

Analysis of Complex Surfaces in the Virtual Laboratory

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1 Introduction

The proposed features of the Virtual Laboratory make it ideally suited for the creating of a distributed centre for the analysis of complex surfaces. Such experiments involve large and complex pieces of physics devices, which constitute valuable resources. Facilities like the nuclear microprobe of the Free University of Amsterdam, the AMOLF mass spectrometer and the infra-red imaging spectroscope (also available at AMOLF) are unique in the Netherlands. Integration of these devices in the Virtual Lab makes it possible to operate these devices remotely in a multiple-user collaboration, and new research opportunities are created by combining results from these devices.

In this case study, we will describe the integration of two devices in the Virtual Lab framework. Requirements regarding shared operation of the apparatus, collaboration or users and combination of results are addressed. This case study was co-developed by the VU nuclear microprobe group and the AMOLF FTIR group.

2 Physics apparatus involved in materials analysis

2.1 Nuclear microprobe for trace-element analysis

The first physical apparatus to be integrated in the Virtual Laboratory is a ‘nuclear microprobe facility’, which will serve as a proof-of-principle. This device provides a highly focused beam of ions, with a spatial resolution in the sub-micrometer range, that can be used to identify trace elements on a surface with a sensitivity of 10^{-15} grammes. A variety of detection techniques, like PIXE/PIGE (particle-induced X- or Gamma-ray emission), RBS (Rutherford back-scattering) and specific nuclear reactions can be employed to measure concentration down to 100 ppm. A schematics of the detectors used is shown in Fig. 1.

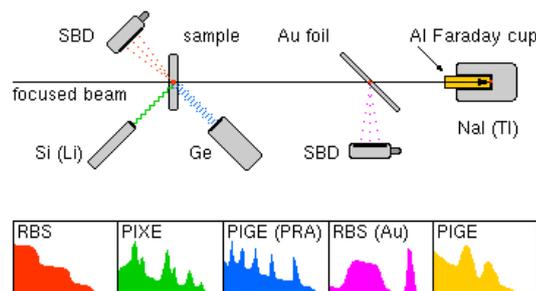


Figure 1: *Setup of various detectors at the beam line of the VU microbeam facility: Surface Barrier Detectors (SBD) used in Rutherford back-scattering experiments; Silicon/Lithium (Si/Li) X-ray detection systems and Germanium (Ge) and Sodium Iodide (NaI) gamma-ray calorimeters. The gold (Au) and Aluminium(Al) targets are added to the setup for calibration purposes.*

This technology yields precise quantitative information on element concentration and isotopic composition. The micrometer position resolution

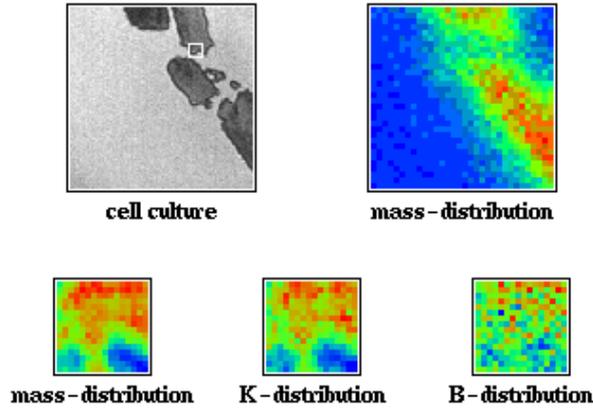


Figure 2: *Distribution of potassium and boron in cells treated with Boron Neutron Capture Therapy (BNCT), a cancer therapy currently under investigation.*

allows ‘scanning’ of a target surface, so that one can ‘see’ the spatial distribution of elements over a surface (*c.f.* Fig. 2).

The technique is suited for the identification of light elements (hydrogen, beryllium, fluoride, etc.) and is as such complementary to other analysis methods, such as e.g. mass spectroscopy and molecular analysis. In addition to its well-established applicability in chemical and applied physics research, this facility has proven to be excellently suited to perform high-precision measurements in biomedical and biophysical research. Some past projects that may serve as an example of the application of microprobe technology are given here.

Fluoride Treatment

The role and effectiveness of fluoride treatment against caries was studied in an extensive program using hamster teeth. Fluoride has been used for the prevention of caries in humans for many years. The desirability of the exposure of babies and young children to fluoride during tooth development has been under debate, since fluoride itself is highly poisonous, even in small doses. The toxicity for the developing tooth germs in children was studied.

Trace Elements in Brain Tissues

Studies of trace elements in brain tissues were made. In order to develop the technique, especially specimen preparation, studies were made initially with healthy and deficient rats, and on bovine liver. In 1997, a microprobe analysis was made of human brain tissue, where the brain tissues gray matter, white matter, nucleus caudatus, putamen, and substantia nigra were analysed. It appeared that the iron concentration in the latter tissue exhibits a complicated pattern.

Hydrogen concentration of switchable mirrors

Thin films of metals like Yttrium, Lanthanum and rare-earth metals show spectacular changes in optical and electrical properties. When loaded with

hydrogen their state changes reversibly from transparent to almost completely reflective in a short time interval. This has earned them the name of ‘switchable mirrors’. The local amount of hydrogen in the films determines these optical properties and elastic recoil detection (ERD), PIXE and RBS techniques, available at the nuclear microprobe facility, allow determination of this hydrogen loading of YH_x films on a micrometer scale.

Forensic Studies of Human Hair

Trace elements in hair are used in forensic studies, e.g. arsenic poisoning can be identified. The trace element content of hair is specific; analysis of hair found at a crime scene may identify the subject. Furthermore, such trace elements play a role in environmental studies (pollutants can leave trace elements in hair), and in biomedical studies. Here, trace elements in hair are seen as a reliable reflection of the total body content and analysis of the hair is used as a diagnostic tool.

2.2 The nuclear microprobe in the Virtual Lab

At present, the microprobe facility is fully operational and in use at the Free University in Amsterdam, although it currently operates as a stand-alone system only. It is the aim that the Virtual Laboratory for microprobe analysis will develop into a national facility for the identification and research of complex surfaces. It is therefore necessary to allow remote operation of this device and to facility sharing of datasets obtained with the various detector setups (PIXE, RBS). This requires the following functionality:

- Ability to access remotely the various hardware controls involved in handling the beam and setting up the detector systems: almost all physics devices feature a large set of controls (dials, buttons, etc).
- Extend the remote control to a level where no manual operator intervention is required (apart from emergency cases). This requires adding to the remote operability of the current setup, *e.g.*, adding remote sample movement.
- Ability to work with several persons together in performing the experiment. This implies that multiple persons should see the current state of the hardware, be able to change it and be updated on each others actions.
- Ability to analyse the datasets obtained with the nuclear microprobe detection systems. In general, the measured data contain too much information and include background and noise. Analysis should convert raw sampled data into quantities and distributions interesting for the experimenters.

2.3 FTIR-imaging micro-spectroscopy in the Virtual Laboratory

A non-dispersive infrared imaging micro-spectrometer is employed to examine the infrared radiation absorbed by complex surfaces. These experiments

provide detailed information on the spatial distribution of infrared active functional groups. The experimental set-up consists of a Michelson-Morley type interferometer equipped with a step-scan mirror, a FTIR microscope and a 64x64 pixel Mercury-Cadmium-Telluride IR array camera (see Fig. 3). In step-scan operation, the moving mirror moves in discrete steps, and the mirror surface stays at a fixed position for a variable period of time. An interferogram is build up from Infrared images at incremental optical path differences (or mirror displacement). After completion of the full scan a dataset is created which consists of a stack of images which is sometimes referred to as a hyper-spectral data-cube. Each pixel stack in this data-cube represents an interferogram, which is subsequently Fourier Transformed to yield the corresponding IR spectrum. Each of the pixels of the IR camera is an individual detector. Hence, it is possible to perform a full multi-channel (4096 channels) FTIR analysis of a 400 x 400 micrometer image with diffraction limited resolution without the need for sample scanning. This mode of operation opens up new possibilities for FTIR micro-chemical imaging which can be employed in a variety of scientific studies.

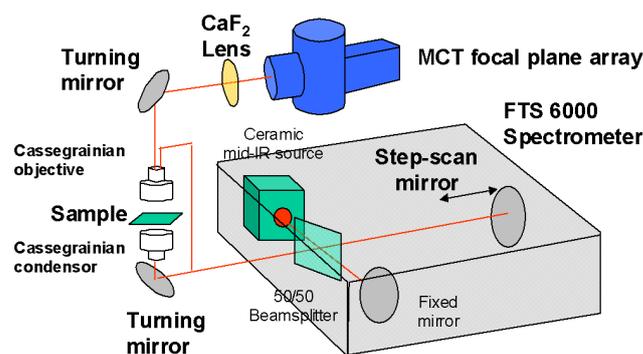


Figure 3: *Mid-Infrared Step-scan imaging spectrometer experimental lay-out*

Computational aspects

The size of one single data-cube ranges from 16 to 100 Mbytes, depending on spectral resolution and acquisition mode. Upto 20 data cubes can be produced per day. Given the magnitude of the data production it is easy to understand that the time it takes to analyse a single dataset in detail is much larger than the actual experiment time. Given this large size, it is near to impossible to distribute the data to individual researchers. A choice to use the computational facility to perform the analysis and only to export the results to the client is obvious for that reason. Several tools for analysis include apodisation, Fourier transformation and background correction. They all need to be developed for or integrated into the virtual laboratory. The high information density in such an experiment additionally requires a more sophisticated approach. Chemometric software tools based on principle component image analysis are developed at AMOLF to visualize the spatially correlated spectral features. These type of expert analysis

systems should be included in the virtual laboratory. The development will focus on the application specific user interface, incorporating both the basic as well as the advanced algorithms.

2.4 Applications

Binding media and pigments in old master paintings

The FTIR imaging facility is currently fully operational as a stand-alone instrument. Its main area of application at AMOLF is the analysis of the binding media and organic pigment distributions in embedded paint cross-section of old master paintings. This work is carried out in the framework of the MOLART program. The virtual laboratory facility can be used to make the results of the MOLART research more readily available to conservation scientists.

Arteriosclerotic deposits in mice

Various experiments have been carried out on biological tissue thin sections. One particular example is the use of FTIR imaging in the identification of arteriosclerotic deposits on arterial walls without the use of chemical staining techniques, shown in Fig. 4. Lewis et. al. have used FTIR imaging to identify silicone in human breast biopsies resulting from leaking breast implants.

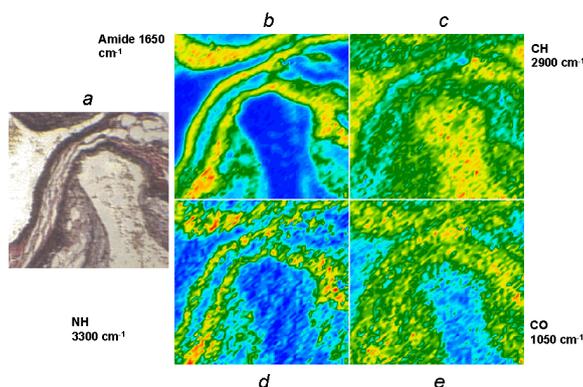


Figure 4: *FTIR transmission images of non-stained arteriosclerotic mouse tissue (a) microscope image of the stained sample (b,d) Protein wavelength bands showing artery wall material, (c) C-H stretch wavelength band showing the embedding material (paraffin), (e) CO wavelength band showing fatty acid deposits on the artery wall.*

Polymer laminate films

FTIR imaging is also a powerful technique to examine synthetic polymer laminates. In a study of laminated polymer films used for food packaging, FTIR imaging was used to determine the thickness distribution of the various layers based on their differences in functional groups. This is the only

way to examine these films as they all have similar optical properties and the different layers in a thin section cannot be distinguished with regular microscopy.

Slow-release of drugs by polymers

Pharmaceutical research is another area of application of FTIR imaging. In various drug formulations the micro distribution of the active compound in a carrier material can be readily determined. Slow-release drugs often use a biodegradable polymer in which an active component (peptides, proteins or steroids) is incorporated. The ratio between active component and polymer is determined as a function of the degradation stage with FTIR imaging.

2.5 The FTIR facility in the Virtual Lab

The variety of applications described above indicates that a large community of researchers from different disciplines has potential use for a FTIR imaging facility. As a result, a number of collaborations already exist with the AMOLF group. These collaborations are complicated by the fact that our partners now depend on our analysis system and our expertise to perform the data-analysis after acquisition. After a virtual laboratory environment has been created, these partners have to use this facility to examine or re-examine the FTIR imaging data in their own working environment, without the intervention of AMOLF scientists.

2.6 Experiments using both devices

Both techniques for surface and materials analysis – μ probe and FTIR – yield complementary information. The microprobe facility uses nuclear reactions and, as a result, is sensitive to element and isotope distributions. The infra-red interferogram technique (FTIR imaging) on the other hand focuses on specific functional groups inside molecules. Combination of the results from both techniques provides researchers with hitherto unknown possibilities. The use of VL infrastructure greatly facilitates the ‘Data Fusion’ possibilities. Although it will still be necessary to physically transport a given sample from one place to the other (since the samples themselves are quite real), the databases integrated in the Lab can store the results.

3 Modelling of physical devices in the VL

An experiment in physics can be logically separated in steps, with have only limited mutual interaction. This logical separation in the microprobe and FTIR experiments in the ‘real-world’ may be used as a basis for modelling these experiments in a Virtual Laboratory environment. In Fig. 5 a simplified data-flow for the (combined) microprobe and FTIR experiment is shown. The experiment configuration suggests implementation of this VL case in a modular way, with the functionalities defined in the boxes of Fig. 5 being modules used as basic Virtual Lab operations.

This simplified picture is not complete. Each module will need some ‘configuration’: settings describing the state of the device or analysis module (one may think of beam position parameters that determine which part

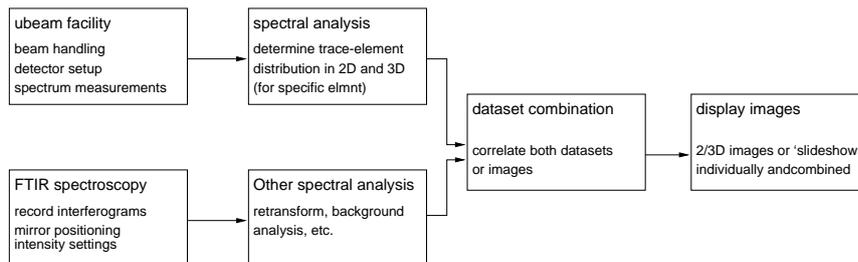


Figure 5: *Simplified data-flow chart for the microprobe and FTIR experiment. The resulting images represent, e.g., mass or isotope distributions.*

of the sample surface is currently under study). As stated in section 2.2, such controls should be available to multiple persons collaborating in the experiment. From an end-user point of view, some easy-to-understand graphical interface should be provided to access these controls.

The layout of the modules in an experiment might also be a good starting point for a user interface. The end-user is presented with a graphical overview of the experiment and can connect and disconnect modules by drag&drop. By selecting experiment modules, their local controls are presented (when allowed by appropriate permission settings).

Also some ‘intelligent’ controls should be provided for easy access to these complex pieces of apparatus. This may either hide or inhibit interaction with the underlying, protected apparatus.

4 Collaboration within the VL

In the preceding section, collaboration essentially focuses on working on ‘shared controls’: the dials and buttons of the devices. Also important is collaboration among the participating end-users of a Virtual Lab experiment. As data are produced, all collaborating scientists should be able to view these data and compare them to data stored in databases, *e.g.*, from previous experiments. Functionality is also required to notify users and (expert) operators in the Virtual Lab of important ‘events’ (failure situations, completion of experiment). Besides, they will want to communicate among themselves (a conference-like situation) as part of the running experiment.

The required functionality for user-collaboration:

- Inspect the data produced in the experiment while the experiment is running. This should include the possibility of inspecting intermediate results.
- Provisions for message event handling.
- Provisions for multi-person conferences, where messages can be exchanged or posted (both text messages and other types of media like pictures).

The preferences and capabilities of each user should be taken into account in all interaction of the VL with that user. Configuration parameters may have access control lists (ACLs) associated with them, limiting their availability to end-users.

User Interface modules (dotted boxes) Various user interfaces and multiple users may be attached to a running experiment. What configuration parameters they see, in what format and whether or not they can view *e.g.*, images coming from the experiment depend on the connection capabilities (web, text-only, phone, etc) and on their level of authorisation.

These modules in the connection layer always have a specific user attached to them.

The main experimental steps are located in the middle part of the figure. The different steps correspond closely to the ones in Fig. 5.

uprobe autotune This module was added to illustrate the configuration abstraction. The parameters of the *uprobe module* are hidden from all users, that only see the parameters of the autotune module. Based on the comprehensible user requirements and using the data generated on-line by the uprobe module, the detailed hardware controls are set. Of course, some controls may just be propagated from the uprobe module to the user by the autotune module. Also, it is not integrated in the uprobe module itself, so as to allow expert users in other experiments to control the uprobe directly.

uprobe module This module actually scans the sample surface and performs the measurements like RBS, PIXE or ERD. From these spectra the element and/or isotope concentrations can be determined.

This module also explicitly produces *status message events*. These events are triggered by, *e.g.*, hardware faults and should be brought to the attention of both end-users (for example broadcast in the running conference) and expert operators. Since operators in general are not involved in the experiment, they need to be contacted autonomously by the VL. This functionality is contained in the *message propagator* module.

uprobe analysis This module converts the measured sample data into mass distributions of specific isotopes. This requires configuration parameters describing, *e.g.*, the isotope name for which the analysis should be done. It produces the spatial distributions underlying the images shown in Fig. 2.

Histo-to-image This module converts the distribution data to a graphical image, and may be attached to a pixel-addressable user interface that will present the final images to end-users.

One module is specifically involved in end-user collaboration: the *Conference Centre*. This conference centre may be thought of as a kind of multi-media chat-box or as a kind of telephony conference. In the end, various media-types (text, image, audio) should be supported, where ‘displaying’ depends on the capabilities of the connected user(s). From the end-user point of view this centre could look like a ‘netmeeting’ like interface when connected via a web-based interface. When that same user connects via a regular phone connection, the text and audio parts of the conference should still be available to him, while visual data (images, drawings) will be suppressed. In

view of the generality of this module, all or part of the required functionality will already exist elsewhere. Integration of these existing tools may provide a good starting point in this respect.

Databases

In the general scheme foreseen for the microprobe case, all kinds of data streams need to be stored in or retrieved from databases. To illustrate this, one of the raw-data streams from the μ probe is (also) directed to a database storage module. Since data stored in a database need some meta-information, the connections to the database may need some end-user configurable parameters. All stream-like data (i.e. all data except for configuration actions) should be storeable in the database, if necessary ‘duplicating’ the outbound streams.

On data retrieval, more user interaction with a database connection is needed, like performing queries and selecting data from generated reports. A database query may always replace a live data stream.

5.1 On the connecting of modules

The modules used in describing the microprobe case above should be reusable in various kinds of experiments. Also, the number of end-users attached to an experiment is not fixed, and may well change even in the course of one experiment. Therefore, the module functionality (‘computation’) should be entirely separate from their interconnections and their runtime order. On the one hand, this will lead to a high degree of re-usability, on the other hand it requires a (rudimentary) ‘experiment controller’ or manager at an early stage of implementation. Trial implementation of a like manager suggests that using this modular concept in a distributed environment is a viable option. Since this is essentially a problem of coordination (on which a lot of research has already been done), existing systems may provide all or part of the functionality required. In Fig. 7 a sample scheme is given on the combination of FTIR data acquisition (DACQ, of which no further details are given) and microprobe results previously stored in a data base.

The ‘experiment controller’ should initially at least

- be able to start modules in a specified order,
- watch run-status and reset/restart if necessary,
- support generic starting/stopping/suspending of modules,
- react in semi-real-time to such requests,
- dynamically make (and break) inter-module connections in a running system,
- be entirely independent of data content.

6 Summary

The integration of various types of physics apparatus provides the Virtual Lab with unique possibilities for combined surface analysis. Several applications in the domains of biophysics, medicine and pharmaceuticals show the

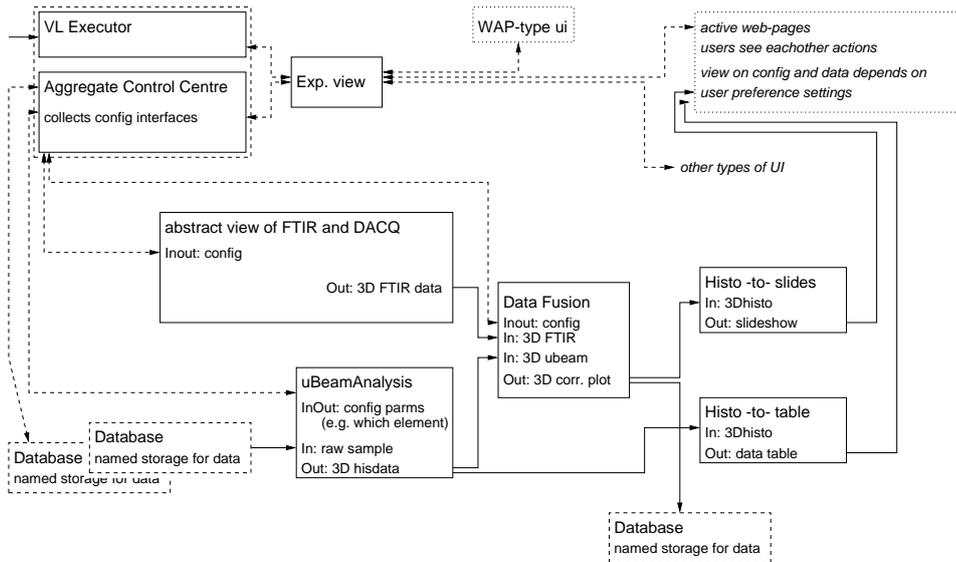


Figure 7: Overview of experiment using FTIR imaging together with results obtained in a previous microprobe experiment and stored in a database.

potential of such a combination in the Virtual Lab environment. The large datasets and the complicated analysis needed to interpret the sample data provides a testing ground for both data transport (networking) and data storage (databases).

The case proposed can well serve to further study the requirements of multiple-user interaction with these devices and the challenges related to the reliable and secure control of such a complex device by external end-users. Collaboration among the participating scientists, related to both device control and to interpretation of experimental results has a prominent role in this scenario.