Modeling Biology

By AMY STULICK Staff Reporter

Simulations Plus makes software to predict how a drug will interact with chemicals in a living organism. John DiBella joined the Lancaster biotech software firm right out of graduate school in 2003. His first assignment was to write computer source code; later, he conducted training seminars for clients and performed consulting work. In 2010, he took on a role in business development, eventually leading marketing and sales for the company. He was named president of the Lancaster facility in 2017.

Question: How does software imitate the body's reaction to drugs?
Answer: It's a combination of equations and parameters. We've done it for a lot of novel, innovative science in our own side to identify equations, whether they are differential equations or algebraic equations, that can help us predict or track what would be the amount of concentrations of a drug within different tissues. In order for us to mimic that virtual human or animal setting, we also need parameter values. There is a lot of really good research that is done in academic labs or with pharmaceutical partners—they're collecting the specific sizes and profusion, or blood flow, rates, the expression levels of enzymes and transporters, and making that information available to us and the public at large.

We are then able to put that into the program as well to differentiate between a rat, a monkey, a dog, or differentiate between an American versus a Chinese versus a Japanese subject.

How well does the software predict the drug's actual effects?
There is going to be certain information about the drug molecule that has to be fed into the system, and so there's a saying in modeling and simulation: Garbage in, garbage out. If we have good info that has been collected in the lab—this will give us good confidence in being able to predict the efficacy or safety of the drug molecules. If there are gaps in that information, we don't have measurements available or predictions are falling outside of what we would call the applicability domain of the model, then you would have to be more cautious in the interpretation of the results.

What challenges did your team face developing the software?
One of the biggest challenges was skepticism from scientists initially. Up until that point, the pharmaceutical research and development was all about cut and try efforts, meaning we're going to try this, synthesize this, and then when we have a certain amount of compound material, we're going to have this powder that we made manufactured into a tablet or capsule, we're going to give that to animals, we're going to run some experiments and collect some more data, and make some decisions on what direction to go into, and then start doing our clinical trials and research. It was all about trial and error. We came along and said, "Hey, a lot of other industries like aerospace and automotive spend a lot of time running computer simulations and using models and maybe trying to apply some of those modeling and simulation principles to pharmaceutical R&D?" People were saying there are a lot of different biological, physical, chemical properties that are interacting, and how do you think you could possibly represent a complex system like a human body or an animal through a set of mathematical equations? It was overwhelming that sort of initial skepticism, that hurdle and showing that we could come up with a set of equations that could predict with a high degree of accuracy what some of these outcomes might be.

How is the software safer than other ways of determining the effectiveness of a new drug?
Unless you're worried about the computer modeling, it's pretty straightforward to run the simulations. Because we've now had decades of knowledge built into our tools and lots and lots of data going in, we're confident that, provided we have good inputs going into the software, there will be good outputs coming back. Using the tools that Simulations Plus is developing, we can hopefully eliminate some portion of animal testing that has historically been done. Instead of doing 100 rat studies, maybe it's down to 25 or 50 rat studies. Instead of doing 12 dog studies maybe we're down to half of that. There are real opportunities to be able to run these simulations, make informed decisions and ultimately have the elimination of unnecessary studies done, the sacrificing of animals, the unnecessary testing on different population groups in humans, especially very sensitive population groups, into the non-pharmaceutical space, so chemical companies or consumer goods companies like Dow Chemical Co. or Procter & Gamble Co.

How do you charge customers?
It is customizable. A company can decide on the configuration that best suits its needs. There are going to be a variety of different modules that they can choose from depending on what their research aims are, what their goals are, how many users they expect. This is an all-subscription-based, so subscription terms can be as short as one month, it can be as long as three years.

How is this software changing biotech?
What we're starting to see now are companies that are really buying into it, appreciating that the use of this kind of technology is not going away. We're really at the ground level right now. As more students become trained in these types of approaches, as they're going through graduate school and come out into the market, companies now are starting to rethink their internal (standard operating procedures), their research SOPs, and how modeling and simulation technology should be integrated from the very beginning of each and every program. What we had historically seen up until a year or two ago, is that our technology would be used when companies were facing a very difficult question. It would be very compound-specific when the technology was called upon. Now, there are a growing number of customers that are saying what they need to do is bring this in as early as possible to all of the programs, and run all of the programs through and use the results to guide what direction to go in at the earliest stage possible.

How will the biotech industry change in the next 10 years?
There's probably going to be more consolidation. It seems like a lot of the larger companies don't have quite the appetite for doing the novel discovery work from the very beginning. They want to leverage the work being done at some of these smaller companies and these academic labs, and then bring in the IP and take over once the program has shown promise. I can see that business model continuing to grow. I think there will be more companies that are virtual. They will have complete confidence in this type of technology and they may be taking some compound that failed for one reason or another and run them through computer models and see if they can somehow be repurposed or see if there are any analogs or backups that could be potentially interesting, and do a lot of virtual work before they start doing substantial investments.

Why Lancaster? Why not a biotech hub?
The reason for Lancaster is because the founder and still chairman of the board, Walter Woltosz, was in the Antelope Valley doing research in the aerospace field using modeling and simulation. When he got the idea to pursue this opportunity, he was already here.

Have you considered alternatives?
In terms of relocating, it comes up. One of the things we've become very flexible with is offering remote commuting opportunities to employees. Even though the headquarters is in Lancaster, we're approaching about 40 percent of our employees in this division being full-time and off-site.

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John DiBella sells software that conducts computer simulations of a drug's reactions inside the body.