Intelligent and Expert Systems in Medicine - A Review

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Abstract. Although medicine is an ancient science, only since the twentieth century there have been technological advances with widespread use in diagnosis, treatment and rehabilitation. However, the introduction of Artificial Intelligence in Medicine did not take place until the second half of the past century. The purpose of this study is to provide an overview of the role of intelligent tools in modern health care systems and to review the current challenges for the field.

1. Introduction

Today, computer technology is involved in almost every activity in the clinical environment. Computers in clinical laboratories have revolutionized the practice of medicine providing computerized imaging techniques, assisting health professionals using advances in artificial intelligence technology, automating clinical laboratories and developing hospital information systems [1].

Artificial intelligence is a branch of computer science capable of analyzing complex medical data. Its techniques can be applied in almost every field of medicine. Their potential to exploit meaningful relationships within a dataset can be used in the diagnosis, treatment and prediction in many clinical scenarios [2].

Agents and multiagent systems (MAS) are becoming increasingly important in the development of dynamic and distributed systems, gaining acceptance in areas such as electronic commerce, medicine, oceanography, business process management, industrial system management, sensoring, robotics, computer simulation and air-traffic control [3]. With regards to the impact in medicine, MAS's offer the possibility to provide highly specialized healthcare professionals with the right information, at the right time, and specifically for the patient. The use of MAS to monitor patients remotely helps to offer early assistance and to reduce medical visits and waiting time.

Today, it can be noticed that most modern hospitals are becoming smart hospitals, digitalizing their administrative processes, incorporating latest technology equipment, storing their images in PACS (Picture Archiving and Communication System) and RIS (Radiology Information System), using diagnostic expert systems, smart labels for tracking patients and mobile medical equipment, and making use of smart clothes to monitor pregnant women, children, elderly and patients with particular physical disabilities [4, 5].

Heterogeneities of hardware/software platforms and software applications are unavoidable in healthcare [6]. To share data between systems in different hospital departments and even between different hospitals, it is necessary that datasets are interoperable among each other. An information tool which permits the integration and communication between such different systems is ontology, which describes and classifies knowledge [7]. In the particular case of its use in health-care systems, the correct term is therefore biomedical ontology.

However, apart from the extensive use of technology and intelligent information systems by hospitals, new innovations require change, for example, in national infrastructure, federal legislation, education and a fast, reliable and uninterrupted communication infrastructure [2].

2. Background

The concept of AI originated at the Theoretical Computer Science Conference, held in 1956 at Dartmouth College. The name was given by John McCarthy, a pioneer in this field. The seminar, in which researchers presented some systems to develop games and prove theorems, served to present to the world the AI and intelligent systems concepts, of which the scientific community expected immediate results [8].

Research into the use of artificial intelligence in medicine (AIM) started in the end of the 1960's and produced a number of experimental systems [8].

- DENDRAL (Stanford University, 1967) deduces the chemical molecular structure of an organic structure from its formula, spectrographical data and magnetic-nuclear resonances.
- INTERNIST (Pittsburgh University, 1974) was a rule-based expert system for the diagnosis of complex problems in general internal medicine. This system covered 80% of the knowledge of internal medicine, but was criticized for the shallowness of their knowledge.
- MYCIN (Stanford University, 1976) was a rule-based expert system to diagnose and recommend treatment for certain blood infections (antimicrobial selection for patients with bacteremia or meningitis).
- CASNET (Rutgers University, 1960) was an expert system for the diagnosis and treatment of glaucoma.
- EXPERT (Rutgers University, 1979) was an extension generalized of the CASNET formalism wich was used in creating consultation systems in rheumatology and endocrinology.
- ONCOCIN (Stanford University, 1981) was a rule-based medical expert system for oncology protocol management. It was designed to assist physicians in treating cancer patients receiving chemotherapy.

Once the idea of knowledge representation had spread, many new expert systems appeared, based on existing and proven intelligent applications. EMYCIN (Essential MYCIN, which is MYCIN but with an empty knowledge base), e.g., was a prototype for PUFF (for lung diseases), CLOT (for coagulation problems) and HEAMED (for psychopharmacology) [8].

Another very influential author whose works have contributed greatly to the spread of AIM is Peter Szolovits. His publications have covered topics such as knowledge representation languages, knowledge-based systems, probabilistic reasoning, information acquisition in diagnosis, artificial intelligence methods for medical expert systems and medical diagnosis, electronic medical record systems via the world wide web, dynamic bayesian models and about the difficulty in representing medical knowledge in a terminological language [9].

3. Artificial Intelligence

The following definition of AI is an adaptation based on the definitions of Russell and Norving in [10]: "Artificial Intelligence is the art of creating machines that run functions that require intelligence when run by humans. It is the automation of activities we associate with human thinking such as perception, reasoning, decision making, problem solving and learning."

AI is based on different disciplines that contribute to this concept with ideas, viewpoints and techniques [10]. These disciplines include:

- Philosophy, provides formal rules to obtain valid conclusions, explains how the mind develops from a physical brain, where knowledge comes from and how knowledge leads to action.
- Mathematics, explains what can be computed and how we reason with uncertain information.
- Economy, analyzes how to make decisions to maximize profit.
- Neuroscience, studies how the brain processes information.
- Psychology, studies how humans and animals think and act.
- Computer Engineering, provides tools to construct efficient computers.
- Control Theory and Cybernetics, study how machines can operate under their own control.
- Language, explains how language relates to thought.

Currently, AIM is an essential component of biomedical informatics and one of the methodologies that can help to solve problems in health care. In [2] Shortliffe says that AI is broadly represented in the biomedical informatics field, in areas such as knowledge representation and ontology development, terminology and semantic modeling of domains, decision support and reasoning under uncertainty, model-based image processing, and many others. It is applied in genetics and molecular medicine, by providing machine learning algorithms, knowledge representation formalism, biomedical ontologies, and natural language processing tools [2].

For the construction of an AI system it is necessary to work with intelligent agents, using standard procedural mechanisms. These allow the modification of processes by simply changing the knowledge base, without rewriting the entire system.

3.1. Intelligent Agents

"An agent is a computer system that is situated in some environment, and that is capable of autonomous action in this environment in order to meet its delegated objectives." [11]. Agents are designed to operate in dynamic and uncertain environments, making complex decisions at run-time. They have the capability to learn, improving their performances over time, thus avoiding repeated negative conditions and persisting on successful behaviors [12].

Alan Turing, the English mathematician, has suggested that a computer had artificial intelligence if it could successfully mimic a human and thereby fool another human. He has created the Turing test with the propose to exhibit intelligent behavior. The test is like a game, which is played with three entities. A human judge has a conversation with a human and with a machine in a natural setting. If the judge cannot distinguish between the machine and the human, then it is possible to conclude that the computer and the human act as intelligent as each other, and therefore they are both similarly intelligent [13].

In [11], Wooldridge mentions that intelligent agents are able:

- to perceive their environment and react in time before changes that occur in it,
- to exhibit goal-directed behavior by taking the initiative, and
- to interact with other agents (and possibly humans).

3.2. Multiagent Systems

Multiagent Systems (MAS) are one of the most interesting technologies for the development of healthcare applications and services. A MAS is a distributed system made up of a number of agents which interact with each other through message interchange using a computer network. That is why they are generally considered an appropriate means for modeling complex and distributed systems. In a MAS, agents may decide to cooperate for mutual benefit, or they may compete to serve their own interests. In these cases agents use their social ability for flexible coordination behaviors that make them able to both cooperate in the achievement of shared goals or to compete for the acquisition of resources and tasks [12].

3.3. Agent Communication Languages

In the early 1990s, the DARPA Knowledge Sharing Effort generated the Knowledge Query and Manipulation Language (KQML), a language and protocol for communication among software agents. It is a message-based language for agent communication, where each message is an object containing a performative (class of the message) and a number of parameters (attribute/value pairs). Several KQML-based implementations were developed and distributed. KQML's imprecise transport mechanisms for messages and their semantics as well as the extensive performative set, were severely criticized which led to the development of a new language by the Foundation for Intelligent Physical Agents (FIPA) [11].

In 1995, the FIPA began its work developing standards for agent systems creating an agent communication language (ACL). The FIPA ACL is similar to KQML. The structure of messages is the same, but the most important difference between the two languages is in the collection of 20 FIPA ACL performatives, providing comprehensive formal semantics, which are intended to promote the interoperation of heterogeneous agents and the services that they can represent [11].

To facilitate the rapid development of MAS using FIPA ACL, several platforms have been developed supporting FIPA messaging. Of these, the best-known and most widely used is Java Agent Development Framework (JADE), which is a free software framework to develop agent-based applications [14].

4. Application of MAS in Medicine

In the last decade MAS's are used for e-health applications like assisted living, diagnostics, smart hospital and smart emergency applications, and expert systems.

4.1. Assisted Living Applications

These applications are offered to elderly or chronically ill people who require telemonitoring. In order to provide a more convenient form of remote monitoring, often with wireless devices and wearable sensors, valuable context information is added for a better interpretation of physiological sensor information.

One of the most interesting projects in this area is CASIS [15]. CASIS is an event-driven, service-oriented MAS framework which goal is to provide context-aware healthcare services to the elderly resident in the intelligent space. It allows family members or healthcare providers to closely monitor and attend to the elder's well-beings anytime, anywhere. The environment tracks the location and activities of the elder through sensors, such as pressure-sensitive floors, cameras, bio-sensors, and smart furniture. Additionally, the elder receives messages through speakers, TV and personal mobile devices.

Another interesting project is MyHeart [16], which focuses on preventing cardiovascular diseases by intensively using e-health applications. Heart rate and physical activity are monitored using sensors integrated in the patients' clothes. The processing consists of diagnosing, detecting trends and reacting on the collected data.

4.2. Diagnosis

Decision support systems (DSS) form a significant part of clinical knowledge management technologies through their capacity to support the clinical process and the use of knowledge, from diagnosis and investigation through treatment and long-term care. Diagnosis needs the integration of different sources of data and the on-line or off-line collaboration of different kinds of specialists. DSSs are typically designed to integrate a medical knowledge base, patient data and an inference engine to generate case specific advice.

One interesting case in this area is a machine learning-based expert system known as Optimal Decision Path Finder [17], which can speed up diagnosis and reduce cost without loss of diagnostic performance and sometimes, with better performance. It is a decision-support tool that shows disease probabilities and actively identifies the minimum set of tests most likely to confirm a diagnosis. The algorithm can learn clinical knowledge directly from a given dataset with minimum human input and consists of three components that work together: lazy-learning classifiers, confident diagnosis, and locally sequential feature selection.

4.3. Smart hospital and smart emergency applications

The applications in a smart hospital try to improve the daily activities of doctors and nurses, providing tools to access patient or clinical records, to track patients and caregivers in a wireless, mobile and context-aware environment.

The hospital "Foundation Son Llàtzer" in Palma de Mallorca [4] is one of the most advanced in Europe in terms of systems integration. Ninety-five percent of the processes that take place in the hospital are made through information tools and without paper. The hospital uses Electronic Medical Records (EMR) as an information vehicle so they can be accessed from all terminals in the center. No clinical task can be done without the system. Consultations are performed with handheld computers (PDA) or Tablet PCs that are connected on-line so that any information entered is recorded by the central system. The hospital has an archive system for digital radiological images, so medical images can be accessed through the patient's EMR. The idea is that any image may be viewed from any point within the medical center.

Another local example of an smart hospital is the Albert Einstein Hospital in Sao Paulo, Brazil. This institution has robots performing delicate operations and simulating patients for medical staff training. Furthermore, the hospital uses a system for tracking mobile medical equipment using smart tags, has a permanent monitoring system for the 200 refrigerators of the hospital, and automatically manages application and dosation of all patient's medicine [5]. Despite Albert Einstein Hospital's progress, there still remain challenges, such as diagnostics and remote surgery or early detection of biochemical changes that help to predict disease. Obstacles to further progress are related to existing infrastructure, e.g., lack of bandwidth availability for the above mentioned special procedures. Additionally, federal legislation concerning above mentioned topics needs to be updated.

Smart emergency management permits that emergency physicians are able to access the records of their patients and current physiological signals ahead of time while the patient is still in the ambulance vehicle.

An example of this case is the AMBULANCE project [18], which consists of a portable medical device that allows the transmission of vital biosignals and still images of the patient from an emergency site to the consultation site. In the hospital, the doctor views data and images received online from the portable device at the emergency scene. He has the possibility to retrieve additional information on the patient's past history, provided that a Hospital Information System HIS/PACS system is available, and thus the system can exchange data with the emergency team on site. The device can telematically consult an expert specialist doctor to the site of the medical emergency allowing him to evaluate patient data and give guidelines to the emergency personnel on treatment procedures until the patient is brought to the hospital.

4.4. Expert Systems

Expert systems were the most important AI technology of the 1980's [11]. Expert systems are knowledge-based systems and are computer programs that simulate the chain of reasoning of an expert in a specific problem domain, or clarify uncertainties where normally one or more human experts would need to be consulted.

The expert system is governed by a set of rules or pre-existing principles derived from the creation of a knowledge base, which consists of all identifiable information relevant to the file in question, like assertions, facts, relationships, caregivers' experience, and assumptions. Then, it uses an inference engine to infer the solution to a problem from a set of assumptions or rules. These systems are capable of manipulating symbolic as well as numerical data and have the ability to interact with the user in something approximating natural language [1].

The power of any expert system lies in its knowledge base. MYCIN, e.g., has five-hundred rules stored in the knowledge base. They were extracted in a time consuming process from experts, which is why it took almost six years to develop MYCIN [1].

5. Uncertainty in the diagnosis

Uncertainty is an important issue in the medical diagnosis. For patients, it is often very difficult to explain to doctors what kind of pain they feel, for nurses and doctors is very difficult to explain what they see, feel or interpret, even for doctors it is often difficult to explain how they have come to a specific diagnosis. Moreover, doctors and medical researchers have not yet come to fully understand how the human body functions.

However, despite all this uncertainty, it is expected that with a given disease the doctor reaches a diagnosis. They reason using their knowledge, their intuition and experience of other similar cases. Based on the observation of the patient and on laboratory findings they arrive at an unambiguous result. This simple reasoning process, with rules easy to explain, is called categorical reasoning [19]. Unfortunately not all decisions are categorical: in 10-20% of cases seen, the process of diagnosis is not as simple [20]. In these cases, decisions are made by carefully weighing all the evidence.

Currently, bayesian networks are used for modeling expert systems in domains with uncertainty [10]. The construction of a bayesian network consists of deciding the domain and the variables that are to be modeled. Then, a tree of nodes describes the relationship of variables to one another. The nodes represent the variables in the system, which can assume only values from a finite set. When a node is created, it can be linked to other nodes. During this process, the table of conditional probabilities are defined, often by educated guesses, and sometimes inferred from data [20]. In a medical ambient, bayesian networks have been used for medical diagnostic decision support [21] and in the intensive care unit to evaluate EEGs [22].

6. Ontology

6.1. What is Ontology?

An ontology specifies a vocabulary with which to make assertions, which may be inputs or outputs of knowledge agents (such as a software program), providing a language for communicating with the agent [23].

Ontology is a kind of controlled vocabulary of well-defined terms with specified relationships between those terms, capable of interpretation by both humans and computers [24]. They provide a unifying knowledge framework to facilitate semantic integration, knowledge-based searching, unambiguous interpretation, mining and inferencing of data using informatics methods [25].

The languages of ontologies are closer in expressive power to first-order logic (semantic level) than languages used to model databases (logical or physical level). This independence of levels enables the integration of multiple, heterogeneous systems and databases, allowing interoperability among disparate systems, and specifying interfaces to independent, knowledge-based services [23]. All this is possible by using explicit semantics, well-defined models for data aggregation, and the possibility to gain new knowledge from raw data [26].

Until this day is possible to see nurses transcribing data from one system to another, because there is no exchange of information between them. Lack of commonly accepted terminologies and ontologies makes exchange and interoperation of information difficult [2].

They have been built and used for many applications, such as scientific knowledge portals, information management, electronic commerce, semantic web services, knowledge management, biology and medicine.

6.2. Ontology Languages

Ontology languages allow users to write explicit, formal conceptualizations of domain models. The main requirements are [27]: (i) a well-defined syntax, (ii) a well-defined semantic, (iii) efficient reasoning support, (iv) sufficient expressive power, and (v) convenience of expression. The most commonly used ontology languages are:

6.2.1. XML - ad hoc ontologies Ad hoc ontologies are created with little effort and for a specific purpose. These ontologies are only a controlled vocabulary, and XML is usually the language of choice for such ontologies. Extensible Markup Language (XML) is not an ontology language, although it can be directly used to define simple ontologies [11].

6.2.2. KIF Knowledge Interchange Format (KIF) is a computer-oriented language for the interchange of knowledge among disparate programs. It has declarative semantics (based on first-order logic), syntactically is based on LISP, and is logically comprehensive. KIF offers the possibility to express: properties of things in a domain (e.g. 'John is a vegetarian' - John has the property of being a vegetarian), relationships between things in a domain (e.g. 'John and Maria are married' - the relationship of marriage exists between John and Maria), and general properties of a domain (e.g. 'everybody has a mother') [11, 28].

6.2.3. RDF In 1998 the World Wide Web Consortium (W3C) published the Resource Definition Framework Schema (RDFS). It is a language which allows the representation of some ontological knowledge. RDF is very simple, which is an advantage because the framework is tractable, but it is also a disadvantage since it means that many are hard to represent using RDF [11].

6.2.4. OWL In order to extend the limited expressiveness of RDF Schema, a more expressive Web Ontology Language (OWL) has been defined by the W3C in 2002 [27]. OWL is a collection of several XML-based ontology frameworks, within which ontologies in these various frameworks can be expressed [11].

There are three main levels of OWL, as follows:

- OWL Full: This is a very expressive framework, providing many features for defining ontologies [11]. It is fully upward compatible with RDF, both syntactically and semantically. But, the disadvantage of OWL Full is that the language has become so powerful as to be undecidable, braking a possibility to have an efficient reasoning support [27].
- OWL DL: It is a sublanguage of OWL Full which restricts the way in which the constructors from OWL and RDF can be used, ensuring that the language corresponds to a well studied description logic. The advantage of this is that it permits efficient reasoning support, but the disadvantage is that it loses full compatibility with RDF [27].

- OWL Lite: It is the simplest and more tractable variant of OWL, which supports only basic ontology features, placing a number of restrictions on the types of axioms one can write [11]. The disadvantage of restricted expressivity is rewarded with a language that is both easier to understand and easier to implement [27].

In 2008 the W3C published a new OWL version: the OWL2 Web Ontology Language. OWL2 is an ontology language for the Semantic Web with formally defined meaning. Its provide classes, properties, individuals, and data values. OWL2 can be used with information written in RDF, and is defined to use datatypes defined in the XML Schema Definition Language (XSD) [29].

6.3. Ontology Applications in Medicine

In hospital software systems it is possible to find a large amount of information saved in multiple forms, like Electronic Health Records, legacy information systems and medical images. Information can come from primary care as well as any other sector of the hospital, and also from sources like home care, geriatrics or other healthcare services. This information, which can be delivered at any time and any place, is especially interesting for patients remotely monitored with wireless sensors.

Ontology in medicine helps greatly in the integration of patient data, facilitating research, hypothesis management, formulation, clinical trials, clinical research, and patient care [26]. Bioinformatics needs computational support for storing, exploring, representing and exploiting this knowledge, because this data is no more suitable for human analysis [7]. Biomedical ontologies are being developed to express data in ways that can be read by computers, and shared between experiments and data sources to accommodate the proliferation of data in this new information age [24].

Stevens et al. describe in [7] some application of ontologies within bioinformatics. They describe the advantage to use ontologies to work with biological data and talk about the complexity of biological knowledge. They characterize the biological data in the following ways: large quantity (i.e. genome sequencing projects), volatility (knowledge about biological entities changes and increases), complexity of data and its relationships, and heterogeneity (biological data is both syntactically and semantically heterogeneous). Additionally, bioinformatics uses a large number of data resources and analysis tools to generate new data and knowledge, resulting in a variety of heterogeneous data.

Kataria et al. propose in [6] a Hospital Intelligent Ward Ontology (HIWO), which addresses the problem of data sharing across wards, hospital departments and administration; alleviates the interoperability problem that arises from semantic heterogeneities; and captures 'context awareness', which is based on the use of data generated from embedded devices, which affect the software application's behavior.

The Translational Medicine Ontology (TMO), a work proposed by Dumontier et al. [26], is another example of ontology applications in medicine. They have demonstrated the utility of ontology in a project, which can answer question by using a prototype knowledge base. It is composed of sample patient data integrated with linked open data. TMO can answer simple questions making queries on a single dataset, but also answers more sophisticated questions using the full integration of diverse datasets. This work provides terms that facilitate interoperability for information, focusing on integrating of existing datasets using a common vocabulary.

7. Current Situation

Although the current DSSs and expert systems have a capacity of reasoning close to that of humans, it is quite difficult to transform them into an algorithm of medical knowledge. Physicians do not base their reasoning on rules like "`if A and B then C`", but also take into account other variables such as that the patient may not be telling the truth or faking symptoms, or may be having more than one disease simultaneously. Medical professionals often have disjointed or incomplete data, and must deduce its meaning by applying knowledge, which not necessarily is logical or has medical sense. Additionally, healthcare specialists also use their senses for decision-making. This may not only includes visual, but also auditory, tactile and olfactory information [30].

There are many technical problems associated with the development of MAS for healthcare, such as user expectations and acceptance, lack of centralized control, and the need to solve legal and ethical issues like privacy, integrity and authentication in the exchange of patient information between agents [12].

When in [2] Shortliffe was asked about his opinion of the current situation of AIM, he said that there are three challenges for the field. First, the need of more professionals who are broadly educated regarding the interdisciplinary nature of biomedical informatics, including its AIM components. Second, the necessity to develop national and international biomedical networking infrastructures for communication, data exchange, and information retrieval. Finally, he said that is important to create credible international standards for communications, data and knowledge exchange, like the globally adopted HL7 standard for medical data exchange.

8. Conclusion

Although there are now many AIM applications developed and installed, they are still not available on a broad scale to all medical institutions. Nonetheless, more and more hospitals are becoming smart hospitals.

There are still many obstacles to further progress like the existing infrastructure, e.g., lack of bandwidth availability for the critical medical procedures, and the federal legislation needs to be updated.

Modeling and reasoning, representation of clinical knowledge and extraction of new information from data are important topics in AIM. Moreover, the difficulty to formalize the medical reasoning is a important factor which represents difficults standarization and massification of smart applications in medicine.

Finally, and not less important, more support for training positions as well as a wide formation of new academic units is necessary. There are still too few people capable of working effectively at the intersection of biomedicine and computer science, even in academic or industrial research roles. Strong interdisciplinary education programs should be further fostered, to improve the quality of researchers and practitioners and to help the dissemination of AI methods and principles in the biomedical informatics community.

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