Report from the Subcommittee on the Evaluation of the Long Term Goal of Demonstrating Progress Toward Developing Computational Models of a Microbe and a Simple Microbial Community

Subcommittee Member: Virginia Torczon

Charge: The subcommittee was asked to evaluate progress toward the long term goal:

> *By 2015, demonstrated progress toward developing through the Genomes to Life partnership with the Biological and Environmental Research program, the computational science capability to model a complete microbe and simple microbial community.*

Evaluation: The subcommittee finds that OASCR has made a good start toward achieving the goal of enabling the computational science capability to model a complete microbe and a simple microbial community. Our PART grade of "Good" reflects our judgment of progress toward validated computational models by 2015. This progress depends essentially on effective integration and collaboration of biological and computational research efforts. We judge ASCR's contribution and progress, in the context of resource constraints, to be outstanding.

ASCR has cooperated with BER on two efforts and started one on its own initiative. The cooperative efforts have involved joint review of research proposals addressing the computational science capability to model a complete microbe and simple microbial community. The Genomics:GTL projects that have been jointly selected with BER include:

- **Carbon Sequestration in Synechococcus: From Molecular Machines to Hierarchical Modeling**
  Principal Investigators:
  G. Heffelfinger, Sandia National Laboratories
  A. Geist, Oak Ridge National Laboratory

- **Development of Computational Tools for Analyzing and Redesigning Metabolic Networks**
  Principal Investigators:
  C. Maranas, Penn State University
  A. Burgard, Genomatica, Inc.

- **Intercellular Genomics of Subsurface Microbial Colonies**
  Principal Investigators:
  P. Ortoleva, Indiana University
  K. Tuncay, Indiana University
  D. Gannon, Indiana University
  C. Meile, University of Georgia

ASCAC and BER also cooperated on the Life Sciences initiative under the recent SciDAC solicitation. The two research awards in support of the *Putting Microbes to Work: Developing microbial communities to generate clean fuel sources and clean up environmental contaminants* initiative, announced in September 2006 (`http://www.scidac.gov/life/life_sciences.html`), are:

- **Predicting the Function of Proteins for Newly Sequenced Organisms**
  Algorithms and engineering for gene function annotation for Joint Genome Institute genomes

  Principal Investigator: Steven E. Brenner
  Lawrence Berkeley National Laboratory

- **Green Energy: Advancing Bio-hydrogen**
  Developing a model of metabolism linked to H2 production in green algae

  Principal Investigator: Michael Seibert
  National Renewable Energy Laboratory

In addition, ASCR has created three institutes for the advancement of computational biology research and education, in support of the ASCR computational biology program, the ASCR-BER DOE Genomics:GTL program, and the broader Office of Science research programs. The institutes support the advancement of computational biology research as an intellectual pursuit and provide innovative approaches to educating biologists as computational scientists. The institutes focus on advancing computational biology research and education as counterbalancing and complementary activities to experimental biology (`http://genomicsgtl. energy.gov/compbioinstitutes/index.shtml`). The three institutes are:

- **Institute for Multi-Scale Modeling of Biological Interactions**
  Johns Hopkins University

- **Center for Computational Biology**
  University of California, Merced

- **BACTER Institute**
  University of Wisconsin, Madison

This effort has been well-received by BER. John Houghton, BER, participated in an informal review of all three institutes during the summer of 2006, even though the funding for all three institutes comes from ASCR. Talks are underway to establish mechanisms to enable interactions between students and researchers in these institutes and researchers directly involved in the Genomics:GTL program.

In general, ASCR is doing all the right things to cooperate with BER, as mandated by the PART measures, to work toward the computational science capability to model a complete microbe and simple microbial community. They are jointly reviewing projects for funding and working together to better integrate the ASCR Institutes for the Advancement of Computational Biology Research & Education into the Genomics:GTL research program. In this regard, ASCR is making every effort to follow the recommendation contained in the 2005 National Research Council (NCR) of the National Academies report *Mathematics and 21st Century Biology* from the Committee on Mathematical Sciences Research for DOE's Computational Biology:

> *Recommendation: Funding agencies supporting mathematical research related to the life sciences should place increased emphasis on funding mechanisms and novel approaches to the organization of interdisciplinary research. The goal should be to foster effective collaboration between mathematical scientists and bioscientists by working to eliminate barriers posed by inadequate communication, disparate timescales for achieving research objectives, inequitable recognition of contributors to interdisciplinary projects, and cultural divisions within universities, research institutes, and national laboratories.*

Furthermore, the relevant program officers from BER also are working toward this goal.

Despite these admirable efforts, there remain some concerns regarding adequate communication and reasonable timescales for achieving research objectives. The effectiveness of the ASCR involvement in the Genomics:GTL program necessarily depends on the involvement of the biology community. The PART measures for ASCR make this clear by stipulating *In partnership with BER* for each of the grades. This creates an explicit dependence on developments in the BER program that makes this measure unusual—perhaps unique—for ASCR. Furthermore it will take more than simply cooperation between program managers in ASCR and BER to achieve success. The biology community must "buy into" the development of computational models, and the need to involve computational scientists from the beginning of the process, for the goals set for 2015 to be met.

The Draft Report of the Biological and Environmental Research Advisory Committee (BERAC) on the Review of the Life Science PART Measure recommends modifying both the charge and the PART measures. The changes are prompted, in part, by the recommendations contained in the 2006 National Research Council of the National Academies report *Review of the Department of Energy's Genomics:GTL Program*, which contained the suggestion that

> *...plant biology research be included in the program, where appropriate, because plants represent a major pathway to the production of bioenergy, play an important role in carbon sequestration and global nutrient cycles, and are potential sources of bioremediation.*

In addition, as noted in the BERAC report

> *...when this PART Measure was developed, the Administration had made hydrogen a priority but had not yet added a focus on liquid transportation fuels such as cellulosic ethanol. BERAC recommends that the Life Science PART measure be modified to include biofuels such as cellulosic ethanol.*

Part of the wording changes for revising the PART measure reflect these two suggestions. Of concern to ASCAC though, is the addition of *Systems biology understanding* to the initial charge of *Develop a computational model*. Developing a computational model that accurately describes the potential of a microbial community (or plant) to clean up waste, sequester carbon, or produce biofuels, and then validating this computational model experimentally by the use or reengineering of that community (or plant) based on model predictions, is an ambitious enough goal to meet by 2015. Adding additional charges raises questions regarding success if focus is split between these two, albeit complementary, goals.