

induction by Spirtes, Glymour, Pearl, Cooper and others has been gaining ground. In 2003, Clive Granger won the Nobel Prize in Economics for his work on the causal analysis of observational economic time series, giving more respectability to the field. Several articles have already appeared in the bioinformatics literature employing causal techniques, and related conferences and workshops (such as the recent NIPS workshop on causal feature selection) have been held.

Several theories of causality have corresponding graphical means for representing causal relations, such as Structural Equation Models and the more recent Causal Bayesian Networks (see Figure 1). Algorithms exist for inducing such networks from observational data. Our recent work has extended learning Bayesian Networks with tens of thousands of variables and unprecedented accuracy. In addition, a growing body of our work is focused on causal variable selection: when the time available or the number of variables does not permit the construction of the full Bayesian Network, algorithms can identify the local causal neighbourhood of a vari-

able of interest in reasonable time, for example, the causes and effects of the expression levels of a gene. The causal local neighbourhood (related to the concept of the Markov Blanket) is under some conditions the smallest variable subset required for optimal prediction. Our algorithms often outperform traditional non-causal variable selection algorithms for prediction, and in addition the selected variables have known causal relations to the target. Our group, along with other researchers, is carrying out theoretical work to accompany this algorithmic work. This includes looking at the conditions under which the relations found correspond to causal relations, lifting or changing the set of assumptions for causal discovery and extending it to different types of data. Algorithms now exist for identifying hidden (unobserved) variables that cause (change the distribution of) the variable of interest, that explicitly model selection bias, model feedback loops and other interesting situations.

We have developed a couple of tools for applying causal data-mining techniques to real data. The first is Causal Explorer, a library of algorithms for learning

Bayesian Networks and identifying the causal neighbourhood of a target variable. The second is the Gene Expression Model Selector or GEMS, which automates the mining of gene expression data with the option of using some of the causal methods mentioned above.

In moving to the Institute of Computer Science at the Foundation for Research and Technology, Hellas and the Biomedical Informatics Laboratory, I will be extending this line of work in several dimensions. In our plans are new algorithms, more theoretical results, and enhanced tools for inducing and mining causality; in addition, the application of such methods to biomedical data to answer specific biological questions. In particular, for the Digital Patient, our methods could identify from data the factors that need to be modeled in order to simulate the development of a disease or a human subsystem malfunction.

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Desktop Virtual Reality for 3D and 4D Medical and Biological Data Analysis

by Jurriaan D. Mulder

The Personal Space Station (PSS™) brings Virtual Reality (VR) to the desktop of the medical and scientific professional. Its purpose is to make VR more useful and accessible for the effective analysis of 3D and 4D data in medical and biological research. To this end, PS-Tech in the Netherlands and CWI are developing and improving new techniques and methods for the application of VR in 3D and 4D data analysis.

Three-dimensional (3D) and time-dependent (4D) datasets are becoming increasingly important in medicine, microscopy, and biology. Such a vast amount of information implies a need for fast, accurate and cost-effective analysis. Visualization - the ability to present complex data as multidimensional images - combined with direct control over that data in VR provides a tool to satisfy that need. In a VR environment the data is presented truly in 3D and users can interact with the data directly in the 3D space. However, traditional VR systems tend to be bulky, difficult to use, and expensive, and their

use has therefore been mainly limited to dedicated VR centres. In other words, the use of VR remained beyond the scope of most medical and biological scientists.

The Personal Space Station was developed at CWI, and is now also commercially available from the CWI spin-off company Personal Space Technologies (PS-Tech) in Amsterdam. The PSS™ is a desktop interface that allows the researcher to interact with 3D and 4D images in a natural and intuitive manner, under normal office working conditions. About the size of a child's school desk, the PSS™ is portable, yet still

large enough to create a virtual environment in the user's personal space. The images are presented to the researcher using a head-tracked, stereoscopic display. In addition, the researcher can control, explore and interact with the data directly in 3D and 4D. Therefore, both the viewing and the interaction with the data are achieved in a transparent and intuitive manner, allowing the researcher to focus on the analysis instead of the user interface.

The PSS™ is now progressing from a scientific concept to a device for medical and biological data analysis. 3D

and 4D datasets from ultrasound, MRI, MRA, CTA and confocal microscopy can be analysed and explored in VR. The user holds a dataset - like a 4D ultrasound dataset of a heart - in one hand and can orientate and position it. The other hand is used to interact with the dataset for manipulation, like slicing, dicing, and pointing. Next to the 3D interaction tools the user has standard 2D tools like a mouse and keyboard. Depending on the task the user selects the appropriate tool (eg menu operations using 2D tools, positioning a data set using 3D tools). The ability to select the right kind of tool for the task at hand not only simplifies the process of working with 3D data, but it also simplifies application development.

Scientists at research institutes, universities and academic hospitals are working with CWI and Personal Space Technologies to create the PSS™ applications needed for the analysis of complex medical and biological data. At the Academic Medical Center (AMC) in Amsterdam, the PSS™ will be used to analyse 4D ultrasound data of quantitatively complex (patho)physiological processes and the effects of genetic background and therapeutic intervention. Processes such as tumour development, atherosclerotic plaque formation in blood vessels, the development of the heart and the effects of genetic background and therapeutic strategies on these processes can be studied effectively in 4D.

At the University of Amsterdam, the PSS™ is used in live-cell imaging to facilitate visualization and analysis of large 3D and 4D data sets obtained with the microscope unit. A controlled light-exposure microscopy (CLEM) microscopy unit combined with the PSS™ is the chosen method that

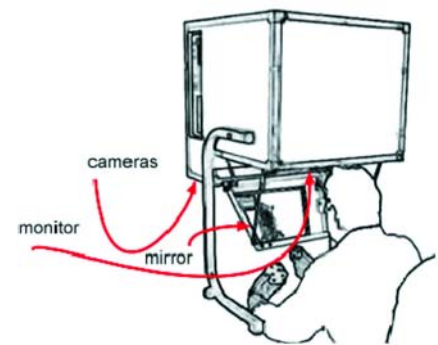


Figure 1: The PSS explained. In the PSS the user holds the image in his hands and manipulates it with tangible interaction devices. The user looks at the monitor via a mirror. This enables the user to bring his hands into the same environment as the virtual 3D-objects without interrupting the visual image. With the use of a custom optical tracking system, the user can interact with the 3D images using wireless, tangible interaction devices. Therefore, interaction with virtual objects can take place in a direct, natural and intuitive way. Hand-eye coordination and 'proprioception' (the subconscious perception of the position of muscles and joints) are used to the full. The user is 'attracted' by the objects he sees; his natural reaction is usually to grab and manipulate them.

enables time-resolved study of fluorescently labelled cells to gain insight into cell dynamic processes. This methodology will allow delicate intracellular processes such as DNA repair, protein aggregation and transport to be more easily studied.

The PSS™ is also used for the analysis and modelling of 3D vascular data, ultrasound analysis in cardiology, brain research, neurosurgery and medical education. With the development of these applications, and the close cooperation between CWI, Personal Space Technologies and the medical and biological research institutes and universities, VR is being brought into the world of the medical and biological professional. The ultimate goal of the project is to bring 3D visualization and interaction within reach of all users of com-

plex 3D and 4D data sets. To achieve this, further research and development is needed in several fields, including human-computer interaction, tracking and display, large dataset management, and automated and interactive image segmentation methods. CWI and PS-Tech will continue to cooperate with scientists from different fields and application areas to continuously improve and develop new techniques and methods for the application of VR in 3D and 4D data analysis.

Link:

<http://www.ps-tech.com>

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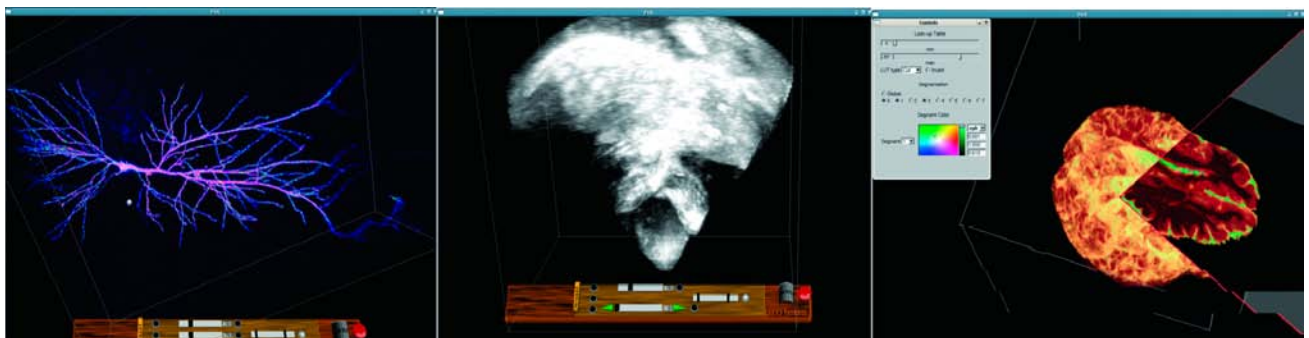


Figure 2: Some examples of interaction and visualization in the PSS. From left: 3D and 4D microscopy; Cardiology, 3D and 4D Ultrasound; Brain Research, segmented CT data.