

The Microscopist's Workstation

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Abstract

This case study looks at the issues involved in operating a sophisticated scientific instrument as a computer peripheral accessible over a high-speed network.

A custom interactive visualization application was constructed to support investigation using a unique computer-controlled high voltage electron microscope. The researcher's workstation forms the visible third of a triumvirate, with the instrument and the compute resource comprising the other two parts. The software was designed to support not only image acquisition, but also many of the tasks that microscope researchers perform in analyzing images.

The result of this case study is the identification of some of the issues regarding interacting with scientific instrumentation over high-speed networks and the construction of custom applications to support many of the tasks within a laboratory's research methodology.

1 Introduction

In scientific investigations, visualization is often performed as a separate process following data acquisition. Even when interactive tools are employed, they are usually applied as a separate process after the experiments have been completed and the data has been manipulated in a form suitable for the visualization programs. [McCo87] [Banc89] [Phil89] [Habe90] [Elvi90]. In this case study we describe the *Microscopist's Workstation* (MWS) project, which we have prototyped for presentation as part of the SIGGRAPH '92 Showcase. The goal of the MWS project is to integrate the high voltage electron microscope (HVEM) at the University of California at San Diego Microscopy and Imaging Resource (SDMIR) into a custom visualization application. In essence, we are adapting the electron microscope to function as a computer peripheral. [Merc92]

The SDMIR microscope is a unique resource. By building an application around it, we hope to achieve two ends. Our primary result will be to extend the capabilities of the microscope. In studying researchers using the microscope, we have found that electron microscopes are used as cameras, to collect data photographically for subsequent analysis. Although the SDMIR microscope is equipped for digital image acquisition, the images are still analyzed off-line, away from the microscope. We hope to create a synergy between interactive visualization techniques and a sophisticated scientific instrument by providing tools for image compositing, comparison, and morphometrics, and by enhancing, via stereopsis and computed tomography, the microscopist's perception of three-dimensional structures during the data collection process at the microscope. The result is a more powerful investigative tool.

Our secondary goal is to extend access to the microscope. The Microscopist's Workstation software is designed to be used either in the same room as the microscope or at a remote site, via a high-speed network. The software is also designed to be used either with the microscope on-line, or independent of the microscope, when the microscope is not available or necessary for a particular task.

2 The Distributed Laboratory

The Microscopist's Workstation project is a collaborative effort between several research sites in San Diego: the San Diego Supercomputer Center, the UCSD Computer Science department and Medical School, and the Scripps Research Institute. Each institution is supplying hardware, networking, software development, and design expertise towards the project. One of the immediate spin-offs of this collaboration has been the installation of higher-speed network connections between all of the sites.

The on-going collaboration and discussions among the sites have lead us to begin to conceptualize a *Distributed*

Laboratory, one that employs high-speed networks to integrate data acquisition, computational resources, visualization, and communication into a seamless, geographically distributed investigative environment. The concept of a Distributed Laboratory leads to many areas of possible investigation, three of which are addressed by the Microscopist's Workstation project: integrating a scientific instrument into the computing environment, seamless management of supercomputing resources, and multi-user collaboration.

Constructing an environment that accesses an instrument as a computer peripheral allows the device to be used by a researcher at a remote site with nearly the same efficiency as is available to an on-site researcher, distributing the facility spatially. If the investigative software also operates both with the instrument on-line and with it off-line, either independent of the instrument or with the instrument available for occasional "batch" processing, the facility is also distributed temporally. The result is the multiplication of single resources.

In order to present to the researcher a unified investigative environment, the management of computing resources must be automatic. Our experience with the NetV software [Elvi91], which transparently distributes volume rendering tasks to high-end rendering resources, is a first step towards hiding the computing power behind the interface. In the MWS project, the workstation interface is the visible third of a triumvirate, the computer-controlled microscope and the supercomputing resources comprising the remaining, hidden, portions (See Figure 1).

Focusing on bringing distributed data acquisition and computational resources to the workstation user interface allows that interface to be replicated among multiple researchers. This creates a collaborative research environment wherein two or more researchers can interact with each other and the instrument.

3 The SDMIR Electron Microscope

SDMIR was developed to support scientific research focused on relating biological function to structure using state of the art computer imaging and electron microscopy. It is a new biology research facility established by the National Center for Research Resources of the National Institutes of Health and is located in the Medical School at the University of California, San Diego. The facilities of the laboratory are available to researchers throughout the United States. The central instrument in the lab is a specially designed and equipped transmission electron microscope (TEM). The TEM has about one thousand times more resolution than a light microscope. A light microscope provides a valuable panoramic view of the paths of nerve fibers from one area of the brain to another and of the jungle of nerve fibers arriving from different

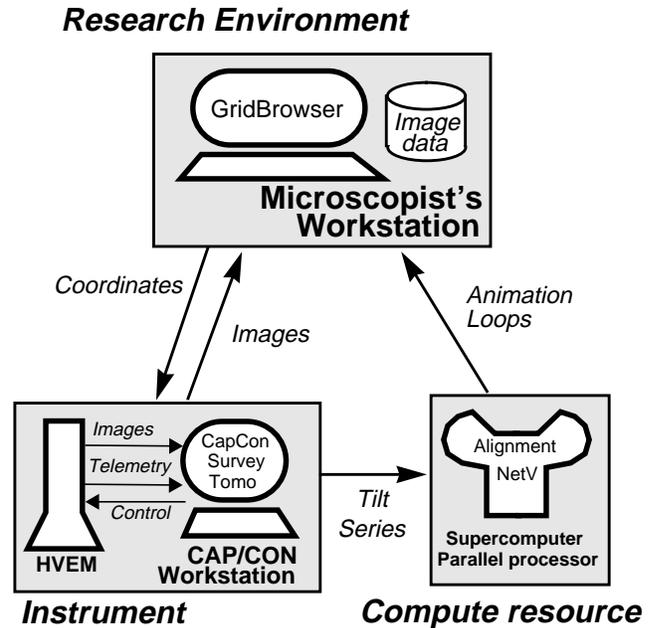


Figure 1: Microscopist's Workstation Triumvirate

sources in the vicinity of the input sites of a particular nerve cell. However, the resolution of a TEM is required to establish which fibers actually form contacts or synapses on the neuron as well as the particular form of the contact. In addition to studies revealing these connections, scientists are currently using the electron microscope at SDMIR to examine the disruption of nerve cell components resulting from Alzheimer's disease [Masl92][Elli90], the structural relations of protein molecules involved in the release of calcium inside of neurons [Mart91], and the three-dimensional form of the Golgi apparatus, where sugars are added to proteins [Elli90][Elli91].

The SDMIR instrument is one of a few High Voltage transmission Electron Microscopes (HVEM) in the US. This instrument, a JEOL 4000EX, can employ a higher acceleration voltage (up to 400KV) than a conventional TEM (100KV). The higher accelerating voltage makes possible penetration and imaging of thicker specimens, up to 3 microns, compared to 0.1-0.25 microns in the conventional TEM. One focus of research at SDMIR is on the development of computer-assisted methods for deriving and exploring the three-dimensional structure residing in these thick sections [Hess92][Carr91]. Because the HVEM has a very large depth of field, the image it forms is an orthogonal projection of the section. The depth dimension is lost. However, it is possible to regain this dimension by obtaining images from different angles of view either by tilting the electron beam relative to the specimen or by mechanically tilting the specimen. In the simplest use of this principle, a stereo pair of images may

be derived. In a more sophisticated approach equivalent to that used in computer-assisted tomography (CAT), a three-dimensional volume of densities is derived from a series of images collected by successively tilting the specimen in small increments about an axis. This axial tomography procedure requires image processing to achieve proper alignment of the tilt series, and computationally intensive operations to derive the volume from the tilt series via filtered back-projection [Fran86].

The SDMIR microscope has been especially designed to accomplish this task. Special deflection coils allow varying the beam entry into the material over sufficient angles to obtain pairs of images for stereo views (± 5 degrees). The objective lens was constructed with a larger gap into which the specimen is inserted to allow rotation over the wider range of tilt angles required to perform axial tomography. The HVEM is also equipped for automated control. The instrument employs an A/D-D/A converter under microprocessor control to read, set, and display parameters such as acceleration voltage, magnification, focus, beam intensity, and astigmatism correction. These parameters can be manipulated with an array of knobs and buttons on the microscope. The parameters can also be set and read remotely with ASCII commands sent over an RS232 serial port. The specimen holder is mounted in a 4 axis (X,Y,Z, and tilt) stage. The positions of the axes can be controlled manually and also by a dedicated IBM PC-AT compatible microcomputer driving four closed loop motor-position encoders. The microcomputer program can be queried via a serial connection to set or retrieve the current stage position.

Microscope control and image acquisition are handled by a dedicated workstation called the CAP/CON (capture/control) workstation. The microscope and stage computer interact via RS232 lines with the CAP/CON, a Sun Microsystems SPARCstation 2 with several special purpose peripherals. CAP/CON also interfaces to an image processor which can acquire microscope images from both a real time 512x512 8-bit video camera and a high resolution 1024x1024 14-bit slow scan cooled CCD camera. Processed images may be viewed on a monitor at the microscope. In addition to providing views with better contrast than those seen by direct viewing at the microscope, the image processor may be used to display previously acquired images and stereo views. These capabilities make possible the design of the Microscopist's Workstation.

4 The Microscopist's Workstation

Our design of the Microscopist's Workstation employs a user-centered approach [Norm86]. We began our investigation into designing the MWS by talking to the scientists who constructed the SDMIR facility and use the

microscope on a regular basis. We also videotaped a microscope session with an expert user, Tom Deerinck, who is adept not only with the SDMIR HVEM, but also with several other electron microscopes. We then transcribed and analyzed the videotape. Microscope users are continuously involved in evaluating our design. The user interviews and video analyses are facilitating our design of a visualization environment centered around the researchers' needs when using the microscope, including tasks currently performed away from the microscope. The MWS will extend the capabilities beyond those of a microscopic camera, to allow performing operations such as image comparison and analysis while on-line with the microscope.

4.1 MWS Network Nodes

The primary application running on the MWS is **GridBrowser**, which supports the display, measurement, and analysis of a large mosaic bitmap of the specimen (*grid*) loaded into the microscope. For a 2mm grid, a 5K x 5K mosaic is constructed, comprised of 0.4μ square pixels. To facilitate interactive browsing of the data, reduced versions of the mosaic are also computed, at several different resolutions, the smallest being a 512 x 512 pixel image.

GridBrowser communicates with a number of other applications (*nodes* on the MWS network) via remote procedure calls (RPCs). There are two levels of MWS nodes supporting GridBrowser. The application at the lowest level is **CapCon**, the microscope control and image capture process running on the dedicated CAP/CON workstation. Also running on CAP/CON are two nodes which invoke CapCon's services to capture sets of images and process them for display.

Survey is responsible for aligning multiple raw images gathered from CapCon to construct a mosaic. The initial 5K x 5K recording of a specimen is gathered in advance by Survey, which is also running while the user is on-line with the microscope. The MWS user can request a higher-magnification mosaic of an area being viewed using GridBrowser. To service this request, Survey starts by capturing and transmitting the central tile of the mosaic, then captures and aligns tiles surrounding the center in a roughly spiral pattern, transmitting each to GridBrowser as it is completed. The process may be interrupted by the user at any time.

The MWS also integrates the microscope's tomography capability into the microscope environment. The user may request a 3-D rendering of a region under the beam by sending a message to **Tomo**. Tomo uses CapCon to gather axial tomography images, which are then sent to an alignment application running on a compute resource (a Cray Y-MP). The aligned images are back-projected to

produce a volume, which is submitted via NetV for rendering on another compute resource (an Alliant FX/2800). NetV renders the volume from a number of viewpoints in a 360 degree rotation and transmits the sequence of images to GridBrowser for display as an animation loop.

4.2 MWS Software Architecture

The RPCs for all of the MWS nodes are assembled into the **NetMan** (network management) library, to facilitate the creation of new nodes and the propagation of changes in the NetMan protocol to all of the nodes. We made a small modification to the RPC code generator to enable the NetMan library to contain both the client and server functions for each node. This allows each node to act as a client employing the services of another instance of itself. For example, this is used by multiple GridBrowsers running on different workstations to interoperate in support of collaborative work.

All of the MWS applications were built using the XView toolkit, and were designed using Sun's DevGUIDE user interface development tool. GridBrowser uses Sun's Sunvision image processing library to manipulate and display images. It also uses Sun's SlingShot extensions to the XView toolkit to handle the drawing of graphics overlays. As a result, GridBrowser was implemented without any coding at the X Windows library level. We have found that relying on higher-level toolkits like XView and Sunvision has sped our development time significantly. [Merc91]

User interface events in an XView application are dispatched via a portion of XView called the Notifier. Event handling is implemented via callback functions that are associated with user interface widgets. A function is provided within the Notifier to enable the handling of RPCs.

All of the dispatch functions, client functions, and dummy versions of the service functions for the applications are compiled into the NetMan library, so a programmer working on an MWS node need only implement the code for each of the service functions. However, the dynamics of RPCs and the needs of our application require that the service functions return as quickly as possible. For example, GridBrowser shouldn't be suspended waiting for CapCon to capture an image. To achieve the appearance of being multi-threaded, each of the MWS nodes contains a polling timer set to be activated as often as possible. The function attached to the timer consists of a simple state machine (a C *switch* statement) with its state stored as a globally-accessible variable. If an RPC service function needs to perform a task which may take an appreciable amount of time, it sets an appropriate timer state and returns. The timer function will then

perform the operation the next time it is invoked. If the client node needs to know when the service task is complete, a follow-up RPC is issued from the service node back to the client. Nodes on the MWS network are thus decoupled. The XView Notifier guarantees that user interface events, RPCs, and the polling timer are all smoothly integrated, making possible an easily extensible event-based program structure.

4.3 MWS Implementation

All of the microscope beam parameters need to be adjusted to align and focus the image correctly, not only at the start of each session, but also continually, as the microscope is being operated. In order to operate the microscope remotely, a real-time video image of the microscope stage would need to be available to the remote microscopist, in addition to facile control over all of the beam parameters. Any perceivable lags or discontinuities in the video signal or in the transmission of the beam control information would make tuning the parameters extremely difficult [Carr92] [Kei191]. Since we presently cannot assume the availability of real-time video, the MWS software design is dependent on the presence of an operator at the microscope site, and includes support for interaction between the on-site operator and the remote researcher. The CapCon node, which is responsible for handling any requests to control the microscope from the other applications on the network, may fulfill a request by prompting the on-site operator and awaiting acknowledgment that the request has been satisfied. In this way, all responsibility for controlling the microscope and capturing images can be encapsulated into CapCon, including those tasks which are not yet capable of being automated.

Two MWSs based on SPARCstations have been assembled. An FDDI ring connects the SDMIR MWS and CAP/CON to SDSC, where they connect to the NSFNet T3 backbone and thus to a remote MWS. The MWSs each have a ViCOM VX graphics accelerator board, 64 MB of host memory, and an FDDI interface. The VX accelerator is based on an Intel i860 processor along with 4 MB of Intel RAM and a 16 MB framebuffer, portions of which are used as a cache when paging blocks of image data to host memory. The resulting configuration affords us a large amount of image storage and manipulation capability.

5 Conclusions

Our goal in the Microscopist's Workstation project is to investigate the potential advantages afforded by tightly coupling a scientific instrument, under computer control, with interactive visualization software. At the time of this

writing, the MWS software is under development. We first demonstrated the remote acquisition of images using MWS in May '92, operating the San Diego microscope from the Argonne National Labs near Chicago. By Visualization '92, we will have demonstrated the MWS prototype at SIGGRAPH '92, as part of Showcase. As the project develops, we expect to be able to draw further conclusions regarding designing a visualization application around a laboratory's users' methodologies, and regarding high-speed network access to a remote scientific instrument.

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