This issue's interview is with Prof. Ivana Bozic, an Associate Professor at the University of Washington. Prof. Bozic is the 2023 recipient of the Akira Okubo Prize, awarded jointly with the Japanese Society for Mathematical Biology, for her significant contributions in mathematical modeling of cancer evolution and her groundbreaking approach in synthesis of theory and data and its impact in the fields of mathematical biology and cancer research.

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

I've always loved math, and initially intended to be a pure mathematician. I obtained my bachelor's and master's degrees in theoretical mathematics at the University of Belgrade in Serbia. However, towards the end of my studies, I had an opportunity to do an internship at the Institute for Infocomm Research in Singapore, as part of a student exchange program. There, I worked on applications of machine learning for the design of peptide vaccines. These vaccines contain a portion of a tumor neoantigen (peptide) and have been used in clinical trials to treat patients with cancer. Owing to the very large number of possible peptides, computational predictions are used to determine which are most likely to trigger an immune response. Coming into this project, I knew very little about the underlying biology and nothing about machine learning – it was a steep learning curve to both understand the specific problem at hand, tools I could use to solve it, and to learn how to communicate with people from different fields. It was my first time applying mathematical thinking to a biological problem and I found it fascinating. After this amazing experience, I decided that I want to do a PhD in mathematical biology.

Your work has some exciting applications in evolutionary dynamics and cancer therapies. Can you tell us more about this?

One of the main goals of my work has been to build a mathematical framework for understanding cancer evolution and using that framework to connect the seemingly disparate observations from clinical, epidemiologic, and genomic cancer data. Recently my group has been working on understanding the evolutionary dynamics of chronic lymphocytic leukemia (CLL) and colorectal cancer (CRC), and we have also started investigating models of cancer immunotherapy. Using a Bayesian approach to analyze tumor burden and genomic data, we discovered that individual CLLs can exhibit diverse growth patterns, namely exponential and logistic growth, each associated with marked differences is genetic composition and clinical outcomes. We also developed a novel methodology to uncover the timing of driver events and

growth rates of individual CLL subclones from sequencing and clinical data, finding that most CLLs are initiated within the first two decades of life.

I am very interested in studying the evolution of colorectal cancer in patients. My group developed a stochastic model of colorectal cancer (CRC) initiation through a complex network of possible premalignant genotypes, employing experimentally measured mutation and proliferation rates, which recapitulates the reported lifetime risk of CRC and the experimentally reported order of mutations in CRC. We are also developing methodology to gain quantitative insight into the success or failure of cancer immunotherapy in patients. Using a dynamical system approach to studying CAR T-cell therapy, we found that the same drug concentrations can lead to vastly different outcomes in patients due to different delivery schedules.

Do you have a favourite paper in your field?

My work has been mostly focused on understanding the evolution of cancer, but I have been deeply influenced by and admire the work of Luria and Delbruck on bacterial evolution. The combination of elegant mathematical modeling and experiments to obtain insight into a fundamental biological question has always fascinated me.

What advice would you give to a junior researcher in the field?

Know what your goal is and work toward it. Work smart by putting the largest effort into things that will make the biggest difference. Try to enjoy the ride.

What is the best part of your job?

The mathematician in me still loves the breakthrough of discovering new mathematical results, especially those that eluded us for a long time. But I also enjoy reading biological and medical literature, hunting for clues into a biological phenomenon, and trying to form a coherent picture of it in my head and a mathematical model that can explain it.

I am also enjoying learning how to be a good mentor to students and postdocs in my group and watching them grow as scientists.

Finally, what does your perfect weekend look like?

Having a slow morning and enjoying good coffee with my husband, going on a small adventure (like visiting a museum or rock hunting) with our daughters.