Delivering the virtual cell to the world

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Although he trained as a medical doctor, Dr. Ion Moraru's only patients now are computers, tasked to perform a host of incredibly sophisticated computing chores for a growing number of laboratories and departments at the Health Center and worldwide.

Born in Romania, Moraru demonstrated an aptitude for math and science early. In high school, as a member of the Romanian team, he won a Bronze medal at the 1981 International Mathematical Olympiad in Washington, D.C.

By the time he arrived at the UConn Health Center in 1991, he had completed medical school and was putting the final touches on a Ph.D. in cell biology. However, fate had another role in mind for him in the nascent field of high-performance computing (HPC).

Originally used to describe computing for scientific research, HPC now is often used to describe cluster-based technical computing. It has become an essential tool for researchers whose work – especially the creation of incredibly life-like "virtual" models and prototypes upon which experiments can be conducted without using actual organic tissue – calls for high-powered computational capabilities as well as enormous amounts of information storage space.

Theoretical modeling

As a faculty member in the Health Center's Department of Surgery, Moraru's first job at UConn focused on experimental research into intracellular signaling mechanisms, the complex chemical communications through which activities within living cells are governed.

"Out of my early work in cell biology came a need for mathematical modeling of intracellular behavior," he says. "That led me to greater interest in theoretical modeling of cell biological phenomena in general. One of the studies entailed the development of theoretical models and computer-assisted simulations."

As a result, Moraru started collaborating with Dr. Leslie M. Loew, in the Department of Cell Biology, who was initiating a project called the "National Resource for Cell Analysis and Modeling," which was funded in 1998 by a National Institutes of Health (NIH) grant.

Loew was on the cutting edge of the fledgling fields of computational cell biology and systems biology that would soon revolutionize cellular and molecular biology. He and James Schaff, an inventive computer science engineer, were working together on what seemed, at the time, a far-fetched idea – a general-purpose program that could create realistic simulations of intracellular processes.

Simulating cell biology

Called the "Virtual Cell" (VCell), their notion soon blossomed into a remarkable computational tool enabling scientists to model and simulate cell biology through a platform that includes sophisticated distributed software and hundreds of servers: some that compute, some that store information, and some with software that can handle the massive calculations necessary to model and simulate cellular processes. Within a few years, VCell became so powerful that it could be used for everything from evaluating scientific hypotheses and interpreting experimental data to the creation of multi-layered models in which scientists evaluate the behavior of complex systems.

By 2000, Moraru was immersed in Loew's project work and had changed his affiliation to join the Department of Cell Biology.

In 2005, funding of the National Technology Centers for Network and Pathways by NIH led to creation of UConn's Richard D. Berlin Center for Cell Analysis and Modeling (CCAM), a multidisciplinary center headed by Loew. The Berlin Center integrates new microscope technologies for quantitative measurement of living cells with both new physical formulations and the HPC tools that make VCell possible.

Moraru was chosen to lead the development of a dedicated computational infrastructure that would enable VCell to support research work not only at the Health Center, but worldwide. The multi-component "brain" Moraru has built over the past decade is currently used by more than 2,000 scientists worldwide.

"VCell is one of the premier platforms for kinetic modeling and simulation of molecules," he says. "We decided, early on, after the first publicly available version, to deploy it as a web-based, client-server design. This had a major contribution to VCell's success within the cell biology community, because biologists were able to create powerful simulations without having their own sophisticated computing hardware or high-end software expertise. It also allowed users to store data in the centralized database at the Health Center. It enables them to easily share models, collaborate, and, as needed, make results publicly available."

Moreover, the web-based design allowed the VCell development team, led by Schaff, to continuously and gradually introduce new features, without having to worry about backwards compatibility and maintenance of many different versions of software.

Blade Servers

In order to serve VCell's external user base, however, Moraru's team has been obliged to build both highly complex, distributed server architecture and maintain a large – and constantly expanding – HPC infrastructure.

"The worldwide distribution of users, and the fact that some simulations often run uninterrupted for many days, have posed a stringent requirement for reliability and high availability," he says.

Those challenges have been addressed, in part, by the increasing power of processers. Cluster technology was still nascent when CCAM deployed its first HPC resources, three racks of processors, about the size of a short row of office file cabinets, back in 1999. Those resources have grown over the years into a multi-million dollar hardware portfolio of increasing sophistication and performance capacity.

The $500,000 worth of new equipment Moraru will add this year, thanks to a new grant from NIH, is composed principally of blade servers, the powerful, stripped down computers that have become the backbone of HPC. One single chassis of 16 blades, a fraction the size of those first racks from 11 years ago, contains 128 processors. And a single energy-efficient blade has four times the power of that entire 1999 array.

The blade technology makes it possible for the capacity of the computational center to grow pretty much unchecked. That's a good thing, says Moraru, because "we fully expect more computational power will be needed."

This summer, Moraru's team relocated the equipment to bright, expansive quarters in the Cell and Genomics Building, the University's new research building on Farmington Avenue, near the Health Center. In addition to the Berlin Center, the new building houses the UConn Stem Cell Institute and the Department of Genetics and Developmental Biology. All of them will benefit from state-of-the-art computing capability that distinguishes the UConn Health Center as one of the region's premier HPC resources. It's a distinction that didn't happen overnight. Ion Moraru has been setting this stage for more than a decade.

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