The Mathematics Behind a Good Night’s Sleep

News from Rensselaer Polytechnic Institute
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Troy, N.Y. – Why can’t I fall asleep? Will this new medication keep me up all night? Can I sleep off this cold? Despite decades of research, answers to these basic questions about one of our most essential bodily functions remain exceptionally difficult to answer. In fact, researchers still don’t fully understand why we even sleep at all. In an effort to better understand the sleep-wake cycle and how it can go awry, researchers at Rensselaer Polytechnic Institute are taking a different approach than the traditional brain scans and sleep studies. They are using mathematics.

Professor of Mathematics Mark Holmes and his graduate student Lisa Rogers are using math to develop a new computer model that can be easily manipulated by other scientists and doctors to predict how different environmental, medical, or physical changes to a person’s body will affect their sleep. Their model will also provide clues to the most basic dynamics of the sleep-wake cycle.

“We wanted to create a very interdisciplinary tool to understand the sleep-wake cycle,” Holmes said. “We based the model on the best and most recent biological findings developed by neurobiologists on the various phases of the cycle and built our mathematical equations from that foundation. This has created a model that is both mathematically and biologically accurate and useful to a variety of scientists.

“This is also an important example of how applied mathematics can be used to solve real issues in science and medicine,” Holmes continued.

To create the model, the researchers literally rolled up their sleeves and took to the laboratory before they put pencil to paper on the mathematical equations. Rogers spent last summer with neurobiologists at Harvard Medical School to learn about the biology of the brain. She investigated the role of specific neurotransmitters within the brain at various points in the sleep-wake cycle. The work taught the budding mathematician how to read EEG (electroencephalography) and EMG (electromyography) data on the brainwaves and muscle activity that occur during the sleep cycle. This biologic data would form the foundation of their mathematic calculations.

She also learned about the role of light and the sleep-wake cycle, a process known as a circadian rhythm. “There are many connections between the sleep-wake cycle and circadian rhythms,” Rogers said. “But scientists have come to realize that the basic parts of the sleep-wake cycle are not light dependent. People will sleep in a dark cave or in constant bright sun. We used this to develop the first mathematical model that is not predicated on daylight or the absence of daylight.”
This research foundation allowed the team to develop a massive 11-equation model of the sleep-wake cycle. They are now working to input those differential equations into an easy-to-use graphic computer model for biologists and doctors to study.

“We have developed a model that can serve other researchers as a benchmark of the ideal, healthy sleep-wake cycle,” Holmes said. “Scientists will be able to take this ideal model and predict how different disturbances such as caffeine or jet lag will impact that ideal cycle. This is a very non-invasive way to study the brain and sleep that will provide important clues on how to overcome these disturbances and allow patients to have better and more undisturbed sleep.”

Rogers will continue her work on the program after receiving her doctoral degree in applied mathematics from Rensselaer this spring. Her work on the mathematics of the sleep-wake cycle has already garnered attention within the scientific community, earning her a postdoctoral research fellowship from the National Science Foundation (NSF). With the fellowship, Rogers will continue her work at New York University and begin to incorporate other aspects of the sleep-wake cycle in the model such as the impacts of circadian rhythms.

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FACULTY NEWS AND NOTES

Roecker to Lead Team to Measure Aftershocks in Chile

Steven Roecker, Professor in the Department of Earth and Environmental Sciences, a seismologist, was asked by the US government to lead a team that will set up a seismic array to measure aftershocks following the recent huge earthquake in Chile. Steve is heading down there on Saturday and will be in the field for ~2 weeks (returning ~April 1).

Chunyu Wang Awarded Research Grant

Chunyu Wang, Assistant Professor in the Department of Biology was awarded a research grant in the amount of $128,845 from the National Institute of General Medical Sciences of the National Institute of Health under the American Recovery And Reinvestment Act of 2009. The project title is: ‘Testing novel hypotheses in Mtu RecA intein splicing’.

Whittet and Cody Co-Organized a Workshop Entitled "The Organic Continuum From the Interstellar Medium to the Early Solar System"

Douglas Whittet, Professor in the Department of Physics, Applied Physics and Astronomy, and George Cody (Carnegie Institute of Washington) co-organized a "Workshop Without Walls" (WWW), held on March 11 and 12, on the topic "The Organic Continuum from the Interstellar Medium to the Early Solar System". The workshop is multidisciplinary, bringing together researchers working in different fields (observational astronomy, laboratory astrophysics, planetary science, meteoritics, geochemistry, and mathematical modeling) to focus on a topic of major scientific interest - the evolution of organic matter from its cosmic origins to the emergence of life on Earth.
Sponsored by NASA's Astrobiology Institute (NAI), the WWW is a new paradigm for workshops involving modern technology, allowing for the widest possible participation whilst minimizing the need for travel. Participants have the option of joining the meeting at their local NAI video conference room (located at RPI, Carnegie Institute of Washington, NASA Ames Research Center, and several other sites within the USA), or simply joining via web browser from any location with full access to live video and audio streams and the ability to ask questions via instant messaging. Some 200 people participated in the meeting.

**Plopper Co-Author of Lewin’s Cells**

George Plopper, Associate Professor in the Department of Biology is a co-author of *Lewin’s CELLS, Second Edition*. The authors are Lynne Cassimeris, Lehigh University, George Plopper, Rensselaer Polytechnic Institute, Vishwanath R. Lingappa, Professor Emeritus, University of California, San Francisco, Chief Technology Office and Co-CEO, Prosetta Bioconformatics, Inc., San Francisco, California.

Completely revised and updated to incorporate the latest data in the field, *Lewin's CELLS, Second Edition* is the ideal resource for advanced undergraduate and graduate students entering the world of cell biology. Redesigned to incorporate new learning tools and elements, this edition continues to provide readers with current coverage of the structure, organization, growth, regulation, movements, and interaction of cells, with an emphasis on eukaryotic cells. Under the direction of three expert lead editors, new chapters on metabolism and general molecular biology have been added by subject specialist. All chapters have been carefully edited to maintain consistent use of terminology and to achieve a homogenous level of detail and rigor. A new design incorporates many new pedagogical elements, including Concept & Reasoning Questions, Methods boxes, Clinical Applications boxes, and more.

**Dr. Daniele J. Cherniak Elected a Geochemistry Fellow**

Dr. Daniele J. Cherniak, Research Professor in the Department of Earth and Environmental Science, has been elected a Geochemistry Fellow by the Geochemical Society and the European Association for Geochemistry. The title is “bestowed upon outstanding scientists who have, over the years, made a major contribution to the field of geochemistry.” This is a significant honor: the number of fellows elected each year is limited to a maximum of ten. It goes on to say “Your work has been recognized by your colleagues as being truly outstanding.”

**Grant to Develop Fluorescent Biosensors**

Chris Bystroff, Associate Professor of Biology, and Jonathan Dordick, Howard P. Isermann Professor of Chemical Engineering, have received a 2-year R21 award from the NIH to design and develop fluorescent biosensors based on green fluorescent protein. A prototype biosensor was created in which "leave-one-out GFP" was immobilized in latex paint. The new material can detect a specific peptide when added exogenously, glowing green within seconds of exposure. The work has sparked to a new collaboration with Lawrence Livermore National Laboratory (LLNL) and the US Army Medical Institute of Infectious Diseases (USAMRIID) to design biosensors against bio-terrorist agents.
Faculty and Students Present at the 54th Meeting of the Biophysical Society

Chemistry major **Karen Cedeno** received a Minority Biophysicists Travel Award to attend the 54th Annual Meeting of the Biophysical Society and to present her research on The Effects of Removal of C-termini of Tubulin for Mitotic Kinesin CENP-E Microtubule Interactions.

**Dr. Douglas M. Swank**, Assistant Professor in Biology, was an invited speaker for the Motility Subgroup at the 54th Annual Meeting of the Biophysical Society in San Francisco, CA. His talk was entitled, “Functional influence of the relay and converter domains revealed by *Drosophila* myosin”.

Graduate students **Catherine Eldred** (BCBP), **Qian Wang** (Biology), **Quiping Zhao** (Biology), and **Chun Ju Chen** (Biology) each presented their research as poster presentations at the 54th Annual Meeting of the Biophysical Society in San Francisco, CA, February 20-24, 2010.

The Structure of a Solar Water Oxidation Intermediate in Nature

**Dr. K. V. Lakshmi**, Assistant Professor in the Department of Chemistry and Chemical Biology and The Baruch ’60 Center for Biochemical Solar Energy Research, presented a research report at the 54th Annual Biophysical Society Meeting that was recently held in San Francisco, CA. The presentation was titled, “The Ligand Environment of the S2 State of Photosystem II: A Study of the Hyperfine Interactions of the Tetraneutral Manganese Cluster by 2D HYSCORE Spectroscopy.” The solar water-splitting protein complex, photosystem II (PS II), catalyzes the highly-efficient light-driven oxidation of water to dioxygen in Nature. The four-electron water oxidation reaction occurs at the tetraneutral manganese-calcium-oxo (Mn4Ca-oxo) cluster that is present in the oxygen-evolving complex of PS II. The mechanism of light-driven water oxidation has been a subject of intense interest. While recent X-ray crystal structures provide a model for the geometry of the catalytic Mn4Ca-oxo cluster, there is limited knowledge of the surrounding protein matrix that participates in the solar water oxidation reaction. Dr. Lakshmi and her team of undergraduate, graduate and postdoctoral researchers at RPI demonstrated the application of two-dimensional (2D) hyperfine sublevel correlation (HYSCORE) spectroscopy to determine the structure of the S2 photochemical intermediate state of catalytic site of PS II. They presented results that, for the first time, identify previously unknown ligands to the catalytic cluster and provide powerful avenues for the refinement of computational and mechanistic models of water oxidation. This research is supported by the Baruch ’60 Center (School of Science) at Rensselaer and the Office of Basic Energy Sciences, United States Department of Energy.
Elucidating the Assembly of a Multi-Subunit Photosynthetic Membrane Protein Complex

Oxygenic photosynthesis is the biochemical process by which solar energy is converted into chemical energy in cyanobacteria and higher plants. The light-driven reactions of photosynthesis are carried out by two transmembrane protein-pigment complexes, termed Photosystem II and Photosystem I (PS I), that operate in tandem. PS I catalyzes the light-induced, transmembrane electron transfer from a luminal (inside the membrane) donor, to a stromal (outside the membrane) acceptor. Cyanobacterial PS I exists in a trimeric form, in which each monomer contains 12 protein subunits and several chlorophyll \( a \) molecules, \( \beta \)-carotenes, lipids, phylloquinones and three iron- sulfur clusters. Efficient functioning of the PS I complex requires the correct assembly of this intricate collection of protein subunits and cofactors, the mechanism for which has remained unclear.

The elucidation of assembly pathways of multi-subunit membrane proteins is of growing interest in structural biology. To date, there have been very few attempts to understand the dynamics of the stromal assembly process of multi-subunit membrane protein complexes. In a recent study, Prof. K. V. Lakshmi and her graduate student, Sarah Dekat in the Department of Chemistry and Chemical Biology and The Baruch ’60 Center for Biochemical Solar Energy Research at RPI and their key collaborators, Prof. J. H. Golbeck (at The Pennsylvania State University) and Dr. Bharat Jagannathan (at the University of California, Berkeley) elucidated the assembly of the multi-subunit membrane protein complex, PS I, using spin labeling EPR spectroscopy. The use of spin labeling EPR spectroscopy provides a unique glimpse of the conformational changes that occur in the stromal subunit (PsaC) when it undergoes a transition from the unbound state to the membrane associated state \textit{in situ}. In addition to monitoring the conformational dynamics of the bioassembly process, they also examine the importance of key binding contacts on the assembly of the PS I subunits. The results of this study provide a comprehensive, stepwise mechanism for the binding of the stromal subunits on the PS I core and, for the first time, elucidate the conformational dynamics of the assembly process of a transmembrane multi-subunit protein complex at the molecular level. This study has recently been published in the American Chemical Society journal, \textit{Biochemistry}. This research is supported by the Baruch ’60 Center (School of Science) at Rensselaer, the Office of Basic Energy Sciences, United States Department of Energy (KVL and JHG) and the National Science Foundation (JHG).
“Fundamentals of Physics” in Farsi

Robert Resnick, Professor Emeritus in the Department of Physics, Applied Physics and Astronomy, received a letter:

“This Farbod, an Iranian postdoc fellow at University of Texas at Austin. I talked to you at FIP reception of last March meeting in 2009. As part of Iranian - American Network Group (IrAP), we are honored to provide you a copy of your "Fundamental of Physics" in Farsi language, which is published in Iran. I was wonder if you are attending the FIP reception at March meeting this year?

We are preparing to award you a letter of recognition for contribution of your book to the Physics society in Iran in addition of the books.

If you are not attending the meeting we are glad to send you the letter and the books through mail.

Thanks a lot
Farbod Shafiei
Treasurer of IrAP Network Group
University of Texas at Austin”

STUDENT NEWS AND NOTES

Society of Physics Students Again Selected as an Outstanding Chapter

The Rensselaer Chapter of the Society of Physics Students was named an Outstanding Chapter for 2008 – 2009. The Chapter whose faculty adviser is Gyorgy Korniss, Associate Professor of Physics, Applied Physics and Astronomy, has repeatedly won this recognition. Eric Dzienkowski was the president in 2008 -2009. Current leadership is: Andrew McAllister - President; Joe Paki - Vice President; Dan Collura - Outreach Coordinator; Eric Dzienkowski - secretary/treasurer; Dan Elton and Dave Hutchinson – Webmasters.

Radiation-Enhanced-Emission-Of-Fluorescence Method Developed

Jingle Liu, Ph.D. student in the Department of Physics, Applied Physics and Astronomy, demonstrated the use of radiation-enhanced-emission-of-fluorescence (REEF) to coherently measure free-space THz radiation. This newly developed remote sensing method at Rensselaer provides a new way to measure a pulsed THz signal at standoff application. Remote pulsed THz sensing was previously considered impossible, due to the water attenuation in atmosphere. REEF, for the first time, made it possible to perform pulsed remote THz sensing. The work will be highlighted by Nature Photonics in a March issue, 2010. Early REEF work was published in Phys. Rev. Lett. Defense Threat Reduction Agency will support an SBIR Phase I project based on this discovery.
Dr. Henry W. Sobel ’62 Awarded the Bruno Pontecorvo Prize

Henry W. Sobel, Professor of Physics and Astronomy at the University of California, Irvine is being awarded the Bruno Pontecorvo Prize from the Joint Institute for Nuclear Research (JINR), Dubna. This award has been given annually since 1995 to "a distinguished scientist for the most significant investigation in particle physics". Dr. Sobel received his Bachelor’s degree in Physics from Rensselaer Polytechnic Institute in 1962.