Expert Systems and Analytical Chemistry: Recent Progress in the ACexpert Project†

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In this paper we discuss the application of expert system technology in the analytical chemistry domain and summarizes the progress made in the implementation of the ACexpert project. We start with a brief description of the software tools that are commonly used in construction of expert system applications as well as the inference mechanisms employed to search the knowledge base. A brief review of the achievements made world wide during the past five years in the development of expert systems for use in the chemistry domain follows. This paper particularly addresses the difficulties found in the knowledge acquisition process. An effective knowledge encoding scheme, named the knowledge domain matrix process (KDM), that has been developed in our laboratory as an knowledge encoding alternative, is described. In the final section, we describe the development of several stand-alone expert system modules based on implementation of the KDM scheme within the framework of the ACexpert project. The importance of the user interface in an expert system program is also emphasized, and graphical user interfaces featuring icons, pull-down menus, and graphical descriptions have been developed for the different modules in the ACexpert project to ensure a user-friendly and self-explanatory environment.

1. INTRODUCTION

Artificial intelligence is the application of mathematical and logic techniques by man-made systems to carry out "reasoning" abilities similar to those of human beings. This includes the ability to recognize objects, phenomena, and situations, to analyze relationships between them, and to make decisions, even to predict the consequences of such decisions, and to disclose new regularities between observations. The major tasks of artificial intelligence can be divided primarily into the following four groups:[1]

pattern recognition,
machine adaptation and learning,
problem solving, and
understanding natural language and communications with machines.

Expert system technology, which is a rich subset of artificial intelligence, is related to the task of problem solving. Expert systems are simply computer programs that are designed to emulate human experts through the integration of the knowledge of domain experts about a rather narrow field of study to furnish such programs with highly specific problem solving abilities.[2] A characteristic difference between an expert system and a conventional computer program is the strict separation of the knowledge from the program code. This principle governs the basic architecture of an expert system; no matter how large or how complex the system, an expert system always contains three fundamental parts: a knowledge base, an inference engine, and a user interface. As shown in Figure 1, the knowledge base of an expert system contains both factual information and heuristic knowledge about a problem domain. In some circumstances, the expert system may need to supplement the heuristic knowledge in the knowledge base by accessing external databases. The inference engine is the reasoning component of an expert system that uses the knowledge in the knowledge base (often in a structured format) to draw conclusions from a set of conclusions in ambiguous situations. The user interface provides system users with an efficient operational environment.

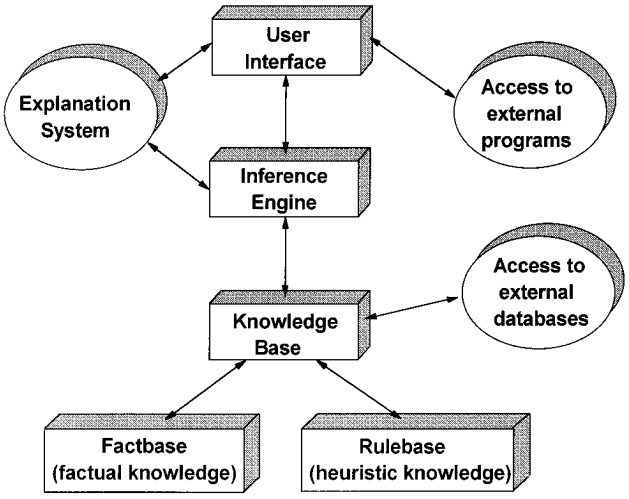

Figure 1. The principal components in an expert system.

2. SOFTWARE FOR THE DEVELOPMENT OF EXPERT SYSTEMS

While it is possible to construct an expert system using a procedural language, such as FORTRAN or C, it is difficult to encode heuristic human knowledge using these conventional languages. The principle of a strict separation of knowledge and control code also determines the nature and structure of the tools that can be used in the development of expert systems. Software tools may be classed into three groups: (i) procedural languages, (ii) higher-level programming languages, and (iii) expert system shells.

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Table 1. Examples of Applications of Expert System Technology in the Chemistry Domain

subarea	topics	examples
structure elucidation and data interpretation	MS,[7−13,27] IR,[14−18,28] NMR,[19−23] UV,[24] Raman,[25] X-ray,[26] GC-MS,[29,30] MS-MS,[32] chromatography[33−35]	DENDRAL,[9,10,27] MYCIN,[13] Meta-DENDRAL,[11,12] HIPS,[21] MAXMASS,[7,8] EXPIRS,[28] PEPTO,[23] AUTARG,[29] ESSESA,[20] PAIRS,[15,18] ESESOC,[31] RASTR,[24] Cathie[35]
computer assisted syntheses	synthesis, retrosynthesis, starting material selection[36−39]	LHASA,[40−42] SYNLIB,[43] SYN-GEN,[44] FOWARD,[44] LILITH[45,154]
analytical method development	HPLC,[46−65] IC,[66] GC, electrochemical analysis,[67−72] UV,[73] IR, ultracentrifugation,[74] sampling,[75] and analysis	CRISEbook,[47] ECAT,[58] ESCA,[57,59−63] RES,[64,65] OPSAES,[75] SpinPro,[74] ChromDream[76]
structure and activity correlation	bioactivity,[77−81,158−159] chromatographic[82−85] behavior vs structure	CRIPES,[84] META,[79,80] CASE,[77] HPLC-METABOL EXPERT,[83] HAZARDexpert[81]
smart chemical database systems	encapsulate standards methods, sample preparation,[87,86] interactive retrieval information[43,88−91,155]	FATE,[88] SYNLIB,[43] SCANNET[89]
experiment design	procedure design,[92−94] method selection[95]	DXPERT[95]
analytical process automation	automation,[25,96−102,156−157] quality control,[103] data comparison,[104] temperature compensation, error diagnosis,[105,106] process control,[112−115] data acquisition[116]	CAFD,[107,108] AAexpert,[100] ACexpert,[109] AAdiagnosis,[110] GCdiagnosis,[111] PAWMI,[102] AUTOMAT,[118] LABGEN,[103] H-FLO,[117] QISMSdiagnosis[119]
tutorial expert systems	interactive, graphical training, and teaching systems[120−122]	DENDRAL,[9,10] LHASA,[40−42] IRexpert[133]
miscellaneous	physico-chemical property,[123] identification,[124] naming,[125] emergency reponse to toxic chemical spills[126]	SOL,[123] SPILLexpert,[126,136] ERexpert[126]

The nature of expert system development requires software tools that can be more efficient at handling data in a symbolic format, rather than at handling numeric calculations in a procedural manner. Theoretically, any algorithm can be programmed using a conventional programming language, nevertheless the use of procedural languages for the development of an expert system is rather inefficient and more or less inappropriate. At a somewhat higher level are the languages that have been developed specifically for effective manipulation of symbolic data. These languages have a rich internal structure, such as lists, chains, sets, trees, mechanisms for returning during state-space searches, and associative memory as well as a range of inference mechanisms. In this category, languages like LISP, PROLOG, SMALLTALK, and OPS among others are the most commonly used.

More recently, the development of universal modular systems, called expert system shells, has made the construction of an expert system much easier.[3] In such shells, some components are prefabricated and fixed without being firmly linked into the functional unit. An expert system shell contains an inference engine, an interface, and knowledge acquisition aids but lacks rules and facts in the knowledge base.[4] In this case, the process of development is centered on the creation and modification of the knowledge base and on linking each of the components into a functional unit. Detailed reviews in this regard have been reported by Settle and van Leeuwan in which they discussed the expert system development tools available to the chemist.[5,6]

3. INFERENCE MECHANISMS

The reasoning mechanisms of an inference engine are normally described as either forward chaining or backward chaining. Some inference engines also support a mixed chaining mode. Forward chaining is also called data-driven reasoning. In a forward chaining system, the inference engine starts by examining the rule's premise and fires those rules that are satisfied, this process runs successively until all the conclusions are identified based on the fact(s) provided by the user. The depth-first search mechanism implies that the search moves from one level of knowledge to another once a rule at that level has been fired. Therefore, this mode of inference will be much faster than a breadth-first approach. However, it is possible that the inference engine may not find an answer, since the search strategy does not access all the knowledge at each level and may travel along a path on which there is no solution. The mixed chaining strategy can reduce this possibility.

Backward chaining or goal-driven reasoning begins with a suspected goal and extends backwards from there in an attempt to find evidence that could match the hypothesis from data in the knowledge base. To avoid a dead-end solution, the system requires that the user supply the missing facts that are necessary for the inference engine to discriminate between responses so that a single goal can be reached.

Mixed chaining refers to an inference strategy that uses both forward and backward chaining mechanisms with a single knowledge base. Normally, the mixed chaining inference process starts in the forward chaining mode, and when the situation arises, e.g., insufficient evidence to satisfy a conclusion, the engine switches to the backward chaining mode that may allow a conclusion to be reached by asking goal-related questions.

4. EXPERT SYSTEM APPLICATIONS IN THE CHEMISTRY DOMAIN

Since the first development of DENDRAL in the late 1960s, expert system technology has been increasingly incorporated into many different applications. In the chemistry domain, such applications span a broad spectrum, ranging from structure elucidation to structure and activity correlation, to data interpretation, synthesis planning, and experiment design. A detailed summary is given in Table 1.

Structure Elucidation and Data Interpretation. One of the earliest cases of heuristic programming in chemistry was the DENDRAL project, which is now considered as a milestone in the history of expert system applications.[27] DENDRAL was originally developed to assist structural organic chemists in elucidating likely structures based on mass spectral data. Presently, DENDRAL is one of the most widely used expert systems that has helped in thousands of chemical structure analyses.[1] In fact, structure elucidation and data interpretation have been very active research areas in which application of expert system technology covers various spectral and chromatographic methods or a combina-

tion of both and results in the generation of powerful new computer-based tools. The table provides a detailed description.

Computer Assisted Synthesis. Computer Assisted Organic Synthesis (CAOS) has become an accepted tool in design of synthetic pathways. Many different approaches are in use; however, they essentially follow the skeletal dissection route in which a target structure is linked to the functionality and reactivity through either synthetic or retrosynthetic reasoning based mainly of the research efforts of Corey and his group.[127−131] LHASA is one such expert system that uses the retrosynthetic route to direct syntheses toward the selection of particular starting materials.[40−42] LHASA is highly interactive allowing unlimited user input and assistance in the decision-making process as syntheses proceed. The program relies on a database of known reactions (about 1100 for LHASA-11) and involves either transform-oriented or structure-oriented strategies to direct the user to simplify molecular structures in terms of size, functionality, internal connectivity, stereorelationships, and chiral centers to reach simpler precursor structures.[128,130]

Analytical Method Development. Within analytical chemistry, chromatography is a particularly active area where research is being undertaken to implement expert system technology. Many applications have been described that provide computer assisted analytical method development.[46−75] The ESCA project (Expert Systems for Chemical Analysis) is supported by ESPRIT (The European Strategic Program for Research and Development in Information Technology), involves a group of experts in a joint international effort to demonstrate the applicability of expert systems in HPLC, and has resulted in the development of a number of subsystem modules.[57,59−65] The project is considered to have been successful and has revealed many useful conclusions that are important for the future development of expert system applications.[59] Among them is the concept of finding narrow focuses for development of modular systems and the systematic integration of these modules into a global framework. Another example in this area is the expert system developed for voltammetric determination of trace metals by Esteban and co-workers.[67−72] This system is built using the KES expert system shell to perform the method development task for both quantitative and qualitative electrochemical analysis of a wide range of metals.

Structure and Activity Correlation. The Quantitative Structure−Activity Relationship (QSAR) program implements expert system technology together with molecular and structural theories to predict trends of the target compounds in either biological activity,[77−81,132,158,159] or chromatographic behavior.[35,82−85] Klopman *et al.* have studied relationships between substructures and bioactivities.[132,77] The META program was developed to predict the sites of potential enzymatic attack and the nature of the chemicals formed by such metabolic transformations.[79,80] The expert system CRIPES was developed to predict retention time properties of organic molecules in reversed-phase HPLC using indices based on an alkyl-aryl-ketone scale derived from empirical quadratic expressions.[84]

Smart Chemical Database Systems. Traditional ways of using database systems only for data and information storage and retrieval can no longer satisfy the growing demand from real world situations. Some have argued about the importance of developing a new generation of database systems that could fully benefit from the power of present day computational techniques.[155] These new systems would not only manage data and information more efficiently but would also implement mathematical, logical, and chemical theories to encapsulate human knowledge and, therefore, be able to extrapolate from the stored data and information to practical situations. Over the last five years or so, a number of such applications have appeared.[43,86−91] SYNLIB is an interactive database system that allows complex chemical synthesis concepts to be presented directly and requires minimal computer expertise on the part of chemists.[43] Settle and co-workers had developed a database of validated microwave sample dissolution methods that can be transferred electronically among different laboratories to reproduce procedures for specific sample types.[91] FATE is an on-line database system for interactive retrieval of kinetic and equilibrium constants that describe the fate of chemicals in the environment that has been developed by incorporation of fundamental chemical structural theories with the expert system SPARC. The resulting program is claimed to be able to provide reliable and environmentally realistic fate constants that have not been available before.[88]

Experiment Design. Deciding on the selection of optimal laboratory procedures is not a simple task even for an experienced analyst in view of the large number of parameters that must be considered.[94] Expert system technology has been implemented in this area to capture the heuristic knowledge applied by the expert. For example, DXPERT, which uses fuzzy logic concepts, has been developed to assist chemists rank 13 experimental designs according to their feasibility for a given project.[95] van den Boagert *et al.* have developed an expert system that assists in the design of experiments using X-ray fluorescence techniques.[93]

Analytical Process Automation. Unattended analysis is one of the ultimate goals of laboratory automation projects.[33] Before an instrument can carry out an automated analysis, the controlling system must be able to perform successfully a series of tasks while unattended. The "successful" part requires that the control software can assess the quality of the results of on-going tasks, which include calibration of the instrument, modification of run-time parameters, analysis of feed-back signals, diagnosis of operational errors, and modification of sample introduction procedures. Various applications have been developed to address such tasks (Table 1). The Analytical Director program has been developed to automate the conversion of "textbook" analytical procedures by applying chemical knowledge in a deep-reasoning-based inference mechanism.[99,156,157] The AAexpert program has been designed to implement totally automated analysis by flame AAS.[100] PAWMI is a program developed to carry out automated identification of bulk organic waste mixtures using IR data as a preliminary screening tool prior to quantitative analysis.[102] A number of instrumental diagnostic expert systems have been developed. For instance, Tsuiji and co-workers had developed a program for troubleshooting HPLC assay methods.[105] Over the last ten years, our laboratory has developed a number of expert systems serving diagnostic purposes for different types of analytical instrumentation including GC, GC-MS, and flame AAS.[109−111,119] Refer to section 6 for a more detailed description.

Tutorial Expert Systems. One of the many advantages of developing an expert system is that expertise from one or

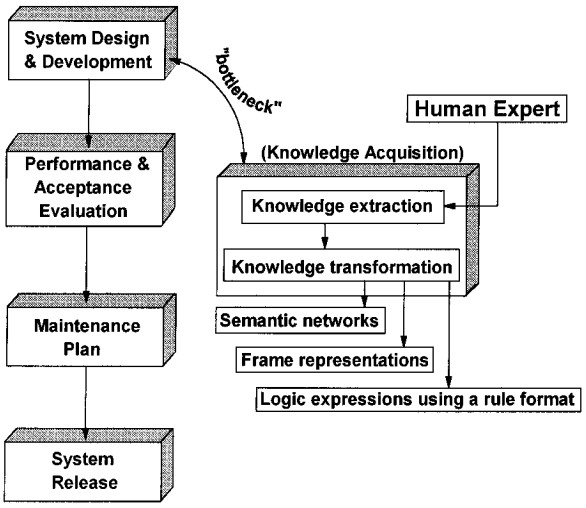

Figure 2. The stages involved in the construction of an expert system application. Knowledge acquisition is a particularly important step that can be the bottleneck for the subsequent development work.

more domain experts is effectively captured and encoded. With the help of graphical functionality, tasks like teaching, simulation, and on-line tutorials can be programmed in a more efficient and direct manner. Programs like DENDRAL,[9,10] LHASA,[40−42] and IRexpert[133] can be used as interactive tutoring systems to train novice laboratory personnel and students.

Miscellaneous. Expert systems have also been applied to a number of other areas. Applications that allow evaluation of physico-chemical properties,[123] characterization of polymers,[124] converting chemical formulas to names,[125] and handling emergency chemical spill accidents[126,136] have been described. Some standard procedures in the chemical decision-making stream can be taken over by expert systems, improving the performance and productivity in laboratories as well as increasing the knowledge sharing probability. The overall success of current applications of expert system technology suggests that this technology will be integrated more frequently into the software support used in chemistry and analytical laboratories.

5. KNOWLEDGE ACQUISITION

Typical problems tackled by expert systems are generally not procedural, instead these problems include information that is vague, complex, incomplete, or even incorrect.[134] Expert systems need to use more than factual knowledge to solve problems that involve some degree of uncertainty. As outlined in Figure 2, the stages in the construction of an expert system include system design and development, evaluation of performance and acceptance, maintenance, and, finally, system release. Knowledge acquisition is an especially important aspect in the early stages of system design and the subsequent development. Later, the knowledge base must be modified to correct ambiguities and extended to reflect new knowledge.

5.1. Knowledge Acquisition and the Bottleneck. In almost every scientific specialty, human knowledge is divided into two categories, namely factual knowledge and heuristic experience.[135] Factual knowledge is that which has been published; the developer can acquire this type of knowledge through research. Private knowledge comprises heuristics (or rule of thumb) that experts apply in manipulating and interpreting factual knowledge. When faced with a practical problem, both the expert and novice soon find that solutions cannot be found solely using factual knowledge; this is when special expertise or heuristic knowledge enters into the problem-solving stream. Unlike factual knowledge, heuristic knowledge does not have a single well defined value and is hard to express and document precisely.[136] One way, and probably the only effective way, to become familiar with heuristic knowledge that is used in a specific domain of expertise is through application of the knowledge in problem solving processes. Experts are experts because they know both the factual and heuristic knowledge that defines their domains.

Knowledge acquisition is the process that transforms expertise (both facts and heuristics) into formalisms that can be used by an inference engine. This process is problematic and known as the "bottleneck" problem mainly because of the following two reasons. The first is the human factor. Initially, a domain expert is primarily proficient in a narrow domain; the expert's knowledge is often insufficient to meet all the requirements of an entire target domain. This problem can be overcome by using a team of experts; however, with an increased number of people, the job of coordinating, meeting, and documenting for the purpose of knowledge transfer rapidly becomes more difficult. A number of other reasons associated with the human factor that complicate this task have been described by Edwards and Cooley: the lack of willingness to share expertise, the difficulties in expressing expertise verbally as it becomes more and more domain specific, and the fact that many domain areas are themselves fields of research that are still poorly understood.[137]

The second reason is the software factor. Although there are a number of expert system shells available that may reduce the amount of work required in the development of an expert system, these shells are themselves rather rigid systems that support prefabricated knowledge representation mechanisms that may not match the requirements of the domain.

Our own results and the reports from other research groups have suggested that the decision-tree structure adopted by most expert system shells may be ineffective for knowledge encoding.[86,110,136] Not only are the logical relations presented in a tree structure rigid so that any changes made to the tree may upset the total relationship but also the connections in a decision-tree are obscure, so that a knowledge engineer may not be able to understand the structure easily. The only feasible way to update a knowledge base developed in this way may be through a major revision from root to tip.

5.2. Knowledge Representation Methods. The challenge is to find a knowledge representation scheme that allows not only smooth knowledge transfer (expert to computer) but also an effective use of the knowledge (computer to user). The choice of the knowledge representation scheme can have a substantial effect on the performance and utility of the resulting expert system. Generally, the methods used to represent knowledge may be divided into three categories, namely semantic networks, frame representations, and logic expressions using a rule format.[138]

A *semantic network* is defined as an oriented graph with evaluated vertices and labeled edges between the vertices. Each vertex of the semantic network represents a concept, object, idea, function, or activity, etc. The edges denote

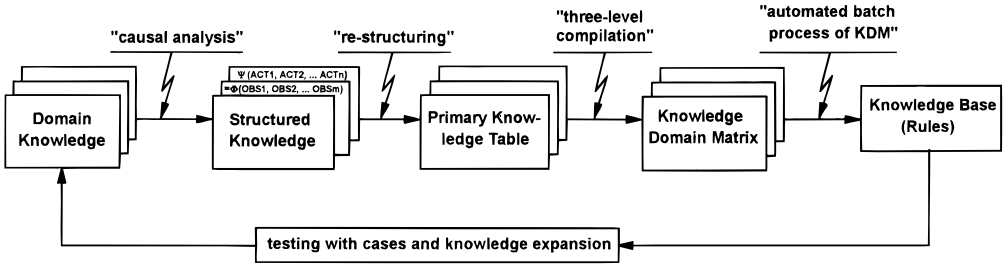

Figure 3. The steps involved in the use of the Knowledge Domain Matrix to process heuristic knowledge of a defined problem domain (adapted from ref 110).

relations between vertices. The problem in using semantic networks arises from the fact that the definitions of the concepts are subjective and difficult to incorporate into a program.[139]

A *frame representation* is a structure of nodes and relations organized in a hierarchy, where the top most nodes represent general concepts and the lower ones represent more specific instances of the concepts.[138] In this structure, knowledge concerning individual objects is represented by instance frames.

The *rule format* knowledge representation scheme uses conditional statements to represent knowledge and is probably the most popular type of knowledge representation technique. In this format, the IF part contains the premise of the rule, and the THEN part indicates the action or conclusion of the rule. Well-written rules can be transparent and the developer of the rule base should be able to see through the syntax to the meaning.

For practical use, several of these knowledge representation formalisms may be combined so that the representation of the domain knowledge is as convenient and appropriate as possible.[140]

5.3. An Alternative—The Knowledge Domain Matrix. In our laboratory, an alternative knowledge representation mechanism has been developed and used in a number of expert system prototypes.[110,111,119,126,136,147] The key to this method is the use of the Knowledge Domain Matrix (KDM) to capture expertise.[110] The way in which heuristic knowledge is used to solve a problem may be represented logically by a causal analysis expression using conditions (OBServerables) and conclusions (ACTions). The resultant decision is a function of conclusions as follows:

$$\text{Decision } \Psi(\text{ACT}_1, \text{ACT}_2, ..., \text{ACT}_n) = \Phi(\text{OBS}_1, \text{OBS}_2, ..., \text{OBS}_m) \quad (1)$$

where OBS_i are the observables and ACT_j are the actions of the decision process Ψ, and where the number n ($n \geq 1$) indicates the total possible conclusions of function Φ based on the number of conditions (m) selected. From time to time, we may observe that a set of conditions can point to several conclusions (the $n > 1$ case) that the inference engine cannot discriminate between, or the singular conclusion (the $n = 1$ case) may not be the actual solution to the problem. Such observables (OBS_m), therefore, are termed as an incomplete set of conditions and the output actions (ACT_n) as primary conclusions. No matter what is the case, further inference is required in order to identify positively a solution or number of solutions to the problem. In this regard, those primary conclusions can be the starting point for a continuous round of the decision process, in which the observables are combined with further observables (OBS_q') so as to derive a more precise (hopefully singular) conclusion. Again, this process may be expressed as

$$\text{Decision } \Psi'(\text{ACT}_1', \text{ACT}_2', ..., \text{ACT}_p') = \Phi\{\text{Decision } \Psi(\text{ACT}_1, \text{ACT}_2, ..., \text{ACT}_n)|\text{OBS}_1', \text{OBS}_2', ..., \text{OBS}_q'\} \quad (2)$$

The number of the output decisions (p) from the function Ψ' should be smaller or equal to that of the previous process (n) provided that the extra observations are relevant to the problem and used correctly by the inference engine in the secondary round of decision process. If a proposed problem does have solution(s), for instance, the band broadening in a gas chromatogram can be caused by a low column temperature, then the repetition of the decision processes such as described in eqs 1 and 2 will finally lead to the positive identification of the solution(s) to the problem.

Equations 1 and 2 suggest a causal model for knowledge analysis that can be followed in the knowledge acquisition phase. This causal model provides the knowledge engineer with a structured approach to extract and organize domain knowledge. Once heuristic knowledge is obtained in this way, it can be easily interpreted as a function of conditions and conclusions and therefore, it becomes possible for it to be represented in a two dimensional matrix. This tabular form is called a knowledge domain matrix. In the KDM scheme, the results of the causal analysis are transferred into an empty matrix in which conditions are listed as the first row in the table and conclusions in the first column of the same table. The logical connections in this form of coding involve three levels.[110] At the primary level, the logical connections between conditions and conclusions are established by filling in the "True" and "False" values in the corresponding cells of the matrix according to the causal analysis results. At this stage, the logical connection are mainly arranged along the diagonal region of the matrix and only valid between individual cells. At the secondary level, conditions and conclusions that were not related previously are connected logically, thus the knowledge represented by a KDM is expanded to cover the off-diagonal regions of the matrix. Sometimes, using the knowledge compiled through the above two steps may result in unexpected conclusions due to the similarities that arise from parallel cases. In this situation additional knowledge is added at the tertiary level to differentiate between the single conditions that make the parallel cases. Blank cells in a KDM represent no connection, neither "True" nor "False", between specified conditions and conclusions.

Figure 3 summarizes the steps involved in the use of the KDM scheme to process heuristic knowledge of a defined

CONDITIONS	CONCLUSIONS	Ion trap contaminated, conditioning overnight	Electronic multiplier gain drop off	Ion trap temperature too low	Filament current too low
Low sensitivity			T	T	T
Noise decreases as column temperature decreases		F			
Short ionization time		T			F
Ionization time varies			T		

Figure 4. An example of a small part of a Knowledge Domain Matrix used in the GC-MS diagnostic expert system.

problem domain. The KDM process takes four steps:[110] (1) Through causal analysis, knowledge of the problem domain is structured in terms of causes and results. In other words, the causal relationships between observables and actions are rationalized and clearly identified. (2) The structured knowledge is translated into a tabular format and forms the primary knowledge table. (3) The primary knowledge table is compiled through three cycles, and the logical connections are, therefore, created. (4) The knowledge represented in the KDM is reformatted into productions rules through an automated batch process.

In fact, the domain expertise represented by a completely filled KDM is much greater than that at the primary level because the knowledge contained in the off-diagonal regions (through both secondary and tertiary compilation) correlates the entire knowledge domain expressed in the KDM. Figure 4 shows a simple example of a compiled KDM structure. However, it may not be possible for the knowledge required to resolve an analytical chemical problem to be represented in a single layer of a KDM. Instead, a series of sequential decisions may be needed. This type of inference process cannot be represented by a one-layer two-dimensional matrix. As described in Figure 5, we have developed a structure in which multiple layers of matrices are designed to address the complexity found in a multistep decision-making process. Conclusions from one level may be inserted as conditions in deeper levels of the knowledge structure. For example, to diagnose a fault in a hyphenated instrument, such as GC-MS, requires, at a minimum, a two-step inferential processes to be performed in tandem. The first step concentrates on diagnosis of the gas chromatographic process and the second focuses on mass spectrometrically related problems. In terms of the KDM, such multiple inference process cannot always be represented by a one-layer two-dimensional structure especially when the decision-making is performed in sequence in which the later inferential process may need to use conclusion(s) of the previous round of inference. Detailed discussions and examples of encoding domain knowledge based on the KDM technique can be found in other publications by our group.[110,111,119,126,136,147]

5.4. The Knowledge Base File. The knowledge in a KDM needs to be transformed before it can be used by the inference engine, EAshell. A KDM is converted into production rules in which the coded heuristic knowledge is represented by a series of IF condition(s) THEN conclusion(s) sentences. A tool kit, named RuleEditor that is part of the shell, has been developed to carry out the conversion of a filled KDM into a knowledge base file (KBF) of rules for use by EAengine automatically.[141]

A KBF file consists of three major sections: a goal section, a logical expression section, and a user query section. The goal section provides information about goals used for backward chaining and contains a set of goal-related variables. The logical expression part is the main rule-based section in which heuristics are represented in IF...[AND/OR]...THEN... rules; an explanation (*EXP*) statement is also

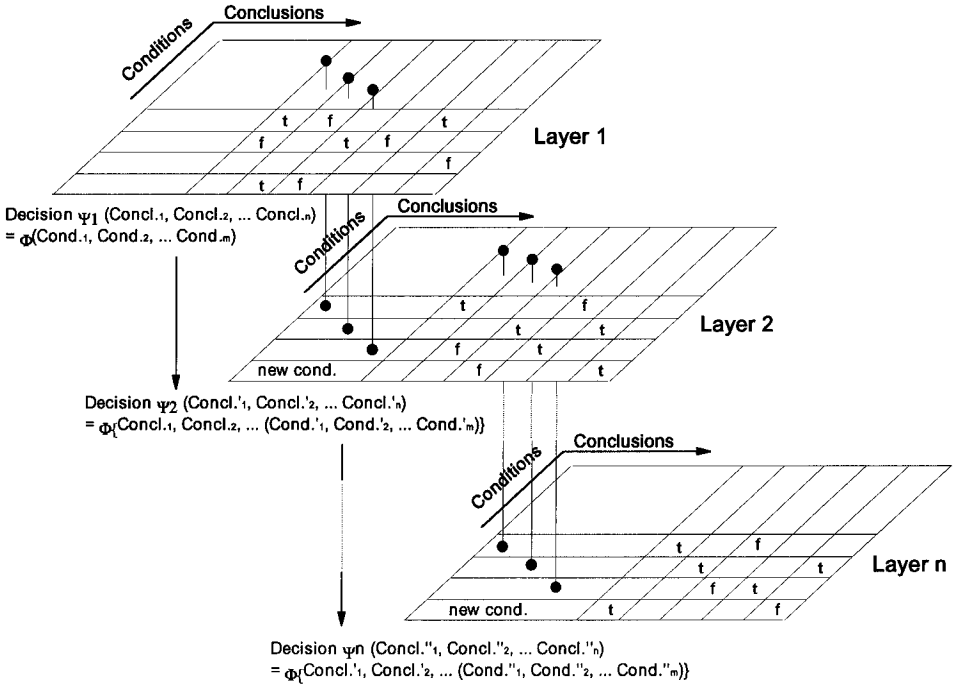

Figure 5. A multilayer knowledge matrix structure designed to incorporate the complexity found in a multistep decision-making process. Conclusions from one level may be inserted as conditions in deeper levels of the knowledge structure.

Table 2. An Example of a KBF File and a Brief Explanation

KBF example	explanation
Goal Section **FIND** Leaking, Inject, Column, IonTrap, CarrierGas, Sample, Communication**;** :	Starts with ***FIND*** and ends with "**;**". Each Goal Variable represents a subarea (part) of the instrument; rules are organized around the goal variables.
Logic Expression Section RULE 29 **IF** Variable1=YES **AND** Variable17=YES **AND** Variable18=YES; **THEN** CarrierGas=Carrier gas flow too high; **EXP** "Optimal gas flow rate is between 0.5 and 2.0 mL/min. Adjust the control on the GC instrument and make sure the gas flow stays within the range." :	This block begins with keyword ***IF***, the premises are connected by ***AND***s or ***OR***s, and the pointer "**;**" ends the block. ***THEN*** indicates the conclusion of a rule. ***EXP*** gives a full explanation of the result immediately after that rule block.
User Query Section **ASK** Variable1 "High background noise masks sensitivity?" **OPTION** YES, NO**;** **ASK** Variable17 "Unresolved peaks?" **OPTION** YES, NO**;** **ASK** Variable18 "Retention time change from run to run?" **OPTION** YES, NO**;** :	The ***ASK*** keyword begins a query block while a "**;**" ends it. Corresponding content of each goal variable is given by the ASK sentence in the Query Section. ***OPTION*** clause provides available answers to questions.

given for the conclusions of each rule. Finally, the user query section provides questions to ask that are related to the facts and provides options as answers for identification. It is important to note that when both *AND* and *OR* are used in a rule, *OR* takes precedence over *AND* as if parentheses surround expressions connected by *OR*. The contents of a KBF file and a brief explanation are given in Table 2.

Table 2 shows the details of Rule 29 from the knowledge base of a diagnostic expert system module developed for use in gas chromatography (GC) and tandem mass spectrometry (MSMS). Rule 29 fires when *high background noise*, *poor resolution*, and *variable retention time* are identified in a chromatogram. The conclusion suggests that the cause for such irregular chromatographic behavior may result from a high carrier gas flow. The explanation suggests a typical range of gas flows and how to adjust the gas flow.

6. APPLICATIONS IN ANALYTICAL CHEMISTRY—THE ACEXPERT PROJECT

For nearly 20 years, our laboratory has been involved in the application of computer technology in instrumental analysis.[100,109−111,119,126,136,141−149] The early work, programs such as CDSCAN, SpectraManager, and Simpfit, were computer programs developed specifically for instrument control and manipulation of spectral data using the concept of spreadsheets.[142−145] These programs dealt with problems that are more procedurally and numerically oriented and common in experimental spectroscopic research. A number of experimental papers have made use of these programs to report spectroscopic data.[152,153] In 1987 we began to encounter problems that were more symbolic in nature as the ACexpert project was developed.[109] We used initially the commercially available expert system shell KDS3 (KDS Corp., 934 Hunter Rd., Wilmette, IL 60091). However, the lack of a graphical user interface made development difficult.[110,136] Therefore, in 1991 we designed an expert system shell that could fit the needs of development of chemical applications for use based on IBM PC or compatible machines running the Microsoft Windows operating environment. EAshell was developed using Microsoft C (version 7.0) and has been central to our work since 1991.[141]

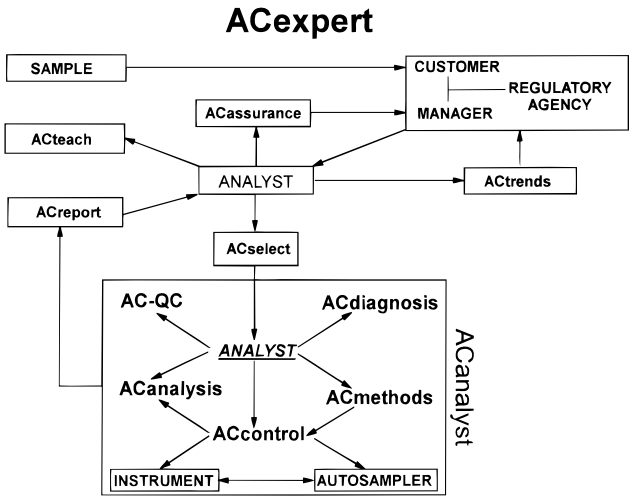

Figure 6. A graphical description of the ACexpert structure in which the principal tasks in a generic analytical process are identified to fit into this global structure.[145]

6.1. A Description of the ACexpert Project. Automation of analytical processes calls for real time communication between the instrument and the control program. The integration of expert systems into automated systems will become increasingly commonplace. The goals of the ACexpert project were to study the feasibility of implementing expert systems to various stages in the chemical analysis process. The development began with an investigation of a generic analytical process.[145] We identified the following stages involved in chemical analysis: (1) sampling, (2) separation and preparation, (3) selection of analytical method(s), (4) performing the analysis, (5) data analysis for QA/QC, (6) reporting analytical results and predicting future trends if applicable, and (7) delivering training for laboratory personnel (optional). According to this definition, the preliminary components of the overall controlling expert system were specified and assembled in a global structure named ACexpert (Figure 6).[109,145,146] Within this structure, each expert system performs a separate task and is capable of acting independently or as a module of the full system. A summary of the roles of the expert system modules and their functions is shown in Table 3.

Table 3. Description of Specific Roles of Expert System Used in ACexpert and the Individual Tasks to be Performed in an Analytical Laboratory[145]

role	module	use
consultation	ACselect	selecting sample preparation and analysis methods from a list of ingredients or procedures
	ACmethod	
control	ACcontrol	directing analytical process control
	ACdiagnosis	diagnosing probable causes for malfunctions or incorrect data values
analysis	ACanalysis	collecting analytical results, evaluating data quality/extracting information, inferring consequences
	AC-QC	from a given situation
report	ACtrend	reporting evaluated analytical data and information, applying guide lines to assure process/production
	ACreport	quality
	ACassurance	
instruction	ACteach	training laboratory personnel or teaching students through simulations and Q&A sessions

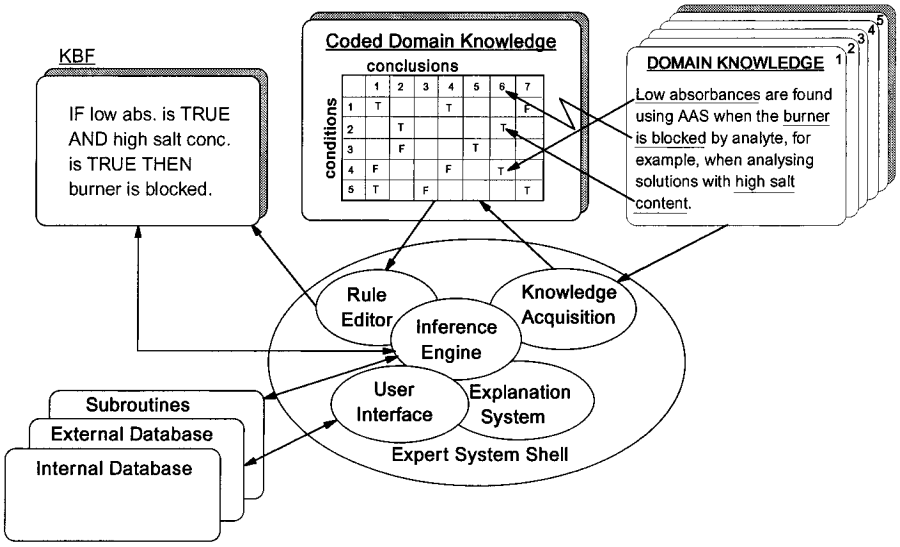

Figure 7. Description of the philosophy used in the development of expert system prototypes under the ACexpert global structure, using EAshell components.

Table 4. A Summary of the Applications Developed in the UWO Laboratory over the Past Six Years

program (personnel)	module	software tool	description
EAshell (G. Huang)	EAengine (136, 141, 148)	C	a Windows-based inference engine, accessible by DLL function call
	TableGenerator (141, 148, 149)	C, Excel	a tool kit for the knowledge acquisition process
	RuleEditor (136, 141, 148)	C	a batch processor to convert a filled KDM into a rule file (KBF)
AAexpert (S. Lahiri)	AAdiagnosis (110)	KDS, EAshell, Visual Basic	a diagnostic expert system for the atomic absorption spectrometer
	AAmethod	EAshell, Visual Basic	an expert system for method selection in flame AAS
	AAcontrol (100, 109, 145)	EAshell, C, Fortran	a control program for automated AAS analysis of trace metals
GCexpert (H. Du)	GCdiagnosis (111, 147)	EAshell, C, Visual Basic	a diagnostic expert system for gas chromatography
	GC-QC	EAshell, C	a module performing data analysis
SPILLexpert (Q. Zhu)	ACselect (146)	Quick Basic, KDS	a module for selection of proper analytical methods based on the matrix, concentration range, and detection limit required
	ERexpert (126, 136)	EAshell, Access, Visual Basic	a program using both an internal database and an expert system module to advise on the best response to an emergency chemical spill accidents
	ACmethod	EAshell, KDS, Access, Visual Basic	an updated version of ACselect comprising a database of methods and an expert system component
GCMSdiagnosis (Q. Zhu)	QISMSdiagnosis (119)	EAshell, Visual Basic	a diagnostic expert system for GC tandem mass spectrometer using the quadrupole ion storage device
	SPECview (119)	Visual Basic	a module directly access the Varian Saturn series of GC-MS data
	DIAGplatform	Visual Basic	a module automatically calculates the conversion efficiency of a GC-MS-MS process

Figure 7 shows the development philosophy that implements (1) the KDM scheme for the knowledge acquisition and representation and (2) a graphical user interface to access internal and external databases and that also provides communication with users for input and output purposes.

6.2. Development of a Windows Based Expert System Shell. The KDM knowledge coding scheme was first implemented in the development of a Microsoft Windows (3.1) based expert system shell, named EAshell.[141] We use 'C' (Microsoft C version 7.0) for the development. The shell

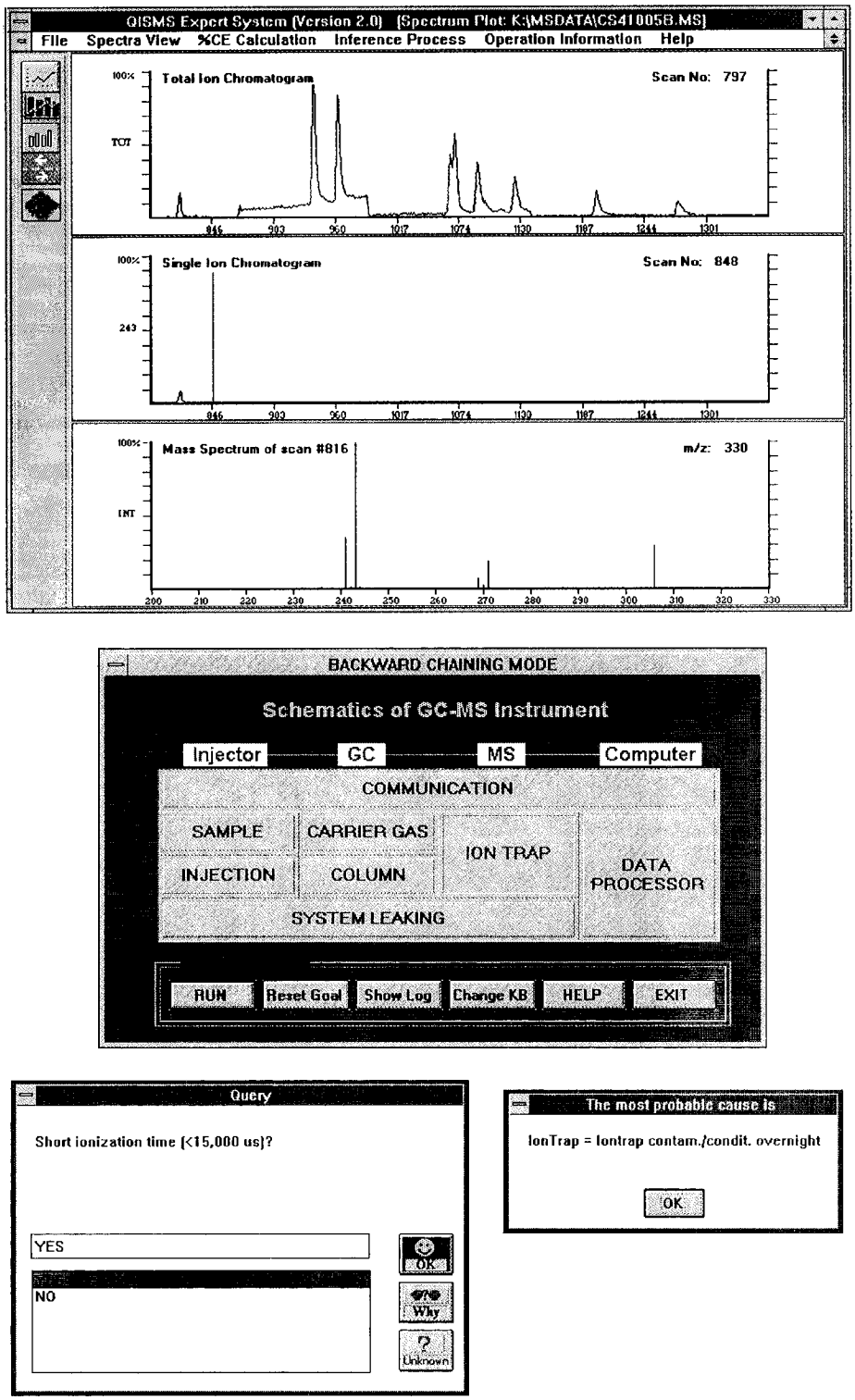

Figure 8. The Windows-based, graphical user interface developed for the program of GCMSdiagnosis, a diagnostic expert system used for diagnosis of faults related to Gas Chromatography Tandem Quadrupole Ion Storage Mass Spectrometry (QISMS, trademark of Varian Associates Inc.). Part A (top) is the data access window of the program that can be used to manipulate data from all Varian GC, MS, or GC-MS instruments directly. In this window, the top trace shows a total ion chromatography, the middle trace shows a single ion (mass 243) chromatography, and the bottom trace is the mass spectum at scan no 816. Part B (middle) is a diagram of a GC-MS instrument that is used by the user to select a goal variable for the Backward Chaining inferential process. Part C (bottom) shows the query box that the inference engine uses to ask specific questions; on the right side is a dialog box used to display the inference results.

currently comprises three components, namely EAengine, TableGenerator, and RuleEditor. EAengine is an inference engine that contains a library of subroutines that functions as a dynamic linked library (DLL) with in Windows. EAengine supports the three inference strategies described above, namely, forward chaining, backward chaining, and mixed chaining. According to the domain problem, these inference strategies can be selected or used interchangeably. The TableGenerator provides a blank tabular matrix for the knowledge engineer to input domain knowledge following

the KDM concept outlined above.[141] RuleEditor[141] is used to convert automatically the encoded knowledge in a KDM into a rulebase of production rules, a KBF.

6.3. Summary of Application Programs Developed under the ACexpert Project. Using the scheme shown in Figure 7 with the inference engine provided by EAshell, a number of Windows-based expert system prototypes have been developed in our laboratory to address task-specific problems in different analytical processes, these include AAexpert,[100,109,110,145] GCdiagnosis,[111,147] SPILLexpert,[126,136] and GCMSdiagnosis.[119] The summary in Table 4 specifies the name of the program, the software tools used, and the analytical tasks these prototype systems addressed as well as the key personnel involved in the development.

To date, we found that use of EAshell components has allowed the successful development of a series of modular systems that address different analytical problems involving both consultation and control. AAmethod and ACselect are modules performing method selection tasks for different analytical problems.[146] AAdiagnosis, GCdiagnosis, and QISMSdiagnosis are programs that diagnose the causes of instrumental malfunction.[110,111,119] AAcontrol automatically controls an AAS analysis process.[100,109,110,145] ERexpert and ACmethod advance our applications by combining expert system technology with database systems to solve specific chemical problems.[126,136] Presently, we are focusing on tasks related to analytical data analysis, data quality evaluation, and trend prediction. In the GCMSdiagnosis expert system shell,[119] SPECview is a module that provides direct data accessibility for the Varian Saturn series of GC-MS instrument. The DIAGplatform program calculates the conversion efficiency of a MS-MS process and can be used as an indicator to provide the operational status of the instrument. Both modules can be connected to QISMSdiagnosis (stands for Quadrupole Ion Trap Mass Spectrometer diagnosis) and when a low conversion efficiency is detected, the diagnostic program can be activated to detect the possible cause(s) of the problem(s) for the user to rectify.

Considerable attention has been paid by our laboratory to the development of user interfaces that are self-explanatory and easy to use. Hochman indicated that useful systems are more user friendly and require less time to master.[150] The applications developed in our laboratory specifically implement the graphical features provided by the MS Windows environment. Figure 8 illustrates several windows of the graphical user interface used in the program GCMSdiagnosis (version 2.0), which was developed using Microsoft Visual Basic. Through the use of icons, pull-down menus, and mouse, the learning curve becomes very shallow, and the workload required for system users to master this program is greatly reduced.

7. CONCLUSION

The implementation of computer technology in the field of analytical chemistry comes in three steps.[151] Computers were initially used in instruments for process control and data logging. Applications soon advanced to the next step in which computers were used for data processing and quality assurance purposes. For example, the implementation of the Fourier-transform algorithm into spectroscopy has brought forth the development of the new fields of measuring technology. Now, computer technology is incorporated into areas in which extensive expertise is involved. This step has been made possible through the implementation of AI techniques, such as is found in expert systems, pattern recognition, neural networks, and machine adaptation and learning. However, the biggest challenge to the widespread implementation of expert system technology into scientific applications comes from translation of heuristic knowledge and established algorithms into a format accessible to the computer program algorithm.

In this paper, we have reviewed recent advances in expert system applications made in the chemistry domain. The results from the implementation of the ACexpert project have been summarized briefly as examples of small, "light" expert systems that we expect will soon be found on computers on the laboratory benches. We have described a knowledge encoding alternatives that has been effective in coding analytical chemical knowledge in a number of projects. The authors believe that expert system technology will be more fully integrated into the chemistry domain in the future, with applications in analytical chemistry leading the way.

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