AUTOMATED PET CHEMICAL SYNTHESIS AT TRIUMF

David B. Morris
TRIUMF
June 22, 1989

A BRIEF HISTORY

The FDG Synthesis System

The automation of PET Chemistry at TRIUMF has evolved over five years. The first system to be built was for the production of 2-Fluoro-2-D-Glucose. The FDG system was specified in the fall of 1984.

At that time the predominant small computer system at TRIUMF was based on the 8080/Z80 microprocessor and the S100 buss. This hardware was used for developing programs that were later installed in permanent memory in single board computers for specific tasks. The systems are still used today, although a lot of system development has moved to different computers in the last three years.

The 8080/Z80 computer was a familiar environment, and there was a complete set of software development tools available. To create the FDG synthesis system, standard components were bought to keep the system compatible with existing hardware. Two non-standard interface boards were bought, but this still kept 70% of the system standard. This helped to reduce the cost of the system because few spare parts had to be purchased.

The system was programmed in a mixture of FORTRAN and Assembler Language. These were the predominant languages, and the tools and resources were freely available.

The operator interface to the FDG system used a common monochrome terminal. The terminal provided a set of line drawing characters which were used to display the components of the system. Bright and dim symbols indicated the active valves, tubes, and components. This was one of the first video screen mimic displays at TRIUMF.

The software was very simple. The synthesis process was broken down into a series of simple steps. At the start of each step, the hardware was configured correctly, and the screen was made to mimic the system. There was little feedback in the system, and there was no way of telling if a valve failed to open. There were two closed loop functions for controlling the heater and the flow controller.

The FDOPA Synthesis System

After the FDG Synthesis System was built and operational, the Fluoro-Dopa Synthesis System was started. There was a lot of common equipment used by both systems, and the initial Fdopa system simply added a few valves and vessels to the existing equipment.

Manual Control

One of the first requirements of the synthesis systems was a version of the program that let the operator manually control each valve. This was important for initial setup, and for post-production clean-up. A simple method of identifying valves and devices was used, and by pressing the proper keys the system could be controlled manually.

THE NEW SYNTHESIS SYSTEMS

In the following four years, computing and process technology has progressed in leaps and bounds. There is little similarity between the small computers of today and those of four years ago. Speed, complexity and capability have increased a hundred fold.

Fdopa Production

In the original Fdopa production system, the automation ended after the product was transferred into a rotary evaporator. The first step to completing the automation of the process was to create a simple automated method of loading and unloading the rotary evaporator. This was done using a motor control system and custom glassware.[1]

Once the rotary evaporator was automated, the other components of the system were fairly simple. The Fdopa system now became the dominant part of the automated synthesis and the new system design has been oriented about this system.

Hardware

The target computer system for this process is an IBM PC or compatible. The PET Chemistry Group owns two IBM PC-XT compatible computers. It was felt one of these computers would be able to control the system and respond at suitably fast rate. A small Carbon-11 system had been built earlier using this system and had worked well.

The configuration of the computer will change to include a high resolution color display. This will bring the video system up to date and enhance the visual capabilities of the computer.

The control equipment used to connect the computer to the process devices is based on OPTO-MUX equipment manufactured by OPTO-22. This equipment uses input and output modules which plug into mounting racks. Each mounting rack contains a communications and control processor. Each processor is connected to a serial communications line that attaches to the IBM PC.

The IBM PC is the only master on this communications line. Each mounting rack has a unique address, which lets the computer access each rack individually. The computer can scan the racks and modules to determine what type of module is installed in each location. An entire rack of modules can be controlled or individual modules can be accessed.

The OPTO-22 product line includes digital and analog modules. There are separate digital and analog mounting racks. Each mounting rack contains 16 positions, which can contain either an input or an output module.

- The digital modules have AC and DC output capabilities, with current ratings of 3 Amperes. The digital input modules have a range of valid input voltages from 2.5 Volts DC to 180 Volts AC.
- The analog modules cover a broad range of analog input and output signals. These include current and voltage inputs, thermocouples, RTD devices and a frequency counter. The output modules provide current and voltage signals.

All these modules are optically isolated so there is no danger of high voltages damaging the computer equipment.

Devices

The majority of devices found in a chemical system are valves. The Fdopa system uses sixteen 24 Volt DC solenoid valves. Each valve is driven by an individual OPTO-22 module.

There are four 110 Volt AC devices. The heater cannot be controlled directly from the OPTO-22 modules because of its high current requirement. A contactor is controlled by an output module to turn the heater on and off. The other devices can be controlled directly by AC output modules.

The flow controller, used to regulate the flow of target gas, uses an analog output module to set the flow rate. It uses an analog input module to indicate what the true flow is. As the target empties, the flow drops below the setpoint. The system monitors the true flow to determine when the target is empty.

[1]Remotely Controlled Evaporation and HPLC Injection for Purification of Radiopharmecuticals. M.J.Adam, T.J. Ruth, S.Jivan, D.Morris and S. Tyldesley, J. Nucl. Med. 30 (1989) 923.

The dosimetry uses an analog input module to return a value proportional to the activity of the product.

Durability

The OPTO-22 equipment is well made and easy to use. The input and output modules are encapsulated, and are secured to the mounting rack with a screw. The mounting racks are tough glass epoxy and come with several locations for attaching them to a panel. The method of mounting the equipment is left up to you. The systems for the PET Chemistry are mounted on a one quarter inch aluminum plate.

The input and output modules are not radiation hardened. They will fail after exposure to radiation. The fields in the chemistry laboratory are not expected to affect the modules. If a module does fail, it can be replaced quickly and easily.

Software

The control program for the synthesis system was written using the Microsoft QuickBASIC 4.0 programming environment. OPTO-22 provides a software support package for the OPTO-MUX equipment called OPTO-WARE, which can be incorporated into the QuickBASIC language. A graphics toolkit[2] was used to enhance the standard graphics functions found in QuickBASIC.

The software was written in a modular form, with separate modules for the display functions, device control, report generation, and step sequencing. The software was developed around the video display and the device control module was added later. This would suggest that the devices mimic the visual display, but the structure was changed to do the opposite.

There are no interrupt routines or sophisticated algorithms used in the process. Whenever a critical process occurs, the program simply spends more time monitoring that process to make sure nothing has gone wrong. The operator can abort or repeat a step and if an error occurs during a step, the operator can abort, repeat or continue the process.

The visual display provides clear indication of the current activity in the system. Active valves and tubes are painted in green, and the tubes have green dots that travel in the direction of flow. Inactive valves and tubes are painted in red. The position of the rotary evaporator and the selector valves are shown.

Each component in the system is labeled. A status panel shows numerical information at the bottom of the screen. Messages to the operator and an error status line are displayed.

The illustrations are not in color, but the different shades of gray in the illustration represent the different colors.

Manual Control

A manual version of the system must be made to allow the operator to control individual valves and devices. This will be developed after the automated version is completed.

The manual version will use a mouse as the primary means of control. The operator can point to a device on the screen and by clicking a button, turn the device on or off. If the device requires a number, then a query will be made for the value.

Using a mouse to control a system like this is much easier than the method used in the original system. It will also provide information about the operator response to the future versions of this system.

[2]Enhanced Graphics Toolkit Version 3.01, Connel Scientific Graphics, Woodinville WA

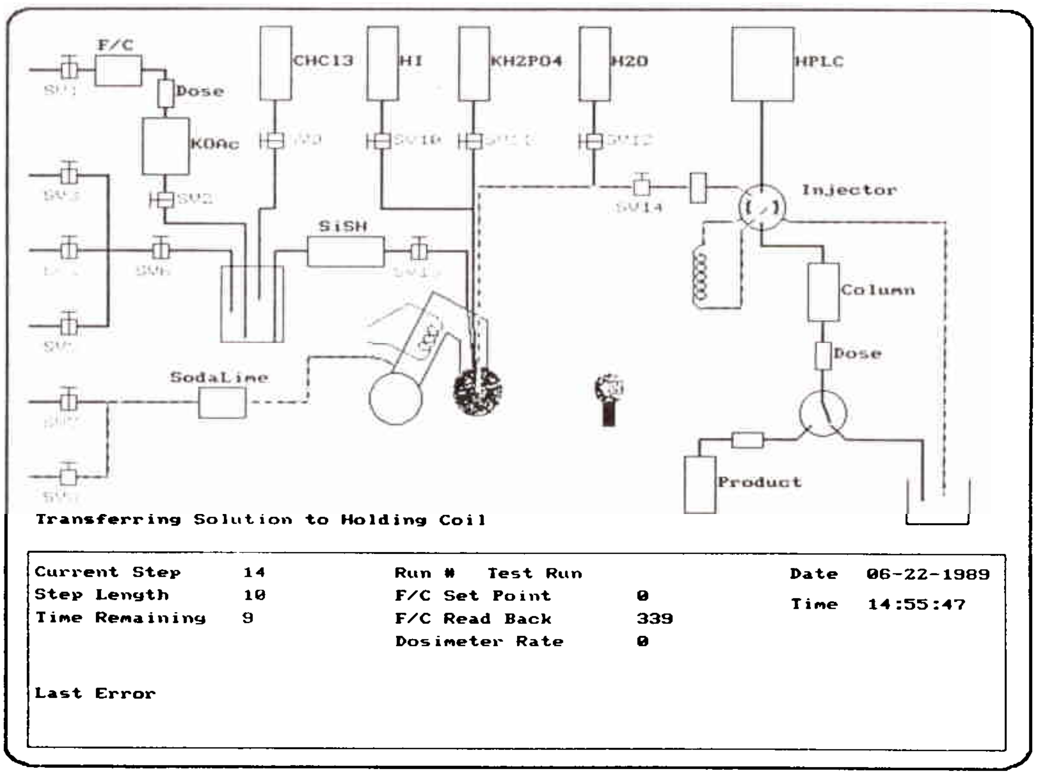

Figure 1 Fdopa Synthesis System Screen

THE FUTURE SYSTEMS

Synthesis Systems

There are several systems to be automated in the next months.

- The FDG system must be re-built to fit in with the Fdopa system.
  This is because of the common components in the two system.
- A Nitrogen-13 system will be assembled, and the Carbon-11 system will be re-built. These two systems will be located in the same hot cell, and can use the same panel of OPTO-22 mounting racks. There will not be any common devices in these two systems.
- An Oxygen-15 system is also proposed.

Each of these systems will run on its own. The systems will use devices that are dedicated to the individual system, or common to other systems.

Computers and Software

Because of the common gases used in these processes, and similar times when the processes must be run, an overlap in system use will occur.

There are several solutions to the problem of two systems running at the same time.

- A separate set of valves and hardware for each system, and a separate computer for each system.
- A common set of valves and separate computers. This requires a sophisticated communications network that allows multiple masters controlling a common set of modules.

- A single computer running several processes on a common communications network.

The last option is the most cost effective in terms of the computer hardware and control equipment, but the software and programming expenses increase. This is the approach that will be taken over the next months.

The intention is to build all systems and have them operate on an individual basis. Once all systems are functional, work will begin on a multiple process system.

The intention is to use the Microsoft OS/2 multitasking operating system in an IBM PC-AT or compatible computer. This operating system has many of the easy and familiar features of the environment that the Fdopa system was developed under. This operating system provides multiple separate windows on a single video screen. Each window can handle a separate process.

The OS/2 environment allows several processes to access a single communications network, to communicate with common modules. Certain devices can be locked out when common processes access the same device. Arbitration of who can communicate can also be handled by the operating system and special software routines.

This route to developing a comprehensive set of synthesis systems will lead to a common operator interface for every process. It will also produce a lower cost solution for any laboratory where several processes are handled by a single operator.