Artificial Intelligence

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Abstract

The history of artificial intelligence is a long one, even going back to the ancient Greeks who sought to mimic human intelligence in a machine, the Automaton. However, much of what we consider to be the story of artificial intelligence encompasses only the last 75 years, when the field of research and practice of artificial intelligence was named as such by the giants in the discipline at the time. This chapter reviews this history, focusing on deductive inference, rather than machine learning; it begins with the proposal for a summer institute on artificial intelligence in 1955, through the development of deductive, rule-based approaches to machine-driven inference, including methods for how these approaches were realized on computers. These approaches, realized as knowledge-based systems, found their manifestation a number of domains, including medical decision making, clinical education, population health surveillance, data representation and integration, and clinical trial support. This history provides the reader with an "family tree" of sorts that shows the evolution of artificial intelligence through the past seven decades and its application to medicine and public health.

Keywords

Artificial intelligence · Rule-based systems · Knowledge acquisition · Knowledge representation · Knowledge-based systems · Deductive inference

The quest has been long for ways to mimic the way humans (and other living organisms, but for now we will focus only on humans) act in response to some environmental phenomenon. This quest has manifested in many ways over the course of history, starting with the ancient Greeks' conception of the Automaton, a machine that acted like a human, and its extension into early conceptualizations of robots that persist to this day. It seems natural that in addition to human behavior, one would consider that thought and intention should be a part of these ideas- that an automaton or a robot would be able to *think*, that is, act intelligently, because after all, that is what humans do. However, no one can really argue that "intelligence" programmed into a machine (computer or otherwise) is not artificial,

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in the sense that it is manufactured and in some way imitates human intelligence.

In this chapter, we acknowledge that artificial intelligence is a very broad domain, including rule- and knowledge-based systems as well as numerous species of machine learning. However, we focus on the former, as manifested in the *expert system*. Expert systems are also known as “rule-based systems”, or “knowledge-based systems”, or “production systems” (in that they systematically produce a conclusion through a reasoning, typically deductive, process.

In 1955, John McCarthy, Marvin Minsky, Nathaniel Rochester, and Claude Shannon wrote a Proposal for the Dartmouth Summer Research Project on Artificial Intelligence [1]. This was a groundbreaking work in that it was the first time the term “artificial intelligence” was coined. Part and parcel of this was “automatic computing”, in retrospect a remarkable idea that would set the stage for work on creating computer systems that reason automatically, like an expert would. These systems would later become known as *expert systems*, in that knowledge obtained from a domain expert could be captured in a language (McCarthy’s term) that could compute- that is, be processed by a computer but in such a way that the language could support reasoning. A year after McCarthy’s proposal, Allen Newell and Herbert Simon developed a system, Logic Theorist, that could mimic human problem solving [2]. Since the Dartmouth Summer Research Project, a number of definitions of expert systems have been offered:

- “A computer system that emulates, or acts in all respects, with the decision-making capabilities of a human expert [in a limited domain].” Attributed to Feigenbaum
- “A computer system that operates by applying an inference mechanism to a body of specialist expertise represented in the form of ‘knowledge’.”—Goodall [3]
- “A program intended to make reasoned judgements or give assistance in a complex area in which human skills are fallible or scarce.”—Lauritzen and Spiegelhalter [4]
- “A program designed to solve problems at a level comparable to that of a human expert in a given domain.”—Cooper [5].

Expert systems have a lengthy history back to 1969, starting with the work of Edward Feigenbaum and Bruce Buchanan with the DENDRAL system, developed at Stanford University in the Heuristic Programming Project. This system was designed to identify unknown organic molecules by analyzing their mass spectra and using knowledge from chemistry. Because of this early work, Feigenbaum is considered the father of expert systems. Three years later, De Dombal developed the first expert system with a medical application, the diagnosis of abdominal pain [6], followed by the work of Edward Shortliffe, Feigenbaum, and Buchanan with the development of MYCIN, an expert system for the diagnosis of a bloodborne infection and recommendations for appropriate antibiotics to treat it [7]. MYCIN was the first to deal with uncertainty, and supported over 400 rules derived from experts; it is considered a landmark system in the history of AI. MYCIN was followed in rapid succession by a number of expert systems for specific clinical applications. This history is explored further in each of the following sections of this chapter.

1 The Anatomy and Physiology of the Generic Expert System

An expert system consists of several components, as shown in Fig. 1. It is helpful to think of the system as an expert consultant that is available to a clinician whenever needed. The knowledge base contains facts, some of which will be obtained from an inanimate source, such as published literature that has undergone peer review or is of equal authority, or even more typically, from consultation with human domain experts during a process known as *knowledge elicitation*. This process can involve interviews, direct observation of experts in action, “think aloud protocols”, or other means borrowed from the social sciences. The knowledge base also

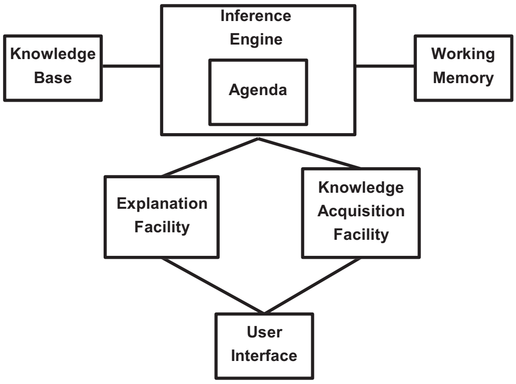

Fig. 1 Schematic of a typical expert system

contains rules, typically expressed in IF–THEN, or antecedent-consequent format. This construction of rules is extremely important for the inference engine which is at the heart of the expert system.

Inference in an expert system is typically deductive, where conclusions follow from premises, and is performed by matching rules and facts with input from the user in the knowledge acquisition facility. Deductive inference follows one of two chaining paradigms. In *forward chaining*, a fact gathered from a user is matched with the antecedent of a rule in in the knowledge base- this causes the rule to be "fired" and the consequent of that rule is then placed in the *agenda*. That consequent now becomes a fact, which itself can be used to match antecedents in the knowledge base and so forth, with additional input from the user, such that a chain is constructed with the ultimate goal of proposing a solution or recommendation back to the user. In clinical systems, just as in clinical reasoning, inference uses *backward chaining*, in that one starts with a hypothesis to be proven or disproven, much like a "rule out" or "rule in" in clinical decision making. In backward chaining, the facts obtained from a user are matched to consequents (as hypotheses), and the inferential chain then works to prove that the antecedents are true (or false). In both cases, there is a working memory that manages the process, which rules are fired, and which facts are included on the agenda. After the system has offered its conclusion, perhaps as a diagnosis, or a recommendation such as a diagnostic procedure to order, an expert system will provide an explanation of its reasoning. MYCIN was the first expert system to include an explanation facility, and has lately been considered a model for new directions in explainable AI.

Creating an expert system is an exercise in knowledge acquisition and the verification and validation of that knowledge. As noted above, the knowledge in an expert system is manifested in rules or facts, either engineered into the knowledge base as a result of the knowledge acquisition process, or obtained from the user in real time, or created through inference in real time by the firing of rules. The process of acquiring knowledge from experts deserves special mention here, and is illustrated in Fig. 2.

Acquiring knowledge from domain experts involves, as noted above, the use of a variety of tools commonly a part of the social scientist's toolkit, such as one would find in ethnography. In addition to the ones mentioned above, these tools also include participant observation, where the person acquiring the knowledge assumes the role of an apprentice to an expert in order to learn her craft. Another tool, more common to the information scientist or librarian is effective searching of the literature, itself considered an "expert". Acquiring knowledge also involves identifying rules and testing them against experts' conceptions of the domain through "what if" scenarios. All of this is conducted by a specially trained knowledge engineer who not

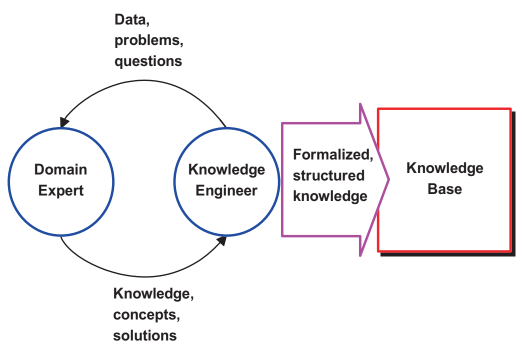

Fig. 2 The knowledge acquisition process

only elicits knowledge from experts but develops computable, formalized representations of that knowledge as a knowledge base. The goal is to create an "expert in a box" that ideally would be undiscernible from a human expert when consulting the system. The evaluation of the expert system, focuses on the verification of the knowledge base (Are the rules in the correct form? Was the system built correctly?) and the validation of the knowledge base as well (Do the rules lead to a correct answer? Was the correct system built?).

It should be evident that knowledge engineering is the Achilles' Heel of any expert system. A breakdown in the specification of rules, or a very large rulebase, can lead to "brittleness", as described by John Holland, where lengthy inferential chains can break, leading to incorrect inferences with catastrophic implications, especially in clinical settings [8]. This is not to say that expert systems do not have a place in clinical applications. As noted below, they are used frequently in medicine, although as a broader type of rule-based system that does not necessarily involve lengthy inferences, is used as frequently in the form of alerts and reminders in electronic health record systems. Broadly speaking, expert systems are a species of *knowledge-based systems*, in that at their heart, expert systems are constructed around a knowledge base. In this chapter, we will use the more inclusive term (abbreviated as "KBS") to refer to any system that uses knowledge to reach a conclusion, offer advice, or make a recommendation. A generic KBS is illustrated in Fig. 3.

The advantages of a KBS are several: Wide distribution of scarce expertise, ease of modification and maintenance, consistency of answers,

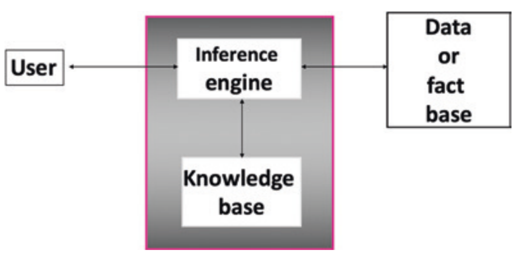

Fig. 3 A generic knowledge-based system

perpetual accessibility, preservation of expertise, solution of problems involving incomplete data, and (usually, but not always) the explanation of solution. However, these advantages come at a cost. First, they are expensive to produce and maintain. In addition, answers might not always be correct for a given clinical problem, and a KBS lacks "common sense". Finally, with few notable exceptions, the KBS cannot learn; this capability is afforded only to knowledge-based systems that incorporate machine learning, which is beyond the scope of this chapter.

This chapter continues with a description of knowledge-based systems as they have been developed for specific clinical or health-related domains: decision support, clinical education, data representation and integration, and clinical trial support. Where appropriate, the history of these systems is discussed as well.

Decision support. In busy or complicated clinical settings, it is often difficult to make consistently accurate and appropriate decisions about diagnosis, treatment, and ongoing management of patients. For this reason, clinical decision making has been and continues to be a target of AI research, application development, and implementation, and the earliest knowledge-based systems focused on diagnosis. The earliest system was INTERNIST-1, which was developed in 1974 by Jack Myers in the 1970s at the University of Pittsburgh for the purposes of training medical students in clinical diagnosis [9]. INTERNIST-1 supported a very broad knowledge base, but it did not find its way into clinical use. Perhaps the best-known early system is MYCIN, developed by Edward Shortliffe, working with Bruce Buchanan at Stanford University. MYCIN was a backward-chaining expert system that focused on decision support for treatment of bacterial infections by capturing information about the bacteria to perform classification, and then recommending an appropriate antibiotic to treat the infection [7].

In the 1980s, an extension and modification to INTERNIST-1, called CADUCEUS, an expert system was created for treating bacterial infections. It was developed at the University of Pittsburgh by Harry Pople with an extensive knowledge base elicited from Jack Myers [10].

Rather than being limited to blood-borne infections, as was MYCIN, CADUCEUS focused on a much broader domain, and supported diagnosis support in as many as 1000 diseases. INTERNIST-1 was also the foundation for another system, the Quick Medical Reference (QMR), developed in the 1980s by Randall Miller, also for use in medical education [11]. Another early system was PUFF, an expert system designed (and put into clinical practice) to analyze pulmonary function tests [12].

Since these early efforts, decision support has been a focus of knowledge-based systems, with many applications in a broad spectrum of clinical applications. Perhaps the broadest use of KBS is in the electronic health record, which supports alerts and reminders to clinicians in real time as they provide care. Even though many such systems are not framed in the architecture of the typical expert system, which relies on chaining to arrive at conclusions (and hence, decisions or recommendations), they are still knowledge-based systems in that they rely on rules, derived from evidence from experts and other sources; they have long captured the attention of clinicians and informaticians, and the work of Safran [13] and Shellum [14] are two early examples. Alert and reminder systems are typically developed using Medical Logic Modules specified in the Arden Syntax [15, 16], which lends a high degree of expressivity to rigorous and specific rule specification [15, 17]. One example of an alert system in pediatrics is CHICA, which was developed to screen patients in while waiting to be seen by the physician so she can optimize her time with the patient [18]. Many other applications have been developed for specific care domains, such as pharmacy, drug prescribing, and adverse event monitoring [19–23], psychiatry [19], infectious disease [20], antibiotic therapy [21–23], anesthesiology [24], intensive care [25, 26], dermatology and obstetrics [27]. In addition, KBS alerts are finding application in remote monitoring and self-reporting of psychiatric symptoms [28], and management of heart failure [29], and diabetes [30]. In addition to the wide application domain of KBS, they have been accepted by physicians as usable and useful in decision support. For example, internal medicine residents judged a decision support system based on DXplain to offer additional or alternative diagnoses in response to heir inputs to the system, and they generally welcomed the possibility of having the system available in practice [31].

Clinical education. As noted above, knowledge-based systems occupied pride of place in the early history of artificial intelligence. Jack Myers' work on INTERNIST-1, CADUCEUS, and QMR truly laid groundwork for the numerous educational and training systems [32]. For example, QMR was incorporated onto a clinical workstation for training students; this system was augmented with material from Scientific American Medicine and anatomic and other images on videodisc [33]. Wolfram's appraisal of INTERNIST-1 and QMR was instrumental in publicizing the value of the latter in undergraduate medical education, even to the extent that it could serve as an "electronic textbook of medicine" [34]. Over the past several decades, there have been numerous calls for incorporating KBS diagnostic decision support systems training in medical education [35], radiology [36], hepatology [37, 38], respiratory failure [39], psychiatry [40], clinical case teaching [41], neonate stabilization prior to transport [42, 43], physical therapy [44], evaluating urinary incontinence [45], and diabetic patient education [46]. Especially with the growth of non-traditional pedagogical methods, such as distance learning and increasing use of multimedia, there is every reason to believe that KBS will continue to play an important role in clinical training.

2 Population Health Surveillance

Public health practitioners and researchers have long been interested in novel ways to conduct disease and risk surveillance. Traditional methods such as manual or even computerized methods of surveillance, which rely on time-consuming data collection, analysis, and dissemination, often fail in providing rapidly actionable information that could identify and forestall emerging infectious or other diseases. As a result, AI, and especially KBS, has attracted the attention of the public health and informatics communities, most recently with the COVID-19 pandemic. One notable example of an expert system in this domain is an expert system that provides clinical guidelines for COVID-19 diagnosis and management, particularly in low-resource settings [47]. Two other expert systems developed for use during the pandemic offer promise for future applications, One used fuzzy logic for early assessment of hypoxemia in COVID-19 [48], and another provides early detection of disease outbreaks with a system that uses a continuously updating knowledge base [49].

However, the COVID-19 pandemic is just one example of a domain where KBS has been applied to population health surveillance. For example, Staudt, et al. developed and evaluated an expert system-based intervention to reduce alcohol use [50]. Another example is a system that performed surveillance using the EHR during the 2002 Winter Olympics; the authors proposed this system as a path toward biosurveillance and improved communication between public health agencies [51]. More broadly, and particularly applicable to the increasing development of health information networks, is a proposal for incorporating expert systems into comprehensive health surveillance networks [52] Finally, a very useful review of AI in global health proposes a conceptual framework for the development of strategies for global AI development and employment [53].

Data representation and integration. Ontologies provide robust frameworks for the integration of data from multiple sources and of different types, not only in terms of their ability to represent concepts but enforce the relationships between those concepts through the use of embedded axioms, or rules. As such an ontology can be used as the structural framework for a KBS. One example is the Unified Medical Language System, which supports domain ontologies with rules that facilitate the creation of knowledge bases in the UMLS that can be used in developing decision support systems [54]. In addition, ontologies themselves can be used as a knowledge base, such as has been accomplished by Ahmed Benyahia, et al. [55], where the ontology-based KBS supported a telemonitoring system that incorporates auscultation sounds in the decisions made by the system. Another remote monitoring application using an ontology as a knowledge base focuses on chronic obstructive pulmonary disease and chronic kidney disease [56]. Other applications include diagnosis [57], knowledge acquisition [58, 59], clinical guideline authoring and retrieval [60–63], evaluation of disability [64], and ultrasound diagnosis in obstetrics [65].

Clinical trial support. Knowledge-based systems have been used in the design and administration of clinical trials. For example, the selection of a clinical trial that is appropriate for a patient can be difficult unless guided by rules that can assist with that process [66–68]. Two early examples of systems that assist with the design of trial protocols is OPAL, which is intended to identify errors in protocol authoring [69] and the Design-A-Trial system which generates a protocol based on an automated interview with the investigator [70]. Several investigators have created such systems to help clinicians identify trials by mapping patient features to the selection criteria for breast cancer clinical trials [71], renal cell carcinoma [72], heart failure [73], and serial graded exercise electrocardiographs [74]. Another example of this application uses natural language processing in the evaluation of patient features to identify cohorts of candidate subjects for clinical trials [75]. The KBS can also be a useful tool in designing a clinical trial where disease progression models need to be taken into account. Such models constitute a knowledge base that could be incorporated in an expert system that would assist a clinical trial designer [76], especially important in complex diseases that manifest a complicated progression [77]. One such example is provided in [78], in which there is the opportunity for community participation of experts in maintaining and enriching the knowledge base.

Another application of KBS is the measurement of response in a multicenter clinical trial can be complex, especially where images are used in this process: there can be considerable variation due to random measurement error, for example. In one study, a KBS was used to guide brain tumor response to radiation therapy and improve on the assessment of that response through MRI; although this study involved a small sample of subjects, the results suggested some promise [79]. Another study using a KBS to monitor progression of disease; in this case, visual analysis of scans for bone metastasis in prostate cancer showed more promise [80]. In addition to response to treatment, trialists are concerned about evaluating side effects, adverse events, and toxicity. A useful review looked at reviewed several KBS that have been used to predict carcinogenic toxicity in clinical trials [81]. Even though individually these systems have demonstrated suboptimal predictive performance, the accepted recommendation is to use them collectively as a composite model using other knowledge sources, including expert advice in real time.

3 Summary

This chapter has offered a view of AI that focuses on knowledge-based approach, especially expert systems. Such systems are at the top of the "family tree" of AI, whether framed chronologically or in terms of scientific inquiry or advancement. In short, it could be argued that KBS are "where it all began", but one must also remember that this domain is not static. Rather than the mere specification and storage of rules, a KBS includes an inference engine of some type- one that reasons with the knowledge in the system and that added to the system by a user in time. The earliest attempts at AI all took into account this requirement that systems must reason- like humans reason- in response to the demands of a current situation, be it a clinical encounter, or student training, or a pandemic. This requirement continues to dominate the field to this day and is manifested in the many machine learning approaches that have been developed over the past 10 years. However, it is good to consider the contributions that efforts manifested in the knowledge-based system branch of the AI family tree- as early as some of these were, continue to influence the development of AI methods and applications.

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