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# Machine Learning in Medical Applications

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## 1 Introduction

Machine Learning (ML) provides methods, techniques, and tools that can help solving diagnostic and prognostic problems in a variety of medical domains. ML is being used for the analysis of the importance of clinical parameters and their combinations for prognosis, e.g. prediction of disease progression, extraction of medical knowledge for outcome research, therapy planning and support, and for the overall patient management. ML is also being used for data analysis, such as detection of regularities in the data by appropriately dealing with imperfect data, interpretation of continuous data used in the Intensive Care Unit, and intelligent alarming resulting in effective and efficient monitoring. It is argued that the successful implementation of ML methods can help the integration of computer-based systems in the healthcare environment providing opportunities to facilitate and enhance the work of medical experts and ultimately to improve the efficiency and quality of medical care. Below, we summarize some major ML applications in medicine.

Medical diagnostic reasoning is a very important application area of intelligent systems [18], [35], [36]. In this framework, expert systems and model-based schemes provide mechanisms for the generation of hypotheses from patient data. For example, rules are extracted from the knowledge of experts to construct expert systems. Unfortunately, in many cases, experts may not know, or may not be able to formulate, what knowledge they actually use in solving their problems. Symbolic learning techniques (e.g. inductive learning by examples) are used to add learning, and knowledge management capabilities to expert systems [5]: given a set of clinical cases that act as examples, learning in intelligent systems can be achieved using ML methods that are able to produce a systematic description of those clinical features that uniquely characterize the clinical conditions. Thus, knowledge can be expressed in the form of simple rules, or often as a decision tree. A classic example of this type of system is KARDIO, which was developed to interpret ECGs [7].

This approach can be extended to handle cases where there is no previous experience in the interpretation and understanding of medical data. For example, Hau and Coiera [11] describe an intelligent system, which takes real-time patient data

obtained during cardiac bypass surgery and creates models of normal and abnormal cardiac physiology to detect changes in patient's condition. Additionally, in a research setting, these models can serve as initial hypotheses that can drive further experimentation.

Learning from patient data one encounters several difficulties, since datasets are characterized by incompleteness (missing parameter values), incorrectness (systematic or random noise in the data), sparseness (few and/or non-representable patient records available), and inexactness (inappropriate selection of parameters for the given task). ML provides tools for dealing with these characteristics of medical datasets [20]. Subsymbolic learning methods, especially neural networks are able to handle these datasets and are mostly used for their pattern matching abilities and their human like characteristics (generalization, robustness to noise), in order to improve medical decision making [1], [21], [22], [26], [31].

Another field of application is biomedical signal processing [9], [17], [24], [30]. Since our understanding of biological systems is not complete, there are essential features and information hidden in the physiological signals that are not readily apparent. Also, the effects between the different subsystems are not distinguishable. Biological signals are characterized by substantial variability, caused either by spontaneous internal mechanisms or by external stimuli. Associations between the different parameters may be too complex to be solved with conventional techniques. ML methods use these sets of data, which can be produced easier, and can help to model the nonlinear relationships that exist between these data, and extract parameters and features which can improve medical care.

Computer-based medical image interpretation systems comprise a major application area providing significant assistance in medical diagnosis [10], [12], [13], [27]. In most cases, the development of these systems is considered as an attempt to emulate the doctor's expertise in the identification of malignant regions in minimally invasive imaging procedures (e.g., computed tomography, ultrasonography, endoscopy, confocal microscopy, computed radiography or magnetic resonance imaging). The objective is to increase the expert's ability to identify malignant regions while decreasing the need for intervention, and maintaining the ability for accurate diagnosis. Furthermore, it may be possible to examine a larger area, studying living tissue *in vivo*, possibly at a distance [8], and, thus, minimize the shortcomings of biopsies, such as discomfort for the patient, delay in diagnosis, and limited number of tissue samples. The need for more effective methods of early detection, such as those that computer assisted medical diagnosis systems aim to provide is obvious. The potential of ML in this area is significantly high since it provides us with computational methods for accumulating, changing and updating knowledge in intelligent medical image interpretation systems, and, in particular, learning mechanisms that will help us to induce knowledge from examples or data. Especially in minimally invasive imaging procedures that apply new imaging principles, such as fluorescence imaging or laser scanning microscopy, ML methods can be useful since algorithmic solutions are not available, there is lack of formal models, or the knowledge about the application domain is poorly defined due to lack of previous experience and/or medical expertise in the interpretation of the acquired images.

In general, it seems that as the healthcare environment is becoming more and more reliant on computer technology, the use of ML methods can provide useful aids to assist the physician in many cases, eliminate issues associated with human fatigue and habituation, provide rapid identification of abnormalities and enable diagnosis in real time.

Next, we will summarize successful applications of ML methods that were presented at the *Workshop on Machine Learning in Medical Applications* held on July 15<sup>th</sup>, 1999, and hosted by the ECCAI Advanced Course on Artificial Intelligence for 1999 (ACAI '99) at Chania, Island of Crete, in Greece. The goals of the workshop were to foster fundamental and applied research in the application of ML methods to medical problem solving and medical research, provide a forum for reporting advances in the area, determine whether ML methods are able to support the research and development on intelligent systems for medical applications, and identify those areas where increased research is likely to yield advances.

The workshop comprised eleven refereed papers [38] and one invited, which looked at the theories and approaches that underpin the use of ML methods in medicine. A number of recommendations for a research agenda were produced, including both technical and human-centered issues. In the next section, a brief description of these contributions is presented and the chapter concludes with a general discussion on the development and use of ML methods in a medical context.

### 3 Overview of the Workshop Papers

The invited talk by Schurr [34] focused on endoscopic techniques and the role of ML methods in this context. The speaker referred to current limitations of endoscopic techniques, which are related to the restrictions of access to the human body, associated to endoscopy. In this regard, the technical limitations include: restrictions of manual capabilities to manipulate human organs through a small access, limitations in visualizing tissues and restrictions in getting diagnostic information about tissues. To alleviate these problems, international technology developments focus on the creation of new manipulation techniques involving robotics and intelligent sensor devices for more precise endoscopic interventions. It is acknowledged that this new generation of sensor devices contributes to the development and spread of intelligent systems in medicine by providing ML methods with data for further processing. Current applications include suturing in cardiac surgery, and other clinical fields. It was mentioned that particular focus is put by several research groups on the development of new endoscopic visualizing and diagnostic tools. In this context, the potentials of new imaging principles, such as fluorescence imaging or laser scanning microscopy, and ML methods are very high. The clinical idea behind these developments is early detection of malignant lesions in stages where local endoscopic therapy is possible. Technical developments in this field are very promising, however, clinical results are still pending and ongoing research will have to clarify the real potential of these technologies for clinical use.

The paper by Moustakis and Charissis [23] surveyed the role of ML in medical decision making and provided an extensive literature review on various ML applications in medicine that could be useful to practitioners interested in applying ML methods to improve the efficiency and quality of medical decision making systems. In this work the point of getting away from the accuracy measures as sole evaluation criteria of learning algorithms was stressed. The issue of comprehensibility, i.e. how well the medical expert can understand and, thus, use the results from a system that applies ML methods, is very important and should be carefully considered in the evaluation.

The paper by Alexopoulos et al. [2] focused on the application of inductive ML methods in medical diagnosis of stroke. The proposed approach was based on the See5 algorithm, which is an updated version of the C4.5 algorithm. In the experiments reported, this approach exhibited the capability to learn from examples and handle missing information by constructing a decision tree, which could be transformed to IF/THEN rules. Special attention was given to the determination of the complexity and comprehensibility of the acquired decision rules by consulting medical experts.

In the paper by Zelič et al. [37], the Magnus Assistant decision tree learner and the Bayesian classifier were used for the diagnosis and prognosis of first cerebral paroxysm. Despite the fact that best predictions were obtained using the naive Bayesian classifier, the most interesting results from a medical point of view were obtained using the Magnus Assistant decision tree learner. Data and attributes that were considered by expert neurologists as obvious and meaningless turned out to be very important for automatic diagnosis and prognosis. In this case, ML methods provided a different estimation of some clinical attributes and motivated clinicians to generate new hypotheses and ultimately to improve their standard diagnostic and prognostic processes.

An interactive system for the ascertainment of visual perception disorders was presented by Ruseckaite [33]. The system performed data analysis and extracted interesting dependencies between visual perception disorder and damage of the brain by applying a modified version of the ML algorithm Charade. Preliminary results indicated the effectiveness of the proposed approach in rehabilitating persons with certain brain anomalies.

The paper by Bourlas et al. [6] extended previous work of the authors on medical expert systems for ECG diagnosis by incorporating ML methods to continuously improve the knowledge base of a medical expert system. According to the reported results, the new system exhibits continual learning capabilities using an extended version of the ID3 algorithm to extract, from time to time, a set to diagnosis rules based on a training set of ECGs. The extracted rules are merged into the older ones and the duplicates are removed. In order to optimize the performance of the system, a knowledge management subsystem provides monitoring of the performance of the final rules, in terms of their diagnostic accuracy, and modifies the knowledge base.

The work presented in Neves et al. [25] demonstrated the need for Health Care Unit's medical imaging models and introduced the concept of a generic and

deductive/inductive model of operation, which supports scheduling, forecasting, and accounting. Following this approach, several agents concurred in generating hypotheses, each one of them having a different role in evaluating parts of the data, and neural networks were used to discover associations in the dataset.

Asteroth and Möller [4] investigated the use of neural network-based approximation of structural information to the identification of individualized models of the human cardiovascular system. This approach allowed them to achieve robust real-time identification.

The problem of identifying the structure of a population of patients with brain disorder was investigated by Prankeviciene [29]. A single layer neural network evaluated the similarity among patients' electroencephalograms (EEGs). Experiments indicated that this approach successfully revealed similarities in the electrical activity of the brain of different patients.

In the paper by Jankowski [14] the use of incremental neural networks was suggested for approximation and classification tasks. The proposed model was based on neurons with a new form of rotated bi-radial transfer functions and was dynamically generated to match the complexity of the training data. In simulation experiments, the model exhibited superior generalization performance in the classification of medical data when compared with other popular methods.

The paper by Karkanis et al. [15] proposed the use of textural descriptors for the discrimination of cancer regions in endoscopic images. Second order gray level statistics were used for texture description and a multi-layer feedforward neural network was employed for classifying regions of interest. In preliminary experiments, this simple scheme was able to detect abnormalities in colonoscopic images with high accuracy.

The paper by Karkanis et al. [16] outlined a new approach to texture classification applied to lung endoscopic images. Feature selection was based on the texture spectrum of the image and a clustering method was used to distinguish the features with the most discriminative ability.

## 4 Discussion

Research in ML methods for medical applications to-date remains centered on technological issues and is mostly application driven. However, in order to answer fundamental questions and acquire useful insight in the performance and behavior of ML methods in a medical context, it is important to enhance our understanding of ML algorithms, as well as to provide mathematical justifications for their properties. Furthermore, we have to cope with a number of difficulties which concern the process of learning knowledge in practice, such as visualization of the learned knowledge, extraction of understandable rules from neural networks and identification of noise and outliers in the data. Other issues that arise in ML applications in medicine, like the

control of overfitting and the scaling properties of the ML methods, so that they can apply to problems with large datasets, and high-dimensional input (feature) and output (classes-categories) spaces need also further investigation.

A common concern for ML applications in a medical context is the need for comprehensibility of the learning outcome, relevance of rules, criteria for identifying applications and assessing their feasibility, integration with the patient records, as well as the description of the appropriate level and role of intelligent systems in healthcare. These issues are very complex, as technical, organizational and social issues become intertwined. Previous research and experience suggest that the successful implementation of information systems (e.g., [3], [28]), and decision support systems in particular (e.g., [19], [32]), in the area of healthcare relies on the successful integration of the technology with the organizational and social context within which it is applied. Medical information is vital for the diagnosis and treatment of patients and therefore the ethical issues presented during its life cycle are critical. Understanding these issues becomes imperative as such technologies become pervasive. Some of these issues are system-centered, i.e., related to the inherent problems of the ML research. However, it is humans, not systems, who can act as moral agents. This means that it is humans that can identify and deal with ethical issues. Therefore, it is important to study the emerging challenges and ethical issues from a human-centered perspective by considering the motivations and ethical dilemmas of researchers, developers and medical users of ML methods in medical applications.

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