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# New Biology for the 21st Century: Transforming Our Energy Future

*Presentation to the National Academy of Sciences  
Board on Life Sciences*

Dr. Raymond L. Orbach  
Under Secretary for Science,  
Department of Energy  
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The Department of Energy has a long history of using research and development in the physical sciences in support of life sciences research.

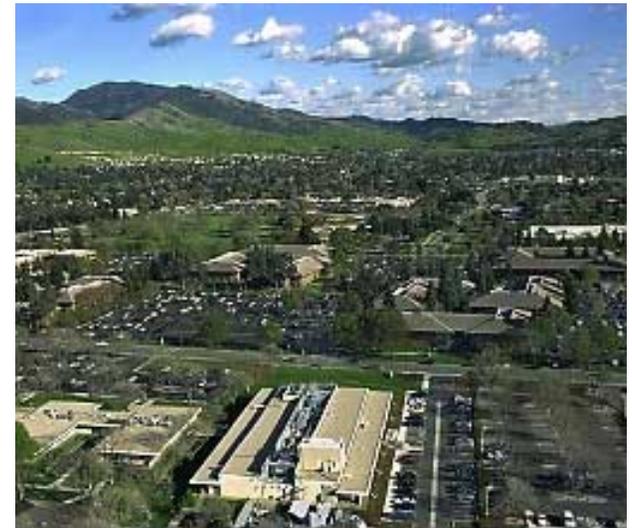
DOE initiated:

- The Human Genome Project
- Ultrafast Genome Sequencing
- Numerous Biomedical Imaging Technologies
- The Artificial Retina Project
- Solution of the Phase Problem in Structural Biology



## The Human Genome Project: A Scientific Revolution

- The Human Genome Project was initiated by DOE to understand effects of radiation and chemical contaminants on genome structure, replication, and repair
- Sequenced 3.1647 billion base pairs and identified ~ 26,000 genes contained in the human genome
- The Joint Genome Institute (JGI) was instrumental in this effort, and now applies ultrafast sequencing to microbes, plants, and intact communities for DOE missions
- In October of 2008 alone, JGI sequenced over 20 billion nucleotides

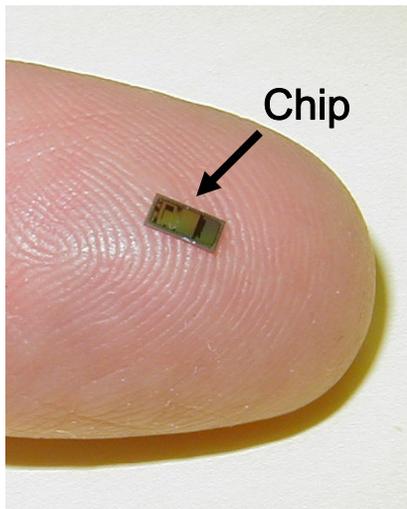




## Biomedical Imaging Technology



- New advances in *in vivo* Positron Emission Tomography (PET) at Brookhaven National Lab
- Miniaturization of PET technology provides a new capability for “wearable PET” in laboratory animals
- Allows real time brain imaging for awake lab rats and correlation of neurochemical stimulations with behavior of the animal
- Further development will provide new tools to study molecular elements as markers of genetic manipulations, biological transformations, and progression of the disease in living animals

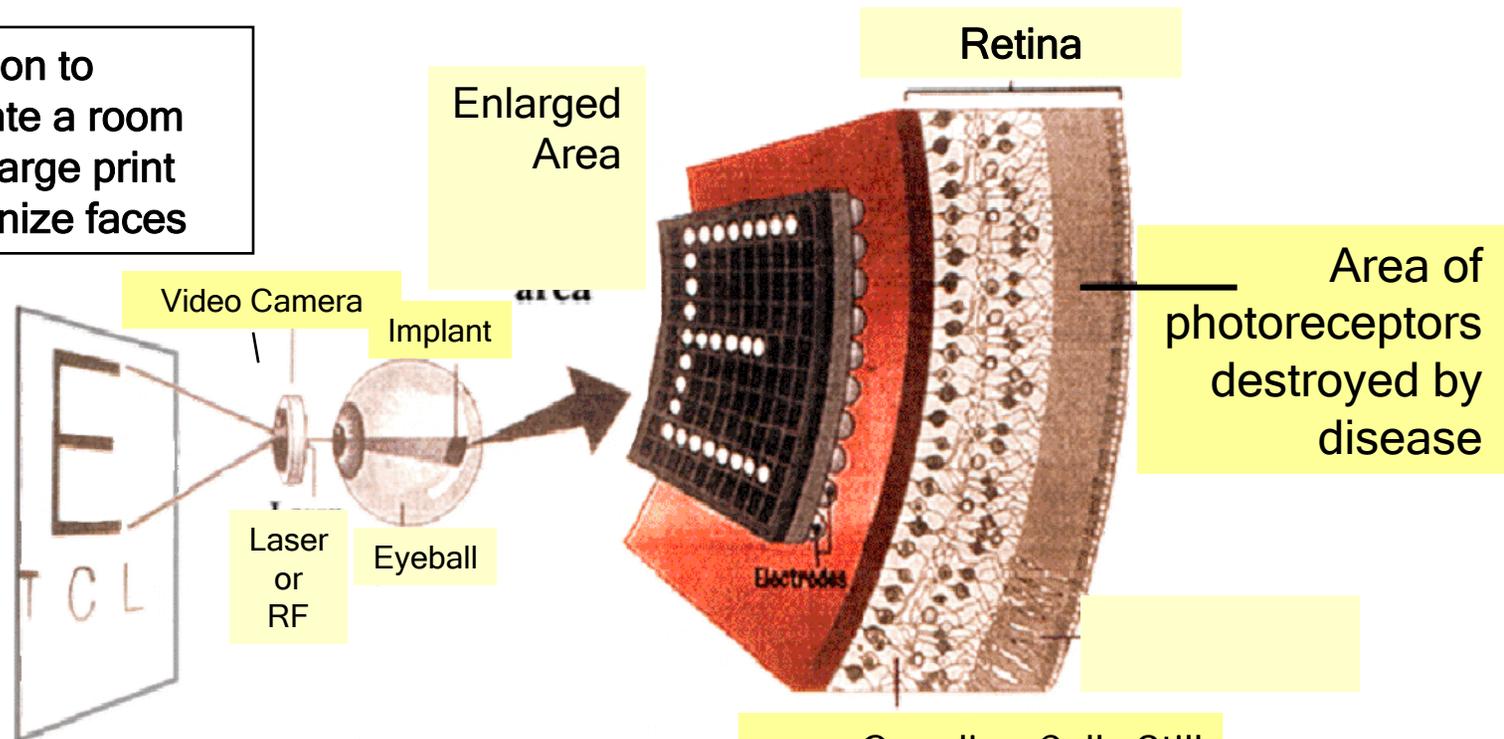




## The Artificial Retina Project: Macular Degeneration

Restore vision to

- Navigate a room
- Read large print
- Recognize faces

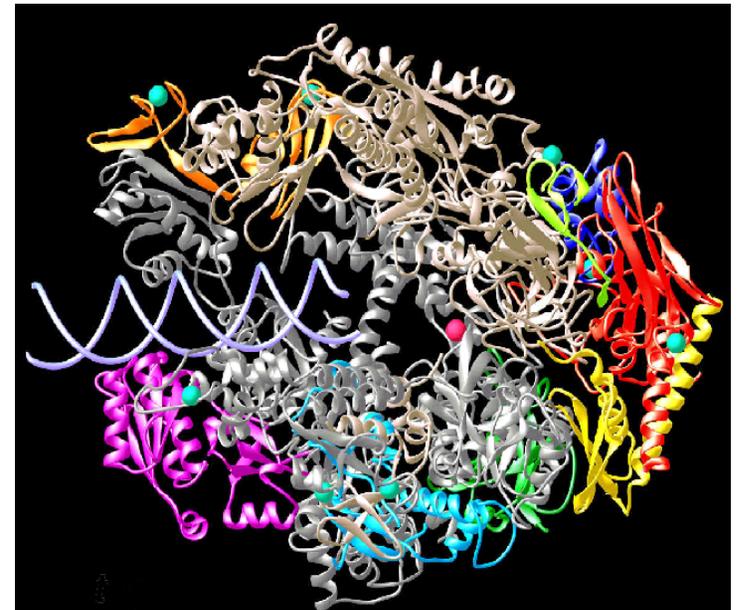


- 200 micron electrodes arrayed on a 2.4 x 4 mm pad
- 60 electrode arrays have been implanted in patients: ability to read large scale print.
- 240 electrode arrays are ready for animal studies
- Phase I clinical trials complete; awaiting FDA approval for phase II



# Structural Biology

- DOE National User Facilities enable new advances in structural biology
- Four Synchrotron Light Sources and three Neutron Beam Facilities
- 40% of users at Light Sources are life scientists
- Solution to the “phase problem” of x-ray crystallography by Keith Hodgson (SLAC) using multiwavelength diffraction
- 2006 Nobel Prize in Chemistry to Roger Kornberg for determining structure of RNA Polymerase II (SSLR and ALS)
- The LCLS (SLAC) will provide new ability to measure chemical dynamics in real time
- NSLS II (BNL) single molecule imaging: real space imaging (1 nm resolution) and energy resolution (1 degree Kelvin)



RNA Polymerase II



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# DOE Bioenergy Research Centers

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## Joint Bioenergy Institute (JBEI)

- Led by Lawrence Berkeley National Laboratory
- Using synthetic biology to engineer microbes that can synthesize next generation biofuels (butanol, hexadecane, etc.) and understanding the molecular structure of plant cell walls

## BioEnergy Sciences Center (BESC)

- Led by Oak Ridge National Laboratory
- Developing switchgrass and poplar as bioenergy feedstocks and Consolidated Bioprocessing for direct conversion of plant material to biofuels

## Great Lakes Bioenergy Research Center (GLBRC)

- Co-Led by University of Wisconsin and Michigan State University
- Research on enhancing the digestability of lignocellulose, engineering microbes for improved fuels synthesis, and sustainability of biofuels production

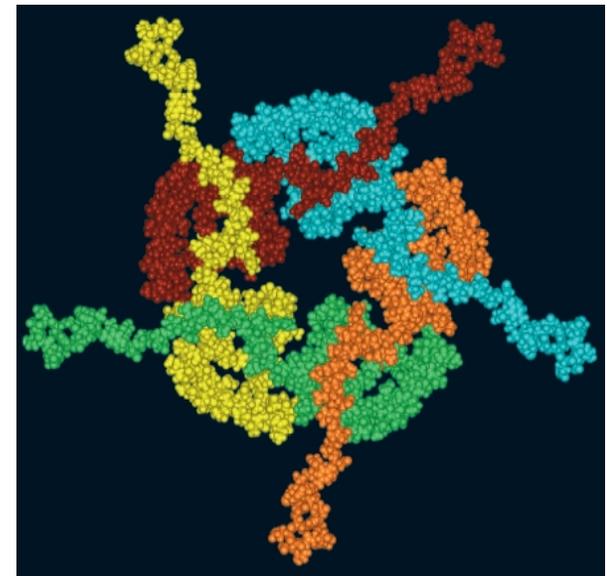


- DOE provides access to world class supercomputing capabilities needed to model complex biological systems at the molecular scale
- Leadership Class Computing facilities at Oak Ridge and Argonne National Labs
  - The Cray XT Jaguar at ORNL is the world's fastest computer for open science: 1.64 petaflops
- INCITE Program: Innovative and Novel Computational Impact on Theory and Experiment
  - Competitive awards allocating time on some of the world's most powerful supercomputers for large-scale computational science projects
  - 400,000,000 processor hours provided in 2008



## Leadership Class Computing: Parkinson's Disease

- An INCITE award to Igor Tsigelny (UC-San Diego) enabled molecular simulation studies on the molecular basis of Parkinson's disease
- Alpha-synuclein (AS) proteins associated with the disease form pentameric rings on the cell membranes of neurons.
- AS rings form pores in the cell membrane, destroying the integrity of the neuron and causing onset of the disease
- Molecular simulation revealed which AS amino acid sequences interact with the cell membrane, providing new targets for drug development and therapy
- These results are applicable not only to Parkinson's Disease, but also Alzheimer's disease, rheumatoid arthritis, type II diabetes, and a host of other diseases.



Alpha-synuclein Pentamer



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# Conclusions

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The Department of Energy has much to offer the “New Biology”:

Through new world-leading large scale facilities:

- Synchrotron radiation light sources

- X-Ray free electron lasers

- Leadership class computers

- High energy accelerators

- Spallation neutron source

Through development of new mathematics

Through provision of radio-nucleotides

Through direct support of research

We look forward to a continuing partnership with the biological community, producing new discoveries and transformational changes in technologies.