Understanding disease states through math

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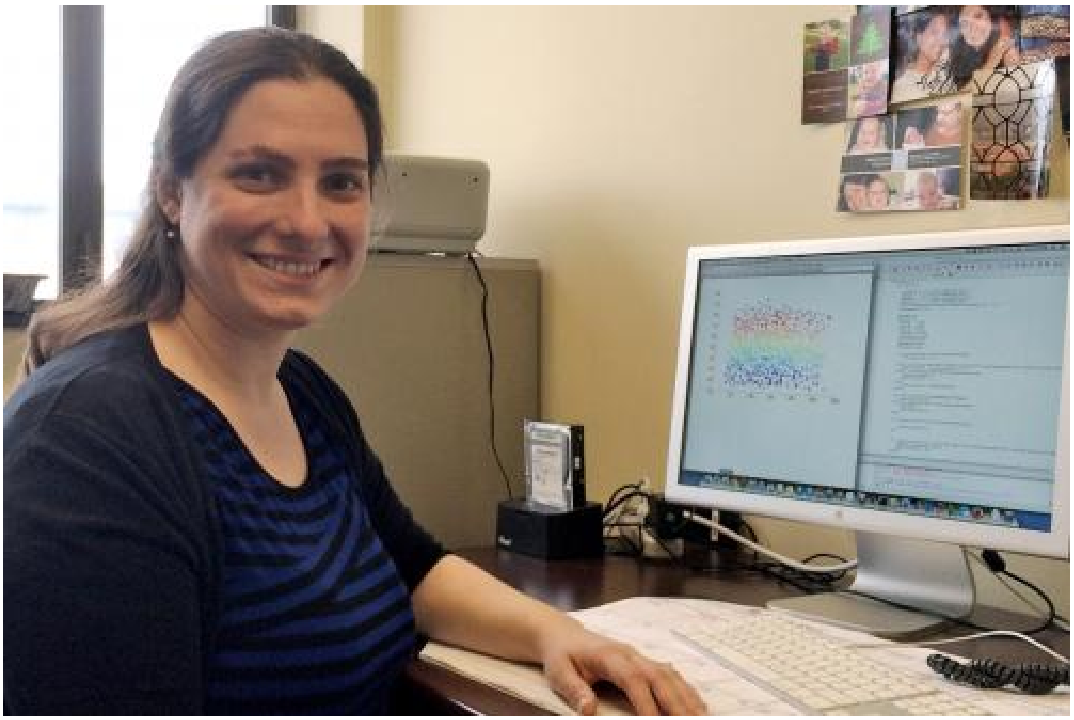

Angela Reynolds, Ph.D.

Angela Reynolds, Ph.D., is in the business of translating math to biology and biology back to math. As an applied mathematician, she can turn chemical reactions into equations.

By working with mathematical tools, Reynolds develops models to better understand wound healing and inflammation found in the lungs of patients who are on ventilators.

But it's work that Reynolds, assistant professor in the Department of Mathematics and Applied Mathematics in the Virginia Commonwealth University College of Humanities and Sciences, can't do alone. She collaborates with experts from the School of Medicine, Medical Center and School of Engineering.

Below, Reynolds discusses her research, the power of multidisciplinary research offered at VCU and advice for up-and-coming researchers.

Q: What is mathematical biology? How do you get from the numbers to understanding diseased states?

Reynolds: Mathematics is generally divided into pure and applied mathematics. I'm what's called an applied mathematician, and I focus on mathematical biology. I develop and analyze mathematical models that account for key biological components such as cells or proteins to determine how they interact and change other factors. I use a type of mathematical equations called differential equations; I look at how fast populations change. For example, I account for how quickly a cell attacks a bacteria. By understanding these types of interactions, I am able to learn what drives the patient's outcome to healthy or diseased state.

I use numbers and equations to quantify how quickly things are happening. Essentially, it's a series of equations that models interactions. Next, I simulate this model on a computer and develop graphs and curves that show what these cell/protein populations look like for different parameters. And so the numbers are there, but the art is actually making models that quantify what biologists understand qualitatively and using these models to make biological hypotheses.

Q: One of your areas of focus is wound healing. How

is math used to understand this process?

Reynolds: In most cases, wounds heal nicely over time, and, once healed, a scar is left behind. But in some cases, wounds do not heal well. My research looks at what happens in those cases – how inflammation interferes with the ability to heal. Mathematically, we're trying to quantify how that inflammatory response is modulating the healing and when is best to intervene and how to intervene.

Our focus is on diabetic foot ulcers. These particular wounds often do not heal. We are examining which treatments are best; for example, when should you use a treatment that delivers oxygen to the wound site to promote healing versus one that eliminates the inflammation.

I create models using math to see why and where things go wrong. Taking the information we gain from this, my colleagues and I are able to develop a hypothesis and method using the model to move towards more effective treatment of wounds.

Of course, those findings are tested experimentally, and that is where my collaborators come in. I work with a lot of collaborators who facilitate the modeling aspect and also test the hypotheses.

Q: What other areas do you focus your efforts on?

Reynolds: Another area of focus is examining how inflammation is triggered in the lung when a patient is on a ventilator. We are developing mathematical models that account for air flow – where the air goes in the lung and how that air flow can affect the tissue.

For example, if the ventilator is pushing air in and is too strong, it may cause damage to the lung tissue and the patient's body will send out cellular signals that give rise to inflammation. We are trying to quantify that inflammatory response so that we can develop protocols that would minimize the resulting inflammation.

As we age, our lungs, tissues and airways are changing and becoming more sensitive. We think that for elderly patients, those changes may play a role in the inflammatory response and how well they respond to ventilation. So our models account for the effects of aging. For this work I am collaborating with experts in engineering and medicine, including Rebecca Heise, Ph.D., assistant professor of biomedical engineering in the VCU School of Engineering; Ramana Pidaparti, Ph.D., professor of mechanical and nuclear engineering in the VCU School of Engineering; and Kevin Ward, M.D., formerly with the VCU School of Medicine and now faculty at the University of Michigan.

Q: Through your research, you collaborate with a broad range of experts. How does that work and what skills are necessary to make that happen?

Reynolds:The atmosphere for collaboration at VCU is very strong. I became heavily involved in collaborative research after coming to VCU in 2008. The research teams I work with include experts in bioengineering, biochemistry, medicine and multiple mathematicians.

The beauty of multidisciplinary collaboration is that everybody knows their field and they know what is important. It would be difficult to know what's important in every single application and also understand all the math and biology that is needed. We each have our expertise, and we bring it together.

In order for collaboration to work, we all need to translate our portion of the work so the others in the group understand. Historically mathematics has been predominantly used in physics, and physicists take a lot of mathematics courses. But, physicians and biologists have not used math as much, so there is a gap in mathematical knowledge and common ground.

Part of the skill of being a math biologist is being able to translate it. I tell my students at all levels that it's important to speak about mathematics so that other people can understand. This is a huge skill to acquire if you are going to be involved with any form of collaboration. Your team must understand – maybe not every detail – but they need to understand what you are trying to do and why you are trying to do it. Half the battle in research is motivating your work and striking interest in others. Once you get people involved and get things moving along, that's when things start to be successful.

Q: What are some of the hot topics in your field now?

Reynolds: There's a push to look at patient-specific treatment/medicine – tailored or individualized medicine. As we are able to gather more and more information with electronic files, health professionals will have a longer history of medical records. Now, we start to wonder how all that information about the patient can be used to better understand how a treatment will work on him or her, rather than taking a one-size-fits-all approach.

Grouping everyone together may not work as well as it has in the past, particularly as drugs are developed that work only on specific receptors. As a mathematician, I see there is variance in a particular population, and something this complex requires mathematics and statistics. This area has a lot of potential if we can quantify patient variability and develop patient-specific treatments using mathematical models.

Q: What advice do you have for students looking to enter the research field?

Reynolds: Diversify mathematically. You cannot take every biology class and every math class and become a biologist and mathematician at the same time, which is what some people think they need to do when they hear biomathematics or mathematical biology.

The applications that people are tackling now are becoming more and more complex and require a variety of mathematical methods. So, as an undergrad, take a variety of courses, learn skills sets such as programming; learn theoretical methods and at the same time you learn how to apply the math, because it's all going to come together no matter what research you do. If you are going to pursue mathematical biology, you need a broad skill set.

Initially, undergraduates may not realize that it will all ultimately come together, but the nature of mathematics is that you have to learn things sequentially and the beauty of it doesn't really come together until you are in the upper-level courses.

At the graduate level, you should be a master of something. Find what you love to do mathematically, become really good at it. There's probably an application for what you are doing. But at the same time, take some classes in related mathematical areas so that when you hit a difficult problem you know what tools will be needed.

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