Greetings from Binghamton University!
Welcome to the 2009 edition of the biochemistry newsletter. The biochemistry major is growing strong, with 35 graduates this May and over 100 students currently enrolled in the major. We now have nearly 900 alumni!

The biochemistry advisory board has been recently reinvigorated, under the leadership of its current president, Rebecca Switzer. This newsletter was compiled by the dedicated members of the BCAB.

We have a new assistant director, Maura Loew. She is an alumna of the biochemistry major herself, and a current graduate student in chemistry. She is helping the BCAB and is open to suggestions for activities for either current students or alumni. You can contact her at mloew1@binghamton.edu to let her know what career path your biochemistry degree has taken you down – we could use your story for the website or the next newsletter. If you are in the area, you could even come speak to current students about what lies ahead of them!

Enjoy the newsletter, and thanks for reading!

Congratulations to our 2009 graduating seniors! We wish you good luck in your future endeavors. Be sure to keep in touch with Biochemistry Department and let us know how you are doing!
Molecular Mechanism of Transmembrane Transport of Amino Acids
by Christof Grewer, Ph.D.

Living cells require a constant supply of nutrients, which are used to meet their energy needs, or as building blocks for the synthesis of biopolymers. Many important nutrient molecules, such as sugars and amino acids, do not freely permeate biological membranes. Thus cells have developed mechanisms to import sugars and amino acids across their cellular membrane. In many cases, this important function is provided by membrane proteins called transporters, which provide a catalytic pathway for the mostly hydrophilic organic molecules through the hydrophobic membrane bi-layer. Membrane transporters often are “active”, which means that they have to move substrates uphill against a concentration gradient. An example is a transporter that moves sugars into a cell already containing high concentrations of sugar. Uphill transport requires work, which is provided by the coupling of substrate transport to the cotransport of Na⁺ ions down their own electro-chemical potential gradient across the membrane.

Recently, significant progress has been made towards our understanding of the molecular architecture through the availability of high-resolution structures of several transporters (see Fig. 1 for the structure of a bacterial glutamate transporter). However, the actual transport mechanism(s) remain elusive. Our aim is to combine functional and structural evidence in order to obtain an understanding of how these transport proteins work.

The systems currently investigated are glutamate transporters, which contribute to the removal of the excitatory neurotransmitter glutamate from the synapse, and the sodium-coupled neutral amino acid transporters (SNATs), which catalyze import or export of glutamine and other important neutral amino acids into or out of cells.

In many cases, membrane transport is associated with stationary or transient transport of charge. We measure this charge transport with electrophysiological techniques, such as current recording from transporter-expressing, voltage-clamped whole cells or excised inside-out patches. In order to investigate transient charge transport, we perturb a pre-existing transporter steady state by applying voltage or rapid substrate concentration jumps and subsequently measuring the kinetics of the relaxation to a new steady state with a sub-millisecond time resolution. A hypothetical transport mechanism that combines evidence from such pre-steady-state functional data with structural information is shown in Fig. 2A for the glutamate transporters. This mechanism predicts that two structural changes are associated with transmembrane glutamate movement: 1) the closing of an external gate after substrate binding, and 2) the subsequent opening of an internal gate, allowing dissociation of substrate to the cytoplasm. A typical example of transport currents generated by glutamate transporters in response to a glutamate concentration jump is shown in Fig. 2B, demonstrating the existence of two separable decay processes (assigned to the state transitions shown in Fig. 2A). We also apply transition state theory to the pre-steady-state kinetics of the transporters. This allows us to get a better understanding of the nature of the structural changes and/or diffusional processes that are associated with transport (Fig. 2C). In addition to investigating the transport mechanism of wild-type transporters, rapid kinetic studies are extended to transporters that are fused to fluorescent proteins or site-specifically mutated by using standard molecular biological techniques. The combination of these techniques allows us to understand the relationship between the structure and the function of the transport proteins and to predict potential cation binding sites.

![Figure 1: Structure of bacterial glutamate transporter](image1)

![Figure 2:](image2)
Hydration of Nucleic Acids: 
How Chemistry Changes the Interactions with Water

by Eriks Rozners, Ph.D.

Nature has optimized nucleic acids to work in an aqueous environment. However, the importance of interactions of the nucleic acid and surrounding water molecules is usually underestimated or even ignored by both biologists and chemists alike. The water molecules in immediate vicinity of the nucleic acid form a well-structured net of hydrogen bonds that contribute to the overall structure and thermal stability of the double helix. Water is an integral part of nucleic acid structure. For many practical applications, such as in vivo probes and gene therapy agents, nucleic acids need to be chemically modified to optimize biophysical or pharmacological properties. In designing the chemical modifications we should consider the effect of our efforts not only on the molecular structure and shape of the nucleic acid, but also its interaction with the aqueous environment.

We are interested in studying how chemical modifications change the hydration of nucleic acids. Specifically, we study the structure and hydration of RNA analogues where the polar phosphates are replaced by non-ionic amide (Figure 1, 1 and 2) and formacetal (3) linkages. We envision that such modifications may have advantageous properties for designing gene therapy agents that target RNA molecules.

To study the hydration we use a method that “dries out” the nucleic acid by diluting the aqueous sample with organic solvent and observes the response of the nucleic acid to the applied osmotic stress. By comparing the response of native and modified nucleic acids to osmotic stress, we obtain valuable insights into how chemical modifications change the interactions of nucleic acids with the surrounding water. We also collaborate with Structural Biologists at Vanderbilt University, who analyze our compounds using X-Ray Crystallography. A crystal structure of formacetal modified DNA and the bound water molecules (spheres) is shown in Figure 2. The modified DNA was synthesized in our lab and crystallized in the lab of Professor Martin Egli at Vanderbilt. Our results suggest that the chemical modifications that fit well with the structure of the double helix also support favorable hydration of the nucleic acid. Our long-term goals are to design novel RNA analogues that will mimic not only molecular structure and shape but also the hydration of nucleic acids.

Chemistry and Biology professors: let us know if you would like your research to be featured in the next newsletter. We would love to hear from you!
Dreading the hassle and expense of buying next year’s textbooks? Not anymore! Borrow your books from the…

Biochemistry Book Swap

Each Semester, the Biochemistry Advisory Board will loan out textbooks for Biochemistry courses, prerequisites and electives (including select courses in Biology and Chemistry). In exchange, the student will be asked to put down a deposit at the beginning of the semester, most of which they will be refunded upon returning each book to the Biochemistry Advisory Board. We reserve the right to keep your deposit if you do not return the book. Books should be returned during finals week of the semester they are borrowed, the exception being the textbooks borrowed for year-long courses (such as Organic Chemistry).

How to borrow: Keep an eye on your inbox at the beginning of next semester for more details about how to get involved

How to donate: If you have an old copy of any Biochemistry, Biology or Chemistry textbook, and are willing to donate it to the Book Swap, please send an email to Maura Loew (mloew1@binghamton.edu).

Example: The used 7th Edition of Organic Chemistry (Carey)
You pay $135
You get back $125 upon returning the book

Thank you to all of our contributors and to Big Daddy’s Pizzeria for their donation to our post-Biochem test pizza party!

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Students involved in research:
We would like to include your work in our next issue. Contact us if you are interested!

Are you a Junior or Senior? Do you have a passion for Biochemistry? Are you interested in helping your Peers?
If you answered yes to all of the above then becoming a Biochemistry Peer Advisor may be right for you. As an Advisor you will be able to help your fellow peers with questions and concerns that they have towards a degree in Biochemistry.
If you are interested, please contact Jacky Chow at JChow1@Binghamton.edu

Find out the most recent Biochemistry information at:
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Proteolytic activity profiling of etiolated and de-etiolated Arabidopsis thaliana seedlings

By Adam Hill

Proteolytic enzymes catalyze the hydrolysis of peptide bonds in proteins, including many whose functions are important in gene regulation, enzymatic action, and amino acid storage. As important as proteolytic enzymes are, the functions of many are unknown. Arabidopsis thaliana serves as a good model system for study of proteolytic activity profiling because it was the first plant species to have its entire genome sequenced. The strategy is to isolate the protein that has proteolytic activity and then subject it to identification by liquid chromatography in-line to tandem mass spectrometry (LC-MS-MS).

Zymograms, which are modified SDS-PAGE gels, can be used to find proteolytic activity. In a zymogram, gelatin and casein are embedded in the matrix of a polyacrylamide gel. The gelatin and casein serve as a substrate for the proteolytic enzymes to break down, producing smaller peptides that will diffuse out of the matrix. When the gel is stained for protein, the lack of gelatin and casein in the gel will leave clear bands that represent the positions of proteolytic enzymes that were able to hydrolyze gelatin and casein.

These detected differences in activity can then be compared among different growing conditions pointing us towards possible functions for the proteases. I am concentrating on the proteolytic activity differences in Arabidopsis seedlings that have been grown entirely in the dark (etiolated) and in a normal 16-hour/8-hour cycle of light and dark. Proteases are characterized according to pH optimum, molecular weight, and mechanistic class. Fractionation by ion-exchange spin column chromatography has been very useful in separating out the large number of proteases in each sample.

Using zymograms I have been able to find a handful of proteases associated with specific classes of small molecule inhibitors. These inhibitors help to determine the mechanistic class. Two proteases, mol wts 157 and 60.3 kD, were sensitive to PMSF, suggesting serine proteases. Both had higher activities in etiolated seedlings. In addition to these two, two o-phenanthroline-sensitive proteases of masses 52.6 and 35.6 were found only in etiolated seedlings. Seedlings grown in a 16 h photoperiod had higher activity levels of the iodoacetamide- and E-64-sensitive 31.4 and 28.7 kD proteases. Finally equal activities between the two conditions were found in two other proteases sensitive to the same cysteine protease inhibitors with masses 38.8 and 41.3 kD.

Now that I have isolated and determined pH optimum, molecular weight, and mechanistic class, in addition to differential activities associated with the two growing conditions I will continue with mass spectrometry based analysis. This can be used in conjunction with databases containing putative and known protein sequences found in Arabidopsis to elucidate the identity of these proteases.

Since plant species evolved from common ancestors, our finding with Arabidopsis can be translated into many other plant species. Proteolytic enzymes are part of the whole process of how plants cope to different environmental conditions. Getting a good grasp on how plants respond to environmental stimulus can be used to help improve agricultural crop growth and productivity. For my specific project, this would be so with regard to seedling viability.
**What can you do with a Biochemistry Degree?**

**By Adam Hill**

Attention prospective and current biochemistry majors, you have made a very wise decision. Biochemistry is an active field driven by the curiosity of life’s little intricacies. In today’s fast paced technology driven world there are countless opportunities for young scientists such as yourself. With the recent explosion of DNA based sequencing we now have access to essentially unlimited amounts of information at our fingertips. Supplementing this profusion of new information there are in place many experimental techniques ripe for the exploitation of this pool of uncharted waters. Utilization of these resources will undoubtedly help to make huge leaps in the health and science fields. Listed below are just a few of the many career fields available to biochemistry majors:

- Research Laboratories
- Biotechnology
- Academia
- Public health entities (i.e. Hospitals)
- Cancer research institutes
- Forensic science
- Chemical manufacturing companies
- Pharmaceuticals
- Human genome project
- And many more!!

We hope you will join us in a quest to drive progress forward and undertake in the bright future as a budding biochemist. As a group we will help to pioneer for the betterment of the human experience and society as a whole!

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**Alumni: Where are they now?**

**By Rachel Georgopoulos**

I am currently a first year medical student at Stony Brook Medical School, having graduated in 2008 from Binghamton University as a Biochemistry major. The biochemistry taught in medical school applies the pathways and biochemical principles that we were taught thoroughly in Binghamton to disease pathways and treatments. My first set of biochemistry exams would have been much more challenging had I not entered this school with the strong foundation in the subject matter that I gained from the faculty and teaching assistants in my undergraduate studies. I remember grueling over learning each step of the Kreb’s cycle and trying to incorporate it into a giant poster board that professor Tan-Wilson recommended that we construct. I brought that poster board here to school with me.

The pathways that took us a week to learn in undergrad, we learned in ½ a class period. Thankfully, I was given the information and study techniques necessary to adjust to the increased pace of medical school. I am very grateful to have received such a wonderful education and support from my undergraduate program. I highly recommend and respect the Biochemistry program at Binghamton University.

**By William Wan**

I feel that the biochemistry program offered at Binghamton has helped me in getting into graduate school by giving me both a good background in biochemistry and allowing me enough room to develop my own interests. The required classes provide the knowledge that any biochemist will need, such as the basic knowledge from the didactic lectures as well as more applicable knowledge from the laboratory classes. While the required courses were rigorous enough to get a good background, there was still enough room to take electives in fields of chemistry and biology that were of particular interest to me such as proteomics and physical chemistry.

Alumni: Would you like to be featured in our next issue? Let us know where the Biochemistry degree has taken you!
The Biochemistry Advisory Board is seeking new members! If you are interested in meeting people with similar interests, taking on leadership roles in creating next year’s newsletter and peer advising, or just chatting about life as a Biochem major, this is the club for you! Contact us if you would like to join!

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