MILLER INSTITUTE NEWSLETTER

Winter 2010

Miller Fellow Focus: Eva Schmid

One of the most memorable experiences for a biologist in training is the first look through a microscope. The object of observation could be a human hair or a small spider, but no matter what it is, it is fascinating and a little scary. One immediately realizes that there is a whole new world of detail opening up in front of one's eyes. Glimpses of this world were first seen in the 1600s by Robert Hooke and Antonie van Leeuwenhoek, who took a big step towards the biology that is still taught in school today. Their observations were further developed by Theodor Schwann and Matthias Schleiden, leading to the 'cell theory', which stated: "All living things or organisms are made of cells."

We now know that some cells are organisms unto themselves (such as bacteria or amoeba), while other organisms evolved to live as a carefully orchestrated consortium of cells, which further specialized into tissues and organs. For this reason, cells are often called 'the building blocks of life'. Cells come in many shapes and sizes. They range from tiny bacteria about 1 µm in length, to nerve cells in giraffes that can grow up to 3 meters long or to the colossal 3 pound single cell comprising an unfertilized ostrich egg. Similar diversity becomes apparent when looking at cellular functions. Cells have become masters at adapting to their surroundings in order to survive in the unlikeliest of conditions.

As diverse as cells are, they have some fundamental features in common. Functionally, they all need to grow and divide. They need to communicate with their surroundings, sense changes and react accordingly. Structurally, all cells have a 'skin' called the plasma membrane, which separates the cell's interior from the environment. On the inside are the working parts, which enable the cell to metabolize and replicate, change shape, move, produce defense molecules, communicate and interact with their surroundings, as well as perform many, many more general or cell-specific functions.

In order to understand biological functions, biologists have often turned to so-called 'model systems'. Those are cells or organisms that are experimentally tractable in the lab and give insight into specific biological questions. So it happened that some selected organisms came to fame in the lab. The most widely used are the bacterium *Escherichia coli*, the bakers yeast *Sacchharomyces cerevisiae*, the fruit fly *Drosophila melanogaster*, the worm *Caenorhaptidis elegans*, the slime mould *Dictyostelium discoideum*, the plant *Arabidopsis thaliana* and the house mouse *Mus musculus*. Each one of them has made great discoveries possible by being a simpler model for a more complex cellular, developmental, neurological or behavioral phenomenon. But even though those model systems are much simpler than for example the human body, a redwood forest or a coral reef, they are still living systems, which are not completely understood and also not 100% controllable. There is a need for an even more reductionist approach in biology. The interdisciplinary collaboration of biologists, chemists, physicist and more recently, engineers, has led to the emergence of a new field known

continued on page 2

INSIDE THIS EDITION

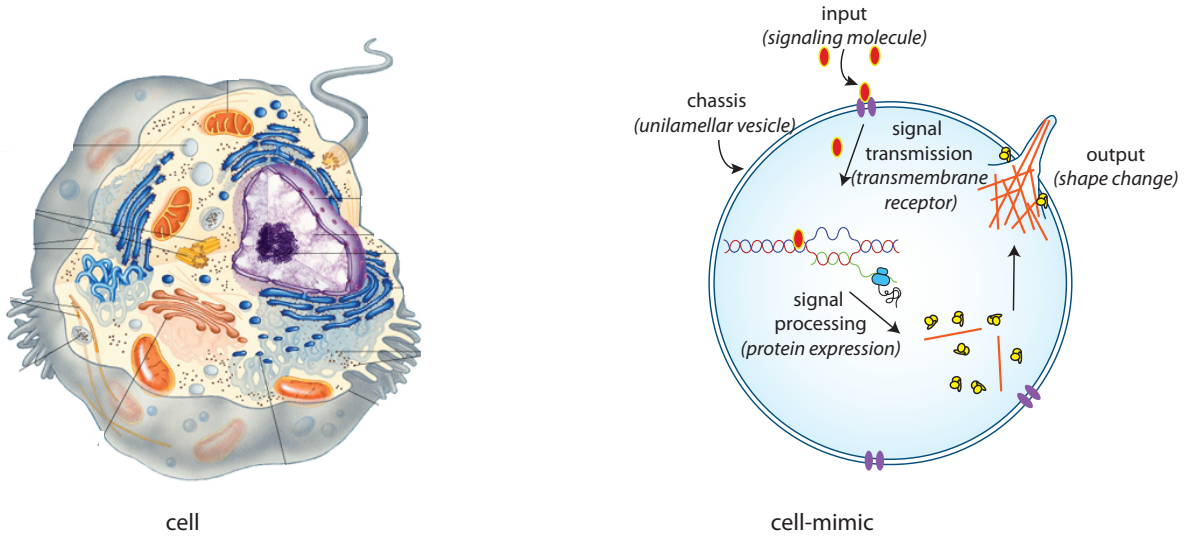


Figure 1: Building cell-like devices. The complexity that underlies cellular fuctions makes cells notoriously difficult to understand and control. The reconstitution of biological processes outside a living system in the form of highly simplified cellular mimics will aid in the understanding of isolated processes.

continued from page 1

by the names of reconstitutive biology or synthetic biology. This field is summarized well with the often-cited Feynman quote: "What I cannot create, I do not understand." It is taking a novel, complementary approach to traditional experimental biology. Rather than taking cells apart to understand cellular functions, scientists now attempt to mimic biological functions by building them from basic parts (Figure 1). This approach has great implications in basic research since it puts existing models of biological functions to the test: if we really understand how a process works, and know all its components, we should be able to build it from scratch. Furthermore, if we can indeed reconstitute biological functions in the lab, a wide field of applications in healthcare, energy and material science comes into reach.

Eva Schmid, a second year Miller Fellow in the Department of Bioengineering, is using this approach to move closer towards a new model system, a 'synthetic cell-like system'. Such a system aims to form the basis for a widely applicable method to test biological models. The system will have to encompass a basic setup of functions: (1) compartmentalization of biological components within micron-sized lipid bilayer vesicle, separating 'inside' from 'outside'; (2) a sensory system, which recognizes a signal from the outside and transmits it to the inside; (3) a signal processing function within the vesicle, which leads to, (4) a visually detectable output (Figure 1 right).
Eva takes advantage of the interaction with physicists and engineers in Dan Fletcher's laboratory. This mix of expertise recently led to the development of a technique that enabled the encapsulation of bio-molecules within membranous compartments, thereby fulfilling the first requirement of a cell-like system.

How is that achieved? The technical principle is somewhat similar to blowing soap bubbles. Just instead of air deforming a soap film, a fluid jet (generated by a piezo-controlled inkjet) deforms a planar lipid bilayer, thereby simultaneously creating and loading unilamellar vesicles (Figure 2). In order to achieve the second requirement there is the need to engineer a sensor system into the vesicles. This is done by incorporating transmembrane proteins into the lipid membrane, thereby enabling controlled communication between 'outside' and 'inside'. Although it sounds straightforward, this task is technically challenging because membrane proteins are very hard to produce and work with. Eva and her colleagues succeeded in demonstrating the proof of principle with simple transmembrane proteins initially (Figure 2a) and are working towards more challenging systems. While this is still in progress, the third and fourth requirement will be approached simultaneously. The team works on a system to enable the vesicle to produce proteins (Figure 2b), which should lead to a change in vesicle shape. Finally, once all individual steps can be reproducibly performed they can be combined and generate the first functional cell-like system, translating an external input into a visually detectable output.

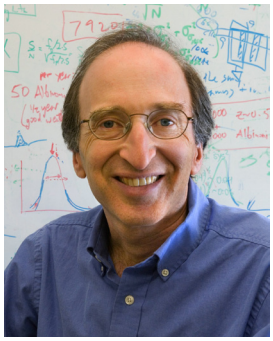
In order to reconnect with more traditional biology Eva also works on two other model organisms whenever there is time. One project investigates the questions on

continued on page 3

2010 Miller Senior Fellowship Announced

The Miller Institute is pleased to name Physics Professor **Saul Perlmutter the 2010 Miller Senior Fellow** for a five-year term beginning July 1, 2010.

Professor's Perlmutter uses astrophysical measurements to probe the make-up and evolution of our Universe. This is demonstrated through his work on supernovae, which has led to the discovery of a form of energy called "dark energy". It is now believed that over 75% of the universe is made of dark energy; a finding that has revolutionized our scientific understanding of the universe. Dark energy is widely acknowledged to be one of the most important recent discoveries in basic science and has profound implications for astronomy, theoretical high-energy physics, general relativity and string theory.



With such pioneering work, Professor Perlmutter has earned many notable awards including the Lawrence Award in Physics from the Department of Energy, the California Scientist of the Year Award in 2003, the John Scott Award, the Padua Prize, the Shaw Prize, the Antonio Feltrinelli International Prize, and the Gruber Cosmology Prize. He has also been elected a Fellow of the American Association for the Advancement of Science and is a member of the American Academy of Arts and Sciences as well as the National Academy of Sciences. He received his PhD from UC Berkeley in 1986 working under Richard Muller (Miller Professor 1990).

As the third Miller Senior Fellow named, Perlmutter will join Randy Schekman, Professor of Molecular and Cell Biology, and Gabor Somorjai, Professor of Chemistry, as part of our community of world-renown scientists. Taking its place alongside the Institute's other programs: the Miller Fellowships, the Miller Research Professorships and the Miller Visiting Professorships, the Miller Senior Fellow Program was established in 2008. Its purpose is to support excellence in basic science at UC Berkeley by providing distinguished faculty on campus with significant discretionary research funds and by involving them in the activities and intellectual fellowship of the Miller Institute. The Miller Senior Fellow Program enhances the Institute's mission by fostering interactions between distinguished senior scientists in different disciplines and our postdoctoral Fellows.

Miller Fellow Focus (continued)

continued from page 2

how moving cells deal with complex environments (such as immune cells in the human body) using the model organism *Dictyostelium discoideum* and microfabricated obstacles. Furthermore, she enjoys a collaboration with a friend from Stanford University where she looks at a model system for coral reef biology, the anemone *Aptasia pallida,* in order to develop a low-cost, easy-to-use-in-the-field, microscopy-based method for coral reef monitoring.

Eva is a second year Miller Fellow in the Department of Bioengineering. After obtaining a degree in Microbiology from the University of Vienna, Austria, she moved to the United Kingdom, where she did her Ph.D. at the University of Cambridge.

In her free time she takes in as much of the Californian sun as she possibly can to make up for 4 years in the English drizzle. She spends a lot of time in her San Francisco neighborhood the Mission (mostly mingling with the hipsters in Dolores Park) or she attempts to conquer the surf in Half Moon Bay. For longer trips she enjoys camping and hiking in national parks.

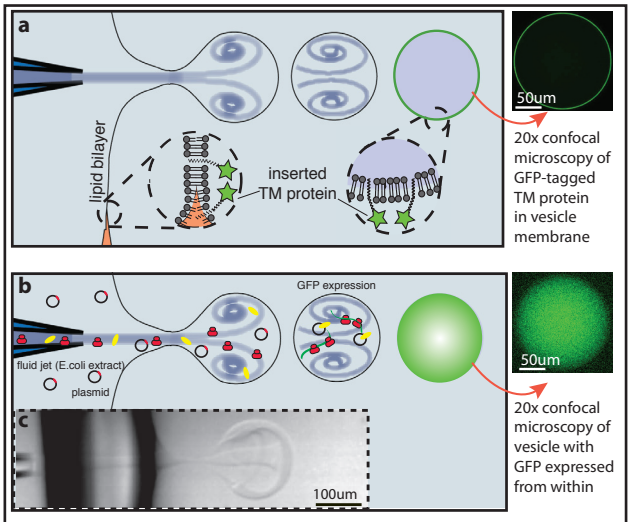


Figure 2: Generation of giant unilamellar vesicles (GUVs) by microfluidic jetting. Analogous to blowing soap bubbles we generate large vesicles by deforming a planar bilayer with a technology typically found in an inkjet printerhead. **(a)** To enable **communication between 'inside' and 'outside'** of the vesicle we need to be able to incorporate transmembrane (TM) proteins into the synthetic lipid bilayer. The incorporated proteins are made visible through fusion to Green Fluoresecent Protein (GFP). **(b)** We encapsulate an E.coli **protein expression** system, which allows us to express proteins inside the vesicle. **(c)** Light microscopy image of a vesicle made by this technique.

The Advisory Board

The Advisory Board of the Miller Institute met on December 7 to select next year's Miller Professors and Visiting Miller Professors. The Board is comprised of four advisors external to UCB: **Elizabeth Blackburn** (UCSF), **Roger Blandford** (Stanford), **Harold Kroto** (Florida State University), and **Simon Levin** (Princeton University); and four internal Executive Committee members: Executive Director **Mimi Koehl**, **Alberto Grünbaum**, **Michael Manga**, and **Richard Saykally**. The Board is chaired by UCB Chancellor, **Robert Birgeneau**.

Miller Professorship Awards

The Miller Institute is proud to announce the awards for Miller Research Professorship terms during Academic Year 2010-2011. These outstanding scientists are released from teaching and administrative duties during their Miller appointments, allowing them to pursue their research, full-time, following promising leads as they develop.

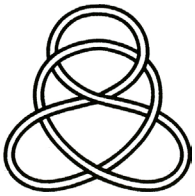
Kathleen Collins
MCB

Allen Goldstein
ESPM

Richard Harland
MCB

Jeffrey Long
Chemistry

Chung-Pei Ma
Astronomy



Bernard Sadoulet
Physics

James Sethian
Mathematics

Daniel Tataru
Mathematics

Visiting Miller Professorship Awards

The Miller Institute is happy to announce the recipients of the Visiting Miller Professorship Award for terms in the 2010-2011 academic year. Selected from an outstanding pool of nominees, these eminent scientists will join faculty hosts on the Berkeley campus for collaborative research interactions.

Eric Agol
University of Washington
Astronomy
Host: Eugene Chiang

Carl August Maria Brenninkmeijer
Max Planck Institute for Chemistry
Chemistry, EPS, and ESPM
Host: Kristie Boering

Jotun Hein
Oxford University
Statistics
Host: Yun Song, Rasmus Nielsen

Marc Kamionkowski
California Institute of Technology
Physics
Host: Uros Seljak

Asit Mazumder
University of Victoria, BC, Canada
Integrative Biology
Host: Mary Power

Eran Rabani
Tel Aviv University
Chemistry
Host: David Chandler

Burkhard Wilking
University of Muenster, Germany
Mathematics
Host: John Lott

Awards & Honors

December 8, 2009: **Ray Jayawardhana** (Miller Fellow 2000 - 2002) was awarded the 2009 Steacie Prize, one of Canada's most prestigious awards in science and engineering.

November 19, 2009: **Paul Alivisatos** (Miller Professor 2001 - 2002) was appointed director of the Lawrence Berkeley National Laboratories.

October 26, 2009: **Nicola Spaldin** (Miller Professor Spring 2007) was awarded the American Physical Society's McGroddy Prize for New Materials "for groundbreaking contributions in theory and experiment that have advanced the understanding and utility of multiferroic oxides."

October 9, 2009: **Gaven Martin** (Visiting Miller Professor Fall 2002) was named director of the New Zealand Institute for Advanced Study.

October 5, 2009: The Miller Institute is proud to share the news that **Elizabeth Blackburn** (Miller Institute Advisory Board Member 2007-2010) won the Nobel Prize in Medicine.

October 1, 2009: **Lucy Pao** (Visiting Miller Professor Fall 2008) was named Scientific Director for the Center for Research and Education in Wind and Richard and Joy Dorf Professor of Electrical, Computer, & Energy Engineering at the University of Colorado - Boulder.

September 22, 2009: **Lakshminarayanan Mahadevan** (Visiting Miller Professor Spring 2006) was selected as a 2009 MacArthur Fellow.

September 21, 2009: **Arunava Majumdar** (Miller Professor 2003 - 2004) was nominated by the White House to become the first director of the U.S. Department of Energy's Advanced Research Projects Agency-Energy (ARPA-E).

September 2, 2009: **Manuel Cardona** (Visiting Miller Professor Spring 2000) was elected a Fellow of the Royal Society of Canada.

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: millerinstitute.berkeley.edu/publications.htm.

Mark Dayel
Miller Fellow 2006 - 2009

Michael Jordan
Miller Professor Fall 2008

Lacey Knowles
Visiting Miller Professor Fall 2009

Adrian Lee
Miller Professor 2008 - 2009

Isamu Matsuyama
Miller Fellow 2008 - 2011

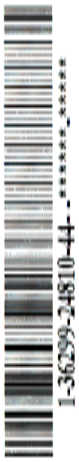
Maryam Modjaz
Miller Fellow 2007 - 2010

Dustin Rubenstein
Miller Fellow 2006 - 2009

Peidong Yang
Miller Professor Spring 2009

Rory Waterman
Miller Fellow 2004 - 2007

Yuanbo Zhang
Miller Fellow 2006 - 2009



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Announcements

September 12, 2009: **Erich Lehmann** (Miller Professor 1962 - 1963, 1972 - 1973), a leading figure in the second generation of modern statisticians, passed away at the age of 91.

December 1, 2009: Congratulations to Kelly and **Josh Eisner** (Miller Fellow 2005 - 2008) on the arrival of their son Colin Arthur Eisner.

December 7, 2009: **Kathryn Day**, Chief Administrative Officer of the Miller Institute, celebrated 20 years of service to the organization. She was presented a plaque at the Institute's Annual Fall Dinner.

December 13, 2009: **Huan Tran** (Miller Fellow 2002 - 2005), an experimental physicist who was featured in the Winter 2004 edition of the Miller Institute Newsletter, passed away.

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."