose production and substrate activity.

**Challenge:** Enhance desired new attributes without sacrificing performance in other areas.

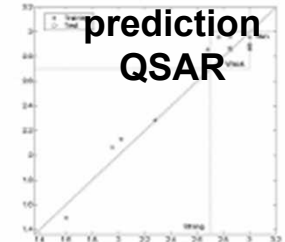
**Approach:** Process for computationally-guided genetic modification and screening.

PI Blake Simmons

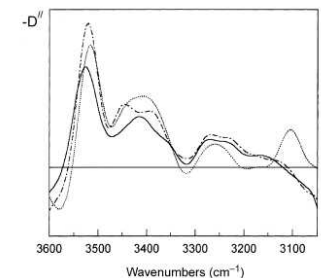
High-throughput  
enzyme production and  
screening



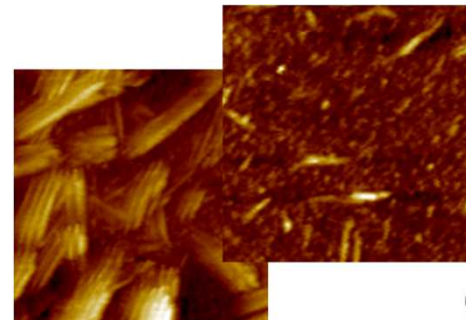
Enzyme activity



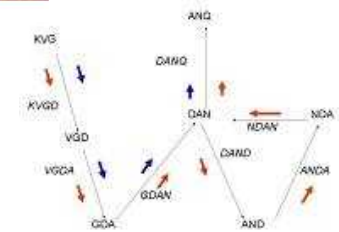
Molecular Biophysics



Imaging/microscopy



Bioinformatics tools:  
annotation &  
functional genomics



# ***Breakdown of Lignocellulose via Mixed-Microbes***

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## **Project Purpose and Approach**

- Address the problem of cellulosic-biomass recalcitrance to processing to ethanol and
- enable efficient use of alternate biomasses for bioethanol production via
- developing new, efficient mixed-microbe system to generate bioethanol from lignocellulose.



Bioreactor run showing degradation of hay substrate

PI Roberto Rebeil



# *Enhanced Production of Ethanol from 5-Carbon Sugars*

## **Project Purpose and Approach**

- Improve the economics of ethanol production from lignocellulosic (C5+C6 sugars) biomass via
- a combination of metabolic engineering, genomics, proteomics, molecular biology and microbiology for
- a novel ethanol tolerant thermophilic bacterium.

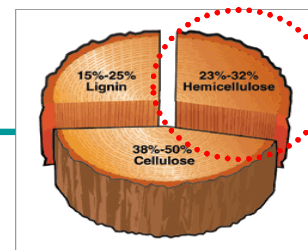
PI Rajat Sapra



Corn Stover  
C-5 sugars  
Xylose, Arabinose

Waste!!  
30-40% goes  
unutilized

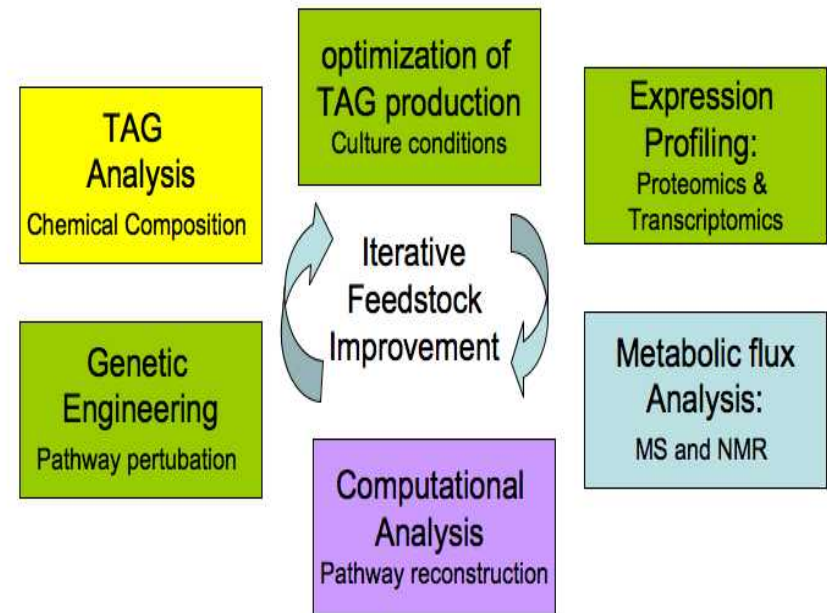
C-5 sugars  
Xylose, Arabinose



# Microalgal Biodiesel Feedstock by Metabolic Engineering

## Project Purpose and Approach

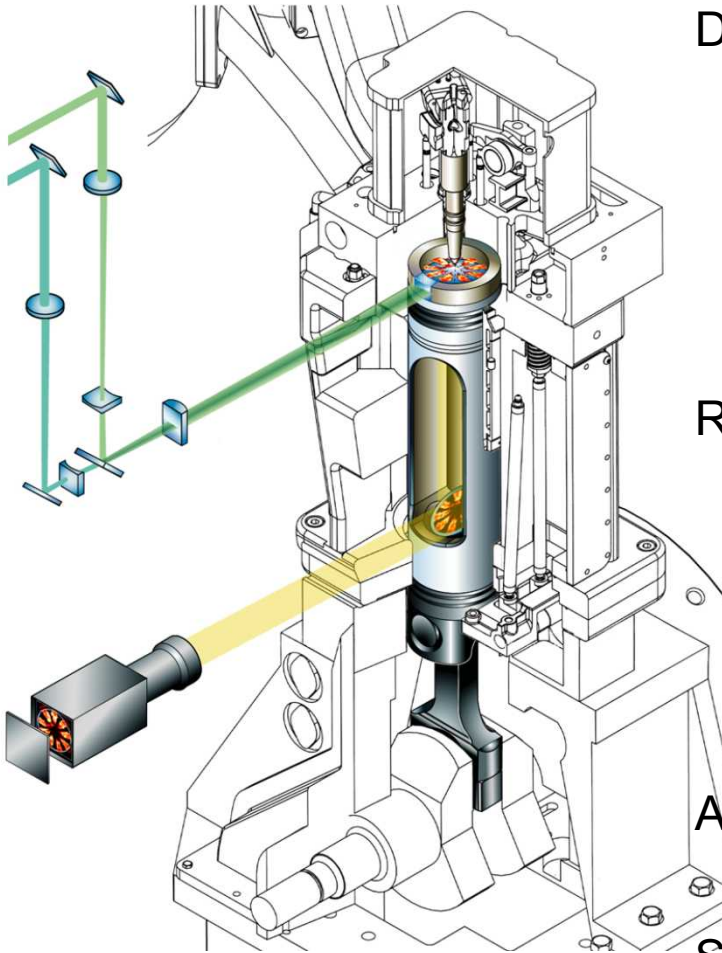
- Address the science issues relevant to using microalgae as a biomass feedstock for biocrude through
- expression profiling and metabolic flux analysis to characterize TAG synthesis pathways and
- reprogramming the diatom to produce TAGs under optimal growth conditions via a suite of molecular tools.



PI Todd Lane

# ***New Light-duty Engine Fuels Research Project Started At Sandia***

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Developing the science-base on in-cylinder combustion/emissions processes that will enable clean, high-efficiency engines for future fuels:

- efficiencies > conventional SI engines
- emissions compliant with 2010 regs

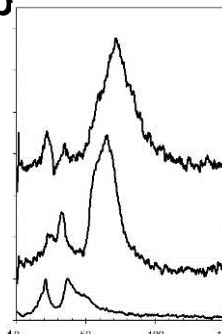
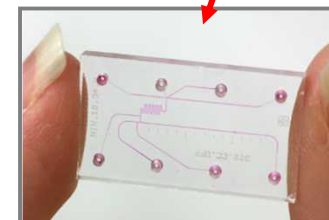
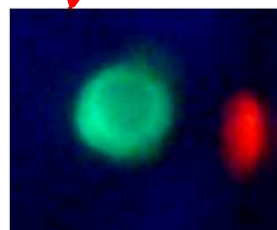
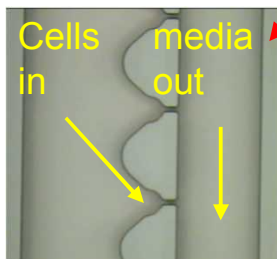
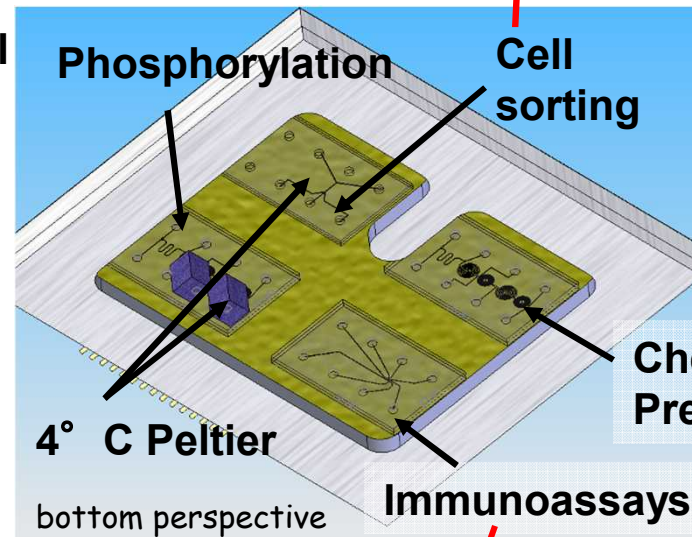
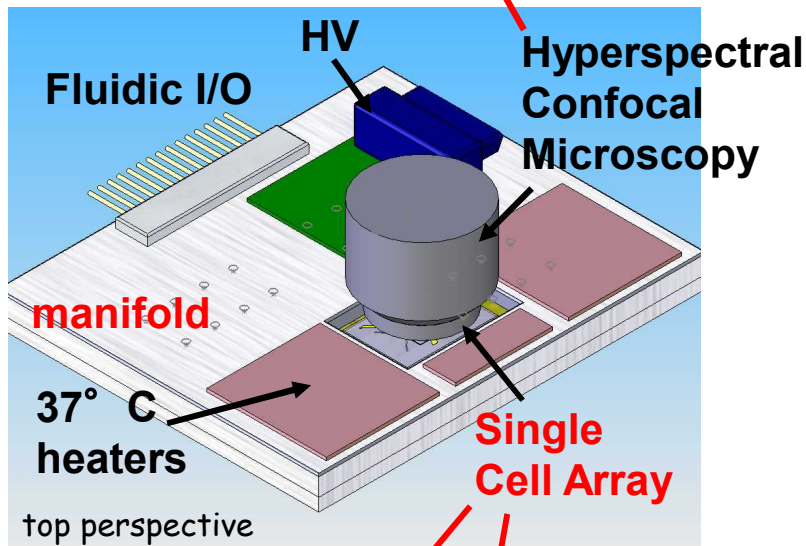
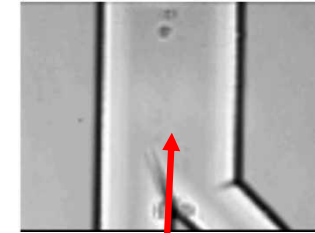
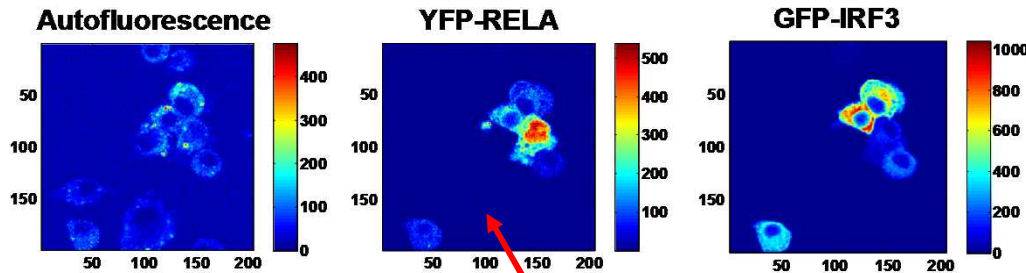
Research directions:

- direct-injection, stratified charge SI engines
- **ethanol and ethanol/gasoline blends**
- future target bio-fuels and non-conventional domestic HC fuels

Approach: Optical diagnostics and realistic engine geometries.

Sponsor: DOE Office of FreedomCAR and Vehicle Technologies

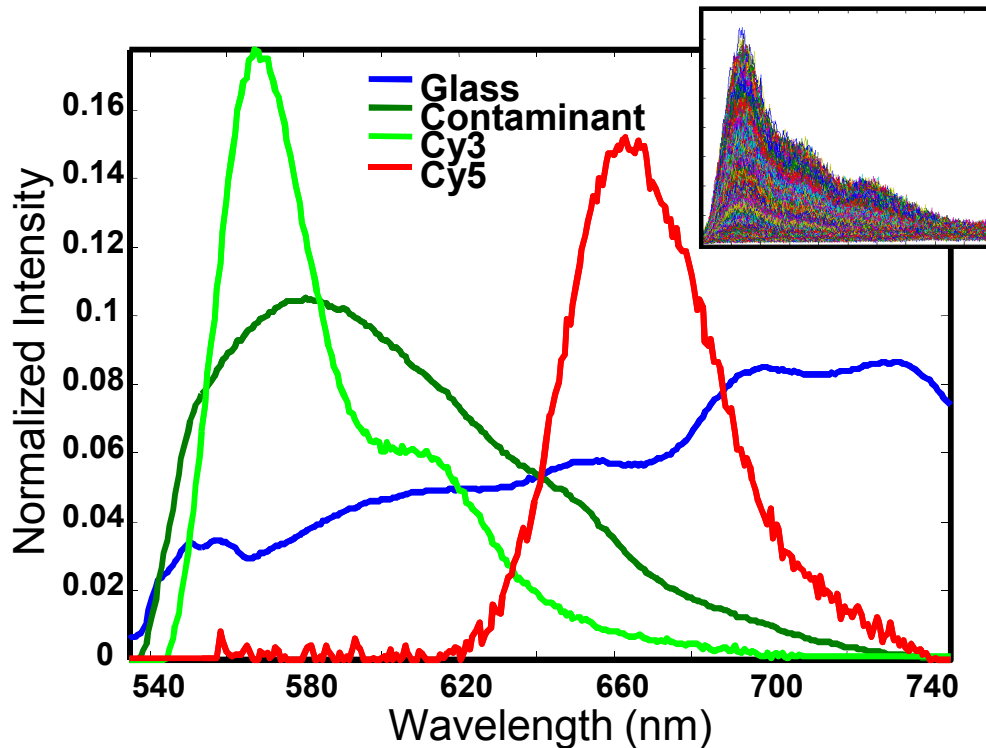
# ***Chips to sort cells, and measure translocation, phosphorylation and cytokines being integrated into a single platform***



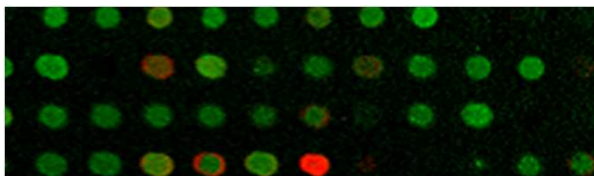
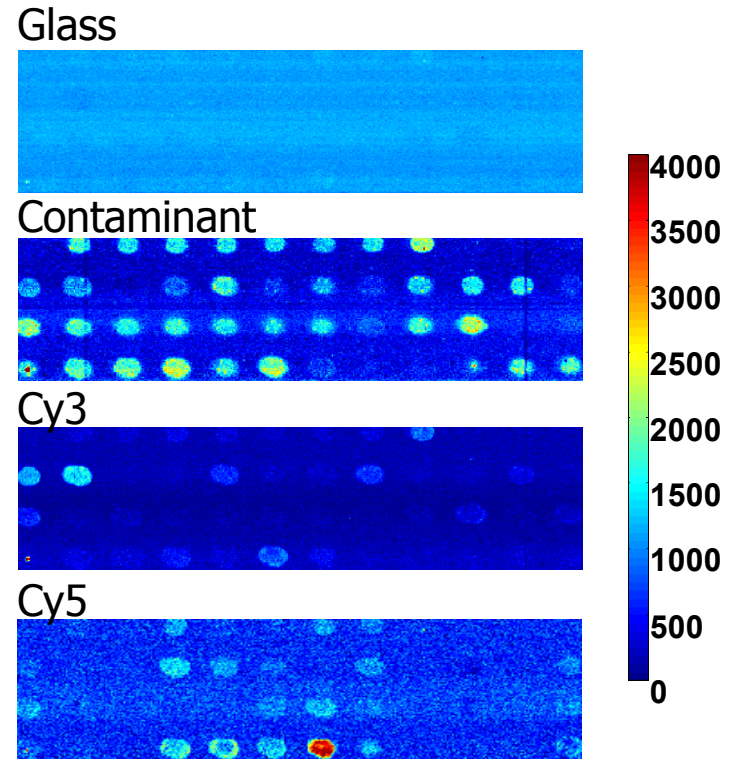


# Application of 2D Hyperspectral Imaging is Ideal for Multiplexed Genetic Profiling.

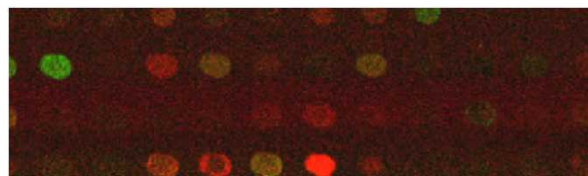
Extracted Emission Spectra



Concentration Maps



Commercial scan



Simulated hyperspectral scan

Contaminant found in  
4 commercial arrays  
and in-house arrays