Mass Spectrometry:
Remote Experimentation and Collaboration
University of Delaware

Project Goal.
The project goal was to provide simultaneous, collaborative, remote control of a MALDI-TOF mass spectrometer located at the University of Delaware. A network-based solution eliminates the need for collaborators to travel to the laboratory in which the large, expensive equipment is housed. Researchers can instead mail their samples (analytes) to the lab. In the initial preparation, an analyte solution is mixed with a matrix solution and allowed to crystallize on a sample plate (probe). After the probe is inserted into the mass spectrometer, all aspects of the equipment control, data acquisition, and analysis can be performed at the instrument itself or at any number of remote locations at which collaborators work.

The control and analysis software is a collection of tightly coupled X Windows applications supplied by the instrument's vendor, Bruker Daltonics **[1]**, and is run on an attached Sun ULTRA-5 workstation. Several approaches were examined to allow the X applications to be controlled and viewed by the remote collaborators. The preferred solution, discussed below, is currently used in joint research by faculty and students at George Washington University, Drexel University and the University of Delaware. The principal investigators are Professor Murray Johnston, Chemistry and Biochemistry Department at the University of Delaware, Professor Akos Vertes, Chemistry Department at George Washington University, and Professor Kevin Owens, Chemistry Department at Drexel University. Other investigators interested in similar use of this equipment should contact Professor Murray V. Johnston, Department of Chemistry and Biochemistry, University of Delaware **[2]**.

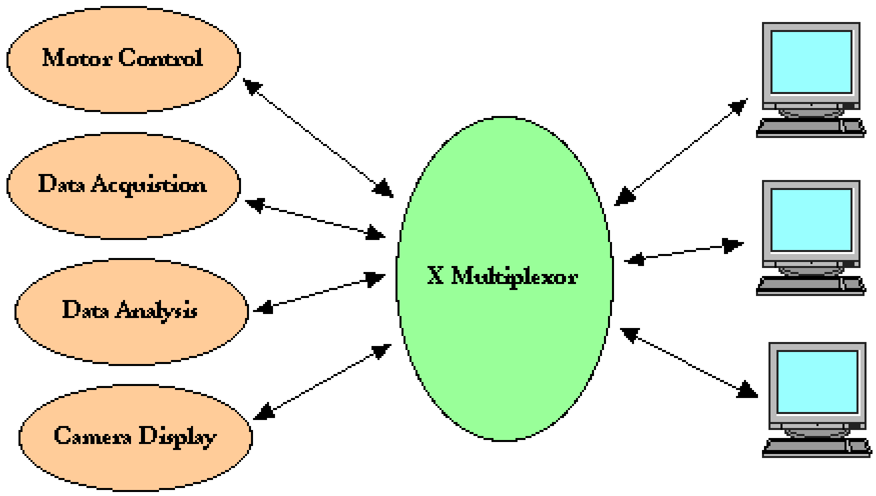
Preferred implementation.
Several commercial and non-commercial software approaches were implemented and tested. While no single approach was ideal, the AT&T Research Laboratory's VNC (Virtual Network Computing) software **[3]** provided the most robust solution. It allowed researchers in multiple locations to take mouse and keyboard control at will. VNC provided a common view of the current windows displayed on the UD laboratory's screen. The researchers were not constrained to use a single workstation manufacturer or operating system. Testing was done on Sun (Solaris), SGI (IRIX), and PC (MS Windows) workstations.

Thanks to the generosity of AT&T Research, the VNC tools are open-source and in the public domain. The tools continue to be maintained by AT&T with contributions by the VNC user community.

Two less-successful, view-and-control-sharing approaches that were investigated were the following:

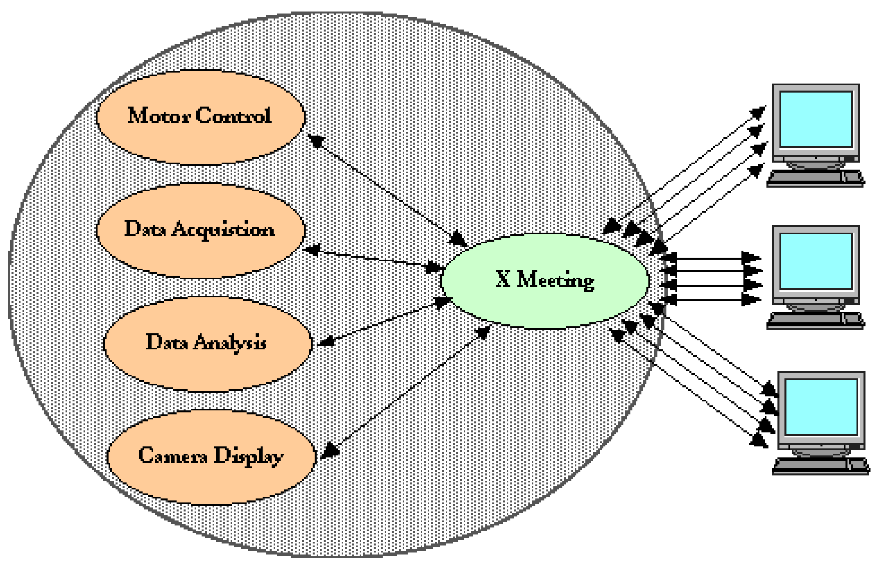
X Multiplexing
This approach did not require any changes to the Bruker software. The sharing is done at the X server level and several X servers can participate in the experiment. The particular implementation used was xmx **[4]**, written by John Basik. The Bruker X clients that were started in the multiplexed XMX server could be shared by each remote participant's xmx client's virtual root window. The xmx software was designed and worked well in a homogeneous collection of workstations, and is heavily used that way in Sun workstation classrooms at Brown University. We encountered problems in our heterogeneous environment, largely associated with variations in color maps and fonts among various hardware and software environments.

X Multiplexing Illustration



X meeting
The particular implementation used was VisualTek's xtvision **[5]**. This approach required that the X meeting control program initiate all of the mass spectrometer's control and analysis programs. Because of the design of Bruker software's start-up Tkl/Tk scripts, this approach would not work well without a major rewriting of the Bruker start-up scripts.

X Meeting Illustration



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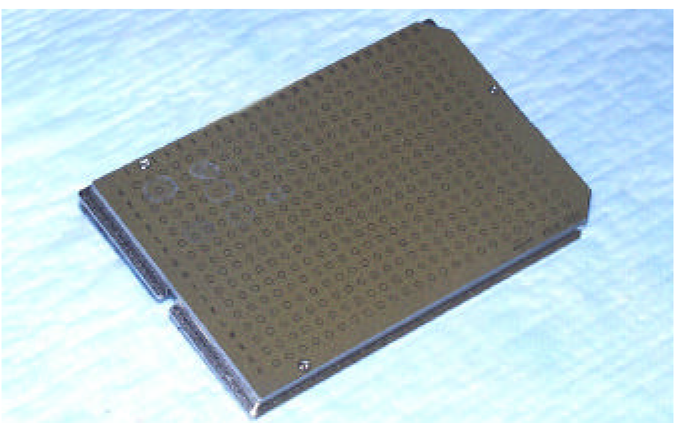
Laboratory Setup:
The Bruker Biflex III MALDI-TOF (Matrix Assisted Laser Desorption Ionization - Time Of Flight) mass spectrometer was designed to be controlled by a single, on-site investigator. The instrument can be operated in either linear or reflecting modes and is capable of post-source decay measurements (MS-MS). This particular instrument has been modified to perform two-laser experiments such as photo dissociation of molecular ions produced by MALDI. It is part of a larger collection in Prof. Murray Johnston's Mass Spectrometry Laboratory **[6]** at the University of Delaware.

The objective of a MALDI experiment is to determine the molecular masses of chemical components in a sample. MALDI generally produces molecular ions of the form (M+H)+ or (M-H)-; in other words, a proton (H+) is added to or taken away from the molecule to produce a molecular ion. MALDI is a versatile ionization method because it can generate these ions for molecules over a wide size range – from less than 500 amu to more than 100,000 amu. By using MALDI to measure the mass-to-charge ratios of molecular ions in a sample, the molecular masses of the corresponding chemical components can be determined. For example, it is possible to run a chemical reaction that breaks a large biomolecule such as a protein or DNA into smaller molecular units. These smaller molecular units are then analyzed by MALDI to determine their molecular masses. The molecular masses allow the biomolecule to be identified and/or sequenced.

MALDI is performed by mixing the analyte solution with a matrix solution, spotting a microliter of the mixture on the probe (sample plate), and allowing the solvents to evaporate. The residue left behind contains analyte molecules imbedded within the (solid) matrix. The matrix enhances the desorption and ionization of sample molecules when the residue is irradiated with a pulsed laser beam at 337nm.



The probe has an array of spots on which dissolved samples are placed. The probe is inserted into the mass spectrometer after the solution dries and the sample crystallizes

The mass spectrometer is controlled by application software, whose results are displayed on the computer monitor (beige). The instrument's internal CCD camera images are displayed on the video monitor (black).

The researcher generally works at the instrument, inserts the sample probe, and runs vendor-supplied X Windows application software on an attached Sun workstation. The X clients control the movement of the probe, start and stop the laser, adjust the high-voltage settings, and acquire and analyze the data. An external, secondary video monitor displays an internal CCD video camera's image of the sample in one spot on the plate.

In theory, once the probe (sample plate) is placed in the mass spectrometer, almost everything else can be controlled by a single user working on any single X display server. On the X desktop display, controls in one window are used to select the cell; controls in a second window provide fine motor control for moving the plate relative to the stationary laser and CCD camera. Other windows on the X desktop are used to control the laser and to display and manipulate a plot of the spectrum as it is acquired. The spectrum is saved and analyzed using a separate "xmass" program. The xmass window is generally iconified since that window nearly fills the screen. The investigator may alternate between use of the xmass window and the acquisition/control windows to improve the coverage or quality of the sampled spectrum. In addition, the resulting data files are sometimes transferred to other systems for subsequent data analysis by the xmass program.

Although control of the instrument by an investigator at a remote X display server is theoretically possible, our experience was that not all X servers worked well with all of the X clients. For example, some of the clients depended on fonts that were not on every X server. Or, the data acquisition software's plotting client would not clear the plotting window on all X servers. All of the X clients did work well, however, when run locally on the attached Sun workstation.

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Overview Laboratory **VNC-based solution**

Coupling the mass spectrometer instrument and software with VNC for remote collaboration:

VNC (Virtual Network Computing) provided the client-server infrastructure that facilitated remote collaboration. This open source software employs a Remote Frame Buffer (RFB) protocol **[7]**, thereby making it potentially applicable to all operating systems, windowing systems, and applications. The RFB protocol allowed us to have several, geographically distant, researchers concurrently

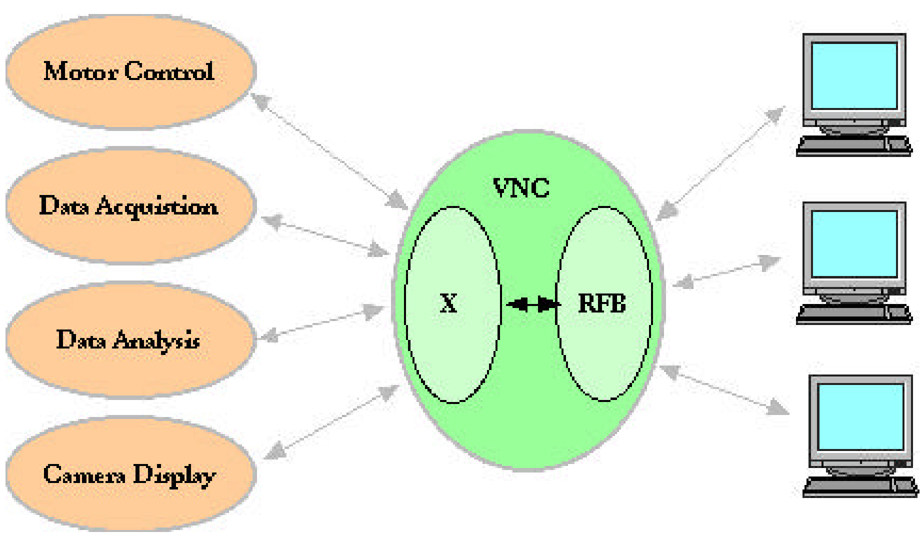
- share the view and control of the mass spectrometer's X desktop; and
- share the view of a separate video stream delivered by an internal CCD camera attached to the mass spectrometer's laser apparatus.

This section describes an actual demonstration performed with three collaborators:

- one researcher in the Johnston mass spectrometry lab at UD, using a Sun workstation (Solaris 7);
- a second researcher using a remote SGI Indy (IRIX 6.5); and
- a third researcher using a remote PC (Windows 98).

A simulation of this scenario is illustrated in a video **[8]** produced at the Internet Spring 2000 Joint Technical Meeting on March 28, 2000. (An earlier presentation using different collaborative tools **[9]** was presented at Internet2 Awareness Day at the University of Delaware on January 19, 2000.)

The VNC components are pictured below:



- A VNC server is run on one workstation in the laboratory to provide a virtual display (i.e., the Remote Frame Buffer or RFB). We run the VNC server on the same Sun workstation that is attached to the mass spectrometer, although the server could be run anywhere.
- The X Windows client applications, supplied by the vendor (Bruker) and used for motor control, data acquisition, and data analysis, are also run on this Sun workstation. The VNC server acts as an X server to the mass spectrometer's X clients and draws each client application's output window in the Remote Frame Buffer.
- A VNC viewer client is run on each collaborator's workstation, including the investigator's workstation in the laboratory. Each VNC viewer pulls its updates from the remote frame buffer, constantly refreshing the VNC window on each collaborator's monitor.
- The internal CCD camera attached to the laser is connected to an Osprey-100 video-capture card. Sun Microsystem's SunVision software (specifically, Xil_display) sends the Osprey's digital video output at 10 frames/second to a second VNC server's RFB. (A successful alternative is to process the Osprey card's JPEG image output by Sun Microsystem's ShowMeTV software. ShowMeTV, run on the workstation attached to the instrument, multicasts RTP -- real time protocol -- packets at 10 frames/second. When the software is configured to send 8-bit, monochrome images, this generates more than 1 megabit/second in network traffic. Remote collaborators can run a Java Media Framework client **[10]** to view the camera image.)

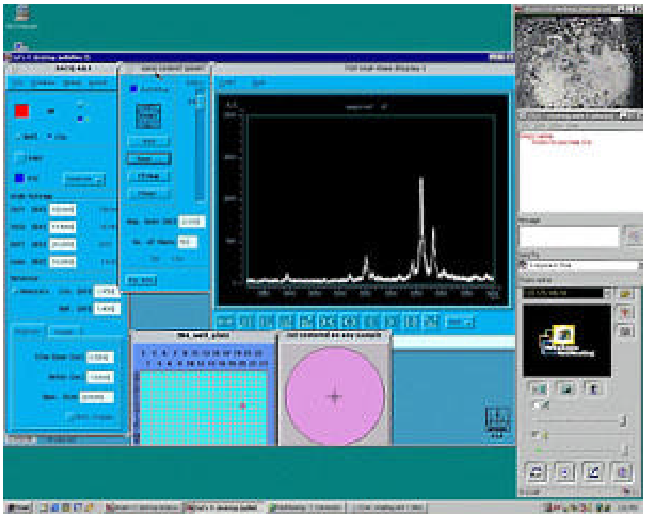
Operationally, the sharing session is started by running the VNC server in the lab. The remote participants can start their VNC viewer clients after learning what port and password the collaborator in the lab has chosen. Collaborators can join and drop out of the sharing sessions as they need to. The collaborators in the UD lab see the camera image on a separate Sony TV monitor. The others start a separate VNC viewer client to connect to the camera's VNC server, which uses a smaller desktop correctly sized for displaying the camera image.

Finally, we have used various ways to provide inter-collaborator communication, including Microsoft NetMeeting's chat and whiteboard, SunForum's similar capabilities, and conference phones. We are currently investigating implementation of H.323-based solutions for conversation among the participants.

Mass spectrometer and workstation in UD laboratory

On the laboratory workstation, the larger monitor displays the X Windows desktop. The workstation is running the X Windows vncview client and showing the VNC virtual desktop. The smaller monitor on the right displays the SVGA camera image that is captured through a direct cable connection to the internal CCD camera. There is also a laptop PC (not shown) which is running Microsoft NetMeeting.

Monitor screen of remote PC (Windows 98)



On each remote machine, the larger vncview window displays the X Windows desktop. The smaller window (upper-right corner) is a second vncview window displaying the camera image. On the lower-right is a chat session managed by Microsoft NetMeeting. NetMeeting is also being used to provide a point-to-point audio link between this PC and the laboratory laptop PC.

VNC viewer clients

All participants must run a VNC viewer client. There are currently three alternatives for the viewer.

- The native vncview client **[11]**, available from AT&T Research. This client is available for the following systems: Windows 9x, Sun (Solaris), MacOS, and generic X Windows (which we used for the SGI (IRIX) platform in our testing).
- A Java applet viewer, included, for example, in JDK 1.1.x **[12]**.
- A Java-enabled web browser (e.g., Netscape 4.x, Internet Explorer 4.x). The Java applet is passed directly from the VNC server to the browser.

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Related Electronic Links

[1] http://www.daltonics.bruker.com/products

[2] E-mail address: mvj@udel.edu

[3] http://www.uk.research.att.com/vnc

[4] http://tux.cs.brown.edu/software/xmx

[5] http://www.visualtek.com/xtvision

[6] http://www.udel.edu/chem/johnston/tour.html

[7] http://www.uk.research.att.com/vnc/howitworks.html

[8] http://i2dv.nwu.icair.org/videospace/research_00.html

[9] http://www.udel.edu/topics/internet2/i2day/realaudio/03-johnston.ram

[10] http://java.sun.com/products/java-media/jmf

[11] http://www.uk.research.att.com/vnc

[12] http://www.java.sun.com/products/jdk/1.1

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