Advancements and Trends in Medical Case-Based Reasoning: An Overview of Systems and System Development

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Abstract

Case-Based Reasoning (CBR) is a recognised and well established method for building medical systems. In this paper, we identify strengths and weaknesses of CBR in medicine. System properties, divided into construction-oriented and purpose-oriented, are used as the basis for a survey of recent publications and research projects. The survey is used to find current trends in present medical CBR research.

Introduction

Ever since Shortliffe's seminal work on diagnosis of infection diseases (Shortliffe 1976), Artificial Intelligence has been applied in numerous applications in the health science domain. In the late 1980's, followed by groundlaying work done by Koton (Koton 1988), and Bareiss (Bareiss 1989), Case-Based Reasoning (CBR) appeared as an interesting alternative for building medical AI applications, and has since been further established in the field. Certainly, one of the intuitively attractive features of CBR in medicine is that the concepts of *patient* and *disease* lends itself naturally to a case representation. Although several advantages of using CBR in medicine has been identified, the medical field certainly is not without its problems, some of them specifically affecting CBR systems.

Gierl and Schmidt (Gierl & Schmidt 1998) identify the following key advantages of medical CBR;

- Cognitive Adequateness. CBR resembles the way physicians are reasoning about patients and the way they use their case expertise.
- Explicit Experience. A CBR system is naturally suited for adjusting itself to the specific requirements of a certain clinic or a surgeon.
- Duality of Objective and Subjective Knowledge. Instead of using the subjective knowledge of one or more experts to build systems (as is done for e.g. rule-based expert systems) CBR systems are built upon existing cases (which may or may not be fully understood).

- Automatic Acquisition of Subjective Knowledge. CBR systems exhibit an incremental knowledge acquisition, and knowledge can be abstracted by generalizing cases.
- System Integration. Patient records are already being collected by hospitals and practitioners and stored on machine readable mediums, which simplifies integration with CBR systems which can utilize them (after varying degrees of modification).

However, a number of disadvantages and problems can also be identified;

- Adaptation. Because of the often extremely large number of features involved in a medical case, adaptation of cases becomes problematic. Generalization and efficient feature identification methods helps to partly remedy this issue, but generally the problem persists. (Schmidt & Gierl 2000)
- Unreliability. Although the reliability of a CBR system increases with the proportion of coverage of the problem domain, reliability cannot be guaranteed. Adding new cases will not necessarily make a system converge towards greater reliability, as cases add only local improvement. Indeed, Bichindaritz argues that the strictly local properties of cases makes convergence an inappropriate notion for CBR systems.(Bichindaritz 2003)
- Concentration on reference. CBR systems are concentrated on reference as opposed to underlying diagnostic factors. Thus, systems cannot function as sources of previous experience unless a suitable case exists in the casebase.

In this paper, we take a look at a number of the most influential medical CBR research projects in late years, with the aim of identifying trends in the development of such systems. Basing our work on the 1998 survey by Gierl and Schmidt (Gierl & Schmidt 1998), we focus primarily on systems created or reported about after 1998. In particular, we are interested in investigating if, and to what degree, the focus has changed on what type of medical CBR systems are constructed, and how they are constructed.

The method of identifying current trends involves examining systems from recent years by focusing on a set of distinctive system properties. We divide system properties into *purpose-oriented* and *construction-oriented*, where the first are characterized by the general type of action the system is supposed to perform (classification, planning, diagnosis, and tutoring), and the second indicate different types of constructions, such as systems supporting adaptation, hybrid systems, varying degrees of autonomicity etc. Additionally, we attempt to find trends of more general importance, looking at medical CBR systems from a broader perspective.

The rest of the paper is organized as follows. Next section contains a description of the different comparison properties used to differentiate a system from another. The section *Recent medical CBR systems* describes a selected number of influential works in the medical CBR domain. In section *Trends in medical CBR*, we present a system property matrix and identify construction-oriented and overall trends.

System properties

Purpose-oriented properties

With purpose-oriented properties, we refer to the separation of overall system purpose into planning, classification, tutoring, and diagnostic.

Diagnostic systems The majority of medical CBR systems belong in the diagnostic systems category. Diagnostic systems attempt to provide the user of the system with various degrees of assistance in the diagnosing process of a medical condition, possibly up to the point of a completely autonomous diagnose.

Classification systems Classification systems attempt to identify the group or group affiliations of real-world cases. One typical example is image classification systems that do not attempt a complete diagnosis.

Tutoring systems A medical tutoring system based on CBR is typically built closely around the concept of learning by examples, providing students with access to real patient cases.

Planning systems Planning systems are characterized by their intention to help in solving a process involving a number of steps. Therapy support is an often seen example of planning in medical systems.

Construction-oriented properties

Looking at medical CBR systems, we are interested not only in which systems have been recently constructed, but also how they were constructed and the motivation behind their construction. Once again, this is done to ease the identification of current trends in the development of medical CBR. However, in some cases it is not possible to derive the state of all these properties from the papers describing the projects in question.

Hybrid systems A hybrid medical CBR system denotes a multi-faceted solution to a problem space, using CBR as one of a number of AI technologies forming a complete system. Many such systems use CBR as the main organizer of data, and data-intense techniques such as neural networks to handle lower-level case identifications. Others match CBR with the Rule-Based Reasoning used in traditional expert systems to gain the advantages of both Rule-Based and Case-Based Reasoning.

Adaptive systems The problem of doing successful adaptation in the medical domain, because of the often enormous amount of features in a case, has been documented by Schmidt and Gierl (Schmidt & Gierl 2000). In the system summary in section *Recent medical CBR systems*, we investigate if and to what degree medical CBR systems from recent years has started to utilize adaptation methods.

Case library size The size of the case library does not only involve the actual number of cases in the case library, but also the degree of case generalisation into prototypes, i.e., the degree to which the system tries to merge existing cases into more general ones.

Autonomicity The degree of autonomicity is arguably of the most importance for diagnostic systems, where it denotes the level of interaction needed with a physician or corresponding medical expert before and after the diagnosis is complete. A purely autonomous system would produce diagnoses that would be accepted and used without having a human expert look at them, which is rarely the case in current systems. The degree of autonomicity implies the need for human intervention in the reasoning cycle and for evaluating its results.

Constraints System constraints concerns reliability and safety-criticality. Safety-criticality denotes the need to always provide correct answers, e.g., whether incorrect system behaviour could potentially create dangerous or even life threatening situations. A system is reliable if it is always operational when needed.

Recent medical CBR systems

As was mentioned in the introduction, the focus of the survey is on systems created or reported about during the last five years. An overview of medical CBR systems before 1998 was done by Gierl et al. in (Gierl & Schmidt 1998). From this overview, we adopted the division of systems into diagnostic, classification, tutoring, and planning systems.

Diagnostic systems

FM-Ultranet (Balaa *et al.* 2003; Balaa & Traphoner 2003) is a medical CBR project implemented with CBR-Works. FM-Ultranet detects malformations and abnormalities of foetus through ultrasonographical examinations. The detection, or diagnosis, uses attributes derived from scans of the mother's uterus, and identifies abnormal organs and extremities. Cases are arranged in a hierarchical and object oriented structure. The hierarchy is organized in 39 concepts, and every concept has one or more attributes. The attributes consists of anatomical features, medical history and general domain knowledge. Similarity between attributes in the concepts (objects) are mathematically calculated or compared through a look up table, depending on the attribute type. A report of the system's findings are generated when the detection (CBR) process is completed.

Perner (Perner 1999) proposes a system that uses CBR to optimize image segmentation at the low level unit according to changing image acquisition conditions and image quality. The system has been used to detect degenerative brain disease in particular Alzheimer disease in CT images of a patient. The cases are comprised of images and image features as well as non-image information about the image acquisition and the patient. The solution of a case is the parameters of the image segmentation unit. The control of the parameter of the image segmentation unit is done by the CBR mechanism. This ensure high image quality of the output image. Similarity is calculated over the image information according to a special image similarity measure and over the non-image information. Finally, both similarity measures are combined to an overall similarity measure. The system was used at the Radiology Department at the University of Halle.

Jaulent *et al.* (Jaulent *et al.* 1997) is diagnosing histopathology in the breast cancer domain. Their system uses cases that are derived from written medical reports. A case has an internal tree structure, and represents a collection of macroscopic area. Every macroscopic area is a collection of histological areas, and each histological area contains a cytological description of subjective features, like a big cell size. The features are also weighted for importance. Cases are compared for structural (structure of the histological tree), surface (semantic resemblance of microscopic areas) and feature similarity. A translation transposes the subjective features into numerical values.

CARE-PARTNER (Bichindaritz 2003; Bichindaritz, Kansu, & Sullivan 1998) is a decision support system for the long term follow-up of stem cell transplanted patients at Fred Hutchinson Cancer Research Center (FHCRC) in Seattle. The CARE-PARTNER system gives medical and decision support to the home care providers that follow up the transplant patients, using the Internet to connect the home care providers with the FHCRC transplant specialists. The system uses a multi modal reasoning framework, combining Case Based Reasoning and Rule Based Reasoning. A safety insurance plan at three levels (a procedural, a software engineering and a knowledge level) is adopted to ensure fault tolerance. One main characteristic of the system is that it uses a rich knowledge base of prototypical cases and practice guidelines to interpret medical cases and guide the case based reasoning.

Schmidt *et al.* deal specifically with prototypes in (Schmidt, Pollwein, & Gierl 1999), where a prototype denotes a generalisation occurring as a result of grouping/clustering single cases into more general ones. The claim is made that generating prototypes is also an adequate technique to learn intrinsic case knowledge, especially if the domain theory is weak. Storing new cases may improve the ability to find solutions for similar cases, but to understand the knowledge included within, generalisation is needed. Schmidt and Gierl have developed several systems focusing on generalising into prototypes, as described in their 1998 medical CBR survey (Gierl & Schmidt 1998), such as **ICONS** (Schmidt, Steffen, & Gierl 2001) for antibiotic therapy advice, **GS.52** for diagnosis of dysmorphic syndromes, **COSYL** for liver patient treatment strategies, and **TeCoMED** for forecasting epidemics of infection diseases. These are all further described in (Gierl & Schmidt 1998) and (Schmidt, Pollwein, & Gierl 1999). In (Schmidt, Pollwein, & Gierl 1999), Schmidt argues that the reason for using prototypes varies with the type of application and task. In areas where the domain theory is weak, prototypes help to guide the retrieval. In other systems, prototypes may correspond directly with the physicians view and be absolutely necessary for the project. Prototypes also help to speed up retrieval by decreasing the number of cases. The general drawback of prototypes is however loss of information when generalizing.

Classification systems

Montani *et al.* has focused on CBR in hemodialysis treatments for end stage renal disease (Montani *et al.* 2003). Their system is applied to the efficiency assessments of hemodialysis sessions. Each new dialysis session, i.e. assessment, is represented as a case in the system. Patterns of failures over time, from the patients past history, and cross references with other patients, can be found with this solution. Features are both statically and dynamically collected. The static features are patient information of a general nature (age etc.), and the dynamical features originates from online measurements in the form of continuous time series. The online features used for assessment is mainly derived from the extracorporeal circuit during a dialysis session, like measuring the arterial pressure.

Costello and Wilson (Costello & Wilson 2003) is focusing on the classification of mammalian DNA sequences, and are using a case library of nucleotide (A,T,G,C) segments. The stored segments are already classified as exons (carrying information on how to create proteins) and introns (junk segments that do not carry any information). The system is identifying exons in a seemingly random mix of exons and introns in strands of DNA. An edit distance calculation of, insertion, substitution and deletion of individual nucleotides in the tested exons is used to evaluate the similarity between the test strand and the store exon cases. Matched exons is then grouped through activation levels (number of similarities) to find new segments of exons in the test strand.

Nilsson *et al.* (Nilsson, Funk, & Sollenborn 2003) address the domain of psychophysiological dysfunctions, a form of stress. The system is classifying physiological measurements from sensors. The system is divided into smaller distinct parts. Measurements, like signals from an ECG, are filtered and improved. A case library of models of distortions etc. is applied to the filters. Features are extracted from the filtered signals (measurements). An additional set of features are extracted from the first set, for trend analysis etc. The features from the first and second set, and patient specific data, are used as a case. The cases are classified with a k-nearest neighbour match.

TeCoMED. Further information about the TeCoMED system was given in (Schmidt & Gierl 2002). Schmidt and Gierl attempt to use a prognostic model to forecast waves of influenza epidemics, based on earlier observations done in previous years. TeCoMED combines CBR with Temporal Abstraction to handle the problem of the cyclic but irregular behaviour of epidemics. Trends are discretized into *enormous decrease*, *sharp decrease*, *decrease*, *steady*, *increase*, *sharp increase*, and *enormous increase*, based on the percentage of change. TeCoMED utilizes former courses and similar cases in a way similar to early kidney problem warnings in the ICONS system. Attempting to commercialize the system, a small software company has incorporated warnings that are generated by the system into web pages of a health insurance scheme and a page of the health authority of the federal state.

Montani *et al.* (Montani *et al.* 2001) attempt to integrate different methodologies into a Multi-Modal Reasoning (MMR) system, used in therapy support for diabetic patients. The authors argue that most systems trying to utilize more than one methodology do so only in an exclusive fashion, with methodologies functioning merely as extensions to one another. Montani argues that a MMR system needs much closer integration of technologies to get the full benefits of a multi-modal solution. Integration allows tackling well known problems of single methodologies, i.e. the qualification problem in RBR and the too-small-a-library problem in CBR. The proposed system tries to use a fuller integration and utilize CBR, Rule-Based Reasoning, and Model-Based Reasoning (MBR).

Perner *et al.* (Perner, Gunther, & Perner 2003) has developed a system for the identification of airborne fungi. The fungal strains have a high biological variability, i.e. dissimilarity between the features of individual fungi is quite extensive. A strain can not be generalised to a few cases because of this variability. The images used originate from microscope enhanced pictures. A case is described by attributes (features) derived from the images. Attributes are in the abstraction level of colour, shape, size etc. New and original cases (descriptions of individual fungi) are retained in the case library, which is constructed by decision tree and prototype learning methods.

Tutoring systems

WHAT (Evans-Romaine & Marling 2003) is a tutoring medical CBR system for the education of sports medicine students. WHAT is designed to give better matching exercise prescriptions than the conservative rule-based approach taught by most books. The system provides two separate recommendations for exercise prescriptions, one which is based on the rules found in the books, the other uses CBR with a stored case base made by an expert. The prescribed exercises are applied to cardiac and pulmonary disease patients, as well as issues of general health and lifestyle. The prescriptions are based on features from the patients' medical history and on physiological tests.

Bichindaritz *et al.* (Bichindaritz & Sullivan 2002) have evolved CARE-PARTNER into a medical training system on the Internet. The intention is to help medical students improve their knowledge by solving practice cases. Prototypical cases consist of clinical pathways, which can be tailored to generate cases of varying levels of complexity. The system is also able to evaluate the solutions given by the students for the practice cases. Due to the unlikelihood that a student solution matches the stored solution exactly, a correctness score is calculated and the student solution is placed into one of three categories: Fails to meet standards, Adequate, and Meets all standards.

Planning systems

The **Auguste** project (Marling & Whitehouse 2001), is an effort to provide decision support for planning the ongoing care of Alzheimer's Disease (AD) patients. The first reported system prototype supports the decision to prescribe neuroleptic drugs for behavioural problems. The prototype is a hybrid system where a CBR part decides if a neuroleptic drug is to be given, and a Rule-Based Reasoning (RBR) part decides which neuroleptic to use. The system uses approximately 100 features, manually extracted from medical charts, in each case for determining the right neuroleptic drug. The patient is initially screened for behavioral problems before a Nearest Neighbour match makes a suggestion on whether or not to give neuroleptics to the patient. If the CBR module finds it appropriate to give neuroleptics and no contradictions are found, e.g., allergies to certain drugs etc., the RBR module determines which neuroleptic (of five available) to use. This prescriptive task, although termed "planning" in the vernacular, may be best characterized as one of design.

Davis *et al.* (Davis *et al.* 2003) are using a planning system based on the ReCall CBR shell. The system decides what kind of SMARTHOUSE devices disabled and elderly people need in their homes for independent living. Features are constructed from manual translations of written reports. The system contains 10 clustered problem space groups and 14 solution groups. Every group is subdivided by a C4.5 decision tree for efficiency and as an easy way to explain the reasoning process.

Trends in medical CBR

Naturally, the selection of papers in the previous section is highly subjective. None the less, certain trends are distinctive enough to deserve mentioning.

Property matrix

The research papers used as underlying documentation for the system descriptions does not always contain sufficient information about whether or not a system exhibits a certain construction-oriented property. For completion, the system authors were therefore contacted and asked specifically about the missing property information. Additionally, the authors were asked about the practical use of the systems in every-day life and whether there had been any attempts at commercialization. The answers to the questionnaire are presented in Figure 1.

Author / System	Cases	Prototypes	Adaptivity	Hybridity
Schmidt/TeCoMED	3000	No (intended)	No (intended)	CBR most imp.
Nilsson/Stress diagnosis	20	No	No	CBR most imp.
Montani/Hemodialysis	1000	No	No	Pure CBR
Montani/Diabetes (MMR)	150	No	No	Hybrid
Costello/Gene finding	948	No	No	Pure CBR
Evans-Romaine/WHAT	25	No (not yet)	No (not yet)	CBR most imp.
Marling/Auguste	28	No	No	Hybrid
Perner/Fungi identification	100	Some extent	No	Pure CBR
Perner/Image segm.	1000	Some extent	No	
El Balaa/FM-Ultranet	130	No		Pure CBR
Bichindaritz/CARE-PARTNER	4000	Some extent	Largely	CBR most imp.

Author / System	Interaction (autonomicity)	Commer-cialisation	Every-day use	Safety criticality	Reliability
Schmidt/TeCoMED	None	Some extent	Largely	No	Soft const.
Nilsson/Stress diagn.	Some extent	No	No	No	No
Montani/Hemodialysis	Some extent	No	No	No	No
Montani/Diabetes	Some extent	No	Some extent	No	No
Costello/Gene f.	None (intended)	No	No	No	No
Evans-Romaine/WHAT	None	No	No	Soft const.	Soft const.
Marling/Auguste	Largely	No	No	Hard const.	No
Perner/Fungi identif.	Some extent	Some extent	Largely		No
Perner/Image segm.	Some extent	Planned	Planned		No
El Balaa/FM-Ultranet	Some extent	No	No	Soft const.	
Bichindaritz/C.-P.	Some extent	No	Some extent	Hard const.	Must work

An empty cell in the matrix denotes that the property could not be determined.

Figure 1: System property matrix.

Notably, the majority of systems are multi-modal. Only one of the systems utilizes adaptation. Generalisation using prototypes appears to be rare; however, in several projects the intention is to extend the system with prototypes at a later stage. The majority of systems are dependant on some level of user interaction in the reasoning cycle. A few of the systems has been commercialized to some degree, but typically the projects are kept on a research level. Safety and reliability constraints are not too common. Systems that do have safety-critical constraints usually depend on operational reliability as well.

Construction-oriented trends

Looking at the previously defined construction-oriented properties, a number of trends can be identified.

Hybrid systems, also commonly referred to as Multi-Modal Reasoning Systems, constitute the majority of medical CBR systems. The combination of CBR with assisting technologies seems especially successful when CBR acts as the top level coordinator at the system level. Medical systems based on a straight CBR approach may suffer from unreliability, since all reference information is concentrated to the cases. Hence, systems like CARE-PARTNER have built in safeguards.

The autonomicity of the majority of systems is relatively low. Considering the inherent problem of unreliability in CBR, and the fact that systems typically does not reach a 100% correspondence with reported correct solutions even for controlled sets of cases, not relying on complete autonomicity appears to be sound.

The use of prototypes through case aggregation seems to be a commonly intended future extension, although only partly apparent in the property matrix. Prototypes are already used by many of the systems created by Gierl and Schmidt (as described in Diagnostic Systems), and prototype support is planned for both TeCoMED and WHAT.

Overall trends

The majority of systems in the purpose-oriented category belong to classifying and diagnostic systems. True to the nature of the domain, the emphasis in the medical AI domain has and probably will continue to be on clinical use, i.e., systems involved in some sort of treatment.

Features and feature extraction is an important part of most CBR systems. One identifiable trend in medical CBR is the continuation of separate pre-processing methods on the input data, whether it is a human or an automated process. The datasets are often too large for a direct CBR analysis, and therefore needs to be pre-processed. Examples of systems focusing on separate feature extraction are the stress diagnosis system by Nilsson *et al.* and the airborne fungi detection system by Perner *et al*.

As was the case in the 1998 medical CBR survey by Gierl and Schmidt (Gierl & Schmidt 1998), medical tutoring systems utilising CBR are rare. The inherent case- and example-based nature and the cognitively plausible model of CBR should be ideal for teaching medical knowledge; still the number of tutoring systems is remarkably low. There is however an increasing number of systems that could partly be seen as tutorial, i.e. the system covers more than one of the purpose-oriented properties, including the Auguste project, WHAT, and FM-Ultranet.

Conclusions

Although the recent five years has not seen any dramatic changes in the construction and use of medical CBR systems, the field is evolving steadily but slowly. The potential for automated systems in clinics is high, but has yet to reach its full potential. Most systems tend to concentrate on diagnostic tasks, but the use of CBR for therapeutic planning appears to be on the increase. Medical tutoring systems based on CBR are still rare.

The clear majority of systems built around a combination of CBR and other AI methods indicates that most medical domain problems looked into by researchers in recent years have been too complex and multi-faceted to handle using CBR alone. Arguably, hybrid systems have been utilized in the CBR health science domain from the very beginning, with early projects such as CASEY (Koton 1988) utilizing a mixture of CBR and RBR. There is, however, an increasing majority of hybrid systems being developed, which appears to reflect the increasing complexity and scope of the problem domains.

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