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AUTOMATING THE ANALYTICAL LABORATORY VIA THE CHEMICAL ANALYSIS AUTOMATION (CAA) PARADIGM

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ABSTRACT

To address the need for standardization within the analytical chemistry laboratories of our nation, the Chemical Analysis Automation (CAA) program within the U.S. Department of Energy, Office of Science and Technology's Robotic Technology Development Program is developing laboratory sample analysis systems that will automate the environmental chemical laboratories. The current laboratory automation paradigm consists of islands-of-automation that do not integrate into a system architecture. Thus, today the chemist must perform most aspects of environmental analysis manually using instrumentation that generally cannot communicate with other devices in the laboratory.

CAA is working towards a standardized and modular approach to laboratory automation based upon the Standard Analysis Method (SAM) architecture. Each SAM system automates a complete chemical method. The building block of a SAM is known as the Standard Laboratory Module (SLM). The SLM, either hardware or software, automates a subprotocol of an analysis method and can operate as a standalone or as a unit within a SAM. The CAA concept allows the chemist to easily assemble an automated analysis system, from sample extraction through data interpretation, using standardized SLMs without the worry of hardware or software incompatibility or the necessity of generating complicated control programs. A Task Sequence Controller (TSC) software program schedules and monitors the individual tasks to be performed by each SLM configured within a SAM. The chemist interfaces with the operation of the TSC through the Human Computer Interface (HCI), a logical, icon-driven graphical user interface. The CAA paradigm has successfully been applied in automating EPA SW-846 Methods 3541/3620/8081 for the analysis of PCBs in a soil matrix utilizing commercially available equipment in tandem with SLMs constructed by CAA. The presentation will include a short video segment showing the operation of the system.
INTRODUCTION

The Chemical Analysis Automation (CAA) program (a program within the U.S. Department of Energy (DOE), Office of Science and Technology's (OST/EM-50) Robotic Technology Development Program (RTDP) is developing a laboratory sample analysis paradigm and robotic systems to address the need for standardization in the analytical chemistry laboratories of our nation.

The current laboratory automation paradigm consists of islands-of-automation that do not integrate into a systems architecture. Thus, today the chemist must perform aspects of environmental analysis manually using instrumentation that generally cannot communicate with other devices in the laboratory. CAA is working towards a standardized and modular approach to laboratory automation based upon the Standard Analysis Method (SAM) architecture. Each SAM system automates a complete chemical method. The building block of a SAM is the Standard Laboratory Module (SLM). The SLM, being either hardware or software, automates a subprotocol of an analysis method and can operate as a standalone unit or as a subunit within a SAM. The CAA concept allows the chemist to easily assemble an automated analysis system, from sample extraction through data interpretation, using standardized SLMs thus eliminating hardware or software incompatibility worries and the necessity of generating complicated control programs. A Task Sequence Controller (TSC) software program schedules and monitors the individual tasks to be performed by each SLM configured within a SAM. The chemist interfaces with the operation of the TSC through the Human Computer Interface (HCI)--logical, icon-driven graphical-user interface (GUI). The CAA paradigm has successfully been applied in automating the Environmental Protection Agencies' (EPA) SW-846 Methods 3541/3620/8081 for the analysis of PCBs in a soil matrix utilizing commercially available equipment in tandem with SLMs constructed by CAA. Another paper titled, "A Standard Analysis Method for the Automated Analysis of PCBs in Soils Using the Chemical Analysis Automation (CAA) Paradigm: Validation and Performance," authored by Charles Rzeszutko, details performance data for the PCB System.

The U.S. Government’s CAA Program, formerly known as the Contaminant Analysis Automation Program, has been an innovative and productive team for over six years now. The program was initially targeted towards the need for remediation and cleanup of the weapons complex site; now its broadened mission includes the automation, integration, and standardization of analytical chemical instrumentation. The CAA team has grown over the years to include an industrial partner to commercialize the technology under a Cooperative Research and Development Agreement (CRADA). Also part of the team are two universities that serve as the research side of the CAA development program.

Scientists have assessed the scope and complexity of automating and integrating the analytical laboratory and with political leaders are working to eliminate the technical barriers to ensure timely waste site remediation and accomplish the next revolution in analytical instrumentation automation.
We think that the solution lies in the development and introduction of multi-vendor fully integrated laboratory automation. Standardized and modular laboratory automation has the potential to bring higher data quality, increased throughput, electronic chain-of-custody, reduced pollution, and enhanced worker safety to those responsible for sample analysis.

Laboratory automation has traditionally been based on a robot-intensive paradigm with systems that are field validated. Within this traditional paradigm, the robot performs the sample preparation steps necessary before introduction to an analytical instrument and systems must be set-up and validated on a case-by-case basis. By relying heavily on the robot, the throughput gain from automation is reduced and reliability of the robotic system becomes limiting. The SLM paradigm for laboratory automation is based on linking chemical workstations together that can autonomously perform sample preparation and analysis steps. These instruments can then be logically grouped as systems processing regulator approved chemical methods, e.g., those detailed in Environmental Protection Agency’s SW846 compendium. Interaction with the robot is minimized in our paradigm. This improves the system throughput, reliability, and component maintainability. Also, by making use of an integration standard, initial chemical validation is less complex and time consuming.

The CAA team is designing and prototyping robotic systems that will standardize and automate the most common environmental chemical methods--both hardware and software.

A Challenge For Industrial Commercialization

The DOE has significant amounts of radioactive and hazardous wastes stored, buried, and still being generated at many sites within the U.S. The DOE has 10,500 potential release sites within 295 geographical areas. The current mid-range cost estimate for a complete cleanup of the DOE legacy is roughly $230 billion. Domestically, the need for environmental cleanup outside of the DOE complex is also significant. The Department of Defense (DoD) has identified about 7200 sites requiring some level of environmental remediation. Other environmental restoration needs include approximately 2400 Resource Conservation and Recovery Act (RCRA) sites and thousands of sites identified under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA).

Before remediation can even begin, waste must be characterized to determine the elemental, isotopic and compound content. Because of the real and perceived danger to the public health, actions must be taken to remediate these sites. Analyses for contaminants are necessary during the numerous phases of a remediation project. These phases include: 1) site characterization, 2) waste characterization, 3) remediation process-development and demonstration, 4) actual remediation of the site, and 5) post-remediation monitoring. The extent of the remediation effort required at each site is determined during the site characterization process. During each phase of the remediation process, stored and buried waste must be analyzed. The requirements for
quality sampling and analysis will increase as DOE undertakes additional environmentally sound remediation efforts. The DOE currently processes one to two million samples per year. 1

With the end of the Cold War in the early 1990s, funding for Environmental Management (EM) increased rapidly and as the nuclear weapons production facilities shut down, cleanup responsibilities increased and the infrastructure functions at sites were transferred to the EM program. As the budget for the program began to level off, EM predicted that funding soon would be insufficient to support increased responsibilities and continued compliance with all legal and regulatory requirements. EM referred to this prospect as the "train wreck scenario."

As limits on funding became increasingly stringent, EM began to focus on increasing efficiency in the performance of its mission. For example, the 1995 estimated cost of cleaning up the Rocky Flats Environmental Technology Site was almost $37 billion (in 1995 dollars) over a 65-year period. Options for streamlining and accelerating cleanup subsequently were identified. The strategy presented for review in this Discussion Draft would allow completion of the proposed remediation and the beginning of long-term stewardship at a cost of about $6 billion. Projections of the cost of cleanup at the Fernald Environmental Management Project have been reduced from $5.9 billion over a 45-year period to the current estimate of $2.6 billion over nine years. The cost savings and reduced cleanup timeframes reflected in these lower-cost options are achieved primarily by enhanced performance and acceleration of schedules rather than by relying on a reduction in the scope of work.

In June 1996, to reconcile the pressing need to reduce spending in the short term while reducing both economic and environmental liabilities over the long term, EM established a vision:

"Within a decade, the Environmental Management program will complete cleanup at most sites. At a small number of sites, treatment will continue for the few remaining legacy waste streams. This unifying vision will drive budget decisions, sequencing of projects, and actual actions taken to meet program objectives. The vision will be implemented in collaboration with regulators, Tribal Nations, and stakeholders." 2

EM has refined the original Ten-Year Plan Vision as it has interacted with Tribal Nations and stakeholders and reviewed site plans. EM assumed that completion of most cleanup activities by 2006 would be possible at all sites, except those having high-level waste and large amounts of transuranic waste.

As draft Site Ten-Year Plans became available, and Tribal Nations' and stakeholders' views became more evident, it became obvious that EM would have to revise those assumptions. For example, the Oak Ridge Reservation could not achieve the 2006 Plan goal, and the Rocky Flats Environmental Technology Site will face challenges in doing so. Nevertheless, the vision has helped focus the EM program by providing a
strong impetus toward completion. When developing the vision, EM recognized that at the major sites numerous activities would continue beyond 2006. In fact, the data revealed that at the Hanford Site in Washington, the Idaho National Engineering and Environmental Laboratory, and the Savannah River Site in South Carolina approximately half the costs will be incurred after 2006 for treatment and disposal of high-level and transuranic waste. Although those activities will not be completed by 2006, one of the primary goals of the 2006 Plan is to reduce the outyear mortgage costs of such activities. In addition, the program, as outlined in the 2006 Plan, does not include facilities and material that currently are not included in the EM program. If a decision is made to transfer additional facilities and material to EM, the 2006 Plan will require revision and the costs of the EM cleanup effort will increase.

The CAA thrust is to address the development of technologies necessary for the automation of the DOE and DOE-contract environmental laboratories. This effort is in response to the significant need for analytical chemical characterization of soil, contents of storage tanks, water, and samples from other waste stream samples that must take place before remediation can be initiated. Los Alamos National Laboratory (LANL) is the coordinating laboratory for the CAA Program. Innovative engineering development in the CAA effort is accomplished by teams at Idaho National Engineering and Environmental Laboratory (INEEL), Sandia National Laboratories (SNL), Oak Ridge National Laboratory (ORNL), as well as LANL.

To understand the magnitude of the required sampling, INEEL estimates that the number of samples requiring analysis will increase from 28,000 to more than 55,000 by 1999, with approximately 65% being radioactive. The Hanford Site predicts that the number of low-level radioactive samples will increase from approximately 50,000 to more than 1,100,000 by the year 2003. Medium and high-level radioactive samples will increase from virtually zero to over 400,000. Without automating current environmental chemistry laboratories, the DOE will have difficulty meeting its needs outlined in the 2006 Plan. Being very resource intensive, this effort is expensive (too expensive to accomplish manually). Remediation is schedule-driven by environmental laws such as the RCRA and Federal Facility Compliance Agreements (FFCAs). The latter is a tri-party agreement between DOE, EPA, and the state where the DOE facility is located. FFCAs specify a timetable for site characterization and compliance with regulations.

The CAA Paradigm
The CAA team came together in early 1990 to identify the analysis methods needing quick attention and to define the standards of modularity that would make the reconfiguration and operation of these automated systems reliable and intuitive. Two EPA methods identified for initial automation due to their frequent use were EPA Method 3540 (the Soxhlet soil extraction) and EPA Method 3550 (the Sonication soil extraction). Both of these methods are organic analyte sample-preparation methods with no automated commercial systems available. Because we deal with potentially mixed waste, i.e. waste that can be radioactive, the possibility of cross-contamination and system containment are factored into the designs.
Initial research by the CAA team revealed that modularized and standardized chemistry (within both the software control and the hardware) were necessary if these automated systems were to be easily integrated, reliable, and transportable. The concept of on-site sample analysis is shown in Figure 1. To provide valid data and timely sample analysis results, the team realized that it would be necessary to harden these systems so that they could be transported directly to the remediation site. Another factor leading toward the modularity concept was the need for systems, which, by leveraging standardization, could be configured by a knowledgeable chemist for a specific method and yet could be operated by a technician not versed in environmental chemistry.

![Mobile Lab](image)

*On-site Sample Analysis*

**FIGURE 1**

The accomplishment of these goals required developing the SAM, which is a glovebox-compatible paradigm grouping of SLMs into a system that will accommodate current technologies. These SLMs behave like modular building blocks that can stand alone, automating a sub-protocol of the full method. The SAM will accept samples from the field as input. After automated sample preparation, the samples are analyzed, and the resulting raw data automatically interpreted by an expert data-interpretation system. The knowledge of the waste site generated by the SAM is then used for execution of the actual remediation. Each SAM will eventually include a sophisticated, object-oriented database. The system controller uses this database to track the sample in all phases of analysis so that a detailed audit trail will be accessible for sample integrity and chain-of-custody verification. Making use of modular, open-architecture software allows the HCI to be much more intuitive and allows the facile addition of new or different system capabilities. A graphical representation of the SAM concept is given in Figure 2. The SAM groups or integrates SLMs in three areas: sample preparation, instrumental analysis, and data interpretation. One advantage of the modular SAM concept is its capability to accommodate emerging technologies. This capability results from the flexibility of the standardized hardware and software.
Integration Using SLMs

When the analysis method being executed by a SAM requires a sample preparation step, this function is subdivided within the SAM into a sample preparation SLM (also known as a Sample Preparation Module (SPM)) as shown in Figure 2. Many of the chemical methods that will be used for the remediation effort will require some sample conditioning or sample preparation. The EPA methods mentioned earlier are examples of sample preparation chemical procedures. In a sample preparation SLM, the actual chemistry is performed and its internal functions are constrained by the method in question. For example, the Sonication SLM will accept a soil sample in a beaker,

\[ \text{Sample In} \rightarrow \text{SPM} \rightarrow \text{Analysis} \rightarrow \text{Data Interpretation} \rightarrow \text{Knowledge Out} \]

*The SAM Concept*

\[ \text{FIGURE 2} \]

add reagents and standards, sonicate the sample, and vacuum transfer the extractant through an indexible filter into a clean beaker. When the SPM scheduler determines that the time is correct, this output beaker will then be taken from the Sonication SLM and input to the High-Volume Concentrator (HVC) SLM. The HVC SLM will then begin its operation. This philosophy of grouping logical tasks into hard-automated work-cells is a departure from traditional laboratory automation in that logical chemical manipulations are combined. Classical laboratory automation is operated on the paradigm of each manipulation being accessed separately (that is, with solution dispensing separate from the sonication, which is separate from the filtration, etc.). This placed a heavy burden on the robot and was not easily reconfigurable or adaptive. By combining logically similar functions in a SLM, robotic conveyance is minimized and the system becomes efficient.

A prepared sample generated by an sample preparation SLM is then ready for the actual physical analysis that takes place in the analytical SLM. This analysis is simply the characterization executed, for example, within a gas chromatograph, liquid chromatograph, atomic absorption spectrometer, or an inductively coupled plasma instrument. Many of these commercial instruments support autosamplers into which the SAM introduces the sample. The analytical SLM usually requires minor software modifications to make it CAA-compliant. These instruments will acquire the data that
must then be interpreted. The Data Interpretation Module (DIM), existing as a software module within the SAM, uses knowledge-based algorithms in an expert system to generate characterization knowledge from the instrumentally generated raw data. The DIM can be configured to use a variety of pattern recognition algorithms and fuse the resulting analysis for verification.

The Concept of Modular Control Software

This software is the key to implementing CAA's plug-and-play strategy. The interface is defined in terms of SLM capabilities, data sets, and message exchanges between SLMs and the TSC. The message content is independent of communications hardware. Once the TSC determines that an SLM can perform a procedure, the TSC initiates the procedure. The TSC is not concerned with how an SLM performs the procedures, only that the SLM can complete the procedure with the given operating parameters. A standardized state diagram is used to describe the interactions of the TSC with SLMs and other system components. These states describe communications, remote and local control of SLMs, SLM processes, and alarms. A set of standard commands and queries for communication between the TSC and SLMs has been defined. SLMs respond to TSC commands and queries through a standard set of events. The commands, queries, and events are primary elements of the software drivers for the TSC and SLMs. Each SLM has a capabilities-data set that describes its functions and operational limits to the TSC. The flow of data and information through the automated system is as important as the flow of samples through the system. Initially the database sends method procedures and parameter values to the TSC. As a sample moves through the system, each SLM sends processing information through the TSC to the database. The instrument, sensing analyte concentrations, sends measurement data through the TSC to the database. This raw data is requested by the DIM, where it is converted into information, and this information is stored in the database. All the information for a given sample generated by the SAM is transferred to the Laboratory Information Management System (LIMS) where it is integrated with other information on the sample, and a final report produced. The flow of data and information conforms to approved validation and archiving procedures such as EPA's Good Automated Laboratory Procedures and ISO 9000 protocols. Since environmental analyses are highly regulated, it is important to capture all pertinent information. In addition to raw data from the measuring instrument and the final analytical results, time stamps indicating when each sample was processed by the system SLMs, other information on processing, and all processing errors are recorded.

Our multitasking environment allows the system to process multiple samples in an optimized fashion. The software architecture is shown in Figure 3.
The automated laboratory interfaces with the site facility through its LIMS. The Method Manager provides translation from high-level chemical method definition to a lower level, hardware-specific script of commands necessary for SLM execution of the method. The TSC performs script processing and supervisory control of the SLMs in the system. The System Database serves as the information store for the automated laboratory. System administrative information, sample tracking, raw results, processed results, and reports are all stored in the database. The GUI provides operator access to the LIMS, Method Manager, Database, and TSC. Each SLM has its own intelligent controller for performing real-time control of the chemical workstation.

**Phasing CAA Technology Introduction**

Many laboratories may not be able to justify the cost of a totally automated system regardless of its flexibility. With this in mind, a path to fully automated systems exists that allows individual SLMs to operate in a standalone mode. Such SLMs can alleviate bottlenecks in sample processing; their embedded microprocessors, keypads, and displays permit direct interaction with operators. Since SLMs are built to standard specifications, they have the capability to become components of larger more automated systems. A mini-SAM represents an intermediate mode of integration between the standalone SLMs and fully automated systems that can perform all tasks associated with a SAM. The mini-SAM is a group of two or more SLMs that perform several procedures required by a method. The mini-SAM shown in Figure 4 extracts...
the analytes from a sample by sonication, rapidly concentrates the resulting solution, and transfers it to a cleanup SLM before gas chromatographic analysis. Samples can be transferred among these SLMs by a technician or a robot. This combination eliminates a common bottleneck in many organic methods. Addition of sample entry, HCl, database, and DIM are required for this mini-SAM to become a fully automated system.

The CAA Mini-SAM

FIGURE 4

Status Of The CAA Project

The overall philosophy for development of CAA technology, shown in figure 5, follows what we refer to as a technology development pyramid. The foundation for this scheme includes development of the necessary CAA standards, requirements, and functionality to support the next higher level of development. The CAA team has completed important fundamental building blocks such as the TSC, HCl, and early SLM prototypes. On the next level of development, the PCB system has been developed and so have several advanced SLMs such as the HVC2 and the advanced Soxhlet SLM. Engineering challenges for the near future include completing the 1) Methods Manager for chemical method script development and monitoring, and 2) the advanced database.
SUMMARY
The CAA team has invested significant time and effort in developing the standards and specifications that form the foundation to our system paradigm. Only through cycles of actual reduction to practice can this iterative process result in a workable and effective commercializable technology. We believe that our paradigm has reached a true prototypical development stage. Our first full SAM for the analysis of polychlorinated biphenyls (PCBs) in soils has undergone the initial stages of operational testing in accordance with a detailed validation plan developed by the Institute For Defense Analyses (IDA) who has been collaborating with the CAA team. Results to date have been encouraging both from the chemical analysis and the system integration perspectives. During FY98 the inductively coupled plasma/atomic emission spectrometer (ICP/AES) Metals SAM will be developed and operated. This system meets the requirements of metals analyses according to U.S. EPA SW-846 Methods 3005 "Acid Digestion of Waters for Total Recoverable or Dissolved Metals for Analysis by Flame Atomic Absorption or Inductively Coupled Plasma (ICP) Spectroscopy," Method 3050 "Acid Digestion of Sediments, Sludges, and Soils," and Method 6010 "Inductively Coupled Plasma Atomic Emission Spectroscopy."

Additional system development includes further refinement and integration of the waters SLM into the Semivol SAM and completion of the operational testing of this system. Enhancements to our system software will also be completed including the semivol DIM enhanced to potentially support olfactory or possibly Surface Acoustic Wave technology within the waters SLM. Integration and testing will make use of the existing Mobile
Environmental Laboratory at a site or sites to be chosen in collaboration with our commercialization partner.

Future plans include the development of a radionuclide analysis system. By developing our paradigm for organics first, we believe that the team has enough experience and depth in implementing the CAA standards that challenges introduced from applying radioanalytical chemistry will be manageable.

From a commercialization perspective, the CAA team is currently developing a CRADA with Advanced Power Technologies, Inc. (APTI) (an E-Systems/Raytheon company). Technologies already developed and future innovations are planned to be directly licensed to APTI, allowing for potential sublicensing to other interested parties.

REFERENCES

1 Based on FY95 sample analysis numbers from the National sample Tracking System, National Sample Management Program, Utilization Management Quarterly Reports, Laboratory Management Division (EM-263)

