MILLER INSTITUTE NEWSLETTER

Winter 2006

Miller Fellow Focus: Josh Shaevitz

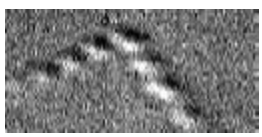
Second-year Miller Fellow Josh Shaevitz studies how motion is produced by living cells. He is hosted by Daniel Fletcher in Bioengineering, Mimi Koehl in Integrative Biology and George Oster in Molecular and Cellular Biology.

In Isaac Asimov's 1966 book *Fantastic Voyage*, a manned submarine is miniaturized and sent into a human body to fight a life-threatening blood clot in the brain of the one man who could decide the fate of the Cold War. While this bit of science fiction is certainly fantastic, nature has already designed a fleet of micron-sized submarines capable of swimming and crawling and equipped with tools for self-replication and all out war with the surrounding environment. These tiny vessels, also known as bacteria, are the most abundant living organisms on our planet and, for many of them, the ability to move is the difference between survival and extinction. Josh's goal is to bring together concepts and techniques from biology, physics and chemistry to unravel the mystery of how these tiny creatures locomote.

Throughout his career, Josh has developed new tools for physically probing biological systems. At the heart of his research lies the optical trap, a device that uses focused laser light to apply controlled forces to biological molecules and cells. Because light carries momentum, an object that deflects light will feel a counteracting force. Micron-size dielectric materials, including cells, at the focus of a high-powered laser beam become trapped and act as if they are held by a three-dimensional spring – a spring made of light. In addition, by measuring the deflection of the laser light one can calculate the position of an object relative to the laser focus.

One beautiful and potentially deadly form of motility is performed by the intracellular pathogens *Listeria monocytogenes*, a major cause of food poisoning from poultry, and *Rickettsia rickettsii*, the agent of Rocky Mountain spotted fever. Both of these bacteria infect eukaryotic cells and commandeer the host cell's actin cytoskeleton, a dynamic network of branched polymers which is integral in a number of biological processes. By expressing a single protein on their exterior these bacteria nucleate a dense network of actin filaments, termed a comet tail, that has the net effect of pushing a bacterium through the host cell's interior. When the bacterium has used up the host cell's resources it uses the same actin cytoskeleton to destroy the host and infect an unsuspecting neighboring cell. While the biochemistry of this process is fairly well understood, significant gaps exist in our physical understanding of how actin network polymerization leads to movement.

Josh has been using his high-resolution optical trapping instrument to track the motion of actin-propelled microspheres in three-dimensions.



Kinked Spiroplasma

Using this data he has experimentally validated the proposal that actin networks grow non-uniformly, moving in fits and starts. Unlike the uniform step size of other motor proteins like kinesin, myosin and RNA polymerase, actin networks move with a variable step size governed by the stochastic nature of filament polymerization.

Bacteria driven by actin polymerization often move in curved paths rather than straight lines. Physical explanations for this phenomenon make specific

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Deadline To Note:

Wednesday, February 8, 2006
Visiting Miller Professorship nominations due

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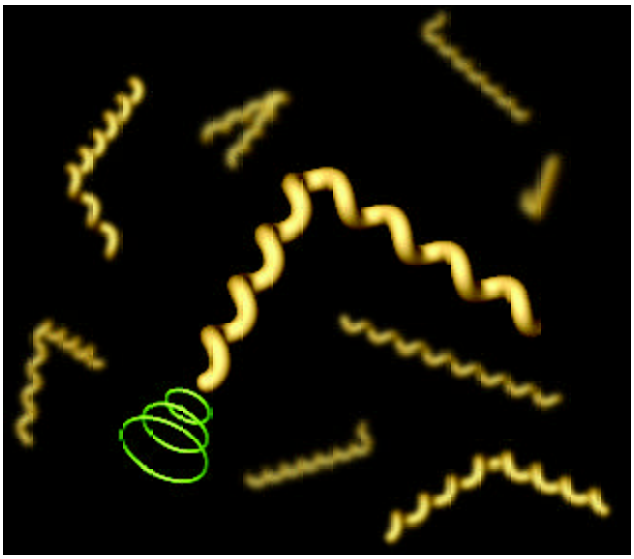
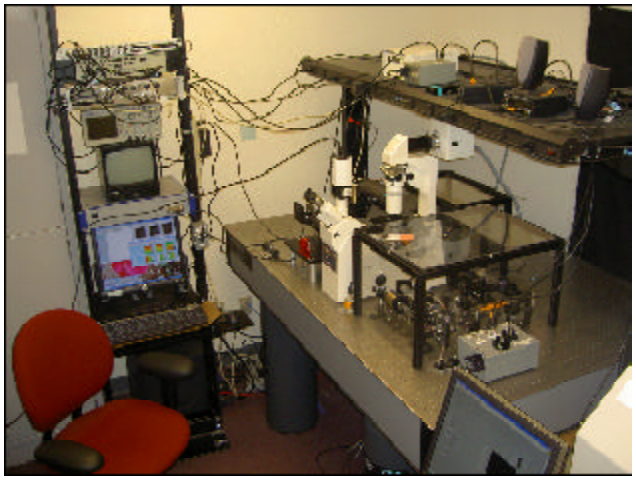
predictions of the curvature explored by a bacterium, but quantitative information about network curvature has been difficult to obtain with traditional techniques. By calculating the instantaneous curvature in his microsphere tracks, Josh has been able to examine the dynamic properties of network curvature. These measurements have been used to rule out several theories of network motion based on the stochastic placement of filaments, but lend support to a feedback mechanism that tends to make actin networks straighter rather than curved. Josh has also used the optical trap to steer actin-propelled microspheres. Compared to the amount of force generated in the forwards direction, surprisingly little force is needed to turn an actin network left or right. This mechanical advantage may be used during the complex processes of chemotaxis and phagocytosis where actin networks need to quickly change their growth directions.

Unlike actin-propelled pathogens, which require the presence of host cell proteins to move, other bacteria can swim freely in water and other inert environments. For a bacterium, swimming is a relatively complex problem of coupling cellular motions to an external fluid environment in order to move. This form of motility is particularly interesting because of the unique requirements placed upon very small swimmers. In this regime, quantified by a very small Reynolds number of about 10^{-6}, inertial forces matter very little and swimming bacteria must rely solely on viscous forces to propel themselves. Bacteria can't coast. If an *E. coli* stops swimming it will slide forward by less than 0.1 angstroms, or about 1/100,000 of its body length. Imagine an Olympic swimmer stopping mid-stroke and coasting only 1/1,000 of an inch! The result of this quirky behavior is that back-and-forth flapping of appendages gets you nowhere. To get around this, many microorganisms swim by spinning or wiggling slender limbs called flagella or cilia. However, very little is known about the swimming mechanism used by those bacteria that lack such appendages.





Optical Trapping Instrument

One such bacterium is called *Spiroplasma* due to its helical shape. These cells are members of a class of very small bacteria that have undergone evolutionary reductionism – shedding their cell walls and shrinking the size of their genomes as well as their physical size. *Spiroplasmas* are incredibly thin, typically 50 nm wide, have a helical pitch of about half a micron and can range from 1 to 8 microns long depending on species. These bacteria possess the ability to swim in environments too viscous for flagellated bacteria to go and are pathogens of plants and insects, causing millions of dollars in damage to corn and citrus crops in the U.S. each year. Despite their tremendous environmental impact, the mechanism that allows them to move in such environments has remained a mystery.

Josh and his coworkers used a high-resolution imaging microscope to visualize *Spiroplasma* cells and watched them swim. Contrary to the belief that these cells corkscrew through viscous media to move, swimming is generated by a processive change in body helicity from right-handed spirals to left-handed ones. This change starts at the front of a cell and sweeps to the back. At the junction point between the two helicities, the cell bodies are bent, like the kinks you find in telephone cords that have gotten twisted up. This bend sweeps fluid from the front of the cell to the back, which in turn imparts a force to the bacterium that propels it forwards. So, while rotation does unwind the helix from right- to left-handed and back, movement of the kink is actually what drives forward progress. Using this mechanism, *Spiroplasma* are able to go where no bacterium has gone before.

This is an exciting time in the interdisciplinary field broadly known as biophysics. New tools, like the ones Josh has developed for studying biological motion, have enabled us to learn about things that we could only dream about a few decades ago. Josh hopes to bring these techniques to other areas of biology in order to learn more about how structure and movement are created in living organisms.

Miller Professorship Awards

The Miller Institute is happy to announce the awards for Miller Research Professorship terms in Academic Year 2006-2007. Recipients are released from teaching and administrative duties, allowing them to pursue their research, following promising leads as they develop.

Donald Backer	Astronomy
Jillian Banfield	Earth & Planetary Science / Environmental Science, Policy, and Management
Cheryl Briggs	Integrative Biology
Richard Saykally	Chemistry
Nicola Spaldin	Materials Science & Engineering (UCSB)
Mark Van Der Laan	Public Health
Alexander Zettl	Physics

Visiting Miller Professorship Awards

The Miller Institute is pleased to announce the Visiting Miller Professorships granted during the Fall competition cycle. The purpose of the Visiting Professorship program is to bring promising or eminent scientists to the Berkeley campus for collaborative research interactions. The recipients will be on campus for terms during academic year 2006-07.

Alice Guionnet *Unité de mathématiques pures et appliquées, Ecole Normale Supérieure de Lyon, France*	Mathematics / Statistics
Yong Baek Kim *University of Toronto, Canada*	Physics
Andrey Kravtsov *University of Chicago, Illinois*	Astronomy
Klaus Müller-Dethlefs *University of Manchester, England*	Chemistry

Announcement

This is the last year that we'll be having a second spring competition cycle for the selection of Visiting Miller Professors. Starting in the Fall of 2006 for award terms in 2007-08 we will hold a single Visiting Miller Professorship competition each year. The Visiting Miller Professor nominations will be considered during the fall, at the same time we consider Miller Professors and Miller Fellows. By conducting all competitions during the fall, we will be better able to make budget decisions that impact the selection process.

This year's competition deadlines are as follows:

Miller Fellowship nomination deadline - Thursday, September 14, 2006
Miller Professorship application deadline - Thursday, September 21, 2006
Visiting Miller Professor nomination deadline - Monday, September 25, 2006

Next Steps

Alex Thompson (Miller Fellow 2003-05) has taken a Research Scientist position with The British Antarctic Survey. The Miller Institute congratulates Alex on her future endeavors.

The Miller Institute Celebrates 50 Years

The Miller Institute celebrated its 50th anniversary on December 9-10, 2005. A reception was held on Friday evening, and Saturday featured an interdisciplinary symposium, followed by a festive dinner and party. To view a more extensive gallery of photos from this event, please visit the Miller Institute's website at: http://millerinstitute.berkeley.edu/50th

Nancy Kopell and Jiaxing Huang

Garniss Curtis and Gilbert Hawkins

Kathryn Miller and Beth Burnside

Douglas Abraham, David Jablonski, Susan Kidwell, and Ellen Simms

Matt Reidenbach, Erin Cunningham, and Rory Waterman

John Barrow

Awards & Honors

Boris Zemva (Visiting Miller Professor Spring 1993) has been selected as the recipient of the 2006 ACS Award for Creative Work in Fluorine Chemistry.

Grigory Barenblatt (Visiting Miller Professor Spring 1996) is the recipient of the Timoshenko Medal for his distinugished contributions to applied mechanics.

Alison Galvani (Miller Fellow 2002-04) was awarded a Young Investigator prize by the American Society of Naturalists.

Venkatesan Guruswami (Miller Fellow 2001-02) was selected for a 2005 Packard Fellowship for Science & Engineering.

B. Lynn Ingram (Miller Professor 2003-04) was elected a Fellow of the California Academy of Sciences.

Nicholas Jewell (Miller Professor Fall 1994, Fall 2004) received the prestigious 2005 George W. Snedecor award for an outstanding publication in biometry.

Michael Manga (Miller Fellow 1994-96) was awarded the prestigious MacArthur Fellowship.

John Prausnitz (Miller Professor 1966-67 and 1978-79) received an honorary doctorate degree from the University of Padua, Italy, in April 2004. At the College of Chemistry Commencement, May 2004, Chancellor Berdahl presented him with the Berkeley Citation.

Mark van der Laan (Miller Professor 2006-07) was presented with the 2005 Presidents' Award by the Committee of Presidents of Statistical Societies.

The following Miller Members were elected as fellows to the American Association for the Advancement of Science:

Bruce Bolt - Miller Professor, 1967-68, 1989 (posthumous award)
Richard Eisenberg - Visiting Miller Professor, Spring 2005
James Haber - Visiting Miller Professor, Spring 2005
Peter Molnar - Visiting Miller Professor, Fall 2005
David Wemmer - Miller Professor, Fall 1998

The Miller Institute is happy to share news of awards and honors received by past members. Please notify us with details of awards you or other past members receive so that we can include them in our list. Additional news on members is listed on our website at http://millerinstitute.berkeley.edu/awards

Obituaries

Serge Lang, Visiting Miller Professor Fall 2004, Emeritus Professor of Mathematics at Yale University, and the most prolific modern writer in his field, passed away on Septermber 12, 2005. He was 78.

Miller Institute News
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Miller Members In The News

Former Miller Professor **Paul Alivisatos**' research on nano-sized semiconductors was featured in Lawrence Berkeley Lab's Research News. To read more about this, see: http://www.lbl.gov/Science-Articles/Archive/MSD-nanocrystal-solar-cells.html

Miller Fellow **Deep Gupta** and his team members' creation of a Bose-Einstein condensate in a storage ring was featured in a UC Berkeley Press Release. For more information, please go to: http://www.berkeley.edu/news/media/releases/2005/09/06_bec.shtml

A sculpture illustrating a 3-D 'shadow' of an object in the fourth dimension, designed by former Miller Fellow **Adrian Ocneanu**, was featured in Science News Daily. Full article is located here: http://www.sciencenewsdaily.org/story-7409.html

Former Miller Professor **Karl Pister** was featured in California Monthly as Alumnus of the Year. To read the whole story, please see: http://alumni.berkeley.edu/calmag/200601/alumnus.asp

Publications

The following Miller Institute members have recently published works resulting from research during their Miller Institute terms. For more information about these publications, please visit the Miller Institute's website at: http://millerinstitute.berkeley.edu/publications.htm

Raghuveer Parthasarathy
Miller Fellow 2002-05

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Joshua Shaevitz
Miller Fellow 2004-07

The Miller Institute is "dedicated to the encouragement of creative thought and the conduct of research and investigation in the field of pure science and investigation in the field of applied science in so far as such research and investigation are deemed by the Advisory Board to offer a promising approach to fundamental problems."