This issue's interview is with Professor Trachette Jackson, Assistant Vice President for Research - DEI Initiatives, Professor of Mathematics and University Diversity and Social Transformation Professor, University of Michigan. Trachette will be a plenary speaker at the 2023 Society for Mathematical Biology Conference, and is this year's awardee of the Leah Edelstein-Keshet Prize. Prof Jackson's research focuses on the use of mathematical models to understand tumour growth and development and to guide therapeutic strategies.

Who or what inspired you to pursue a career in mathematical biology?

My inspiration came from a visionary leader, dynamic speaker, and transcendent scholar. When I first saw James D. Murray, F.R.S. speak, I immediately knew that I wanted to solve problems and create new biological knowledge using mathematics.

What is your favorite research paper (by another mathematical biologist)?

"Education is not the fill of a pail, but the lightening of a fire*[1]." The paper that changed the course of my education and lit the mathematical biology fire in me as a sophomore in college was, How the Leopard Gets Its Spots, by James D. Murray. I changed my major from pure to applied mathematics because of this paper.

Your work has some exciting applications for improving cancer therapies. Can you tell us about any interesting potential therapies that your models have suggested may be an improvement to current treatments?

To improve therapeutic outcomes for cancers, a substantial amount of research is now focusing on the molecular biology of the tumors and treatments that selectively target pathways involved in tumor progression. Some new approaches aim to inhibit tumor growth and spread by targeting the tumor microenvironment. In contrast, others focus on specific proteins or signal transduction pathways associated with tumor cell proliferation and survival. Intending to address critical challenges related to targeted molecular therapeutics, my collaborators and I have developed a suite of data-driven mathematical models designed to optimize the use of targeted drug treatment strategies and determine which drugs are the best candidates for clinical trials. Evidence of our computational efforts' impact is that our multiscale mathematical model of the VEGF-CXCL8-BCL-2 pathway suggested that metronomic dosing of a small molecule inhibitor (SMI) of the pro-survival protein BCl-2 could provide optimal efficacy. These computational model predictions were validated in preclinical studies and led to their application in a clinical study.

In a current NIH-funded project, we are interested in developing predictive methods for optimizing combination immunotherapy and therapies that target receptors that are frequently mutated in bladder cancer. Clinical trials using drugs that inhibit these mutated receptors lead to promising clinical responses for some patients, but dose scheduling remains challenging. At the same time, immunotherapies that use monoclonal antibodies to target the PD-1/PD-L1 pathway achieve approximately 25% response rates for patients with advanced bladder

[1] *A quote from William Butler Yeats

cancer. One reason for these less-than-ideal response rates is that the aggressive mutations associated with some advanced bladder cancers can hinder the impact of immunotherapy. Leveraging the excitement around these approaches and the challenges each therapeutic option faces, our mathematical models show that a co-acting combination of potent immune checkpoint inhibitors and specific inhibitors that target the mutation can offer significant improvement over either monotherapy.

Have you ever encountered any surprising results in your research?

Several years ago, my team became very interested in cancer stem cells (CSCs), which function as putative drivers of tumor initiation, therapeutic evasion, metastasis, and recurrence. Though they are an appealing conceptual target, CSC-directed cancer therapies remain scarce. We developed and validated a multiscale mathematical model that predicts the responses of head and neck squamous cell carcinoma to combination therapy consisting of tocilizumab, which targets cytokines that enhance CSC function, and cisplatin, the standard of care chemotherapy. This computational platform provides a framework for preclinical cisplatin and tocilizumab dose and frequency evaluation to be tested in future clinical studies. Our results suggested that the commonly used dosing strategy of co-treatment of the two drugs was antagonistic. By carefully considering the pharmacokinetic attributes of each drug, we discovered non-intuitive treatment schedules that optimized the synergism between drugs, CSC reduction, and tumor shrinkage.

You've published with collaborators across multiple specialties. Do you have any advice on forming and maintaining inter-disciplinary collaborations?

Be proactive! Don't be afraid to reach out, for example, to an experimental group in hopes of forming a collaboration, and when you do so, have your pitch ready. That is, be able to:

- Describe your research in a few sentences without jargon.
- Give a brief example of one of your latest projects or a specific question you want to explore.
- Explain how collaboration could be mutually beneficial.

Once a collaboration is underway, intra-team communication is critical to its lasting success. I like having multiple avenues of communication, e.g., email, Slack Channel, etc. I also think showing a genuine interest in your collaborators' day-to-day work is essential, as is understanding where specific data sets come from – so visit the lab! Finally, the culture and camaraderie of the team are also critical. Ensure you earn trust, develop mutual respect, and demonstrate reliability, commitment, and flexibility.

Alongside research, you have worked to improve educational programs and initiatives to train a diverse workforce in mathematical biology. Can you comment on where the field is heading (or should be heading) in this regard?

As mathematical biologists, our research products have the potential to find new and creative answers to challenging biological questions facing our world. Our community's resolve to synergize mathematics, scientific computing, biology, and medicine for societal impact should be inseparable from our commitment to diversity, equity, and inclusion (DEI). Significant further diversification of our field requires increasing the number of researchers from marginalized backgrounds pursuing doctoral degrees, securing academic positions, and advancing through the ranks in these intersectional areas. For example, as late as 1999, only four African Americans were among the more than 900 faculty members in the mathematics departments of the nation's 25 highest-ranked universities. To begin shifting these numbers, we need to capitalize on the momentum and progress of DEI efforts of our disciplinary societies while recognizing that new approaches are required to significantly and sustainably transform the DEI landscape throughout our field. As a community, we should construct a theory of change model that helps us better align the strategic DEI objectives with our values

as a community. Doing so will allow us to infuse DEI genuinely and organically into all aspects of who we are, what we do, and how we serve.

Can you tell us about your approach to mentorship?

For every student I mentor, I aim to bring to light the talent, ability, and creativity I see in them so their full potential shines through.
My mentoring approach involves always:

- keeping lines of communication open,
- helping to set realistic goals and expectations,
- providing honest feedback, and
- offering continuous support.

Finally, what does your perfect weekend look like?

My perfect summer weekend involves a boat, a lake, my family, sunshine, and blue skies. In the winter, a cozy fire, and a good book!