Success Story

The University of Toronto's MDIT: SGI® Visualization Technology Speeds Drug Discovery and Delivery

When the Molecular Design and Information Technology (MDIT) Center of the University of Toronto moves into its new facilities in 2005, 100 scientists will be able to interact in real time with three-dimensional molecular models in a theater environment using an SGI® Reality Center™ display. Until then, molecular visualizations on the original Reality Center system will continue to play to packed houses in a much smaller theater with limited seating but unmistakable excitement. Members of the University of Toronto's Leslie Dan Faculty of Pharmacy, who are using the new visualization facility for drug discovery and drug delivery research, are finding immersive visualization a difficult tool to put down. "This is addictive," says MDIT Director Dr. Lakshmi Kotra. "True. You can't go back," says Associate Director Dr. Christine Allen.

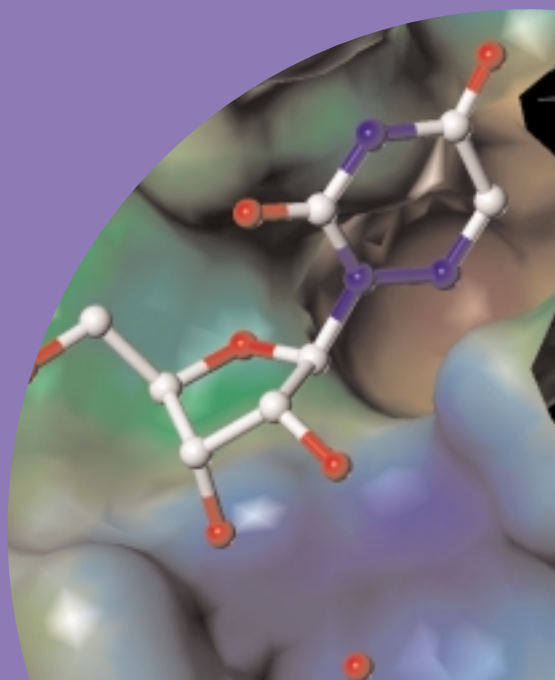
"I've been using SGI's smaller workstations, especially Octane systems, for a number of years, Pretty much every computer modeler has used them. But this project was conceived on a much bigger scale, and from a number of points of view SGI was the only choice."

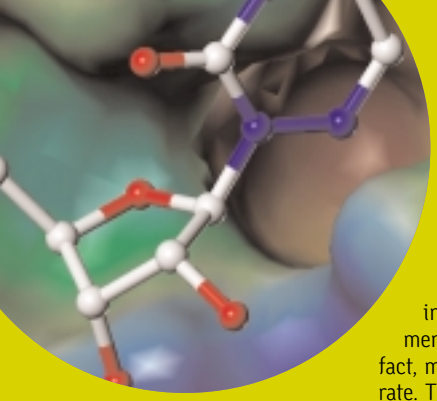
—Dr. Lakshmi Kotra, Director, MDIT

MDIT: Catching the Next Wave in Life Sciences

The faculty's research work focused primarily on bench chemistry until 2000, when university visionaries began planning a long step into the future. After Dr. Kotra's arrival that year, the school organized a campaign to equip MDIT with cutting-edge molecular modeling technology. The Ontario Innovation Trust, founded by the Province of Ontario to help universities, hospitals, colleges, and research institutes to enhance research infrastructures, provided major funding for computer and visualization systems, complemented by assistance from SGI and its technology partner Tripos, Inc. MDIT's first SGI Reality Center facility came online in September 2002. A 44-processor SGI® Onyx® 3800 system with 44GB of memory and an InfiniteReality3™ graphics pipe now generates stereo images projected onto a 5x12-foot screen. The system can display a single large image or three side-by-side images. Viewers wearing Stereographics CrystalEyes® glasses interact with molecules in an immersive environment. An SGI® TP9400 RAID provides a terabyte of storage backup.

There was never any doubt that MDIT visualization center would be an SGI facility. "I've been using SGI's smaller workstations, especially Octane systems, for a number of years," says Kotra. "Pretty much every computer modeler has used them. But this project was conceived on a much bigger scale, and from a number of points of view SGI was the only choice."





The faculty committee wanted to tackle post-proteomic problems to accelerate drug discovery. The goal was the creation of a combined high-performance computing/visualization facility for the structure-based study of large molecular systems, including drug-protein and drug-polymer interactions. The faculty wanted an environment in which a sizeable number of people—in fact, more than one research group—could collaborate. They also identified the software that would best serve the faculty's researchers for computational and visualization purposes and the hardware platform on which it could deliver the best performance. "Obviously, when we put all these things into the equation, they all pointed to SGI integrated processing power and graphics capabilities," says Kotra. "Tripos Sybyl was the key software on which we built this solution."

From Number-Crunching to Immersive Visualization

The SGI Onyx 3800 system in the Reality Center facility at MDIT is used primarily for drug discovery, including heavy number-crunching for computational chemistry using Tripos and other software applications. But the visualization capability is considered essential.

"In the past, we've concentrated on speeding up the computational work," says Kotra. The next generation of research is to assimilate all this information. The excitement for us is that we can start to look visually into the structures of these large, complex biomolecular systems. At any stage of computational chemistry, drug design, biophysics, or drug delivery research, all our projects are connected to the 3D structure of molecules. Large-scale visualization is the key to greater understanding, and this is what Reality Center brings to us." The SGI Reality Center platform has the capability of generating visualizations in context with Tripos drug-discovery compute applications such as bioinformatics and structure-activity relationship software.

MDIT projects involving the Reality Center system include studies of orotidine monophosphate decarboxylase (ODCase), a highly efficient enzyme present in virtually all species. Because it is a target for a variety of viruses, it has value in fighting bioterrorism. In developing synthetic molecules as potential replacements for insulin, researchers conduct docking studies using a very large 3D insulin-receptor structure for which the University of Toronto holds an exclusive patent. Faculty member Dr. Peter Pennefather, a biophysical chemist, is using the Reality Center system to study nerve-cell response to stress conditions. Dr. Regis Pomes conducts studies in cell membrane proteins and ion channels. The facility's processing and visualization power has also attracted interest from industrial companies, who have contracted with MDIT for basic research work using the Reality Center facility.

Drug Delivery Research: Cutting Costs, Saving Time

Drug delivery research works in tandem with drug discovery at MDIT. When a potentially useful drug is designed or discovered, it must be delivered in a way that maximizes its ability to benefit patients. Dr. Christine Allen, with a background in industrial materials research, uses Tripos' Sybyl® software and Reality Center visualizations to study drug-polymer interactions, then models polymer materials that will provide an effective delivery-vehicle formulation.

"Most people are using trial and error to discover effective formulations," says Allen. "They try various drugs-materials combinations and run studies to see how they perform, which involves a great deal of time and money. We're avoiding trial and error and fast-tracking the process by using software. We don't synthesize polymers randomly." Allen's group uses the compute and visualization power of the SGI system to create a virtual library of materials fragments and screen them against anticancer drugs, selecting the most compatible materials for synthesization.

The Road Ahead: Accelerated, Cost-Effective Discovery

"The addition of this integrated HPC and immersive visualization facility has given the faculty a far more effective way to investigate molecular interactions," says Pennefather. "We can now clearly visualize the three-dimensional structures we're working with and arrive at insight much more quickly. We feel that immersive visualization represents the next wave in life sciences research."

Although the Reality Center system has only been up and running for a few months, MDIT has already increased the number of its processors from 36 to 44. MDIT has 10 Silicon Graphics® Octane® workstations, including two that provide remote access to the system from the Chemistry and Biochemistry departments. MDIT's new quarters are already under construction, which demonstrates the commitment of the Province of Ontario and the university to MDIT's work. The cost-efficiency of SGI Reality Center visualization and its ability to accelerate discovery continues to impress MDIT researchers.

"It's amazing that more pharmaceutical companies don't use visualization to guide formulation development," says Allen. "To some extent we're still in the development stages."

Corporate Office
1600 Amphitheatre Pkwy.
Mountain View, CA 94043
(650) 960-1980
www.sgi.com

North America 1(800) 800-7441
Latin America (52) 5267-1387
Europe (44) 118.925.75.00
Japan (81) 3.5488.1811
Asia Pacific (65) 6771.0290

3464 (03/11/2003)

J14234