VIIBRE

SyBBURE

Systems Biology and Bioengineering Undergraduate Research Experience

John P. Wikswo

http://www.vanderbilt.edu/viibre/SyBBURE.html

Parents & Grandparents Leadership Committee
September, 2006

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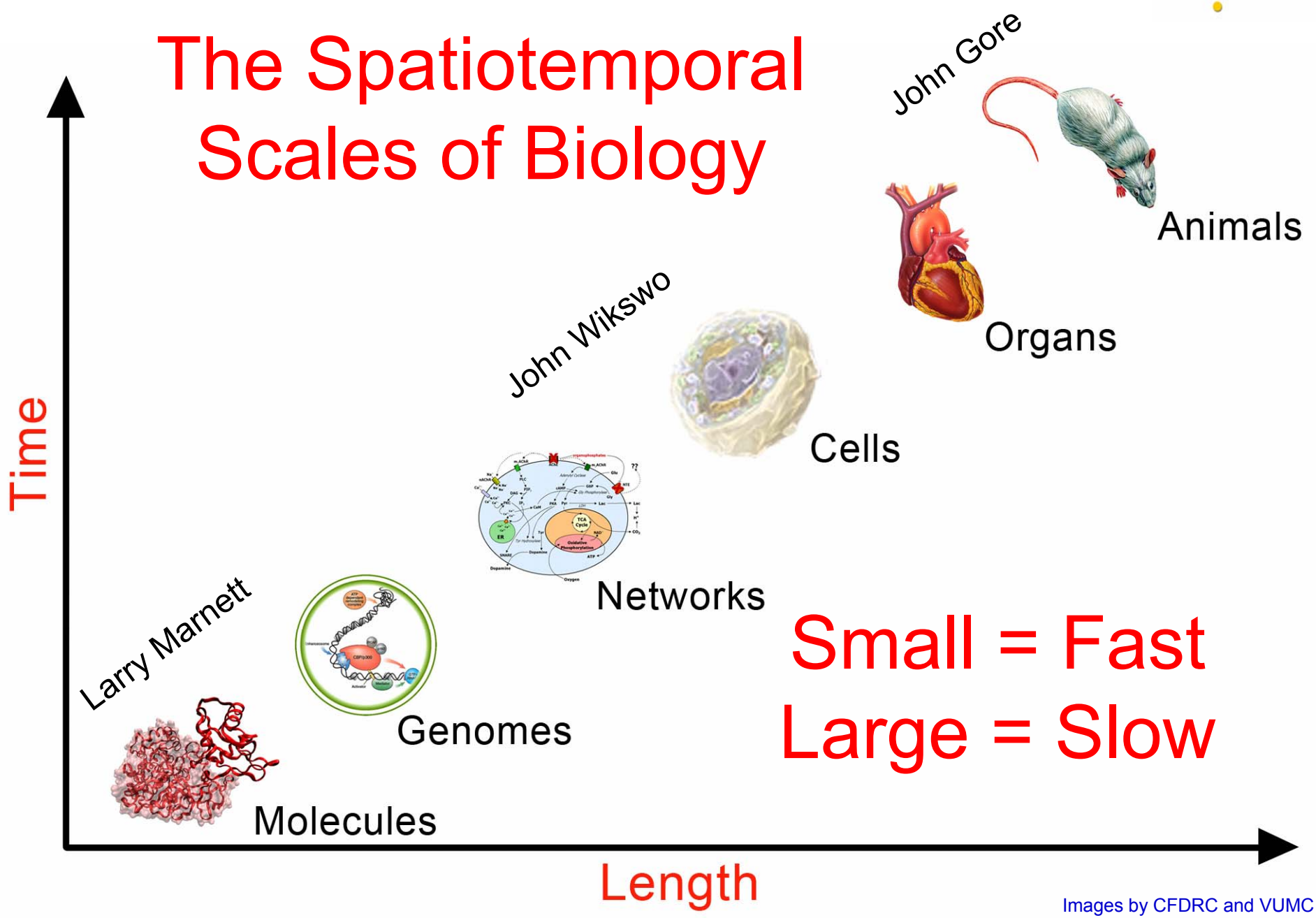
The Spatiotemporal Scales of Biology



Images by CFDRC and VUMC

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Biology is Complicated

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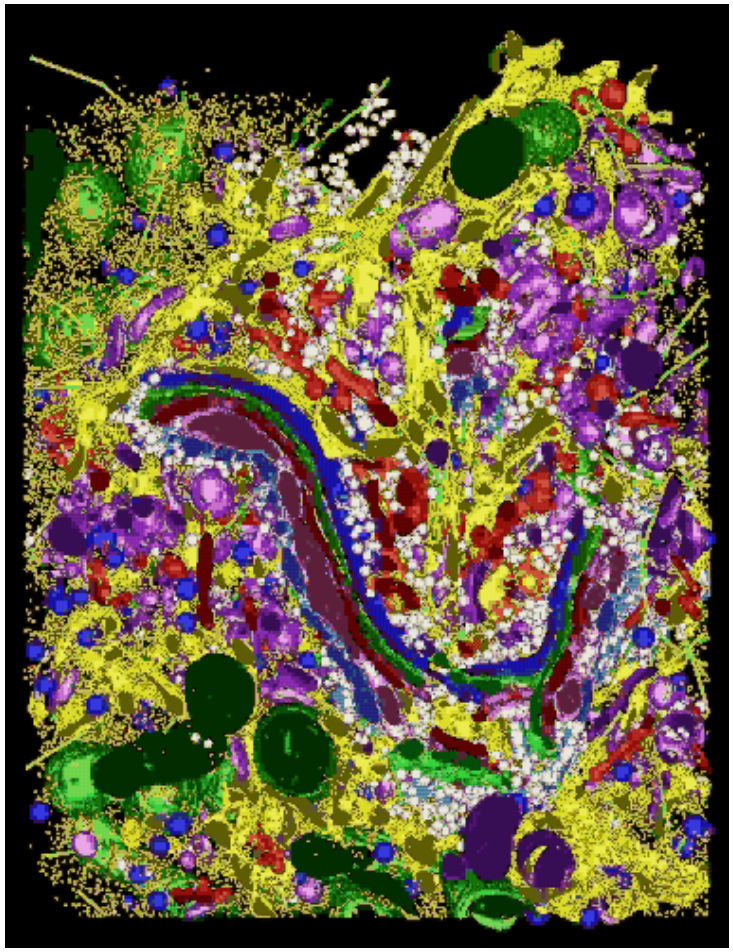
The Hardware

The protein processor inside a cell

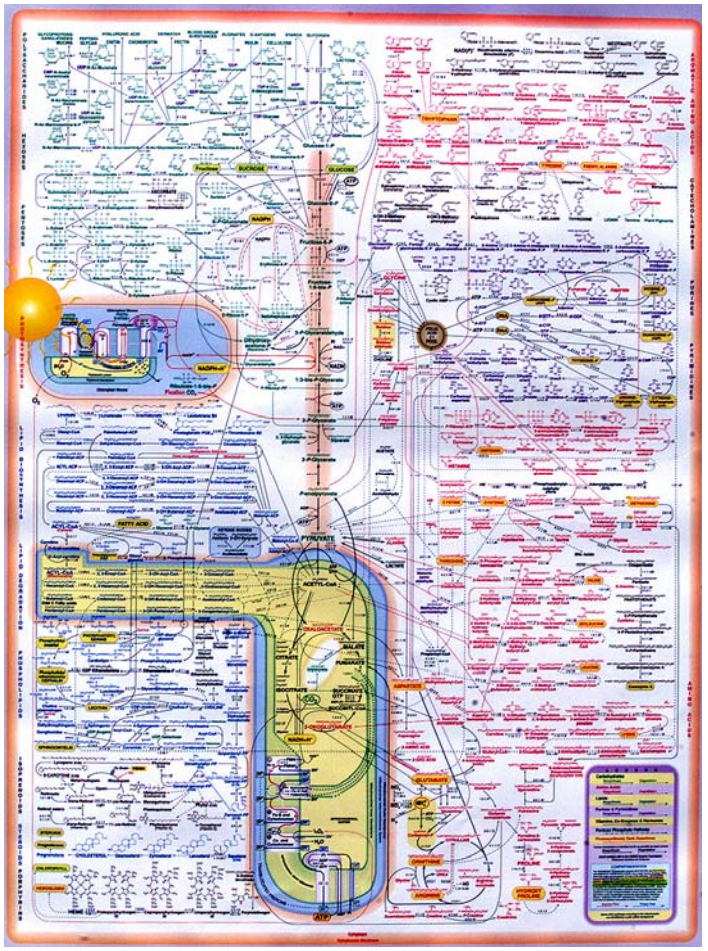


~ 1/30 the diameter of a human hair

B.J. Marsh, *et al.,* PNAS 98 (5):2399-2406, 2001.

The Software

Cellular metabolic network



1 cell ≈ 1 million equations

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Teaching Philosophy

The mind is not a vessel to be filled but a fire to be kindled.

Mestrius Plutarchus (c. 46- 127)

You cannot teach a man anything; you can only help him to find it within himself.

Galileo Galilei (1564-1642)

Education is what remains after one has forgotten everything one learned in school.

Albert Einstein (1879-1955)

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SyBBURE Goal

To provide undergraduate students, as early as possible in their academic careers, with training in specific research tools and active participation in interdisciplinary scientific research

- Students need to learn research tools and techniques BEFORE their senior year.
- Research training is intensive, hands-on.
- Near-peer mentoring: Students trained in SyBBURE can, as juniors and seniors, train sophomores.
- Honors theses and senior design projects will benefit from a cadre of pre-trained students.

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SyBBURE Components

- Peer-taught workshops in research tools
- Research teams of five undergraduates each, focusing on interdisciplinary projects involving quantitative measurements on living cells
- Topical seminar in journal club format
- $4,000/summer research stipend
- $1,000/semester academic year stipend
- Travel to conferences
- On-campus informal gatherings and other activities
- Poster presentations with VUMC, VUSE, VUSRP

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SyBBURE Statistics

- Summer 2006
  - 18 students, 13 sponsored full or in part by SyBBURE
  - 16 Vanderbilt (7 A&S, 9 VUSE),
    1 UCSD, 1 Freed-Hardeman U
  - 7 majoring in BME (6 VU, 1 UCSD)

- Fall 2006
  - Application required for admission
  - $1,000 stipend per semester
  - Academic credit available (Senior Design, BME 290C)
  - Can be part of a senior/honors thesis
  - Student instructors of formal workshops will be paid
  - 50 applications, 21 students accepted, with many continuing from the summer

SyBBURE VIBRE

SyBBURE Faculty and Staff

- Faculty
  - John Wikswo
  - Franz Baudenbacher
  - Chris Janetopoulos
  - Stacy Klein
  - Kevin Seale
  - Dmitry Markov
- Staff
  - Bryan Gorman
  - Raghav Ventkataraman
  - Phil Samson
  - Tobias Meyer
  - Don Berry
  - Allison Price

Undergraduate research that involves the development and application of technology requires intense supervision
… as does all levels of all research

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Summer 2006 Projects

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- **Jeff Chamberlain** – Division of Jurkat T-cells in a microfluidic Device. Mentor: Kevin Seale
- **Timothy Chen** – CD69 expression of individual T Cells activated simultaneously within a microfluidic device. Mentor: Kevin Seale.
- **Jennifer Colby** – Visualization of heterotrimeric G protein activation in living cells. Mentor: Chris Janetopoulos
- **Sara Davis** – Haptotactic component of cancer invasion. Mentor: Vito Quaranta
- **William Hooper** – Quantification of intracellular junction strength using a microfabricated spring assembly. Mentor: Franz Baudenbacher
- **Matt Houston** -- The effect of media flow rate on CD4+ T cell viability in microfluidic devices. Mentor: Kevin Seale
- **Michael Hwang** – Real-time computer control of pH in a microfluidic environment. Mentor: John Wikswo
- **Rachel Kochert** – Effects of PI3k on cytokenesis and chemotaxis pathways in *Dictyostelium discoideum*. Mentor: Chris Janetopoulos
- **Ruby Kwak** – Cellular chemotaxis. Mentor: Chris Janetopoulos
- **Adam Liegner** – Cell adhesion and pH control testing in microfluidic bioreactors. Mentor: John Wikswo
- **Alex Makowski** – Measurement of sarcomere length changes in cardiac myocytes. Mentor: Franz Baudenbacher
- **Steven Manual** – Failure testing of a microfluidic TURN valve. Mentor: John Wikswo
- **Rebecca Martinie** – Characterization of slug movement using a silicone bed of nails. Mentor: Chris Janetopoulos
- **Matt Pfister** – Primary CD4+ T cells calcium released activated calcium (CRAC) channel dynamics. Mentor: Kevin Seale
- **Erik Schneibel** – Microfluidic bioreactor for measuring yeast oscillations
- **Laura Smith** – Oxygen-sensitive films for microfluidics. Mentor: Dmitry Markov and Phil Samson
- **Jeremy Walker** – Evaluation of the local excitation global inhibition (LEGI) model of cell chemotaxis. Mentor: Chris Janetopoulos
- **Candice Weiner** – Quantification of separation forces between E-Cadherin mediated cell-cell pair adhesion. Mentor: Franz Baudenbacher

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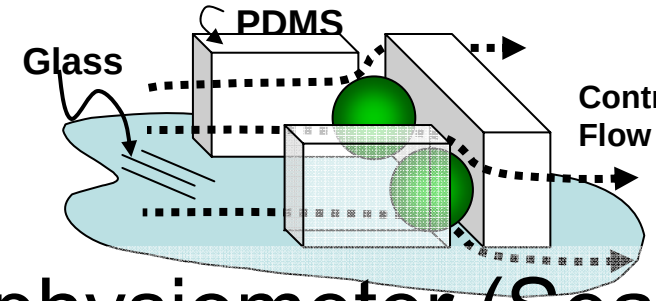
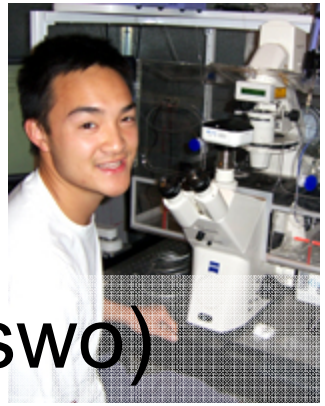
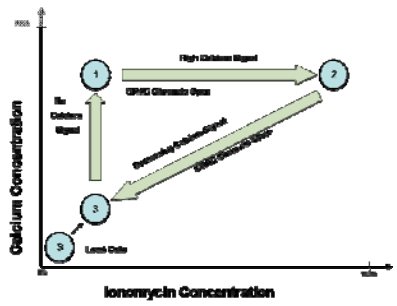
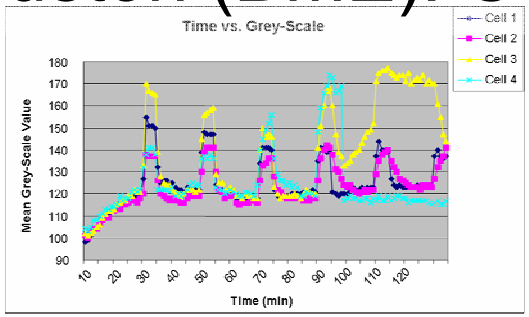
T-Cell Activation

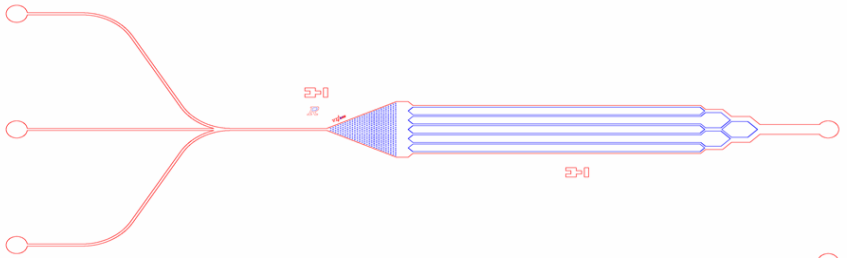




- T-Cell Nanophysiometer (Seale, Wikswo)
  - Jeff Chamberlain (BME): Jurkat cell division
  - Matt Pfister (BME): CRAC channel dynamics
  - Tim Chen (BME): CD69 T-Cell activation assay
  - Matt Houston (BME): Cell viability vs. flow rate







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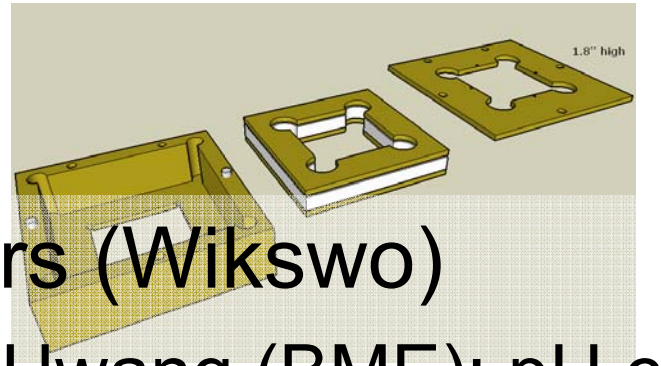
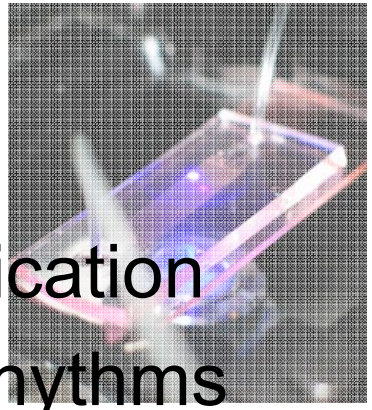
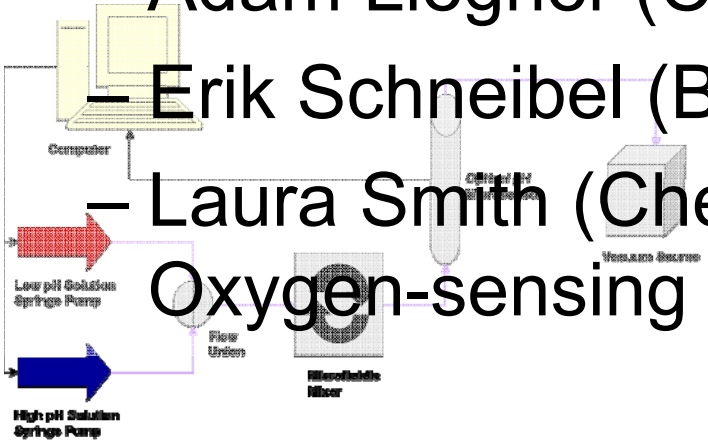
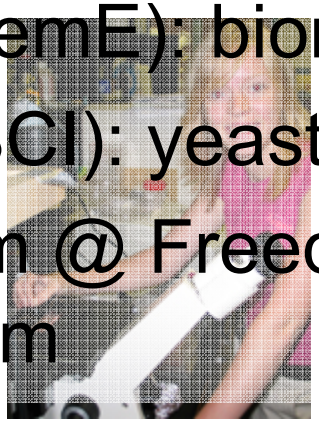
Bioreactor

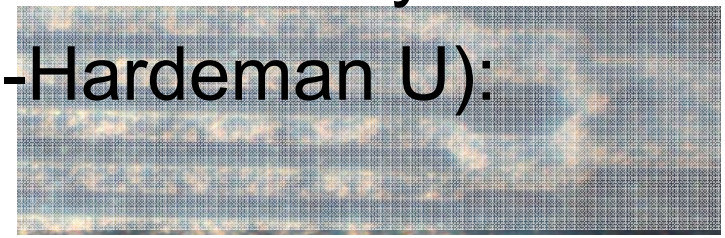


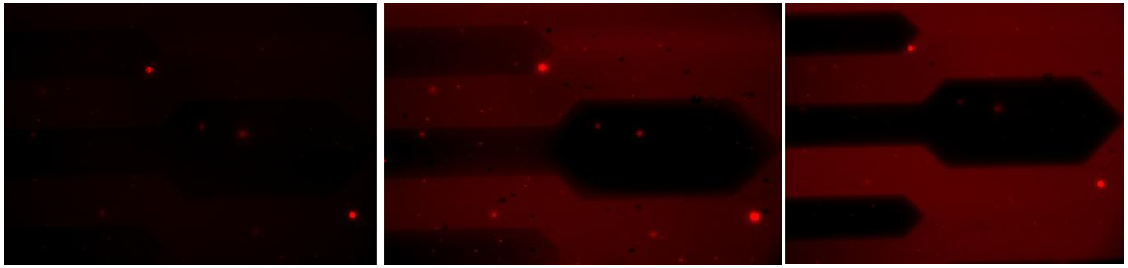
- Bioreactors (Wikswo)
  - Michael Hwang (BME): pH controller
  - Adam Liegner (ChemE): bioreactor fabrication
  - Erik Schneibel (BSCI): yeast circadian rhythms
  - Laura Smith (Chem @ Freed-Hardeman U): Oxygen-sensing film

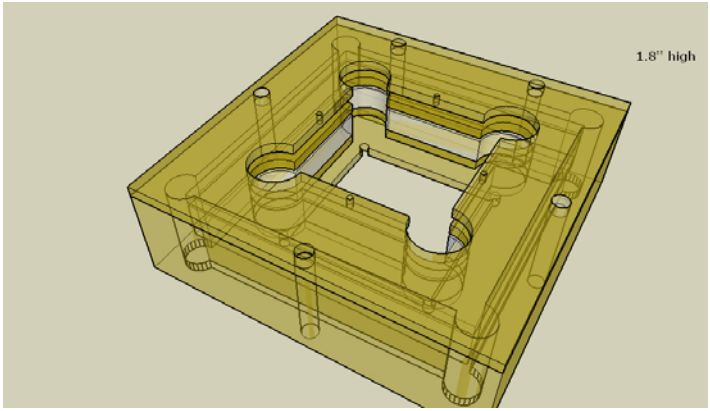












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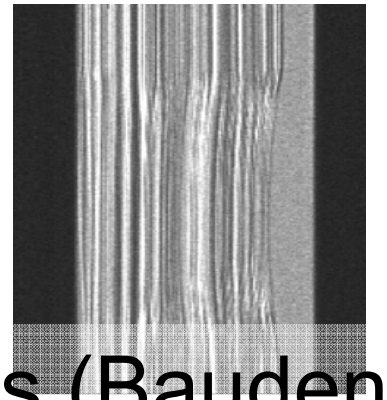
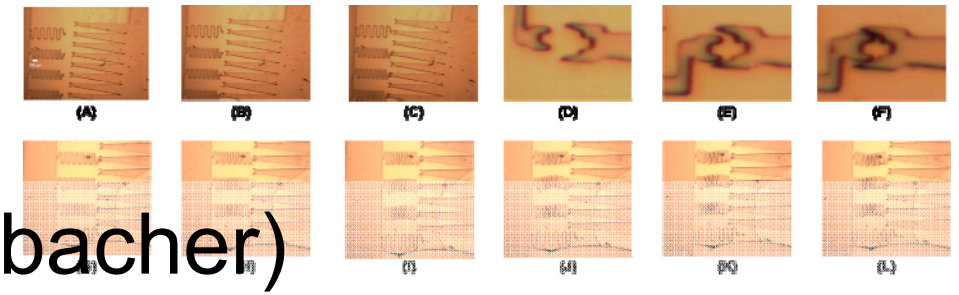
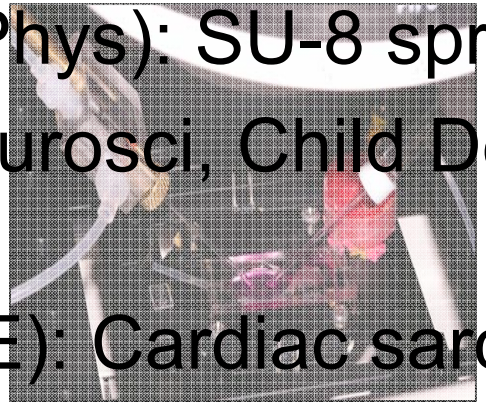
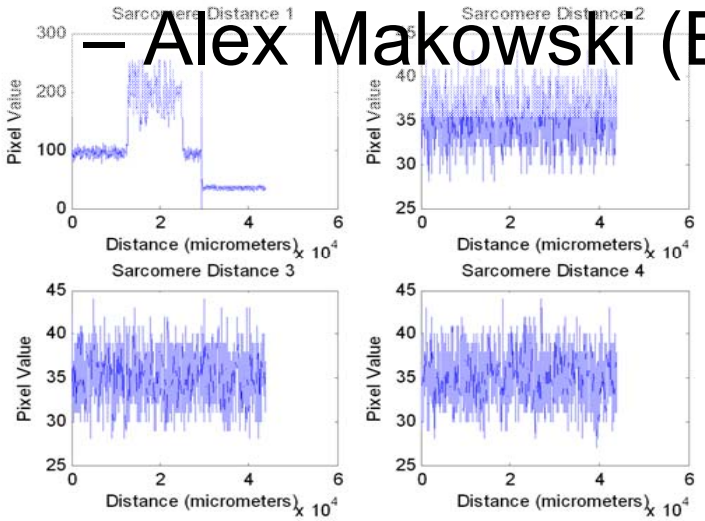


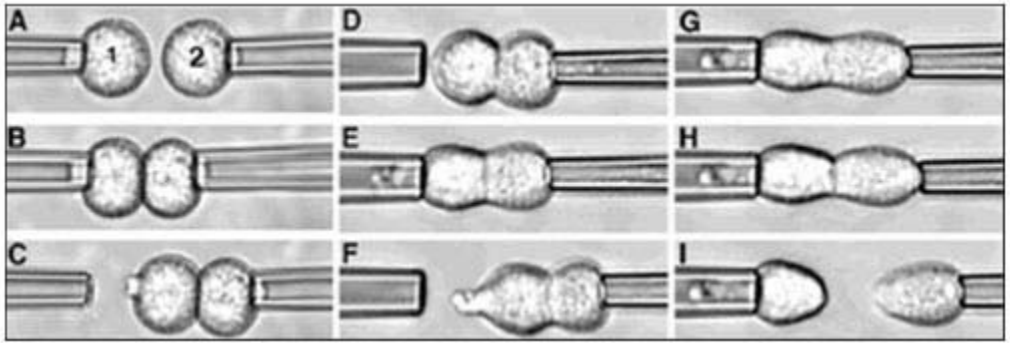
Cell Forces



- Cell forces (Baudenbacher)
  - Blake Hooper (ES, Phys): SU-8 springs
  - Candice Weiner (Neurosci, Child Dev.): Magnetic tweezers
  - Alex Makowski (BME): Cardiac sarcomere length







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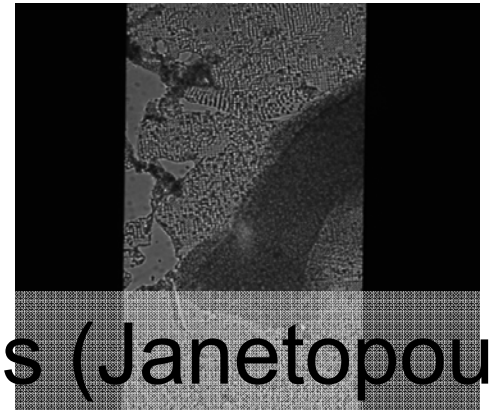
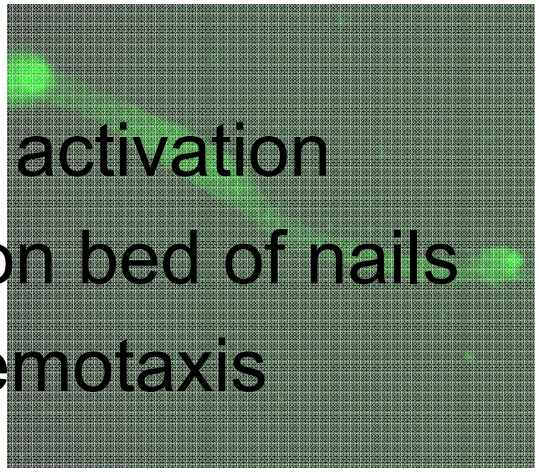
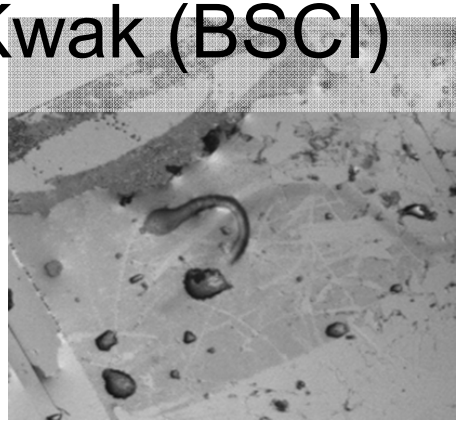
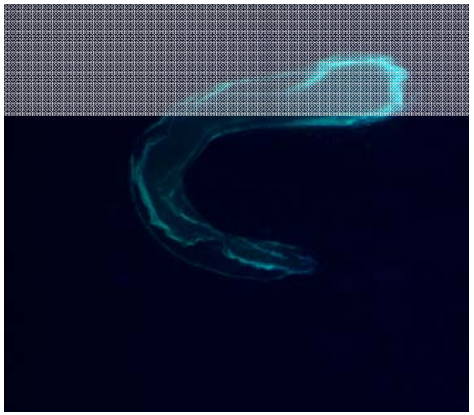


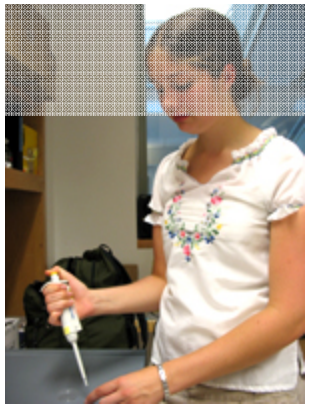
Chemotaxis

- Chemotaxis (Janetopoulos)
  - Jennifer Colby (BSCI): G-protein activation
  - Rebecca Martinie (BSCI): Dicty on bed of nails
  - Jeremy Walker (BSCI): Dicty chemotaxis
  - Rachel Kochert (BSCI)
  - Ruby Kwak (BSCI)









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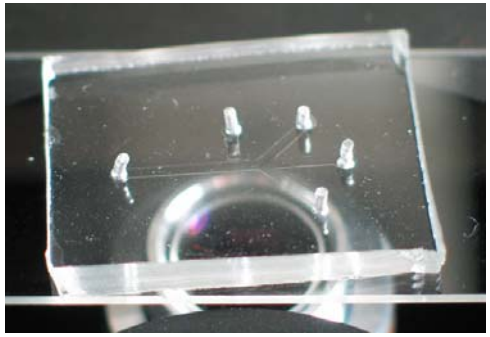
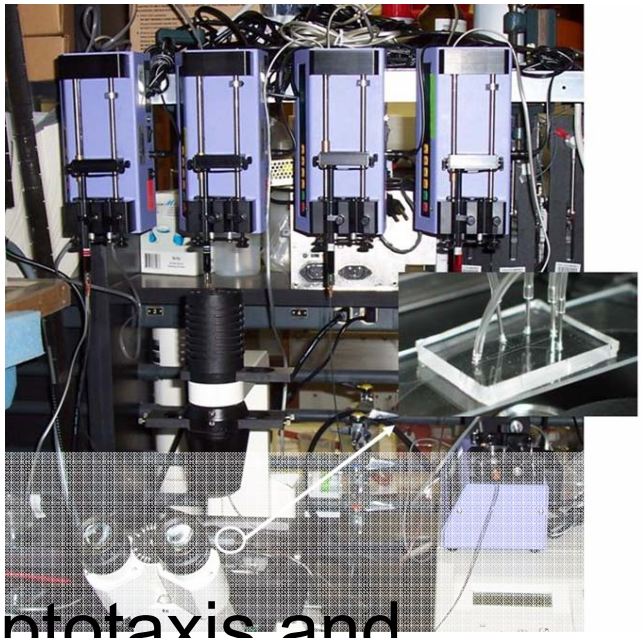
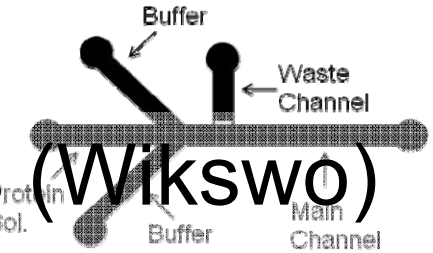
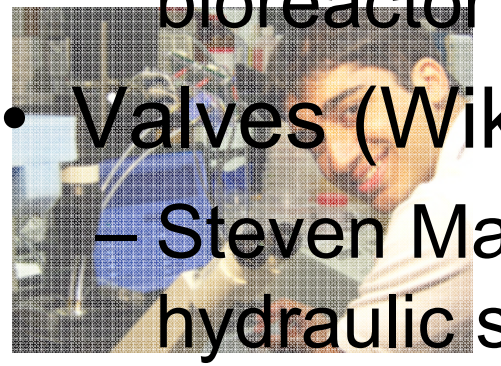
Computer Control of Microfluidics

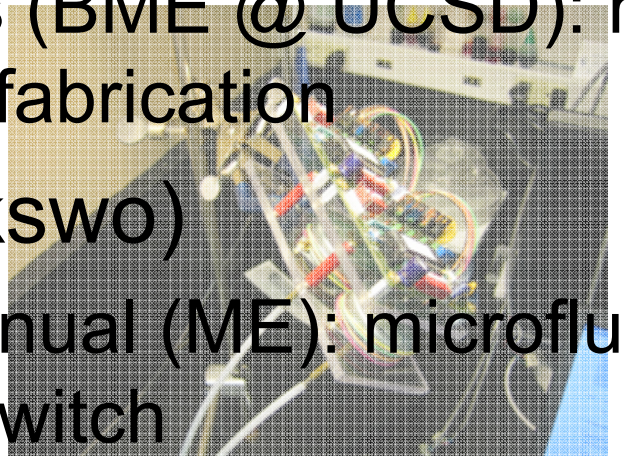


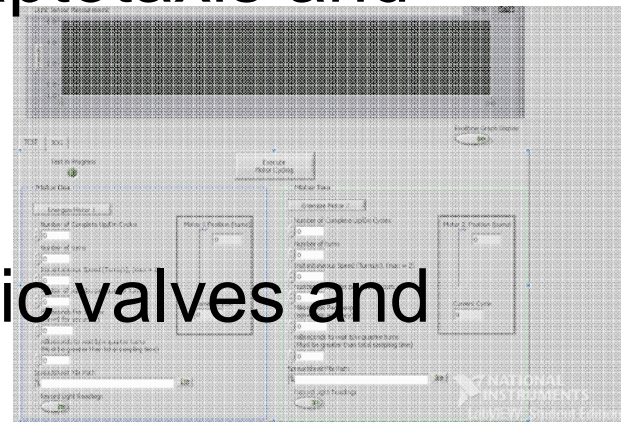




- Haptotaxis (Wikswo)
  - Sara Davis (BME @ UCSD): haptotaxis and bioreactor fabrication
- Valves (Wikswo)
  - Steven Manual (ME): microfluidic valves and hydraulic switch







Workshops

- **Developed and taught by students**
- Summer 2006:
  - Microfabrication
  - Java/ImageJ
  - AutoCAD
- All three workshops will be taught in Fall 2006
- Additional workshops under consideration
  - LabVIEW
  - MATLAB
- Seeking instructors
  - SyBBURE
  - **Underrepresented minorities**

Workshops Offered - Summer 2006

Date	Topic	Instructor	Course Materials
On demand	Microfabrication	Bryan Gorman	1. Sia,S.K. and Whitesides ,G.M. (2003) Microfluidic devices fabricated in poly(dimethylsiloxane) for biological studies. *Electrophoresis* 24, 3563-3576. 2. Beebe,D.J. et al. (2002) Physics and Applications of Microfluidics in Biology. *Annu. Rev. Biomed. Engr.* 4, 261-286.
On demand	AutoCAD	Laura Smith	N/A
2006_07_03	Java/ImageJ	Sara Davis	Tutorial PowerPoint: ImageJ_Tutorial

Weekly Journal Club

- Ten journal club sessions during summer, weekly during academic year
- Pizza
- Topics:
  - Ethics in science
  - Strong inference
  - Slidesmanship
  - T-cells
  - Chemotaxis
  - Microfluidic bioreactors
  - Cardiac myocytes
  - Efficient technical reading techniques
  - Student presentations
- Discussion/mentoring

SyBBURE

Systems Biology and Bioengineering Undergraduate Research Experience

SyBBURE Journal Club - Summer 2006

Number	Date	Topic	Discussion Leader	Article(s)
1	2006_06_08	T-Cells	Kevin Seale	1. K. Sachs, et al., "Causal protein-signaling networks derived from multiparameter single-cell data," *Science*, vol. 308, no. 5721, pp. 523-529, Apr.2005. 2. J. Wright, "Journal Clubs - Science as Conversation," *N Engl J Med*, vol. 351, no. 1, pp. 10-12. 3. A.D. Sokal, "Transgressing the Boundaries: Toward a Transformative Hermeneutics of Quantum Gravity," *Social Text* #46/47, pp. 217-252 (spring/summer 1996). 4. J. Stribling, et al., "Rooter: A Methodology for the Typical Unification of Access Points and Redundancy," *The Journal of Irreproducible Results*, vol. 49, no. 3, pg 5-8, May 2005.
2	2006_06_15	Chemotaxis	Rachel Kochert	1. C. Janetopoulos, et al., "Chemoattractant-induced phosphatidylinositol 3,4,5-trisphosphate accumulation is spatially amplified and adapts, independent of the actin cytoskeleton." *Proc Natl Acad Sci U S A*, 101(24), 8951-6, 2004. 2. J.D. Watson, "Succeeding in Science: Some Rules of Thumb," *Science*, New Series, vol. 261, no. 4129, pp.1812-1813, Sep. 1993.

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Access to Key Data

VIIBRE

Faculty Database | Employment | Services | News

VIIBRE

Vanderbilt Institute
for Integrative Biosystems Research and Education

VANDERBILT UNIVERSITY

About VIIBRE | Organization | Programs | Publications / Presentations | VIIBRE Funding | People

SyBBURE Master Page

We provide access to the following articles for individual educational use only under the Fair Use provision of the U.S. copyright law.

Item	Link	Notes
0	SyBBURE Directory	List of SyBBURE Students and Staff
1		Fill out VIIBRE Lab User Form (Ron Reiserer)
2	VandySafe	Mandatory Safety Training
3	VIIBRE Orientation	Read to be sure you understand staff to contact, access policies, phone numbers, etc
4		Turn in VandySafe certificate and schedule Lab Orientation with Ron Reiserer
5	VIIBRE Member Support	The central entry to VIIBRE facilities
6	Topical Reading	A repository of articles relevant to VIIBRE projects
7	BioMEMS Reading Lists	A list of pages that contain info on VIIBRE BioMEMS
8	SyBBURE_Projects	The internal-use SyBBURE student project reports
9	SyBBURE_Posters	Archive of all SyBBURE student posters
10	SyBBURE_Journal_Club	SyBBURE Journal Club articles and discussions
11	SyBBURE Workshops	Workshops offered by SyBBURE students, staff, and faculty

Automated/Shared Student Reports

VIBRE SyBBURE

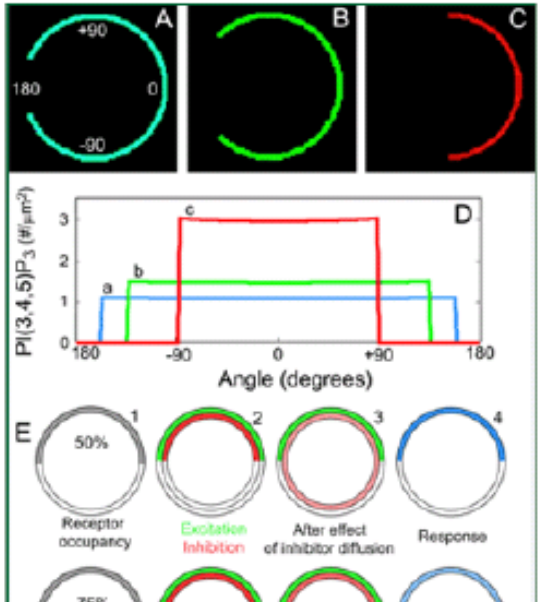
Jeremy Walker

Evaluation of the Local Excitation Global Inhibition (LEGI) model of cell chemotaxis

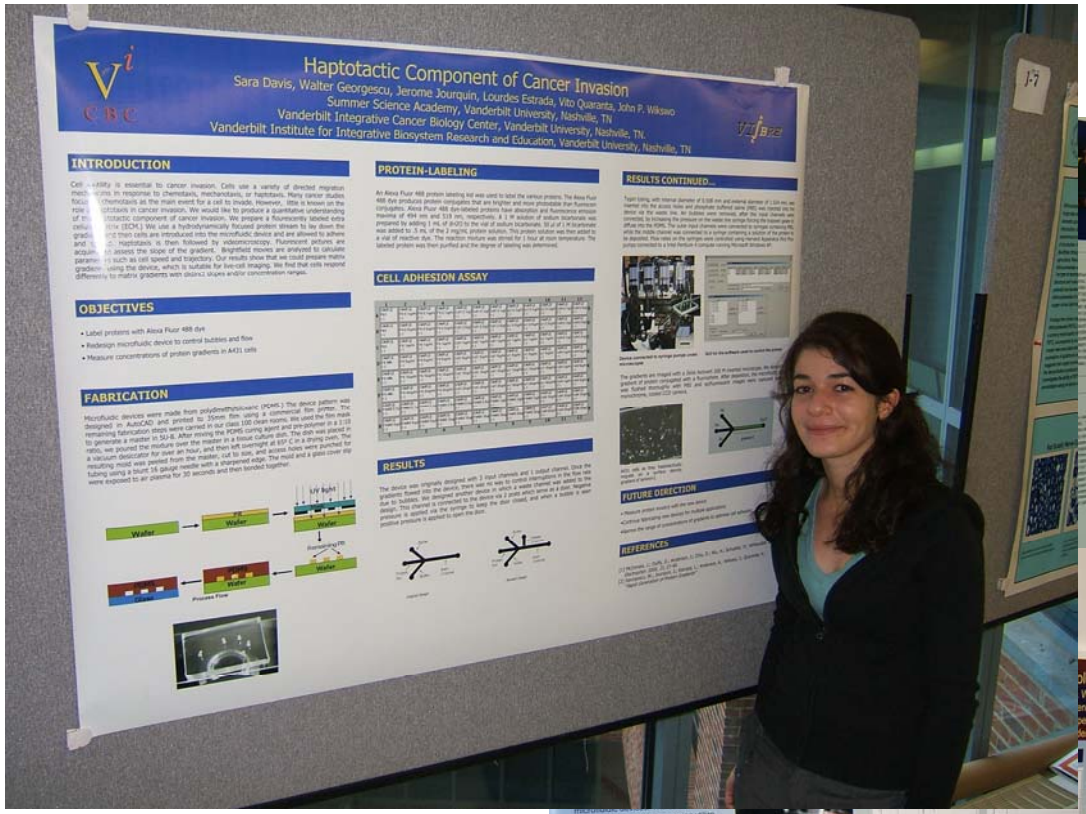
Abstract

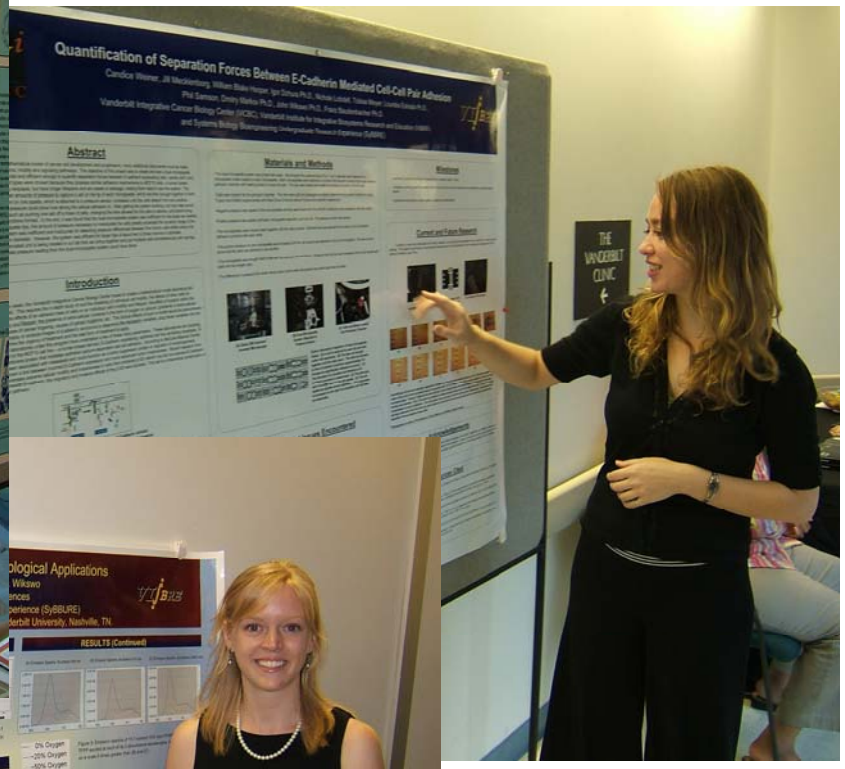
Many cell types have the ability to move in reaction to chemical gradients. This process, known as chemotaxis, is sensitive even to very shallow gradients (1). Chemotaxis plays a vital role in immunity, embryological development, and wound healing and is also involved in inflammation, allergic responses, and cancer metastasis (2, 3). In order to better understand these processes, it is necessary to understand the mechanism by which cells sense and respond to external chemical gradients. By studying chemotaxis in *D. discoideum* , we hope to illuminate the pathways involved in chemotaxis in humans.

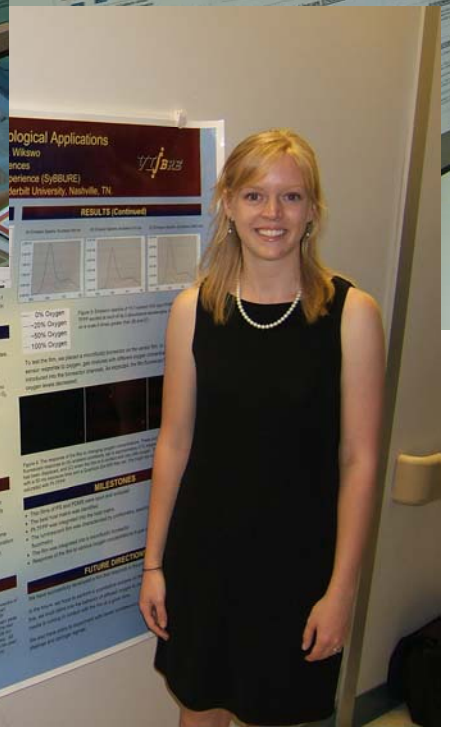
D. discoideum , an amoebic slime mold found in soil and leaf litter, was chosen as the model system for studying chemotaxis because of its hardiness and because its genome can be altered with reasonable ease. Also, the pathways involved in *Dictyostelium* chemotaxis bear significant resemblances to the pathways involved in human neutrophil chemotaxis (4). In both cell types, it is evident that directional sensing is marked by the accumulation of phosphatidylinositol 3, , 5-trisphosphate [PI(3,4,5)P 3] on the plasma membrane, regulated by a heterotrimeric G-protein pathway (5). This G-protein pathway allows for significant amplification of the chemical gradient. [PI(3,4,5)P 3] is created by the phosphorylation of [PI(4,5)P2] by PI3 kinase (PI3K) (5). Once formed, [PI(3,4,5)P 3] recruits several other proteins to the membrane, ultimately leading to actin polymerization and the extension of pseudopodia. Using the GFP-labeled pleckstrin homology (PH) domains of one



SyBBURE Posters – VUMC Session

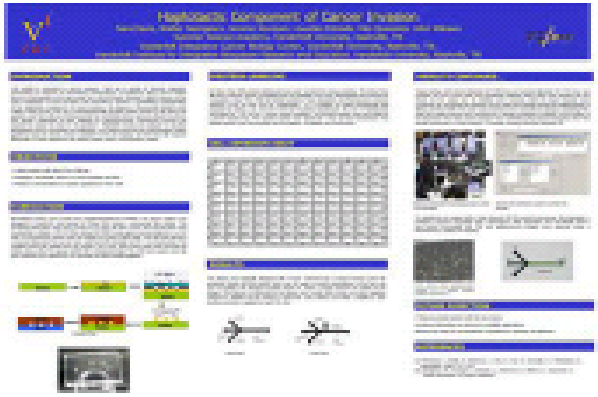
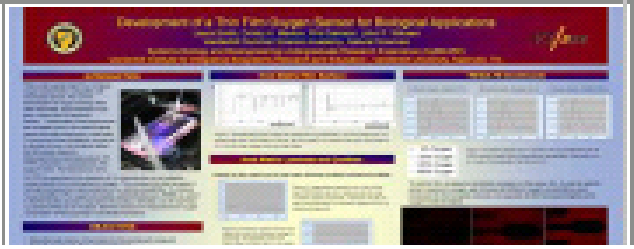






SyBBURE Students Teach Students

-- Poster Repository --

SyBBURE Poster Repository		
See Also: VIIBRE Poster Repository		
NEW: INSTRUCTIONS FOR VUSRP (SEPT 6) POSTER SESSION Poster dimensions: 42 inches high and 48 inches wide Posters will be presented in rooms B&C of the Grand Ballroom of the Student Life Center from 4-5:30 PM. Please set up a poster and present even if you can only be there a few minutes!		
Primary Author(s), Title, and Presentation Date	**Thumbnail**	**PPT file (size)**
Davis, Sara Haptotactic Component of Cancer Invasion August 4, 2006		SyBBURE_POSTER_2006_Davis_Sara (7.05 MB)
Smith, Laura Development of a Thin Film Oxygen Sensor for Biological		SyBBURE_POSTER_2006_Smith_Laura (8.03 MB)

SyBBURE

VIBRE

The Future

- Continue with this format – construct a pipeline of research-active undergraduates, beginning with the summer after the freshman year.
- Add a small number of non-science students
- Maintain *Transinstitutional* emphasis
- Devise additional workshops
  - LabView
  - Machine shop
  - Electronic instrumentation
- Develop evaluation tools
- Extend workshops to non-SyBBURE students
- …

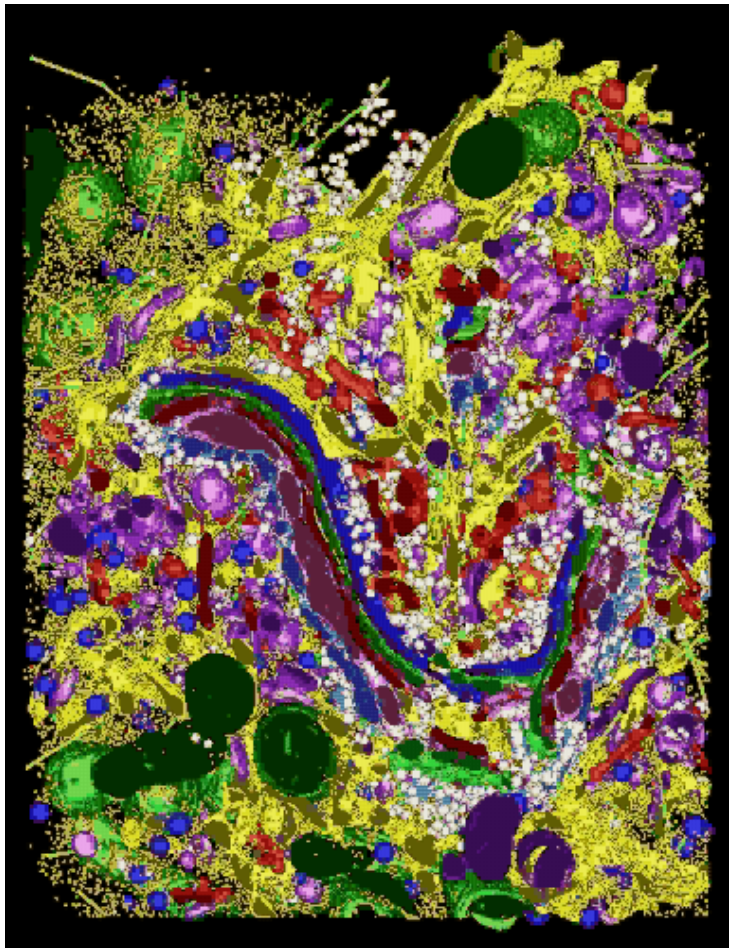
SyBBURE

Biology is Complicated

VIBRE

The Hardware

The protein processor inside a cell

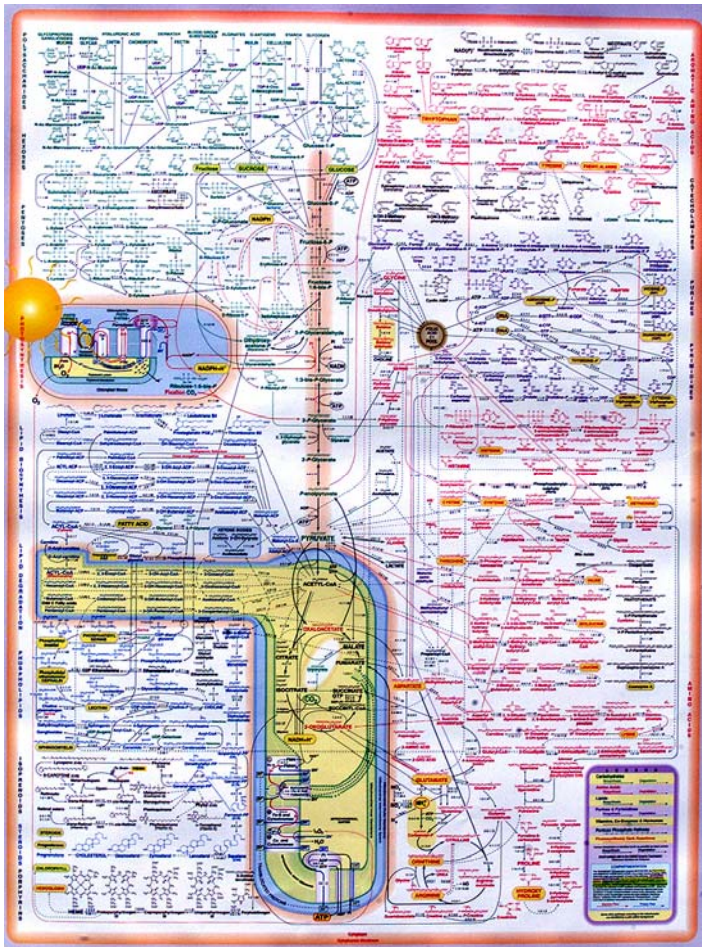


~ 1/30 the diameter of a human hair

B.J. Marsh, *et al.,* PNAS 98 (5):2399-2406, 2001.

The Software

Cellular metabolic network



1 cell ≈ 1 million equations

End of Presentation. Click to go beyond the end

SyBBURE VIBRE

Question 1 - What are the most important things that you learned during the SyBBURE summer?

Students identified three main areas of learning:

- the overall experience of working in a research environment
- the development of lab skills and techniques
- a better understanding of what constitutes scientific research.

- “I learned that research is not just a 9-5 job. You really need to have passion for a field that does not have many immediate conclusions and rewards.”

SyBBURE VIBRE

Question 4 - What were the best aspects of the SyBBURE summer?

Most students commented positively on the independence they experienced in the program, commenting particularly on the control they had over their own projects. Most liked the team aspect of the program and working with peers who, like them, had little experience in a lab setting and conducting research.

- "I really enjoyed the fact that we got a mentor and a small team to work with. I found it really helpful to ask my mentor and team members questions."
- "Effective structure of teams under a common PI – we each had our own project but still worked together to make our experiments run smoothly."

Question 11 - Please offer your opinion on the overall strengths of the program specifically and of undergraduate research more generally.

The most common strength mentioned is the insight into graduate research life that the interns receive.

- “This program is a great look at how grad school will be. Because we worked closely with grad students, we were able to see a glimpse of what we are in for if we choose to attend grad school.”
- “The primary strength of the program is that it truly introduces undergraduates to the research environment and overall process involved. Learning the basics seems to be one of the more arduous tasks with conducting research, and I think that this early introduction as an undergraduate is extremely important.”

SyBBURE VIBRE

Question 12 - Has the SyBBURE program altered either your views towards science and/or engineering, or your professional aspirations? If so, how?

Most respondents said that participation in the program had not altered their aspirations but rather clarified what they can expect from attending graduate school and conducting research. Only a few felt that this clarification would deter them from following the path to graduate school and advanced research.

- "SyBBURE has definitely altered my views on research. I learned that research is not exactly the profession with the most immediate results and that passion and interest are key to a successful life in research."
- "I think it has jaded me on research. Over this summer, I got a picture of what research would be like for a job and have decided that I do not want to go that route."
- "Yes, research did not seem very appetizing before I participated in the summer program. I found that research becomes more interesting once you understand the topic in more depth."