◇ *Quantifying uncertainty in modeling cell-biological decisions to divide, differentiate, or die during organogenesis, as influenced by underlying modularized networks of interacting gene products, with Dr. Michael J. McConnell, Harvard University:*

The future integration of bioinformatics and systems biology will rely heavily on insights from pure, applied and computational mathematics. To this end, studying the potential influence of DNA damage and repair on developmental timing during cortical neurogenesis has instructed me in the challenges mathematical biology faces. Formulating models of cell fate control is, in essence, an inverse problem in need of a systematic computational framework. In recent work, I have reviewed the molecular bases of proliferation, differentiation, and programmed cell death, in the specific cellular context of cortical development in a mouse. In doing so, model uncertainty due to reduction in both spatial and network complexity is explored. Two nested qualitative networks were introduced and, employing the simplest of these, two mathematical formulations of the dynamics were proposed. Each formulation, derived from an incomplete qualitative network, is viewed as a discretization of the inverse problem of cell fate determination. Options for mathematical translations to describe the network dynamics were discussed, including stochastic and hybrid continuous/stochastic methodologies. After confirming that qualitative properties are displayed, a model validation framework is proposed that bridges intracellular and cell population scales using a portfolio of objective functionals to guide in sampling parameter space. In particular, validation is underway using cortical neuron lineage relationships, as well as karyotype distributions that characterize the mosaic composition of aneuploidy; that is, they characterize cell population diversity defined with respect to loss and/or gain of chromosomes. By focusing on the developmental timing influence of a cell's response to DNA damage, which is always present, signaling associated with proliferation, differentiation, and programmed cell death can be integrated. Moreover, double-stranded breaks of DNA are directly implicated in chromosome segregation defects . The ultimate ability to traverse among hierarchies of models, testing their validity, or plausibility, within an optimization setting, will lead to greater understanding of how the balance between division, differentiation, and death emerges from intrinsic and extrinsic factors of cell cycle and cell fate control. There is much room for future work on this project and, as it epitomizes the grand challenge to mathematical systems biology, development of such a framework for other cellular contexts should be explored. Importantly, given the complexity of biology, the aim of modeling is not to replace experiments but rather to supplement them, ideally accelerating understanding in a perpetual, null-hypothesis driven cycle of model development and validation. In future work, I will draw heavily on model reduction strategies for quantifying uncertainty that owe their development to fluid flow control and optimization, and this direction is elaborated in my recent article.

◇ *Adaptive meshfree first-order system least-squares (FOSLS) using centroidal Voronoi generators and a partition of unity, with Max Gunzburger and John Burkardt, Florida State University:*

The FOSLS methodology caters a formulation to algebraic multigrid solvers and directly provides *a posteriori* error estimation, due to the FOSLS functional's ellipticity to a *div-curl* Sobolev norm. A dual version, FOSLL$^*$, is preferable to FOSLS when solution regularity is restricted, as can be the case in nonlinear elasticity and electromagnetics. Application to a wide range of partial differential equations has been very successful, and the community of research has a large presence in the DOE national labs. Meshfree, or meshless, discretization methods are in vogue due to the prospect of bypassing complications in adaptive mesh generation. Using a covering defined by generators, or nodes, of a centroidal Voronoi tessellation, along with corresponding support radii, we construct a partition of unity basis and conduct quadrature in the resulting lenticular overlap of elements to discretize a FOSLS minimization principle. Given the local estimates a FOSLS functional provides by design, and given the ease with which Voronoi nodes can be added, this approach may realize the potential of meshless computing.

---

Confident it would keep all doors open, I completed an undergraduate degree in mathematics, despite lacking much perspective to relate topics in abstract algebra, complex analysis, and topology to the real world. While in graduate school, I was fortunate to find mentors, Tom Manteuffel and Steve McCormick, who eagerly demystified mathematical abstractions important to understanding their applied mathematics research. Offering such context and perspective early in undergraduate mathematics courses is imperative to recruiting and retaining many potential mathematics majors, students who will then likely benefit, regardless of their careers, from fluency in both qualitative and quantitative reasoning. This is a defining consideration in my teaching, because a supportive individual contact with a professor can be the only encouragement a student needs before deciding to invest in learning mathematics.

Last spring, I volunteered to teach the second semester of undergraduate numerical analysis at FSU. By the end of the course, the students saw how concepts learned over the course of the year—approximation theory, numerical integration, orthogonality of functions, and preconditioned iterative methods—are all utilized in the finite element solution of Poisson's equation. Their sense of accomplishment in the final weeks was palpable. The class was small, with a handful of senior mathematics majors, allowing for low key lectures with frequent interruptions that often led to enriching segues. I composed my own detailed notes as a narrative and maintained a lively presentation, integrating examples and homework assignments into each lecture. For more details on this course, including copies of exams, programming assignments, and a handout reviewing matters for the final exam, please visit *http://www.csit.fsu.edu/~macmilla/teaching.html*.

In addition to providing context, a teacher of mathematics must instill patience, particularly to promote literacy. Many capable students mistakenly assume they are otherwise when, at their first exposure to analysis, for example, they find themselves in the unfamiliar position of having to reread a single page or proof many times before understanding the relevance of each sentence. Students need to be reminded that wringing each statement for meaning, usually with paper and a pen in hand, does take time. To promote this patience while a teaching assistant in graduate school, I once composed a playfully worded translation of a proof of an existence and uniqueness theorem for a simple class of ordinary differential equations. Many students who would have otherwise never tried to follow the proof offered in the textbook could see, through my translation, that the underlying concept is in fact quite logical and simple, but that it is just enshrouded in language they are unpracticed in reading. At both undergraduate and graduate levels, such literacy empowers a student to not only explore interfaces within mathematics but also those between mathematics and science. A computational scientist or engineer, for example, if interested in how well he/she can trust a solution their model provides, would be well served by the ability to study alternative formulations along with their corresponding solution methods.

I look forward to a career of teaching and learning in an academic environment that encourages creative research. In addition to the calculus sequence, ordinary differential equations, and numerical analysis, I am ready and interested to teach special topics courses on numerical linear algebra, multigrid methods, finite elements, and partial differential equations. Moreover, I would especially like to develop and teach an interdisciplinary course, perhaps in conjunction with a biologist, on current trends in mathematical systems biology.