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DISTRIBUTED MICROPROCESSOR AUTOMATION NETWORK FOR SYNTHESIZING RADIOTRACERS USED IN POSITRON EMISSION TOMOGRAPHY

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INTRODUCTION

This presentation describes the engineering concepts underlying an evolving distributed microprocessor network for automating the routine production synthesis of radiotracers used in Positron Emission Tomography brain studies at the Chemistry Department of the Brookhaven National Laboratory in New York. As an introduction to the distributed system, we will first present a brief overview of the PET method for measuring biological function, and then outline the general procedure for producing a radiotracer. Following this, the paper will then identify the several reasons for our automating the syntheses of these compounds, that is, it will define the major problems which we have encountered in carrying out the syntheses manually. Next, there will be a description of the distributed microprocessor network architecture chose and the rationale for that choice. Finally, we will speculate about how this network may be exploited by ourselves and others to extend the power of the PET method from the large university or National Laboratory to the biomedical research and clinical setting.

An Overview of Positron Emission Tomography

PET (Positron Emission Tomography) has become one of the most important quantitative imaging tools in nuclear medicine, because with PET the clinician and the medical investigator can now measure physiological processes going on in the tissues of living and intact men and animal subjects (1). In particular,

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using the PET method, scientists are identifying and measuring many of the processes by which the normal and abnormal brain works.

In a nuclear medicine imaging procedure, a radiotracer enters the subject's circulatory system either through an intravenous injection or by inhalation. PET, as does other nuclear medicine techniques, generates images of the spatial distribution of the radiotracer within an organ. But unlike most other nuclear medicine imaging methods, PET quantitates the distribution of the positron-emitting radiotracer. PET produces maps of the brain, for example, that depict the regional concentration of the radiotracer in units of nano curies per gram of tissue, not merely relative densities as a Gamma Camera or SPECT produce.

A radiopharmaceutical becomes a positron-emitting radiotracer by having one of its natural atoms replaced by a radionuclide. The most common of the radionuclides used in PET are ^{15}O, ^{13}N, ^{11}C and ^{18}F whose half-lives are 2.03, 10.3, 20.4 and 109.8 minutes, respectively (2). The short half-lives of these radionuclides offer a great advantage over those of typical radionuclides used in nuclear medicine for studying physiological function because even an initially very active tracer decays away quickly. This characteristic makes it possible to administer a high activity tracer, and then to measure the compound's distribution within the subject's brain tissue using a PET camera, while the counting rates are still high to obtain images of good statistical quality. The exposure to the subject is limited since the radioactivity of the tracer decays away rapidly. In other words, little radioactivity is retained in the tissue after the images have been measured.

In addition to having shorter half lives, the commonly used positron emitting radionuclide labels offer other advantages over the more commonly used isotopes in nuclear medicine. As has been noted, the radionuclides most commonly used as tracers are isotopes of oxygen, nitrogen, carbon and fluorine. Except for fluorine, these can be considered as the elements of life: atoms that are found in living tissue and most nutrients. Compounds including these atoms in their molecules can often participate in biochemical processes. Since living tissue can't distinguish between the normal atom and its isotope a chemist can synthesize a tracer in which the carbon, oxygen, nitrogen or a hydrogen atom is replaced by its positron-emitting isotope. Except for iodine, most radionuclides commonly used in nuclear medicine imaging don't actually participate in the usual metabolic pathways. Technitium and indium are not elements that are accepted by living systems.

But, we named fluorine as one of the useful radionuclides, and one might ask how fluorine fits into this category of atoms involved directly in life processes because, except for its being sequestered in the bones and teeth, this element is strange to most living cells. The answer is that when a chemist replaces a naturally occuring hydrogen atom in a compound with a fluorine atom, the living cell usually accepts the so-labeled molecule in much the same way as it does the natural one.

From the technical viewpoint of quantitative nuclear medicine imaging, the most important advantage that a positron-emitting radionuclide offers over the more commonly used single photon-emitting atom stems from the fate of a positron after it evolves from the decay of the radionuclide. Within a very short time after it has been generated, a positron is annihilated by encountering a nearby electron (a negatron). The masses of these particles are then converted to two photons (gamma rays) of 511 kilo-electron volts each. These photons travel in almost opposite directions to one another, that is their trajectories fall on a common line in space. Since the positron travels only a few millimeters in the tissue before its annihilation, this line passes very near to the point in the tissue at which the positron was generated. One can detect the decay, and hence the tracer activity, along a line by counting the number of times that a coincident-pair of photons are detected along that pathway. The time coincident photon detection of PET identifies electronically the line in space along which the activity decayed. To measure many such lines, one places a ring of coincidence detectors (the PET camera) around the subject's body - in our studies the head - in which tissue the positrons are being generated and annihilated. From an accumulation of the number of many coincident photons that are detected in a given time interval along each of the possible lines-in-space passing through the head, one can compute the two dimensional spatial distribution, a slice, of the radiotracer by applying a mathematical tomographic reconstruction algorithm to the measurements. The algorithms employed to reconstruct PET images are similar to those that reconstruct computed tomography (CT) x-ray images. Both imaging techniques involve reconstructing slice images from a set of planar profiles passing through the body.

In contrast, single photon nuclear medicine imaging such as by gamma cameras or single photon emission tomography (SPECT) achieves this collimation by interposing thick lead plates having parallel channels between the subject being studied and the photon detectors. Only photons traveling down a channel reach the detector. Photons traveling in any other direction are absorbed by the lead and thereby wasted. Accordingly, single photon cameras lack the sensitivity of PET cameras, and as well, their spatial resolution is degraded for objects beyond the

collimator plate, that is at different depths in the organ. PET offers greater sensitivity, more uniform quantitative measurement of images, and less exposure to the subject than does any single photon method yet devised.

Major Steps in Producing a Positron-Emitting Radiotracer

The first step in a PET study begins with the bombardment of material in a target vessel by a beam of elementary particles from an accelerator, usually a cyclotron. There follows the transfer of the resulting radionuclide precursor to the synthesis apparatus. Then the radiotracer is synthesized and a sterile, pyrogen free pharmaceutical delivered to the PET. The tracer is administered to the subject and its regional concentration measured by PET. The last step is the interpretation of data on the resulting set of PET quantitative images by the team of scientists and physicians.

The new generation of medical cyclotrons, often called Baby Cyclotrons, are almost completely automated. In contrast to the large control room with a myriad of gauges, meters, and adjustment knobs that we recall from research cyclotron installations, the Baby Cyclotron has only a small panel from which a single technician selects the beam current and particle for the target bombardment. A microprocessor actually tunes the cyclotron and monitors beam, radiofrequency and vacuum parameters without human intervention. After a period of irradiation by the proton or deuteron beam, the original target material will have been converted to the desired precursor radionuclide, that is to ^{15}O, ^{13}N, ^{11}C or ^{18}F.

The atomic species or compound, now highly radioactive, is transferred from the cyclotron shielding vault to the radiotracer synthesis apparatus in the so-called Hot Lab. Whatever the particular configuration of this apparatus may be depends upon the kind of radiotracer to be produced and the particular synthesis procedure to be followed. The operations to be performed, whatever they are specifically, are typically those that are carried out in a chemistry laboratory. Severns and Hawk (3) identify these as LUO (Laboratory Unit Operations). The general categories of LUO's include: manipulation, liquid handling, separation, pulverization, weighing, measurement of physical properties, modifying and controlling the sample environment, using measurements to modify the procedure, conversion of raw data to useful information, and creating records for subsequent retrieval.

LUO's are building-block procedures from which an entire synthesis may be assembled. Once a module procedure works, it can be used repeatedly. For example, moving a liquid between

vessels by creating a pressure difference works for a wide variety of vessels and liquids.

At this time, most radiopharmaceutical syntheses are performed manually by remote control, frequently confused with automation, by chemists and technicians.

Since personnel must manipulate highly radioactive materials during the synthesis, a primary consideration is the safeguarding against radiation exposure. The glassware, columns, evaporators, piping, heaters and sensors for a synthesis are assembled within a heavily-shielded lead box for that reason.

Operators open and close valves, or reposition components inside of the box by means of mechanical manipulators while they view the apparatus through a thick leaded glass window. Reagents are added to reaction vessels from syringes mounted outside of the box, and liquids are transferred from one vessel to another within the box by positioning valves to cause a pressure difference to exist between the vessels.

Once the chemical synthesis has been completed, the radiotracer product, now appropriately diluted with saline for administration to the PET subject, is forced through a bank of micropore filters into a sterile collection ampule or syringe. The filters remove organisms and pyrogenetic agents as well. Samples of the product are withdrawn and immediately assayed for chemical purity, absolute activity, and specific activity.

A growing Demand for Radiotracers for PET Studies

The current literature cites over 200 positron-emitting tracers with application to PET studies. Many being used routinely each day in more than sixty PET installations throughout the world (2). Even though the variety of tracers is numerous, the most widely employed today are the analogues of glucose, 2-deoxy-2[^{18}F]fluoro-D-glucose (^{18}FDG) and 2-deoxy-D-[1-^{11}C]glucose (^{11}CDG) for measuring regional tissue glucose metabolic rates (4,5). Also widely used are the compounds of oxygen-15, H_2O, CO, and O_2, for determining regional blood flow, blood volume and oxygen consumption (6). Recently available neuroreceptor binding drugs (7) are being applied to study neurotransmitter-receptor physiology by PET in the continuing effort to understand biochemical processes of normal and abnormal behavior. The demand to produce large quantities of these labeled compounds to support both research and clinical diagnostic program grows each day as the PET method proves its promises. The primary obstacle to extending the PET method from the

research and development laboratory where it is now practiced to the setting of the major medical institution is the synthesis of radiotracers. As has been stated, Medical Cyclotrons are now automated and simple to operate. Modern commercially-available PET cameras are easy to operate, and the quantitative image processing of the raw profile data into physiological maps proceeds mostly without human intervention. Only the synthesis of the radiotracers continues to be carried out by chemists and technicians.

The Problems of Manually-Performed Syntheses

Before describing the distributed microprocessor system for automating routine production of radiotracers, let us identify the major problems we intend to solve by that automation.

Since the half-life of the positron-emitting nuclides is short and because the activity of the labeled tracer must be sufficient to obtain high statistical quality PET images, the synthesis must begin with a high activity precursor, and it must proceed rapidly and efficiently. It follows that the problems include working with high activities, working quickly, and working carefully so as not to waste the compound during the synthesis. The high activities present a risk of chronic radiation exposure when one works with the compounds every day.

Even though the syntheses are complex and demand skill, good judgment and vigilance, carrying them out day after day is boring, and boredom promotes human errors. For example, reagent supplies can become exhausted during a synthesis because we forget to check. A procedural step can be neglected, or we can even damage the apparatus by a clumsy movement of the mechanical manipulator. Also, not to be disregarded is the time the technical staff must spend teaching new staff members to perform old syntheses, and to learn new ones themselves.

Clearly, a major problem in routine radiotracer production, as it is mostly managed today, is the waste of professional staff in their performing of robot-like operations. Since all of the steps in a synthesis can be defined in terms of LUO's, and because each LUO can be automated, we believe that the manually performed steps involved in routine syntheses can be replaced by automated physical modules, and that these modules can then be integrated into a totally automated system.

AN AUTOMATED RADIO SYNTHESIS SYSTEM

There are several ways one can automate a complex process such as a radiotracer synthesis. A primitive approach is to hard-wire a set of discrete components to perform a single

process. An apparatus resulting from this approach would be much like an American Pinball Game: it would play one game and would require rewiring to change the rules of that game. This style of automation has rarely been applied to radiopharmaceutical synthesis, because it is inherently inflexible, complex and expensive to manufacture. Finding a fault in a pinball machine is a nightmare for an engineer.

To avoid the pitfalls of the hard-wired approach to implementing a process control system, system designers began to apply the mainframe digital computer. The superiority of this concept was, and still is, that with a stored program computer, numerical and logical manipulations to carry out the process can be designed by programming and then implemented on general purpose hardware. Developing and refining a computer-controlled process becomes mostly a software engineering job instead of anelectronics circuitry and mechanical engineering one. A problem encountered in using this kind of automation is the expense of acquiring, operating, and maintaining a mainframe computer. The high expenses were, and still are, spread among several users by timesharing the single computer, but this is achieved at the cost of operating system complexity and increased system response times. Even more important than the expenses, is the reliability of a shared large computer. Since one or more processes are controlled by a single computer and its software, any failure will compromise all of the applications. Computer hardware was costly but no longer a direct consequence of LSI (Large Scale Integration) semiconductor chips.

LSI minicomputers can be economically dedicated to a single process thereby avoiding the complexity of timesharing software and the relative unreliability of electronic circuitry wired from discrete components. LSI chips cost less, operate more reliably, and are usually faster than their discrete component counterparts. In spite of the advantage offered by the procedure-dedicated hardware approach of automation, the minicomputer still requires a multi-tasking operating system and still suffers some degree of the conflicts which plague the timeshared mainframe controller. Nevertheless, the few successful radiotracer synthesis systems that exist today, for example that of (8), employ a single minicomputer as a multitasking controller. As successful and economical as the dedicated minicomputer is, once again, new semiconductor technology, very Large Scale Integration, makes possible an even more modular approach.

Distributed Microprocessor Architecture

Our approach to automation is based on a system architecture that is an extension of the process-dedicated minicomputer: a network of elementary subtask-dedicated microprocessors. In this

architecture, individual microprocessors take responsiblity for elementary subtasks. For example, one microprocessor in a network can control and monitor the valves for purging, filling, and emptying a precursor target. That is the limit of its responsibility. This processor receives its command to begin, and the parameters it needs from another microprocessor. It is on the periphery of a network of other processors. The target controller, for example, is connected locally to the valves, and pressure gauges of the target being controlled and it controls the apparatus by executing the program that it holds in its ROM (Read Only Memory). In modern computer vernacular, this ROM program is called firmware in distinction to the terms hardware and software. Another peripheral microprocessor might control the temperature cycling of a reaction vessel, or it could direct a manipulator such as does the Zymark Robot (3,9).

Each task-dedicated module receives commands and data from another module, and in return sends measurements and its task status to other modules. Modules communicate with one another to form an integrated system.

There are three kinds of basic communication linkages over which modules in a distributed intelligence system can exchange information (10). The simplest involves a central microprocessor module having individual data connections to one or more satellite modules - a star pattern. The success of this network depends upon the central module's being able to intercept, interpret and reroute messages to and from the satellites.

A second network communication scheme is one in which every module has a direct line to every other module. In this configuration, command and integration of the network can be vested in either one of the modules or among several. A problem is that each module must include a hardware and software interface for each fellow-processor.

The third communication linkage is the data highway to which each module is attached. The familiar IEEE 488 protocol (11) is an example of a data pathway as is the CAMAC bus. Each microprocessor in a network is attached to the data highway through an interface. A module places a message intended for another module onto the data highway in a packet. The packet includes the destination module's address. The data highway method lends itself to fiber optics, microwave or coaxial cable transmission lines through which message packets may be conducted at very high speeds over a single bit channel.

We have chosen an architecture that combines the first and second network scheme communication linkages. A coordinating microprocessor (IBM PC) exchanges information with task-dedicated

peripheral modules (Z-80 STD Bus crates) over individual full-duplex serial input-output cables using either the EIA (Electronics Industries Association) RS-232 or RS-427 protocols, a common way that computers send character codes to terminals. In addition to the link with the IBM PC, a peripheral module is connected directly to the sensors and effectors in the apparatus through STD (Simple to Design) Bus interfacing cards. A peripheral module resides physically near to the apparatus it controls, and the PC is close to the personnel who oversee the synthesis. It is through the PC that the system operator initiates a synthesis and monitors its progress. This configuration minimizes the amount of signal wiring that must be installed in a laboratory because the numerous channels from the microprocessor to the apparatus are short and the EIA RS-232 connections only require double twisted pair cables.

Eventually, when the automated synthesis system is extended to control several syntheses simultaneously, and when the synthesis network exchanges information with the PET scanner and the cyclotron, some kind of PC-to-PC communication linkage must be established. Perhaps the data rates and volumes will require a data highway link, but more likely a serial EIA RS-232 or RS-422 connections among the PCs will still be adequate.

Hardware Engineering

As has been described, the radiotracer synthesis system is a growing network of STD Bus microprocessors clustered about an IBM PC coordinating computer. Our choice of these elements was based on commercial availability, reliability, and simplicity of use. For example, STD Bus Z-80 microprocessor boards and crates are supplied by over 200 companies in the United States, and they are manufactured in high volume for industrial and military applications. The Z-80 microprocessor chip itself is over 10 years old, but is still well supported. As well, several of us know how to program it, and the Z-80 commands are subsets of the more modern 8086, 8088 and 80286 microprocessors, an advantage should we wish to update the peripheral modules. Each Z-80 microprocessor-based peripheral module is housed in a STD Bus mother board crate, and along with the single board computer are the interface boards and power supplies.

Since so many boards are available for interfacing, we have needed to build only a few signal-conditioning circuits. These were engineered to the STD Bus standards, and are installed in the STD Bus crate.

The Z-80 single board microprocessor includes the ROM for the crate program, read-write random access memory (RAM), three timers, and the chips to manage the STD Bus. A typical crate includes the processor and several digital input-output boards

such as those manufactured by PROLOG, and an analogue signal interface. A typical peripheral crate includes the following PROLOG (12) digital boards.

7804 Z80 - Single board microprocessor
7504 TRIAC - Optically isolated ac power switches
7301 RS-232 - Serial input-output interface
7602 TTL - Parallel output
7603 TTL - Parallel input
7501 DC - Driver card, open collector power transistors

Incoming analog signals are digitized and placed on the STD Bus by a Data Translation (13) DT-2722, and the Z-80 sends analogue signals to the external apparatus through a DT-2726.

The homemade analogue-conditioning boards convert signals from thermistors or thermocouple probes, from strain gauge bridges, position potentimeters, and from radiation detectors into voltages suitable for being measuring by the DT-2722 analogue-to-digital conversion cards.

One other module must be mentioned in this description of the automation network, it is the Spectracom 8170 (14) synchronized time-of-day master clock and its slaves. This clock broadcasts a time-of-day and date message each second over an independent RS-488 network to several stations throughout the entire cyclotron-PET project. A coordinating PC in the tracer synthesis network reads this clock message through one of its Serial Input Ports.

The IBM PC coordinating processor hardware includes the standard monochome display as well as a TV graphic display. The PC also includes six Serial Input-Output Ports, two 5-1/4" floppy disks and 256 kbytes of RAM.

Software Engineering

The software supporting the distributed microprocessor radiotracer synthesis system is, as is the hardware, modular and task-dedicated. We have carried the concept of modularity beyond the hardware-identifiable levels down into the structure of the subprocedures themselves with the intention that the system, physical and algorithmic, will be assemblies of simple building blocks. In other words, we have attempted to engineer the system in the fashion of a modern structured computer program.

The programs executed by the peripheral microprocessors are written in MOSTEK Z-80 assembly language (15); the IBM PC

coordinating processor code is written in Microsoft BASIC (16). As is well known, the advanced BASIC available for a PC does not lend itself to structured programming, but by adhering to a set of Programming Standards (17), we have been able to achieve a well understood structure (18) in all programs. The Standards identify the naming of variables, specify how values are exchanged between procedures and how one allocates specific blocks of line numbers for often-used building block procedures. Also, by adopting a structure of IF-GOTO, ELSE GOTO in the PC BASIC, we have been able to simulate the IF-THEN-ELSE structures of more modern languages. The WHILE-WEND construct of PC BASIC, and its relaxed variable naming restrictions also help in the quest for structure.

Because of its conversational nature, we find that new procedures and programs can be developed more quickly by running them initially in interpretive BASIC than by employing the traditional sequence of EDIT - COMPILE - LINK - RUN while testing and debugging. Once a new program meets its design specifications while executing under interpretive BASIC, it can be compiled (19). The resulting machine code will execute much faster and use less memory storage space than the interpretive version. The IBM PC operates under Microsoft DOS-2.1. There is no operating system in the Z-80s.

Other provisions in the Programming Standards for the project are concerned with data quality. For example, any procedure (or subroutine) that receives a value from another procedure - or from those rare instances of an operator's keyboard entry - tests the range of that datum. A valid numerical value usually falls within an absolute or a relative prescribed range of values. For example, the cyclotron can't develop 200 milliamperes of beam current. An entry requesting that current is rejected. A reaction vessel doesn't hold three liters of a precursor. Strings of numbers must not include letters of the alphabet.

There are other examples of how the programming helps to insure data quality. As an example, a peripheral processor verifies that the analogue signal it sends to a heater controller (or any other device) in the chemistry apparatus, is the intended magnitude. It does this by measuring that signal level through its analogue-to-digital conversion channel. To carry the self-checking concept further, since the electrical signal sent to the heater controller is supposed to raise the temperature of a vessel, the peripheral processor can also monitor that vessel's temperature, just to be sure that the heater and thermistor are working properly. We could cite many other examples of this quality control, but the underlying principle is that the system closes a feedback loop on any process it is controlling whether it be an algorithmic or a physical one.

Each physical module sends the results of its own performance checks and to its task-dedicated controlling module. For example, a peripheral processor tests the electrical continuity between two pins of each of its cable connectors to insure that the plug has been inserted. It measures its own power supply voltages, and tests its own memory and microprocessor chip. These self-checks are a continual background job for the modules. The success or failure of each such test is recorded in the status part of the message sent to the PC, and the PC logs its own status periodically on a disk file.

Several of these algorithmic checking procedures are more complex than the ones we have just described. For example, the gas target handling peripheral processor checks for gas leaks in the vessels and piping by analyzing a series of pressure measurements that have been acquired for a 30 second interval after the target has been filled. None of the pressure data points may fall outside of a predetermined pressure range if the valves have been positioned correctly and no leaks exist.

System Activity Log and Restart Files: Each coodinating PC writes a system status file on a floppy disk every two minutes during a synthesis. The ensemble of these files provide data entries for a detailed log of the process. The most recently recorded file also helps the system or the human operator to restart the synthesis after an abnormal interruption such as from a temporary power failure. The time-annotated log of system states and measurements also are valuable for trouble-shooting the procedures of a synthesis and for refining the control system. When things go wrong, this log makes for a useful postmortem.

Menu Driven Control: The automated system carries on dialogues with the chemistry staff operators through the display screens and keyboard entries at a PC coordinating microprocessor. For example, to begin a synthesis, the operator selects the tracer to be produced, the procedure to be followed, and the conditions under which it is to be performed from a series of plain-language menus. As well, once the process has begun, the operator can monitor the current state of that synthesis by viewing a continually updated schematic representation of the process on the graphics display screen. The operator can also request that specified numeric values describing the process be posted on the text screen.

Communication between the PC and an operator is not limited to menu selection alone. When a manual procedure must be performed in which the operator must participate, such as calibrating a transducer or carrying out certain steps in the synthesis yet to be automated, the system guides the operator through an interactive plain-language prompting protocol. This step-by-step

prompting minimizes what an operator must learn about using the system and insures that no part of a procedure is neglected.

Simple Remote Control: A rudimentary manual mode of performing a set of steps is also available to the operator for a backup use when some fault has occured or as a tol for developing a new procedure. In this mode, the coordinating and peripheral microprocessors serve only as a manually operated panel for controlling the valves and other devices in the synthesis apparatus. The screen display indicates the positions of all valves and it also posts any measurements being made by the peripheral processor. While monitoring this display, the operator can control valves and set points by entering appropriate keystrokes at the PC. To install this kind of remote operation costs far less than does building the more conventional hard wired remote controller, and the rudimentary system lends itself more readily to the ultimate automation of the synthesis than does the hard-wired panel. All of the peripheral and communication wiring will already be in place when automation begins.

Alarms: Warning and alarm messages appear on the lowest two rows of the text screen. No other messages appear in that region. To signal the staff that a message has been posted, the PC emits a set of annunciating sounds (the command BEEP in BASIC). In the coming months, we will test the usefulness of a speech synthesis board for the PC. This PC compatible board uses a VOTRAX phoneme chip to generate both voice alarm messages and to "read back"keyboard-entered values as a help to the operator. It is likely that this embellishment provide us with more fun than usefulness.

Application Programs: The application programs that actually direct and monitor the steps in a synthesis are a set of modular procedures. Most of these are simple and involve little mathematical sophistication. For example, the programs in ROM executed by one of the peripheral processors acquire analogue and digital measurements from the chemistry apparatus, control valves and other effecting devices, verify that subsystem is functioning properly (as we have already discusseed), and communicate with the PC coordinating microprocessor. We designed a general purpose peripheral processor that performs this task. It measures 16 (external and internal) analogue signals and 16 digital states, sends to the apparatus 8 analogue signals and 32 digital states. While this continuous measuring and sending is proceeding it also waits for a message to arrive from the coordinating PC over a Serial Input-Output channel. That message instructs the peripheral processor to update the settings of the digital and analogue output signals, and once, the values have been updated, the peripheral processor returns a message to the PC describing the newly-measured output signal values (presumably

the latest set) and the most recent sensor measurements from the apparatus being controlled. Whether the peripheral microprocessor controls 32 valves or none, it still executes the same program and must send the same message format. The advantage of having these general purpose modules on the shelf is that a new system or an expansion of an existing one can be implemented in hardware and software in the time necessary to make the electrical connections.

In another version of a peripheral processor, the Z-80 crate subsystem replaces a commercial temperature controller. In this role, its task is to raise a reaction vessel to a predetermined temperature as (measured by a thermistor). To do this the peripheral processor measures the thermistor temperature and controls the electrical power delivered to a heating element. The instantaneous power applied is computed by a PID (Proportional-Integral-Derivative) control algorithm (20). The coefficients in the PID algorithm can be trimmed dynamically by a program to take into account the variety of masses that may need to be heated.

EXPECTATIONS FOR THE SYSTEM

A short-term expectation for this project is that once the synthesis of the basic cerebral metabolic function tracers (FDG, CDG, and the oxygen-15 compounds) has been completely automated, that final obstacle to bringing the PET method into major clinical centers will have been removed. Also, because in building the system to produce these compounds, the basic communications and controls modules will have been defined for synthesizing other positron-emitting pharmaceuticals. By reconfiguring the already-implemented LUOs, the hardware and software task dedicated modules for producing new physiological tracers can be easily integrated into the existing network.

The longer range expectations involve connecting the distributed microprocessor synthesis network to the cyclotron controller and to the PET to form a totally integrated PET research and diagnostic facility. It is a replica of this system that we believe could be installed in a medical-research institution without the need for the highly-specialized staff of chemists and technicians.

Taking advantage of our automated facility, we at BNL will be able to produce large quantities of high-quality radiotracers for both ourselves and for extramural PET studies as well so that regional medical institutions will then be able to measure organ function in subjects with their own PET scanners, using the radiotracers produced at the BNL Center. The precedence and feasibility for such an extra-mural use of BNL radiotracers is well established. For several years, the BNL Chemistry

Department has air transported FDG to the National Institutes of Health, to the University of Pennsylvania, and to Massachusetts General Hospitals. Using a helicopter, we have even delivered CDG to the State University of New York at Stony Brook. For studies involving very short half-life radionuclide tracers, such as oxygen-15 and nitrogen-13, a regional medical institution would refer subjects to the BNL Center for the PET measurements, and then analyze the resulting images at their home laboratory.

The network can easily be installed into a clinical center whose patient care program includes using the PET method as a diagnostic aide and to track the results of therapy. Only those radiotracers of proven clinical usefulness need to be automated by attaching the task-dedicated modules to the supporting network.

SUMMARY

We have proposed a way to minimize the involvement of professional staff members in the routine production of positron-emitting radiotracers by assigning the required operations to automated apparatus controlled by a network of task-dedicated microprocessor modules. The modules are assembled from general purpose microprocessor components and commercially available hardware interfaces. The task-dedication of a microprocessor module is achieved both by virtue of the kinds of sensors and effectors to which it is connected, and by the software procedures it executes.

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