Kyle McWilliams
Ben Goodrich
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Designing Drugs in the Cloud

University of Tennessee professor Jerome Baudry opens a terminal on his computer and types a few strange-looking words—he's logging into one of the world's fastest supercomputers, a machine with giant capabilities aptly known as Kraken. Using supercomputers, Baudry and his students have, over years, carefully crafted a virtual world that is not unlike the hyper-realistic worlds of today's video games, but with a far greater purpose.

This virtual world is designed to simulate the rules of chemistry and physics, modeling the interactions between large, complicated protein molecules and their corresponding ligands, small molecules that bind selectively to specific proteins. A visit to this world allows scientists to discover new drugs and pharmaceuticals that can eventually help physicians treat many deadly illnesses.

Like a video game, the virtual world of drug interaction must be programmed before it can be "played." While computational drug design has been evolving since the 1980s, the codes that create these digital biological worlds are still underdeveloped.

"The codes already exist, but they don't run well," Baudry explains. He likens using these outmoded codes on today's supercomputers to equipping a Volkswagen Beetle with a Saturn V rocket motor: "The car isn't going to run faster; it's just going to explode." Baudry and his colleagues have taken on the challenge of modifying

these types of programs to run efficiently on machines with hundreds of thousands of processors.

Researchers commonly seek a substance that can inhibit the function of a target protein, perhaps one that's strongly associated with malaria or cystic fibrosis or cancer. Traditionally, this search has required long and expensive chemical experiments in a lab. Drug researchers could quickly end up out of money with nothing to show for their efforts.

Computer simulations provide a new tool in the field of drug discovery. They allow researchers to screen for and predict which drugs are likely to work before actually testing them in expensive lab experiments. "We can now easily screen a million compounds a day with a reasonable amount of accuracy. One million simulated compounds could easily save $10 million and several years for a task team to develop [in a lab]."

Dr. Baudry explains that while the simulations are not yet able to pinpoint what compound will become a successful drug, they allow the focus to be on a much smaller pool of possibilities. "The haystack is made much smaller so it's possible to find the needle," he says.

Improvements in the algorithms that drive computational drug screening have made it possible to screen compounds for interaction on many proteins, not just the target, allowing scientists to find new applications for existing drugs. "A drug that is known to bind to protein A can also bind to protein B which might be involved in another disease," Baudry says. He also notes that computers could help with modifying an existing drug compound it to make it work better.

But Baudry's main concern is that drug design applications, the codes that create the virtual world, are simply not as developed as the machines on which they run. "The hardware doesn't help when we don't have applications that can make use of it." From their discoveries and mistakes, Baudry and his colleagues constantly work to enhance their applications and build a solid bridge between the machine and their ideas.