Experimentation from hundreds of miles away

Remote data acquisition offers some researchers access to instruments usually out of their reach

BY JIANFEI (JEFFREY) ZHAO

Picture this: You're in your pajamas, sitting in front of a computer. After a cup of coffee, you turn on the computer, log in to a secure website, start your favorite instrument remotely and begin to collect data. You then turn your attention to analyzing the data you acquired and downloaded from your earlier experiments. Occasionally, you check the progress of your experiment and modify some of the instrument parameters accordingly. And voilà, several hours later, the new data are ready for your next round of analysis.

Is this a dream? Science fiction? Admittedly, for most biomedical researchers, it is not yet reality, but for some privileged scientists, especially structural biologists, the remote access of rare and expensive instruments is both a reality and a necessity.

Remote X-ray crystallography

"You need an X-ray source with high intensity to solve the three-dimensional structures of large macrobiomolecular complexes at angstrom resolution," explains Roy Mariuzza, a professor of cell biology and molecular genetics at the Institute for Bioscience and Biotechnology Research at the University of Maryland, College Park. "The X-ray source we need is only available in a few national labs in the U.S."

Although in-house X-ray crystallography equipment is ubiquitous, it cannot generate X-rays with intensity high enough for the Mariuzza group's research. "The molecular packing of the crystals of my protein complexes is often defective to various degrees," says Yiyuan Yin, who recently graduated from the Mariuzza lab.

Yin wants to understand the interactions between CD4, MHC II and the T-cell receptor — three proteins involved in multiple sclerosis — by solving the crystal structure of a CD4-MHC II-T-cell receptor complex. After producing preliminary data using a local X-ray diffractometer, Yin relies on the Advanced Photon Source, a synchrotron facility at the Argonne National Laboratory, to refine the structure at a higher resolution.

She describes the synchrotron as a giant ring where electrons are accelerated to near light-speed to produce high-energy X-ray beams. With a nearly $1 billion construction cost and an 80-acre footprint, it would be impossible for most academic institutions to build a synchrotron. Indeed, by the latest count from lightsource.org, a high-energy light source facility advocacy group, only five synchrotron facilities in the U.S. have the capability to solve the structures of proteins with imperfect crystallization that Yin creates.

However, using NoMachine, a commercially available desktop virtualization and remote-access management program, in combination with JBluice-EPICS, the beamline control software developed by APS and the Stanford Synchrotron Radiation Lightsource, Yin can control the X-ray beamline — a section of the synchrotron — and collect data through a secure network at her lab in Maryland without the hassle and cost of traveling. "The software is very user-friendly," says Yin. After initially being supervised by a colleague who is an experienced APS user, Yin was approved to independently operate the machine remotely.

Nagarajan Venugopalan, a crystallographer at the APS, says that, to schedule beamline time, Yin had to submit a proposal that was evaluated for scientific merit. After the proposal was approved, Yin was given a specific time during which she could

use the synchrotron. The usage of the beamline is free for users who are funded by the National Institutes of Health.

When the appointment approaches, Yin packs her crystals in a specially designed rack that can be handled by a robot system at the APS and ships the rack in a liquid nitrogen tank to Argonne. As Yin's host scientist, Venugopalan loads the crystals onto the beamline machine. From there, Yin takes over the machine through JBluice-EPICS and usually runs three continuous eight-hour sessions. "Running the marathon experiments in the familiar setting of our own lab reduces a lot of stress," says Yin.

During the experiment, Venugopalan is on call to assist Yin with any technical questions. He also provides scientific advice for data analysis and develops new X-ray technologies to help beamline users. Venugopalan explains that the beamlines undergo constant improvements. "We are in the planning phase of upgrading one of our beamlines to achieve a 1-micron X-ray beam size," he says. "It will help in achieving diffraction from extremely small crystals and also help in the reduction of radiation damage to the crystals."

Remote microscopy

For a few lucky scientists working with Sriram Subramaniam, a senior investigator at the National Cancer Institute, remote access to electron microscopes from home and around the clock is becoming the norm. With Virtual Network Computing, a desktop-sharing system, researchers in Subramaniam's group can remotely control the workstation that physically connects with the microscope and see the exact same screen that pops up on the microscope's workstation. Joel Meyerson, a graduate student working in the Subramaniam lab, says that the remote control provides flexibility to the lab members, especially to scientists who have young children.

Remote servicing

For Bruker Daltonics and Waters, two analytical instrumentation providers, remote access means cost efficiency and uninterrupted workflow. Doug Boyd, a sales representative at Bruker Daltonics, explains that Bruker service engineers use WebEx, a commercial software package similar to Virtual Network Computing and NoMachine, to diagnose their instruments remotely and help customers troubleshoot. "The engineers may detect a faulty part, order a replacement and even remotely teach the customer to install the part, which could potentially save the customer hundreds of dollars or more," he says, adding that remote work also saves time because many inquiries are "resolved without the need for parts or an onsite service visit."

Weibin Chen, principal chemist of the Biopharmaceutical Sciences group at Waters, says that remote access allows scientists at Waters to change parameters, such as solution gradients, of mass spectrometers and even to reset the instruments. When Chen, like most Bostonians, was kept at home by the heavy snowfall this past winter, he was able to control his mass spectrometer remotely and conduct his planned experiments.

For the David H. Murdock Research Institute in Kannapolis, N.C., the desire to offer remote access to some of its state-of-the-art instruments arises from its vision for collaboration. Mike Luther, president of the DHMRI, says that the institute supports research and development projects with partners who are located both on and off campus. The cost of each project is decided on a case-by-case basis.

Zhong Wang of the Bio-Imaging Facility at Hunter College, City University of New York, wants external users to share the facility's high-end microscopes, because smaller universities "may not have enough funding to support expensive instruments." Wang says that outside researchers can remotely access the confocal microscopes equipped with WebEx and a video-conferencing system.

The future of remote

The remote access of sophisticated instruments, except in the case of synchrotron facilities, largely remains off limits for academic researchers. Some instrumentation experts speculate that the low availability partly is due to the complexities of the operations. "Each lab member undergoes months of intense training before he or she can operate the electron microscope independently or remotely," notes graduate student Meyerson.

However, there is a growing need for remote access, as sophisticated instruments are "starting to cost more both in terms of purchase and maintenance," says Tobias Starborg, senior experimental officer of the electron microscope facility at the University of Manchester. He adds that "the only way new techniques get developed [by the facilities is to have] a constant flow of users wanting to try different things."

Remote control of instruments could be a double-edged sword, however. Chen predicts that remote control via smartphone will be the next step. "[But] would I really like to control the mass spectrometer on the beach?" asks Chen with a smile.

Jianfei (Jeffrey) Zhao (zhao_jianfei@yahoo.com) is a postdoctoral fellow at the National Cancer Institute.