University of California San Francisco

CURRICULUM VITAE

February 2011

Name: **Christopher A Voigt, PhD**

Position: **Associate Professor**
Department of Pharmaceutical Chemistry
School of Pharmacy

Joint Appointment
Department of Bioengineering and Therapeutic Science
School of Pharmacy

Bioengineering, Chemistry and Chemical Biology, Tetrad, iPQB
(Biophysics, Bioinformatics, Systems Biology)

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EDUCATION:

1994-98 University of Michigan, Ann Arbor BSE Chemical Engineering
Graduated Summa cum laude

1998-02 California Institute of Technology PhD Biochemistry and Biophysics
(advisors: Frances Arnold, Zhen-Gang Wang, Stephen Mayo)

2002-03 University of California, Berkeley postdoc Bioengineering
(advisor: Adam Arkin)

LICENSES, CERTIFICATION:

N/A

PRINCIPAL POSITIONS HELD:

2003-2008 University of California, San Francisco Assistant Professor
Department of Pharmaceutical Chemistry

2008-present University of California, San Francisco Associate Professor
Department of Pharmaceutical Chemistry

OTHER POSITIONS HELD CONCURRENTLY:

2005-present Lawrence Berkeley National Labs
Chemist Scientist Faculty
2003-present Biophysics Graduate Program Faculty
2003-present Biomedical Informatics Graduate Program Faculty
2003-present Chemistry and Chemical Biology Graduate Program Faculty
2006-present Bioengineering Graduate Program Faculty
2007-presemt Tetrad Graduate Program Faculty
2008-present Korea Advanced Institute of Science and Technology
Adjunct Professor
Chemical and Biomolecular Engineering

HONORS AND AWARDS:

1996-98	Omega Chi Epsilon Chemical Engineering Society
1996-98	Tau Beta Pi Engineering Society
1998	James B. Angell Scholar
1998	Landes Writing Award
1998	Kucher Award for Engineering Research Excellence
1999-02	NSF Graduate Research Fellowship
2000-02	Computational Molecular Biology Pre-Doctoral Training Grant
2001	Everhart Series Lecturer
2002-04	Sloan/DoE Postdoctoral Fellowship in Computational Molecular Biology
2005-07	Sloan Research Fellow
2006-present	Pew Scholar
2006-present	NSF CAREER Award
2006-present	Packard Fellow
2006	Dean's Award for Excellence in Teaching
2006	MIT Technology Review 35
2007-12	Packard Fellow
2009	Vaughan Lecturer (Caltech)
2009	Honorary Fellow, Imperial College
2010	World Class University (WCU) Professor (Korea)
2010	"Top 10 Technologies of 2009" The Scientist

KEYWORDS/AREAS OF INTEREST:

Biotechnology, genetic engineering, synthetic biology, systems biology, biophysics, material and chemical production, cellular engineering, metabolic engineering, microbiology

PROFESSIONAL ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

Memberships:

2006-present Institute of Biological Engineers
2006-present American Institute of Chemical Engineers
2006-present American Chemical Society

Service to Professional Organizations:

2002	**Santa Fe Institute**	**Workshop Co-Chair**
2003	**Bay Area Signaling**	**Meeting Organizer**
2005	**Keck/National Academies**	**Meeting Organizer (Chair)**
2005-09	**BioBricks Foundation**	**Director**
2006	**Synthetic Biology 2.0**	**Meeting Organizer**
2006-08	**Institute of Biological Engineers**	**Scientific Board**
2007	**RECOMB Conference**	**Meeting Organizer**
2007-08	**Synthetic Biology 4.0**	**Meeting Organizer**
2008	Steering Committee, iGEM competition	
2008-present	Program Committee, Workshop on BioDesign Automation	
2009	Program Committee, International Conference in Systems Biology (ICSB)	
2009	Program Committee, Metabolic Engineering VIII	
2009	Participant, National Academies Futures Initiative Meeting, Synthetic Biology (Irvine).	
2010-present	Co-chair, Metabolic Engineering X	

SERVICE TO PROFESSIONAL PUBLICATIONS:

2007-10 Ad hoc referee for Science (3 papers in past 3 years), Nature (5 papers in 3 years), Journal of Molecular Biology (2 papers in 3 years), Proc. Natl. Acad. Sci USA (6 papers in 3 years), Journal of Molecular Evolution (1 paper in 3 years), Nature Chemical Biology (2 papers in 3 years), Molecular Systems Biology (3 paper in 3 years), Nature Biotechnology (2 papers in 3 years), Biotechnology and Bioengineering (1 paper in 3 years), EMBO J (1 paper in 3 years), PLOS (1 paper in 3 years), PLOS One (3 papers in 3 years), Journal of Bioengineering (1 paper in 3 years), Nature Nanotechnology (1 paper in 3 years), Nature Methods (2 papers in 3 years), Biotechnology Journal (1 paper in 3 years)
2006-present Editor, Systems and Synthetic Biology
2007-present Editor, Blackwell Synthetic Biology
2008-present Editorial Board, Journal of Biotechnology
2009-present Advisory Board, Journal of Chemical Biology
2010-present Editorial Board, BMC Systems Biology
2010-11 Editor, Methods in Enzymology, Volume on Synthetic Biology

INVITED PRESENTATIONS:

INTERNATIONAL:

2002 Workshop on Theoretical Evolution, *Peking University*, Beijing, China (invited).
2004 World Conference on Molecular Engineering, Los Cabos, Mexico (invited).
2005 World Conference on Molecular Engineering, Los Cabos, Mexico (invited).
2005 World Conference for Theoretically Oriented Chemists, Capetown, South Africa, (invited).
2005 International Symposium on Strategies of Life, Okayama, Japan, (invited).
2006 Workshop on Systems Properties and Evolution in Cell Signaling, Beijing, China (invited).
2006 20th IUBMB Congress and 11th FAOBMB Congress, Kyoto, Japan (invited).
2007 SysBioSys Conference, Manchester, England (invited, keynote).
2007 Synthetic Biology Symposium, VTT, Helsinki, Finland (invited, keynote).
2007 Pew Scholars Meeting, Puerto Vallarta, Mexico (invited).
2007 Seminar, Biological Engineering, ETH, Zurich, Switzerland (invited).
2007 Synthetic Biology Conference, Göteborg, Sweden (invited).
2007 BioKorea Symposium, Seoul, South Korea (invited, keynote)
2008 Lorne Proteins Conference, Melbourne, Australia (invited).
2008 12 Hong Kong High Schools, HKUST (invited).
2008 Department of Chemical and Biomolecular Engineering, KAIST, South Korea (invited).
2008 BioMalaysia, Kuala Lumpur, Malaysia (invited).
2008 Korean Institute of Chemical Engineering Annual Meeting, Busan, South Korea (invited).
2008 Wellcome Trust Workshop on Synthetic Biology, London, England (invited).
2008 Workshop on Synthetic Biology, Groningen, Netherlands (invited).
2008 Synthetic Biology 4.0, Hong Kong (invited).
2009 Seminar, Sick Kids Hospital, U Toronto, Toronto (invited).
2009 Workshop on Synthetic Biology, Imperial College London, (invited, keynote).
2009 DECHEMA conference, Frankfurt, Germany (invited).
2009 Seminar, DSM, Delft, Netherlands (invited).
2009 WCU Program Workshop, South Korea (invited).
2009 Department of Chemical and Biomolecular Engineering, KAIST, Korea (invited).
2010 University of British Columbia, Vancouver, Canada (invited).
2010 Pew Meeting, Costa Rica (invited).
2010 Metabolic Engineering VIII, Jeju, Korea (invited).
2010 EPFL Life Science Symposium, Lausanne, Switzerland (invited).
2010 International Conference on Synthetic Biology, Paris, France (invited).

NATIONAL:

2000 Working Group on Evolvability, Santa Fe Institute, Santa Fe, NM (invited).
2001 5th Lake Tahoe Symposia on Molecular Diversity, Lake Tahoe, CA (invited).

2001 Microbiology Seminar, California State University - Northridge, Northridge, CA (invited).
2001 Everhardt Lecture Series, California Institute of Technology, Pasadena, CA (invited).
2001 Robustness Advisory Meeting, Santa Fe Institute, Santa Fe, NM (invited).
2001 Seminar, Maxygen, Redwood City, CA (invited).
2001 Robustness and Evolvability of Molecules and Microbes, Santa Fe Institute, Santa Fe, NM (invited).
2002 Interview seminars, University of Illinois – Urbana-Champaign, Georgia Institute of Technology, University of California – Berkeley, University of California – San Francisco, University of Michigan – Ann Arbor, Massachusetts Institute of Technology, University of Texas – Austin, University of Wisconsin – Madison (invited).
2002 Seminar, Xencor, Monrovia, CA (invited).
2002 Bioinformatics Seminar, University of Southern California, Los Angeles, CA (invited).
2004 Biology Seminar, Purdue University, West Lafayette, IN (invited).
2004 Astrovirology Workshop, Mammoth Lakes, CA (invited).
2005 Chemical Engineering Seminar, Rice University, Houston, TX (invited).
2005 American Chemical Society Meeting, San Diego, CA (invited).
2005 American Chemical Society, San Diego, CA (invited).
2005 International Conference of Systems Biology, Boston, MA (invited).
2005 Seminar, Synthetic Biology Lecture Series, Berkeley, CA
2006 Biochemistry Seminar, California Institute of Technology, Pasadena, CA, (invited).
2006 Synthetic Biology 2.0, Berkeley, CA (invited).
2006 American Chemical Society, San Francisco, CA (invited).
2006 AiChE meeting, San Francisco, CA (invited).
2006 Meeting on Engineering Principles in Biological Systems, Cold Spring Harbor, NY (invited).
2007 Chemical Engineering Colloquium, University of California - Berkeley (invited).
2007 Plant and Microbiology Seminar, University of California - Berkeley (invited).
2007 Physics Seminar, Rockefeller University, New York City, NY (invited).
2007 Georgia Tech, Atlanta, GA (invited).
2007 California Institute of Technology, Pasadena, CA (invited).
2007 Synthetic Biology Symposium, Boston University, Boston, MA (invited).
2007 Science Foo Camp, Google, Mountain View, CA (invited).
2007 National Academies Frontiers in Science Symposium, Irvine, CA (invited).
2008 Department of Bacteriology, U Wisconsin, Madison, WI (invited).
2008 Department of Chemical Engineering, Texas A&M, College Station, TX (Lindsey Lecture, invited).
2008 Department of Chemical Engineering, Stanford, Palo Alto, CA (invited).
2008 Office of Naval Research, Washington D.C (invited).
2008 Gas Reaction Technologies, Santa Barbara, CA (invited).
2009 Life Technologies (Invitrogen/ABI), Carlsbad, CA (invited).

2009 Department of Chemical Engineering, Caltech, Pasadena, CA (invited).
2009 Department of Chemical Engineering, University of Michigan, Ann Arbor, MI (invited).
2009 Department of Chemical Engineering, University of Minnesota, MN (invited).
2009 Microbiology, Harvard, Boston, MA (invited).
2009 Department of Chemical Engineering, Stanford, Palo Alto, CA (invited).
2009 Santa Fe, NM (public science seminar, invited).
2009 Los Alamos National Labs, NM (invited).
2009 International Conference on Systems Biology (ICSB), Stanford, CA (invited).
2010 Department of Chemical Engineering, UCLA, CA (invited).
2010 Dow Agrosciences, Indianapolis, IN (invited).
2010 Genencor, Palo Alto, CA (invited).
2010 Bayer CropScience, Raleigh, NC (invited).
2010 Rice University, Houston, TX (invited).
2010 Biophysical Society, San Francisco, CA (invited).
2010 Bioengineering Department, MIT, Cambridge, MA (invited).
2010 Invited Talk, Science@Interface: Optogenetics, University of Chicago, IL (invited).
2010 Office of Naval Research Meeting, Alexandria, VA (invited).

REGIONAL AND OTHER INVITED PRESENTATIONS:

2003 Bioengineering Seminar, UCSF
2004 Faculty Lunch Talk, UCSF
2004 Asilomar Seminar, UCSF
2004 Invited Talk, Bay Area Signaling Symposia, Stanford Research Institute
2004 Invited Talk, NCI Nanotechnology Workshop, Half Moon Bay, CA
2005 Seminar, Kosan Biosciences, Hayward, CA
2005 Seminar, DNA 2.0, Hayward, CA
2005 Invited Talk, Life Engineering Symposium, UCSF
2006 QB3 dinner talk, UCSF
2007 Faculty Lunch Talk, UCSF
2007 Asilomar Seminar, UCSF
2008 Faculty Lunch Talk, UCSF
2008 Asilomar Seminar, UCSF
2008 QB3 Physics Talk, UCSF
2009 Cell Propulsion Laboratory, Meeting Talk, UCSF
2009 Faculty Lunch Talk, UCSF
2009 Presentation to School of Pharmacy Board, UCSF
2010 Seminar, Art-Science Symposium, UCSF

GOVERNMENT and OTHER PROFESSIONAL SERVICE:

2005 California GREAT Fellowships Reviewer
2006 *ad hoc* National Science Foundation Grant Reviewer
2007 *ad hoc* National Science Foundation Grant Reviewer

2008-present Site Review Team, Engineering Research Centers, National Science Foundation
2009 NSF-EPSRC Synthetic Biology Sandpit
2009 *ad hoc* NIH Grant Reviewer (challenge grants)
2010 Panel Review Member, BBBE, National Science Foundation
2010 *ad hoc* NIH Grant Reviewer (challenge grants)
2010-present Study Section Member, Biomaterials and Biointerfaces (BMBI), NIH
2010-present Panel Review for Biological and Environmental Research (BER) DOE

UNIVERSITY AND PUBLIC SERVICE:

UNIVERSITY SERVICE:

SYSTEMWIDE:

UCSF CAMPUS-WIDE:

2004 QB3/Systems Biology Faculty Search Committee
2004-05 Biophysics/CCB Seminar Committee
2004-06 Director, UCSF International Genetically Engineered Machines (iGEM) Team
2005 Neuroscience Theory Faculty Search Committee
2005-06 Graduate Council
2005-present Biophysics Academic Committee
2006 Systems Biology Faculty Search Committee
2006 Pew Fellowship Reviewer
2006 Pew Fellowship Internal Reviewer
2006-present NIBIB Graduate Program Development
2007-present Systems Biology Faculty Search Committee

SCHOOL OF PHARMACY:

2004 PharmD Graduation
2006 Interviewer for PharmD program
2006-08 Faculty Council
2010 PharmD Graduation
2010 Industrial Liaison Advisory Committee

DEPARTMENTAL SERVICE:

2006-07 Pharmaceutical Chemistry Nanotechnology Faculty Search Committee
2007-09 Pharmaceutical Chemistry Physical Chemistry Faculty Search Committee
2009 Pharmaceutical Chemistry Retreat Planning Committee
2010-present Vice Chair, Pharmaceutical Chemistry

PUBLIC SERVICE:

2005-06	**UCSF High School Internship Program (Mission High School)**
2010	**Host, High School Teachers for Curriculum Development, Industry Initiative for Science and Math Education (IISME).**

SUMMARY OF SERVICE ACTIVITIES:

I have served to develop a new graduate program, which merges the existing Biophysics and BMI programs with a new Systems Biology option. This has centered on committees to develop and write the NBIB grant and curriculum development. The core of this effort is the development of a new course structure. Within this effort, I have led the development of a new core course (BP205).

TEACHING and MENTORING:

FORMAL SCHEDULED CLASSES FOR UCSF STUDENTS:

Qtr	Acad Yr	Course No. & Title	Teaching Contribution	Units	Class Size
F	**2003**	**PC111: Physical Chemistry**	**Lab Instructor; 10 three hour labs**	**1**	**30**
F	**2003**	**BP241: Statistical Thermodynamics**	Lecturer; 8 1.5 hour lectures	**4**	**25**
W	**2004**	**PC205: Bioinformatics**	Lecturer; 2 1.5 hour lectures	**1**	**20**
S	**2004**	**BP205: Complex Systems in Biology**	Lecturer; 4 two hour lectures	**3**	**25**
F	**2004**	**PC111: Physical Chemistry**	Lecturer; 15 one hour lectures	**5**	**120**
W	**2005**	**BP201: Cellular Biophysics**	Lecturer; 3 1.5 hour lectures	**3**	**20**
S	**2005**	**BP205: Complex Systems in Biology**	Lecturer; 8 two hour lectures	**3**	**25**
F	**2005**	**PC111: Physical Chemistry**	Lecturer; 15 one hour lectures	**5**	**120**
W	**2006**	**BP201: Cellular Biophysics**	Lecturer; 3 1.5 hour lectures	**3**	**20**
S	**2006**	**BP205: Complex Systems in Biology**	Lecturer; 8 two hour lectures	**3**	**25**
F	**2006**	**PC111: Physical**	Lecturer; 15	**5**	**120**

		Chemistry	one hour lectures		
S	**2007**	**BP205: Dynamical Systems in Biology**	Lecturer; 10 1.5 hour lectures	**3**	**20**
W	**2008**	**BP205: Molecular Dynamics of the Cell**	Lecturer 20 1.5 hour lectures	**3**	**20**
F	**2009**	**BP241: Statistical Thermodynamics**	Lecturer 8 2 hour lectures	**4**	**25**
W	**2011**	**BP205: Molecular Dynamics of the Cell**	Lecturer 20 1.5 hour lectures	**3**	**20**

POSTGRADUATE AND OTHER COURSES:

W 2007 Synthetic Biology Team Challenge

POSTDOCTORAL AND OTHER SUPERVISED OR MENTORED:

2003-07 J. Christopher Anderson, Postdoc Advisor
Assistant Professor, UC-Berkeley, BioE
2004-05 Soon Ho Hong, Postdoc Advisor
Assistant Professor, Ulsan University, Korea
2006-07 Danielle Tullman-Ercek, Postdoc Advisor
Assistant Professor, UC-Berkeley, ChemE
2006-10 Jeff Tabor, Postdoc Advisor
Assistant Professor, Rice University, BioE
2007-09 Howard Salis, Postdoc Advisor
Assistant Professor, Penn State, ChemE
2007-10 Travis Bayer, Postdoc Advisor
Assistant Professor, Imperial College, BioE
2007-present Dehua Zhao, Postdoc Advisor
2009-present Chunbo Lou, Postdoc Advisor
2010-present Tae Seok Moon, Postdoc Advisor
2010-present Robin Prince, Postdoc Advisor
2010-present Byrnne Stanton, Postdoc Advisor
2010-present Ying-Ja Chen, Postdoc Advisor
2010-present Virgil Rhodes, Research Scientist

PREDOCTORAL STUDENTS SUPERVISED OR MENTORED:

2003-2008 Eli Groban, Biophysics, graduate student, PhD Advisor
Scientist, LS9 (South San Francisco)

2004-2009 **Anselm Levskaya, graduate student, Biophysics, PhD Advisor**
Postdoctoral Fellow (Stanford)
2004-2010 **Elizabeth Clarke, graduate student, Biophysics, PhD Advisor**
Scientist, LS9 (South San Francisco)
2005-2010 **Daniel Widmaier, graduate student, CCB, PhD Advisor**
Founder, Refactored Materials (San Francisco)
2006-present **Ethan Mirsky, Biophysics, graduate student, PhD Advisor**
2006-present **Karsten Temme, Bioengineering, graduate student, PhD Advisor**
2007-present **Alvin Tamsir, Tetrad, graduate student, PhD Advisor**
2009-present **Felix Moser, Bioengineering, graduate student, PhD Advisor**
2009-present **Brian Caliando, Tetrad, graduate student, PhD Advisor**
2010-present **Daniel Kaemmerer, graduate student, PhD Advisor**

INFORMAL TEACHING:

2004-08 **International Genetic Engineering Machines (iGEM) competition (ad hoc summer competition held by MIT for competing teams of high school, undergraduate, and graduate students)**
2005 **Xiaoyan Liu, high school student (Mission High School), summer internship advisor, now at UC-Berkeley Bioengineering**
2006 **Chia Hseih, high school student (Mission High School)**
2006 **Patrick Visperas, undergraduate student, REU Advisor**
2007 **Ryan Clarke, high school student (City Arts and Technology)**
2008 **Ryan Clarke, high school student (City Arts and Technology)**
2008 **Hannah Tabakh, high school student (Lowell High School)**
2009 **Hannah Tabakh, high school student (Lowell High School)**
now at UC-Berkeley (Bioengineering)
2010 **Ryan Clarke, undergraduate student (Iowa State)**
2010 **June Park, high school student (Piedmont High School)**
2010 **Jacqueline Tam, undergraduate student (UC-Berkeley)**

TEACHING AWARDS AND NOMINATIONS:

2006 Dean's Award for Excellence in Teaching
2007 **Nomination, Postdoctoral Mentorship Award**

SUMMARY OF TEACHING HOURS:

2003-04: 128 total hours of teaching (including preparation).
Formal class or course teaching hours: 53 hours
Informal teaching hours: 300 hours

2004-05: 128 total hours of teaching (including preparation).
Formal class or course teaching hours: 36 hours
Informal teaching hours: 300 hours

2005-06: 128 total hours of teaching (including preparation).
Formal class or course teaching hours: 36 hours

Informal teaching hours: 300 hours

2006-07: 192 total hours of teaching (including preparation).
Formal class or course teaching hours: 30 hours
Informal teaching hours: 350 hours

2007-08: 120 total hours of teaching (including preparation).
Formal class or course teaching hours: 30 hours
Informal teaching hours: 400 hours

2008-09: 120 total hours of teaching (including preparation).
Formal class or course teaching hours: 30 hours
Informal teaching hours: 600 hours

2009-10 64 total hours of teaching (including preparation)
Formal class or course teaching: 16 hours
Informal teaching hours: 600 hours

TEACHING NARRATIVE
My Pharmacy teaching requirement has focused on Physical Chemistry 111. I teach a half-quarter of this class, which focuses on the fundamentals of thermodynamics. I have taken a pedagogical approach to developing new material for this course, including the development of new lecture topics and visual approaches to learning.

I have built two new graduate classes that have not previously existed at UCSF. The first is listed as a Biophysics course, which focuses on complex systems analysis in Biology. As part of the new NBIB program (see service), I am developing a new core class for the incoming Biophysics/BMI/Systems Biology students. This course teaches the fundamentals of kinetics, transport, and non-linear dynamics.

RESEARCH AND CREATIVE ACTIVITIES:

RESEARCH AWARDS AND GRANTS:

Voigt, Christopher A.

ACTIVE SUPPORT

R01 GM095765 (Voigt) 12/01/2010 – 11/30/2015 $1,158,750 Total Award
NIH
Characterization of Gradient-Responsive Genetic Programs Using Synthetic Light Sensors
The main goal of this proposal is to identify the design principles by which genetic programs convert gradients into patterns of gene expression. Our approach will harness two new tools that we have developed. The first is a set of orthogonal light sensors (red and green) that activate a signaling pathway in a graded manner as a function of light intensity. Simple circuits will be combined to

create many permutations and the robustness and evolvability of their ability to convert gradients into patterns will be assayed.

2011 LDRD Program (Simon/Voigt) 11/01/2010—10/31/2013 $370,800 Total Award
LBNL/DOD
Engineering Yeast to Produce Methyl Formate for Conversion to Fuels and Chemicals
This research is to build a synthetic four gene pathway to convert SAM to methyl formate, which is a volatile precursor for fuels and chemicals. Synthetic metagenomics will be applied to screen the sequence databases to identify enzymes that can perform each step of the pathway.

P50 GM81879 (Lim/Voigt) 09/01/2010 - 06/30/2015
NIH
"Exploring Design Principles of Cellular Control Circuits" $941,800 Total **Award**
We use mathematical modeling to guide the construction of synthetic adaptive circuits, and apply these to optimize metabolic flux.

A114510 (Voigt) 04/1/2010 – 03/31/2012 $394,066 Total **Award**
Life Technologies Corp. .
“Computational and Experimental Tools for Synthetic Biology”
We will create and experimentally verify new biophysical and mathematical methods for part design (terminators and orthogonal phage polymerases) that will be integrated into a Computer Aided Design (CAD) software package.

N00014-10-1-0245 01/01/2010 – 12/31/2012 $449,640 Total **Award**
DOD Office of Naval Research
Powerful Combinatorial Sensors to Program Microbes
We propose to develop methods to rewire the circuitry of bacteria to harness their sensing power for applications relevant to the Navy. This will be achieved by developing a platform by which synthetic genetic circuits can be rapidly constructed to respond to a pattern of sensor activities that is a signature from a desired environment or chemical.

BES-0547637 (Voigt) 04/01/2006 – 03/31/2011 $400,000 Total **Award**
NSF CAREER
Multi-input Multi-output Cellular Control: Bacterial Type III Secretion as a Model System
The major goals of this project are: 1. to determine how multiple inputs are integrated by the Salmonella SPI-1 regulatory network, and 2. to determine how individual cells bifurcate between the expression of SPI-1, SPI-2, and flagella as a function of the environmental conditions.

EEC-0540879 (Keasling/Voigt) 07/01/2006 – 06/30/2016 $2,549,846 Total **Award**
UCB/NSF
NSF Engineering Research Center
SynBERC: Synthetic Biology Engineering Research Center
The major goals of this project are to develop a foundation to expand the complexity of functions that can be engineered into cells. Specifically, we will construct new genetic logic gates, mathematical models to characterize parts (ribosome binding sites), and methods to refactor gene clusters (Klebsiella nitrogen fixation).

CCF-0943385 (El-Samad/Voigt) 01/01/2010 – 1/1/2013 $267,833 Total **Award**
NSF Sandpit
A Programmable Rhizosphere: Highly integrated genetic programs for spatio-temporal control
The goals of this project are to create programmable NAND gates that can be connected to produce higher logic operations and to apply this to integrating sensors that are relevant to the genetic engineering of rhizosphere bacteria.

CBET-0943302 (Voigt) 09/01/2009—08/31/2012 $419,747 Total **Award**
NSF Sandpit
Collaborative Research: Cyberplasm – An autonomous micro-robot constructed using synthetic biology The goal of this project is to create genetic circuits that enable cells to send and receive signals to an electronic interface.

R01AI067699 (Voigt) 01/01/2007 –12/31/2011 $1,505,895 Total **Award**
NIH/NIAID
System Dynamics of the Salmonella Virulence Regulatory Network
The major goals of this project are to study the temporal dynamics of the SPI-1 regulatory controlling Salmonella invasion.

2006-30537 (Voigt) 11/01/2006 – 10/31/2011 $775,000 Total **Award**
The David and Lucile Packard Fellowship for Science and Engineering
Programming Cells: Building a Bacterial Nose.
The major goals of this project are to determine if multiple two-component sensors can interact to perform combinatorial sensing, where general signals are integrated by a regulatory network to identify a specific microenvironment.

(Voigt) 04/30/2009 – 07/31/2011 $240,000 Total **Award**
Pew Scholars Program
Programming the Dynamics of Bacterial Type III Secretion

The major goals of this project are to re-engineer the type III secretion system to alter the number of needles that are produced per cell, the fraction of the population that turn on, and the strength of the feedback in the effector pathway.

PENDING SUPPORT

(Weiner) 12/01/2010 – 11/30/2015 $1,831,145 Total **Award**
NIH R01
A toolkit for Light Control of Molecular Processes in Living Cells
The goal of this research is to expand the toolbox for the use of light sensors in eukaryotic cells. To do this, we will port mutations from bacterial phytochromes that respond to different colors (blue, green) to the plant phytochrome PhyA such that three colors can be used simultaneously to control protein-protein interactions. In addition, we will use protein engineering to build orthogonal PhyA-PIF pairs, will move the PCB metabolic pathway into eukaryotic cells, and will develop a toolbox of signal sequences to enable light to direct proteins to different eukaryotic organelles.

COMPLETED RESEARCH SUPPORT

(Voigt) 09/01/2007 – indefinite $75,000 Total **Award**
Helios Research Fund
Reverse Engineering of Rhodobactor Photosynthesis
The major goals of this project are to reverse engineering of a photosynthetic organism to create chemical fuel directly from sunlight.

(Voigt) 09/01/2006 – 08/28/2009 $270,566 Total **Award**
UC Discovery Grant (UCOP/Amyris Biotech)
Microbial Biopolymer Factories
The major goals of this project are to optimize Salmonella type III secretion for the expression and secretion of heterologous proteins, including silk fibroins.

N000140710066 (Voigt) 11/01/2006 – 11/01/2009 $300,000 Total **Award**
Office of Naval Research
A Bacterial Nose: Combinational Sensing in Single Cells
The major goals of this project are to demonstrate that combinational sensing is achievable and then to explore the degree to which is can be engineered.

(Voigt) 09/16/2005 – 09/15/2007 $45,000 Total **Award**
Sloan Research Fellowship
Design and Evolution of Bacterial Therapeutics

The major goals of this project to build genetic circuits that enable therapeutic bacteria to sense the correct microenvironment, integrate this information, and deliver a therapeutic to diseased cells

PN2 EY016546 (Lim) 09/30/2004 – 09/29/2010 $724,710 Total
Award
NIH
Engineering Cellular Control: Synthetic Signaling and Motility Systems
The major goals of this project to create protein-based synthetic genetic circuits that control eukaryotic cell motility. My role in this grant is to build mathematical models to characterize the spatial self-assembly characteristics of natural and synthetic genetic circuits.

(Voigt)
Sandler Program in Basic Sciences 02/15/2004 – 02/14/2006 $200,000 Total
Award
Preceding and Building transferrable bacterial control systems.

PEER REVIEWED PUBLICATIONS:

1. Voigt, C. A., and Ziff, R. M. (1997) Dynamic behavior of the monomer-monomer surface reaction model with adsorbate interactions. *Journal of Chemical Physics*, 107: 7397-7401.
2. Voigt, C. A., and Ziff, R. M. (1997) Epidemic analysis of the oxygen poisoning critical point in the Ziff-Gulari-Barshad model. *Physical Review E*, 56: R6241-R6244.
3. Voigt, C. A., Gordon, D. B., and Mayo, S. L. (2000) Trading accuracy for speed: a quantitative comparison of search algorithms in protein sequence design. *Journal of Molecular Biology*, 299: 789-803.
4. Voigt, C. A., Mayo, S.L., Arnold, F.H., and Wang, Z-.G. (2001) Computational method to reduce the search space of directed protein evolution, *Proc. Natl. Acad. USA*, 98, 3778-3783.
5. Voigt, C. A., Martinez, C., Mayo, S.L., Wang, Z-.G., and Arnold, F.H. (2002) Protein building blocks preserved by recombination, *Nature Structural Biology*, 9: 553-558.
6. Meyer, M. M., Silberg, J. J., Voigt, C. A., Endelman, J. B., Mayo, S. L., Wang, Z-G., and Arnold, F. H. (2003) Library analysis of SCHEMA-guided protein recombination, *Protein Science*, 12: 1686-1693.
7. Otey, C. R., Silberg, J. J., Voigt, C. A., Endelman, J. B., Bandara, G., and Arnold, F. H. (2004) Functional evolution and structural conservation in chimeric cytochromes P450: Calibrating a structure-guided approach, *Chemistry & Biology*, 11: 309-318.
8. Voigt, C. A., Wolf, D. M., and Arkin, A. P. (2005) The B. subtilis sin operon: An evolvable network motif, *Genetics*, 169: 1187-1202.

9. Levskaya, A., Chevalier, A.A., Tabor, J.J., Simpson, Z.B., Lavery, L.A., Levy, M., Davidson, E.A., Scouras, A., Ellington, A.D., Marcotte, E.M., and Voigt, C. A.. (2005) Engineering E. coli to see light, *Nature*, 24: 441-442.
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4. Voigt, C. A., Bayer, T.S. Industrial production of organic compounds using recombinant organisms expressing methyl halide transferase, pending 2009
5. Voigt, C. A., Bayer, T.S. Cell-based systems for production of methyl formate, pending 2009

6. Voigt, C. A., Lim, W.A., Levskaya, A., Light Regulated System for the Spatiotemporal Control of Signalling Proteins and their Activities, pending 2009

OTHER CREATIVE ACTIVITIES:

Our 'bacterial photography' project has become a central component of the teaching curriculum of high schools, undergraduate programs, and science museums. For example, we have disseminated the necessary materials to MIT and the London Science Museum.

In 2010, we received a National Academies Keck Future Initiative (NAKFI) grant to develop a set of visual genetic engineering project that our develop as high school labs. This is done in collaboration with two embedded high school teachers that are participating in the Industry Initiatives for Science and Math Education (iiSME), which is a formal program for curiculum development. These teachers worked with a high school student and undergraduate over the summer to create a lab based on the photographic bacteria. This involved both the integration of educational material, as well as some engineering to utilize low-cost components.

AREA OF FOCUS

Genetic engineering is undergoing a revolution, where next-generation technologies for DNA and host manipulation are enabling larger and more ambitious projects in biotechnology. Automated DNA synthesis has advanced to where it is routine to order sequences >100,000bp where every base is user-specified, the turnaround time is several weeks, and the cost is rapidly declining (Figure 1). Recently, this facilitated the synthesis of a complete 1 Mbp genome of a bacterium and its transfer into a new host, resulting in a living cell. However, while whole genomes can be constructed, the ability to design such systems is lagging. The focus of my lab is to develop new experimental and theoretical methods to push the scale of genetic engineering, with the ultimate objective of genome design. This will impact the engineering of biology for a broad range of applications, including agriculture, materials, chemicals, and medicine.

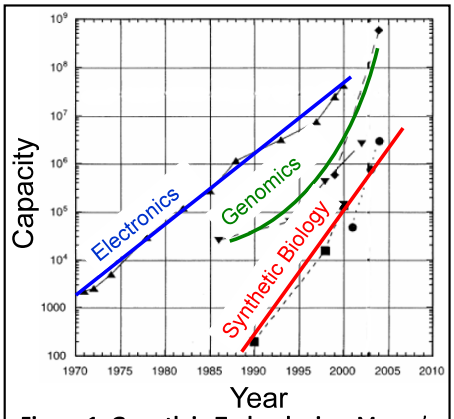

Figure 1: Growth in Technologies. Moore's law (# of transiters per chip) is shown in blue. In comparison, the capacity (bp per person per day) for DNA sequencing (green) and DNA synthesis (red) is shown (Carlson, 2003). DNA synthesis has been doubling every 1.1 years.

My lab is roughly divided into two groups. The first is focused on the development of a programming language for cells. A genetic "program" consists of a combination of genetic circuits, each of which uses biochemistry to

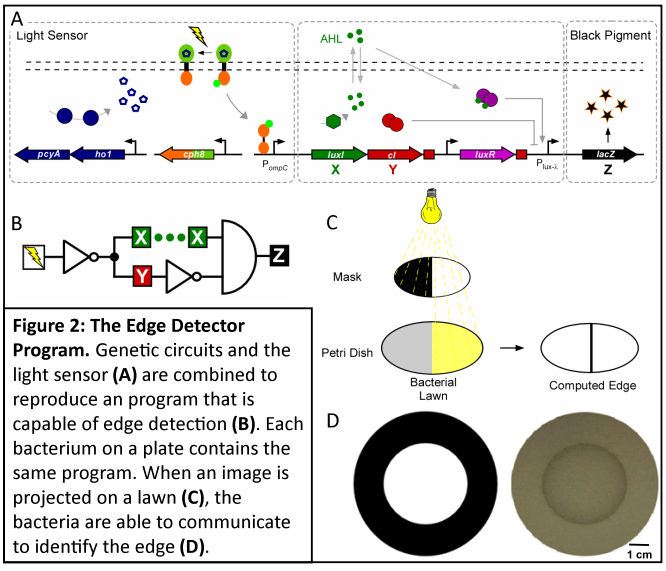

Figure 2: The Edge Detector Program. Genetic circuits and the light sensor **(A)** are combined to reproduce an program that is capable of edge detection **(B)**. Each bacterium on a plate contains the same program. When an image is projected on a lawn **(C)**, the bacteria are able to communicate to identify the edge **(D)**.

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replicate a function analogous to an electronic circuit (*e.g.*, a logic gate). Combining circuits yields more complex signal processing operations. For example, we combined 4 circuits to build an "edge detection program" in *E. coli* that enables cells to draw the light-dark boundaries of an image projected on a plate (Figure 2). Our near-term objective is to develop the foundations by which 20-30 circuit programs can be reliably built. This will require new classes of circuits that can be rapidly connected and are sufficiently simple and robust to be assembled by computer algorithms. We are also developing biophysical models that can map the sequence of a genetic part (*e.g.*, a ribosome binding site) to its function. These models can be used to connect and optimize circuits and programs.

The second group in my lab is focused on applying these tools to problems in biotechnology. This encompasses new approaches to old problems (*e.g.*, nitrogen fixation) as well as more futuristic ideas (*e.g.*, re-programming bacteria as a drug delivery device). Currently, we are focused on harnessing the functions encoded within prokaryotic gene clusters. These are contiguous stretches of DNA in the genome that (ideally) contain all of the genes necessary and sufficient for that function. These clusters consist of diverse functions requiring ~20+ genes, including elaborate nano-machines and metabolic pathways. We are applying principles from synthetic biology to rebuild these functions from the ground up, in order to eliminate complex and often uncharacterized native regulation, gain complete control and understanding of the cluster, and to facilitate its optimization and transfer between organisms. To do this, we use the same computational tools, genetic circuits, and construction methodologies developed by the foundational half of the lab. This work represents a step towards whole genome design, where our vision is that the future designer would mix-and-match modular clusters to build a synthetic organism.

CONTRIBUTIONS AND IMPACT

Research

1. A Programming Language for Bacteria

The goal of genetic programming is to gain control over the logic and dynamics of cellular processes, in order to harness the capabilities of living cells. The first genetic circuits have been built over the last decade, and now the focus is on how to reliably assemble them into multi-circuit programs. Building such programs remains an art. Our goal is to couple circuit design with biophysical models and computational algorithms to automate the assembly of integrated circuits. This would be abstracted from the user, making genetic programming a routine component of biotechnology projects.

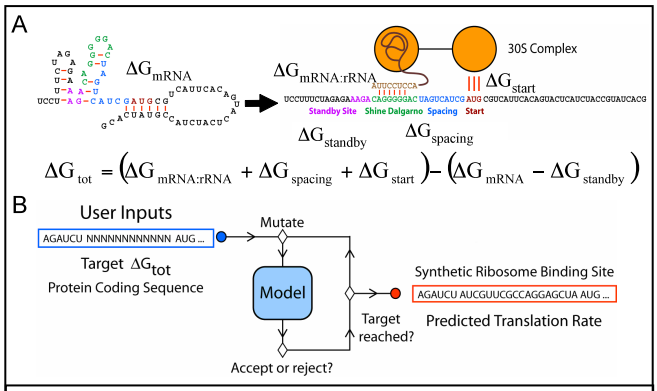

Figure 3: The RBS Calculator. The model predicts the free energy of ribosome binding to mRNA (ΔG_{tot}). **(A)** The calculated contributions to ΔG_{tot} are shown and include the unfolding of the mRNA. **(B)** A search algorithm identifies a sequence that achieves a target ΔG_{tot}.

In choosing experiments, we follow

a design cycle that allows us to iteratively improve our ability to program cells. The aim is to advance the *process* of programming, so we focus this research on "toy problems," where there is no particular application for the end product. The design cycle involves: 1. construction of a program, 2. identification of a design principle, 3. development a formal theoretical basis to address the design principle. For toy problems, the deliverables are those tools developed at step 3, which are often licensed to companies. An example of a toy problem is the edge detector. Building this program elucidated the design principle that in order two connect two circuits their dynamic ranges need to match. This led to the construction of a thermodynamic model, which can predict DNA sequences that will functionally connect circuits (Figure 3). Subsequently, it has been licensed to Bayer Cropscience, DSM, Life Technologies, and Genomatica.

(i) *Next-generation genetic circuit design*.
We have been designing architectures for genetic circuits that can be used in different permutations to build programs. The circuits need to be: 1. flexible, representing a function that is applicable to many programs, 2. extensible, where the inputs and outputs are the same, such that they can be layered, 3. scaleable, where the same architecture can

be re-used to build many gates, 4. fast and reliable. To this end, we designed transcriptional NOR and AND gates that satisfy these constraints. Many gates are being constructed by varying the component transcription factors. The number of gates that can be used simultaneously in a program is dictated by the number of available orthogonal transcription factors. To identify these, we have a research agreement with Life Technologies to use DNA synthesis to build libraries at no cost. We are applying a variety of *in vivo* and *in vitro* techniques to identify and characterize orthogonal gates.

(ii) *Biophysical models of genetic parts*.
Modeling in systems biology involves kinetic models that capture the dynamics of cellular regulatory networks. Harnessing these models for synthetic biology is difficult because, even if the need for a particular kinetic parameter is quantified, it is difficult to "reach down" to suggest a particular mutation or part substitution in the DNA. We have been developing thermodynamic models that can map the DNA sequence of a genetic part to its function. One example is the RBS Calculator, which can predict the strength of a ribosome binding site based on its sequence. This can be converted to an expression rate that provides a direct link to the kinetic models, which can predict the impact on circuit or program dynamics. We are also developing models for other fundamental parts, including promoters and terminators.

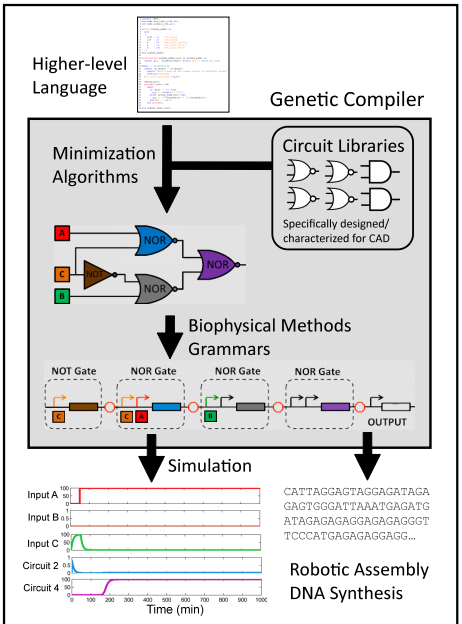

Figure 4: The Genetic Compiler. The user would use a higher-level language to specify a desired circuit. The output is a DNA sequence, which can be synthesized.

(iii) *Algorithms for automated part selection and device combination*.
The vision of this research is to completely abstract the programmer from the biochemical details of the program. The circuit libraries (i) and biophysical methods (ii) will form the theoretical backbone of a "genetic compiler" (Figure 4). The input to the compiler will be a higher-level language and the output is a DNA sequence. The compiler also deploys other algorithms to deconstruct and assemble the circuits. Some of these will be taken from other fields. For example, we have been using the ESPRESSO logic minimization software developed in Electrical Engineering to deconstruct multi-input multi-output truth tables into integrated 2-input circuits.

2. Applications in Biotechnology: Moving to Genome-scale Engineering

The ability to build and program cells enables a variety of applications in agriculture, fuels/chemical production, and medicine. For each project, we focus exclusively on the genetic engineering in my lab and form either an academic or industrial collaboration for downstream optimization. For example, we have done work with the engineering of spider silk proteins in my lab, and the spinning of threads is being performed by a company founded by my students. Similarly, we have started a company around our work to produce methyl halides in yeast that will focus on fermentation, purification, and their catalytic conversion to chemicals and fuels.

Currently, we are focused on "refactoring" gene clusters from bacteria. Refactoring is a term borrowed from software engineering that refers to the rewriting of code to achieve the same overall function. Here, we are applying the concept to re-engineer gene clusters in bacteria that encode valuable functions. These clusters range from ~15-100,000 bp with ~20+ genes. Their expression is highly controlled by the native regulatory network. This ensures that the cluster is only active under conditions where it is needed by the organism. For example, a protein secretion needle may only be expressed for a short period during an infection and it is difficult to overcome this to use it to export proteins during fermentation. The regulation is redundant and many regulatory interactions are unknown; thus, it is difficult to engineer in a piecemeal manner. Also, many gene clusters that appear in sequenced genomes are "cryptic" meaning that there are no known conditions under which they are expressed. It would be valuable to be able to "wake up" these clusters.

The process of refactoring consists of several steps, all of which are performed on the computer. Starting from the DNA sequence of the wild-type cluster, we remove the non-essential genes (if known), regulatory genes, and non-coding DNA. Next, each gene is "codon randomized" to identify a sequence that is as far away as possible from wild-type. This is to eliminate unknown regulation internal to the gene. The genes are organized into operons and synthetic parts (promoters, RBSs, terminators) are used to control their expression. (In practice, this step still

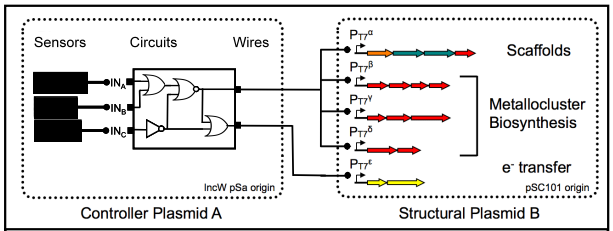

Figure 5: The Blueprint of a Refactored Nitrogen Fixation Gene Cluster. Synthetic sensors, circuits, and T7 wires form the "controller," which regulates the 15 genes required for nitrogenase maturation and function.

requires enormous efforts of trial-and-error, but we are getting progressively better in automation). Finally, a "controller" is constructed from synthetic sensors and circuits to integrate environmental signals and implement expression dynamics. The output of the controller is linked to the refactored gene cluster using polymerases.

We are focused on two gene clusters: nitrogen fixation in *Klebsiella* and type III secretion in *Salmonella*. Fixed nitrogen is a critical input to agriculture and requires significant energy and carbon resources to produce. Many microorganisms are able to fix atmospheric nitrogen. We are refactoring the gene cluster (Figure 5) with the objective of transferring it into a rhizomal bacterium or chloroplast. Protein secretion in gram negative bacteria is difficult because proteins need to traverse two membranes. For many applications, protein secretion is a critical tool to export proteins that: 1. act on substrates that cannot diffuse into the cell, 2. self-assemble into fibrils, 3. need to be recovered in highly-purified form. We have engineered the type III secretion system from Salmonella to export recombinant protein, including spider silk proteins. However, it is strongly repressed by glucose and only turns on for a few hours in *Salmonella*, making it not suitable for fermentation. For both systems, the gene clusters are being refactored to gain complete control of their functions, while maintaining the critical regulation

There are numerous gene clusters that encode a range of functions of interest to biotechnology, including pharmaceutical production pathways, the construction of metallic nanoparticles, light harvesting in photosynthesis, and hydrogen production. The work that we are currently doing provides a platform to access and engineer these functions. Gene clusters also provide a mechanism by which improvements in the process enable the engineering progressively larger systems with the ultimate objective of simplifying and engineering whole genomes.

3. Education

My primary interest in education is thermodynamics and statistical mechanics and their application to problems in biology and biological engineering. I have also developed and taught courses in the area of kinetics, transport phenomena, and non-linear dynamics. These topics are directly applied in my research program. My views of the organization and teaching of these topics have been shaped both by my formal training in Chemical Engineering and by my development as a teacher at UCSF, where the students largely come with backgrounds in Biology (or are Pharmacists!).

As a teaching philosophy, *statistical mechanics and molecular processes should be incorporated earlier in thermodynamics education.* In many fields, students benefit from an early molecular view; notably, in biological engineering. The impedance of doing this has been the advanced mathematics required to appreciate the derivations. Until recently, it has been difficult to observe processes at the single molecule level and this has hampered the incorporation of examples backed by data, especially for biological examples. The deluge of single molecule data in the last decade as well as single-cell measurements have led to derivations in the literature for fundamental process. This warrants revisiting the organization and teaching of thermodynamics.

UCSF does not have undergraduates. The closest experience I have had is in teaching PC111: Physical Chemistry to a class of 120 first year pharmacy students. The material in this course is very close to a chemistry undergraduate program. It is a 5 credit course, involving 3 one hour lectures and a 4 hour lab per week. For this course, I was awarded the "Dean's Award for Excellence in Teaching."

I have also developed a new core course, BP205: Molecular Dynamics of the Cell, which is taught as part of the Biophysics Graduate Program. My teaching mentor is Ken Dill (author of the innovative "Molecular Driving Forces" textbook) and I started teaching at UCSF in his BP241: Statistical Mechanics course. This course is intended as a sister course to 241, with an emphasis on kinetics and transport phenomena. The focus is on molecular phenomena that occur at the scale of single cells. A reoccurring theme is that the cell is right at a scale that is at the boundary of interesting physical transitions (*e.g.*, low Re swimming, Pe = 1 for equal contributions between advection and diffusion, small numbers of molecules). BP205 started in 2004 as a 1 credit seminar course, has grown each year, and was made a 3 credit required core course in 2009.

I founded the UCSF iGEM (international genetically engineered machines competition) team in 2004. UCSF does not have undergraduates, so these teams have consisted of high school students embedded into my lab. The projects included: "photographic bacteria," "a genetic thermometer," and "remote control of chemotaxis." In summer 2010, I hosted two high school teachers sponsored by IISME (Industry Initiatives for Science and Math Education), which is a formal program for high school curriculum development. These teachers worked with a high school student and undergraduate over the summer to create a lab based on the photographic bacteria. This involved both the integration of educational material, as well as some engineering to utilize low-cost components. The long-term objective is to compile multiple labs that will be part of a high school biotechnology lab class**.**