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Synergistic case-based reasoning in medical domains

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ABSTRACT

This paper presents four synergistic systems that exemplify the approaches and benefits of case-based reasoning in medical domains. It then explores how these systems couple Artificial Intelligence (AI) research with medical research and practice, integrate multiple AI and computing methodologies, leverage small numbers of available cases, reason with time series data, and integrate numeric data with contextual and subjective information. The following systems are presented: (1) CARE-PARTNER, which supports the long-term follow-up care of stem-cell transplantation patients; (2) the 4 Diabetes Support System, which aids in managing patients with type 1 diabetes on insulin pump therapy; (3) Retrieval of HEmodialysis in NEphrological Disorders, which supports hemodialysis treatment of patients with end stage renal disease; and (4) the Mälardalen Stress System, which aids in the diagnosis and treatment of stress-related disorders.

1. Introduction

Case-based reasoning (CBR) systems have long found fertile ground in health sciences domains (Begum, Ahmed, Funk, Xiong, & Folke, 2011; Bichindaritz & Marling, 2010; Montani, 2008). Eight international Workshops on CBR in the Health Sciences have highlighted the challenges and showcased the applications of CBR in biomedical fields. At the 2012 workshop, held at the International Conference on Case-Based Reasoning (ICCBR-12) in Lyon, several exemplary systems were featured (Lamontagne & Recio-García, 2012). In the spirit of CBR, which promotes reasoning and learning from concrete examples, four of these systems were selected as cases of medical CBR systems. These systems are:

- CARE-PARTNER, which supports the long-term follow-up care of stem-cell transplantation patients.
- The 4 Diabetes Support System, which aids in managing patients with type 1 diabetes on insulin pump therapy.
- Retrieval of HEmodialysis in NEphrological Disorders, which supports hemodialysis treatment of patients with end stage renal disease.
- The Mälardalen Stress System, which aids in the diagnosis and treatment of stress-related disorders.

In this paper, we present each of these systems in turn. Then we explore the synergies enabled and exemplified by these systems. We find a tight coupling of Artificial Intelligence (AI) research with medical research and practice. We see integration of multiple AI and computing technologies. We find that complex domains demand complex knowledge structures. We identify a need to fully leverage small numbers of available cases. We encounter time series data and develop new ways to harness it for reasoning. We integrate numeric data, including biosensor signal data, with contextual life-event data and subjective patient perceptions. In essence, the synergistic intertwining of CBR and medicine in these systems has led to new insights in both CBR research and development and medical practice. It is our hope that these experiences will be retrieved, reused, revised and retained (Aamodt & Plaza, 1994) for future CBR research and system development.

2. CARE-PARTNER

CARE-PARTNER is a decision support system for the long-term follow-up of oncology patients who have undergone stem cell transplantation (Bichindaritz, Kansu, & Sullivan, 1998). This system was built between 1996 and 2000 at the Fred Hutchinson Cancer Research Center, at the University of Washington, in Seattle. Three physicians, Keith Sullivan, Paul Martin, and Emin Kansu, and a physician assistant, Muriel Siadak, served as the domain experts. While CARE-PARTNER is no longer an active project, the ideas it pioneered have been carried over into the ongoing Mémoire project

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(Bichindaritz, 2006, 2007) and have influenced numerous other CBR systems in health sciences domains.

2.1. CARE-PARTNER system functionality and goals

CARE-PARTNER assists clinicians with the long-term follow-up (LTFU) of stem cell transplant patients once they have returned to their home communities. It provides online answers to questions from home care providers, who previously had to telephone nurses, who would then relay their questions to LTFU clinicians before getting back to them with clinical answers. The electronic contact management system developed to replace the old phone and paper-based system provides advantages for research and documentation and serves as an example of a medical knowledge management system.

CARE-PARTNER's decision-support is based upon proven and validated practice, helping to implement evidence-based medicine (Sullivan et al., 1997). It provides the following types of decision support:

- Interpretation for each laboratory test and procedure result.
- List of differential diagnoses, ranked by likelihood; these diagnoses are often not incompatible, since several diagnoses co-occur to cover all the signs and symptoms exhibited by the patient.
- List of steps of laboratory tests and/or procedures for diagnostic assessment.
- List of steps of planning actions for treatment.
- List of pertinent documents hyperlinked to the previous elements, such as guidelines, or textbook excerpts.

An important system requirement for CARE-PARTNER is the management of risk. A physician not specialized in a domain may not be able to critique or challenge system advice, and may not notice even severe mistakes. In the domain of stem-cell transplantation, transplant complications were quite unfamiliar to home care providers. These complications can be rapidly life-threatening, thus imposing very high standards of safety to protect patients. Therefore, the reliability and safety of the system were of paramount importance.

2.2. CARE-PARTNER system design

Fig. 1 shows CARE-PARTNER's reasoning cycle. This multimodal reasoning cycle combines case-based reasoning, rule-based reasoning, and information retrieval. CARE-PARTNER's reasoning steps are generalizations of the steps defined in these respective methodologies. The cooperation of the different knowledge sources is driven by the LTFU domain, in which, as in most medical domains, knowledge takes several forms:

1. **Practice guidelines:** A practice guideline is composed of systematically developed textual statements, designed for practitioners and patients, which will be helpful in making clinical decisions on the prevention, diagnosis, treatment and management of selected conditions. Guidelines are represented as rules that are embedded in prototypical cases.
2. **Practice pathways:** A practice pathway covers the same type of knowledge elements as a practice guideline, but it is specialized to the LTFU domain. While practice guidelines are represented via text, practice pathways are expressed in the knowledge representation formalism of the decision support system. Practice pathways were created by a group of LTFU experts exclusively for the CARE-PARTNER system. Pathways correspond to prototypical cases, and they are represented as cases in the system.
3. **Practice cases:** A practice case is an example of a problem-solving situation as solved by an expert or possibly a group of experts. It is essentially a real patient problem-solving situation, and not a prototypical one as for a practice guideline or a practice pathway. It is represented as a case in the system.
4. **Medical textbooks:** A collection of documents serves as documentation and explanation during the reasoning process, often in hyperlinked form.

Intensive knowledge elicitation efforts were required to build the case base around a knowledge base of the domain. It was determined early on in the project that cases were not available in electronic format at a level of detail required for CBR. For instance, the patient database did not include patient treatments, or most of the signs and symptoms, but only the main events abstracted from the paper charts. The project team had to come up with prototypical cases to bootstrap the system, which took over two years to develop at a level of thoroughness and consistency needed to achieve high quality decision support.

This system was unique because its proposed recommendations spanned not only diagnosis, but also lab result interpretation, and treatment planning. An extensive ontology was developed including 1109 diseases, 452 functions (also known as signs and symptoms), 1152 labs, 547 procedures, 2684 medications, and 460 sites. Most of the terms naming these objects were standardized using the Unified Medical Language System (UMLS) semantic network (National Library of Medicine, 1995). Only terms not corresponding to objects in the UMLS were added to the domain specific ontology. In particular, the planning actions used in the treatment part of a prototypical case did not exist in the UMLS and were all created for the system.

The cornerstone of the knowledge acquisition process was the conception of prototypical cases, or clinical pathways. The 91 implemented clinical pathways primarily correspond to clinical diagnostic categories, with some of them corresponding to essential signs and symptoms requiring specific assessment or treatment actions. The clinical pathways are knowledge structures represented using the ontology described above. A prototypical case comprises three parts:

1. A list of findings, corresponding to signs and symptoms.
2. A diagnosis assessment plan, which is a plan to follow for confirming (or informing) the suspected diagnosis.
3. A treatment/solution plan, which is a plan to follow for treating this disease when confirmed, or a solution when the pathway does not correspond to a disease.

The diagnosis assessment part and the treatment part of the case can also be viewed as simplified algorithms, since they use *if-then-else* structures, *loop* structures, and *sequence* structures of actions in time. When instantiated with an actual patient's data, this provides a diagnosis assessment plan or treatment plan tailored to the specific patient. In this way, the knowledge structure allows for sophisticated adaptation when reusing a prototypical case.

2.3. CARE-PARTNER evaluation

Table 1 shows the results of an evaluation in which two expert clinicians rated the system using the scale *Fails to Meet Standards/Adequate/Meets All Standards* (Bichindaritz, 2006). This evaluation covered 163 different clinical situations or cases, corresponding to contacts between the system and a clinician, for three patients. As seen in Table 1, the system was rated 82.2% of the time as *Meets all Standards* and 12.3% of the time as *Adequate*, for a total of 94.5%