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and

Metabolic Engineering Working Group Inter-Agency Conference on Metabolic Engineering 2006

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Welcome to GTL-MEWG Workshop

Welcome to the 2006 joint meeting of the fourth Genomics:GTL Contractor-Grantee Workshop and the sixth Metabolic Engineering Working Group Inter-Agency Conference. The vision and scope of the Genomics:GTL program continue to expand and encompass research and technology issues from diverse scientific disciplines, attracting broad interest and support from researchers at universities, DOE national laboratories, and industry. Metabolic engineering's vision is the targeted and purposeful alteration of metabolic pathways to improve the understanding and use of cellular pathways for chemical transformation, energy transduction, and supramolecular assembly. These two programs have much complementarity in both vision and technological approaches, as reflected in this joint workshop.

GTL's challenge to the scientific community remains the further development and use of a broad array of innovative technologies and computational tools to systematically leverage the knowledge and capabilities brought to us by DNA sequencing projects. The goal is to seek a broad and predictive understanding of the functioning and control of complex systems—individual microbes, microbial communities, and plants. GTL's prominent position at the interface of the physical, computational, and biological sciences is both a strength and a challenge. Microbes remain GTL's principal biological focus. In the complex "simplicity" of microbes, we find capabilities needed by DOE and the nation for clean and secure energy, cleanup of environmental contamination, and sequestration of atmospheric carbon dioxide that contributes to global warming. An ongoing challenge for the entire GTL community is to demonstrate that the fundamental science conducted in each of your research projects brings us a step closer to biology-based solutions for these important national energy and environmental needs.

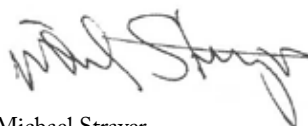
This year marks an important milestone for GTL with release of the roadmap that will help guide and justify the GTL program to a broad audience of scientists, policymakers, and the public. This important document was developed through a process of broad community participation that included many of you. It traces the path from DOE mission science through systems microbiology to the promise of emerging technologies, integrated computing, and a new research infrastructure. It describes opportunities, research strategies, and solutions related to this new science as applied to microbes and the complexities of mission problems.

To make GTL science and biological research broadly tractable, timely, and affordable, GTL will institute four user facilities to deliver economies of scale and enhance performance. These facilities will provide advanced technologies and state-of-the-art computing needed to better understand genomic capability, cellular responses, regulation, and community behaviors in any environment. Another important step forward for GTL is the solicitation of applications for development of the Facility for Production and Characterization of Proteins and Molecular Tags, first of the four planned.

This year's GTL-MEWG workshop provides an opportunity for all of us to discuss, listen, and learn about exciting new advances in science; identify research needs and opportunities; form research partnerships; and share the excitement of this program with the broader scientific community. We look forward to a stimulating and productive meeting and offer our sincere thanks to the organizers and to you, the scientists, whose vision and efforts will help us all to realize the promise of this exciting research program.



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Contents

Welcome to GTL-MEWG Workshop	iii
---	-----

Workshop Abstracts	1
---------------------------------	---

Milestone 1

Organism Sequencing, Annotation, and Comparative Genomics	3
--	---

Poster

1 U.S. DOE Joint Genome Institute Microbial Sequencing: Genomes to Life Projects	3
David Bruce* (dbruce@lanl.gov), Tom Brettin, Patrick Chain, Cliff Han, Loren Hauser, Nikos Kyrpides, Miriam Land, Alla Lapidus, Frank Larimer, Jeremy Schmutz, Paul Gilna, Eddy Rubin, and Paul Richardson	
2 High Throughput Genome Annotation for U.S. DOE Joint Genome Institute Microbial Genomes	4
Miriam Land* (landml@ornl.gov), Loren Hauser, Phil LoCasco, Gwo-Liang Chen, Denise Schmoyer, and Frank Larimer	
3 Understanding Microbial Genomic Structures and Applications to Biological Pathway Inference	5
Z. Su, F. Mao, H. Wu, P. Dam, X. Chen, T. Jiang, V. Olman, B. Palenik, and Ying Xu* (xyn@bmb.uga.edu)	
4 The BioCyc Collection of 200 Pathway/Genome Databases and the MetaCyc Database of Metabolic Pathways and Enzymes	7
Peter D. Karp* (pkarp@ai.sri.com), Christos Ouzounis, and Sue Rhee	
5 Bioinformatic Methods Applied to Prediction of Bacterial Gene Function	8
Michelle Green* (green@ai.sri.com), Balaji Srinivasan, Peter Karp, and Harley McAdams	
6 Pipelining RDP Data to the Taxomatic and Linking to External Data Resources	10
S. H. Harrison, P. Saxman, T.G. Lilburn, J.R. Cole, and G.M. Garrity* (garrity@msu.edu)	

<u>Poster</u>	<u>Page</u>
7 Geobacter Project Subproject I: Genome Sequences of <i>Geobacteraceae</i> in Subsurface Environments Undergoing <i>In Situ</i> Uranium Bioremediation and on the Surface of Energy-Harvesting Electrodes	12
Jessica Butler* (jbutler@microbio.umass.edu), Regina O'Neil, Dawn Holmes, Muktak Aklujkar, Ray DiDonato, Shelley Haveman, and Derek Lovley	
8 Geobacter Project Subproject III: Functional Analysis of Genes of Unknown Function	14
Maddalena Coppi* (mcpoppi@microbio.umass.edu), Carla Risso, Gemma Reguera, Ching Leang, Helen Vrionis, Richard Glaven, Muktak Aklujkar, Xinlei Qian, Tunde Mester, and Derek Lovley	
9 Comparative Genomic Analysis of Five <i>Rhodopseudomonas palustris</i> Strains: Insights into Genetic and Functional Diversity within a Metabolically Versatile Species	16
Yasuhiro Oda* (yasuhiro@u.washington.edu), Frank W. Larimer, Patrick Chain, Stephanie Malfatti, Maria V. Shin, Lisa M. Vergez, Loren Hauser, Miriam L. Land, Dale A. Pelletier, and Caroline S. Harwood	
10 Functional Analysis of <i>Shewanella</i>, a Cross Genome Comparison	17
Margrethe H. Serres* (mserres@mbl.edu) and Monica Riley (mriley@mbl.edu)	
11 Comparative Genomic and Proteomic Insight into the Evolution and Ecophysiological Speciation in the <i>Shewanella</i> Genus	18
James M. Tiedje* (tiedjej@msu.edu), Konstantinos T. Kostantinidis, Joel A. Klappenbach, Jorge L.M. Rodrigues, Mary S. Lipton, Margaret F. Romine, Sean Conlan, LeeAnn McCue, Patrick Chain, Anna Obraztsova, Loren Hauser, Margrethe Serres, Monica Riley, Carol S. Giometti, Eugene Kolker, Jizhong Zhou, Kenneth H. Nealson, and James K. Fredrickson	
12 Microbial Genome Sequencing with Ploning from the Wild: A Progress Report	19
Kun Zhang* (kzhang@genetics.med.harvard.edu), Adam C. Martiny, Nikkos B. Reppas, Kerrie W. Barry, Joel Malek, Sallie W. Chisholm, and George M. Church	
13 Application of a Novel Genomics Technology Platform	20
Karsten Zengler, Marion Walcher, Carl Abulencia, Denise Wyborski, Trevin Holland, Fred Brockman, Cheryl Kuske, and Martin Keller* (mkeller@diversa.com)	
Microbial-Community Sequencing	21
14 Ribosomal Database Project II: Sequences and Tools for High-Throughput rRNA Analysis ...	21
J.R. Cole* (colej@msu.edu), B. Chai, R.J. Farris, Q. Wang, S.A. Kulam, D.M. McGarrell, G.M. Garrity, and J.M. Tiedje	
15 Community Genomics as the Foundation for Functional Analyses of Natural Microbial Consortia	23
R.J. Ram, V.J. Denef, I. Lo, N.C. VerBerkmoes, G. Tyson, G. DiBartolo, E.A. Allen, J. Eppley, B.J. Baker, M. Shah, R.L. Hettich, M.P. Thelen, and J.F. Banfield* (jill@seismo.berkeley.edu)	

<u>Poster</u>	<u>Page</u>
16 Environmental Whole-Genome Amplification to Access Microbial Diversity in Contaminated Sediments	24
Denise L. Wyborski, Carl B. Abulencia, Joseph A. Garcia, Mircea Podar, Wenqiong Chen, Sherman H. Chang, Hwai W. Chang, Terry C. Hazen, and Martin Keller* (mkeller@diversa.com)	
17 Domestication of Uncultivated Microorganisms from Soil Samples	25
Annette Bollmann* (a.bollmann@neu.edu), Lisa Ann Fagan, Anthony Palumbo, Kim Lewis and Slava Epstein	
18 Metagenomic Analysis of Microbial Communities in Uranium-Contaminated Groundwaters	26
Jizhong Zhou* (jzhou@ou.edu), Terry Gentry, Chris Hemme, Liyou Wu, Matthew W. Fields, Chris Detter, Kerrie Barry, David Watson, Christopher W. Schadt, Paul Richardson, James Bristow, Terry C. Hazen, James Tiedje, and Eddy Rubin	
19 Understanding Phage-Host Interactions Using Synergistic Metagenomic Approaches	27
Shannon J. Williamson* (shannon.williamson@venterininstitute.org), Douglas B. Rusch, Shibu Yooseph, Aaron Halpern, Karla Heidelberg, Cynthia Pfannkoch, Karin Remington, Robert Friedman, Marvin Frazier, Robert Strausberg, and J. Craig Venter	
20 The Impact of Horizontal Gene Transfer: Uniting or Dividing Microbial Diversity?	28
Rachel J. Whitaker (rwhitaker@nature.berkeley.edu), Dennis Grogan, Mark Young, and Frank Robb	
Protein Production and Characterization	29
21 Genes to Proteins: Elucidating the Bottlenecks in Protein Production	29
M. Hadi* (MZhadi@sandia.gov), K. Sale, J. Kaiser, J. Dibble, D. Pelletier, J. Zhou, B. Segelke, M. Coleman, and L. Napolitano	
22 High-Throughput Production and Analyses of Purified Proteins	30
F. William Studier* (studier@bnl.gov), John C. Sutherland, Lisa M. Miller, Michael Appel, and Lin Yang	
23 A Combined Informatics and Experimental Strategy for Improving Protein Expression	31
Osnat Herzberg, John Moulton* (moulton@umbi.umd.edu), Fred Schwarz, and Harold Smith	
24 High-Throughput Optimization of Heterologous Proteome Expression	32
Robert Balint (rfbalint@sbcglobal.net) and Xiaoli Chen	
25 Development of Genome-Scale Expression Methods	34
Sarah Giuliani, Elizabeth Landorf, Terese Pepler, Yuri Londer, Lynda Dieckman, and Frank Collart* (fcollart@anl.gov)	

<u>Poster</u>	<u>Page</u>
26 A Novel Membrane Protein Expression System for Very Large Scale and Economical Production of Membrane Proteins	35
Hiep-Hoa T. Nguyen* (hiephoa@its.caltech.edu), Sanjay Jayachandran, Randall M. Story, Sergei Stolyar, and Sunney I. Chan	
27 High-Throughput Methods for Production of Cytochromes <i>c</i> from <i>Shewanella oneidensis</i>	36
Yuri Y. Londer, Sarah Giuliani, Elizabeth Landorf, Terese Pepler, and Frank R. Collart* (fcollart@anl.gov)	
28 Towards the Total Chemical Synthesis of Helical Integral Membrane Proteins	37
Erik C.B. Johnson* (erikj@uchicago.edu) and Stephen B.H. Kent	
29 Selecting Binders Against Specific Post-Translational Modifications: The Sulfotyrosine Example	37
John Kehoe, Jytte Rasmussen, Monica Walbolt, Carolyn Bertozzi, and Andrew Bradbury* (amb@lanl.gov)	
30 Progress on Fluorobodies: Intrinsically Fluorescent Binders Based on GFP	38
Csaba Kiss, Minghua Dai, Hugh Fisher, Emanuele Pesavento, Nileena Velappan, Leslie Chasteen, and Andrew Bradbury* (amb@lanl.gov)	
31 High Throughput Screening of Binding Ligands using Flow Cytometry	39
Peter Pavlik, Joanne Ayriss, Nileena Velappan, and Andrew Bradbury* (amb@lanl.gov)	
Molecular Interactions	40
32 Exploring the Genome and Proteome of <i>Desulfitobacterium hafniense</i> DCB2 for its Protein Complexes Involved in Metal Reduction and Dechlorination	40
James M. Tiedje* (tiedje@msu.edu), John Davis, Sang-Hoon Kim, David Dewitt, Christina Harzman, Robin Goodwin, Curtis Wilkerson, Joan Broderick, and Terence L. Marsh	
33 Comparison of Conserved Protein Complexes Across Multiple Microbial Species to Evaluate High-Throughput Approaches for Mapping the Microbial Interactome	42
D. Pelletier* (pelletierda@ornl.gov), G. Hurst, S. Kennel, L. Foote, P. Lankford, T. Lu, W. McDonald, C. McKeown, J. Morrell-Falvey, D. Schmoyer, E. Livesay, F. Collart, D. Auberry, K. Auberry, Y. Gorby, B. Hooker, E. Hill, C. Lin, P. Moore, R. Moore, R. Saripalli, K. Victry, V. Kery, S. Wiley, and M. Buchanan	
34 Advanced Technologies for Identifying Protein-Protein Interactions	43
R. Hettich* (hettichrl@ornl.gov), G. Hurst, W. McDonald, H. Connelly, D. Pelletier, C. Pan, N. Samatova, G. Kora, V. Kertesz, S. Gaucher, T. Iqbal, M. Hadi, M. Young, G. Orr, M. Romine, D. Panther, S. Reed, D. Hu, E. Livesay, B. Hooker, S. Wiley, S. Kennel, and M. Buchanan	

<u>Poster</u>	<u>Page</u>
35 Complementary Assays for Validating Protein Interactions Identified by High-Throughput Screening Techniques	45
Mitchel J. Doktycz* (doktyczmj@ornl.gov), Jennifer L. Morrell-Falvey, W. Hayes McDonald, Gurusahai Khalsa-Moyers, Dale A. Pelletier, Stephen J. Kennel, Vladimir Kery, Galya Orr, Dehong Hu, Margaret F. Romine, David J. Panther, Brian S. Hooker, H. Steven Wiley, and Michelle V. Buchanan	
36 Computational Approaches for Aggregating and Scoring Protein-Protein Interaction Data	46
William R. Cannon* (william.cannon@pnl.gov), W. Hayes McDonald, Don S. Daly, Denise Schmoyer, Gregory B. Hurst, Manesh B. Shah, Brian S. Hooker, Vladimir Kery, Stephen J. Kennel, H. Steven Wiley, and Michelle V. Buchanan	
37 The Microbial Interactome Database: An Online System for Identifying Interactions Between Proteins of Microbial Species	46
G.B. Hurst* (hurstgb@ornl.gov), D.A. Pelletier, D.D. Schmoyer, M.B. Shah, W.H. McDonald, N.E. Baldwin, N.F. Samatova, A. Gorin, B.S. Hooker, V. Kery, W.R. Cannon, D.L. Auberry, K.J. Auberry, K.D. Victry, R. Saripalli, H.S. Wiley, S.J. Kennel, and M.V. Buchanan	
38 Investigation of Protein-Protein Interactions in the Metal-Reducing Bacterium <i>Desulfovibrio vulgaris</i>	48
Sara Gaucher* (spgauch@sandia.gov), Masood Hadi, Swapnil Chhabra, Eric Alm, Grant Zane, Dominique Joyner, Adam Arkin, Terry Hazen, Judy Wall, and Anup Singh	
39 Protein Complex Analysis Project (PCAP): High Throughput Identification and Structural Characterization of Multi-Protein Complexes During Stress Response in <i>Desulfovibrio vulgaris</i>.	49
Project Overview	
Dwayne Elias, Swapnil Chhabra, Hoi-Ying Holman, Jay Keasling, Aindrila Mukhopadhyay, Tamas Torok, Judy Wall, Terry C. Hazen, Ming Dong, Steven Hall, Bing K. Jap, Jian Jin, Susan Fisher, Peter J. Walian, H. Ewa Witkowska, Mark D. Biggin* (mdbiggin@lbl.gov), Manfred Auer, Robert M. Glaeser, Jitendra Malik, Jonathan P. Remis, Dieter Typke, Kenneth H. Downing, Adam P. Arkin, Steven E. Brenner, Janet Jacobsen, and John-Marc Chandonia	
40 Protein Complex Analysis Project (PCAP): High Throughput Identification and Structural Characterization of Multi-Protein Complexes During Stress Response in <i>Desulfovibrio vulgaris</i>	50
Microbiology Subproject	
Terry C. Hazen* (tchazen@lbl.gov), Dwayne Elias, Hoi-Ying Holman, Jay Keasling, Aindrila Mukhopadhyay, Swapnil Chhabra, Tamas Torok, Judy Wall, and Mark D. Biggin	
41 Protein Complex Analysis Project (PCAP): High Throughput Identification and Structural Characterization of Multi-Protein Complexes During Stress Response in <i>Desulfovibrio vulgaris</i>	52
Multi-Protein Complex Purification and Identification by Mass Spectrometry	
Ming Dong, Steven Hall, Bing K. Jap, Jian Jin, Susan Fisher, Peter J. Walian, H. Ewa Witkowska, and Mark D. Biggin* (mdbiggin@lbl.gov)	

<u>Poster</u>	<u>Page</u>
42 Protein Complex Analysis Project (PCAP): High Throughput Identification and Structural Characterization of Multi-Protein Complexes During Stress Response in <i>Desulfovibrio vulgaris</i>	53
Data Management and Bioinformatics Subproject	
John-Marc Chandonia* (JMChandonia@lbl.gov), Adam P. Arkin, Steven E. Brenner, Janet Jacobsen, Keith Keller, and Mark D. Biggin	
43 Protein Complex Analysis Project (PCAP): High Throughput Identification and Structural Characterization of Multi-Protein Complexes During Stress Response in <i>Desulfovibrio vulgaris</i>	54
Imaging Multi-Protein Complexes by Electron Microscopy	
Kenneth H. Downing* (KHDowning@lbl.gov), Manfred Auer, Robert M. Glaeser, Jitendra Malik, Jonathan P. Remis, Dieter Typke, and Mark D. Biggin	
44 A Hybrid Cryo-TEM and Cryo-STEM Scheme for High Resolution <i>in vivo</i> and <i>in vitro</i> Protein Mapping	56
Huilin Li* (hli@bnl.gov), James Hainfeld, Guiqing Hu, Zhiqiang Chen, Kevin Ryan, and Minghui Hu	
45 Optical Methods for Characterization of Expression Levels and Protein-Protein Interactions in <i>Shewanella oneidensis</i> MR-1	58
Natalie R. Gassman* (ngassman@chem.ucla.edu), Younggyu Kim, Sam Ho, Nam Ki Lee, Achilles Kapanidis, Xiangxu Kong, Gopal Iyer, and Shimon Weiss	
46 Protein Interaction Reporter Studies on <i>Shewanella oneidensis</i> MR-1	59
James E. Bruce* (james_bruce@wsu.edu), Xiaoting Tang, Wei Yi, Gerhard Munske, Devi Adhikari, Saiful Chowdhury, Gordon A. Anderson, and Nikola Tolic	
47 Implementation of a Data Management and Analysis System In Support of Protein-Protein Interaction Studies of <i>Shewanella oneidensis</i> MR-1	60
Nikola Tolic* (Nikola.Tolic@pnl.gov), Shaun O'Leary, Bryce Kaspar, Elena Peterson, Gunnar Skulason, Roger Crawford, Gordon Anderson, and James Bruce	
48 Cell-Permeable Multiuse Affinity Probes (MAPs) and Their Application to Identify Environmentally Mediated Changes in RNA Polymerase and Metal Reducing Protein Complexes	62
M. Uljana Mayer, Baowei Chen, Haishi Cao, Seema Verma, Ting Wang, Ping Yan, Yijia Xiong, Liang Shi, and Thomas C. Squier* (thomas.squier@pnl.gov)	
49 <u>Molecular Assemblies</u>, <u>Genes</u>, and <u>Genomics</u> Integrated <u>Efficiently</u>	63
John Tainer* (jat@scripps.edu), Mike Adams, Steve Yannone, Nitin S. Baliga, Gary Siuzdak, and Steve Holbrook	

<u>Poster</u>	<u>Page</u>
50 The MAGGIE Project: Identification and Purification of Native and Recombinant Multiprotein Complexes and Modified Proteins from <i>Pyrococcus furiosus</i>	64
Francis E. Jenney Jr.* (fjenney@arches.uga.edu), Farris L. Poole II, Angeli Lal Menon, Rathinam Viswanathan, Greg Hura, John A. Tainer, Sunia Trauger, Gary Siuzdak, and Michael W. W. Adams	
51 Systems Approach in a Multi-Organism Strategy to Understand Biomolecular Interactions in DOE-Relevant Organisms	65
Nitin S. Baliga (nbaliga@systemsbiology.org) and John Tainer	

Milestone 2

OMICS: Systems Measurements of Plants, Microbes, and Communities	67
52 Meta-Proteomic Study of a Microbial Community Response to Cadmium Exposure	67
C.M.R. Lacerda, L. Choe, and K.F. Reardon* (reardon@engr.colostate.edu)	
53 Investigating Novel Proteins in Acidophilic Biofilm Communities	68
Christopher Jeans, Clara Chan, Mona Hwang, Jason Raymond, Steven Singer, Nathan VerBerkmoes, Manesh Shah, Robert L. Hettich, Jill F. Banfield, and Michael P. Thelen* (mthelen@lnl.gov)	
54 Proteomics Measurements of a Natural Microbial Community Reveal Information about Community Structure and Metabolic Potential	70
Nathan C. VerBerkmoes* (verberkmoesn@ornl.gov), Rachna J. Ram, Vincent J. Deneff, Gene W. Tyson, Brett J. Baker, Manesh Shah, Michael P. Thelen, Jillian Banfield, and Robert L. Hettich	
55 Computational Algorithms and Software Tools for Quantitative Shotgun Proteomics	72
C. Pan, B. Zhang, G. Kora, N.C. VerBerkmoes, D. Tabb, W.H. McDonald, D. Pelletier, E. Uberbacher, G. Hurst, R. Hettich, and N.F. Samatova* (samatovan@ornl.gov)	
56 High Throughput Comprehensive and Quantitative Microbial Proteomics: Production in Practice	74
Richard D. Smith* (rds@pnl.gov), Joshua N. Adkins, David J. Anderson, Gordon A. Anderson, Kenneth J. Auberry, Michael A. Buschbach, Stephen J. Callister, Therese R.W. Clauss, Jim K. Fredrickson, Kim K. Hixson, Navdeep Jaitly, Gary R. Kiebel, Mary S. Lipton, Eric A. Livesay, Matthew E. Monroe, Ronald J. Moore, Heather M. Mottaz, Angela D. Norbeck, Daniel J. Orton, Ljiljana Paša-Tolić, Kostantinos Petritis, David C. Prior, Samuel O. Purvine, Yufeng Shen, Anil K. Shukla, Aleksey V. Tolmachev, Nikola Tolić, Harold R. Udseth, Rui Zhang, and Rui Zhao	
57 H₂O₂-Induced Stress Responses of <i>Shewanella oneidensis</i> MR-1	76
T. Li, J. Guo, D. Klingeman, L. Wu, X. Liu, T. Yan, Y. Xu, A. Beliaev, Z. He, T.C. Hazen, A. P. Arkin, J. Zhou* (jzhou@ou.edu)	

<u>Poster</u>	<u>Page</u>
58 Application of High Resolution Proteomics to Characterize Microbial Systems for Metal Reduction and Photosynthesis	77
Mary S. Lipton* (mary.lipton@pnl.gov), Margie F. Romine, Stephen J. Callister, Kim K. Hixson, Samuel O. Purvine, Angela D. Norbeck, Joshua N. Adkins, Matthew E. Monroe, Yuri A. Gorby, Carrie D. Goddard, Richard D. Smith, Jim K. Fredrickson, Derek Lovley, Richard Ding, Timothy Donohue, Miguel Dominguez, Christine Tavano, Samuel Kaplan, Xiaihua Zeng, Jung Hyeob Roh, and Frank Larimer	
59 VIMSS Applied Environmental Microbiology Core Research on Stress Response Pathways in Metal-Reducers.....	79
Terry C. Hazen* (tchazen@lbl.gov), Carl Abulencia, Gary Andersen, Sharon Borglin, Eoin Brodie, Steve van Dien, Matthew Fields, Jil Geller, Hoi-Ying Holman, Rick Huang, Richard Phan, Eleanor Wozei, Janet Jacobsen, Dominique Joyner, Romy Chakraborty, Martin Keller, Aindrila Mukhopadhyay, David Stahl, Sergey Stolyar, Judy Wall, Denise Wyborski, Huei-che Yen, Grant Zane, Jizhong Zhou, E. Hendrickson, T. Lie, J. Leigh, and Chris Walker	
60 The Virtual Institute of Microbial Stress and Survival (VIMSS): Deduction of Stress Response Pathways in Metal/Radionuclide Reducing Microbes.....	82
Carl Abulencia, Eric Alm, Gary Andersen, Adam P. Arkin* (APArkin@lbl.gov), Kelly Bender, Sharon Borglin, Eoin Brodie, Romy Chakraborty, Swapnil Chhabra, Steve van Dien, Inna Dubchak, Matthew Fields, Sara Gaucher, Jil Geller, Masood Hadi, Terry W. Hazen, Qiang He, Zhili He, Hoi-Ying Holman, Katherine Huang, Rick Huang, Janet Jacobsen, Dominique Joyner, Jay Keasling, Keith Keller, Martin Keller, Aindrila Mukhopadhyay, Richard Phan, Morgan Price, Joseph A. Ringbauer Jr., Anup Singh, David Stahl, Sergey Stolyar, Jun Sun, Dorothea Thompson, Christopher Walker, Judy Wall, Jing Wei, Denise Wolf, Denise Wyborski, Huei-che Yen, Grant Zane, Jizhong Zhou, and Beto Zuniga	
61 Nitrate Stress Response in <i>Desulfovibrio vulgaris</i> Hildenborough: Whole-Genome Transcriptomics and Proteomics Analyses	85
Qiang He, Zhili He, Wenqiong Chen, Zamin Yang, Eric J. Alm, Katherine H. Huang, Huei-Che Yen, Dominique C. Joyner, Martin Keller, Jay Keasling, Adam P. Arkin, Terry C. Hazen, Judy D. Wall, and Jizhong Zhou* (jzhou@ou.edu)	
62 Bacterial Nanowires: Novel Electron Transport Machines that Facilitate Extracellular Electron Transfer.....	86
Yuri A. Gorby* (yuri.gorby@pnl.gov), Svetlana Yanina, Dianne Moyles, Matthew J. Marshall, Jeffrey S. McLean, Alice Dohnalkova, Kevin M. Rosso, Anton Korenevski, Terry J. Beveridge, Alex S. Beliaev, In Seop Chang, Byung Hong Kim, Kyung Shik Kim, David E. Culley, Samantha B. Reed, Margaret F. Romine, Daad A. Saffarini, Liang Shi, Dwayne A. Elias, David W. Kennedy, Grigoriy E. Pinchuk, Eric A. Hill, John M. Zachara, Kenneth H. Nealson, and Jim K. Fredrickson	
63 VIMSS Functional Genomics Core Research on Stress Response Pathways in Metal-Reducers.....	87
Aindrila Mukhopadhyay, Eric J. Alm, Adam P. Arkin, Edward E. Baidoo, Peter I. Benke, Sharon C. Borglin, Wenqiong Chen, Swapnil Chhabra, Matthew W. Fields, Sara P. Gaucher, Alex Gilman, Masood Hadi, Terry C. Hazen* (tchazen@lbl.gov), Qiang He, Hoi-Ying Holman, Katherine Huang, Rick Huang, Zhili He, Dominique C. Joyner, Martin Keller, Keith Keller, Paul Oeller, Francesco Pingitore, Alyssa Redding, Anup Singh, David Stahl, Sergey Stolyar, Jun Sun, Zamin Yang, Judy Wall, Grant Zane, Jizhong Zhou, and Jay D. Keasling* (keasling@Berkeley.edu)	

<u>Poster</u>	<u>Page</u>
64 Comparative Analysis of Bacterial Gene Expression in Response to Environmental Stress.....	89
Eric J. Alm* (ejalm@lbl.gov), Edward E. Baidoo, Peter I. Benke, Sharon C. Borglin, Wenqiong Chen, Swapnil Chhabra, Matthew W. Fields, Sara P. Gaucher, Alex Gilman, Masood Hadi, Terry C. Hazen, Qiang He, Hoi-Ying Holman, Katherine Huang, Rick Huang, Zhili He, Dominique C. Joyner, Jay D. Keasling, Martin Keller, Keith Keller, Aindrila Mukhopadhyay, Paul Oeller, Francesco Pingitore, Alyssa Redding, Anup Singh, David Stahl, Sergey Stolyar, Jun Sun, Zamin Yang, Judy Wall, Grant Zane, Jizhong Zhou, and Adam P. Arkin	
65 Evaluation of Stress Responses in Sulfate-Reducing Bacteria Through Genome Analysis: Identification of Universal Responses.....	90
J.D. Wall* (wallj@missouri.edu), H.-C. Yen, E.C. Drury, A. Mukhopadhyay, S. Chhabra, Q. He, M.W. Fields, A. Singh, J. Zhou, T.C. Hazen, and A.P. Arkin	
66 Cellular Responses to Changing Conditions in <i>Desulfovibrio vulgaris</i> and <i>Shewanella oneidensis</i>.....	90
M.E. Clark, Q. He, Z. He, K.H. Huang, E.J. Alm, X. Wan, T.C. Hazen, A.P. Arkin, J.D. Wall, J. Zhou, J. Kurowski, A. Sundararajan, A. Klonowska, D. Klingeman, T. Yan, M. Duley, and M. W. Fields* (fieldsmw@muohio.edu)	
67 Probing Gene Expression in Single <i>Shewanella oneidensis</i> MR-1 Cells.....	92
X. Sunney Xie* (xie@chemistry.harvard.edu), Paul Choi, Jie Xiao, Ji Yu, Long Cai, Nir Friedman, Jeremy Hearn, Kaiqin Lao, Luying Xun, Joe Zhou, Margaret Romine, and Jim Fredrickson	
68 Phosphoproteome of <i>Shewanella oneidensis</i> MR1.....	94
Gyorgy Babnigg* (gbabnigg@anl.gov), Cynthia Sanville-Millard, Carl Lindberg, Sandra L. Tollaksen, Wenhong Zhu, John R. Yates III, Jim K. Fredrickson, and Carol S. Giometti	
69 The <i>Shewanella</i> Federation: Functional Genomic Investigations of Dissimilatory Metal-Reducing <i>Shewanella</i>	95
James K. Fredrickson* (Jim.Fredrickson@pnl.gov), Margaret F. Romine, Carol S. Giometti, Eugene Kolker, Kenneth H. Nealson, James M. Tiedje, and Jizhong Zhou, Monica Riley, Shimon Weiss, Christophe Schilling, and Timothy S. Gardner	
70 An Integrated Knowledge Resource for the <i>Shewanella</i> Federation	97
Nagiza F. Samatova* (samatovan@ornl.gov), Nicole Baldwin, Bing Zhang, Buyng-Hoon Park, Denise Schmoyer, Yuri Gorby, Grigoriy E. Pinchuk, Timothy S. Gardner, Mary S. Lipton, Samuel Purvine, Angela D. Norbeck, Margaret F. Romine, Gyorgy Babnigg, Carol S. Giometti, James K. Fredrickson, and Ed Uberbacher	
71 Physiological Characterization of Genome-Sequenced <i>Shewanella</i> Species	99
Radu Popa, Rodica Popa, Anna Obratzsova, A. Hsieh, and Kenneth H. Nealson* (knealson@usc.edu)	

<u>Poster</u>	<u>Page</u>
72 The Use of Microbial Fuel Cells (MFCs) for the Study of Electron Flow to Solid Surfaces: Characterization of Current Producing Abilities of Mutants of <i>Shewanella oneidensis</i> MR-1, of Other Strains and Species of <i>Shewanella</i>	100
Orianna Bretschger*, Byung Hong Kim, In Seop Chang, Margaret F. Romine, Jim K. Fredrickson, Yuri A. Gorby, Samantha B. Reed, David E. Culley, Soumitra Barua, and Kenneth H. Nealson	
73 Characterization of <i>c</i>-Type Cytochromes in <i>Shewanella oneidensis</i> MR-1	101
Margaret F. Romine* (margie.romine@pnl.gov), Samantha B. Reed, Soumitra Barua, Samuel O. Purvine, Alex S. Beliaev, Haichun Gao, Zamin Yang, Yunfeng Yang, David E. Culley, David W. Kennedy, Yuri Londer, Tripti Khare, Sandra Tollaksen, Claribel Cruz-Garza, Jun Li, Mandy Ward, Jizhong Zhou, Frank Collart, Mary S. Lipton, James M. Tiedje, Carol S. Giometti, and Jim K. Fredrickson	
74 Genome-Wide Transcriptional Responses to Metal Stresses in <i>Caulobacter crescentus</i>	103
Gary L. Andersen* (GLAndersen@lbl.gov), Ping Hu, Eoin L. Brodie, Yohey Suzuki, and Harley H. McAdams	
75 Host Gene Expression Responses: Unique Identifiers of Exposure to Biothreat Agents	104
Rasha Hammamieh* (rasha.hammamieh@na.amedd.army.mil), Steven Eker, Patrick Lincoln, and Marti Jett	
76 High Throughput Fermentation and Cell Culture Device	104
David Klein and Stephen Boyer* (sboyer@gener8.net)	
77 Genome-Wide Biochemical Characterization of Plant Acyl-CoA Dependent Acyltransferases	105
Chang-Jun Liu* (cliu@bnl.gov), and Xiao-Hong Yu	
78 The MAGGIE Project: A Mass-Based Platform for Protein and Metabolite Characterization	106
Gary Siuzdak (siuzdak@scripps.edu), Sunia Trauger, Francis E. Jenney Jr., Steven M. Yannone, Daojing Wang, Nitin S. Baliga, Steven R. Holbrook, Chris H.Q. Ding, Angeli Menon, John A. Tainer, and Michael W.W. Adams	
79 Organisation of Heavy Metal Resistance Genes in the Four Replicons of <i>Cupriavidus metallidurans</i> CH34	106
Sébastien Monchy, Nicolas Morin, Mohammed A. Benotmane, Sébastien van Aelst, Max Mergeay, Tatiana Vallaeys, Ruddy Wattiez, Safyih Taghavi, John Dunn, and Daniel van der Lelie* (vdlelie@bnl.gov)	
80 <i>Geobacter</i> Project Subproject II: Expression of <i>Geobacteraceae</i> Genes Under Diverse Environmental Conditions	108
Dawn Holmes* (dholmes@microbio.umass.edu), Brad Postier, Regina O'Neil, Kelly Nevin, Barbara Methe, Jessica Butler, Shelley Haveman, and Derek Lovley	

<u>Poster</u>	<u>Page</u>
81 Comprehensive Study of <i>recA</i> Expression in <i>Deinococcus radiodurans</i> with Single Cell and Population Level Analyses	110
Emily H. Turner* (emilyt@u.washington.edu), Haley Pugsley, and Norman J. Dovichi	
82 Directed Evolution of Radioresistance in a Radiosensitive Species	111
J.R. Battista* (jbattis@lsu.edu) and Michael M. Cox	
83 Development of a <i>Deinococcus radiodurans</i> Homologous Recombination System	112
Sanjay Vashee* (SVashee@venterinstitute.org), Ray-Yuan Chuang, Christian Barnes, Hamilton O. Smith, and J. Craig Venter	
84 Studies on the Fe Acquisition Mechanisms in <i>Nitrosomonas europaea</i> Derived from the Genome	112
Xueming Wei, Neeraja Vajrala, Norman Hommes* (hommesn@onid.orst.edu), Cliff Unkefer, Luis Sayavedra-Soto, and Daniel J. Arp	
85 Large Scale Genomic Analysis for Understanding Hydrogen Metabolism in <i>Chlamydomonas reinhardtii</i>	114
Michael Seibert* (mike_seibert@nrel.gov), Florence Mus, Alexandra Dubini, Maria L. Ghirardi, Matthew C. Posewitz, and Arthur R. Grossman	
86 Single-Molecule Imaging of Macromolecular Dynamics in a Cell	116
Jamie H.D. Cate and Haw Yang* (hawyang@berkeley.edu)	
87 Probing Single Microbial Proteins and Multi-Protein Complexes with Bioconjugated Quantum Dots	116
Gang Bao* (gang.bao@bme.gatech.edu), Grant Jensen, Shuming Nie, and Phil LeDuc	
88 Hyperspectral Imaging of Photosynthetic Pigment Molecules in Living Cyanobacterial Cells	118
Jerilyn A. Timlin, Michael B. Sinclair, Howland D.T. Jones, Linda T. Nieman, Sawsan Hamad, David M. Haaland* (dmhaala@sandia.gov), and Wim F.J. Vermaas	
89 The Cyanobacterium <i>Synechocystis</i> sp. PCC 6803: Membrane Biogenesis, Structure and Function	120
Wim Vermaas* (wim@asu.edu), Robert W. Roberson, Sawsan Hamad, Bing Wang, Zhi Cai, and Allison van de Meene	
Metabolic Network Experimentation and Modeling	122
90 Metabolic Engineering of Light and Dark Biochemical Pathways in Wild-Type and Mutant <i>Synechocystis</i> PCC 6803 Strains for Maximal, 24-Hour Production of Hydrogen Gas	122
P.S. Schrader, E.H. Burrows, F.W.R. Chaplen, and R.L. Ely* (ely@enr.orst.edu)	

<u>Poster</u>	<u>Page</u>
91 Geobacter Project Subproject V: <i>In Silico</i> Modeling of the Growth and Physiological Responses of <i>Geobacteraceae</i> in Complex Environments	123
Radhakrishnan Mahadevan* (rmahadevan@genomatica.com), Maddalena Coppi, Daniel Segura, Steve Van Dien, Bernhard Palsson, Christophe Schilling, Abraham Esteve-Nunez, Mounir Izallalen, and Derek Lovley	
92 Development of Computational Tools for Analyzing and Redesigning Biological Networks	125
Priti Pharkya, Madhukar Dasika, Vinay Satish Kumar, Narayanan Veeraghavan, Patrick Suthers, Anthony Burgard, and Costas D. Maranas* (costas@psu.edu)	
93 Next Generation Computational Tools for Biochemical Network Models	127
Ravishankar Rao Vallabhajosyula, Frank Bergmann, and Herbert M. Sauro* (hsauro@kgi.edu)	
94 Cyclic AMP-Dependent Regulatory Networks of <i>Shewanella oneidensis</i> MR-1 Involved in Anaerobic Energy Metabolism	129
Alex S. Beliaev* (alex.beliaev@pnl.gov), Daad A. Saffarini, Lee Ann McCue, Amoolya H. Singh, Yang Zhang, Matthew J. Marshall, Grigoriy E. Pinchuk, and Jim K. Fredrickson	
95 Engineering <i>E. coli</i> to Maximize the Flux of Reducing Equivalents Available for NAD(P)H-Dependent Transformations	130
Patrick C. Cirino* (cirino@enr.psu.edu), Costas D. Maranas, and Jonathan W. Chin	
96 A New MILP Based Approach for <i>in Silico</i> Reconstruction of Metabolic Networks and Its Application to Marine Cyanobacterium <i>Prochlorococcus</i>	131
Xiaoxia (Nina) Lin* (xiaoxia@genetics.med.harvard.edu), Aaron Brandes, Jeremy Zucker, and George M. Church	
97 Optimizing Central Metabolic Pathways in Yeast	132
Thomas W. Jeffries* (twjeffri@wisc.edu), Chenfeng Lu, Karen J. Mansoorabadi, Jennifer R. Headman, Ju-Yun Bae, and Haiying Ni	
98 Multi-Scale Models for Gene Network Engineering	133
Yiannis N. Kaznessis* (yiannis@cems.umn.edu)	
99 Generalized Computer Models of Chemoheterotrophic Bacteria: A Foundation for Building Genome-Specific and Chemically-Detailed Bacterial Models	134
Jordan C. Atlas, Evgeni V. Nikolaev, and Michael L. Shuler* (mls50@cornell.edu)	
100 Determination of the Most Probable Objective Function for Flux Analysis of Metabolism Using Bayesian-Based Model Discrimination	135
Andrea Knorr and Ranjan Srivastava* (srivasta@enr.uconn.edu)	
101 In silico Analysis of <i>Escherichia coli</i> Metabolism to Optimize Electron Production	136
David Byrne* (dbyrne@bu.edu), Daniel Segre, and Timothy Gardner	

<u>Poster</u>	<u>Page</u>
102 Reverse-Engineering the Central-Metabolism Network of <i>Shewanella oneidensis</i> MR-1	137
J.F. Penders and T.S. Gardner* (tgardner@bu.edu)	
103 Genome-Scale Metabolic Model of <i>Shewanella oneidensis</i> MR1	138
Brian Gates* (bgates@genomatica.com), Grigoriy E. Pinchuk, Christophe Schilling, and Jim K. Fredrickson	
104 A Phylogenetic Gibbs Sampler for High-Resolution Comparative Genomics Studies of Transcription Regulation	139
Sean Conlan* (sconlan@wadsworth.org), William Thompson, Lee Newberg, Lee Ann McCue, and Charles Lawrence	
105 Integrated Computational and Experimental Approaches to Facilitated Model Development	140
R. Mahadevan* (rmahadevan@genomatica.com), T. Fahland, Y. Kwan, J.D. Trawick, I. Famili, and C.H. Schilling	
106 New Technologies for Metabolomics	140
Jay D. Keasling* (jdkeasling@lbl.gov), Carolyn Bertozzi, Julie Leary, Michael Marletta, and David Wemmer	
107 Metabolomic Functional Analysis of Bacterial Genomes	142
Clifford J. Unkefer* (cju@lanl.gov), Pat J. Unkefer, Munehiro Teshima, Kwasi Godwin Mawuenyega, Norma H. Pawley, Rodolfo A. Martinez, Marc A. Alvarez, Daniel J. Arp, Luis Sayavedra-Soto, Xueming Wei, and Norman Hommes	
108 Linking Nano-Scale Patterns of ¹⁵N and ¹³C Metabolism to Bacterial Morphology	143
Jennifer Pett-Ridge* (pettridge2@llnl.gov), Stewart J. Fallon, Juliette Finzi, Doug Capone, Radu Popa, Ken Neelson, Ian D. Hutcheon, and Peter K. Weber	
109 Animal Gene Regulatory Networks	144
R. Andrew Cameron* (acameron@caltech.edu) and Eric H. Davidson	
Regulatory Processes	147
110 VIMSS Computational Core: Comparative Analysis of Regulatory Systems in Environmental Microbes	147
Eric J. Alm, Inna Dubchak, Alex Gilman, Katherine Huang, Keith Keller, and Adam P. Arkin* (APArkin@lbl.gov)	
111 Genome-Wide Mapping of Transcriptional Networks in <i>Escherichia coli</i> and <i>Shewanella oneidensis</i> MR-1	149
G. Cottarel, M.E. Driscoll* (mdriscoll@bu.edu), J. Faith, M.A. Kohanski, B. Hayete, J. Wierzbowski, C.B. Cantor, J.J. Collins, and T.S. Gardner	

<u>Poster</u>	<u>Page</u>
112 Computational Approaches to Investigating Transcription Regulatory Networks and Molecular Evolution of the Metal-Reducing Family <i>Geobacteraceae</i>	150
Julia Krushkal* (jkrushka@utm.edu), Marko Puljic, Ronald M. Adkins, Jeanette Peebles, Bin Yan, Radhakrishnan Mahadevan, and Derek R. Lovley	
113 Geobacter Project Subproject IV: Regulatory Networks Controlling Expression of Environmentally Relevant Physiological Responses of <i>Geobacteraceae</i>	152
Byoung-Chan Kim* (bckim@microbio.umass.edu), Katy Juarez-Lopez, Hoa Tran, Richard Glaven, Toshiyuki Ueki, Regina O'Neil, Ching Leang, Gemma Reguera, Allen Tsang, Robert Weis, Marianne Schiffer, and Derek Lovley	
114 Advances in System Level Analysis of Bacterial Regulation	154
Lucy Shapiro, Michael Laub, Ken Downing, Alfred Spormann, and Harley McAdams* (hmcadams@stanford.edu)	
115 A System-Level Analysis of Two-Component Signal Transduction	157
Michael T. Laub (laub@cgr.harvard.edu), Lucy Shapiro, and Harley H. McAdams	
116 The Bacterial Birth Scar, a Spatial Determinant for the Positioning of a Polar Organelle at the Late Cytokinetic Site	158
Edgar Huitema, Sean Pritchard, David Matteson, Sunish Kumar Radhakrishnan, and Patrick H. Viollier* (Patrick.Viollier@case.edu)	
117 Anaerobic Respiration Gene Regulatory Networks in <i>Shewanella oneidensis</i> MR-1	158
Jizhong Zhou* (jzhou@ou.edu), Haichun Gao, Xiaohu Wang, Yunfeng Yang, Xiufeng Wan, Zamin Yang, Dawn Klingeman, Alex Beliaev, Soumitra Barua, Ting Li, Christopher Hemme, Yuri A. Gorby, Mary S. Lipton, Steve Brown, Margaret Romine, Kenneth Nealson, James M. Tiedje, Timothy Palzkill, and James K. Fredrickson	
118 Uncovering the Regulatory Network of <i>Shewanella</i>	161
Gary D. Stormo* (stormo@genetics.wustl.edu), Jiajian Liu, and Xing Xu	
119 Integration of Control Mechanisms and the Enhancement of Carbon Sequestration and Biohydrogen Production by <i>Rhodospseudomonas palustris</i>	162
F. Robert Tabita* (Tabita.1@osu.edu), Caroline S. Harwood, Frank Larimer, J. Thomas Beatty, James C. Liao, Jizhong (Joe) Zhou, and Robert L. Hettich	
120 High-Resolution Physical Mapping of Transcription Factor Binding Sites in Whole Bacterial Genomes	164
J. Antelman, X. Michalet* (michalet@chem.ucla.edu), S.B. Reed, M. Romine, and S. Weiss	

Milestone 3**Computing Infrastructure and Education**.....167**121 Research Highlights from the BACTER Program**..... 167

Julie C. Mitchell* (mitchell@math.wisc.edu), Timothy J. Donohue, George N. Phillips Jr., Nicole Perna, Qiang Cui, David Schwartz, Mark Craven, Paul Milewski, and Stephen Wright

122 UC Merced Center for Computational Biology..... 168

Michael Colvin* (mcolvin@ucmerced.edu), Arnold Kim, Masa Watanabe, and Felice Lightstone

123 The BioWarehouse System for Integration of Bioinformatics Databases..... 169

Tom Lee, Valerie Wagner, Yannick Pouliot, and Peter D. Karp* (pkarp@ai.sri.com)

Communication..... 171**124 Communicating Genomics:GTL**..... 171

Anne E. Adamson, Shirley H. Andrews, Jennifer L. Bownas, Denise K. Casey, Sherry A. Estes, Sheryl A. Martin, Marissa D. Mills, Kim Nylander, Judy M. Wyrick, Anita J. Alton, and Betty K. Mansfield* (mansfieldbk@ornl.gov)

Ethical, Legal, and Societal Issues..... 173**125 *The DNA Files*[®]** 173

Bari Scott* (bariscot@aol.com)

126 Science Literacy Project for Public Radio Journalists..... 175

Bari Scott* (bariscot@aol.com)

	<u>Page</u>
Appendix 1: Participants	177
Appendix 2: Web Sites	187
Author Index	189
Institutional Index	196

Workshop Abstracts

This is the first Genomics:GTL workshop for principal investigators since the release of *Genomics:GTL Roadmap: Systems Biology for Energy and Environment* in October 2005 (www.doe-genomestolife.org). Abstracts and posters for this workshop are organized around the GTL goal and milestones shown below and in the roadmap on pp. 42–55. Many of the research projects are essentially pilots or proof-of-principle studies for systems biology, technology and methods development, computing, and facilities.

Most computing abstracts, instead of comprising a separate category, are associated with appropriate experimental topics. Overarching computing infrastructure and education abstracts are under Milestone 3, GTL Computational Biology Environment.

Abstracts of the Metabolic Engineering Working Group (MEWG), an interagency approach to understanding and using metabolic processes, are identified as such and intermixed with GTL abstracts in relevant program categories.

Genomics:GTL Overarching Scientific Goal

Achieve a predictive, systems-level understanding of biological systems to help enable biobased solutions to DOE mission challenges.

Science and Technology Milestones

Milestone 1: The Code—Understand Gene Structure and Functional Potential of Plants and Microbes and Their Communities

- Organism Sequencing, Annotation, and Comparative Genomics
- Microbial-Community Sequencing
- Protein Production and Characterization
- Molecular Interactions

Milestone 2: The Response—Understand Function, Regulation, and Dynamics in Plants and Microbes and Their Communities

- Omics: Systems Measurements of Plants, Microbes and Communities
- Metabolic Network Experimentation and Modeling
- Regulatory Processes

Milestone 3: GTL Computational Biology Environment

- Computing Infrastructure and Education

Communication

Ethical, Legal, and Societal Issues

The following table is a simple summation of how GTL science and DOE missions align (GTL Roadmap p. 40).

Summary Table. GTL Science Roadmap for DOE Missions

DOE Mission Goals		GTL Science Roadmaps	
Selected Processes	Biofuels Processes to convert cellulose to fuels <ul style="list-style-type: none"> Understanding and improving cellulase activity Improving sugar transportation and fermentation to alcohols Integrated processing Microbial processes to convert sunlight to hydrogen fuels <ul style="list-style-type: none"> Understanding photolytic fuel production Designing photosynthetic biofuel systems 	Science Objectives	<ul style="list-style-type: none"> Characterize genes, proteins, machines, pathways, and systems <ul style="list-style-type: none"> Conducting genomic surveys and comparisons Mining natural systems for new functions Producing and characterizing proteins Analyzing interactions, complexes, and machines Understand functions and regulation <ul style="list-style-type: none"> Measuring molecular responses: Inventories Performing functional assays Develop predictive mechanistic models <ul style="list-style-type: none"> Conducting experimental design Designing and manipulating molecules Using cellular and cell-free systems
	Environmental Remediation Microbial processes to reduce toxic metals <ul style="list-style-type: none"> Understanding microbe-mineral interactions Devising restoration processes 		Mission Outputs
Natural Systems' Behavior	Subsurface microbial communities' role in transport and fate of contaminants <ul style="list-style-type: none"> Understanding fate and effects Supporting remediation decisions 	Science Objectives	<ul style="list-style-type: none"> Analyze communities and their genomic potential <ul style="list-style-type: none"> Sequencing and comparing genomes Screening natural systems for processes Producing and characterizing proteins Understand community responses, regulation <ul style="list-style-type: none"> Comparing CO₂, nutrients, biogeochemistry cycles Producing cellular and community molecular inventories Performing community functional assays Predict responses and impacts <ul style="list-style-type: none"> Building interactive and predictive models Applying natural and manipulated scenarios
	Carbon Cycling and Sequestration Ocean microbial communities' role in the biological CO₂ pump <ul style="list-style-type: none"> Understanding C, N, P, O, and S cycles Predicting climate responses Assessing impacts of sequestration Terrestrial microbial communities' role in global carbon cycle <ul style="list-style-type: none"> Understanding C, N, P, O, and S cycles Predicting carbon inventories and climate responses Assessing sequestration concepts 		Mission Outputs

A capsule summary of systems being studied, mission goals that drive the analysis, generalized science roadmaps, and outputs to DOE missions. To elucidate design principles, each of these goals entails the examination of thousands of natural primary and ancillary pathways, variants, and functions, as well as large numbers of experimental mutations.