



This issue's interview is with Dr Chengyue Wu, a Postdoctoral Research Fellow at the Oden Institute, UT Austin. Dr Wu is the 2023 recipient of the H. D. Landahl Mathematical Biophysics Award for her extremely creative, exciting, and high impact contributions for both diagnosing breast cancers and predicting their response to therapy.

Who or what inspired you to pursue a career in biomedical engineering?

There are multiple factors leading to my decision of going for a career in biomedical engineering. First, my undergraduate study provided me a strong, interdisciplinary background in math, physics, chemistry, biology, and computer science. The program I was recruited in didn't necessarily have a major – instead, our curriculum of first two years contained the core, courses from all science majors (which is very stressful but fun), then we get to build our own curriculum of the next two years with guidance and research interest. This background made me very enthusiastic to explore opportunities in interdisciplinary research, especially to solve biophysical problems. I got to learn many biomedical imaging and bioinformatics techniques during the undergraduate research. After graduation, I was extremely lucky to be able to join my current supervisor, Dr. Tom Yankeelov's group for PhD study in the biomedical engineering major. My first project was to develop a MR image processing and kinetic modeling system to help breast cancer diagnosis. Later I combined this tech with a fluid dynamics model to better understand how blood flows around a tumor and within its supporting tissue. This allowed me to further explore the delivery of treatment drugs through the bloodstream, and to build more models for predicting how varying therapeutic regimens would affect the cancer response. Now it has been almost nine years I got into the infinite world of biomedical engineering, and the opportunities and challenges in this field never fail to make me excited.

Your work has some exciting applications in biomedical imaging and breast cancer diagnosis. Can you tell us the challenges and benefits of combining medical imaging and computation methods?

Combination of medical imaging and computation methods is one of the most practical strategies to apply mathematical/computational models for clinical oncology. Tons of brilliant models have been developed to investigate the mechanisms under tumor growth, response, evolution, etc. However, we all know cancer is a highly heterogeneous disease, both across different patients and within a single tumor. If we want to use these models in clinical cancer healthcare, it's necessary for the models to represent the tumor behaviors in each specific patient. A natural solution to this demand is to calibrate model parameters using patients' data, and medical imaging is an ideal type of data that can be used to calibrate tissue-scale models. First, medical images (e.g., MRI, ultrasound, x-ray, CT, PET) can provide a lot of information about the anatomical morphology and pathophysiological functions (like blood supply, cell density, metabolism, etc.) of the tumors and diseased organs. Such information is very valuable for informing models that representing related biophysical phenomena.

Second, medical images are widely used in the standard clinical cancer healthcare, so they are highly available. Using the clinically available data to inform computational models will make the application/translation of these models much easier. Of course, these are also disadvantages of using mere medical images for computational calibration. Most importantly, due to the resolution of medical images, they usually cannot provide detailed information of small-scale biophysical mechanisms. For example, if you want to build a model describing intracellular signal pathways, medical images probably won't provide too much usable information. Thus, the future direction might be to combine multi-modality data (e.g., medical images, histology, genomic sequencing) with multi-scale models.

Have you ever encountered any surprising results in your research?

Well, most results in research are surprising – even you have designs and hypotheses, things never go exactly as expected :)

I think the most surprising result I encountered is in a recent study on optimizing catheter placement for delivery of radioactive nanoparticles in recurrent glioblastoma (GBM) treatment. GBM is the most common and deadliest of all primary brain cancers. Even more unfortunately, despite treatments, recurrence of GBM is inevitable and the prognosis is quite poor. A promising treatment strategy for recurrent GBM is convection-enhanced delivery (CED) to deliver large, localized doses of therapeutics. It's well known that the success of CED treatment relies on proper catheter placement for therapy delivery to maximize tumor coverage and minimize the leakage to healthy tissue. To address this, there have been some commercial tools using pre-delivery images to plan for the location of catheter placement. In this study, we seek to develop a more systematic optimization approach to find the best place to put catheters on a patient-specific basis. We indeed expected our approach to improve the outcome a little bit (measured by the balance between treatment efficacy and side-effect toxicity), but we were kind of surprised that the final *in silico* evaluation indicated the optimization would improve the outcome by over 30% - which was more than we expected, and implied the current administration is far from optimal. This might explain the low success rate of clinical trials investigating CED-based therapy in the last two decades. This surprising observation also provides us more confidence on the potential of computational modeling to significantly improve cancer healthcare.

What do you see as the biggest challenges in your field in the future?

By now, I feel the biggest challenge in the translation of mathematical cancer modeling is to build trust between computational researchers and the clinicians. Applying computational modeling in clinical cancer healthcare requires collaboration of people with very different expertise, and needs to address many concerns about safety, efficacy, and ethics. Fortunately, there are great leaderships in the field who are devoting to building such interdisciplinary collaborations - some lead to clinical trials aiming to validate the ability of computational models to guide/improve cancer treatment outcomes. I'd be grateful to see wider success of such collaborations in future.

What is the best part of your job?

I feel one best part of my job is I always feel motivated. Being able to work on research problems related to clinical cancer healthcare is an exciting thing. You can always see why these problems are very important, and you can see the hope to help solve them with your knowledge and expertise – even though that probably will take tons of effort and time. Also, the atmosphere of our group is super encouraging and enjoyable – having colleagues who are kind and willing to share ideas with each other is another best part of my job.

Finally, what does your perfect weekend look like?

I enjoy art and history as a hobby. So a perfect weekend for me would be wandering in a museum to see all the fantastic artworks and antiques, learning where they come from, what cultures or historical events they represent, or what the artists want to express when they created these works – moreover, to understand and to feel being free from limitations of space, time, and all kinds of barriers. I also enjoy going out to make landscape painting or architecture sketching – of course, not in a weather as hot as Texas' summer though.