Guest-editorial

Challenges for future intelligent systems in biomedicine

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New perspectives and applications for artificial intelligence (AI) have appeared over the last decade in biomedicine. AI applications in medicine and biology (including genetics and genomics) were separate fields of research until recently. Neither did professionals of the two disciplines, medical informatics and bioinformatics, have much contact. Considering medical applications, AI research focused on topics such as modelling medical reasoning, creating novel methods for uncertainty management, building intelligent approaches to medical image diagnosis and prognosis in sets of clinical data, representations of medical terminologies, case-based reasoning based on large libraries of medical cases and other techniques. Meanwhile, bioinformatics (BI) has been especially successful in developing techniques for information retrieval from large genetic databases and machine learning applications for genomic research.

Recalling the past of AI in medicine, we have seen how academically successful systems, like MYCIN [1], were scarcely used in clinical practice – although its architecture and related tools were commercialised and adapted to many areas. Some of those pioneer expert systems also introduced novel heuristic models of uncertainty management that in most cases facilitated subjective expert weighting of evidence. Hundreds of medical expert systems have been built since the 70s, but not many have been used in routine clinical practice. Medical informatics (MI) professionals long ago learned the complexities of applying intelligent systems in medicine [2]. The "oracle" approach that dominated the 70s and 80s, endeavouring to build systems that could act as medical specialists, was later modified. A software engineering approach emerged, aiming to build practical and commercial applications to solve real problems related to biomedical research and patient care.

MI professionals realised that they could help medical practitioners to satisfy the computational needs of many areas and health issues rather than creating artificial substitutes for physicians. Although the pioneering medical expert systems were rarely applied in practice, they did get the field of knowledge engineering off the ground. They were disregarded by a few AI pioneers in the early years, but they did contribute to introducing methodological advances that were essential to AI, too. Regarding medicine, they helped to model clinical reasoning, adding to the understanding of the cognitive processes carried out by physicians.

Medical reasoning mechanisms are sometimes fuzzy, usually based on experimental evidence and difficult to model. Medical experts use a variety of reasoning processes that AI researchers have tried to emulate using neural networks, case-based reasoning, qualitative reasoning and other methods. While they performed quite well compared to physicians in some cases, the actual processes of medical reasoning remain a challenge for research.

From a different perspective, MI professionals have invested a huge effort in modelling clinical manifestations of disease care and less in modelling the pathophysiological processes of diseases in terms of information processing [3]. Meanwhile, "low-level" processes, ranging from biochemistry to physiology, have

been a major interest of biologists and BI professionals. In the face of challenges such as the Human Genome Project, BI professionals have focused their efforts on building tools to enhance basic scientific research by biologists [4].

Biological AI applications were boosted by the conception and development of the Human Genome Project. Tasks such as DNA sequencing, protein structures prediction, gene sequences comparison and matching or molecular interactions modelling called for the use of novel intelligent-based approaches. The use of sophisticated programs and high-performance computers played a significant role in bringing forward the scheduled completion of the Human Genome Project [5].

From its very beginning, some 15 years ago, bioinformatics has focused on the study of a variety of issues: (1) biological sequences, polypeptides or genes, (2) analysis of models of metabolism, regulation and physiology, (3) structural biology, and (4) databases of molecular sequences. AI approaches and techniques have significantly contributed to furthering research into these questions [5,6].

Genomic research and results promise to contribute to discovering the complexity of life and developing different approaches to molecular medicine. This type of molecular medicine will include new diagnostic procedures and drugs that could be personalised for specific patient groups. Genetic information may soon be incorporated into computerised medical records, giving physicians additional data of great clinical interest [7]. The addition of decision support systems could provide patients with tools for health advice and reminder indications, related to personal health habits and disease prevention. Tools like these could be embedded in different devices, computers and personal digital assistants (PDAs).

MI and BI have used similar methods and tools for many research issues, yielding quite different results. By way of an example, data mining applications have been widely used in genomics with excellent results. In genomics, data analysis is central to the design of future experiments that test focused, scientific hypotheses. Meanwhile, similar methods and tools have been used for clinical issues, although more difficulties have been encountered because of the complexity of medical data and the characteristics of patient care within complex environments and settings [3]. Furthermore, clinical medicine is usually devoid of the kind of focused principles that characterise genomics.

Both perspectives – from MI and BI – are different but complementary. Collaborative efforts are needed to set up an interaction between medical and biological informatics applications. The expertise and lessons learned by MI professionals over 30 years of AI applications in medicine could be added to the recent developments in intelligent approaches for processing and managing biological information [8]. Without this knowledge, BI professionals could repeat some of the mistakes that MI professionals have learned by trial and error.

Over the last decade many applications have been developed in MI and BI using similar methods and techniques. The "reinvention of the wheel" has been a characteristic of many applications of both disciplines over the years [9]. Thus, increased collaboration could enhance results for future biomedical efforts in research, management, education and care. An integrated approach could lead to synergy.

Such collaborative efforts are an objective of this special issue of the Journal of Intelligent and Fuzzy Systems. Six papers, written by distinguished researchers in their specific fields, are presented. One introduces a method with a dual application, for both medical and biological objectives. Another two papers are focused on biological issues. The final three papers deal with medical applications. An underlying characteristic of all the papers is their potential application and use for both medicine and genomics.

In the first paper, titled "Set covering submodular maximization: an optimal algorithm for data mining in bioinformatics and medical informatics", Genkin, Kulikowski and Muchnik present an algorithm designed to optimise problems that can be viewed as finding the optimal covering of a finite set. The generalisation proposed in the paper has potential applications to a variety of MI and BI problems.

After this paper, readers will find two papers dealing with microarrays, a technology which is increasingly used in BI to analyse gene expression. In the second paper, "Classification of gene expression data using fuzzy logic", Ohno-Machado, Vinterbo and Weber introduce a classification scheme using fuzzy logic, which can be applied to different types of measurements in genomic research.

Inza, Sierra, Blanco and Larrañaga contribute the third paper, "Gene selection by sequential search wrapper approaches in microarray cancer class prediction". They have used a variety of machine learning methods to analyse large sets of microarray data. With this approach, the authors aim to improve classification results in cancer prediction.

The fourth paper, by Gamberger, Lavrač and Krstačiç is titled "Confirmation rule induction and its applica-

tions to coronary heart disease diagnosis and risk group discovery". The method provided by the authors is designed to enhance rule discovery and improve accuracy in machine learning algorithms.

The title of the fifth paper, "Temporal constraints in clinical diagnosis", by Keravnou, addresses an important topic within AI and MI: the representation of time in models for medical diagnosis. The paper presents a new approach to relating temporal constraints and causal reasoning in medicine, which has been an important issue since the earliest days of medical expert systems.

The final paper in this special issue, "Rule generation and model selection used for medical diagnosis", presents a method to address a classical issue within AI in medicine. Since the early 80s, AI researchers have been debating how to automatically generate knowledge from data sets, avoiding biases and inconsistencies in knowledge acquisition from medical experts. Paetz and Brause present a neural network approach for classification and rule generation in the medical domain of septic shock.

As can be seen from some of the papers of this issue, the borders between MI and BI are blurring. There are more and more research groups and reports engaged in analysing problems common to both areas. And there appears to be a similar trend within medicine and biology, since new models of molecular medicine and personalised health care, based on genomic research, are being proposed.

A different philosophical purpose has driven experimental research in AI in medicine and genomics until now. Regarding medical AI applications, the huge quantities of medical data available to practitioners have launched initiatives for data reduction and knowledge extraction. For instance, clinical prediction rules have been proposed for prognosis in specific diseases using different data mining methods [10]. Meanwhile, the use of some AI methods in genomics – e.g., machine learning algorithms and tools – also aimed to analyse data, as well as developing theories that could help to explain and predict what genes and proteins do from a physiological perspective.

We have proposed elsewhere that the theoretical foundations of BI – and biology, too – may be stronger than those of MI and medicine [11]. Thus, new approaches to medical issues could benefit from considering their biological foundations. By contrast, the emphasis of MI professionals on developing clinical

applications could provide a transfer of expertise for developing genomic-based applications in medicine.

This special issue is an example of recent proposals to bring together and exchange AI initiatives that address both medical and biological issues and problems that need innovative solutions. Similar collaborative efforts are being launched by international institutions, such as the European Commission – e.g., via the BIOINFOMED project – [12] and US organisations such as the American Medical Informatics Associations and the American College of Medical Informatics.

Finally, we would like to thank the editors and staff of the Journal of Fuzzy and Intelligent Systems for their collaboration. Our special thanks go to the co-Editor-in-Chief, Prof. Tim Ross, for his support and suggestions throughout the whole process that has led to the publication of this special issue.

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