MINUTES

Biological and Environmental Research Committee (BERAC) Meeting
Office of Biological and Environmental Research
Office of Science
U.S. Department of Energy

DATE: December 3-4, 2002

LOCATION: American Geophysical Union, Washington, DC. The meeting was announced in the Federal Register on November 15, 2002

PARTICIPANTS: Approximately 85 people were in attendance for part or all of the meeting. Seventeen BERAC members were present:

Keith Hodgson	Roger McClellan
James Adelstein	Jill Mesirov
Eugene Bierly	Louis Pitelka
Michelle Broido (by phone)	Lisa Stubbs
David Burgess	James Tiedje
Ray Gesteland	Nora Volkow
Richard Hallgren	Warren Washington
Leroy Hood	Barbara Wold
Steven Larson	

Eight BERAC members were not present:

John Ahearne	Jonathan Greer
Carlos Bustamante	Willard Harrison
Charles DeLisi	James Mitchell
Robert Fri	Janet Smith

(Information on the BERAC membership can be found at:
http://www.science.doe.gov/ober/berac/members.html)

Tuesday, December 3, 2002

Keith Hodgson, Chair, BERAC

- Welcome to new members – Nora Volkow (medicine, medical imaging), Robert Fri (energy policy, global change), John Ahearne (risk analysis, environmental cleanup)

GENOMES TO LIFE PRESENTATIONS ON PROPOSED NEW FACILITIES

Marvin Frazier, Director, Life Sciences Division, OBER - Overview

- Growing mandate to move biology forward – OMB/OSTP, American Academy of Microbiology
- This new document is a DOE response to a previous BERAC subcommittee report/discussion (David Galas, Barbara Wold, etc.) – see minutes from BERAC meeting spring 2002 (http://www.sc.doe.gov/production/ober/berac/04-02mins.pdf)
- DOE has broad needs in energy, climate change, environmental cleanup for which biotechnology can contribute solutions
- DOE has a historical role in microbial genomics – "microbes are us." Began the Microbial Genome program in the fall of 1994. First public funding to sequence a microbe.
- Pilot research projects and technology development projects have been underway in our program for a number of years.
- We have a plan – science, technologies, facilities, management
- Four facilities to be described today
    - Production and Characterization of Proteins – *high throughput*
    - Whole Proteome Analysis – *high throughput*
    - Characterization and Imaging of Molecular Machines – *high throughput*
    - Analysis and Modeling of Cellular Systems – *high technology*
- Overall funding profile proposed rises to approximately $200M per year for construction followed by facility operation that increases for inflation. Current plan calls for completion of facilities in approximately 8 years at a total cost of $800M+.
- Pending SC approval BER will investigate the possibility of attracting other funding sources outside of DOE including third party funding and shared funding with other agencies, e.g., NIH, NSF
- Open and rapid access of data, tools, and resources – fundamental principles.

Questions/Comments

- Concern that we are not attracting the best scientists because of the specific focus on DOE mission needs. Does this DOE-centric focus also impact the broader applicability of the science/technologies to medicine? Need for more careful wording of announcement? Downplay specific microbial systems somewhat?
    - Clinical microbiology community becoming much more open to sorts of interests that DOE has. Not as clear a distinction between medical and environmental microbiology as there has been in the past. This is a good time because of where people are intellectually today.
    - Essentially everything in calls is applicable across end applications whether soils or medicine.
    - Facilities will be valuable to many including bioweapons defense though our specific focus and responsibility in this area has been transferred to the Department of Homeland Security.

- Possibility of excluding a fraction of funds for people outside DOE focus areas?
- Justification for these facilities is to underpin the research base of GTL and as user facilities for the broader research community.
- These facilities will interface with other programs supported by DOE, e.g., targeted tracers for medical therapy.

Eric Ackerman, Pacific Northwest National Laboratory – Facility 1: Production and Characterization of Proteins

- High throughput protein production and affinity reagents
- Deliverables – validated clones and expression protocols for proteins and affinity reagents; proteins (though not generally a protein export facility); affinity reagents
- 10-25,000 full-length purified proteins per year as a goal.
- Affinity reagents to study protein interactions, dynamics, complex isolation/identification. Still major technical problems/challenges to be solved.
- High throughput = high quality = reduced cost
- Computation to track and monitor and improve future production
- Pilots – NIH/NIGMS Structural Genomics Centers, cell-free efforts in Japan ("feeder" of proteins to NMR "farm"), yeast surface and phage display cellular methods; Japanese interests in collaborating since they have little mass spectrometry interface or computation so far.

Questions/Comments

- 70-80% of microbial proteins insoluble. A significant problem that has not yet been cracked. Facility to use experience-guided approaches. New uses of detergents? Production of several proteins simultaneously? Japanese produce proteins in high throughput but only at small screening levels – may provide some help.
- Facility itself will not be dispersed but there are diverse elements needed to successfully develop this facility. Pilot efforts are currently dispersed at different sites but no one method has yet emerged. DOE's Joint Genome Institute began with three separate DNA sequencing protocols.
- Issue of posttranslational modification and high throughput – results in structural changes. Need to identify what those modifications are. General modifications can be incorporated into protocols but very specific modifications will be a much greater challenge.
- Affinity tags as a key issue. Aptamers? Is DOE looking at this specifically? Not a current pilot but certainly a consideration. Aptamers seem even a greater challenge to produce than antibodies though they work well once good ones found. Founder of aptamer company says that production of large numbers of high affinity aptamers going well.
- Will cell-free expression systems work well for broad range of G+C content DNAs? Hasn't been a problem in Japan so far.

Michelle Buchanan, Oak Ridge National Laboratory – Facility II: Whole Proteome Analysis

- Would like to be able to analyze hundreds of microbial proteomes each year under a variety of conditions.
- Microbes grown under controlled conditions, high throughput sample preparation and analysis, computational tools for interpretation and modeling
- Revolutionary impact of mass spectrometry (MS). MS not the limiting step at this point. Need for high throughput sample preparation, novel cell cultivation, on-line analysis of metabolites, robotics/automation, chip expression assays, microsample handling, single cell analysis (?), imaging, computation/informatics (petabytes of data per day soon)
- *D. radiodurans* success story – proteins from 83% of predicted open reading frames have been identified using high performance MS
- Microfluidics example – opportunity for single cell analysis, potential for interfacing with MS analysis
- Impact – high fidelity, openly accessible, "pedigreed" data to the scientific community; economy of scale; information base for facilities III and IV

Questions/Comments

- How will protein quantitation be done? Still not routine.
- A strength/value of DOE labs has been the things that they can/have exported. Certainly a goal here as well – technology transfer.
- Will want to quantify/integrate other types of data, e.g., mRNA, on same cells in addition to just proteome analysis
- Can we actually detect proteins from single cells yet? Some proteins but not comprehensive yet.
- Proteomics only as good as the quality of the material being analyzed. How will environmental conditions be identified? Need for collaboration with organism experts for example.
- Microbes in nature generally grow on surfaces not in solution.

Lee Makowski, Argonne National Laboratory – Facility III: Characterization and Imaging of Molecular Machines

- Isolate the repertoire of molecular machines and characterize their composition and organization
- Will require a variety of analytic and imaging technologies together with computational/modeling tools
- Example of the 3D ribosome structure – the individual components in the ribosome are in configurations that would be unstable if they were not in the ribosomal complex.

Questions/Comments

- How do you measure protein-protein complexes? Seems that so much of what is being talked about is incredibly immature just as sequencing was in the early phases of the genome project. Protein-protein mapping is an immature field though not saturated. Facility III will not be available for 7 years so time for technology development between now and then important a key to success. Nano technology approaches will also play a major role, e.g., micro cantilevers with attached proteins. Need to get beyond 50% current success rates. DNA-protein interactions also essential. Need to ensure that flexibility is in place so that the best and most promising technology can be incorporated into facility.
- In vivo imaging also essential.
- At what level is data distribution anticipated. Often several orders of magnitude difference between primary and processed data. Having primary data available is important as shown by the genome program. There are limits as to what is practical to send over the web.

Jim Fredrickson, Pacific Northwest National Laboratory – Facility IV: Analysis and Modeling of Cellular Systems

- More technology driven and GTL end-use than other three facilities
- Single cells to entire complex communities
- Final component of an integrated network for systems biology. Microbes rarely live as monocultures except in our laboratories.
- High throughput cultivation (issue of unculturability in the lab – though organisms must grow in nature at some point in time), imaging (spatial/temporal analyses)
- Investigators, students, teams of scientists viewed as using this facility
- Coupling of experiment, analysis, and theory

Questions/Comments

- Trade offs in imaging between spatial and temporal resolution. DOE Spring imaging workshop (http://www.doegenomestolife.org/technology/imaging/GTLimaging2002.pdf) addressed many of these issues. Many technologies that are not directly imaging, e.g., micro spectroscopies. There are limits and clever ways to try to address them.
- Lots of the same technologies being described here as in other 3 facilities. Is focus here more on living cell than extracts? Yes. There is technology overlap but not in facility mission. "All" will have imaging needs for example but they are quite different in each case. This reads more like a research facility than a facility. Have been through this argument but are convinced that Facility IV will bring together lots of technologies not likely to be found in any individual project. Seems like this could benefit from being a multi site "facility." Have talked about this too. Why limit to a single site model? Development of the capabilities represented here is the key in the end.

- Discovery science versus systems biology. Systems biology is a well integrated, iterative effort. Nice to be able to do all in one place. Hard to see how it could work optimally in a distributed way. Goal is to make this a user facility as well as the others.
- Don't want to duplicate what is being developed elsewhere including industry. Partnerships and coordination will be critical.

Ed Uberbacher, Oak Ridge National Laboratory – GTL Facilities and Computing

- Computation links and underpins GTL and GTL facilities
- Computation to be integrated within each facility not built as a separate facility. Will also leverage broad capabilities and expertise found in the Office of Advanced Scientific Computing Research (ASCR).
- High performance computing for both capacity (lots of cycles, trivially parallel problems) and capability (biophysical problems, communication between processors and speed of that communication is essential – an ASCR mission responsibility). Leveraging mathematics and algorithmic expertise found in ASCR to help address the current and future challenges in biology and GTL.
- Data organization and storage a huge challenge. Much greater complexity than in the human genome project. Integration of large datasets is a precursor to predictive modeling.

Questions/Comments

- At least two NIH institutes (NIGMS and NHGRI) are already planning large training efforts to meet the human resource needs of the future of biology. How will we attract the computational biologist to this problem when the industry and disease communities have the same/competing needs? Belief that energy and climate change issues will become increasingly important. Capabilities and resources found in GTL will also be major attractors to scientists.
- How important will high end computing be to all of this? What parts actually need high performance computing? Some do and many don't. Working with ASCR to plan next generation of machines and computing.
- Challenges – How will complex models and data really be compared? Modeling of incomplete data sets will have errors that we don't yet know how to model. Important to learn how to pull of this together. Integration of mathematics, computing, and biology really key.
- This is not something that can wait. We are already collecting data, developing models, integrating data sets. How do we do this as transparently as possible? The community needs to be able to use these but doesn't need the details. Relational technologies likely. ASCR projects looking at ways to do this.

Abigail Salyers, Past President American Society of Microbiology

- Comments from a perspective of the microbiology community. Microbiology has a remarkable track record that has produced antibiotics, the germ theory of life, and huge industries. No reason to assume the future won't be equally productive.
- Plans for these facilities (and in Genomes to Life) are a source for inspiration and dreaming. A source of new technologies for the entire research community.
- A program like this may be able to draw scientists from clinical research if it represents inspiration and excitement. Students don't know much about microbiology beyond medicine – this can help.
- As technology gets more complex it gets harder for the individual laboratory to do everything well and most efficiently.
- Consider making facilities accessible to students for training. This needs to be included as part of overall facilities planning.

Questions/Comments

- Ultimately what drives this is a set of capabilities that leads to breaking science that can't be done other ways. This was certainly a lesson from the synchrotron structural biology beamlines.

General Discussion on GTL Facilities Presentations/Plans

- Overall the vision is really attractive. Need more details on the execution and the leadership at the facilities. Genome facilities had outstanding intellectual leadership. A critical part of facility siting will need to be people who understand the science and have the respect of the relevant scientific fields. Training important. Provides an opportunity to play a leadership role and have a major impact on the field and future users. Flexibility and how this is attained is also key. High level outside oversight committees useful. How do you recruit first-class scientists to come use them. Has to be more than "if you build it they will come." Early evolution of technology critically important to a field. Much more complicated than with DNA sequencing. Need to be able to attract people to apply for DOE support and to play roles at the facilities.
- Need to avoid problem of getting locked into a noncompetitive mode of operation once a facility is sited. How do you keep these fresh, cutting edge, and competitive. Risk of losing funding still needs to be an option once facilities are sited.
- How will facilities be managed as a group and not just as individual facilities?
- Dissemination of information and value early, from the beginning, to the broad research community. Lesson from the genome project has been that many only saw practical value relatively recently and not at the beginning.
- Need to reconsider the overall staging of the four facilities since modeling is so important and shouldn't necessarily wait until the end. Each facility will include a computational/modeling aspect. Each is so complex that we can't afford to merge them all by trying to do everything at once.

- This will be a very large management challenge. Peer review and advisory committee input will be critical. Flexibility was key to the genome program. Critiques from advisory groups are slow so need to build in a rapid scientific feedback process from the beginning.
- Seems that locating facilities at different places makes the management challenges even greater. This is so much more complex than sequencing the genome. The genome centers weren't really training scientists. Research appears to be the goal here. What about distributed centers like the NIGMS structural genomics initiative? It may be appropriate for the staff to consider the pros and cons of siting all four facilities at the same physical location.
- Details of the draft report makes the differences between the facilities clearer than they seemed previously. Example of genome sequencing center with associated (rather than separate from) research.
- There is also a Genomes to Life research program in addition to these proposed facilities. Together these make the program. The facilities are enablers of the research by developing and providing technology and high throughput capabilities. There is a large group of Genomes to Life scientists who will be using these facilities. Need for new methodologies and management strategies for integrating across the program. Has BER been in touch with the Alliance for Cell Signaling?

Ari Patrinos, Associate Director for Biological and Environmental Research, Office of Science, DOE, perspectives on GTL facilities

- Significant shift in the way BER does business. We have limited facilities experience – only EMSL and the "mouse house" at Oak Ridge.
- Confident in the value of these facilities. Natural home that these facilities would have in BER and the Genomes to Life program.
- Encouraged by our partnership with ASCR.
- Don't know about the long term viability or chances for getting these facilities approved. As always, times are interesting. Marvin Frazier and his team have done all the right things to position us well to move ahead with these facilities.
- Dr. Orbach has asked if some or all of these facilities could be sponsored jointly with NIH. Anything is possible and we need to determine if it makes sense. Would be useful to have BERAC weigh in on this issue.
- Useful to have input from BERAC on our ability to carry an effort like this through to the end. BER has had limited experience and has a limited track record in this area.
- What feedback has been received from colleagues at NIH on these facilities? Earlier summary versions of these facilities were sent to Dr. Zerhouni. They were circulated among several institute directors (certainly) under the assumption that these would be funded entirely by DOE since we had not talked about doing anything together. All comments we got back were quite favorable. We will wait to see what happens next within DOE before approaching NIH about doing anything jointly.

Additional comments/thoughts

- Important to understand the diversity of particular key functions of microbes, not just what goes on inside them. Synergistic or parallel effort to what has already been described. Example – methane oxidation. We only study organisms that do a good job of using high concentrations of methane. In Facility I could look at a series of related proteins for example.
- University involvement in these kinds of centers? A group of universities could become a core partner for example with impacts on hiring strategies and education programs. Analogy with what NIH has done with glue grants. This all comes back to effective and timely management.
- These facilities are completely open for any and all science but a key aspect does need to focus on integrated program challenges in Genomes to Life.
- General enthusiasm? Is this the right strategy? Yes. There were lots of reasons given why the genome project shouldn't start and how it would waste money. This is no different. DOE should go forward. A spectacular opportunity for DOE to make a substantial contribution. Attracted to the idea of doing something together with NIH. Pattern that DOE will set now will be a great contribution.
- This is a big project, but only in the context of biology not in the bigger picture of big projects. This investment is just not that much for the scale of what is being attempted. An exciting project.
- Need to focus on integration and not fragmentation. How do you create a management structure that will move it forward? Need to start almost de novo. Don't start with the baggage of any one organization.
- What has already been proposed in Genomes to Life is already ambitious without these facilities. These are needed to achieve what has already been proposed in Genomes to Life. These facilities need to be integrated not only with each other but with the entire program. This needs to be an integral part of the Genomes to Life program. In the end, the program needs to be well served – this is the principle goal.
- There is a great opportunity here but considerable thought and effort needs to be put forward to make it happen and to be a success in the end.
- This would be a lot less exciting if all of the technologies were already in hand. The innovations and surprises that come along with the development of these new technologies will be one of the great benefits.

Dave Reichle – Review of Free-Air Carbon Dioxide Enrichement Facilities (FACE)

- Environmental research facilities to conduct controlled CO_2 release in defined ecosystems. Have enabled research on intact ecosystems under natural environmental conditions.
- Originally designed as individual experiments but with time became user facilities. Collectively constitute a distributed user facility. Allow for long-term continuous measurements at ecological sites.
- Five questions -
    - Are these facilities considered and recognized as facilities?

    - Are the operated effectively?
    - Does their distributed nature offer significant opportunities to scientists?
    - Can they be enhanced to attract more users?
    - Can FACE sites be enhanced as a distributed user network?

- Four sites / ecosystems
    - Duke – loblolly pine
    - Oak Ridge – Sweetgum
    - Nevada – desert
    - Rhinelander, Wisconsin – Aspen, birch
- Summary of responses to questions asked of each site:
    - Steering committees evolving at each of the sites
    - General mechanisms for inter-site operational and scientific collaboration are in place.
    - Clear points of contact for each site.
    - Mixed review process of facility operation and performance.
    - Mixed evaluation of the site's scientific products and outcomes.
    - Mix of people responsible for measurements and QA.
    - Mixed data management and QA program documentation.
    - Sites archive and share data with users.
    - Mixed data use policy.
    - General publication credit acknowledgement procedure.
    - Sites do advertise and encourage users.
    - Good access and proposal evaluation.
    - Mixed procedures for user feedback.
    - Publication of annual site progress reports
- Key findings:
    - Accessible and valuable to the user community
    - Facility and infrastructure support provided
    - Long term continuity in measurements and data availability
    - Could accommodate and attract more users
    - Should better track users and user satisfaction
    - Should better coordinate operational and experimental protocols across sites
    - Would improve performance as a network with a coordinating committee
- 60-125 users per site during life of these facilities (5-8 years). About 20 users have used more than one site. 20-125 peer reviewed publications during same time periods. 19 total theses have been completed to date.
- A couple of other FACE sites have been funded – former USDA site, another BER site that was not renewed since research relevant to DOE was completed. A few in Germany and Switzerland. DOE has funded 9 total of which 4 remain today.
- Recommendations:
    - Establish a cross-site coordinating committee
    - Separate operational and research funding
    - Ensure adequate and appropriate support staff
    - Coordinate and promote FACE with other federal bodies, e.g., Forest Service

Questions/Comments

- Any comments on external monies received by investigators since nothing in report though was one of the questions asked? Some modest investments from other DOE technology programs. Some NSF funding. Most operational funding from BER with larger amounts of research support from others.
- What is the trajectory of the need for these types of facilities in the future? Have already gone from 9 to 4 sites. Opportunity for future, unique science still exists. A fairly low cost program. DOE is still in a unique position to bring about a seed change in the conduct of integrated environmental research.
- Need for long-term research to see many environmental effects. Opportunity to begin linking environmental genomics to environmental effects.
- Good report. Agree with overall evaluation. Strong message to DOE and sites – If you want to be considered a distributed user facility then you need to start acting like one. Every site welcomed greater Headquarters involvement. No objections to preliminary report from any of the sites.
- Well done report. Do need to make these types of reports in the context of the program funds involved. Not even a sense of the order of magnitude of funding involved.
- Why aren't multiple CO_2 concentrations a key variable in these studies? This seems like a serious scientific flaw as the program goes forward. There has often been criticism that this program is observational versus experimental. BER simply doesn't have the budget to study additional CO_2 concentrations without cutting other programs.
- BERAC should weigh in on whether this program is asking the right questions. Is the right and the best science being done?
- Report was approved with a recommendation to include budgetary information.

Steve Larson, BERAC Member, Memorial Sloan-Kettering Cancer Center – Science Talk – Molecular Imaging: Dawn of an Era in Cancer Research

- Molecular imaging has become an established part of cancer research. Focus here will be on nuclear imaging, e.g., PET/SPECT, especially PET (positron emission tomography). Believe that nuclear imaging will be the way that we translate many advances in molecular biology into medicine.
- DOE/AEC contributions – nuclear medicine, gamma camera, PET camera, radiotracers, and many diagnostics.
- Combination of PET and CT in oncology valuable since it combines anatomical and functional detail. Growing use of PET for diagnosis of many cancers now reimbursable by Medicare – a driver for future use and development.
- Imaging gene expression and signaling pathways.
- Examples of tumor PET imaging pre- and post-treatment
- Developing a rich inventory or radiolabeled markers that can be used to image a wide variety of key biomolecules that are potential therapeutic targets. DOE funds used to develop radiotracers and NIH funds used for clinical trials.

- Molecular imaging and targeted therapy go hand in hand.

Gene Bierly, BERAC Member, American Geophysical Union – UAV (Unmanned Aerospace Vehicle) Subcommittee Report

- This is another one of DOE's risk taking programs like many we have already heard about today. The whole point of the Atmospheric Radiation Measurements (ARM) program was to take a look at clouds.
- UAV fills a unique in acquiring atmospheric data from "above" to complement ground-based measurements. UAV measurements effectively "put the lid on the box" of measurements taken from below by ARM sites.
- Does UAV research support the fundamental goals of ARM?
- Recommendations:
    - UAV should be continued as part of the ARM program. (Many of these vehicles are not always available because of competing national needs.)
    - Would be nice to have the UAVs owned by the government. Most are rented. Would be much more available for BER needs if government owned. Would also save insurance costs since the government is self-insured.
    - Would be nice if FAA could/would certify them. Limited air space availability now for these to fly their missions.
    - Remarkable ability of national labs to create instrumentation was noted by the committee.
    - People doing UAV research do not have separate funding for the analyses of the data. Committee recommends that the ARM infrastructure and ARM-UAV budgets be merged into a single budget to allow greater flexibility.
- Report approved by BERAC pending inclusion of questions raised during the discussion.

Ed Oliver – Associate Director, Office of Advanced Scientific Computing Research

- INTRODUCTORY NOTE – This presentation is an opportunity for BERAC to have broader perspective on how it fits in with the rest of the Office of Science. Margaret Wright, Chair of the ASCR Advisory Committee was invited to speak but came down with laryngitis so Ed agreed to step in at the last minute.
- Large data sets across SC programs.
- ASCR needs far exceed commercial market capabilities. Applied math. Computer science for high end use. Networking research. Collaboratories – communication across large geographical areas. ES-NET – connecting SC scientists. Facilities, e.g., NERSC (National Energy Research Scientific Computer).
- Scientific Discovery through Advance Computing (SciDAC) – Initiated in FY 2001. Performance gap between peak performance and real performance. SciDAC addressing this performance gap for real applications such as climate modeling.
- Genomes to Life – Very important to ASCR. Far from where it should be today in terms of ASCR funding. $8M in ASCR's FY03 budget.

- Computational Nanoscale Science – new FY03 activity.
- Early Career Principal Investigator Activity - $1.6M/year for 3 years. Within 5 years of Ph.D. 17 awards to date. Goal of steady state of 45-50 investigators.

- Earth Simulator – Took lots of people by surprise though not in the computer world. When announced in spring of 2002 it shocked many. 42 Tflops peak performance. Most shocking thing is its sustained performance levels – 12-26 Tflops for fusion, turbulence, and climate problems. Biggest jump (5x) in a big machine ever. This is not a single use/single purpose computer.
- $350-400M over 5 years. $60M/year operating. An order of magnitude more than US has invested. This machine was built for science. The Japanese are very anxious to interact with US scientists. 35% on climate. 15% on geoscience. 2% on computer science. The balance for other uses to be determined.
- ASCR Advisory Committee thinks that this is a critical challenge to US leadership in computational science and to national security and economic vitality.
- Embarking on a science-driven program of ultrascale simulation. Dr. Orbach sees high end computing as a key thing to be doing.
- Have had a series of meetings with the Access Grid – experts in different scientific disciplines to identify needs of their science.
- Doing an inventory of who uses what machines and how they are performing for their specific applications – http://www.appsmatrix.info/matrix/top_matrix.cgi.

Questions/Comments

- Vector versus scalar – With a scalar machine you reach out and get 2 numbers and you process by adding or multiplying and then send them out and speed is dependent on the total of these individual operations. Vector machines are more like an assembly line in that they can perform the same operation on whole lists of numbers (vectors) in one operation.

Public Comment

None

Adjourned at 5:49 PM.

Wednesday, December 4, 2002

Dr. Ray Orbach

- Thanks to BERAC for your service to DOE and the Office of Science
- Genomes to Life has received broad accolades and justifies DOE's role in the conduct of biological research. BERAC efforts over a number of years to get this important program up and running are greatly appreciated.

- Handout of materials describing the Office of Science programs and some of our key opportunities and challenges have been provided.
- SC research is judged on the quality of its science. Part of our strength is due to our diverse and unique facilities. About half of the SC budget supports our facilities. The other half is split about equally between universities and national laboratories.
- Science education is something that all of us needs to be concerned about. More than half of our science and engineering graduates are foreign nationals. We are blessed that they are contributing to the broad science infrastructure but where are the US students?
- Nanoscale science part of a grand challenge and opportunity in science. We are working closely with other agencies. Five nanoscale science centers at our national laboratories are planned.
- The artificial retina project is a perfect example of why DOE should be involved in biomedical research.
- The Earth Simulator has achieved unprecedented sustained performance levels far exceeding anything we have achieved in this country. It should be possible to develop capabilities to work at 50-100 Tflops sustained speeds to provide unprecedented opportunities in many fields of importance to SC, including climate modeling, protein folding, astroparticle physics, fusion, etc.
- SC is currently going through a process for the development of the next generation of large-scale facilities. Each Associate Director has been asked to provide their recommendations for the facilities needed over the next 20 years. Fifty-three recommendations were made. Will be asking advisory committees for comments, especially in each committee's area of expertise.
- Would like BERAC to address the question of what a light source would be like if BERAC, and not physicists, were designing the source for BER/biology-related needs. All machines we have were designed by physicists and biologists were then been invited to use them. What instruments? time scale? spot size? frequency? intensity? Now is the time for this type of feedback. By spring we will have a roadmap for these new facilities.
- New charge for the future of radiopharmaceutical research has been given to BERAC.

Questions/Comments

- BERAC did spend a lot of time yesterday reviewing the Genomes to Life facilities plans. DOE had the vision and insight at the beginning of the genome project to make it happen as well as developing key technology. DOE again is positioned to help take a lead in the post-genomic era. New technology development can be driven by facilities that bring together capabilities and expertise in one place. DOE's role is critical at this juncture. There are challenges today but there were also challenges and nay sayers at the beginning of the genome project. These facilities have taught us how important it is to make cross disciplinary scientists speak a common language. Appropriate to set bold goals. Developing technology and collecting new data both needed to even get to the position where we can use our incredible computational capabilities to model and understand biology.

Jim Tiedje, BERAC Member, University of Michigan – NABIR Subcommittee Reports

- Do funded project support the goals articulated in the NABIR Strategic Plan for the Community Dynamics and Microbial Ecology element?
- Funded projects fall into one of two general categories
    - Development of molecular and biochemical methods to characterize microbial communities
    - Evaluation of microbial communities in relevant contaminated environments and those involved in bioremediation
- These two activities clearly support the overall goals of this research element. Early emphasis has been placed on molecular and analytical tools development. Good choices were made. In contrast the community dynamics research portfolio only partly supports the strategic goals. Some of the older projects are not well aligned with the rest of the program.
- Are relevant areas being adequately addressed?
- Generally yes. Additional areas for consideration by the NABIR program were suggested, e.g., other organisms/communities; broader consideration of geochemistry, hydrology, chemical contaminant speciation; additional community dynamics during and after biostimulation; microbial community characterization at representative, contaminated DOE sites
- How can this research element be better integrated with the other elements?
- Need for more (not less) alignment with DOE sites.
- Future program calls asking for cross-element research projects.
- How can this research element take better advantage of field sites?
- Development of a long-term plan for use of methods that have been developed would facilitate research at the NABIR Field Research Site and at UMTRA (Uranium Mill Tailings Remedial Action) sites.
- There is a need for more and more diverse smaller scale research sites.
- EMSL facilities are being used in some of the NABIR research. More will be used in the future. High performance computing has not been used to date but will likely be used in the future.
- UMTRA report – 21 of these sites in the western US.
- Can do valuable, low cost field research at these sites.
- More advantage should be taken of these sites.
- There are some challenges with access to these sites at times.
- The NABIR subcommittee has completed its review of all elements of the program and is officially being disbanded as a new committee will be formed to cover the entire scope of the new Environmental Remediation Sciences division.
- The report was approved by BERAC.
- BERAC thanks Jim and the NABIR subcommittee for the excellent work they have done over the past few years.

Medical Science charge

- DOE has been the major source of radiopharmaceuticals in past years. NIH supports the resulting clinical trials using these materials.
- A recent workshop identified a national need in this area.
- The charge:
    - Future need for radiopharmaceutical development and how BER can remain at the forefront
    - Evaluate impact of shortage of trained radiochemists and BER role
    - Role other agencies
    - Identify current national impediments to efficient entry of promising new compounds into clinical feasibility studies
- Steve Larson will chair BERAC subcommittee to address this charge. Roger McClellan and Jim Adelstein will also serve on the subcommittee.

General Discussion

- Importance of making Ray Orbach aware of nontraditional facilities and the need for operating funds that don't simply eat into research dollars.
- Aren't there still GPP (General Plant Project) funds available? Yes, but these are small and used for very basic repairs such as roof and air conditioning types of repairs.
- An OSTP study is just getting underway that may help the recognition of our nonconventional facilities.
- There are some downsides to giving too much exposure to any general type user facility regarding metrics and expectations but in aggregate BER feels that this increased exposure would be of general benefit to BER.

Ari Patrinos, Associate Director for Biological and Environmental Research, Office of Science, DOE

- The state of BER is ok.
- This is not an all encompassing or all inclusive report. Making the news isn't always the best thing.
- Continuing resolution still in effect so no FY 2003 budget yet for 11 of 13 appropriations bills. No new starts. Some optimism now that resolution is in sight. Senate may agree to lower number than what they had previously passed. Anticipate end early in 2003. Senate approved a $10M increase for Genomes to Life along with very complimentary language. We have also lost $20M in support of the new Department of Homeland Security. The Senate also approved additional increases above the President's request, e.g., $7M for low dose radiation research. These increases may or may not hold in the final resolution.

- FY 2004 passback from OMB last night. Embargoed until budget delivered to Congress. Don't know if loss for Homeland Security will continue in FY 2004 and beyond.
- Comings and goings in BER –
    - Mike Viola now a federal employee (Senior Medical Officer) after several years as an IPA
    - Peter Kirchner now primarily at NIH (National Institute of Biomedical Imaging and Bioengineering)
    - Jeff Amthor has joined the Climate Change Research Division as a federal employee (currently detailed to the Adminstration's new Office of Climate Change Science Program at Commerce)
    - Teresa Fryberger is the director of the new Environmental Remediation Sciences Division
    - Dave Bader is on sabbatical at the National Center for Atmospheric Research
    - Henry Shaw (from LLNL and recently from Basic Energy Sciences) is an IPA for the Environmental Remediation Sciences Division.
- Rushing to finish the human DNA sequence. Final product to be delivered in April 2003. Joint celebration with NIH on April 14-15 in Washington, DC. Genomic sequence analyses of Ciona intestinalis (sea squirt) and Fugu (the puffer fish) as cover articles in *Science* magazine representative of recent successes in genomics.
- Genomes to Life – Public thanks to Marvin Frazier for his leadership and for his team over the past several years. Five multi institutional awards were made in the summer of 2002 by Secretary Abraham. Microbial Cell projects are now part of the Genomes to Life program. A new request for proposals is pending. At some time in the not to distant future BERAC will be asked to look at our process for reviewing proposals and tracking progress. Related, in part, to the new emphasis on performance metrics.
- Climate Change Research news – Climate Change Science Program = USGCRP + Climate Change Research Initiative. NOAA's Jim Mahoney heads the CCSP. Ongoing planning workshop for scientists and stakeholders. Should know better by the end of the day tomorrow where the Administration's plan stands.
- About $8M invested in climate modeling SciDAC effort with ASCR. We have been discussing new ideas about ecological research – cascade of scales research. Have done well on large scale ecosystem research and on molecular scale research but the time has come to bridge these extremes of scales. Have asked BERAC subcommittee to review BioSphere II facility in Arizona (led by Bob White) with regard to its potential for use as an ecological research user facility. 25th anniversary of DOE CO_2 program on January 24, 2003.
- Medical Sciences news – Prominently represented in DOE strategic plan in spite of concerns about long-term viability of the program within DOE. Developing partnership with NIH/NHBIB. Possible (NIH/BER) JASON study next summer on imaging and the computational aspects in particular – Dr. Zerhouni (NIH Director) gave a presentation at the recent JASON fall meeting on biomedical imaging. Need for a workshop on molecular biology for medical imagers? Opportunity for BER lead? Note that BER already has a long-standing and productive relationship in imaging with NCRR at NIH.

- Environmental Remediation Sciences – Delay in transfer of EMSP and SREL to BER because of the continuing resolution. Ongoing strategic planning activities for this Division to be discussed extensively at the spring meeting. A new BERAC subcommittee chaired by Michelle Broido will be formed.
- Office of Science news – A restructuring of the Office of Science is underway in keeping with the Administration's management initiative. New role for field and site offices being developed/debated. Hopefully we will know much more by the spring meeting. There is an ongoing Office of Science strategic planning exercise though time is very limited. Performance measures are showing up in all areas of the budget and budget process. These last two items are closely linked.
- BER Strategic Themes
    - Biotechnology for Energy and Environmental Needs
    - Responding to Earths Changing Climate
    - Smart Strategies for Environmental Remediation
    - Powerful Tools for a Healthier Nation
- Interagency activities still a large component of the BER program – NIH; USDA (sequencing at the JGI); EPA (sequencing, environmental toxicology); NSF, NOAA, NASA, etc. (CCSP); DHS
- Other issues –
    - JASON nano biology study (ASCR, BES, BER);
    - possible new role for EMSL (new ways to "use" EMSL user facility, challenges to the scientific community to use EMSL capabilities to solve significant problems);
    - Institute for Biological Energy Alternatives (one of Craig Venter's new ventures) minimal genome grant based on the sequencing and analysis of *Mycoplasma genitalium* to get something that is small enough genetically so that we have a better chance of getting a handle on the modeling of a biological system – possibility of a BER in the news section of the web site?;
    - review of INEEL's subsurface facility – INEEL now a Nuclear Energy laboratory; Teresa Fryberger will coordinate this review
    - Washington Area Advisory Group review of Ameriflux network ongoing
- New BERAC charge has been discussed
- FY 2003 solicitations issued and planned across the BER program
- Eddy Rubin has agreed to take on the role of Director of the Joint Genome Institute.
- Congratulations to Keith Hodgson on receiving the 2003 Lawrence Award

Questions/Comments

- Is there a specific Office of Science plan to increase the budget? Obviously need to dovetail with the Administration's plan. A bill has been introduced by Representative Biggert (Illinois) to substantially increase the Office of Science budget. This bill is being used as a framework for internal planning activities. This bill has about 100 signatories in the House so far. Support from scientific societies as well – Federation of American Societies for Experimental Biology (FASEB), American Physical Society.

- Radiopharmaceuticals – Is there a possibility for liaison within DOE? Sometimes these radionuclides become commercialized too some. For example iodine-123 much more accessible in Europe than in the US because companies say they can take production on but aren't adequately prepared. This is an area of significant concern for BER – BER is not involved in isotope production. This is the responsibility of the Office of Nuclear Energy.

Kevin Crowley – National Academies of Science

- Personal views based on experience at the National Academy
- Four reports on Environmental Management Science Program (EMSP) have been published and one more is on the way.
- What are intractable problems? Depends on the audience. Scientist – knowledge or technology not available; Policymaker – time or budget shortages; Regulators – risks to people or violations of regulations involved
- Over 100 sites and 5,000 facilities. Five high cost sites – Hanford, INEEL, Oak Ridge, Nevada Test Site, Savannah River
- Clean up is not just about contaminant removal but about contaminant stability. Work on the most difficult problems has not even begun. Clean up program not about science – 7,000 milestones, bias toward baseline approaches, never enough time, budget constrained in spite of money being spent
- Very large waste volumes and diversity of waste forms
- Current DOE acceleration plans call for completion in 2028 instead of 2070 and $100B cost reduction – less time for science that can be used to cleanup; 11 sites have signed letters of intent to accelerate cleanup; Strategies for future cleanup often decided now.
- Intractable problem 1 – High level waste: 340,000 cubic meters, 2.4 billion curies; little is currently stored in robust containers; Should this all be retrieved? Will more contamination be caused as a result? Don't even know what is in all of the tanks.
- Intractable problem 2 – Buried waste: though not in DOE view today. 6.2 million cubic meters, 50 million curies. Poor characterization. Variable stability. Remediation and monitoring issues.
- Intractable problem 3 – Contaminated soil / groundwater: This waste is already in the environment. Don't have technologies to remove or stabilize in most cases.
- Other problems – deactivation and decommissioning (solvable) ; orphan waste streams and materials (solvable); radiation effects (research is not likely to lead to changes in standards in time to affect the clean up program); long-term stewardship (could go on indefinitely especially as cleanup times are shortened and trade offs are made)
- Science needed for clean up - Solving problems associated with remediation baselines but may not know what there are until failures occur. Developing alternative approaches. Understanding the consequences of action or inaction.
- Science needs to be anticipatory and proactive that is "inside" the EM fence and in synch with clean-up plans/schedules. Value of balance between program driven and investigator driven program.

Comments/Questions

- Tritium problems do have advantage of 12 year tritium half life. Problematic radionuclides are the mobile ones – tritium, technicium, iodine. Transuranics don't move much. There is a lot more in storage than in the environment so we need to make sure it stays stored.

Wrap up comments

- BERAC comments on draft materials?
- Continue to invite other program or advisory committee representatives? Yes.
- Dates for next two meetings? April 30 – May 2 time frame? Before Thanksgiving – first two weeks of November? Members will be contacted.
- Handling of Ray Orbach's verbal charge? BERAC has an unresolved structural biology charge. Part of what Ray asked BERAC to do relates to this charge. Perhaps broadening this activity could accommodate this activity. Keith Hodgson will contact Jonathan Greer to see if he has time or needs to be replaced as chair of this group.
- Genomes to Life facilities response to Ray Orbach will be prepared in the next few weeks.

Public Comment

- Bob Marianelli – Need for better / stronger interaction among advisory committees. From 3 years spent at OSTP it is embarrassing to realize that offices often don't know what the others are doing. This shouldn't be happening. Many areas of mutual interest exist.

Meeting adjourned at 11:50 AM.