Personal Statement
Georgia Institute of Technology
Biology Ph.D. Program

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Note: I have been transferred to Quantitative Biosciences Ph.D. program at Georgia Tech before accepting the offer from its Biology Ph.D. program, because I think QBioS would be a better fit for my future scientific career.

Research experiences

My path of biology started with encountering Thompson's On Growth and Form that led me to touch upon my inner fascination with complex biological structures and my built-in comparative mindset eager for pursuing general principles. After a short stay in Dr. Liang Cai's Lab of cytoskeleton, I realized my preference to making sense of the complex biological structures in terms of their formation rather than their dynamics, so I joined Dr. Yufang Zheng's Lab of developmental neuroscience. I politely turned down an offered project due to disinterest and tried coming up with my own ideas. At the same time, I became interested in how a population of individuals undergoes division of labor during the formation of complex structures, and I even explored this topic in the context of microbial communities and ant colonies. And when I came across the interesting phenomenon of interkinetic nuclear migration in a pool of neural progenitor cells (NPCs), I instantly linked it with the subsequent cell fate choice of NPCs on self-renewal or differentiation, an idea unfortunately reflected in a Cell article in 2008. When I discussed with Dr. Zheng on further questions, she told me her mice might not be suitable for addressing such dynamic embryonic processes, and recommended me to visit Dr. Su Guo who studied zebrafish.

In my first meeting with Dr. Guo, a question I posed about her work was developed into my first project, studying the molecular mechanisms of intra-lineage Notch signaling, which determines the asymmetrical fates of paired daughter cells produced by asymmetric cell division (ACD) of a NPC. The essence of development is symmetry

breaking, Lionel Harrison said in his Kinetic Theory of Living Pattern, and I think such intra-lineage property exhibits a special, if not new, kind of asymmetry. I hypothesized that it might be rooted in the co-localization of Notch ligands (DeltaA) and receptors (Notch1b) at the membrane interface between paired daughter cells, and the key to testing this idea is to label and visualize DeltaA and Notch1b. With my research mentor mostly in her another lab abroad in UCSF, inconvenience gradually turned into independence during those months of sending problems with potential solutions for her suggestions, previewing thoroughly and discussing with graduate students on molecular or genetic experiments, and even requesting protocols to establish an electroporation system myself for sparse labeling of paired daughter cells. As for labeling DeltaA and Notch1b, their dosage sensitivity made exogenous fluorescent fusion proteins result in cell fate alternation, and antibodies were either unavailable or unworkable. Knockin of fluorescent protein sequences was ideal. After noticing a newest paper on CRISPR/Cas9 MMEJ knockin highlighting both efficiency and accuracy in zebrafish, I tested this method but had no success. Despite frustration with these negative results, their conclusiveness conferred by controls and logic give me the confidence in that these methods are indeed not suitable in my case, and other knockin methods will be tried.

In order to further understand the mechanisms regulating the asymmetrical fates of paired daughter cells from a NPC, my current project in Dr. Su Guo's Lab in UCSF focuses onthe potential centrosomal localization of DeltaD during its asymmetrical segregation in ACD. In order to trace the dynamics of DeltaD in vivo, I have developed the first antibody uptake assay in the embryonic zebrafish forebrain. Despite extensive discussions and consulting another group's experience in the zebrafish spinal cord, trials and errors abounded. Even after the first appearance of the expected result, I was not able to reproduce it for the next two weeks. But had it not been these two frustrating weeks, I might not have noticed previous errors in imaging settings and antibody preparation. It was my belief in that contingent success and continuous improvements that led to a highly reproducible assay. Using this assay and time-lapse confocal imaging, I have successfully captured the asymmetrical segregation of DeltaD in ACDs, the colocalization of DeltaD with centrosome in some cases, and an unexpected potential ciliary localization of DeltaD that is worthy of further investigation. Moreover, in discussions with lab colleagues, I became aware of the importance of considering alternative explanations to data, especially in a complex multicellular context and for a new assay. In the coming months in UCSF, I plan to study the dynamic spatial relationship of DeltaD and centrosome, its regulation and its functional significance to ACDs of NPCs.

During these times, taking courses ranging from development, evolution, to computational biology and philosophy of sciences continued to broaden my mind.

Charmed by Eric Davidson's work on how genetic network rewiring shaped the animal body plan evolution, I started to consider the formation of complex biological structures, not only as their revelation during development, but also as their emergence through evolution. John Maynard Smith and Eors Szathmary's papers further struck my mind by viewing the hierarchy of biological complexity as the result of a series of major evolutionary transitions (METs) where individuals integrate into a new level of individuality. As an example of METs, the transition to multicellularity intrigued me the most. So when I heard Dr. Zhixi Su was studying the role of phosphotyrosine (pTyr) signaling in the origin of animal multicellularity, I immediately joined his lab this summer. As a preparation, I wrote a review article on this topic, where I tried blending into a flavor of signaling and a comparative view to other multicellular lineages. In the lab, I learned the foundations of protein domain predictions, phylogeny construction and enrichment analyses using tyrosine kinome and phosphoproteome data of Monosiga brevicollis, a unicellular ancestor of animals. I also tested the expansion of pTyr signaling system and the increase of genomic GC content as two alternative explanations to the proteomic tyrosine loss in evolution, which is correlated with the increase of biological complexity. Compared to previous studies, I extended the focus from metazoan to eukaryotic evolution, and tried to avoid statistical bias of selecting close species that caused elevated correlation coefficient. I developed R programs to calculate the tyrosine and GC4 content of selected species. With previous experience in C and Matlab, I tried a task-directed learning of R that comprises an exciting loop of learning and problem solving, and I was surprised at how troubleshooting experience back in wet lab could facilitate debugging. As a result, I found that the increase of genomic GC content might be a better explanation for the decrease of proteomic tyrosine content in the eukaryotic evolution, while the expansion of pTyr signaling system still held some significance in the holozoan and metazoan evolution.

Why have you chosen to apply to Georgia Institute of Technology?

I believe Georgia Tech is ideal for my graduate study.

Georgia Tech is renowned for its persistent efforts for integrative biological researches. This emphasis in collaboration is not only between sub-disciplines within biology, but also extending to mathematics, computer science and engineering, which is reflected in the researches of its faculty members as well as its well-designed coursework, like Evolutionary Development Biology, Mathematical Biology and Evolutionary & Synthetic Biology. My mind will certainly be broadened in this exciting environment, and my multi-

disciplinary background (in molecular and cell biology, development, and evolution) will also contribute new perspectives to the program.

More importantly, Georgia Tech has several scientists (e.g., Dr. William Ratcliff, Dr. Frank Rosenzweig, and Dr. Matthew Herron) whose work matches my research interest in the evolution of multicellularity, and the experimental evolution they use represents an emerging and powerful approach in this area. Moreover, the NASA CAN-7 Team in Montana, which studies the experimental evolution of major transitions, has recently moved to Georgia Tech. So it's really a party (instead of a solo as in many other research institutions) for studying how major evolutionary events have shaped who we are today. And I am really looking forward to being a part of this exciting adventure.

What are your primary interests - research, career goals, etc?

My research interest lies in the evolution of multicellularity. As the beginning of all development and a representative of evolutionary transitions in individuality, the multicellular origin holds important implications for the development and evolution of biological complexity. Besides, the emerging approaches like comparative genomics and experimental evolution combined with genetics, phylogenetic analyses, mathematical modeling are making this problem seem answerable in the foreseeable future. Moreover, this problem fits my personal qualities. I could hardly find another problem that can satisfy my broad biological interests in cell biology, development and evolution, and that can allow me to work in a multi-disciplinary environment where I can utilize various approaches and collaborate with interesting people from different disciplines.

Georgia Tech has several scientists using experimental evolution to study this problem. Experimental evolution has the unique power of elucidating not only how multicellularity evolved in history but also how it can be evolved in principle, as well as of documenting the multicellular evolution in real time. I would love to be a part of this exciting adventure, evolving the nascent multicellularity into complex structures and division of labor, and probably adding a flavor of synthetic biology.

What have you done thus far to prepare yourself for graduate study?

Through coursework, I have built up a rigorous foundation in biology as well as mathematics and other natural sciences. My undergraduate GPA is among top ten in our grade, and I obtained A in all courses ended with a final essay. Since the courses allowed

in the above “Biology Course” section is limited, I have typed some biology courses in “Chemistry Course” and “Biochemistry Course”, and they are distinguishable by Course# with a prefix “BIOL”.

Aiming for a research-oriented career, I have joined three labs and performed independent research projects. They helped develop my scientific thinking skills and forge my perseverance through trials and errors. I am also selected as a member of the National Top Talented Undergraduate Training Program, which is reserved for very top undergraduate students in China.

With respect to my research interest in the evolution of multicellularity, I have read many papers, and joined in a research project on the role of pTyr signaling in the origin of animal multicellularity. In the ASCB (American Society of Cell Biology) Annual Meeting 2016, I discussed with graduate students from Dr. Nicole King’s Lab in UC Berkeley, which studies the origin of animal multicellularity using choanoflagellates. In the reply to my e-mail, Dr. Nicole King said, “It sounds like you’ve done a great deal of reading and thinking about multicellularity. That’s great!”