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Synopsis

Decision Support, Knowledge Representation and Management

Information technology provides powerful tools to the medical community to build up and steadily enhance medical knowledge for the sake of better healthcare. Obviously, the human abilities extended by the immense amount of knowledge represented in computer compatible form may support both the routine and even the computation intensive complex diagnostic and therapeutic decisions. All these combined with modern telecommunication infrastructure enmeshing wide areas, render knowledge dissemination possible in a cost-effective way. Through these tools, information technology can not only improve the institutional framework of classical healthcare, but essential services can reach the patients even at home [1].

The four selected papers of this section address different novel technologies of Knowledge Management & Decision Support.

1. In the paper by Morrison et al. [2] the accuracy and consistency of diagnostic decisions are improved in a problem where the grading of morphological variables plays an important role.
2. Peleg et al. [3] compile a new methodology of hierarchical process knowledge in biology, utilizing software components originally developed in non-biological areas.
3. Peters et al. [4] combine medical and statistical knowledge for the improvement of diagnostic performance while limiting the number of tests to be applied.
4. In the fourth paper, Prado et al. [5] introduce a novel telehealthcare architecture for renal assistance. In their solution the improved diagnostic and therapeutic features stem from the involvement of quantitative models for patients and therapy equipment in the relevant knowledge base.

The paragraphs below briefly summarize each selected paper in turn.

Expert system support using a Bayesian belief network for the classification of endometrial hyperplasia

The paper by Morrison et al. [2] attempts to improve the accuracy as well as the consistency of histopathological classifications by a decision support system (DSS) based on Bayesian belief networks [6]. In general, the framework of Bayesian Belief Networks (BBN) defines various events, the dependencies among them, and the conditional probabilities involved in those dependencies. A BBN can use this information to calculate the probabilities of various possible causes being the actual cause of an event.

The motivation of the work described comes from previous studies showing considerable intra- and inter-observer variation in the classification of endometrial hyperplasias. Since adequate treatments vary widely between the different categories of hyperplasia, the consequences of the erroneous classification might be crucial, so the improvement of the underlying histological diagnosis has an importance. The principal source of human decision uncertainties can be traced back to the difficulty in objective grading of morphological histological abnormalities. In the DDS proposed by the authors the prerequisites of a more objective grading are realized by a set of carefully validated reference images of proliferative endometrium, simple hyperplasia, complex hyperplasia, atypical hyperplasia and grade 1 endometrioid adenocarcinoma. These diagnostic outcomes are stored in the decision node. In the BBN four morphological features were selected as diagnostic clues used routinely in the discrimination of endometrial hyperplasias. These represented the evidence nodes and were linked to the decision node by conditional probability matrices. The system was designed with a computer user interface (CytoInform) where reference images for a given clue were displayed to assist the pathologist in entering evidence into the network. Reproducibility of diagnostic classification was tested on 50 cases chosen by a gynecological pathologist. These comprised ten cases each of proliferative endometrium, simple hyperplasia, complex hyperplasia, atypical hyperplasia and grade 1 endometrioid adenocarcinoma.

The testing of the DSS was confined to four pathologists with varying experience and two medical students. The utility of DSS in the improvement of decision accuracies and consistencies was assessed by the intra- and inter-observer „weighted" kappa values. Both consultant pathologists had slightly worse weighted kappa values using the DSS, while both junior pathologists achieved slightly better values using the system. Taking the original diagnoses of the consultant gynecological pathologist as the 'gold standard', there was excellent or moderate to good inter-observer agreement between the 'gold standard' and the results obtained by the four pathologists using the expert system. Due to the limited number of observers and cases, the results introduced should be considered as promising but preliminary results. According to the authors, decision support systems like this may improve the diagnostic performance of inexperienced observers.

The system seems to have an important application in the training of pathologists or undergraduates, mainly because the system highlights critical points in the diagnostic process where the errors have been made. Obviously, an increase in the number of carefully selected reference images and/or the computation of suitable morphologic parameters might still have further advantages.

Modeling biological processes using workflow and Petri Net models

In order to understand essential mechanisms of biological systems, it is not enough to develop an advanced knowledge representation describing elementary processes, as there is a need for the representation of the interrelationships of elementary building blocks of complex processes as well. In the paper by Peleg et al, [3] a novel framework has been introduced for the representation of knowledge about complex biological processes in terms of their components. The methodology advised relies on a Workflow model (mappable to Petri Nets) elaborated earlier for non-biological applications and on a component called TAMBIS, which serves as a biological concept model. By these two components, all the requirements for a dynamic model for high-level biological processes can be fulfilled.

The Workflow Model section of the compound model represents high-level biological processes in a form suitable for automatic manipulation. The term "high-level biological process" covers a set of linked component processes that are responsible for a biological behavior, normally within the context of a cell or organism, defining functional roles and relationships among cellular substances. The organization of component processes as a network provides a dynamic model. The subflow activities that represent high-level processes are hierarchically pasted into lower-level component processes. The process participants are specified in the organizational model that provides the static-structural aspect of the workflow. A participant may be an individual (biomolecule), a group of individual molecules that are assembled into a unit (organizational unit in the original Workflow definition and a biomolecular complex in a biological system), or a functional role. The process definition is often graphically displayed, as a flowchart of activities, which eases understanding. The current model is a qualitative model to illustrate the interconnection of elementary biological processes; it does not represent cellular concentration of reactants, or kinetic coefficients that are required to formalize quantitative models. The utility of the compound model was demonstrated by representing malaria parasites invading host erythrocytes, and composed queries, in five general classes, to discover relationships among processes and structural components.

Diagnosis of Glaucoma by Indirect Classifiers

In the third paper by Peters et al. [4] the framework of "indirect classification" has been applied to the problem of glaucoma classification. The framework combines medical and statistical (a priori) knowledge.

In the case of a suspected glaucoma the patient is examined with several tools. Keeping in mind cost-effectivity, the first aim is to reveal the relationship among different examinations in order to decide whether some medical examinations can be disregarded. A priori information extracted from this procedure offers the opportunity to build an indirect classification rule based on a reduced set of examinations. The result of this procedure is a classification rule based on a reduced set of necessary diagnostic tests but incorporating the a priori medical information about the full set of measurements.

The set of variables from different examination tools has been structured into explanatory, intermediate and response variables. The classification has been performed considering an important aspect of glaucoma, i.e. patients do not usually detect its onset. However, early detection is of main importance, since adequate therapy can slow down the progression of the disease. Because damages in the optic nerve head precede visual field defects of the patients, even a cost effective classification strategy should be based on such measurements which are able to detect early damages in the retinal nerve fiber layer. The Heidelberg Retina Tomograph (HRT) is an appropriate tool to detect early damages [7]. Hence, the ideal explanatory variables are the HRT and anamnestic variables. The definition of the disease is based on the optic nerve head morphology and the visual field defects of the patient. The three intermediate variables employed in the procedure also belong to these two areas.

In the example considered, misclassification errors are reduced by the indirect classification compared to similar direct approaches. The direct classification methods utilized in the problem of glaucoma diagnosis are linear discriminant analysis, classification trees and bootstrap aggregated classification trees.

Virtual Center for Renal Support (VCRS): Technological Approach to Patient Physiological Image

In this work Prado et al.[4] presented a novel telehealthcare architecture for renal assistance. The sophisticated high-tech architecture is not limited to patient telemonitoring, but yields a more deep knowledge about patients and therapy equipment by means of modeling and simulation technologies. The paper has been focused on the novel idea called patient physiological image (PPI) technology, which is the base of the VCRS.

The PPI is a concept which manages the knowledge of the virtual center for renal support. Renal patients have reliable access to the VCRS through a public switch telephone network—X.25 gateway. The design complies with the universal access requirement, allowing an efficient and inexpensive connection even in rural environments and reducing computational requirements in the patient's remote access unit. VCRS provides support for renal patients' care, increasing the quality and quantity of monitored biomedical signals, predicting events as hypotension or low dialysis dose, assisting them further by an online therapy modification and easing diagnostic tasks. Finally, the presented system serves as a computational aid for quantitative knowledge acquisition in renal physiology.

PPI describes aspects of human physiology by means of mathematical models which emphasize feedback relations as well. The model is built on differential-algebraic equations or partial differential equations, depending on the lumped or distributed nature of the simulated physiological topic.

Classical telehealthcare systems provide communication networks and services together with biomedical signal monitors to improve patient supervision and increase interaction between physicians and remote patients. The VCRS is a telehealthcare system which shares these initial goals, adding new capabilities for detecting dysfunction in machines, therapies and patients and also for diagnosis assistance. All these capabilities are mainly supported by the PPI-based simulator. The VCRS facilitates trials of new and personalized therapies. The major objective of the system is to provide a more adequate dialysis therapy to end-stage renal disease patients, overcoming current limitations on the application of kinetic and hemodynamics mathematical models.

Conclusion

The papers presented represent significant contributions to the development of knowledge representation and decision support in Medicine and Biology. Although the problems addressed are important from a clinical point of view, they just represent the diversity of application areas in this compilation of novelties. However, the methodologies applied i.e. Bayesian belief networks, Petri nets, workflow models etc. represent a solid theoretical and practical background for the solution of other problems as well.

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