SERIOUS GAMES AND BIOMEDICAL RESEARCH: What Do Game Developers Bring to the Table?

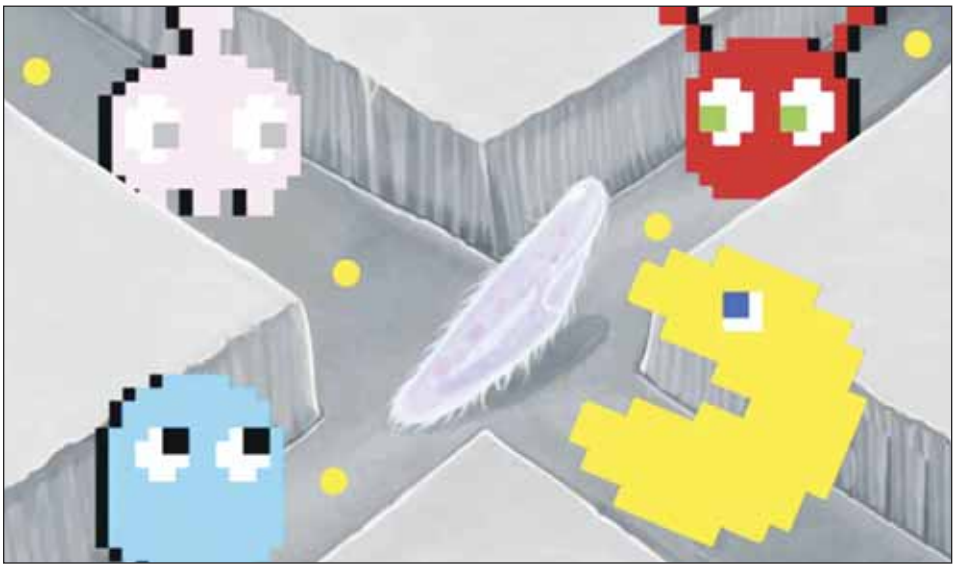
By Alexander Gelfand

Some biomedical researchers are serious about games.

"Just because something is a game does not mean it is childish," says **Ingmar Riedel-Kruse, PhD**, assistant professor of bioengineering at Stanford University.

Indeed, the so-called serious games movement has established that games in general—and electronic games in particular—can serve as tools for accomplishing meaningful goals, like helping people to improve their eating habits or understand the federal budget.

For his part, Riedel-Kruse has developed a number of "biotic games" that employ real biological materials. Right now, these are primarily educational in nature, allowing players to influence, observe, and understand the behavior of simple living organisms. In PAC-mecium, for example, players use something resembling a conventional videogame controller to herd a flock of actual paramecia, single-celled organisms that live in ponds and respond readily to mild electrical stimulation. The paramecia are represented on a monitor by a digital image of a fish; and while players can also watch real-time video of the tiny creatures swimming about and changing direction in response to electrical fields, the fun lies in using their digital fish avatar to gobble up virtual yeast pellets while trying to avoid the bite of a predatory zebrafish.



In the biotic game PAC-Mecium, players redirect the movements of actual live paramecia by changing the surrounding electric potential. Reprinted from H. Riedel-Kruse, A. M. Chung, B. Dura, A. L. Hamilton and B. C. Lee, Design, engineering and utility of biotic games, Lab Chip, *11:14-22 (2011).*

There have been a handful of notable cases in which researchers have used online games to crowdsource solutions to big biological problems. The most famous of these, Foldit, relies on players (or citizen scientists, as they are known in research circles) to find novel ways of folding proteins. EteRNA, developed by scientists at Stanford and Carnegie Mellon University, does something similar with RNA molecules; and EyeWire, which was spearheaded by Princeton neuroscientist **Sebastian Seung, PhD**, has gamers map the three-dimensional structure of neurons in the retina. The results can be impressive: In a paper published last year in the journal *Nature*, Seung and his co-authors drew on the work of thousands of EyeWire players to help explain how eyes detect motion.

Still, games that are used to advance biomedical research remain rare enough to garner attention just for their sheer novelty. But that may be about to change.

Last December, the National Institutes of Health (NIH)sponsored a two-day workshop at the National Cancer Institute's (NCI) Shady Grove facility in Rockville, Maryland. On the agenda: exploring how games could be used for biomedical research, and how the methods and technologies that game developers rely upon might also be exploited by scientists.

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The benefits could be substantial. The avalanche of data available to researchers is fueling demand for new and better tools to analyze and understand it—tools that use methods such as crowdsourcing and data visualization to discover patterns and solutions that might otherwise go unnoticed. As it turns out, game developers have been refining such methods for years.

Bringing Game Thinking to Biomedicine

"Game developers are computer scientists who just happened to go into a slightly different field," says **David Miller, PhD**, AAAS Science and Technology Policy Fellow at the NCI and one of two lead organizers of the December event. His fellow organizer, **Jennifer Couch, PhD**, who leads the Structural Biology and Molecular Applications Branch at the NCI, adds that biomedical researchers have watched with considerable envy as game developers have succeeded in visualizing and manipulating complex systems for

entertainment purposes, getting large numbers of people to work together online.

Riedel-Kruse, meanwhile, points out that game developers are also highly adept at motivating players, designing incentives to keep them engaged, and building interfaces that help them learn how to play as they progress through the game itself. Both science and games involve problem-solving, he says, but game developers are the ones who have figured out how to encourage voluntary participation by making their products fun, even if they may also be frustrating. That skill could prove useful not only for building online research-oriented games capable of marshaling thousands of citizen scientists, but also for developing digital tools to make the more tedious tasks involved in biomedical research—like tracking the positions of individual cells in a sample—more bearable for professional scientists toiling away in their labs.

In EteRNA, developed by scientists at Stanford and Carnegie Mellon, players design complex new RNA molecules. The best designs are then synthesized in the lab.

The workshop, which was sponsored by the NIH's Big Data to Knowledge (BD2K) initiative—a program that aims, among other things, to develop the methods and tools necessary to analyze biomedical Big Data—and formally titled "BD2K Think Tank: Game Developers and Biomedical Researchers," was therefore intended not only to generate ideas for new games that could help solve specific problems, but also to explore how scientists might benefit from what game developers sometimes call game thinking. "The way that game developers think about problems is different from the way in which bioinformaticians think about problems," Couch says. "How can we bring some of that thinking into biomedical research?"

Making that happen will require a good deal of effort on both sides. The workshop participants—nine biomedical researchers and ten game developers—were all chosen in part for their open-mindedness, but that didn't mean they knew much about their counterparts' work or methods. Indeed, just getting up to speed on the basic science involved in biomedical research is going to be a challenge for game developers, says **Ben Sawyer**, a leading figure in the realm of serious games who co-chaired the event and recruited the developers—though he adds that they're up to the task, and even look forward to it. (Sawyer co-founded Games for Health, a grassroots network funded by the Robert Wood Johnson Foundation that supports the development of health games and technologies.) Researchers, meanwhile, are going to have to get their minds around an entirely different way of approaching problems. Whereas scientists tend to begin by looking at big questions and try to design experiments that will answer them, says Couch, game developers work more iteratively, jumping right into a project and allowing the solution to reveal itself—often in a form that they might not have envisioned. "We're just worlds apart," says **Markus Covert, PhD**, an associate professor of bioengineering at Stanford who rounded up the researcher contingent and acted as co-chair.

Gamifying Research

In an effort to bring those worlds a bit closer together at the workshop, Covert and Sawyer engaged in a sample dialogue about Covert's work, which involves computational models of cellular activity and plenty of live-cell imaging. Their back-and-forth led first to a lively discussion among the assembled game developers about how Covert's research could be "gamified," followed by a round of speed-dating sessions that teamed each researcher up with several game developers to brainstorm how games might be used to help solve problems involving large data sets. The topics ranged from genomics to organic chemistry, and the sessions touched upon everything from the objectives of cancer researchers to the potentially useful characteristics of games like Pokémon and SimCity.

In some cases, game developers were able to quickly see the potential for turning particular research problems into games. And participants on both sides walked away having made connections that could lead to future collaborations. Riedel-Kruse, for example, met a number of developers whom he believes could potentially help refine his biotic games; while **Nick Fortugno**, a prominent game developer and entrepreneur who teaches game design at The New School's Parsons School of Design, is already in discussions with several different researchers who attended the meeting. But perhaps just as important, the various parties involved also left with a better understanding of the opportunities—and challenges—that lie ahead.

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Sawyer, for example, points out that research-oriented games pose a unique problem for game developers: whereas the latter typically know all of the rules of a game before they design it, they won't have that luxury when constructing games meant to facilitate scientific discovery—games whose very purpose will be to help lift the veil on the unknown. Yet building games in the absence of all the rules not only flies in the face of traditional game design; it could also result in games that upend traditional norms of gameplay. "Imagine if you only knew 30 percent of the rules of chess," says Sawyer, "and I arranged the board in some weird way that was still valid, and I said, 'How did we get there?'"

Fortugno explains that this kind of uncertainty about basic ground rules will make it harder for game designers to evaluate the solutions that players come up with, and therefore to design incentives that will keep them engaged. And the fun won't stop there: Once they've succeeded in establishing evaluative criteria based on the limited information that researchers can provide, the developers will still have to gamify those criteria in ways that will not only motivate players to win, but also produce scientifically relevant results. "This," says Fortugno, "is an odd way to make games."

On the other hand, researchers and developers alike see great potential in open-ended, discovery-oriented games. Among other things, such games could be used to test researchers' hypotheses and models by having large numbers of people run amok in gamified versions of them, identifying aberrations and inconsistencies as only game-obsessed players can. "That's the process of game design," says Couch. "You build a game and put it out there, and players find all the glitches and exploits very quickly, figuring out where it's broken." Similarly, research games could be extremely useful tools for attacking nebulous problems involving large piles of data. "We as humans are very, very good at seeing anomalies given the right type of data, presented in the right way," Miller says. And Sawyer contends that that the unusual challenge posed by research games could spur developers to discover new ways of designing systems to deal with unknown rules and data structures, resulting in games—and outcomes—that go beyond anything achieved thus far.

Where this may lead, only time will tell; and there will be plenty of practical hurdles to overcome, like finding ways of connecting scientists and game developers who inhabit completely different professional networks, and figuring out how to fund their collaborations. But Couch and Miller are already considering ways of continuing the conversation between researchers and developers, perhaps through boot camps or short courses. And in a telling sign, the BD2K initiative recently announced a new funding opportunity to support the development of "new or significantly adapted interactive digital media that engages the public, experts or non-experts, in performing some aspect of biomedical research via crowdsourcing."

Let the games begin. □

Game developers who attended the NCI think tank pondered whether popular, open-ended games such as SimCity (pictured) and Minecraft could serve as models for biomedical research games.

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