

## Series of Formal Talks Launched

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A series of exciting formal talks were held in the fall of 2006 on topics ranging from neurodegeneration to intelligent design. These presentations, held for the first time on such a regular basis throughout the semester, were launched by Eukaryon,  $\beta\beta\beta$ , the Biology Department, and the Center for Chicago Programs. Students were exposed to the latest research of distinguished scientists in fields such as neurodegeneration and psychology. Many students majoring in biology, psychology and chemistry attended these talks. The presentations also attracted students from the social sciences and humanities.

The interactive nature of the presentations added to the rich liberal arts education at Lake Forest College and emphasized the importance of out-of-classroom learning experiences. These presentations highlighted the mission statement of the Biology Department to help "students embark on hypothesis-driven journeys of discovery where answers are found not in textbooks, but in the lab and the field". All of the speakers spoke in simple language, and welcomed questions from the audience, which also included professors and on occasion members of the public. A brief summary of the six talks is given below:

Stress and Aging in Neurodegenerative Disease  
Dr. Richard Morimoto, Bill and Gayle Cook Professor of Biology, Northwestern University



Have you ever wondered if stress affects the 30 trillion cells of your body? What happens when you are stressed? Can stress increase your chances of getting neurodegenerative diseases, like Alzheimer's disease or Parkinson's disease? Dr. Richard Morimoto, professor of biochemistry and molecular and cell biology at Northwestern University, addressed a packed auditorium of students in the first of a series of six talks.

Specifically, the particular kind of stress being spoken of was physiological stress, which includes a number of factors like temperature, viruses, genetic factors, and heavy metals to mention a few. Primarily, stress affects a diverse class of molecules called proteins, whose function depends on their natural shape or conformation. At the molecular level, cells in

our bodies respond to a plethora of "stressors" like temperature and lack of nutrients, using special proteins called receptors. These receptors induce different protective responses for the varied stressful stimuli our cells experience. They can initiate mechanisms enabling the cell to survive or mechanisms to commit suicide through a systematic process known as programmed cell-death, or apoptosis.

On average, our cells contain  $10^{13}$  proteins! Many of these proteins function in multiple pathways. Different proteins are also assembled into protein machines, which help carry out cellular processes. Dr. Morimoto explained that in order to make so many proteins so rapidly and with diverse functions, the cell has protein quality control machinery which makes sure that proteins are folded correctly, have the right shape, and are functioning well. Those that do not meet these requirements are degraded. When proteins are synthesized in our cells, about 10% have missense mutations, which occurs when a protein building block is misplaced in the sequence of building blocks. Thus, the most important process in the cell is error prone. Proteins with missense mutations, as a result, fold differently and may have different functions. Lightening up the mood in the auditorium, Dr. Morimoto compared our cells to a Ford motor plant, rather than a Toyota motor plant!

Proteins somehow know how to fold by themselves and we are yet to discover how and why this process happens. Misfolded proteins cause "proteotoxic stress" due to their altered shape and function. These misfolded proteins, if not degraded by the cell, can be toxic, which is the major hypothesis for the cause of some neurodegenerative diseases, like Huntington's, Alzheimer's and Parkinson's. To prevent misfolding from occurring, cells have a special class of proteins called chaperones, which help with correct folding. Explaining how proteins can change shape when thermally heated, Dr. Morimoto used an example of making eggs where heating up the protein (or eggs), changes its shape, form, and function. We certainly don't want that happening in our brains! Thankfully, heat shock factors, or HSFs, help cells regulate protein's shape in cases of stress. As we age, these HSFs do not function as efficiently, thus increasing "proteotoxic stress" in our cells and subsequent toxicity.

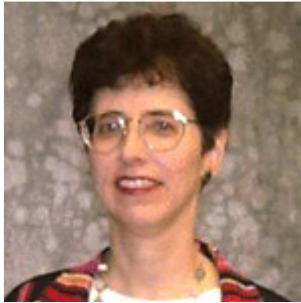
Dr. Morimoto uses *C. elegans* to study HSFs. He explained that this nematode is a good model system to study diseases as each organism has only 959 somatic (non-gonadal) cells and 302 nerve cells. Further, the worms are transparent and the fate of each cell in the worm has been determined. *C. elegans* have about 160 chaperones. He showed data from his lab, where knocking out a heat shock factor, HSF-1 led to the formation of many aggregates in the worm nervous system. Overexpressing lots of HSF in the worms gave them a longer life span!

This presentation tied in concepts from a number of biology courses, including Organismal Biology, Diseases around the Globe and Cell and Molecular Biology. The importance of protein shape and its relationship to the proteins' function was a review for students of Organismal Biology. Students who had taken Diseases around the Globe had a clear idea of the diseases Dr. Morimoto mentioned, while Cell and Molecular Biology students could easily recall protein formation in the cell!

Junior Sina Vahedi, thought that the presentation was very good but he would have wanted to see more data and details about the experiments. However, Sina understood that the talk's lack of experimental detail made it more accessible to the many non-science majors in the audience.

Dr. Morimoto's presentation was simple and easy to understand. It explained the connection between stress, protein misfolding, and neurodegenerative diseases. Dr. Morimoto's sense of humor, calm disposition, and the tone and pace of his voice made this presentation both educational and enjoyable.

Yeast as Small "Mad Cows" Demonstrate Protein-Based Inheritance  
Dr. Susan Liebman, Distinguished University Professor,  
University of Illinois-Chicago



Did you know that we have a dogma in biology? Yes, the central dogma of molecular biology says that heredity is controlled by DNA, which spells out protein formation. Dr. Liebman explained that in Mad Cow disease, a pathogen, a prion (PrP), lacks nucleic acids, yet can change a protein's original formation. There are many cousins of PrP diseases, like Creutzfeldt-Jakob disease, kuru, fatal familial insomnia, scrapie of sheep, mad cow disease of cattle, and chronic wasting syndrome of deer, all of which are known as transmissible spongiform encephalopathy's.

Dr Liebman's talk was as exciting as it was easy to follow. She explained that proteins can exist in a normal or prion shape. Prions are infectious (self-perpetuating) proteins which form fibers that can be seen under the microscope. Comparing the DNA paradigm to the prion paradigm, Dr. Liebman pointed out that in the case of a DNA mutation, a protein can lose function or gain new function. However, in the case of prions, a normal protein can change shape and induce other molecules of that same protein to change shape as well. There can also be mutations which predispose proteins to change shape and act like a prion.

Different strains of PrP cause different disease pathologies in inbred animals. These prion strain differences appear to be due to different heritable prion conformations. Showing data from her lab, Dr. Liebman pointed out that prion proteins in yeast are infectious.

So why use yeast? Well, yeast contain proteins that are highly conserved. In addition, many cellular processes like DNA synthesis and repair, cell-cycle progression, protein synthesis and processing, and protein transport are also highly conserved. Yeast grow by mitotic budding and propagate proteins that are in the prion shape.

Increasing the amount of proteins in the cell yields a greater chance of getting prions. However, the fibers formed by these prions need to be broken in order for it to be given to the daughter cell.

Dr. Liebman explained that a nonsense mutation is one where there is an extra stop codon in the DNA sequence. In her laboratory, when a mutation was made in the sup35 gene, the protein was still made, despite the stop mutation! Dr. Liebman's lab also discovered that a chaperone protein that dissolved protein aggregates was required to propagate the prion. The chaperone breaks the fiber and thus helps in propagation of the protein. Inhibition of the chaperone protein by hydrochloric acid leads to decreased prion propagation.

This presentation touched on many topics covered in Cell and Molecular Biology, as well as those explored in Ecology and Evolution. Why does our protein synthesis and degradation machinery differ only slightly from that of yeast? Evolutionarily speaking, how similar are we to yeast?

Dr. Liebman spoke in simple language and explained cell biology terms throughout her talk. She frequently asked the audience questions. This helped almost everyone to understand the talk, and it also made the presentation an unforgettable learning experience.

How our Hands Help us Think  
Dr. Susan Goldin-Meadow, Ruml Distinguished Service  
Professor, University of Chicago



Dr. Susan Goldin-Meadow presented her talk amid the excitement of the campus-wide Brain Awareness week at Lake Forest College. Her presentation was at the peak of this outreach campaign organized by the first-year studies Medical Mysteries class and Molecular Neuroscience students. She shared exciting data from her research, which studies the process of mismatch learning in children.

It was discovered that gestures change when children or learners are "in transition." Therefore gestures are associated with learning. Dr. Goldin-Meadow presented data to show that a gesture is not only a reflection of human thought, but also a mechanism of learning. Using data she collected, Dr. Goldin-Meadow explained that in a child with gesture-speech match, the speech of the child about moving and the gestures show the actual movement that happened. However, in a gesture-speech mismatch, the gesture of the child describing movement does not correspond to the actual movement. Interestingly, children with gesture-speech mismatch are more likely to learn after training than children with gesture-speech match.

Dr Goldin-Meadow found that while teaching, one strategy in speech is a lot better than two. She also discovered that gestures are powerful in their ability to shape the way we think! If the children learned only the gesture, they tended to learn much better than those who repeated only the speech. In another experiment, children were told to gesture everytime they were trying to solve a problem. Interestingly, the number of new strategies was much greater in those told to gesture. Further, she found that children who are told to gesture during a lesson remember what they learn. Also, children remember more when they gesture, in addition to coming up with new strategies to solve a problem. She pointed out that making gestures encourages experimentation and adding more ideas.

Dr. Goldin-Meadow mentioned that gesturing lightens the cognitive load in the same way that writing down a problem on paper does. Another benefit of gestures is that they provide a second representational formation. Further, notions in gesture can go unchallenged.

This talk attracted a great number of questions from the audience. One student requested that Dr. Goldin-Meadow replay tapes of classroom experiments involving children being taught by gesturing and non-gesturing teachers.

#### Feeding and Gloating for More: Intelligent Design Vs Evolution

Dr. Jerry Coyne, Professor of Ecology and Evolution, University of Chicago



Do you accept evolution as a scientific theory well supported by evidence or not? Well, only 1 in 5 Americans believes in evolution. And only 12 percent of Americans think that evolution should be taught in schools. Dr. Coyne pointed out that the theory of evolution should be compared to the atomic theory of matter, which is accepted by almost 100 percent of Americans. This is because, like any other scientific theories, it makes sense of wide-ranging data that were previously unexplained, makes testable predictions and is vulnerable to falsification. However, no evidence has yet been found to falsify the theory of evolution.

Dr. Coyne's talk was reminiscent of the college's Ecology and Evolution class! He explained that there are four parts to the theory of evolution. First, evolution occurred; that is, living species descended from a common ancestor. Second, there were very gradual changes in each descending generation. Third, speciation occurred; that is, a single ancestor gives rise

to a new species. Last, the only force causing evolutionary change is natural selection.

Dr. Coyne went on to present data supporting the theory of evolution. He mentioned that the Archaeopteryx which has a pelvis bone, indicating that it evolved from dinosaurs. In embryology, scientists can see that dolphins develop hindlimb buds, which then regress. Further, humans develop a Lanugo (a coat of hair), which we shed. Dr. Coyne pointed that vestigial organs serve as "the senseless signs of evolutionary history," for example the kiwi is a flightless bird. Dr. Coyne also cited the development of antibiotic resistance in bacteria as evidence for natural selection.

Intelligent Design, or ID, claims that an "intelligent agent" designed some of the features of modern organisms. ID states that some features are "irreducibly complex" and could not have evolved in a stepwise fashion. They include such features as the eye, the blood clotting system, the immune response pathway and the bacterial flagellum. However, due to new fossil evidence the vertebrate jaw can now be explained. The problem with ID is that if we can't think of a way a feature evolved, then the intelligent designer is credited with its creation. Another problem is that nothing is known or can be known about the designer's goals and methods. Thus, claims by ID are not testable.

Dr. Coyne was very careful not to downplay the important role of religion in society. He said that Bible must not be taken literally and that we can reconcile our beliefs with scientific evidence. Like a true scientist, Dr. Coyne was very comfortable with discussing evidence that would falsify or refute the theory of evolution. He mentioned that a fossil in the wrong place would be one. For example, a human fossil that is older than 10 million years old!

#### Alzheimer's Disease: A Tangled Problem Dr. Lester Binder, Abbott Professor of Biology, Northwestern Feinberg School of Medicine



Dr. Binder's talk on Alzheimer's disease (AD) was the opening talk of an exciting one-day workshop on neuroscience. Dr. Binder, who studied the control elements of tau tangles found in AD patients, enlightened the audience about the culprit thought to cause the disease. Tau protein binds microtubules and stabilizes them. Tau also aggregates to form filaments that compose the neurofibrillary tangles found in brains of AD victims. Phosphorylation of this protein controls its binding to microtubules. Phosphorylated tau leads to dynamic instability which allows for plastic changes to the cell's architecture. Hyperphosphorylation is a hallmark of AD. In addition to the tangles, plaques

(amyloid) are also seen. The axons and dendrites of the neurons are filled with tau tangles. The density of these tangles correlates with the degree of dementia in the AD patient. Tau mutations also cause certain forms of familial frontotemporal dementias (FTDs).

In an experiment involving neurons, neurodegeneration is absent when tau is absent. Tau is known to come off the microtubules. What is not known is whether the disassociation or the aggregation of tau is the problem. Thus, the role of tangles and other tau aggregates in AD is still unknown.

In his laboratory, Dr. Binder designs and conducts experiment using antibodies which recognize tau conformations, modifications, and truncations. It was found that one conformation of tau, ALZ50, was a polymer. When tau is cleaved, the rate of assembly of aggregates is increased. However, if the tail peptide is added back, the rate of assembly is inhibited! Studies in Dr. Binder's laboratory indicated that making a tangle is protective to the cell.

Other interesting data from Dr. Binder's laboratory indicated that the N terminus of tau facilitates the assembly of full-length tau. And the deletion of a region in the N terminus of the protein decreases the rate of assembly. Findings from Dr. Binder's laboratory have made valuable contributions to AD research and provided many targets for potential therapy.

Dr. Binder's enlightening presentation was a synthesis of concepts students had come across in Cell and Molecular Biology. Students of Molecular Neuroscience were able to appreciate Dr. Binder's research on AD to a greater extent than the others.

Neuroscience in Search for a cure for drug addiction  
Dr. T. Celeste Napier, Professor of Pharmacology,  
Loyola Stritch School of Medicine



Dr. T. Celeste Napier presented the last talk in the fall series of formal seminars and the closing talk of the day for the Neurofrontiers workshop. Her presentation elicited many questions from students who thoroughly enjoyed her talk. Dr. Napier mentioned that an astonishing 9 percent of the population, or an estimated 21.6 million people aged 12 or older, can be classified with dependence or abuse on psychoactive substances (alcohol or illicit addictive drugs). Recently, there has been a large increase in ER visits for methamphetamine related cases. Methamphetamine, which is a most potent psychostimulant, is also called meth, crystal, and crank.

Dr. Napier clarified that addiction refers to the pattern of self-administration. Addiction is a behavioral

pattern of drug abuse characterized by overwhelming involvement with the use of the drug (compulsive use), the securing of its supply, and high tendency to relapse after withdrawal. This pattern is thought to be "learned."

In her laboratory, Dr. Napier used rats and mice to study addiction. A drug was put at a certain place so that the rats learned to associate environmental cues with the drug. Drugs were given in repeated, intermittent doses to induce addiction. This led to the progressive enhancement of motor activity. The animals were observed visiting this location even in the absence of the drug.

Dr. Napier's laboratory also carried out research using amphetamines. Amphetamines have common mechanisms in action. These bind to receptors and are taken up, and subsequently displace the transmitters. Thus there is a great increase in transmitters. In other words, the brain is beefed up in a very big way! It was found that rats could be weaned off methamphetamine addiction by administration of the drug mirtazapine!

Dr. Napier's research and her promising results with mirtazapine generated many intelligent questions from the audience, who still seemed addicted to neuroscience after a whole day workshop!

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