GST looks forward to Fall 2015

Friends of GST,

A new academic year is upon us, and with it a new class of GST! The eleven students who are joining us this Fall are the largest cohort that GST has admitted in the last five years, a sign of the health of the program and of the ‘omics and computational research community at UT and ORNL. Snapshots of our incoming ‘fresh(wo)men’ follow below. Please welcome the new students to GST. As faculty members, you are particularly encouraged to open your lab for rotation experiences.

Over the past year, GST again proved very attractive to new faculty members. Our faculty was embellished by ORNL scientists Drs. Xiaolin Cheng, Jessy Labbé, and Dan Jacobson, and UT faculty members Drs. Sarah Lebeis (Microbiology), Colleen Jonsson (Microbiology, NIMBioS), Maitreyi Das and Francisco Barrera (both BCMB), and Steven Ripp (Center for Environmental Microbiology). All of them have already started to become active in GST affairs. GST can use all the help it can get. This is particularly true now, that a committee of GST faculty has completed work on GST’s 2015-2020 Strategic Plan.

Meanwhile, GST students have been busy presenting their explorations to the science community in the form of papers and conference presentations. Further below, Weili Xiong, Sarvesh Iyer, and Alfredo Blakeley-Ruiz share their impressions about recent meetings they were able to attend. The last year also saw a substantial uptick in first author publications by GST students. Congratulations!

Also exciting are new developments in the formal and informal course offerings that GST faculty and students are putting forth for the UT community. Although many ongoing efforts deserve mention, in the interest of space let me focus on a few recent and upcoming events surrounding next-generation sequence analysis: In the Spring of 2014, GST students offered the first tutorial in next-gen sequencing within the GST Colloquium. Due to popular demand, this was followed in May 2015 by a 2-day workshop on RNA-Seq analysis taught by Meg Staton with the assistance of staff members and GST students. Aside from a more general ‘skills’ workshop taught under the Software Carpentry initiative (August 10-11), Meg is also preparing for a semester-long course in next-gen sequence analysis this Fall (ERP622/LFSC696). Last Spring, Chongle Pan and colleagues taught a well-subscribed 600-level course on ‘omics at ORNL, while this Fall, Vitaly Ganusov is offering a journal club on mathematical modeling (MICRO606). Please take advantage.

A the core of this newsletter are spotlights on two of the many sparkling facets of the GST faculty. As a neighbor to Dr. Barry Bruce, I regularly get to enjoy Barry’s informal yet enthusiastic accounts of his latest discoveries, and I have learned that Barry is a master of forging collaborations. This newsletter contains an interview that captures how some of these collaborations come about. Second, Dr. Dave Ussery returned to the US and joined GST and ORNL two years ago after a productive faculty career in Denmark and Norway. His experiences are contributing an unusual perspective to our program. I hope you enjoy both of these conversations.

With best wishes for a productive Fall semester,

Albrecht von Arnim
Faculty Spotlight: Barry Bruce—Threading The Needle

Dr. Barry Bruce is a Professor in UT’s Department of Biochemistry Cellular and Molecular Biology and has trained GST students since the beginning of the program. A mainstay of research in the Bruce lab has been to decipher the mechanics of protein import into chloroplasts, the green organelles responsible for plant photosynthesis. Award-winning advances were recently accomplished by Dr. Bruce’s GST student, Prakitchoi ‘Non’ Chotewutmontri. A second area of research in the Bruce lab is ‘Applied Photosynthesis’, harnessing the highly efficient natural process of photosynthesis to generate electrical potential or chemical energy in a variety of hybrid materials. Much of this research relies on key (inter)national alliances that Dr. Bruce is a master of crafting and nurturing. This interview lifts the veil on how some of these alliances came about. The interview was edited for clarity and brevity.

Barry, please summarize the gist of Non’s contribution to the field of chloroplast protein import.

Non came in with an unusual background. With prior degrees in experimentally based genetics and in computer science, he embodied in many ways the ideal union of the GST program, in that he could do experimental work as well as computational work. So, the question that my lab has struggled with for 20 years is how do the class of proteins that possess transit peptides as plastid targeting sequences function in a concerted fashion. This has been an enigmatic question, because the bioinformaticists cannot find any conserved motif in them, yet we know that all of them are recognized by, and imported into, the chloroplast through the same pathway. My lab has designed ways to differentiate means of physicochemical recognition and means of sequence based recognition. Around the time that Non started, I had the clever idea that I had seen used as an undergraduate student where people created “reversed-sequence” genes, the first amino acid becomes the last and so forth. If we make reversed-sequence transit peptides, then we don’t perturb the physico-chemical properties but we completely obliterate their sequence. Non basically investigated the physico-chemical characteristics as well as the in vivo properties of two reverse transit peptides. What we discovered was that both answers were correct, that there was a specific physico-chemical interaction and a second one that was more sequence based. Non’s work teased that out, and using bioinformatics he realized that this is a global feature of one major class of transit peptides. What does it give you a dual lock and key mechanism, a low-specificity, high-frequency collisional encounter, which will capture the protein and then more specific sequence added on top of that, which will allow the protein to be translocated. That gives the cell a kinetically favorable system that also has very high fidelity. And it is probably one that can evolve quite easily de novo, given that we still don’t know where these transit peptide sequences came from.

You have always been very open to bring in bioinformatics approaches into your lab. Some investigators in the biophysical arena feel that “Genome Science” is beyond the scope of their research. How do you see it?

Maybe that’s true, but I don’t really see a reason for it. I think I understand the bioinformatics toolkits, I know what can be done and needs to be done. You have to realize that evolution is out there, and evolution is a great instructor for what’s important, so digging deep into genome space is like going into the library.

What was the key event that triggered you to return to your roots, so to speak, and re-engage in photosynthesis research?

It goes to one particular event, serendipity, truthfully. My wife worked with Rick Woychik and Liane Russell, mouse geneticists at Oak Ridge National Lab. She would bring home these very glossy quarterly magazines that the lab put out - I would never look at them. Except one day I was vacuuming the seats of her truck and one of those magazines was stuck underneath the seat. As I threw it out, it opened, and the centerfold was a story talking about Elias Greenbaum who was taking pieces of chloroplasts, and using a chemical treatment with hexachloroplatinate, he functionalized them in such a way that they became light dependent hydrogen evolving nanomaterials. I knew Elias Greenbaum a little bit, so I called him and said “Elias, this is really interesting, it must be photosystem one” (PS I, one of two core complexes in photosynthesis) that is responsible for generating hydrogen. And he says, “No, PS I alone had no activity”—basically a negative result. I said that doesn’t make sense. Having done my graduate work on PS I, I convinced him to let me try again. It so happened that I recruited a chemistry student from Maryville College, Jennifer Millsaps, who initially just wanted some opportunity for research, and then became a GST student.
We isolated PS I, we platinumized it, and sure enough when we did it in my lab PS I alone was a blockbuster complex for hydrogen production.

**How did you then become involved in the development of photovoltaic cells?**

As this was the first paper showing PS I dependent hydrogen production, it got a lot of publicity, because PS I was a nanoparticle, and it was stable. Elias and I and others then went on and got a DARPA grant (from the Department of Defense), originally to use PS I as a source of sustainable energy. I didn’t receive much funding from that DARPA grant but as part of the team I met an electrical engineer at MIT, Mark Baldo. We decided if PS I can make hydrogen it ought to be able to also make electricity, if only we could place an electrode close to PS I. The beauty of PS I is that it undergoes the largest photochemical free energy change of any biological particle and delivers over 1 electron-volt per photon captured. It is a very efficient process. The challenge is how do you take these biochemical, relatively soft, squishy macromolecules and attach an electrode at the right distance so that the electron goes in the right direction without going backwards. At some point I just started working directly with Mark, I flew up to Boston and over the course of maybe four days we mapped out a grant to the National Science Foundation. We got this grant, over 3.5 million dollars, and in the course of this work we were able to demonstrate that we could make a solid state photovoltaic device that underwent true charge separation.

The photosynthesis research is much more team-based and collaborative than your protein import work. How do these key alliances come about?

Nine months ago, I was headed to Europe and intentionally flew via Paris where I spent three days to meet the new director of the Paris Culture Collection at the Pasteur Institute, which is the largest and oldest collection of cyanobacteria in the world. I also knew of a scientist at the collection, Rosie Rippka, who had moved to Paris from UC Berkeley together with the original founder of the collection maybe forty years ago. And now we are formally collaborating. We are very interested in the structural stability and integrity of PS I, so I said maybe there are thermophilic organisms out there that have very stable PS I complexes.

What do you see as the key challenges of this kind of interdisciplinary work?

Perhaps the most exciting application of these photovoltaic devices are low power needs in remote sites. Think of the two billion people on this planet who do not have electricity. There are two challenges. The first is that the quantum efficiency is still low. Only around 0.2% of the light energy is captured, while nature can capture up to 37%, so nature is on our side, but we are still in the first generation of these devices. Basically, the challenge is to interface the biological materials into a photovoltaic ‘sandwich’ so as to capture the electrons effectively. There is a tuning process, where the electrical engineers and the biologists need to work together; I’m building the hand, and they the glove, so to speak. The problem is getting the material scientists cognizant of the challenges of working with biological materials, because a lot of things they want to do we simply cannot do. We cannot put our stuff into an oven and heat it up to 700 degrees. Also, we want to work with earth abundant materials, elements that are not resource limited. Typical solar cell technology uses rare elements, like ruthenium, gallium, of which there is simply not enough on planet earth to build a solar panel the size of Nebraska. The material scientists have a tendency to rely on those kinds of reagents for proof of concept for the inorganic side of the photovoltaic sandwich. Now, PS I is a renewable reagent. Nature understood resource limitation. Nature’s electron transport components work with elements like iron that are earth abundant. So, again, we have nature and evolution on our side, showing us that it can be done.
Making the most of the conference experience

This season, GST students were well represented at the annual meetings of the American Society for Microbiology (ASM) and the American Society for Mass Spectrometry (ASMS). We'd like to thank Alfredo Blakeley-Ruiz, Weili Xiong, and Sarvesh Iyer (all members of the Hettich lab) for answering a few of our questions about their experiences at the meetings.

In a nutshell, what did you present at the meeting?


Alfredo: I presented a poster on an analysis of the metaproteome of two Crohn's disease patients before and after (intestinal) resection surgery. The main point of the poster was looking at how the proteome changes over time at varying resolutions with the highest resolution being discrete protein groups and the lowest resolution being broad functional gene ontology groups.

How did your audience respond to your work?

Alfredo: Although our data was pretty preliminary, the audience was still for the most part excited about our work. Metaproteomics is a fairly new field and people are excited to find out what kind of biological information can be provided.

Weili: Yes, metaproteomics has emerged as a powerful tool to globally study the microbial community composition, function, and how microbes interact in situ and respond to their environment. Since most of my audience had a background in microbiology, they were very excited about the technique and showed great interest in understanding how the process worked and how it could be applied to their own work.

Sarvesh: I presented improvements to the chromatographic separation pipeline. Poor separation of peptides is one of the major bottlenecks in discovery proteomics. My optimized protocols involved simple modifications in steps which can be adopted by any lab. Hence it was met with a pretty good response.

At a large meeting like this, how do you make contact (planned or unplanned) with people that are interesting to you?

Weili: I usually look up the topics or the contacts that I am interested in and make a schedule. I will attend their presentations or stop by their posters. I like to ask them questions about their studies and also introduce what I am doing, to see how our studies relate.

Alfredo: The easiest way to make contact with people is to approach them during their poster sessions. ASMS has a tradition where people leave their business cards at posters that interest them, which can open the door for further discussion after the conference.

Sarvesh: Yes, by chatting with the presenters at the poster sessions, it also enables us to get an idea of the other projects going on in their group.

We all like a good buzz around our poster. Do you have tips for how to attract a good crowd?

Weili: An informative title that summarizes the topics, techniques, and conclusions usually attracts the audience. A balance between figures and word descriptions help the audience better follow the poster. Also, some highlights on the novelty and uniqueness of the study are very helpful.

Alfredo: I agree, craft a good title that interests people. Also people tend to be excited about buzz topics: human health, alternative fuel, and integrated omics are examples.

What was most valuable about attending? What do you wish you had known before going?

Alfredo: This was my first time attending ASMS. It is interesting because the conference does not cover a specific field. Instead it covers an analysis technique that can be applied to a wide variety of fields. This means that you get to see what a lot of different scientists are doing while still gathering information that helps you with your specific work. I wish I had known how important it was to bring a notebook to the meeting. Conferences are long and you are bombarded with a lot of information. It is important to jot some things down to help you retain all the possible information you can get at the conference.

Weili: I attended ASMS meetings a few times before. ASM is a much larger meeting. Although not so many topics were relevant to mass spectrometry technology, ASM broadened my view of proteomics in the context of microbiology and human health.

Was New Orleans a good venue for the meeting?

Weili: Yes, New Orleans is one of the biggest cities in the South. It’s a convenient location for meetings. There was good representation from local institutions of higher education and large corporations, which provides special opportunities for making contacts and seeking jobs.
GST Faculty Continues to Snowball

Dr. Francisco (Fran) Barrera arrived in UT’s BCMB department in August 2013 as an Assistant Professor after postdoctoral work with Don Engelman at Yale. He is a biochemist studying the interaction of peptides and other small molecules (drugs or drug candidates) with biological membranes and membrane bound receptors.

Dr. Xiaolin Cheng is a Staff Scientist at ORNL. His research has focused on the molecular dynamics of protein structure, using high performance computing. He has already been a valuable co-advisor of a handful of GST students in the Computational Molecular Biophysics group.

Dr. Maitreyi Das is an Assistant Professor in BCMB. She came to UT in 2013 after postdoctoral research at the University of Miami. Maitreyi studies the regulation of cell division in fission yeast, building on work, published in Science, which showed oscillations of the small GTPase Cdc42 at the cell tips. She uses computer modeling in her investigations.

Dr. Dan Jacobson is a Staff Scientist in the ORNL Biosciences Division. He joined ORNL in 2014 from Stellenbosch University (South Africa), where his research centered on yeast biotechnology. Dan has a broad range of experiences, including appointments in industry, which he has begun to share with GST researchers at ORNL.

Dr. Colleen Jonsson is a Professor of Microbiology. After a prior appointment at the University of Louisville she took over the helm of the National Institute for Mathematical - Biological Synthesis (NIMBioS) at UT from its founding director, Lou Gross. Her own research interests have revolved around viruses and image analysis.

Dr. Jessy Labbé is a Staff Researcher in the Plant-Microbe Interaction group at ORNL. He joined ORNL in 2009 after earning his PhD in fungal genetics from the University of Lorraine, France. He is well published in the field of plant-fungal (mycorrhizal) symbioses.

Dr. Sarah Lebeis entered Microbiology as an Assistant Professor in 2014. Her interests in the innate immune response have taken her from a PhD in vertebrate immunology into a postdoc on plant-microbe interactions (Arabidopsis root microbiome). She is also cultivating collaborations with current GST faculty members at ORNL and UT.

Dr. Steven Ripp is a Research Associate Professor in the Center for Environmental Biotechnology. As a senior research staff in the CEB, he has already been working with a number of GST students since 2001. His research spans a broad range of interests and technologies, among which bioluminescent biosensors and their application in pathology and biomedicine are a focal point.

Recent Publications

GST students and recent graduates have been publishing in the top journals in their fields. Following is a partial list of recent journal articles.


Dr. David Ussery joined ORNL in 2013 as the Comparative Genomics Group Leader in the Biosciences Division at ORNL. He came to us from a faculty appointment at the Technical University of Denmark, located in the hamlet of Lyngby, a suburb of Copenhagen. Enthusiastic about graduate training, he recruited a number of PhD students to his group, took the reigns on a segment of the GST I core course 'Genetics and Genomics', and also guided members of his group to become engaged in the GST program.

Thank you, Dave, for answering a few questions for me. First up, how did you experience the transition from academia to a national lab?

In Denmark, my group was primarily centered on PhD students, 4-5 students at any given time, plus one or two postdocs and maybe a programmer. I probably graduated a total of 30 students over the years. Whereas here, it actually took a while to sink in that supervising PhD students comes much lower on the priority list, in terms of job expectations. I’ve also discovered that the typical way to motivate and nurture PhD students is actually quite a bit different from what I find necessary here, where more of the core activities are delivered by staff scientists. With students I feel more like a gardener - this student needs water, that student needs fertilizer etc. The challenges are different. Also, it appears to me that at ORNL before my arrival, scientists had to adjust from a system where an individual researcher was largely responsible to contribute to one large block grant to a system where funding comes and goes and individuals must contribute productively to a number of different projects at any given time. But this is actually quite difficult to do and people tend to focus on what’s right in front of them at any one time, and sometimes lose track of the ‘big picture’. When I arrived I initially focused on building my own comparative genomics group. More recently, I got the chance to seek out the experimentalists at ORNL at a deeper level in order to coordinate how we can work together. For a series of recent presentations, we have structured the talks in such a way that each experimental talk has the computational aspects integrated into it, rather than keeping those separate. I believe this helps people to think of the computational component as an integral part or tool of the project.

Has your research interest shifted to any degree during this transition?

It has. One of the reasons I came here was a gene finding program that Doug Hyatt and his colleagues had written, called Prodigal; it is the best in the world. Another reason I came is for the scale of computing power that is accessible here. Although I have worked on comparing genomes for 20 years, here and now we have the opportunity to build a world class bioinformatics group that will work at the exascale (10^18 operations per second), which is essentially 1000 times faster than the current supercomputers in the world. This is a key directive also from DOE headquarters, to develop the biological applications for this scale of computing. We will soon have a million different bacterial genomes to compare. People are considering transforming these DNA sequence data into a data structure that can be analyzed by graph algorithms, rather than traditional alignment methods, where genes and their transcripts and their encoded proteins are considered coordinates of multidimensional vectors. In the end we may be comparing genomes by comparing graphs of vectors, which may be very effective, but may well require exascale-computing power.

You were trained in the US, but left the US for Europe after earning your PhD, the exact opposite of my life in science. Have you been surprised by how science and science training is (still being) done here?

I’ve actually quite enjoyed my 21 years of “5-star socialism”, as a friend of mine likes to call the Scandinavian system. In academia, some of the differences are perhaps cosmetic, others are not. On the surface it seems striking that 96% of PhD students in Denmark take only three years to complete their degree, but typically they complete a 2 years
Masters first, so in essence the length of their program overall is not all that different from ours. On that topic, when I completed my PhD in molecular biology in the US 20 years ago, aspects of it were really quite brutal, the lack or uncertainty of funding for example. In Denmark, PhD students earn what seems like a very comfortable salary - professors don’t really earn a whole lot more - and are treated more like regular employees. One aspect that is less cosmetic is that at the outset PhD students must present a very detailed 3-year plan for completing their research, broken down by 6-month milestones. And the program has support staff that will actually keep track of that progress, although just like here plans always change when reality strikes.

As you compare students with whom you have worked in Denmark with students you meet here, do you see differences in their career goals, or outlook on life?

As you may be aware, in Europe, young people realize earlier than in the US, basically as teenagers, where they are headed, career-wise. As they enter university they are set for a particular discipline, and thus by the time they start graduate school they have already been thinking of themselves as scientists. Whereas in the US it is more common for people to change careers later in life, and so they may enter grad school with different life experiences.

Some European universities seem to offer opportunities for students to cultivate a relationship with industry, more so than is customary here. Do you see what is needed to be successful in this area?

Yes, Denmark had an interesting model where PhD students can earn their degree while basically working on a project in a company. The company gets a tax break for supporting the PhD student. There are lots of opportunities. For example several of my students have worked for Novo-Nordisk, a manufacturer of enzymes and many of them now have jobs in the company. I have a Danish student I’m co-supervising, who is doing an industrial Ph.D. with Christian Hansen, a company that sells bacterial strains for the dairy industry, products such as cheese and yoghurt. They have proteomics data on the types of proteins produced in this very applied setting and wanted to know which bacterial strain was contributing which protein. These are interesting yet doable projects that one would not come across in an academic setting. That said, there can be sticky issues to resolve, conflicts between the company’s desire to patent the work or restrict the intellectual property and the student’s and the university’s motivation to publish the work. The key requirement the way I see it is the question of trust between the company and the university. Is there enough trust to realize that their common interests outweigh the effort needed to resolve the potential sticking points.

You have probably graduated as many if not more Bioinformatics students than anyone in our community. What is your advice for students who are entering this career path?

First of all, my general advice is that students need to be passionate about a specific project. And second, in bioinformatics it is perhaps not so common for a student to find a single mentor who can advise them optimally on both the biological and the computational side of their project. Therefore, I advise students to seek out two mentors that will cover both of those areas. I think it makes sense to learn from the professionals. Here at ORNL, the professionals are people in the computer science department, who work literally on ‘big data’ and some of the largest computing facilities on the face of the planet—we can all learn a lot from them—as well as the professionals who work with experimental areas, such as proteomics, microbial ecology, plants and animals. A good bioinformatics education requires experience in both areas.
As always, we’re very happy to announce our newest class of incoming students. The admissions committee is always delighted to receive a large number of applications each year, and works very carefully to ensure that accepted applicants are up to the challenges and opportunities that lie before them.

This year we have a large and diverse group of extremely talented and highly motivated scholars, eager to make their mark in 21st century life science. You will read about their achievements as they progress through the program. Please join us in welcoming them to Genome Science & Technology and to The University of Tennessee.

Aditya Barde has both Bachelor’s and Master’s degrees in Biotechnology from The University of Nagpur. Before coming to UT, Aditya was a research associate and Head of Operations at “Eugeniks Genetics Laboratory” in Nagpur, Maharashtra, India where he specialized in prenatal diagnosis of single-gene disorders in amniotic fluid or chorionic villi samples.

Ming Chen studied previously at Baylor University in Waco, TX before transferring to UT. His BS and MS degrees are from Yangtze University and the Chinese Academy of Sciences, respectively. He arrived earlier this summer for a project in computational genomics in the Staton lab.

Sarah Cooper is a graduate of The University of New England with a BS in Biochemistry and Neuroscience & Mathematics. She began working at ORNL with Jerry Parks in the molecular biophysics group.

Alex Cope comes to UTK from Centre College in Georgetown, KY where he earned a BS in Mathematics and Computer Science. He chose to apply to the GST program after working as a research intern with Kwai Wong and learning that UT would be a great place to pursue his interests in computational biology.

Maddie Denney has a BS in Biochemistry and English from Purdue University, and participated in the bioinformatic analysis of genomes for evolutionary phylogenetic research at Indiana State University before applying to the GST program. In 2012, she won an award from Purdue’s Biology Department as an Outstanding Teaching Assistant.

Amanda DeVolk, originally from Gunter, Texas, has a BS from Rutgers University where she double majored in Genetics and Spanish. She will build on prior experience in studying fertility in the genetic model organism, C. elegans, a nonparasitic nematode (roundworm) that lives in temperate soil environments.

David Fouth comes to the GST program from Southern Illinois University in Carbondale, IL. He has a very strong computational interest, especially for understanding a wide variety of statistical methods for inferring, analyzing and modeling gene regulatory networks derived from microarray and RNA-Seq data.

Grace McSween is originally from Knoxville, and she has earned a BS in Biology and History from Samford University in Birmingham, AL. Grace’s research has taken her far beyond normal university labs—she has visited Peruvian rainforests on more than one research trip to investigate both the medicinal properties of the “Sangre de grado” tree as well as bioluminescence of certain fungi.

Shantanu Shukla earned an MS in Bioinformatics from Pondicherry University in Puducherry, India. Having already gained quite a bit of experience in Next Generation Sequencing (NGS), Shantanu seeks to apply these skills in the bacterial genomics arena.

Yaojin Sun is a graduate of Shanghai JiaTong University, where he earned a BS in Biotechnology/Bioinformatics. He comes to GST with prior computational experience in molecular modeling and principal component analysis as well as hierarchical clustering algorithms. His primary interests lie in computational and systems biology.

Ricardo Urquidi Camacho has a BS in Bioengineering and Physics from The University of Arkansas at Fayetteville as well as an MS in Biomedical Engineering from The University of Twente in the Netherlands, where he developed bio-computational models, experience that led him to apply to GST.