Miller Institute Newsletter

ISSUE Fall 2012 Miller Fellow Focus: Franziska Bleichert

The underlying mechanisms of body function have fascinated scientists for centuries. In the seventeenth century, scientists believed that all body functions were performed by minute machines. With the advances in modern biology over the last half century, we now know that this idea is not that far-fetched.

Machines we encounter in the macroscopic world are composed of different individual parts that, when assembled in a specific way, give rise to threedimensional objects that use energy to perform work. The same holds true for the molecular machines found in the cells of living organisms, which have evolved naturally over time to execute diverse tasks essential to life. The building blocks of these biological machines are proteins, nucleic acids, sugars and lipids. Of these, proteins are considered the powerhouses because they can perform an astounding variety of functions. So it is not surprising that most molecular machines are actually protein machines, ranging from relatively simple systems containing individual or few proteins to very large (in the microscopic world), complex assemblies with hundreds or more different





proteins. To make things even more complicated, additional building blocks such as nucleic acids can assemble with proteins into nucleoprotein machines.

Molecular also h machines are highly dynamic. They contain flexible parts that can undergo highly coordinated movements fueled by chemical energy. The sum of these movements ultimately results in work, which can vary greatly depending on the type of molecular machine. For example, some molecular machines move along cellular structures to a) transport cargo molecules between different areas within cells, b) actively alter cell shapes or c) alter conformations of other molecules. These machines are best described as processive motors. Others are large factories, synthesizing new mol-

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ecules, helping molecules to fold into the correct three-dimensional structure, or degrading unnecessary or damaged molecules. Different from the examples above, but still considered molecular machines, are molecular switches, which cycle between "on" and "off" states and thereby act as regulators of cellular processes. All in all, molecular machines perform highly diverse functions and they work together in a highly coordinated fashion in order to ensure cell survival. Understanding how this is accomplished at the molecular level is the focus of Miller Fellow Franziska Bleichert.

How are molecular machines put together from a limited number of building blocks? How can this result in such a broad spectrum of functions? What are the dynamics of these machines, or in other words, how do these machines change

during their work cycle? And how are these movements translated into work? These are some of the questions that fascinate Franziska and that she hopes to answer with her research in the long-term.

The molecular machinery that Franziska is currently studying is involved in

DNA replication, the biological process by which the genetic information is duplicated before it can be passed on to daughter cells during cell division. Errors in DNA replication are detrimental to cell survival, as they can result in cell death, cancer, and in the onset of other genetic diseases. At the beginning of each round of DNA replication, multiprotein complexes, so-called replication initiation complexes, assemble on specific regions of double-stranded DNA in a stepwise manner and mark these DNA regions as start sites for DNA replication (Figure 1). The replication initiation complex is a molecular machine that is essential for loading of the DNA helicase. During DNA replication, the DNA helicase unzips the DNA double-strand so that another enzyme, DNA polymerase, can read the genetic information encoded in each DNA strand and synthesize new DNA encoding the same information as the template DNA. Without the replication initiation machinery, DNA replication cannot occur. In the laboratories of Dr. James Berger and Dr. Eva Nogales, Franziska is investigating the mechanism of how replication initiation complexes in eukaryotic organisms accomplish these tasks.

The three-dimensional shape, or structure, of I molecules is well known to dictate their function. Thus, knowledge of the three-dimensional structures of proteins and large protein machines helps us understand how they perform their tasks and provides insight into fundamental mechanisms in biology. To get a glimpse of the shape of the initiation machinery, Franziska purifies these protein complexes from cells and directly visualizes them by transmission electron microscopy. By combining the images of different views of thousands of identical copies of these protein complexes, she can calculate their three-dimensional structure. The resolution of such structures (typically 8-30Å) can be adequate to pinpoint individual protein components, providing valuable information on how large

> molecular machines are assembled from subunits. However, even in the case of the best behaved biological samples, the resolution commonly does not reach atomic scale, i.e. it is not good enough to resolve individual amino acids within proteins or individual nucleotides within nucleic acids. Ultimately, this kind of information

is needed to fully understand the fundamental operating principle of a protein or protein machine. Consequently, Franziska is also trying to obtain atomic-resolution structures of the replication initiation machinery using another visualization technique called X-ray crystallography. In contrast to transmission electron microscopy, this method requires that biological molecules are arranged in a well-ordered three-dimensional lattice, most commonly in the form of crystals. It is difficult, and sometimes even impossible, to produce crystals of large molecular machines composed of many different subunits, so Franziska is targeting more amenable individual subunits or subcomplexes of the initiation machinery with this method. In combination with lower resolution structures obtained by electron microscopy, such crystal structures of subunits allow interpretation of the whole complex at a "pseudo-atomic" scale and is a powerful tool in exploring the dynamics of molecular machines.

With the ability to decipher entire genomes or proteomes obtained over the last decade, a



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Direct questions to Kathryn Day at the Miller Institute office: (510) 642-4088 or millerinstitute@berkeley.edu

Miller Research Fellowship 2013-2016 Online Nomination Deadline: Thursday, September 6, 2012

The Miller Institute for Basic Research in Science invites department chairs, faculty advisors, professors and Ph.D. research scientists at institutions around the world to submit nominations for the Miller Research Fellowship in the basic sciences. Fellowships are intended for exceptional young scientists newly awarded the doctoral degree and are selected on the basis of their academic achievement and the promise of their scientific research. The Miller Institute seeks to discover and encourage brilliant and imaginative individuals of outstanding and original talent, and to provide them with the opportunity to pursue their research on the Berkeley campus. Miller Fellowship terms must be completed within 5 years of receipt of the doctoral degree.

The Miller Institute is the home administrative department for each Miller Fellow who is hosted by an academic department on the Berkeley campus. All research is performed in the facilities provided by the UC Berkeley academic department and host faculty. The Fellowship term must commence between July 1 and October 1, 2013. Early nominations are encouraged to allow the candidates more time to prepare and submit their online applications and request references by deadline. Nominations cannot be made by students or postdocs. Direct applications and self-nominations are not accepted.

The nomination must be completed online. Nominators will need the following information to complete the process:

- Nominee's complete full and legal name
- Nominee's complete and current active E-mail address
- Nominee's current Institution, mailing address including postal code and telephone number(s)
- Nominee's Ph.D. Institution and (expected) date of Ph.D. (month & year; P.h.D. must be received by 9/30/13 to be eligible for nomination).
- The nominator's letter of recommendation and judgment of nominee's potential. This letter is included in the nominee's file as a letter of reference.
- Nominator's current active email address, title, and professional mailing address (include zip code/campus mail code)

Successful nominations will be confirmed by email within 24 business hours. Eligible nominees will be invited to submit an online application which will be due October 5, 2012. An announcement of awards will be made in the spring.

Nomination & Application details for all Miller Institute programs can be found at: http://millerinstitute.berkeley.edu/

Miller Research Professorship 2013-2014 Online Application Deadline: Thursday, September 13, 2012

The purpose of the Miller Professorship is to release members of the faculty from teaching and administrative duties and allow them to pursue research 100% time. Miller Professorships are open only to faculty of the University of California, but are not restricted to Berkeley faculty. The Miller behest requires, however, that research be conducted on the Berkeley campus. Extended absences from the campus should not be planned for the term of appointment. Other UC campus faculty must seek sponsorship of a Berkeley campus academic department before making an application and must solicit an endorsement letter from the Berkeley campus Department Chair as well as their home campus Department Chair. The term of appointment is for either the full academic year, beginning July 1, 2013, or one semester of Academic Year 2013-2014. Professorial salary and benefits for a regular 9/12 academic year or semester will be paid by the Miller Institute. Note: Miller Professors do not accrue time towards sabbatical leave. Applications are judged competitively and awards will be announced in December.

Visiting Miller Research Professorship 2013-2014 Online Nomination Deadline: Friday, September 14, 2012

The Miller Institute for Basic Research in Science invites Berkeley faculty to submit online nominations for Visiting Miller Research Professorships and the Gabor A. and Judith K. Somorjai Visiting Miller Professorship Award. The purpose of the Visiting Miller Professorship is to bring promising or eminent scientists to the Berkeley campus on a short-term basis for collaborative research interactions. The purpose of the Somorjai Award is to support the collaborative research of an early-career visiting scientist within the broad field of chemical sciences for a one-month term. It is required that awardees be in residence at Berkeley during their entire Miller Institute appointment term and that the visit must run in consecutive weeks. It is the academic department host faculty member's responsibility to ensure the visitor's presence on campus. Travel during the appointment is not allowed and will result in adjusted stipend and living expense payments.

Terms of VMP appointments range from a minimum of thirty days to a maximum of one semester (120 days). Somorjai Award appointments are limited to 30 days. Appointments must take place during the regular academic year 2013-2014 (Fall 2013 or Spring 2014). It is not appropriate to request a starting date between semesters or during the summer, and the visit must run in consecutive weeks. Non-US citizens must be eligible for J-1 Scholar visa status. Visitors cannot be supported on H1B or B visa status. Nominations are judged competitively and awards will be announced in December.

From the Executive Director

I feel very honored to have the opportunity to serve as a member of the Executive Committee for what is easily the very best job that anyone on the Berkeley Faculty could ask for. The Miller Institute's three goals are simply to bring the best and brightest postdoctoral fellows to Berkeley across all disciplines of science, to support more established scientists from around the world so



that they can enhance our environment, and to provide support for our own scientists with a semester of relief from non-research responsibilities during critical junctures in their careers. It is a delight to participate in the selection of our Miller Fellows and Faculty and enjoy the weekly venues for interaction that constitute the core of the Institute.

The past year has been thrilling for all of us as we witnessed the discovery of what may well be the elusive Higgs boson, and for sharing the joy of having Saul Perlmutter, one of our Miller Senior Fellows, share last year's Nobel Prize in Physics with former Miller Fellow Adam Riess. The June Symposium was another highlight, and planners for next June's meeting have already secured a slate of fantastic speakers. We expect the excitement of the coming year to continue at the same level as past years. We would also be happy to help the Swedish Academy in their deliberations with suggestions of other past or present members of the Miller Institute for their consideration.

The opportunities for advances in science have never been better. Nevertheless, we are all concerned about the future of science funding, and the Sequestration that may happen in January 2013 could likely have very unfavorable consequences. What we do as scientists is expensive and depends upon public and private support. Faculty and Fellows associated with the Miller Institute have made many contributions and discoveries over the 55 years of the Institute's existence which have helped build the foundation for public support of science. The fantastic success of our Fellows in securing appointments at top research institutions is irrefutable evidence of the value our investment in their careers. However, for science as a whole

it is unlikely that continued business-as-usual will be enough to continue the scientific enterprise as we have known it, especially considering the many fiscal challenges facing the nation. I look forward to working with the members of the Miller Institute to find ever more effective ways of communicating the successes, challenges, and promise of scientific discovery to an ever-wider audience. That would be good for science and fun for us.

I would like to take this opportunity to thank sincerely Simon Levine of Princeton University for his dedicated service as member of our External Advisory Board. Simon stepped down in June and will be replaced by David Botstein, also of Princeton University, beginning July 2013. Rich Saykally, Professor of Chemistry and Michael Manga, the previous Executive Director of the Miller Institute and Professor of Earth & Planetary Science will both be on sabbatical for the coming academic year, and we wish them both a most productive year. Joining me and Craig Evans of the Mathematics Department on the Executive Committee, we welcome Eliot Quataert of Astronomy and Bob Bergman of Chemistry in their stead.

~ Sincerely, Jasper Rine, Professor of Genetics, Genomics & Developmental Biology and Executive Director of the Miller Institute for Basic Research in Science

Miller Fellow Focus (continued)

great challenge facing biologists today is to understand how all the proteins of a cell cooperate and function to sustain life. By understanding their normal physiological function, we will be able to better understand how disruption of protein function leads to diseases. Franziska's research contributes directly to meeting this challenge.



In the News

July 24, 2012: Eliot Quataert (Miller Executive Committee, Miller Professor 2009-2010) and Alice Guionette (VMP 2006) were awarded \$500,000 open-ended grants from the Simons Foundation to further their research. Dr. Quataert is a theoretical astrophysicist with interests in black holes, stellar physics, plasma astrophysics and galaxy formation, among other topics, and is the director of the UC Berkeley Theoretical Astrophysics Center. Dr. Guionette is the Research Director at CNRS and responsible, with Florent Georges Benaych and Bertrand Eyard, for the ANR project Granma dealing with large random matrices.

July 24, 2012: **Josef Dufek** (Miller Fellow 2006-2008) & **David Shelly** (Miller Fellow 2007-2008) were named the distinguished honorees of the James B. Macelwane Medal. "These individuals are recognized for their outstanding contributions to the advancement of Earth and space science and for their service to the scientific community." They have distinguished themselves through their extraordinary achievements and are role models for future generations of scientists."

July 23, 2012: **Jesse Thaler** (Miller Fellow 2006-2009), Massachusetts Institute of Technology Assistant Professor and Theoretical Particle Physicist, was named a recipient of the Presidential Early Awards for Scientists and Engineers, the highest honor bestowed by the United States Government on science and engineering professionals in the early stages of their independent research careers.

In the News (continued)

July 19, 2012: Tanja Cuk (Miller Fellow 2007-2010), UC Berkeley Assistant Professor of Chemistry, "...received a Baker Fellowship to advance her research on 'supercapacitors'. Cuk's goal is a new generation of supercapacitors optimized for both power delivery and energy storage."

July 13, 2012: Julius Lucks (Miller Fellow 2007-2010), Cornell Assistant Professor at the School of Chemical and Biomolecular Engineering, was named a 2012 DARPA Young Faculty Award recipient. The DARPA Young Faculty Award (YFA) program aims to identify and engage rising stars in junior faculty positions in academia and expose them to Department of Defense (DoD) needs. In June Dr. Lucks was named a James C. and Rebecca Q. Morgan Sesquicentennial Faculty Fellow in honor of the generous gift of the Morgans for recruiting emerging "stars" to the Cornell Faculty as part of the Faculty Renewal Sesquicentennial Challenge.

June 12, 2012: Ray Jayawardhana (Miller Fellow 2000-2002), University of Toronto Professor and Canada Research Chair in Observational Astrophysics, delivered this year's Whidden Lectureat McMaster: "Rocks, Ice and Penguins: Searching for Clues to Planetary Origins in Antarctica."

May 13, 2012: Gil Navon (Visiting Miller Professor Fall 1997), Tel Aviv University Professor Emeritus of Chemistry was awarded the Mif'al HaPayis Landau Prize for pioneering developments in magnetic resonance imaging.

May 1, 2012: The American Academy of Arts and Sciences announced the election of new members, which include the following Miller Institute Members: AAAS

Miller Professors:

- Bjorn M. Poonen (Fall 2005) •
- Bernard Sadoulet (Spring 2011)
- Peidong Yang (Spring 2009)

Visiting Miller Professors:

- Philip H. Bucksbaum (Fall 1996) •
- John B. Pendry (Fall 1991) •
- Richard L. Taylor (Spring 1999)

May 1, 2012: The National Academy of Sciences announced the election of members, which include the following Miller Institute Members: NAS

Miller Fellows:

Miller Professors:

Visiting Miller Professors:

- William Bialek (1986-1987) • John Clarke (1975-1976, Fall 1994 & 2007) • Matthew Fisher (Spring 1991) Guinevere Kauffmann (1993-1994) • Mary Power (Spring 2002) John F. Hartwig (Fall 2009)
 - Bernard Sadoulet (Spring 2011)

April 17, 2012: Barbara Romanowicz (Miller Professor Spring 2010), UC Berkeley Professor of Earth & Planetary Science, received The Reid Medal at the 2012 annual meeting of the SSA in San Diego, California. The Harry F. Reid Medal is the highest honor of the Seismological Society of America (SSA) and awarded for "outstanding contributions to seismology and earthquake engineering." Dr. Romanowicz was honored as an exceptional scientist who has made fundamental contributions to theoretical seismology, seismology infrastructure and global geodynamics.

March 8, 2012: Rich Saykally (Miller Professor 1985-86, 1997-98, Fall 2006, Executive Committee), UC Berkeley Professor of Chemistry, was awarded the 2012 Royal Society of Chemistry (RSC) Faraday Lectureship Prize. The RSC is the largest organization in Europe for advancing the chemical sciences.

March 5, 2012: Nicholas P. Jewell (Miller Professor Fall 1994, Fall 2004), UC Berkeley School of Public Health Professor of Biostatistics and Statistics, was awarded the Harvard School of Public Health's 2012 Marvin Zelen Leadership Award in Statistical Science.

March 5, 2012: Marvin L. Cohen (Miller Professor 1969-70, 1976-77 & 1988), UC Berkeley Professor of Physics and Senior Faculty Scientist at the Lawrence Berkeley National Laboratory, and one of the most influential condensed matter physicists in the world, was awarded 2011 Dickson Prize in Science.

March 2012: John Prausnitz (Miller Professor 1965-66 & 1978-79), UC Berkeley Professor of the Graduate School Dept. of Chemical and Biomolecular Engineering, was announced as the honoree of the 2012 Lifetime Achievement Award in ChE Pedagogical Scholarship from the Chemical Engineering Division of the American Society for Engineering Education.

16th Annual Interdisciplinary Symposium



James Bullock, Claude-André Faucher-Giguère, Phil Hopkins, & Genevieve Graves



Nick Piro, Rachel Pepper, August Johansson, & Yogesh Surendranath



Jack Szostak & Saul Perlmutter





Adam Day & Robert Griffiths



Tom Baker



Franziska Bleichert, Louise Glass, Timofey Frolov

Interdisciplinary Symposium Speakers



Carl Bergstrom



Steve Cowley

Peter Olson

Tom Seeley



Jack Szostak

The Adolph C. and Mary Sprague Miller Institute for Basic Research in Science

Kristin Scott



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Birth Announcements

Alexandra Turchyn (Miller Fellow 2005-2008) & Vitaliy Turchyn announced the birth of their daughter, Annika V. Turchyn, born July 3rd.

Rory Waterman (Miller Fellow 2003 - 2006) & Sarah Waterman announced the birth of their daughter, Mae Eleanor Waterman, born April 30th.

Phil Starks (Miller Fellow 1999-2002) & Caroline Blackie announced the birth of their son, William Philip Blackie Starks, born June 14th

Scott Morrison (Miller Fellow 2009- 2012) & Kate Liesinger announced the birth of their daughter, Ruth Anna Morrison, born April 24th.

Obituaries

Ned Birdsall, ERG Co-Founder (Miller Professor 1963-64, Electrical Engineering)

What's New

The Miller Institute is now



Online Newsletter

The Miller Institute invites you to enjoy our previous e-newsletters by visiting millerinstitute.berkeley.edu.

Select NEWS.

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."