From *SIAM News*, Volume 43, Number 6, July/August 2010

Teacher, Research Mathematician, Mentor: A Groundbreaking Career in Computational and Mathematical Biology

When Trachette Jackson walks with her two sons in Ann Arbor, she is following paths traced six decades ago by Marjorie Lee Browne, who made history at the University of Michigan as one of the first African American women to earn a PhD in mathematics (in 1949). Trachette too has made history at the University of Michigan: She joined the mathematics department as an assistant professor in 2000 and was the first African American woman to become a full professor there (in 2009).

Expanding our Scope

By Carlos Castillo-Chavez

Marjorie Lee Browne (1914–1979) earned a "traditional" PhD in mathematics, with a dissertation, "Studies of One Parameter Sub-groups of Certain Topological and Matrix Groups," written under the supervision of G.Y. Rainich. On graduating, she joined the faculty of North Carolina College, or NCC (now North Carolina Central University), becoming chair of the mathematics department in 1951—a position that she held for nearly two decades. Marjorie Lee Browne's academic path was not straightforward. She received a master's degree from Michigan in 1939 and then, while teaching mathematics at Wiley College in Marshall, Texas, worked on her PhD from a distance and over the summers.

Trachette is not a "traditional" mathematician; she works in computational and mathematical biology—a field that crossed a critical threshold as Marjorie Lee Browne was beginning her career at NCC. This "push" was the result of at least two nearly simultaneous events: invention of the "computer experiment" by Enrico Fermi, John Pasta, and Stanislaw Ulam at Los Alamos National Laboratory and discovery of the chemical structure of DNA by James D. Watson and Francis Crick, both around 1953. Some of the great advances from the start of the second half of the 20th century are intimately connected to what Steve Strogatz* called a "third way of doing science":

> "Suddenly the computer became a telescope for the mind, a way of exploring inaccessible processes . . . —phenomena that are too large or too fast to be visualized by traditional experiments and too complex to be handled by pencil-and-paper mathematics. The computer experiment offered a third way of doing science. Over the past 50 years, it has helped scientists to see the invisible and imagine the inconceivable."

The use of the "computer experiment," Strogatz continued, has enhanced scientists' ability to make use of the intrinsic capacity of nonlinear systems for self-organization:

Using mathematical modeling, numerical simulation, and in vivo tumor vascularization experiments, Trachette Jackson and her research collaborators are working to provide a deeper understanding of tumor growth and vascular structure at the molecular, cellular, and tissue levels. As the 2010 recipient of the Blackwell–Tapia Prize, Jackson is honored both for her research and for her efforts on behalf of underrepresented minorities in the mathematical sciences.

> "The resulting technology has spawned the world's most sensitive detectors, used by doctors to pinpoint diseased tissues in the brains of epileptics without the need for invasive surgery, and by geologists to locate oil buried deep underground. But perhaps the most important lesson of Fermi's study is how feeble even the best minds are at grasping the dynamics of large, nonlinear systems. Faced with a thicket of interlocking feedback loops, where everything affects everything else, our familiar ways of thinking fall apart. To solve the most important problems of our time, we're going to have to change the way we do science. For example, biologists working alone will not cure cancer. Its solution will require a melding of both great discoveries of 1953. Many cancers, perhaps most of them, involve the derangement of biochemical networks that choreograph the activity of thousands of genes and proteins."

It is in the study of cancer dynamics that Trachette Jackson has found her calling as a scientist and mathematician. How did this come about? Following a nomadic youth as the child of parents in the military, Trachette settled at the age of 12 into what she considers her hometown: Mesa, Arizona. It was in Arizona that she met the first of the three (male) mathematicians who would guide her efforts to find her path as a teacher, research mathematician, and mentor.

At 15, Trachette met Joaquín Bustoz Jr., the first university professor who was to have a significant impact on her life. Joaquín was a native of Tempe, Arizona, the son of farm workers and school caretakers who were deeply loved and respected by the community. (It was Joaquín who brought me to Arizona after 18 years at Cornell University, so that we could carry out our joint schemes as a "Latino dynamic duo." His untimely death, four months before my arrival, was a tremendous loss to the Latino, minority, and mathematical sciences communities, to the state of Arizona, and to our nation. Holding the first endowed professorship named after this U.S.-born, raised, and educated Mexican–American mathematician is an immense honor for me.) In 1985, to provide first-rate educational opportunities in the mathematical sciences to minority and economically disadvantaged students, Joaquín established the Mathematics Science Honors Program (MSHP) and then the Institute for Strengthening the Understanding of Mathematics and Science (SUMS). SUMS has expanded the mentoring and academic support available to MSHP alumni after they enroll as full-time

*In a 2003 op-ed piece for *The New York Times*, "The Real Scientific Hero of 1953."

students at Arizona State University. Joaquín's efforts were recognized with a Presidential Award for Excellence in Science, Mathematics and Engineering Mentoring in 1996; SUMS, as an organization, received the same award in 2003.

Trachette vividly remembers meeting Joaquín for the first time. "A cocky 15-year-old kid," she signed up for a five-week calculus course, having taken a math placement test in one of the ASU dorms. Shocked at her score of 98%, she marched up to a man wearing Levis and Birkenstocks to ask whether anyone had earned 100%. Joaquín replied, "Yes, Miss Jackson, two or three students received a perfect score, but they all took calculus during their senior year of high school, and I understand that you still have one year of HS left and have yet to take a calculus course." Surprised that Joaquín knew her name, Trachette had no idea to whom she was speaking, and could not have predicted the profound impact that he would have on her life. "That's how I first met and came to know Joaquín Bustoz, the person to whom I owe much of my mathematical career."

In a land of opportunity, access and excellence cannot be present only at institutions that serve the few. Access and excellence must be key elements, the *main* ingredients, and ever present at all public institutions. Access at Hispanic-Serving Institutions, Historically Black Colleges and Universities, Tribal Colleges and Universities, and some public universities must always be accompanied by excellence—otherwise, the promises of our democracy will rarely reach huge segments of the American population. Trachette, one of the top students in a class of more than 800 who graduated in 1990 from Mesa High School, chose to stay at Arizona State University. She explains:

Joaquín Bustoz Jr., the first of three university professors to have a significant impact on Trachette Jackson's life.

"So, I took calculus at ASU that summer and came back the following summer to take a longer eight-week math course. By then I had already decided to go to ASU for my BS. (I registered as an engineering major, which earned me a trip to Dr. Bustoz's office where we had the first talk that changed my life—and my major to math.) My fellow academic Top 20 high school graduates went to places like Caltech, the University of Chicago, and Stanford, but I knew that ASU was the right place for me."

What helped make it right, she says, was a network of friends, mostly underrepresented minorities, who had goals similar to hers: "to be the first person in my family to graduate from college."

Programs like MSHP and institutes like SUMS respond to what the Reverend Martin Luther King referred to as "Life's most urgent question . . . what are you doing for others?" Trachette addresses this question often: "The Math–Science Honors Program and Dr. Joaquín Bustoz are the reasons I have made it as far as I have today. The SUMS program gave me every type of support (financial, emotional, etc.) and enabled me to complete my BS and my PhD." Trachette has been involved in almost every aspect of the MSHP, as student, mentor, tutor, and teacher.

Trachette has followed a mathematical education-through-research path that is distinct from Marjorie Lee Browne's. It provides a solid example of alternative powerful ways for bringing underrepresented minorities into the mathematical sciences. Tenets of this model for recruitment and career success include the following: The relevance of mathematics must shine through its application to the most challenging scientific problems of the day; training must be interdisciplinary, possibly cross-disciplinary, a philosophy to which many SIAM members adhere but one that is still not common (and not possible to implement in many mathematics departments—how do we find time for learning a third way of doing science, for acquiring significant knowledge of disciplines outside mathematics?); the graduate program must involve mathematics students in the study of scientific questions for which it is evident that progress will come through mathematics; and the mathematical profession must find ways for students to do all of the above in *five years* (that is, at least for this kind of applied mathematics, we must abandon in many cases the successful but often one-dimensional "cloning" model of mathematics education that dominates our graduate programs).

James Murray, a native of Scotland, has inspired generations of computational, mathematical, and theoretical biologists at the Centre for Mathematical Biology at Oxford and, later, at the University of Washington. Jim became Trachette's PhD adviser at the University of Washington. His description of their interactions also gives a close look at his perspective on the field of mathematical biology:

"I was struck immediately on first meeting Tracé by her genuine enthusiasm and her strong wish to get involved in real mathematical biology research as quickly as possible. Her progress exceeded my expectations. Normally I find that students require considerable help in identifying a suitable thesis project. Tracé, on the other hand, read widely and came up with a highly suitable proposal almost entirely on her own. Not only that, she also found an enthusiastic first-rate experimental collaborator in the Seattle area, who was very keen on collaborating with us. The collaboration involved in her thesis work proved very fruitful for everybody involved in the project and some of the results were published in the prestigious *British Journal of Cancer*, a journal not noted for publishing articles in mathematical modelling. An important aspect of her research is the close connection she always maintains with the real experimental world. Her approach to research is fundamentally practical. She has a real talent for constructing models from real experiments and biological facts. She is also a superb communicator with non-specialists and can explain with clarity what is important, how a complex phenomenon is modelled and what the results mean biologically. She has very high standards and, unlike many of her contemporaries, only publishes when she has something new and relevant to say. Tracé is a first-rate mathematical biologist and excellent interdisciplinary collaborator. . . ."

It is not surprising that a student with the interests and motivation of Trachette would wind up working with somebody like Jim. She recalls meeting him when, as an undergrad at ASU, she saw a flyer for a seminar whose speaker was going to describe, using mathematics, "how the leopard got its spots." After attending this talk, by Jim, Trachette knew that math biology would be her future: "This was the first time that I had seen this type of application of mathematics and it excited me." Jim was an extremely positive and supportive PhD adviser, she says: "He was always full of ideas and pushed me to think deeply about the underlying biology of my work by saying in his signature accent, 'Ahh, Tracé, but have you thought about . . . ?' " Today, she continues to strive to construct models that capture as much of the relevant biology as possible.

In general, identifying the right academic/professional match and finding ways to implement it are not so simple. Even for the best informed students, a "correct" path does not always emerge directly.

In seeking postdoctoral positions, Trachette identified several opportunities and experienced some confusion and anxiety. She recalls not being sure which offer to accept. She then took *the* call, from Michael Reed of Duke University (a distinguished mathematician, mathematical biologist, and champion of women in academia). He and I "talked on the telephone that first time for a very long time," Trachette recalls. "I immediately felt that this was a person who had my best interests in mind. I trusted him from his very first words to me." Mike facilitated Trachette's transition from recent PhD to independent researcher, introducing her to key people in Duke's Medical School and at the Environmental Protection Agency and making sure that she had the resources she needed to succeed.

Mike's perspective on Trachette's trajectory also gives some insights on his views on mathematical biology:

"Some mathematicians are not really interested in biology but use biology as a source of new and interesting mathematical questions, which is fine. Another group is really interested in biological problems, but they don't get too close to the biology; they tend to work in areas where the biology is fairly well understood or on methods. The reason they don't get too close is that biology is really difficult, very complicated, and knowledge is changing rapidly in the important areas. Thus one must devote enormous amounts of time to learning new things and just keeping up. This is time taken away from proving theorems, making models, running simulations, developing numerical methods, i.e., all the things that bring rewards in the applied mathematics community. Who would do this? Only a relatively small number of mathematicians, those who are absolutely driven to try to understand the biology, follow this path. They naturally head for big important problems where the biology is not well understood. Cancer is, of course, such a problem. And Tracé Jackson is such a mathematician."

As to Trachette's current research, she and her colleagues work in a world in which new strategies for treating cancer are a more pressing need than ever. Despite advances in early diagnosis, aggressive surgical treatment, and application of additional non-surgical modalities, the prognosis for many cancers remains dismal. Several issues related to the complexity of tumor growth and the development of novel molecular targets cannot, and most likely never will, be fully understood through experiment or through mathematical modeling alone. Mathematical and computational modeling must be intertwined with ongoing experimental research if we are to piece together the related cellular processes that cut across multiple biological scales in facilitating the progression of cancer.

Using mathematical modeling, numerical simulation, and in vivo tumor vascularization experiments, Trachette and her research collaborators are working to provide a deeper understanding of tumor growth and vascular structure at the molecular, cellular, and tissue levels. More specifically, the researchers have quantified the (usually dramatic) effects of variations in pro-angiogenic factor gradient profiles on capillary sprout morphology; predicted the dependence of average sprout extension speed on the proximity of the proliferating region to the sprout tip and on the coordination of cellular functions; and helped to demonstrate the mechanism by which inhomogeneities in extravascular tissue lead to sprout branching and anastomosis, emergent properties of developing vessel sprouts.

This work has implications for the selection of drugs that will be the best candidates for clinical trials. Trachette and her collaborators have introduced models connecting the molecular events associated with VEGFR2 dimerization and intracellular signaling with temporal changes in endothelial cell proliferation, migration, and survival, and linking these dynamics to tumor growth and vascular composition. They developed these models in an attempt to decrease the cost and reduce the time required to devise and evaluate therapies targeting pro-angiogenic proteins. The models are providing rapid and rigorous answers to questions about the therapeutic potential and optimal timing and dosing for these new therapies. In essence, Trachette's research has the potential to get new small-molecule inhibitor therapies to cancer patients faster—and in doing so to save lives.

Trachette's influence in the relevant biological communities keeps growing. Her recent remarks on the relation between mathematical and systems biology, for example, were featured in an article in *Nature Reports Stem Cells* ("Stem Cells, Systems Biology and Human Feedback"), and she and Sofia Merajver spearheaded the introduction of a regular Mathematical Oncology subsection in the journal *Cancer Research*. Her career lives at the interface of collaborative research and educational activities that cut across traditional disciplinary boundaries.

Trachette's work has been recognized many times. Most recently, she is the 2010 recipient of the David Blackwell–Richard Tapia Prize—the first woman in a distinguished list of awardees: Arlie Petters, Rodrigo Bañuelos, Bill Massey, and Juan Meza. The prize will be awarded at the NSF-supported Mathematical Biosciences Institute, host of the 2010 Blackwell–Tapia Conference, November 5–6.

Trachette's career has not prevented her from raising a family. Her first son was born while she was a postdoc, and the birth of her second did not stop the tenure-track clock at Michigan. "Things are a bit easier to balance now," she says, "but achieving balance is something I consciously strive for every day."

Marjorie Lee Browne had a brilliant career at a time when opportunities for women, particularly women of color, were exceedingly rare. But 60 years—three generations—would elapse between her 1949 PhD from the University of Michigan and the awarding of a tenured full professorship to another African American woman. My daughter, Gabriela Citlalli Castillo-Londono, recently celebrated her 11th birthday. It is my hope, as I am sure it would be the hope of any parent, that she will live in a world in which women of color no longer have to think in terms of generations as they strive to fulfill their dreams and aspirations.

Expanding our Scope is a new column devoted to stories that highlight the efforts of individuals to broaden participation in the mathematical sciences. Carlos Castillo-Chavez, Regents Professor and the Joaquin Bustoz Jr. Professor of Mathematical Biology at Arizona State University, is the editor of the new column. He welcomes submissions and ideas for future columns (chavez@math.asu.edu).