U.S. DEPARTMENT OF ENERGY | Office of Science

The Department of Energy's Activities Supporting the Life and Medical Sciences

Presentation to the Secretary of Energy Advisory Board

June 17, 2015

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Office of Science
By the numbers

Shown is a portion of SLAC's two-mile-long linear accelerator (or linac), which provides the electron beam for the new Linac Coherent Light Source (LCLS) – the world's first hard x-ray, free-electron laser. For nearly 50 years, SLAC's linac had produced high-energy electrons for physics experiments. Now researchers use the very intense X-ray pulses (more than a billion times brighter than the most powerful existing sources) much like a high-speed camera to take stop-motion pictures of atoms and molecules in motion, examining fundamental processes on femtosecond timescales.

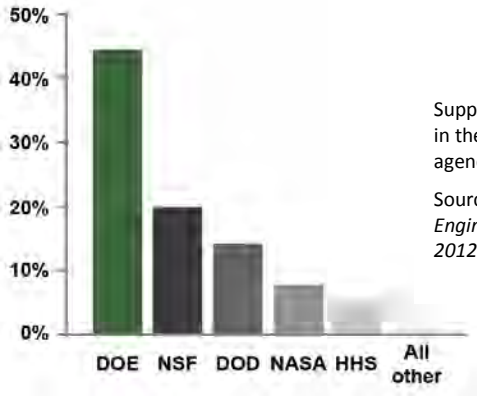
SC's mission is to deliver scientific discoveries and major scientific tools to transform our under-standing of nature and advance the energy, economic, and national security of the U.S.

Research

- SC supports 47% of the U.S. Federal support of basic research in the physical sciences;
- ~22,000 Ph.D. scientists, grad students, engineers, and support staff at >300 institutions, including all17 DOE labs;
- U.S. and world leadership in high-performance computing and computational sciences;
- Major U.S. supporter of physics, chemistry, materials sciences, and biology for discovery science and for energy sciences;

Scientific User Facilities

- The world's largest collection of scientific user facilities operated by a single organization in the world, used by 31,000 researchers each year.



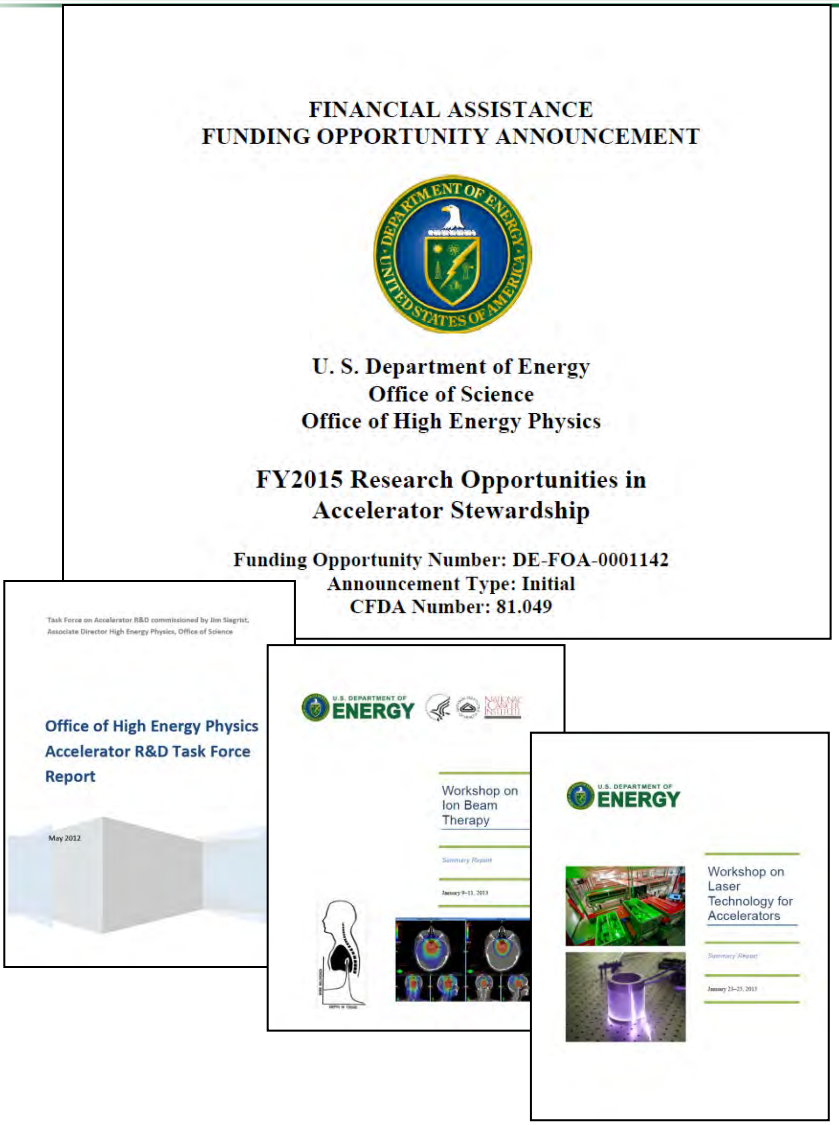
Support for basic research in the physical sciences by agency.

Source: *NSF Science and Engineering Indicators 2012*

Research Areas of Mutual Interest to DOE and NIH

- Accelerator stewardship
- Medical isotopes
- Materials and imaging
- Structural biology
- Genomics and bioinformatics
- Computational analysis and infrastructure

Accelerator Stewardship - High Energy Physics



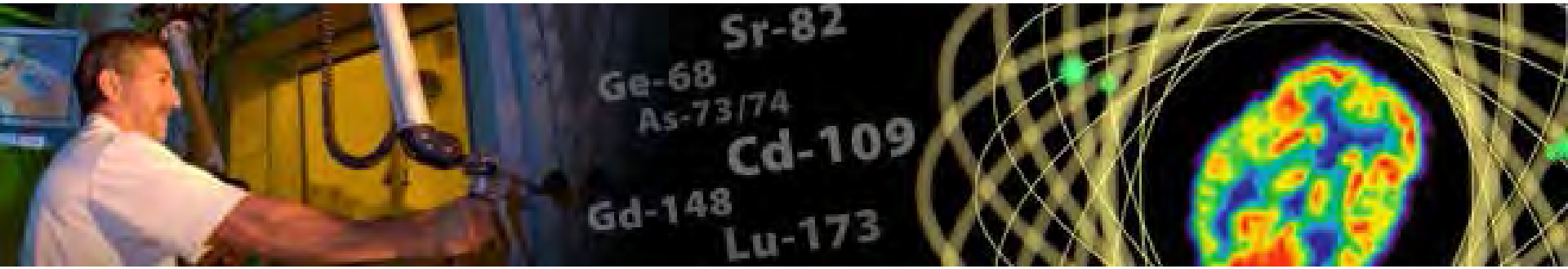
- **Track 1: Applied R&D**
  - **Particle Therapy Beam Delivery Improvements**
    - Less massive and more compact beam delivery systems capable of delivering ion beams
    - Technology that can provide for rapid (seconds) scanning of the beam over a tumor
    - Beam diagnostic technologies for ion beam therapy
  - **Ultrafast Laser Technology Program**
    - Ultrafast gain materials capable of very high average power,
    - Increased robustness and reduction in size of optical components,
    - Innovations in laser architectures
    - Wavelength extension further into the infrared
    - Improvements in laser quality
  - **Energy Efficiency Improvements Compatible with SC Accelerators**
    - Reduce accelerator power consumption through innovations in power conversion technology
- **Track 2: Basic R&D**
  - **Significant increases in accelerator performance** (flux, brightness, polarization, coherence, stability, reliability, flexibility) and **decreases in cost** (construction cost, operating cost, physical size, complexity) are sought.

NIH-NCI issued call for proposals addressing the radiobiological (ongoing R01) and clinical aspects (targeted P20) identified by these workshops.

DOE-HEP executed two awards ($2.8M/3 years), selected with input from NIH-NCI, each involving a DOE-funded R&D institution and a cost-sharing U.S. industrial partner.

DOE-HEP and NIH-NCI plan continued coordination in this area. Future Accelerator Stewardship Funding Opportunity Announcements will continue to call for translational R&D to transfer accelerator technology into medical use.

The DOE Isotope Program (Office of Nuclear Physics)



- **Research, development, and production of stable and radioactive isotopes is provided for science, medicine, industry, and national security.**
- Support continues for R&D competitive awards to universities and laboratories, as well as support to laboratory research groups at LANL, BNL, and ORNL.
- Development of production techniques for alpha-emitting radionuclides for medical therapy continues to be a priority, implemented through collaborative R&D at the national laboratories, particularly at BNL, LANL, and ORNL.
- Research at universities and national laboratories is supported for new isotope production technologies. Funding increases to enhance core research capabilities at the national laboratories and universities, and the program of competitive R&D, in order to address the high priorities especially with regard to the research to produce Ac-225.
- Maintains the infrastructure required to produce and supply isotope products and related services.
- Provides technical support to the National Nuclear Security Administration (NNSA), which has responsibility for the establishment of a domestic supply of Molybdenum-99 (Mo-99).

R&D Creates New Production Method for Actinium-225

- A new isotope project at LANL shows promise for rapidly producing major quantities of a new cancer-treatment agent, actinium 225.
- Using proton beams, LANL and BNL could match current annual worldwide production of the isotope in just a few days.
- A collaboration among LANL, BNL, and ORNL is developing a plan for full-scale production and stable supply of Ac-225.
- Ac-225 emits alpha radiation. Alpha particles are energetic enough to destroy cancer cells but are unlikely to move beyond a tightly controlled target region and destroy healthy cells. Alpha particles are stopped in their tracks by a layer of skin—or even an inch or two of air.

Basic Energy Sciences: 12 Scientific User Facilities

- Available to all researchers *at no cost* for non-proprietary research, regardless of affiliation, nationality, or source of research support
- Access based on external peer merit review of brief proposals
- Coordinated access to co-located facilities to accelerate research cycles
- Collaboration with facility scientists an optional potential benefit
- Instrument and technique workshops offered periodically
- A variety of on-line, on-site, and hands-on training available
- Proprietary research may be performed at full-cost recovery

Light Sources

- Advanced Light Source (LBNL)
- Advanced Photon Source (ANL)
- Linac Coherent Light Source (SLAC)
- National Synchrotron Light Source-II (BNL)
- Stanford Synchrotron Radiation Laboratory (SLAC)

E-Beam Microcharacterization Centers administratively merged with NSRCs in FY 2015

Neutron Sources

- High Flux Isotope Reactor (ORNL)
- Spallation Neutron Source (ORNL

Nanoscale Science Research Centers

- Center for Functional Nanomaterials (BNL)
- Center for Integrated Nanotechnologies (SNL & LANL)
- Center for Nanophase Materials Sciences (ORNL)
- Center for Nanoscale Materials (ANL)
- Molecular Foundry (LBNL)

Capabilities at the Nanoscale Science User Facilities

- Advanced synthesis of nanoscale materials
  - Clean room fabrication including lithography
  - Atomically controlled synthesis
- Wide range of characterization techniques
  - Microscopy, NMR, spectroscopy, etc.
- Specialized analytical tools
  - Discovery platforms (SNL CINT)
- Theory, Modeling and Simulation
- Coupled to x-ray and neutron scattering facilities
- Specialized capabilities for biological systems
  - Deuteration for neutron scattering (ORNL CNMS)
  - Biological imaging

Structural Biology Resources

- Support of synchrotron and neutron beamlines for structural analysis of key biomolecules and complex cellular components
- Develop new instrumentation for structural biology applications that take advantage of unique capabilities at DOE user facilities
- Support user access to end stations at light source beamlines
- DOE SC-BES, SC-BER, and NIH-NIGMS partnership

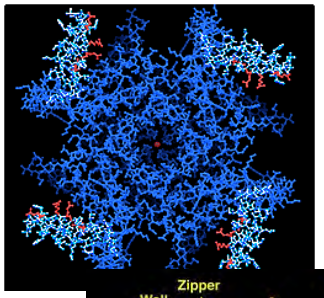
4 Nobel Prizes in 10 Years Using SC Light Sources

2003: Roderick MacKinnon (Chemistry) for “structural and mechanistic studies of ion channels.”
Used NSLS beamlines X25 and X29.

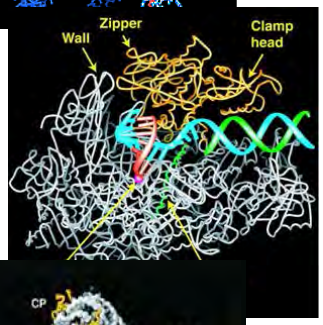
2006: Roger Kornberg (Chemistry) "for his studies of the molecular basis of eukaryotic transcription.”
Used SSRL macromolecular crystallography beamlines.

2009: Venkatraman Ramakrishnan, Thomas A. Steitz, and Ada E. Yonath (Chemistry) "for studies of the structure and function of the ribosome.”
Used all 4 DOE light sources.

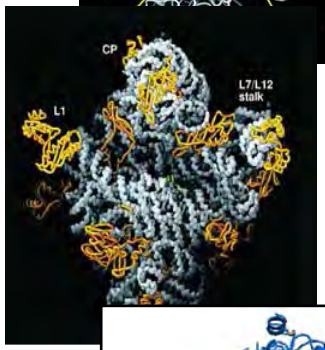
2012: Robert J. Lefkowitz and Brian K. Kobilka (Chemistry) "for studies of G-protein-coupled receptors.”
Used APS beamline 23-ID.



The overall view of a voltage-dependent potassium ion channel.



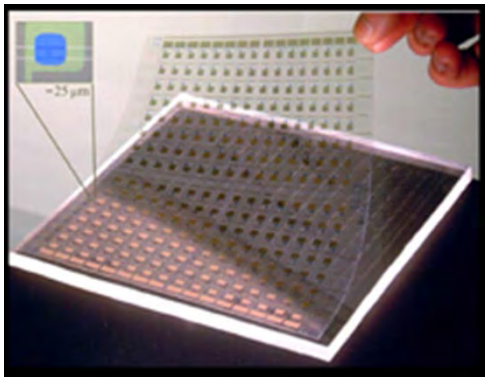
The visualized transcription process.



The 50S subunit structure at 2.4Å resolution.

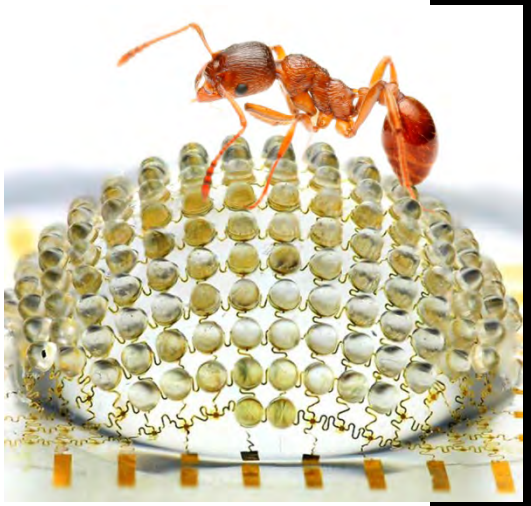
The structure of the β2AR-Gs complex.

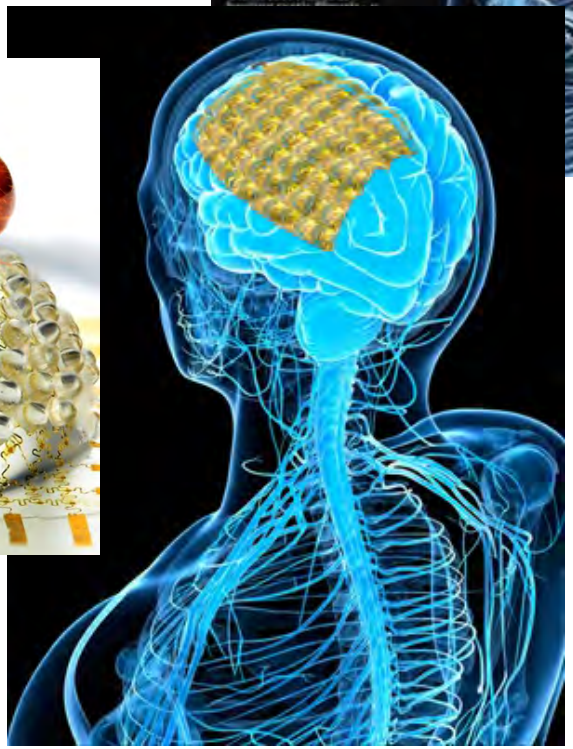
BES-supported Research on Flexible Electronics



New Electronics Can Stretch, Flex and Even Dissolve in the Body

– John Rogers, U of Illinois





- BES-supported materials research at UIUC has resulted in an extensive intellectual property (IP) portfolio related to printable, flexible electronics.

- The basic research knowledge base includes key materials-centric aspects of a micro-transfer printing process for single crystalline silicon and other semiconductors, dielectrics and metals.

Electronic monitors now in development could mold to the brain's surface to sense aberrant electrical activity.
Sciepro/Getty Images and Jay Smith/Discover

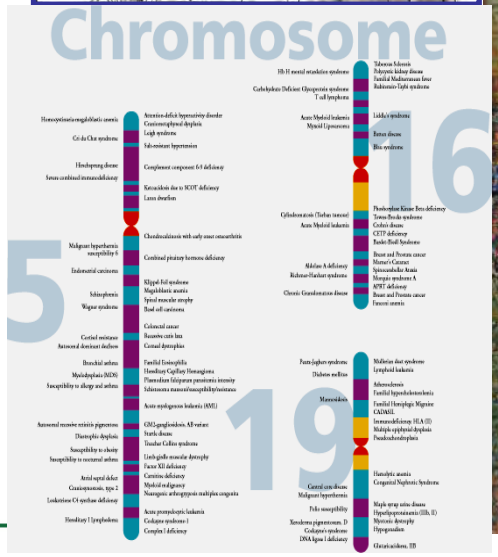
Important Dates in Genomics

1986 DOE announces Human Genome Initiative

1990 DOE & NIH join forces and launch the Human Genome Project (HGP)

2000 Completion of the working draft by the HGP and Celera

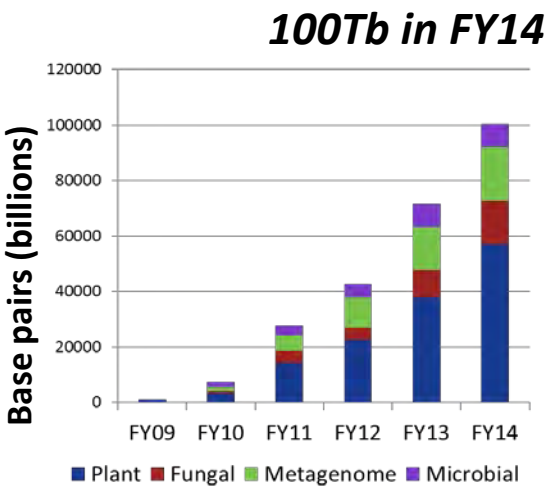
2003 **Finished human genome delivered on the 50th anniversary of the Watson-Crick paper**

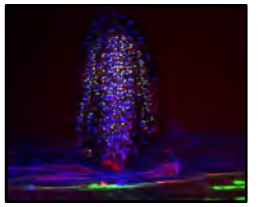


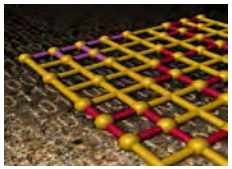
User Facilities—Biological and Environmental Research

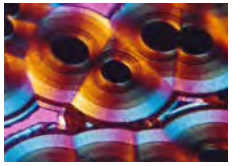
The Joint Genome Institute (JGI) enables genome sequencing and genome science on plant, rhizosphere and microbial communities for energy and environment.

- Developing new strategies for complex genome assembly using next-generation sequencing platforms and analysis tools.
- Supporting biosystems design for biofuels and environmental process research
- Metagenome (genomes from multiple organisms) sequencing to analyze complex, inter-dependent microbial communities to elucidate individual and collective function.









The Environmental Molecular Sciences Laboratory (EMSL) enables molecular-scale experimental and theoretical research on aerosol chemistry, biological systems, geochemistry/biogeochemistry, and interfacial and surface science.

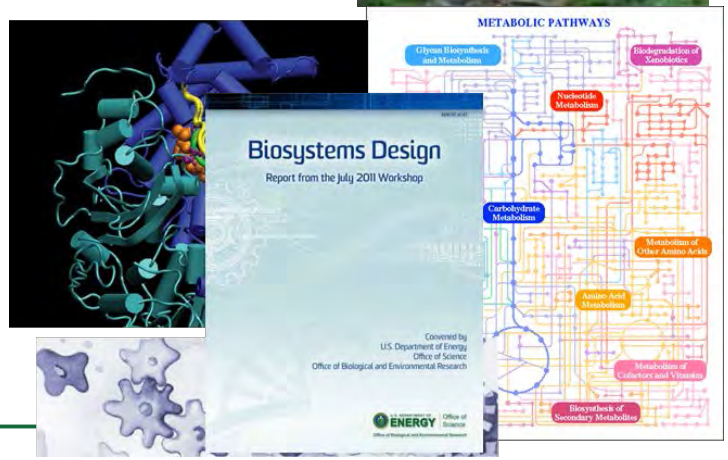
- Core experimental capabilities include:
- Microscopy, Deposition and Microfabrication
- NMR, EPR, Mass Spectrometry, Spectroscopy and Diffraction
- Cell Isolation and Systems Analysis
- Molecular Science Computing
- Radiochemistry Annex
- Quiet Wing for ultrasensitive microscopy instruments

Genomic Science in Biological and Environmental Research

- Determine the genomic properties, molecular and regulatory mechanisms, and resulting functional potential of microbes, plants, and biological communities central to DOE missions
- Develop the experimental capabilities and enabling technologies needed to achieve a genome-based, dynamic system-level understanding of organism and community functions
- Develop the knowledgebase, computational infrastructure, and modeling capabilities to advance the understanding, prediction, and manipulation of complex biological systems

Biosystems Design Tools for Plant & Microbial Systems

- Research to establish biological design rules will enable the predictive design of innovative natural and hybrid systems for clean energy production.
  - New synthetic biology methods
  - New genetic toolkits
  - Predictive integration of components and processes
  - Verify & validate computer-aided design toolkits
  - Testbeds to prototype performance and function



Leadership Computing Today – Advanced Scientific Computing Research

- Providing the Facilities **– High-End and Leadership Computing**
  - **National Energy Research Scientific Computing Center (NERSC)** at Lawrence Berkeley National Laboratory
    - Delivers high-end capacity computing to entire DOE SC research community
    - Over 5,000 users and 400 projects
  - **Leadership Computing Centers at Argonne National Laboratory (ALCF) and Oak Ridge National Laboratory (OLCF)**
    - Delivers highest computational capability through **Innovative and Novel Computational Impact on Theory and Computation (INCITE)** program
      - » Open to national and international researchers, including industry
      - » No requirement of DOE or Office of Science funding or topic area
      - » Peer and computational reviews
    - Over 300 users and 25-30 projects at each center
- Linking it all together
  - Energy Sciences Network (ESnet)

Science Drivers Requiring Capable Exascale High Performance Computing

NIH-NSF-DOE (ASCR) Request for Information to identify scientific research topics that need High Performance Computing (HPC) capabilities that extend 100 times beyond today's performance on scientific applications.

- Information will be used to assist agencies to construct a roadmap, build an exascale ecosystem required to support scientific research, and inform the research, engineering and development process. It is likely that a range of advanced capabilities will need to be developed to respond to the varied computing needs across science disciplines.
- To be released shortly, pending discussions with OSTP

DOE Systems Biology Knowledgebase (KBase)

Building a Community Resource for Predictive Biology

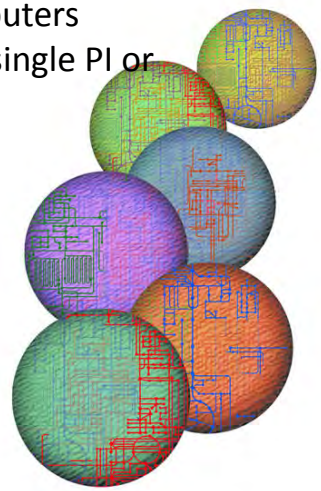
An open-source and open-architecture computational environment for integrating large, diverse datasets, generated by the Genomic Sciences program and other sources, and for using this information to advance predictive understanding, manipulation, and design of biological systems for energy and environment.

Accelerates the use of complex data by biologists:

- encourages best science practices: access to data, sharing, publishing, reproducibility of analyses
- provides access to the best tools for the analysis of large, complex data sets
- provides metrics for success and utility of data, tools etc.
- lowers the bar for the analysis of complex data sets and modeling with high performance computers
- synthesizes biological data from the community to answer questions beyond the ability of the single PI or small teams of researchers

KBase includes (to date):

22,253 microbial genomes
96 eukaryotic genomes (56 plants)
15,462 metagenomic datasets
13,111 public reference models
28 analysis services
60+ point-and-click analysis functions



KBase
PREDICTIVE BIOLOGY
DOE Systems Biology Knowledgebase

- MOA with the National Institute of Allergy and Infectious Diseases (NIAID) Office of Cyber Infrastructure and Computational Biology (OCICB) to continue collaboration on genome analysis tools and techniques.

Analytics of Extremely Large Graphs

- **Large scale graphs in various fields**
  - US Road network : 58 **million** edges
  - Twitter follow-ship : 1.47 **billion** edges
  - Neuronal network : 100 **trillion** edges

large

Social network

Twitter

61.6 million vertices
& 1.47 billion edges

- **Fast and scalable graph processing** by using **HPC**

Neuronal network @ Human Brain Project
89 billion vertices & 100 trillion edges

US road network
24 million vertices & 58 million edges

Cyber-security
15 billion log entries / day

Image: Illustration by Mirko Ilic

DOE - NIH Coordination and Collaboration Inputs and Drivers

- NSTC – Committee on Science
- Community workshops and Principal Investigator Meetings
- Federal Advisory Committee and National Academy Workshops and reports
- Scientific Meetings convened by federal agencies, scientific professional societies, nonprofit foundations
- Office of Science and Technology Policy (OSTP) initiatives