To my Family and Parents

Preface

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Mobyen Uddin Ahmed
Västerås, November 15, 2011

Publications by the Author

The following articles are included in this thesis:

A. Case-Based Reasoning Systems in the Health Sciences: A Survey on Recent Trends and Developments, Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Mia Folke. International *journal* of "IEEE Transactions on Systems, Man, and Cybernetics-Part C: Applications and Reviews", vol 41, Issue 4, 2011, pp 421 - 434.

B. A Hybrid Case-Based System in Stress Diagnosis and Treatment, Mobyen Uddin Ahmed, Shahina Begum and Peter Funk. Accepted in the "IEEE-EMBS International Conference on Biomedical and Health Informatics (BHI2012)", 2012.

C. Case-based Reasoning for Diagnosis of Stress using Enhanced Cosine and Fuzzy Similarity. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong, Bo von Schéele. International *journal* of "Transactions on Case-Based Reasoning on Multimedia Data", vol 1, Number 1, IBaI Publishing, ISSN: 1864-9734, 2008, pp 3-19.

D. A Multi-Module Case Based Biofeedback System for Stress Treatment. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong, Bo von Schéele. International *journal* of "Artificial Intelligence in Medicine", vol. 51, Issue 2, Publisher: Elsevier B.V., 2010, pp 107-115.

E. Fuzzy Rule-Based Classification to Build Initial Case Library for Case-Based Stress Diagnosis. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong. In the proceedings of "9th International Conference on Artificial Intelligence and Applications (AIA)", 2009, pp 225-230.

F. A Case-Based Retrieval System for Post-operative Pain Treatment, Mobyen Uddin Ahmed and Peter Funk. In the proceeding of "International Workshop on Case-Based Reasoning CBR 2011", IBaI, Germany, New York/USA, Ed(s):Petra Perner and Georg Rub, September, 2011, pp 30-41.

G. Mining Rare Cases in Post-Operative Pain by Means of Outlier Detection, Mobyen Uddin Ahmed and Peter Funk. Accepted in the "IEEE International Symposium on Signal Processing and Information Technology", 2011.

Additional publications, not included in the thesis:

Journals:

1. A Decision Support System Based on ECG Sensor Signal in Determining Stress. Shahina Begum, Mobyen Uddin Ahmed and Peter Funk, Submitted to the journal of Expert Systems with Applications. Elsevier. ISSN: 0957-4174, 2011.
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14. Classify and Diagnose Individual Stress Using Calibration and Fuzzy Case-Based Reasoning. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Bo von Schéele. In proceedings of 7th International Conference on Case-Based Reasoning, Springer, Belfast, Northern Ireland, August, 2007.
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List of Figures

List of Abbreviations

ABS	Absolute
AI	Artificial Intelligence
AIM	Artificial Intelligence in Medicine
ANN	Artificial Neural Networks
ANFIS	Adaptive Neuro-Fuzzy Interference System
CBR	Case-Based Reasoning
CDSS	Clinical Decision Support System
DSS	Decision Support System
EEG	Electroencephalography
ECG	Electrocardiography
EMG	Electromyography
ETCO2	End-Tidal Carbon dioxide
FCM	Fuzzy C-Means Clustering
FIS	Fuzzy Inference System
FL	Fuzzy Logic
FRBR	Fuzzy Rule-Based Reasoning
FT	Finger Temperature
HR	Heart Rate
HRV	Heart Rate Variability
IPOS	Integrated Personal Health Optimizing System
IR	Information Retrieval
MFs	Membership Functions
NN	Nearest Neighbour

NVAS	Numerical Visual Analogue Scale
RBR	Rule-Based Reasoning
RSA	Respiratory Sinus Arrhythmia
SNS	Sympathetic Nervous System
tf-idf	term frequency – inverse document frequency
VSM	Vector Space Model
VAS	Visual Analogue Scale

Table of Content

PART 1

Thesis

Chapter 1.

Introduction

This chapter presents an introduction of the thesis, the aim and objective of the research, problem descriptions and research questions, research contributions and an outline of the thesis.

MEDICAL KNOWLEDGE is today expanding so quickly to the extent that even experts have difficulties in following the latest new results, changes and treatments. Computers surpass humans in their ability to remember and such property is very valuable for a computer-aided system that enables improvements for both diagnosis and treatment. A computer-aided system or Decision Support System (DSS) that can simulate expert human reasoning or serve as an assistant to a physician in the medical domain is increasingly important. In the medical domain diagnostics, classification and treatment are the main tasks for a physician. System development for such a purpose is also a popular area in Artificial Intelligence (AI) research.

DSSs that bear similarities with human reasoning have benefits and are often easily accepted by physicians in the medical domain [8, 26, 68, 69, 73, and 74]. Hence, DSSs that are able to reason and explain in an acceptable and understandable style are more and more in demand and will play an increasing role in tomorrow's health care. Today many clinical DSSs are developed to be multi-purposed and often combine more than one AI method and technique. In fact, the multi-faceted and complex nature of the medical domain motivates researchers to design such multi-modal systems [70, 72 and 74]. Many of the early AI systems attempted to apply pure Rule-Based Reasoning (RBR) as 'reasoning by logic in AI' for decision support in the medical area. However, for broad and complex domains where knowledge cannot be represented by rules (i.e. IF-THEN), this pure rule-based system encounters several problems. Knowledge acquisition bottleneck is one of the one of the most critical problems since medical knowledge evolves rapidly, updating large rule based systems and proving their consistency is expensive. A risk is that medical rule-based systems become brittle and unreliable. One faulty rule may affect the whole system's performance and is also important to consider [17, 101]. Artificial Neural Networks (ANN) can be used in the medical domain as "reasoning by learning in AI". However, it requires large data sets to learn the functional relationship between input and output space. Moreover, transparency is another issue since the ANN functions as a so called black box i.e. it is very difficult to understand clearly what is going on [101]. Case-Based Reasoning (CBR) is a promising AI method that can be applied as "reasoning by experience in AI" for implementing DSSs in the medical domain since it learns from experience in order solve a current situation [29]. CBR is especially suitable for domains with a weak domain theory, i.e. when the domain is difficult to formalise and is empirical. In CBR, experiences in the form of cases are used to represent knowledge. A case is defined by Kolodner and Leake as "a contextualised piece of knowledge representing an experience that teaches a lesson fundamental to achieving the goals of the reasoner" [59]. In practice, clinicians often reason with cases by referring and comparing previous cases (i.e. experiences). This makes a CBR approach intuitive for clinicians. A case may be a patient record structured by symptoms, diagnosis, treatment and outcome. Some applications have explored integration of CBR and RBR, e.g. in systems like CASEY [60] and FLORENCE [16].

This thesis focuses on the application of AI techniques in two domains i.e. stress management and post-operative pain treatment. It proposes a multi-modal and multipurpose-oriented Clinical Decision Support System (CDSS) for both domains. Both the CDSSs have been designed and developed in order to perform diagnostic and treatment tasks. Moreover, the proposed approach is able to handle multimedia data formats where information is collected from complex data sources. For example, the CDSS for stress management is based on 1) Finger Temperature (FT) from a sensor signal, 2) patient's contextual information (i.e. human perception and feelings) in a textual format and 3) patients feedback on how well they succeeded in carrying out the test using a Visual Analogue Scale (VAS). Again, in developing CDSS in post-operative pain treatment, 1) information is collected through questionnaires both in numerical and textual formats and 2) pain measurements using a Numerical Visual Analogue Scale (NVAS). Both the CDSSs apply CBR as a core technique to facilitate experience reuse and decision explanation by retrieving the previous “similar” cases. Besides CBR, the proposed approach has incorporated Fuzzy Logic (FL) in order to calculate the similarity between two cases, which handles vagueness and uncertainty which is inherent in much of human reasoning [PAPER B] [PAPER F]. In the stress management domain, reliability of the system for decision making tasks is further improved through textual Information Retrieval (IR) with ontology [PAPER C]. A three phase computer-assisted sensor-based system for treatment including biofeedback training in stress management is proposed in [PAPER D]. A part of the research work has made an effort to improve the performance of the stress diagnosis task when there are a limited number of cases. The proposed multimodal approach introduces a fuzzy rule-based classification scheme into the CBR system in order to increase the size of the case library by generating artificial cases [PAPER E]. In post-operative pain treatment, besides CBR, clustering techniques and approaches are used in order to identify rare cases [PAPER G].

1.1 Problem Descriptions

In the stress management application domain, FT is a popular measurement used by some clinicians to determine stress. Medical investigations have shown that FT has a correlation with stress for most people [14]. During stress, the sympathetic nervous system is activated, causing a decrease in the peripheral circulation, which in turn decreases the skin temperature. During relaxation, the reverse effect occurs i.e. the parasympathetic nervous systems activates and increases the FT. However the effect of FT changes is very individual and there are some other factors such as the patient’s feelings, behaviours, social facts, working environments and lifestyle which also plays a role in the diagnosis of stress. Besides the sensor measurements, such information can also be collected using text and VAS input. VAS is a measurement instrument (a scale ranging between 0 and 10) which can be used to measure subjective characteristics or attitudes. This data captures important information of an individual that is not contained in measurements and also provides useful supplementary knowledge to better interpret and understand sensor readings. It also allows the transfer of valuable experience between clinicians that is important for diagnosis and treatment planning. So, CDSSs in this domain should be capable of dealing with textual information besides biomedical sensor signals. Biofeedback is today a recognised treatment method for a number of physical and psychological problems. Stress is a more complex area for biofeedback as a treatment and different patients have very different physical reactions to stress and relaxation. In the stress area, a clinician commonly supervises patients in biofeedback and together with the patient they make individual adjustments to measurement and treatment. The results are largely experience based and a more experienced clinician often achieves better results. Less experienced clinicians may even have difficulty to initially classify a patient correctly. Often there are only a few experts available to assist less experienced clinicians. Consequently, there is a need to have a computer-assisted biofeedback system to assist in the process of classification, parameter setting and biofeedback training.

In the post-operative pain treatment domain, before an operation the clinician makes a pain treatment plan using guidelines (following a standard protocol) and an evidence-based approach and makes observations to the patient's response afterwards. However, approximately 30% of the population does not fit the recommended pain treatment procedures due to some hidden individual factors or unusual clinical situations. Cases that do not follow the standard protocol can be classified as a “rare case”. These “rare cases” often need personalised adaptation to standard procedures. A CDSS that uses these rare cases and generates a warning by providing references to similar bad or good cases is often beneficial. This will help a clinician to formulate an individual treatment plan. The quality of an individual's post-operative pain treatment can be improved if relevant similar cases and experience are presented for the clinician, especially if the patient needs special medical consideration.

CBR together with fuzzy logic have been applied in this research (for both domains) as a core technique. However, CBR has its limitations that in terms of accuracy, performance can be reduced due to a small amount of available reference cases in the case library. In the initial phase of a CBR system there are often a limited number of cases available which reduces the performance of the system. If past cases are missing or very sparse in some areas the accuracy is reduced. Another problem is that CBR may fail to classify a case due to lack of similar cases in the case library. In order to overcome the problem for instance, for a stress diagnosis task when there are a limited number of initial cases it is necessary to apply another method besides the CBR approach to improve the performance of the system.

1.2 Aims and Objectives

Stress management and post-operative pain treatment are complex medial domains where diagnosis, classification and treatment are the main tasks for clinicians. The overall goal of this research is to propose an approach that can be used to design and develop CDSSs both for stress management and post-operative pain treatment for improved health care.

There is an increasing demand for a computer-aided system in the stress domain. However, the application of such systems in this domain is limited so far due to weak domain theory. In clinical practice, balances between the sympathetic and parasympathetic nervous systems are monitored as a part of the diagnosis and treatment of psychophysiological dysfunctions (i.e. stress). Hence, the rise and fall of FT can help to diagnose stress-related dysfunctions. However, FT changes are so individual due to health factors, metabolic activity etc. Interpreting/analysing FT and understanding large variations of measurements from diverse patients require knowledge and experience. Without having adequate support, erroneous judgments could be made by a less experienced clinician. Since there are large individual variations when looking at FT, it is a worthy challenge to find a computational solution to apply in a computer-based system. Thus, one of the main goals of this research is to propose methods or techniques for a multipurpose-oriented CDSS i.e. a system that supports in the diagnosis and treatment of stress. Other important issues such as reliability and performance of the system in the diagnosis and decision making tasks for stress management are also addressed here.

Since 30% of the whole population need personalised adaptations to standard procedures for pain treatment a CDSS and can help to offer better treatment for these rare cases. Hence, the CDSS here retrieves and presents these rare situations together with regular cases and generates a warning alarm to physicians when they prepare a treatment plan.

1.3 Research Questions

Research questions are formulated based on the problem description (section 1.1) and aims and objectives (section 1.2). There are three main research questions together with sub- questions and they are as follows:

RQ 1. What ***approaches, methods and techniques*** can be used to design and develop CDSSs where the domain knowledge is weak e.g. stress management and post-operative pain treatment.

After analysing the content of both application domains and through discussions with experts, it is observed that both domains are complex and knowledge is very weak. So, in order to design and develop CDSSs for such domains, it is necessary to identify the proper approaches, methods and techniques.

RQ 2. How can a CDSS be ***designed, developed and validated*** for complex medical decision making tasks (i.e. diagnosis/classification and treatment) in stress management using FT measurement?

RQ 2. 1. How can a computer-based system provide more reliable solutions in the stress diagnosis task? In particular, could the CDSS framework handle textual information capturing e.g. human perceptions and feelings and use these with biomedical signals e.g. FT measurements to support the diagnosis of stress?

RQ 2. 2. What ***methods and techniques*** can be used to design a system to assist in treatment e.g. bio-feedback training in stress management using FT sensor signals?

RQ 2. 3. How can the CDSS be useful from the start even if there are a limited number of cases available?

CDSS for stress management (i.e. diagnosis and treatment of stress) is problematic to design and develop since it is a multipurpose system which applies data in multi-media formats (i.e. FT measurement from sensor signals and human perceptions and feelings from textual information). Hence the research explores a hybrid framework design, capable of handling multi-media data.

A CBR approach has many advantages but according to Watson [101], the system needs enough cases in the case library to enable a good level of performance. In many domains only a limited number of cases are available for a considerable time. A limitation first disappearing when the CDSS is widely used. Thus, to have a better performance from the start of the system a supplementary method is needed to populate the case library.

RQ 3. How can the proposed multimodal approach be enriched to fit other medical domains such as post-operative pain treatment?

The last research question is mainly aimed at applying the implemented approach (in stress management) to other medical application domains. Depending on the domain and application needs the proposed approach may need to be modified, adapted and enhanced and these issues are addressed by this research question.

In this research, CBR has been chosen as the core technique which works well when the domain knowledge is not clear enough. In both the domains even experienced clinicians have difficulty expressing knowledge explicitly. Textual Information Retrieval (IR) is added to the CBR system to make a more reliable diagnosis and improve decision making tasks in the stress management domain. Fuzzy Rule-Based Reasoning (RBR) is incorporated to support the system in its initial condition to classify patients. Fuzzy set theory is also used to compose an efficient matching method for finding the most relevant cases by calculating similarities between cases. A combination of the FCM algorithm and Hierarchical clustering algorithm is applied in order to identify rare cases. Thus the combinations of such AI techniques are applied to build a multi-modal computer-aided CDSS for multi-purpose tasks i.e. diagnosis, classification and treatment for both medical domains.

1.4 Research Contributions

A brief description of the contributions of this research work is presented in Part 2 through the included papers. A short summary of each paper is also presented in Chapter 5. There are several research areas such as Artificial Intelligence (AI), Medical Informatics and Decision Support System (DSS), which have contributed to this research work. The main contributions of this thesis can be summarised as follows:

RC 1. A literature study has been done for both the domains in order to understand the content of the domains and how the diagnosis and treatment have been conducted in a real clinical environment (presented in [CHAPTER 2]).

RC 2. A comprehensive survey (between the year 2004 and 2009) has been done in the research area of CBR in Health Sciences. The survey investigates current trends, developments, pros and cons of CBR systems in the medical domain [PAPER A].

RC 3. Implementation and validation of the proposed multimodal approach to show the usefulness of the proposed approach in stress management using FT measurement. [PAPER B].

RC 3.1. The textual data (i.e. human perceptions and feelings) of a patient capture important information that may not be available in the sensor measurements such as using FT measurement. So, a hybrid system is required to address this issue. The research addresses the design and evaluation of such a hybrid diagnosis system capable of handling multimedia data. By using both mediums (sensor signal and textual information) the clinician can be offered more relevant previous cases. Thus it enables enhanced and more reliable diagnosis and treatment planning [PAPER C].

RC 3.2. A multi-module computer assisted sensor-based biofeedback decision support system which can assist a clinician as a second option to classify patients has been developed. The system can estimate initial parameters and make recommendations for biofeedback training using FT measurements. The intention of the system is to enable a patient to train themselves without particular supervision [PAPER D].

RC 3.3. A CBR system could diminish its performance if a case library doesn't contain enough cases similar to the current patient's case. In this research, methods are explored to overcome this problem. A set of rules is used to generate hypothetical cases in regions where a limited number of cases are available. This method has also been evaluated and showed better performance in the task of diagnosing stress [PAPER E].

RC 4. Used the proposed case-based intelligent retrieval approach for assisting clinicians in making a better assessment of patients and to select a treatment plan to improve the quality of the individual's post-operative pain [PAPER F].

RC 4.1. An approach to automatically identify rare cases in post-operative pain [PAPER G] using a clustering based approach. Here, 18% of the cases are identified as 'rare' using the automatic approach.

Table 1 illustrates the interconnections among the research questions, research contributions and included papers.

Table 1. Interconnection among the research questions and contributions.

Research Questions	Research Contributions	Included Papers
What ***approach, methods and techniques*** can be used to design and develop CDSSs	***Literature review*** and a ***comprehensive survey*** have been done in the research area of CBR in health sciences.	PAPER A Case-Based Reasoning Systems in the Health Sciences: A Survey on Recent Trends and Developments. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Mia Folke, In the international ***journal*** on IEEE Transactions on Systems, Man, and Cybernetics-Part C: Applications and Reviews, vol 41, Issue 4, 2011, pp 421 - 434.
How can a CDSS be ***designed, developed and validated*** in stress management and used in a multi-purpose oriented task using FT measurement.	***Approaches, methods and techniques*** have been identified in order to design and develop a CDSS that can assist clinicians in their decision making tasks i.e. ***diagnosis, classification and treatment*** in the stress management domain using FT measurement. Moreover, ***reliability*** of the diagnosis task and ***performance of the classification*** task are also enhanced.	PAPER B, C, D and E A Hybrid Case-Based System in Clinical Diagnosis and Treatment Mobyen Uddin Ahmed, Shahina Begum and Peter Funk, Accepted in the IEEE-EMBS International **Conference** on Biomedical and Health Informatics (BHI2012), 2012. Case-based Reasoning for Diagnosis of Stress using Enhanced Cosine and Fuzzy Similarity. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong, Bo von Schéele. International ***journal*** Transactions on Case-Based Reasoning on Multimedia Data, vol 1, Number 1, IBaI Publishing, ISSN: 1864-9734, 2008, pp 3-19. A Multi-Module Case Based Biofeedback System for Stress Treatment. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong, Bo von Schéele. In the international ***journal*** on Artificial Intelligence in Medicine, vol. 51, Issue 2, Publisher: Elsevier B.V., 2010, pp 107-115. Fuzzy Rule-Based Classification to Build Initial Case Library for Case-Based Stress Diagnosis. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong. In the proceedings of the 9th international ***conference*** on Artificial Intelligence and Applications (AIA), 2009, pp 225-230.
How can the **proposed multimodal approach be enriched** for post -operative pain treatment	***Similar approach*** has been implemented in this domain. A ***novel approach to identify rare cases*** is also included in the system.	PAPER F and G A Case-Based Retrieval System for Post-operative Pain Treatment Mobyen Uddin Ahmed and Peter Funk, In the International ***Workshop*** Case-Based Reasoning CBR 2011, IBaI, Germany , New York/ USA, Editor(s):Petra Perner, September, 2011 Mining Rare Cases in Post-Operative Pain by Means of Outlier Detection Mobyen Uddin Ahmed and Peter Funk, Accepted in the IEEE International ***Symposium*** on Signal Processing and Information Technology, 2011

1.5 Outline of the Thesis

The thesis is divided into two parts; the first part is organized as: an introduction chapter which presents the aim and objective of the research work, problems, research questions and research contributions. Chapter 2 provides a background of the domains and related work. Chapter 3 presents a detailed description of the methods and techniques applied in this research. Chapter 4 presents information of the proposed Clinical Decision Support Systems (CDSSs) both for the stress management and the post-operative pain treatment domains. Chapter 5 provides the research contributions along with a summary of the included papers. Chapter 6 discusses the whole research and concludes the first part of the thesis along with the limitation and future work. The second part of the thesis contains the completed versions of the seven included papers.

Chapter 2.

Background and Related Work

This chapter presents a short description of the problem in terms of domain knowledge both for stress management and post-operative pain treatment. The related works about CDSSs in these domains are also discussed here.

CLINICAL DECISION Support Systems (CDSSs) are computer-based systems that are typically designed for medical knowledge, patient's data/information and an inference engine in order to assist clinicians in their decision making tasks namely diagnosis and treatment. In order to develop such CDSSs it requires clinical knowledge of the application domain. Medical, biological and/or physical background of a particular disease and its treatment is one example. Moreover, process and factors are considered in order to make diagnosis and treatment of a patient in a clinical environment, which is also important. The researcher had a great opportunity to work with two different medical application domains. So, there are two CDSSs and they are 1) CDSS for stress management and 2) CDSS for post-operative pain treatment.

2.1 Stress Management

In our daily lives we are subjected to a wide range of pressures. When the pressures exceed the extent that we are able to deal with then stress is trigged. A moderate level of stress is always good since it helps our body and mind work properly.

However, a high level of stress or severe stress during long periods is very risky or even life-endangering for patients with e.g. heart disease or high blood pressure. Stress has a side effect of reducing awareness of bodily symptoms and people on a heightened level of stress may often not be aware of it and one may notice it weeks or months later when the stress has already caused more serious effects on the body [98]. A computer-aided system that helps early detection of potential stress problems would bring essential benefits for the treatment and recovery of stress in both clinical and home environments.

2.1.1 Stress

According to Hans Selye, stress can be defined as “the rate of wear and tear within the body” [91]. He first introduced the term ‘stress’ in the 1950s when he noticed that patients suffer physically without having only a disease or a medical condition. He defined stress as "non-specific response of the body to any demand" [91]. We have an inborn reaction to stressful situations called the “fight or flight” response. That means we can react to certain events or facts that may produce stress and our body’s nervous system activates and then stress hormones are released to protect ourselves. The wear and tear is a physiological reaction such as rise in blood pressure, rise in heart rate, increased respiration rate and muscles get ready for action.

The human nervous system is divided into two main parts, the voluntary system and autonomic system. The autonomic nervous system is further divided into the sympathetic and parasympathetic nervous system. Walter Cannon described in [99], that the Sympathetic Nervous System (SNS) activates the body for the “fight or flight” response to perceived threats for physical or emotional security. Thus the SNS works to protect our body against threats by stimulating the necessary glands (i.e. thyroid and adrenal glands) and organs. It decreases the blood flow to the digestive and eliminative organs (i.e. the intestine, liver, kidney etc.) and enhances the flow of blood to the brain and muscles. The thyroid and adrenal glands also supply extra energy. As a result it speeds up the heart rate, increases blood pressure, decreases digestion and constricts the blood vessels i.e. vasoconstriction which slows down the flow of blood etc. The SNS thus activates the body for the fight-or-flight response to stress. The parasympathetic nervous system counteracts the fight-or-flight response to return the body to its normal state. It stimulates digestion, the immune system and eliminative organs etc. to rebuild the body [62].

2.1.2 *Good vs Bad Stress*

Stress is not always bad. It is almost impossible to live without some stress because it gives life some spice and excitement. A moderate amount of stress is often positive because it helps our bodies and minds to work well and to contribute to our mental health. Thus, good performance can be achieved but high level of stress reduces our performance that may harm our personal relationships, and enjoyment of life. A relationship curve between performance and stress is shown in Fig. 1. The explanation of the traditional performance-stress relationship curve can be: at zero or low level of stress, a person has low performance which usually means that the person is either sleeping or meditating. At a high level of stress the person also has zero performance i.e. the person may be experiencing panic.

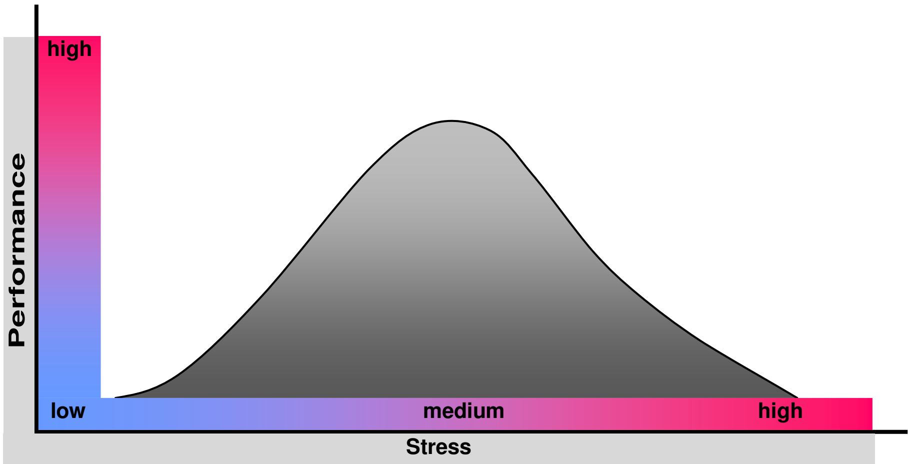

Figure 1. Stress versus performance relationship curve [107].

So, to achieve a good performance it is better to have a moderate amount of stress. This means if any person can accomplish any activity such as driving a car with a moderate level of stress, he/she could do it with good performance. Such kind of stress experiences can be treated as good or short-term stress. But long-term stress, for example constant worry about work or family is bad for our health because it may drain energy and decreases our ability to perform well. So, if suffering from extreme stress or long-term stress, the body will eventually wear itself down.

2.1.3 Stress Diagnosis and Treatment

The diagnosis of stress is often multi-factorial, complex and uncertain due to large variations and personalisation. According to [76], there are three methods that can be used for the diagnosis of stress: questionnaires, biochemical measures and physiological measures. A face-to-face interview with questionnaires and a checklist are traditional ways to diagnose stress. Rudolf E. Noble in [76], mentioned various biochemical parameters e.g. corticosteroid hormones which can be measured from body fluids, blood, saliva and urine. Since the autonomic nervous system is activated by a stress response various physiological parameters of the SNS can be used in the diagnosis of stress. The physiological parameters are commonly measured using skin conductance, skin temperature, respiration e.g. end-tidal carbon dioxide (ETCO2), electromyography (EMG), electrocardiography (ECG), heart rate e.g. calculating respiratory sinus arrhythmia (RSA) and heart rate variability (HRV), electroencephalography (EEG), brain imaging techniques, oculomotor and pupilometric measures etc. In this research, both stress diagnosis and biofeedback treatment have been conducted using the skin temperature i.e. finger temperature (FT) since the intention of the research was to design and develop a CDSS for stress management which should be simple, inexpensive and easy to use.

There are several methods to control or manage stress e.g. exercise or training. In our everyday lives we need to control our stress in many situations, for instance when we are sitting at our desk or behind the wheel of a car getting stuck in traffic. In such a situation or in other environments, biofeedback training is an effective method for controlling stress. It is an area of growing interest in medicine and psychology and it has proven to be very efficient for a number of physical, psychological and psycho-physical problems [2, 63]. Experienced clinicians have achieved good results in these areas and their success is largely based on many years of experience and often thousands of treated patients. The basis of biofeedback therapy is to support a patient in realising their self-ability to control specific psychophysiological processes [54]. The general strategy is that, patients get feedback in a clear way (e.g. the patient observes some measurements visualising some physical processes in their body) and behaviourally train the body and mind to change the biological responses to improve the condition. Sensor-based biofeedback is drawing increasing attention within this field of research and one reason is the development of sensors which are able to measure processes in the body which we have previously not been able to measure.

An area where biofeedback has proven to give results is the area of practicing relaxation. There is a correlation between skin temperature and relaxation. The changes in skin temperature reflect the state of the peripheral blood vessels which in turn are controlled by the SNS. A biological significant decrease in the SNS i.e. relaxation activity results in an increased diameter in the peripheral blood vessels. This increase in the peripheral blood vessels in turn results in an increased blood flow and skin temperature. Therefore, FT measurement is an effective biofeedback parameter [45, 71] for self-regulation training and has a clinical consensus as an important parameter in stress treatment. This research also investigates biofeedback training by employing FT measurements for stress control.

2.2 Post-Operative Pain Treatment

Approximately 40 million patients are undergoing minor to major surgical operations every year in Europe[1]. At least half of these patients from children to elderly have suffered with a moderate or severe amount of post-operative pain. The degree of post-operative pain differs for various patients, operation site and the type of operation. For example, an operation on the thorax and upper abdomen is more painful than the lower abdomen [20]. There are different types of operations but in this project we will only focus on the following operations:

Surgery without preoperative pain

1. Thoracotomy for lung cancer
2. Breast surgery for cancer
3. Inguinal hernia repair
4. Hysterectomy
5. Colectomy
6. Appendectomy

Surgery with potential preoperative pain

1. Cholecystectomy

[1] http://pain-out.med.uni-jena.de/index.php/about-pain-out/research

2. Total knee arthroplasty
3. Knee arthroscopy
4. Lower limb amputation
5. Sternotomy for valve replacement or CABG

According to Hawthorn and Redmond [43], pain might often be a useful thing, a "protective mechanism", a biological signal, which is essential when we for example learn not to touch a stove in order to protect us from being injured. However, pain can also be a bad thing; pain after surgery obstructs the healing-process for example resistance to mobility, loss of sleep, decreased food intake, depression and loss of morale can be a consequence of post-operative pain among many other negative consequences that might occur. Pain is considered to be an obstacle to recovery and also requires significant health care resources to manage. It is generally defined as an unpleasant sensory or emotional state due to actual or potential tissue damage. The measurement of pain is very subjective and multidimensional experience and unique to every individual [22, 61]. For example, someone may experience heavy pain after a small operation and need extra medication since they have very low capacity to cope with pain. On the other hand, others may have better capacity for pain tolerance and be happy with small doses of medication. Post-operative pain has different levels and ranges starting from a minor pain to a very major acute pain. There are different ways to measure pain even if it is very subjective and individual. For example, for adults a Numerical Rating Scale (NRS) [42] or a Visual Analog Scale (VAS) [50] or Brief Pain Inventory (BPI) [23] is used and for children and elderly patients a Facial expression [53] approach can be used. The *NRS* is a self-report scale asking patients to say a number between 0 and 10 to express the intensity of their pain. The *BPI* is a medical questionnaire used to measure pain, information on the intensity of pain as well as the degree to which pain interferes with function. The BPI also asks questions about pain relief, pain quality, and patient's perception of the cause of pain. It also used a NRS scale between 0 and 10 but questionnaires are asked at different times. The *VAS* is a psychometric response scale that is used in questionnaires. Here, patients cannot see any numeric value rather two end-points. An assessment is done by patients indicating a position along a continuous line between those two end-points. The *Facial expression* is a pictogram of six different faces with expressions between happy and tearful. Patients are asking to point out any of these faces as an experience of their pain.

Pain is a subjective experience which includes individual's sensory, emotional and behavioural factors along with the tissue injury. Understanding patient's experiences about pain is essential since the physiological basis of pain is helpful for both the sufferer and health provider in providing appropriate medication. Individual variations in response to pain can be achieved and the variation is influenced by the patient's culture, tradition, food habits, age and gender. Postoperative pain can be divided into two parts as follows [53]:

- Acute pain: patients experience this kind of pain immediately after an operation which can be last up to one week.
- Chronic pain: this pain lasts for a long time i.e. more than 3 months after the operation.

Both short and long term pain has negative effects and they are listed below:

1. Physical and emotional suffering by the patient.
2. Problem in sleeping.
3. Cardiovascular problem such as hypertension.
4. Oxygen consumption can be increased.
5. Impaired bowel movement.
6. Problem in respiratory system
7. Delayed mobilisation
8. Severe pain can be develop chronic pain
9. Behavioural changes for children in long-term pain.

In practice, a number of factors such as clinical, local and patient-related questions are asked to a patient by a healthcare provider before the operation to decide a proper treatment plan in pain relief. The healthcare providers use a questionnaire which comprises the following: information about the patient's history, medical history, pre-medications, screening, and demographics. Depending on the question-answer by the patient, operation sight and other clinical factors, the health care providers make a plan for treatment that is what medication and in what quantity will be used before, during the operation, and in the recovery room and ward. This pain treatment plan is then observed and a pain measurement along with the patient's perception of pain is carried out after the operation. Depending on the pain outcome the medications in the recovery room and/or in ward are altered. In order to provide a good treatment for post-operative pain recovery both non-pharmacological and pharmacological medicine are used. Moreover, good nursing and drug combinations are also necessary to provide adequate pain relief. There are different pharmacological options that are used in pain treatment such as non-opioid analgesics, weak opioids, strong opioids, and adjuvants. These opioids are given in different modes such as intravenous with continuous or incessant infusion, infusion, orally and by injection. The detailed information about different drugs, drug combination, quantity and application methods are used in pain treatment can be found in [53].

2.3 Related Works about DSS in Medical Applications

The design and development of Decision Support Systems (DSSs) or intelligent systems in medicine is very challenging and complex. Even though the area is evolving day-by-day they are most often limited to research level. CDSSs using AI started in the early 1970s and produced a number of experimental systems; the MYCIN [17] was one of them. The HELP [36] system is one of the longest running and most successful clinical information systems. According to a literature study presented in [106], different AI techniques have been applied in the clinical DSSs such as 1) rule-based reasoning [3, 4 and 17], 2) bayesian theory [18], 3) bayesian belief networks[64], 4) heuristic, 5) semantic network, 6) neural networks [19], 7) genetic algorithms [84] 7) fuzzy logic [3, 18] and 8) case-based reasoning. Some of the recent medical DSSs using CBR approach are presented below: a) ExpressionCBR [30], the system is a decision support system for *cancer diagnosis* and *classification*. It uses Exon array data and classifies *Leukemia patients* automatically to help in the diagnosis of various cancer patients. b) GerAmi [26] 'Geriatric Ambient Intelligence', is an intelligent system that aims to *support healthcare facilities for the elderly*, *Alzheimer's patients and people with other disabilities*. This system mainly works as a multi-agent system and includes a CBR system to provide a case-based planning mechanism. c) geneCBR [31, 38], is focusing on *classification of cancer*, based on a gene expression profile of microarray data. The system is aiming to deal with a common problem in bioinformatics i.e. to keep the original set of features as small as possible. d) ISOR [90], the system *identifies the causes of ineffective therapies and advises better recommendations* to avoid inefficacy to support in *long-term therapies in the endocrine domain*. The system is exemplified in diagnosis and therapy recommendations of Hypothyroidism patients treated with hormonal therapy. e) the KASIMIR project [28], is an effort to provide decision support for *breast cancer* *treatment based on a protocol in Oncology*. The adaptation of protocol is an important issue handled here to provide therapeutic decisions for cases those are out of the protocol. f) Song et al. [96], proposes a DSS in *radiotherapy for dose planning in prostate cancer.* Their system is able to adjust appropriate radiotherapy doses for an individual while, at the same time, it reduces the risks of possible side effects of the treatment. The system is implemented in cooperation with the City Hospital at the Nottingham University Hospital. g) Marling et al. in [69], described a case-based DSS to assist in the daily management of *patients with Type 1 diabetes on insulin pump therapy*. In adjusting patient-specific insulin dosage the system considers a real-time monitor of the patients' blood glucose levels and their lifestyle factors. In [70], the authors presented different research directions and development paths. In order to develop a proper DSS for the patient with Type 1 diabetes they have included naive Bayes classification and support vector regression into the existing CBR system. Before that through the Auguste Project the authors also developed a DSS for the care of patients suffering from *Alzheimers* [68].

2.3.1 CDSS in Stress Management

According to literature study, clinical DSSs and/or intelligent systems in stress management i.e. for diagnosis and treatment is still limited. A web-based intelligent stress management system has been found in [51], where the system is claimed as the world's first intelligent stress management system. Here, the system takes the input of several pre-defined stress related symptoms basically in 4 categories; a) behavioural, b) emotional c) mental and d) physiological. These symptoms are then weighted and a score is calculated and finally, an overall stress level is presented as a percentage of each symptom's category. Moreover, the system also provided some exercises in audio format for relaxation and monitoring can be done several times in a day. Stress diagnosis using questionnaires can be found in [9, 24], which is mainly to calculate and identify the level of stress (i.e. work and physical related stress). Stress detection using human voice is outlined in [108], where the authors have applied several features such as loudness, fundamental frequency, power spectral density zero-crossing rate, etc. Further, the system has applied Artificial Neural Network (ANN) and Adaptive Neuro-Fuzzy Interference System (ANFIS) to provide an intelligent solution. However, stress diagnosis using physiological parameters such as skin conductance, skin temperature, respiration and heart rate is limited so far. A procedure for diagnosing stress-related disorders using physiological parameters has been put forward by

Nilsson et al. [79], where stress-related disorders are diagnosed by classifying the Respiratory Sinus Arrhythmia (RSA) i.e. the interaction of the heart beat with breathing cycle. This was an initial attempt to use a DSS in psycho-physiological medicine domain i.e. using physiological parameters. The system is used as a research tool and is more suitable in a clinical environment for diagnosis of stress. DSS for only diagnosing stress based on the finger temperature (FT) measurement is addressed in Begum et al. 2007 [8], the authors have also included Heart Rate Variability (HRV) in order to measure individual stress levels and is addressed in [10]. However, an enhance DSS both for diagnosis and treatment (i.e. biofeedback) using FT as physiological parameters is focused in this research [PAPER B], [PAPER C] and [PAPER D]. Moreover, besides the physiological parameters, patient's contextual information provided in a textual format is also included in this research [PAPER C] and [PAPER B].

2.3.2 CDSS in Post-Operative Pain Treatment

Recent advancements of clinical DSSs in pain treatment have been investigated through a literature study. The authors in [94] have presented a review on DSS for chronic pain management in primary care, where 8 systems are studied. According to the paper, all 8 DSSs are designed to assist physicians in pain management. Most of them have applied artificial intelligence techniques such as CBR, RBR, and fuzzy logic. A DSS in pain management for cancer patients is described in [12]. In their proposed system, daily pain assessment has been conducted through a NVAS and the system assists physicians in recommending correct deviations from pain therapy guidelines. A recent DSS in the domain of palliative care addressed by Houeland and Aamodt [48] is an advice-giving system that supports physicians to improve pain treatment in lung cancer patients. The proposed system incorporates rule-based and model–based methods into the CBR approach. Elvidge in [33] also describes a system to help healthcare providers in improved pain and symptom management for advanced cancer patients. His web-based DSS incorporated CBR with evidence-based standards for end-of-life cancer care. To my knowledge, CDSS in post-operative pain treatment is limited. So far, from this study no intelligent systems were found that addressed assistance with post-operative pain treatment. Therefore, it is a challenging issue. The proposed system in this research considered both the rare and regular cases which have already been collected and/or automatically identified [PAPER G] and stored into the case library of the system [PAPER F]. The system presents most similar cases (both regular and rare) to physicians as a solution of a new case presented in section 4.2 [CHAPTER 4].

Thus the system provides support in selecting proper individual treatment plans in order to improve post-operative pain treatment.

Chapter 3.

Methods and Approaches

This chapter presents a short description of the background of the related methods investigated in this research work. Here, Case-Based Reasoning (CBR) as the core technique of this research is described. Beside CBR, several others Artificial Intelligence (AI) techniques are also presented such as, textual information retrieval, fuzzy logic, fuzzy rule-based reasoning and clustering approaches.

SEVERAL ARTIFICIAL intelligence methods and techniques have been investigated in order to design and develop the CDSSs. However, a CBR approach is used for both the CDSSs as a core technology to build the basic framework. Depending on the nature of the application domain, requirements and data formats and considering the functionalities and performance of the CDSSs, other AI methods and approaches have been applied and combined with the CBR approach. For example in the stress management application domain, information retrieval techniques are applied with a CBR approach in order to handle human perceptions and feelings in a textual format. Again, in this domain, a fuzzy rule-based reasoning approach is included beside the CBR approach in order to create artificial cases to instate the case library. This helps to get a better performance in stress diagnosis tasks when the CDSS contains only a few reference cases. On the other hand, in the post-operative pain treatment application domain, research has applied a clustering approach to group the cases and identify rare cases since the CDSS in this domain contains more than 1500 patient cases. Here, clustering approaches are combined with a CBR approach. Thus beside the CBR approach other AI methods are working as tools to improve the systems' performance and reliability in decision making tasks by the clinicians of each domain.

3.1 Case-Based Reasoning (CBR)

Case-Based Reasoning (CBR) is a problem solving method that gives priority to past experiences for solving current problems (solutions for current problems can be found by reusing or adapting the solutions to problems which have been solved in the past). Riesbeck & Schank presented CBR as, "A case-based reasoner solves new problems by adapting solutions that were used to solve old problems" [85]. The CBR method in a problem solving context can be described as follows: 1) given a particular problem case, the similarity of this problem with the stored problems in a case library (or memory) is calculated 2) one or more most similar matching cases are retrieved according to their similarity values 3) the solution of one of the retrieved problems is suggested for reuse by doing revision or possible adaptation (if needed e.g. due to differences in problem descriptions) 4) finally, the current problem case and its corresponding solution can be retained as a new solved case for further use [65].

CBR is not only a powerful method for computer reasoning, but also a common human problem solving behaviour in everyday life; that reasoning is based on the past personally experienced cases. CBR is inspired by a cognitive model based on the way humans solve certain classes of problems e.g. solve a new problem by applying previous experience adapted to the current situation. Watson and Marir have reported in [102] that CBR is attracting attention because:

- It does not require explicit domain knowledge but gathering of cases.
- Simple and easy implementation because significant features describe a case.
- Database Management Systems or DBMS could help to handle a large volume of information.
- Systems can easily learn by obtaining new knowledge as cases.

The root of CBR can be traced from the work of Schank and his student at Yale University in the early 1980s but Watson presented in [102] that the research of CBR began in 1977. CYRUS [56, 57] developed by Janet Colodner, is the basic and earliest CBR system. She employed knowledge as cases and used an indexed memory structure. Other early CBR systems such as CASEY [60] and MEDIATOR [92] have been implemented based on CYRUS. In the medical domain around the 1980s, early CBR systems were developed by Konton [60], and Braeiss [5, 6].

The medical domain is suitable and at the same time challenging for a CBR application. Doctors often recall similar cases that he/she has learned and adapted them to the current situation. A clinician may start their practice with some initial past experiences (own or learned solved cases), and attempt to utilise this past experience to solve a new problem, which simultaneously increases their experience. One main reason that CBR is suitable for the medical domain is its adequate cognitive model and cases may be extracted from the patient's records [37]. Several research works i.e. in [13, 37 and 72] have investigated the key advantages of CBR in the medical domain. Moreover, the recent trends and advancements are investigated and presented in [PAPER A]. The motivations to apply CBR methods in the above domain are listed below:

1. The CBR [1, 101] method can solve a problem in a way similar to the normal behaviour of human problem solving e.g. it solves a problem using experience.
2. Such a CBR system could be valuable for a less experienced person because the case library can be used as knowledge.
3. A CBR system can start working with few reference cases in its case library and then learn day by day by adding new cases into the library. Similarly, a doctor or an engineer might start their practice with a few cases and gradually increases their experiences.
4. A CBR system can provide more than one alternative for a similar problem which is beneficial for the clinician.
5. CBR can help to reduce the recurrence of a wrong decision because the case library could contain both success and failure of cases.
6. Knowledge elicitation is most of the time a bottleneck in the health science domain since human behaviour is not always predictable. The CBR method can overcome this because prediction is based on the experience or old cases.
7. It is useful if the domain is not clear i.e. CBR does not depend on any rules or any models [46].

8. Systems using CBR can learn new knowledge by adding new solved cases into the case library, so domain knowledge is also updating in time.

However, medical applications offer a number of challenges for CBR researchers and drives research advances in the area. Important research issues are:

1. *A limited number of reference cases* – even though a CBR system can work with a small number of reference cases, the performance might be reduced due to a limited number of available cases [101].
2. *Feature extraction* – cases are formulated with a number of features or a feature vector, so the big issue is to dig out features from the complex data format (i.e. images, sensor signals etc.).
3. *Adaptation* – the medical domain is often complex knowledge and recommendations in the medical domain evolve with time, cases often consist of a large number of features, and therefore it is a real challenge to apply automatic adaptation strategy in this area [34].

3.1.1 The CBR Cycle

According to Kolodner in [58] a case is a "contextualised piece of knowledge representing experience that teaches a lesson fundamental to achieving the goals of the reasoner". Representation of a case structure can be done in various ways. The most common and well known way is to present a case only with a problem and a solution description. The *problem* part describes the condition of a case and the *solution* part presents advice or a recommendation to solve a problem. Some systems could also add an outcome besides the solution to evaluate a new state. The outcome describes the state after the case had taken place [102]. A comprehensive case structure has been proposed by Kolodner in [58] as follows: 1) a state with goal, 2) the solution 3) the outcome 4) explanations of results and 5) lessons learned. Further ahead, Bergmann et al [11] classified case representation in the following three categories: a) feature vector representations or propositional cases b) structured representations or relational cases, and c) textual representations or semi-structure cases [11].

A schematic or life-cycle that presents the key processes involved in the CBR method is shown in Fig 2. Aamodt and Plaza [1] have introduced a four-step model of CBR in a cyclical process comprising the four REs: Retrieve, Reuse, Revise and Retain.

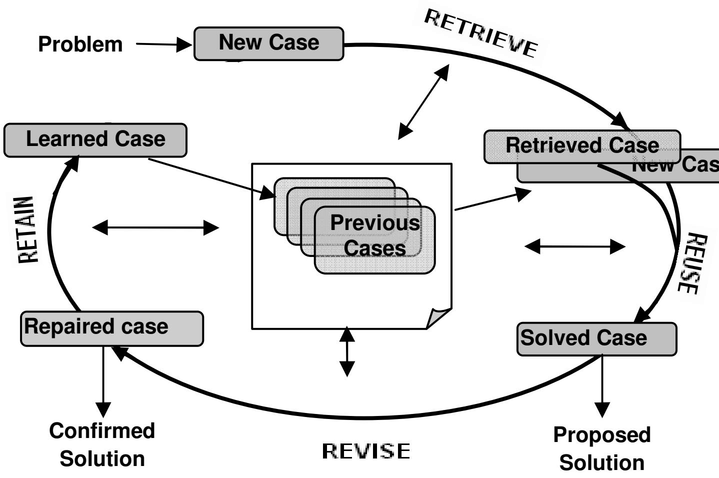

Figure 2. CBR cycle. The figure is introduced by Aamodt and Plaza [1].

Fig 2. illustrates these four steps that present the key tasks to implement such a cognitive model. The current situation is formulated as a new problem case and matched against all the cases in a library, depending on the similarity value of the cases one or more of the most similar cases are retrieved. Matching cases are presented with their corresponding solutions and a solution is then proposed to be reused and tested for success. If the retrieved case is not close enough to the new problem case, the solution will probably be revised and/or adapted. Finally, the new solved case is retained in the case library. The steps are described below with the aspect of CBR in the health science.

The *Retrieval* step is the major part of a CBR cycle and it is the most common for many CBR systems. Retrieval is essential since it plays a vital role for calculating the similarity of two cases. One popular way to the retrieve most similar cases is that the retrieval algorithm computes the similarity value for all the cases in a case library and retrieves the most similar cases against a current problem. The similarity value between cases is usually represented as 0 to 1 or 0 to 100, where “0” means no match and “1 or 100” means a perfect match. One of the most common and well known retrieval method is the *nearest neighbour* (or kNN) [101] which is based on the matching of a weighted sum of the features. For a feature vector, local similarity is computed by comparing each feature value and a global similarity value is obtained as a weighted calculation of the local similarities. A standard equation for the nearest-neighbour calculation is illustrated in Eq 1.

$$Similarity\ (T, S) = \frac{\sum_{i=1}^{n} f(T_i, S_i) \times w_i}{\sum_{i=1}^{n} wi} \tag{1}$$

In equation 1:

T is the target case

S is the source case

n is the number of attributes in each case

i is an individual attribute from *1 to n*

f is a similarity function for attribute *i* in cases *T* and *S*

w is the importance for weighing of attribute *i*.

The weights allocated to each feature/attribute provide them a range of importance. But determining the weight for a feature value is a problem and the easy way is to calibrate this weight by an expert or user in terms of the domain knowledge. However, it may also be determined by an adaptive learning process i.e. learning or optimizing weights from the case library as an information source.

Looking from the classical CBR cycle in Fig 2, the *Reuse* step comes just after the retrieve step. This step is reusing one of the retrieved cases from the case library and returning it as the proposed solution for a current case. But in some cases, this phase can become more difficult, especially when there are notorious differences between the current case and the closest one retrieved. An adaptation of the obtained solution is required in order to provide a solution for the current problem. For adaptation, it could calculate the differences between the retrieved case and the current case. Then it is possible to apply algorithms or rules that take the differences into account to suggest a solution. This adaptation could be done by an expert/user in the domain. The expert determines if it is a reasonable solution to the problem and they can modify the solution before approval. After that the case is sent to the *Revise* step where the solution is verified and evaluated for the correctness and presented as a confirmed solution to the new problem case [101].

The term *Retain* becomes the final stage which functions as a learning process in the CBR cycle, and it incorporates the new solved case into the case library for future use. The most common way to retain a case is to simply record the information concerning the target problem specification and its final solution (assuming that the solution given was accurate and correct) [65]. If the solution retrieved is not as reliable as it should be, additional information might be stored into the case library such as the changes made to the retrieved solution. So, the information to be saved has to be considered carefully [77].

3.2 Textual Case Retrieval

As we mentioned above, Bergmann et al [11] have proposed that a case could be represented as a textual or semi-structural format. Textual case retrieval could be defined as matching a user query against a bunch of free-text cases. Text retrieval is a branch of Information Retrieval (IR) if the information is stored in the form of text. IR is a science used for searching documents and/or for information within a document or metadata about the document. In this research the knowledge of IR is used to search and retrieve cases with features containing information in a textual format. The idea of this process begins when a query is entered by a user into the system through a user interface. Then the system extracts information from the query. The extracted features may match with several objects (cases) in the collection (case library) with different degree of relevance. The degree of relevance can be computed by the system as a numerical value that shows how well each case is matched with the query. Finally, according to this numerical value, all the cases will be sorted and the top ranked cases will be presented to the user [93]. There are several ways to find a match between a user query and the stored cases, such as Boolean model, fuzzy retrieval, vector space model, binary retrieval etc. [93]. The Vector Space Model (VSM) [87] is the most common and well known method that has been used in information retrieval.

VSM or term vector model is an algebraic model that represents textual cases in a vector of terms. It identifies similarity between a query case Q and the stored cases C_i. One of the best known schemes is the *tf-idf* (term frequency – inverse document frequency) [88] weighting used together with cosine similarity [103] in the vector space model [87] where the word "document" is treated as a case. The *tf-idf* is a traditional weighting algorithm and is often used in information and/or textual retrieval. The similarity/relevancy is measured from the cosine angle between a query case Q and the stored cases C_i inside a vector i.e. a deviation of angles between the case vectors. "$\cos\theta = \frac{Q.C_i}{\|Q\|\|C_i\|}$" is a general equation to calculate the cosine similarity where $Q.C_i$ is the dot product and $\|Q\|\|C_i\|$ is the magnitude of the vectors (a query and the stored case), i is the index of the cases in the case library. The value of the similarity lies in the range of -1 to +1, where -1 means no matching and +1 means exactly the same. In terms of IR, the cosine similarity of two cases will range from 0 to 1, since the *tf-idf* weights cannot be negative. The final result 1 is a full match and 0 means no words match between Q and C_i. To measure the similarity we need two things, the weight of each term in each case and the cosine similarity between the cases inside a vector space.

The terms are words, keywords, or long phrases in a case and the dimension of the vector is the number or frequency of each term in the vocabulary of cases. If a term occurs in a case the value will be non-zero in the vector. Each word *tf* is the relative frequency of the word in a specific case (document represent as a case) and it presents the importance of the word inside the case. *idf* is the inverse proportion of the word over the whole case corpus which presents the importance of the word over the entire case pool. The weight vector for a case c is $V_c = [w_{1,c}, w_{2,c}, \ldots, w_{N,c}]^T$ and $w_{t,c} = tf_t \cdot \log \frac{|C|}{|\{t \in c\}|}$ where tf_t is the term frequency or the number of times a term/word t occurs in a case c and $\log \frac{|C|}{|\{t \in c\}|}$ is the inverse case frequency. The symbol "$|C|$" is the total number of cases in the case library and $|\{t \in c\}|$ is the number of the cases containing the term t i.e. case frequency.

3.2.1 Advantages, Limitations and Improvements

There are a number of advantages for using this model which makes it attractive to use in textual retrieval. These advantages are summarised below:

1. VSM represents both the query and the stored cases in a weight vector where weights are non-binary and terms are weighted by importance.
2. Stored cases can be ranked according to their similarity value.
3. Retrieval can be done with partial matching, that is, cases can be retrieved even if they don't contain a query keyword.

4. It is simple to compute.

Even though VSM is an easy and well known method in text retrieval, there are a number of limitations and the limitations are as below:

1. When the information in a document or case is very long, a similarity measure is difficult or poor because of a high dimensional vector with small dot product.
2. Keywords from the user query must exactly be matched with the keywords from the stored documents/cases, so prefix/suffix words or parsing can affect the similarity results.
3. A similar information/context can contain both in a query and the stored cases using different words (for example synonym of words) may result in poor dot product.
4. The order of each term that appears in the document/case is lost in the vector during the representation.

In terms of processing time VSM also has some limitations, they are as follows:

1. From a computational point of view the system requires a lot of processing time if all the processes are going to be done in run time making response times in this domain too long.
2. When adding a new case or a new term into the case library or term space, all vectors need to be recalculated.

Most of the limitations discussed above have been overcome by improving the model presented in this research (see contribution [PAPER C]). A short summary is as follows:

1. Stored cases are formulated and retained by a human expert; only essential information is used and the cases are not very large.
2. Extracted number of significant keywords represents a stored case, so the cases do not contain high dimensional term vectors.
3. Less significant and common words such as "a", “an”, “the”, "in", "of", etc. are named as stopwords and are removed.
4. Necessary terms are stemmed to their root or basic form i.e. suffix/prefix the words such as "stemmer", "stemming", "stemmed" as based on "stem".

5. Added a dictionary such as "WordNet" to get a semantic relation among the words that are synonyms of the words.
6. Altered the term vector using expert defined domain specific ontology. The domain specific ontology provides relational strength among the special words in the domain to identify similarity between cases in a similar context.
7. Used a user defined similarity threshold or select a number of retrieved cases, so that only the relevant cases can be retrieved.
8. When adding a case or altering the ontology, a background process starts updating the case library by re-calculations the weightings. The next time the case library is used these calculations are already performed which reduces response time.

3.3 Fuzzy Logic

Information can be incomplete, inconsistent, uncertain, or all of these three and it is often unsuitable for solving a problem. For example, "The motor is running *really hot* or Tom is a *very tall* guy." Most people rely on common sense when they solve problems. To deal with such vague and uncertain information exact mathematical techniques are not sufficient, we need a technique that uses a much closer concept of human thinking. Fuzzy logic is specifically designed to mathematically represent this uncertainty and vagueness. So, fuzzy logic is not a logic that is fuzzy, but a logic that is used to describe fuzziness. It is a theory of fuzzy sets, sets that calibrate vagueness. Moreover, it is a form of multi-valued logic with more than two truth values to deal with reasoning i.e. an approximate value rather than an exact value. Opposite to the binary or crisp logic, it handles the concept of 'Partially Truth' i.e. the values between completely 'true' and completely 'false'. The degree of truth of a statement can range between false (0) and true (1) and considers more than two truth values.

Aristotle was the first to realise that logic based on "True" or "False" alone was not sufficient. Plato left the foundation of a third region beyond the true and false [86]. Multi-valued logic was introduced by a Polish philosopher Jan Lukasiewicz in the 1930s. He introduced logic that extended the range of truth values to all real numbers in the interval between 0 and 1 [66, 67]. In 1965, Lotfi Zadeh a professor in the University of California at Berkley, published his famous paper “Fuzzy sets”. He extended the work on possibility theory into a formal system of mathematical logic, and introduced a new concept for applying natural language terms. This new logic for representing and manipulating fuzzy terms was called fuzzy logic [110, 111]. The term “fuzzy logic” derives from the fuzzy set theory or the theory of fuzzy sets. The fuzzy set theory has successfully been applied in handling uncertainties in various application domains [52] including the medical domain. The use of fuzzy logic in medical informatics has begun in the early 1970s.

Fig. 3 represents binary logic with a crisp boundary of 4 different seasons in Sweden; where the X-axis corresponds to dates according to the month of the year and the Y-axis represents the probability between zero and one. In binary logic the function that relates to the value of a variable with the probability of a judged statement is a ‘rectangular’ one. The output probability for any input will always be ‘one’ i.e. only one season and ‘zero’ for the rest of the seasons. The crisp boundary of the season winter drawn at 31st March and 20th March is winter with the probability of one.

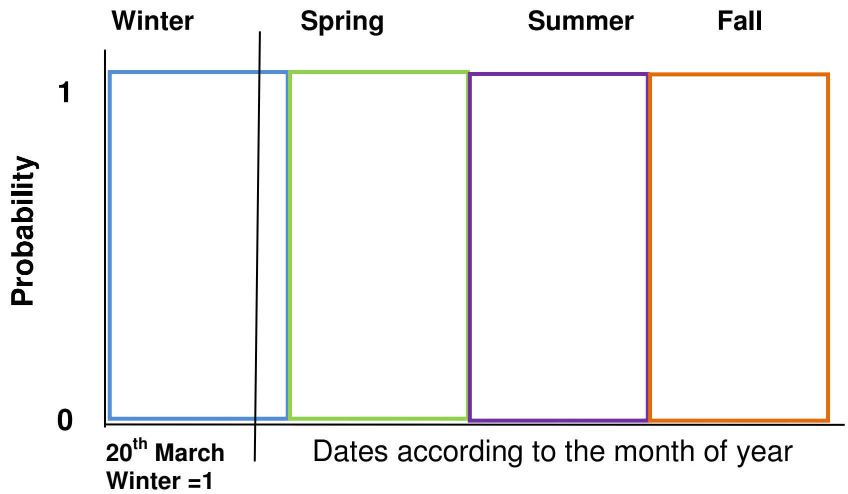

Figure 3. Binary or crisp logic representation for the season statement.

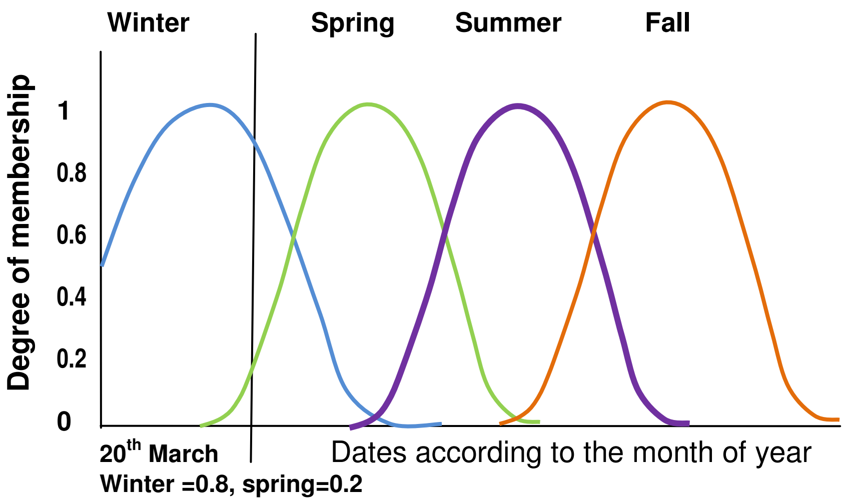

Figure 4. Fuzzy logic representation of the season statement.

In fuzzy logic the function can take any shape. As the season example illustrated, with the Gaussian curve in Fig 4, here, the X-axis is the universe of discourse which shows the range of all possible days for each month in a year for an input. The Y-axis represents the degree of the membership function i.e. the fuzzy set of each season's day values into a corresponding membership degree. In fuzzy logic, the truth of any statement becomes a matter of degree. Considering the 20th March as an input in the fuzzy system, it is winter with the degree of truth 0.78 and at the same time spring with the degree of truth 0.22. So according to Zadeh [110], "*Fuzzy logic is determined as a set of mathematical principles for knowledge representation based on degrees of membership rather than on crisp membership of classical binary logic*".

3.4 Fuzzy Rule-Based Reasoning (RBR)

Fuzzy Rule-Based Reasoning is a combination of the fuzzy logic approach with traditional Rule Based Reasoning (RBR) which is also called Fuzzy Inference Systems (FIS). Fuzzy inference is a computer paradigm based on fuzzy set theory, fuzzy if-then-rules and fuzzy reasoning. A traditional RBR system contains a set of if-then rules in a crisp format. A general form of a rule is "If <antecedent> then <consequence>". An example of such a rule is; "If speed is > 100 then stopping distance is 100 meters". In 1973, Lotfi Zadeh outlined a new approach to analyse complex systems, where human knowledge is captured as fuzzy rules [109]. A fuzzy rule is a linguistic expression of causal dependencies between linguistic variables in the form of if-then conditional statements. If we consider the previous example in a fuzzy format "If *speed* is ***fast*** then stopping *distance* is ***long***". Here the term '*speed*' and '*distance*' are linguistic variables, while '***fast***' and '***long***' are linguistic values determined by fuzzy sets. Therefore '*speed* is ***fast***' is the antecedent and 'stopping *distance* is ***long***' is the consequence.

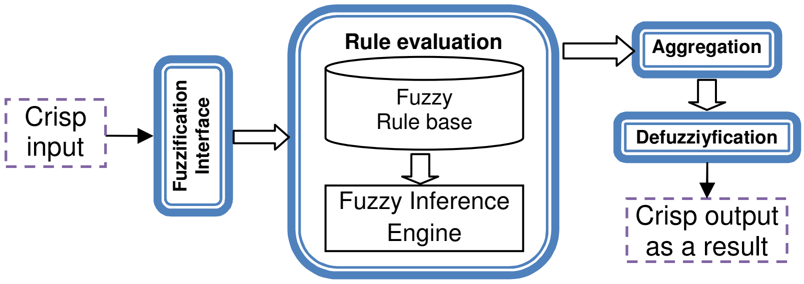

Figure 5. Steps in a Fuzzy Inference System (FIS).

Fuzzy decision making or inference systems can be defined as a process of mapping a given input to an output with the help of the fuzzy set theory i.e. fuzzification → fuzzy reasoning → defuzzification [52]. Well known inference systems are the Mamdani-style and Sugeno-style but both of them perform the 4 step process as described in Fig 5which illustrates the steps of a fuzzy inference system for the Mamdani-style. As can be seen from Fig 5, the first step is the fuzzification of an input variable i.e. crisp input is fuzzified against appropriate fuzzy sets. Given an input in a crisp format, *step1* computes the membership degree with respect to its linguistic terms. Consequently, each input variable is fuzzified over all the Membership Functions (MFs) used by the fuzzy rules. In a traditional rule-based system, if the antecedent part of a rule is true then the consequent part is also true. But in a fuzzy system, the rules are met to some extent. If the antecedent is true to some degree of membership then the consequent is also true to that degree.

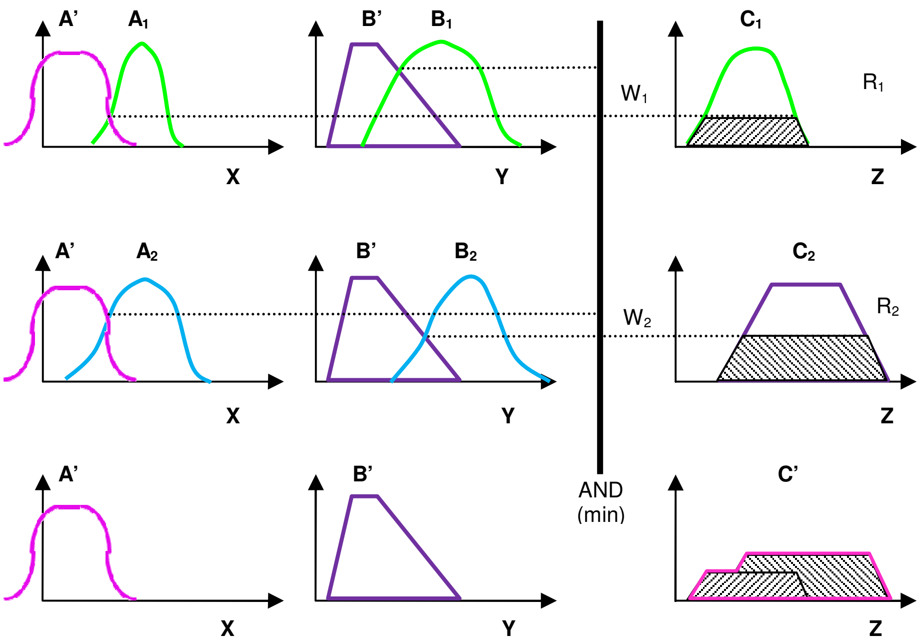

Figure 6. Graphical representation of an example of fuzzy inference.

Step2 is the rule evaluation where it takes fuzzified inputs and applies them to the antecedent part of the fuzzy rules. So it compares facts with the antecedents of the fuzzy rules to find degrees of compatibility. The value or firing strength is a single number from each rule represented in the result of the antecedent evaluation. This number is then applied to generate consequent MFs. Aggregation in *step3* is the process that merges all the output MFs for all the rules i.e. all outputs are combined into a single fuzzy set. The last and final phase (*step4*) in the inference process is defuzzification that determines a crisp value from the output membership function as a solution. The input for defuzzification is the aggregate fuzzy set and the output is a single number.

A simple example of fuzzy inference with multiple rules and multiple antecedents is illustrated in Fig 6. The rules and inputs are as follows: Rule 1: if x is A_1 and y is B_1 then z is C_1 and Rule 2: if x is A_2 and y is B_2 then z is C_2; Inputs: x is A and y is B then z is C (?). First the inputted crisp values (A and B) are converted into the fuzzy sets A' and B'. Then for the rule R_1 and R_2, A' and B' are fuzzified with the fuzzy sets A_1, B_1 and A_2, B_2. The dotted line in Fig. 6

presents the clipped area of the membership functions in the antecedent part of the rules. As the rules contain multiple antecedents with AND operators, fuzzy intersection is used to obtain a single number that represents the evaluation result of the antecedents. W_1 and W_2 are the evaluation results applied to the MFs in the consequent part of the rules. Upward and downward diagonal patterns in the fuzzy sets C_1 and C_2 show the firing strengths for the rule's evaluation. After aggregation, the clipped fuzzy set C_1 and C_2, and the new fuzzy set C' are obtained. A defuzzification algorithm could convert this fuzzy set into a crisp value which is a single number that represents the final output.

3.4 Clustering Approach

Clustering is an approach in which a set of data is divided among several subsets where the data within one subset are similar to each other and are different from the data of other subsets. The clustering approach or cluster analysis is not an algorithm itself rather it is a task to be solved by applying various algorithms. It is a task that assigns a set of data points to a group. A formal definition can be presented as "These clusters should reflect some mechanism at work in the domain from which instances or data points are drawn, a mechanism that causes some instances to bear a stronger resemblance to one another than they do to the remaining instances" [105]. A mathematical definition of clustering as stated in [40], which can be express as follows: let $X \in R^{m \times n}$ in a set of data representing a set of m points x_i in R^n. The goal is to partition X into K groups and C_k so that all data that belongs to the same group are more "alike" than data in different groups. Each of the K groups is called a cluster and the result of the algorithm is an injective mapping $X \mapsto C$ of data items X_i to clusters C_k. Several algorithms are available in literature with many different classifications. However, one simple classification of clustering can be divided into two classes as: 1) parametric and 2) non-parametric clustering.

Parametric clustering helps to minimise a cost function where the main goal of this kind of algorithm is to solve an optimisation problem in a satisfactory level imposed by the model. However, this algorithm requires a better understanding about data distribution and a proper probability distribution. This class can be further divided into two groups: a) generative or probability-based model and b) reconstructive models. In the probability-based model, the model relies on a guess that the data comes from a known distribution, but this is not true for many situations. So, this model cannot be usefully applied where the probability distribution is not known and/or the data are not numerical. The Gaussian mixture model is one example of such model. However, a proper probability distribution in data can be achieved using this algorithm. On the other hand, the reconstructive model aims to minimise the cost function. A most common and basic algorithm is K-means as an example of reconstructive models. For non-parametric clustering, the hierarchical algorithms or an agglomerative and divisive algorithm is a good example. The algorithm works based on dis-similarities among the current clusters for each iteration. The agglomerative algorithm merges and the divisive algorithm divides the clusters depending on similarities. Both of them also produce dendograms, which presents clusters in a tree structure as bottom up or top down. A detailed elaboration of parametric and non-parametric clustering can be found in [35] and the difference between parametric and non-parametric clustering can be summarised in Table 2.

Table 2. Comparison of parametric and non-parametric clustering.

Criteria	Parametric	Non-parametric
Algorithm	• Optimises a cost function • Most costs are NP-hard problem • Assumes more detailed knowledge of cluster shape • Assumes K is known • Gets harder with larger K • Older, more widely used and studied	• Density-based method • No cost function • Does not depend on initialisation • K and outliers selected automatically • Requires hyper-parameters
When to use	• Shape of clusters is known • K not too large or known • Clusters of comparable size	• Shape of cluster is arbitrary • K is large or has many outliers • Cluster size in large range • Lots of data

A summary of the 4 common and well-known clustering algorithms 1) K-means clustering, 2) Fuzzy C-means clustering, 3) Gaussian mixer model and 4) Hierarchical clustering are presented here:

1) K-means clustering: K-means clustering formulates groups in a numeric domain and partitions data samples in disjointed groups. The main objective of the algorithm is to minimise the cost objective function and it requires the number of clusters and its initial centre points. The centre points can be given manually or randomly in the initial stage of the algorithm and later in each iteration the algorithm will automatically adjust in order to minimise the value of the distance matrix. Considering the distance matrix values, each iteration is repeated and as soon as the two distance values (previous and next) become the same, the algorithm stops. The Euclidean distance function is used in this algorithm in most of the cases and performance of the algorithm is strongly depends on the distance value. Although the algorithm is easy to implement and takes less time to compute compared to others, it has a drawback that it can be stuck in a local minimum since the algorithm depends on the provided initial centre point. The algorithm starts work by giving a set of initial cluster numbers and the centre points for each cluster. Then the centre points are replaced by the mean point for each cluster. These steps are repeated until the two distances become the same. The algorithm can be illustrated as below [39]:

- Step 1. Choose K initial cluster centres $Z_1, Z_2, \ldots\ldots, Z_k$ randomly from the n points $\{X_1, X_2, \ldots, X_n\}$.
- Step 2. Assign point X_i, $i= 1, 2, \ldots, n$ to the cluster C_j, $j \in \{1,2,\ldots K\}$, if

  $$\left\| X_i - z_j \right\| <= \left\| X_i - z_p \right\|, \; p=1, 2, .., K \text{ and } j \neq p$$

- Step 3. Calculate new cluster centres:

  $$z_i^{new} = \frac{1}{n_i} \sum_{X_j \in C_i} X_j \quad i=1, 2, .., K$$

- Step 4. Continue step 2 and 3 and If $\left\| z_i^{new} - z_i \right\| < \varepsilon$, $i=1, 2, .., K$ then stop.

2) Fuzzy C-means (FCM) clustering: FCM is also referred to as soft clustering; it is an unsupervised clustering algorithm that has been applied to a wide range of problems involving feature analysis, clustering and classifier designs. It is similar in structure to the K-means algorithm and also behaves in a similar way [95, 97] except that fuzzy behaviour is also considered. It is a clustering algorithm where each data point belongs to a cluster to a degree specified by a membership grade whereas traditional clustering algorithms assign each data point to one and only one cluster. It is a clustering method that allows one piece of data to belong to two or more clusters. It associates each element that represents a set of membership levels. Thus it creates the concept of fuzzy boundaries which is opposite from the traditional concept of well-defined boundaries. The algorithm is presented in several steps in Fig. 7.

Step 1: U=[u_{ij}] matrix is initialize, $U^{(0)}$
Step 2: At k-step: calculate the centre vectors $C^{(k)}=[c_j]$ with $U^{(k)}$
Step 3: Update $U^{(k)}$, $U^{(k+1)}$
Step 4: If || $U^{(k+1)}$ - $U^{(k)}$||< δ then STOP; otherwise return to the step 2,

where m is any real number greater than 1, u_{ij} is the degree of membership of x_i in the cluster j, x_i is the i^{th} of d-dimensional measured data, c_j is the d-dimension centre of the cluster, and ||*|| is any norm expressing the similarity between any measured data and the centre. The equation of the cluster centres c_j and the updated membership matrix function u_{ij} are given bellow:

$$c_j = \left(\sum_{i=1}^{N} u_{ij}^{m} . x_i\right) / \sum_{i=1}^{N} u_{ij}^{m} \qquad \text{and} \qquad u_{ij} = \frac{1}{\sum_{k=1}^{c} \left(\left\|x_i - c_j\right\| / \left\|x_i - c_k\right\|\right)^{2/(m-1)}}$$

Figure 7. Algorithm and steps of the FCM clustering technique are taken from [97]

3) *Gaussian mixer model:* It is an example of a generative model where data are presented by a calculated Gaussian Mixture distribution of data points. Each distribution represents a different cluster and during clustering it computes the expectation maximisation of a data point. It is associated with fitting a set of data and identifies a set of Gaussian distribution that presents the highest probability for the data. The data is fitted using an expected maximisation algorithm that assigns probability to each component based on individual observations. This probability is sometimes also called as membership score or rank. Each data point has a membership score of belonging to each cluster. It appears to solve many problems related to other clustering techniques and has been identifying as yielding a more stable cluster especially when the requested number of clusters changes. The details of the model and the basic algorithm can be found in [35].

4) Hierarchical clustering: The algorithm clusters data over a variety of scales by creating a hierarchical structure (tree) or dendrogram. The tree is not a single set of clusters, but rather a multilevel hierarchy, where clusters at one level are joined with clusters at the next level [21]. It is then further divided into two categories; bottom up i.e. agglomerative and the top down i.e. divisive clustering. This algorithm does not require any initialisation of centre points. To group the data together, a suitable proximity measure is used that estimates firstly the similarity between points and secondly the similarity between groups of points. It has several advantages, such as it starts with the number of clusters equal to the population of the initial data points then through an iterative process of grouping similar data points it finally ends up with a single cluster containing all the given data points. It makes it easy to catch the distance between clusters. If the agglomeration occurs between clusters at a greater distance than the previous agglomeration, one can decide whether to stop when the clusters are too far apart or when there is a sufficiently small number of clusters. However it is not very efficient when it comes to dealing with large data. To perform agglomerative hierarchical clustering on a data set the algorithm uses the following procedures:

1. It calculates the distance between every pair of objects in the data set in order to find similarity or dissimilarity.
2. It collects or groups the objects into a binary, hierarchical cluster tree. Here, pairs of objects that are close to each other are linked. Since all the objects are paired into the binary clusters, newly formed clusters are grouped to larger clusters until a hierarchical tree is formed.
3. It determines the cutting position of the hierarchical tree into clusters. Here, it prunes the branches off at the bottom of the hierarchical tree, and assigns all the objects below the cutting point to a single cluster.

In the hierarchical algorithm, the distance between pairs of objects is generally calculated using Euclidean distance. However, there are some other distance functions which can be used and available in MATLAB function ‘pdist’, such as Standardised Euclidean distance, cityblock, cosine, hamming , jaccard etc. Similarly, the linkage function applies ‘single’ (i.e. shortage distances) as a default parameter which determines the objects in the data set that should be grouped into clusters. However, other linkages can be used and available in MATLAB, such as average, centroid, complete etc. [35]. Finally, a cluster function is applied to group the sample data set into clusters where it specifies the cluster’s number.

Chapter 4.

Clinical Decision Support Systems

This chapter provides information about the approaches, methods and frameworks of multi-modal Clinical Decision Support Systems (CDSSs). Using Finger Temperature (FT) in the stress management domain, it describes how the multipurpose-oriented system performs complex tasks such as diagnosis, classification and treatment by combining CBR with other artificial intelligence techniques. The CDSS in the post-operative pain treatment domain is also discussed here where the approach shows how CBR is combined with a clustering-based approach.

HUMAN EXPERIENCE is a valuable asset and could be even more valuable if stored and reused in an efficient way. Clinicians/doctors have experience which may have been collected over many years. As an example, when a less experienced clinician is confronted with a new problem (for example symptoms that are not familiar) the clinician might start to analyse the whole situation and try to make a diagnosis by using their education and experience (with some solved cases). This may be a very time consuming task and may result in not finding a proper diagnosis. In that case the clinician needs to find other sources for help and a very common way is to ask senior colleagues who have more experience. A professional (more experienced clinician) might start to think to himself: "Have I ever faced any similar problem and in that case, what was that solution?" and refer the problem with their past solution to the less-experienced clinician. The less-experienced clinician then solves the problem and learns the new experience and saves it in their memory for future use. Thus a clinical experience can be shared and reused to make a quick and correct diagnosis in the domain of health care. Cases may also be hypothetical, e.g. hypothetical cases containing some rare/unusual symptoms and tests which could result in the wrong treatment with severe consequences. It is essential for staff to be alerted to such similar "negative" cases. Therefore, a computer-based system for experience reuse in health care would be valuable both for junior clinicians and as a second opinion for professionals.

4.1 CDSS in Stress Management

A difficult issue in stress management is to use a biomedical sensor signal in the diagnosis and treatment of stress. Clinicians often base their diagnosis and decisions on the manual inspection of signals such as, ECG, heart rate, finger temperature (FT) etc. However, the complexity associated with a manual analysis and interpretation of the signals makes it difficult even for experienced clinicians. A computer system, classifying the sensor signals is a valuable property to assist a clinician. Diagnosis and treatment of stress is such an example of a complex application domain. An important focus of this research is to develop tool based methods reducing stress to levels that are safe in the long term and thus improve the health of an individual. Moreover, diagnostic methods and techniques are important in order to adapt and personalise any health improving recommendations and exercises e.g. biofeedback treatment. The research interest lies in employing several AI techniques and methods to physiological time-series data for diagnosis, classification and treatment of stress. Case-Based Reasoning (CBR) is especially suitable for domains with a weak domain theory, i.e. when the domain is difficult to formalise and is empirical. The advantages of CBR in the medical domain have been identified in several other research works i.e. in [13, 37, 47, 73, and 82]. For some applications the integration of CBR and rule-based reasoning have been explored, e.g. in systems like [16, 69]. Cases comprising textual features or textual cases and introducing ontology into the CBR system, to get the advantages, are also implemented in systems such as in [68, 78]. The use of fuzzy logic in medical informatics began in the early 1970s. In fuzzy CBR, fuzzy sets are used in similarity measurement e.g. [15, 32, and 100].

The construction of multi-purposed and multi-modal medical systems is also becoming a hot topic in current applied CBR research, using a variety of different methods and techniques to meet the challenges from the medical domain. The research contribution through [PAPER A], presents some of the recent medical case-based reasoning systems alone with their classifications according to their functionality and development properties. It shows how a particular multi-purpose and multi-modal case-based reasoning system solves certain challenges in the medical domain. The research efforts in this direction can be demonstrated by Fig. 8 which presents the steps to develop a hybrid multi-purpose CBR system to support the diagnosis and treatment of stress-related disorders [PAPER B].

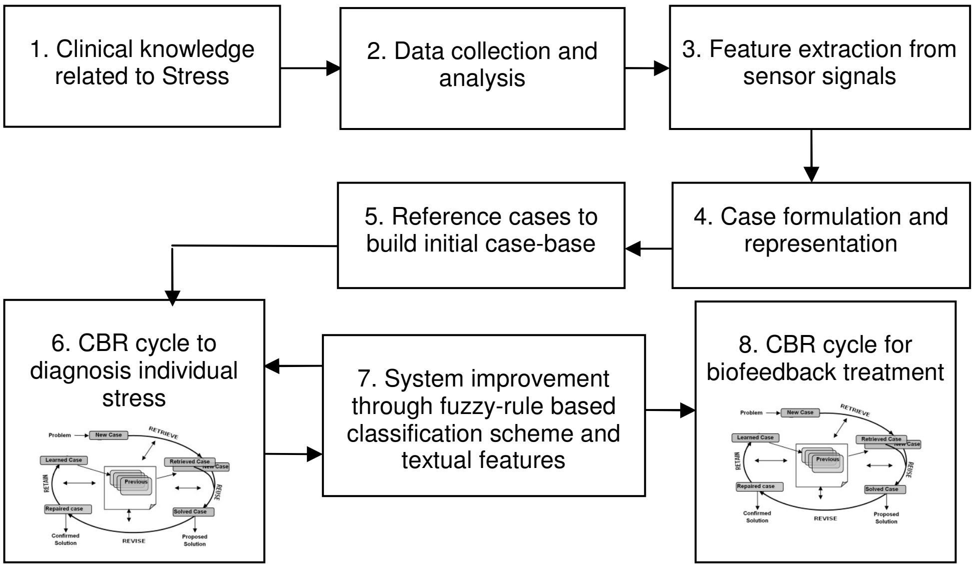

Figure 8. Schematic diagram of the stress management system.

Step 1: The signal employed in this research is finger temperature (FT) and clinical studies shows that the FT decreases with stress in general. This is one of the psychophysiological parameters clinically used to determine stress-related disorders [14]. Analysing/interpreting finger temperature and understanding large variations of measurements from diverse patients requires knowledge and experience. Without adequate support, erroneous judgments could be made by less experienced staff.

Steps 2 and 3: The measurements are collected from 46 subjects using a temperature sensor in six steps (i.e. Baseline, Deep-breath, Verbal-stress, Relax with positive thinking, Math-stress and Relax) in the calibration phase [7]. 12 women and 34 men within the age range of 24 to 51 participated in this experimental study [PAPER B]. The number of individual parameters identified and features extracted from the complex data format are briefly presented in section 4.1.1.1

Steps 4 and 5: A new problem case is formulated by the 19 features (17 extracted features from the signal and 2 other features) in total. The problem description part of a case contains a vector of the features extracted from the FT measurements and the solution part provides a level of stress. The levels of stress are denoted as Very Relaxed, Relaxed, Normal/Stable, Stressed and Very Stressed and the initial case base, with 68 reference cases from 46 subjects, is classified by a domain expert.

Step 6: To diagnose an individual's stress level [8], a new FT measurement (formulated as a problem case) is inputted into the CBR cycle. The new problem case is then matched using three different matching algorithms: 1) *modified distance* function, 2) *similarity matrix* and 3) *fuzzy similarity*. The Nearest Neighbour (NN) algorithm is applied for the retrieval of similar cases. A detailed evaluation of these three local similarities is conducted and presented in [PAPER B] and in [PAPER C]. Finally, the top ranking case or the case selected by a clinician will provide a classification of the FT measurement as output. A detailed description of the diagnosis of stress is presented in section 4.1.1.

Step 7: A fuzzy rule-based classification scheme [PAPER E] and textual information retrieval [PAPER C] are introduced to provide improved performance and increased reliability in diagnosing individual stress. Section 3.2 and 3.3 provide a detailed discussion about fuzzy rule-based classification and textual information retrieval.

Step 8: The last step in Fig 8 focuses on the CBR system in biofeedback treatment. A three phase CBR framework [PAPER D] is deployed to classify a patient, estimate initial parameters and to make recommendations for biofeedback training. A detailed description on the three phases is given in section 4.1.4

4.1.1 Diagnosis of Stress Levels with FT Sensor Signal

Stress influences the Sympathetic Nervous System (SNS). In general, the temperature of the finger decreases when a person is stressed and increases during relaxation or in a non-stressed situation.

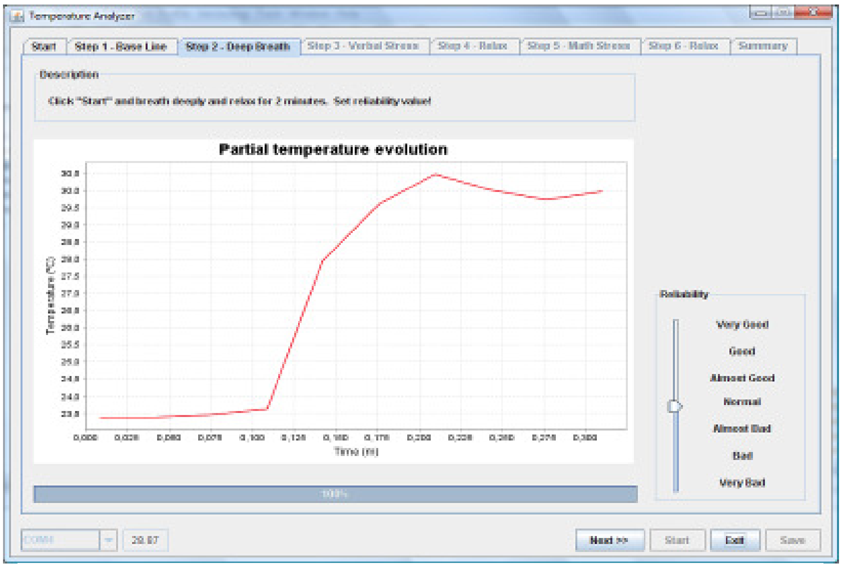

Figure 9. User interface to measure FT through the calibration phase.

A calibration phase [7] helps to establish an individual stress profile and is used as a standard protocol in the clinical environment. The protocol comprises different conditions in 6 steps, they are as follows: *baseline, deep breath, verbal stress, relax, math stress, and relax*. Fig. 9 demonstrates the user interface developed using the JAVA programming language to collect FT measurements with the conditions of each step. In this phase a number of individual parameters are identified to establish an individual stress profile. The *baseline* may be seen as indicating the representative level for the individual when they are neither under significant stress nor in a relaxed state. Clinicians let the person read a neutral text during this step. In the step *Deep-breath*, the person breaths deeply which under guidance normally causes a relaxed state. The step *Verbal-stress* is initiated by asking the individual to talk about some stressful events they experienced in life. During the second half of the step a person thinks about some negative stressful events in their life. In the *Relax* step, the person is instructed to think of something positive, either a moment in life when they were very happy or of a future event that they look forward to experiencing. The *Math-stress* step tests the person's reaction to directly induced stress by the clinician where the person is requested to count backwards. Finally, the *Relaxation* step tests if and how quickly the person recovers from stress.

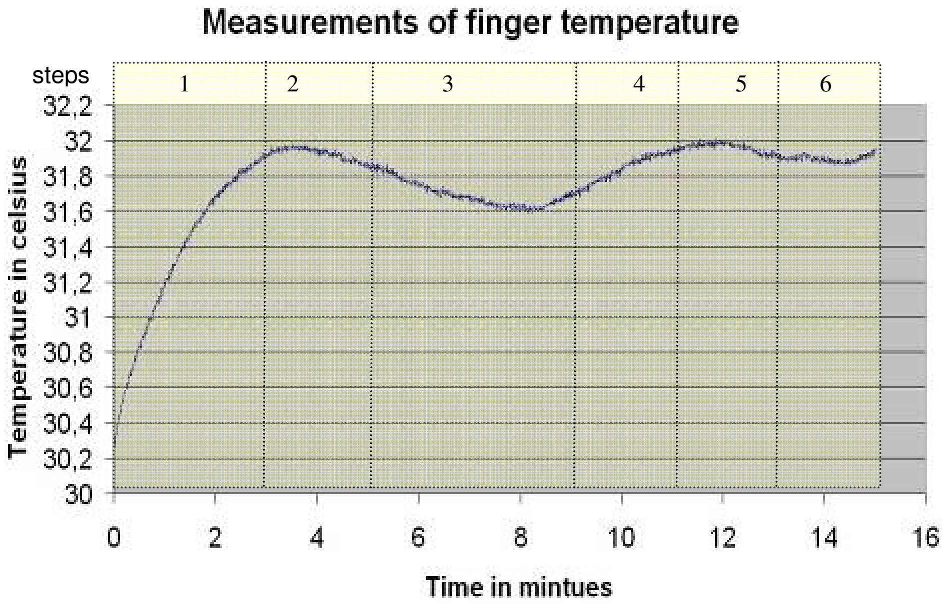

Figure 10. An example of a finger temperature measurement during the six different steps of a calibration phase. Y-axis: temperature in degree Celsius and X-axis: time in minutes. 1, 2, ..6 are six differences steps.

An example of the changes in finger temperature during the calibration phase is illustrated in Fig. 10. As mentioned earlier in this section, it can be observed from the figure that during step 3 in the *Verbal-stress* condition the finger temperature decreases, and it increases during step 4 i.e. in the *Relax* condition.

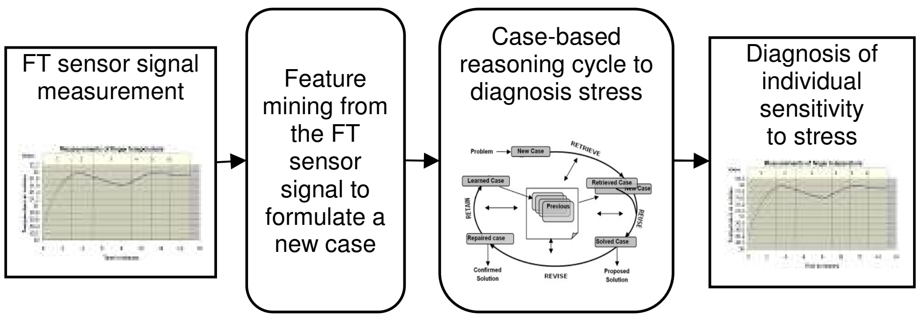

Figure 11. Schematic diagram of the steps in stress diagnosis.

The proposed computer-based stress diagnosis system uses CBR and fuzzy logic to assist in diagnostic and/or classification tasks. It performs several steps to diagnose an individual's sensitivity to stress as shown in Fig.11. The system consists of a thermistor, sensing the finger temperature [27]. The sensor is attached to a finger on the subject and is connected to an electronic circuit that is connected to a USB-port on a computer. The system takes the finger temperature measurement as an input and identifies essential features and formulates a new problem case with the extracted features in a vector. The feature extraction technique from the biomedical sensor signal is illustrated in the following subsection 4.1.1.1

CBR solves a new problem by applying previous experience adapted to the current situation [101]. Most of the CBR systems follow the reasoning cycle discussed in the earlier chapter with Retrieve, Reuse, Revise and Retain as shown in Fig. 2. A case represents a piece of knowledge and plays an important role in the reasoning process. This new problem case is then passed into the CBR cycle to *retrieve* the most similar cases. The case (feature vector extracted for FT signal) in this system is matched using three different matching algorithms. A *modified distance* function uses Euclidean distance to calculate the distance between the features of two cases. Hence, all the symbolic features are converted into numeric values before calculating the distance for example, for a feature 'gender' male is converted to one (1) and female is two (2). The function *similarity matrix* is represented as a table where the similarity value between two features is determined by a domain expert. For example, similarity in same gender (i.e. if both are male or female) is defined by 1 otherwise 0.5. In *fuzzy similarity*, a triangular membership function (*mf*) replaces a crisp value of the features for new and old cases with a membership grade of 1. In both the cases, the width of the membership function is fuzzified by 50% in each side. Fuzzy intersection is employed between the two fuzzy sets to get a new fuzzy set which represents the overlapping area between them.

$$sim(C_f, S_f) = s_f(m1, m2) = \max(om/m1, om/m2) \qquad (2)$$

Similarity between the old case (S_f) and the new case (C_f) is now calculated using equation 2 where *m1*, *m2* and *om* is the area of each fuzzy set. For the interested reader, an elaborated description of fuzzy similarity can be found through the research contributions in [PAPER-C].

Cases matching with current case **2008-11-12_11-12-45_erikO.xml**				
<< Previous Next >>				
Case	Percent	Evaluation	Times reviewed	Score
Case 15	71.8	very_stressed	0	0
Case 23	70.8	very_stressed	0	0
Case 9	70.4	very_stressed	0	0
Case 24	69.6	stressed	0	0
Case 4	65.8	very_stressed	0	0
Case 31	65.5	stressed	0	0
Case 35	62.8	normal	0	0
Case 27	57.5	very_stressed	0	0
Case 5	57	normal	4	3
Case 28	56.8	stressed	0	0
Case 7	56.7	normal	3	2
Case 32	56.3	stressed	0	0
Case 18	56	stressed	0	0
Case 13	53.5	normal	0	0
Case 17	52.2	stressed	0	0

Figure 12. The most similar cases presented in a ranked list with their solutions.

A similarity measurement is taken to assess the degree of matching and creates a ranked list containing the most similar cases retrieved according to equation 3.

$$Similarity\ (C,S)=\sum_{f=1}^{n} w_f * sim\,(C_f,S_f) \tag{3}$$

Where C is a current/target case, S is a stored case in the case base, w is a normalized weight defined by equation 4, n is the number of the attributes/features in each case, f is the index for an individual attribute/feature and $sim\ (C_f,\ S_f)$ is the local similarity function for attribute f in cases C and S.

$$w_f=\frac{lw_f}{\sum_{f=1}^{n} lw_f} \tag{4}$$

Here, a *Local weight (lw)* is defined by experts, assumed to be a quantity reflecting importance of the corresponding feature, *Normalised weight (w)* is calculated by equation 4.

Similarity matchings with current case **2008-11-12_11-12-45_erikO.xml**									
Attributes	Local weight	Normalized weight	Current case 43	Stored case 15	Similarity function	Weighted similarity	Stored case 23	Similarity function	Weighted similarity
Gender	5	0.03	F	M	0.5	0.01	M	0.5	0.01
Maximum temperature	10	0.06	23.99	24.61	0.987	0.06	24.84	0.983	0.06
Minimum temperature	10	0.06	23.18	24.24	0.978	0.06	24.58	0.971	0.06
Difference	10	0.06	0.81	0.37	0.627	0.04	0.26	0.486	0.03
Start temperature	10	0.06	24.98	25.24	0.995	0.06	25.49	0.99	0.06
End temperature	9	0.05	23.23	24.1	0.982	0.05	24.5	0.973	0.05
Hours since last meal	10	0.06	0	4	0	0	3	0.4	0.02
Before_after meal	0	0	unknown	unknown	1	0	unknown	1	0
Room temperature	0	0	0	0	1	0	0	1	0
Step1_part1	4	0.02	-9.858	-13.281	0.852	0.02	-16.843	0.738	0.02
Step1_part2	4	0.02	-7.704	-7.714	0.999	0.02	-13.823	0.716	0.02
Step1_part3	4	0.02	-4.101	-6.266	0.791	0.02	-9.112	0.621	0.01
Step1_reliability	0	0	8	5	0.769	0	5	0.769	0
Step2_part1	10	0.06	-9.786	-5.96	0.757	0.05	-8.936	0.955	0.06
Step2_part2	10	0.06	-8.825	-5.956	0.806	0.05	-8.04	0.953	0.06
Step2_reliability	0	0	6	5	0.909	0	5	0.909	0
Step3_part1	6	0.04	-5.804	-6.484	0.945	0.03	-6.228	0.965	0.03
Step3_part2	6	0.04	-6.553	-6.818	0.98	0.03	-5.898	0.947	0.03
Step3_part3	6	0.04	-8.102	-6.268	0.872	0.03	-6.2	0.867	0.03
Step3_part4	6	0.04	-5	-4.666	0.965	0.03	-5.43	0.959	0.03
Step3_reliability	0	0	5	5	1	0	5	1	0
Step4_part1	9	0.05	0.22	-3.961	0	0	-5.574	0	0
Step4_part2	9	0.05	-7.216	-4.591	0.778	0.04	-4.95	0.814	0.04
Step4_reliability	0	0	7	5	0.833	0	5	0.833	0
Step5_part1	6	0.04	-7.392	-5.901	0.888	0.03	9.369	0	0
Step5_part2	6	0.04	-6.427	-5.072	0.882	0.03	-4.41	0.814	0.03
Step5_reliability	0	0	8	5	0.769	0	5	0.769	0
Step6_part1	9	0.05	14.764	-4.816	0	0	-7.548	0	0
Step6_part2	9	0.05	-6.416	-4.037	0.772	0.04	-4.412	0.815	0.04
Step6_reliability	0	0	7	5	0.833	0	5	0.833	0
	Update				Global similarity case 15	**71.755**		Global similarity case 23	**70.78**

Figure 13. Comparison between a new problem case and the most similar cases.

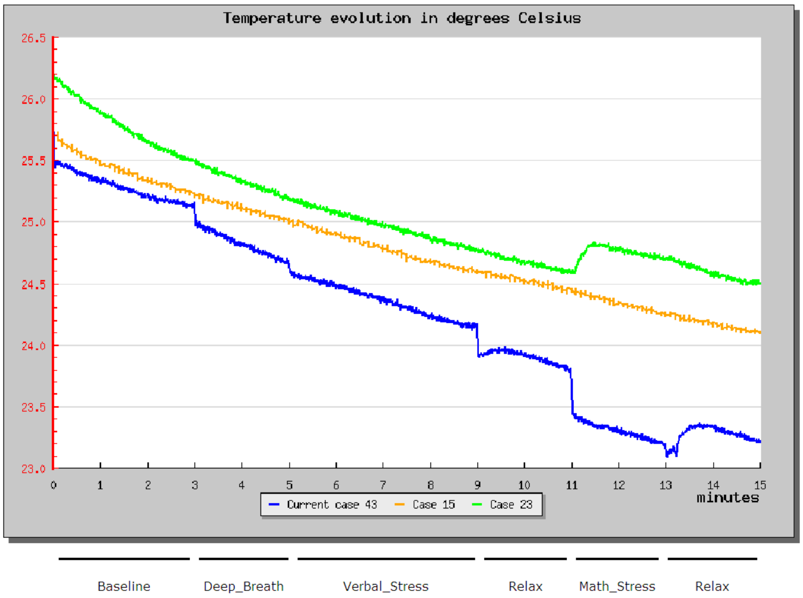

Figure 14. Comparison in FT measurements between a new problem case and old cases.

The system provides a matching outcome in a sorted list of the best matching cases i.e. a ranked list by the system for a current/new case matching all the other cases in the case base as shown in Fig 12. The CBR approach is developed using the PHP programming language and the case library is built in a MySQL database. A ranked list of cases is presented on the basis of their similarity value and identified classes. The solution for a retrieved old case i.e. the diagnosis and treatment recommendations are also displayed by the system. It also shows the number of times each case is reviewed by an expert as well as the number of times each case solution is used to solve a new problem as a score of the case. Moreover, by clicking a case id, the user can see detailed information of that case and a comparison between the new problem case and the selected case. A screen shot of such information is presented in Fig 13. It also provides a better visualisation of the comparison of FT measurement between a new case and an old case through a plotted line chart using the signals (see Fig 14). The user can apply different matching algorithms by selecting a specific method. Details information regarding the matching provides an opportunity to see the similarity between the cases (a current case and old cases) more clearly, which may assist clinicians/users to determine if a solution is reusable or requires an adaptation for the new problem. The example described in Fig 12, 13 and 14 shows the similarity matching of a current case (Case Id 43) with the previous cases (Case Id 15 and 23) in a ranked list. For the current case, the system establishes with 71.8% similarity that the patient is categorised under the *Very stressed* condition. Finally, as output, the top matching case is displayed which provides the classification of the individual stress level for the diagnosis of individual sensitivity to stress.

Clinicians can adapt solutions i.e. it could be a combination of two solutions from the list of the retrieved and ranked cases in order to adjust a solution to the current problem case. Then clinician/expert determines if it is a plausible solution to the problem and the solution can be modified before approval. Then the case is sent to the revision step where the solution is verified manually for correctness and presented as a confirmed solution to the new problem case. In the retention step, this new case with its verified solution can be added to the case base as new knowledge.

4.1.1.1 Feature Extraction from the Biomedical Sensor Signal

Clinicians normally observe the FT signal on a computer screen and analyses this signal manually, which is a very tedious task and often requires time and experience.

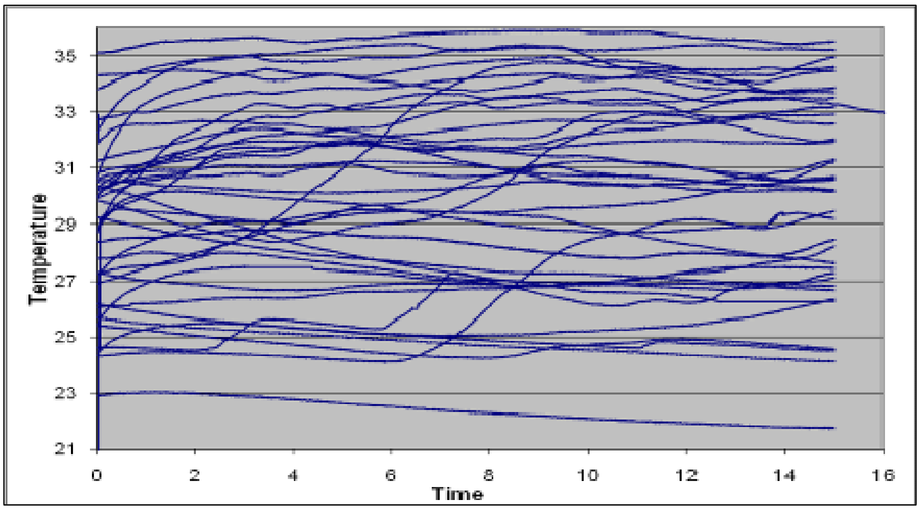

Figure 15. FT sensor signals measurement samples are plotted.

After analysing a number of finger temperature signals, a large individual variations was found, but also a similarity in the pattern that the temperature decreases during stress and increases during relaxation for most people. That is an important feature which needs to be identified by an automatic classification algorithm searching for "similar" patients. The variation of FT can be seen in Fig. 15 where 39 measurements are plotted in one chart. The indication of a person's stress might be found both from the low or high temperature signals. The different techniques applied to investigate the similarity between the signals are discussed below.

Point-to-point matching has been applied between two signals. But it shows some disadvantages in identifying similarity/differences for this kind of signal:

i. Each and every point needs to be calculated i.e. the difference between two cases can be achieved by calculating the difference for 1800 samples in our case. So the computational time is an important issue here.
ii. The similarity in pattern between two cases is not calculated. Let's consider this example, one case with 15 minutes of sample data where the finger temperature lies between 33^0 C and 35^0 C, with the same pattern considering another case where finger temperature lies between 24^0 C and 28^0 C is not similar according to their different temperature values. But they are similar in pattern.
iii. If the finger temperature for a new problem case lies at a higher level (e.g. 35^0 C) then the system will not consider any cases where finger temperature lies at a lower level (e.g. 23^0 C) and vice versa.
iv. This similarity method does not consider any variation in FT when calculating the difference between two cases, whereas the change in finger temperature is an important factor for classifying stress.

The mean value or standard deviation of the FT measurement may not be a clear indicator of stress. For instance, consider two signals, one is increasing from 20^0 C to 30^0 C, and the other is decreasing from 30^0C to 20^0C.Both have the same mean/standard deviation value in the duration, but indicate opposite stress levels. As an alternative, this research suggests that the mean of the slope value might be a feasible feature to convey a relation with stress. If the mean slope is sufficiently positive, it will be an indication of a relaxed state, otherwise an indication of stress. But if the mean slope is around zero, it shows a situation with high uncertainty for decision making or a weak decision.

We have applied case-based reasoning where two cases (i.e. signals) are matched depending on the feature values that define a case. An experienced clinician often classifies a FT signal manually without intentionally pointing out all the features used in the classification process. However, extracting appropriate features is of great importance when performing accurate classification in a CBR system. To determine important features the system uses 15 minute measurements (time, temperature) in 3600 samples, together with other numeric (i.e. age, room-temperature, hours since last meal, etc.) and symbolic measurements (i.e. gender, food and drink taken, sleep at night, etc.) parameters. According to closer discussion with clinicians, the derivative of each step of the FT measurement (from calibration phase) is used to introduce a "degree of changes" as an indication of the FT changes. A low angle value, e.g. zero or close to zero indicates no change or a stable finger temperature. A high positive angle value indicates a rising FT, while a negative angle, e.g. -20° indicates falling FT. The total signal, except the baseline, is divided into 12 parts each with a one minute time interval. A case is formulated with 19 features in total in which 17 features are extracted from the sensor signal (i.e. *Step2_Part1*, *Step2_Part2*, *Step3_Part1*, …, *Step6_Part1*, *Step6_Part2, start temperature*, *end temperature*, *minimum temperature*, *maximum temperature* and *difference between ceiling and floor*) and 2 are the human defined features (i.e. *sex*, *hours since last meal*). This new formulated case is then applied into a CBR cycle of the CDSS to assist with the diagnosis and treatment plan of stress.

4.1.2 Fuzzy Rule-Based Reasoning for Artificial Cases

The composition of a case library is one of the key factors that decide the ultimate performance of a CBR system. The cases stored in the case library should be both representative and comprehensive to cover a wide spectrum of possible situations. One of the limitations of CBR is that it depends on a case library; enough cases in a case library gives better results (with the purpose of accuracy) otherwise it may reduce the performance due to a lack of knowledge. Initially, when a system starts only with a small number of cases, the performance may be reduced so an algorithm that automatically classifies new cases would be valuable. Fuzzy rule-based reasoning is introduced into the CBR system to initiate the case library with artificial cases providing an improved performance in the stress diagnosis task. The details of this research effort are presented in [PAPER E]. In this research, the rules used in the classification process limit the number of cases in the matching procedure. Furthermore, a sharp distinction in the classification of individual sensitivity to stress may lead to misclassification. The system overcomes the problem by introducing fuzzy rules in the classification scheme. Instead of sharp distinction everything in fuzzy logic appears as a matter of some degree or degrees of truth.

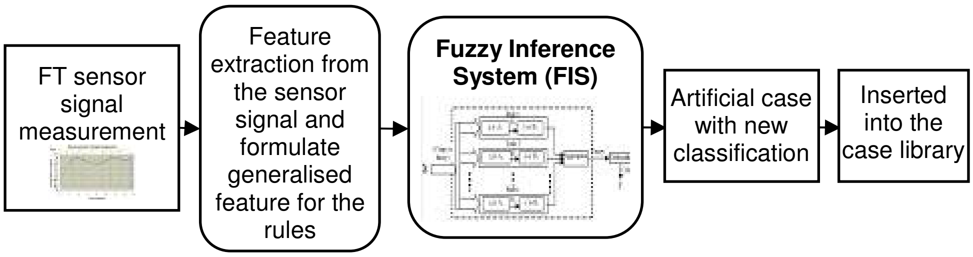

Figure 16. Steps to create artificial cases in a stress diagnosis system.

Fuzzy rule-based reasoning to create artificial cases functions as follows: 1) A FT sensor signal is measured through the calibration phase presented in the earlier section, 2) Features are extracted from the sensor reading and formulated into a generalised feature, 3) The generalised feature is then supplied into the Fuzzy Inference System (FIS) to classify a new case, 4) The output from the FIS is the new classification defined in a feature vector and, 5) Finally, this case is saved into the case library as an artificial case (See Fig. 16). The rules used in this classification process are defined by a domain expert and formulated with a generalised feature allowing sensor signal abstraction. A detailed description of these steps is presented as a research contribution in [PAPER E].

A single-input single-output Mamdani fuzzy model is implemented in which the percentage of a negative slope (feature) is considered as the input variable and the corresponding stress class as the output. The parameters of the IF–THEN rules (known as antecedents or premise in fuzzy modelling) define a fuzzy region of the input space, and the output parameters (known as consequent in fuzzy modelling) specify a corresponding output as shown in Table 3.

Table 3. Rules for the fuzzy inference system.

Fuzzy rules for classification
1. if **X** is *VeryHigh* then **Y** is *VeryStress* 2. if **X** is *High* then **Y** is *Stress* 3. if **X** is *Medium* then **Y** is *Normal/Stable* 4. if **X** is *Low* then **Y** is *Relax* 5. if **X** is *VeryLow* then **Y** is *VeryRelax*
X= Percentage_Negative_Slope, and Y= Stress_Condition

The crisp rules of these fuzzy rules are available in the included article [PAPER E]. Percentage_Negative_Slope and Stress_Condition are the linguistic variables with the universe of discourse {0, 100} and {1, 5} respectively. *VeryHigh*, *High*, *Medium*, *Low* and *VeryLow* are the linguistic values determined by the fuzzy sets "TriangleFuzzySet" with the universe of discourse of Percentage_Negative_slope. *VeryStress*, *Stress*, *Normal/Stable*, *Relax* and *VeryRelax* are the linguistic values determined by the fuzzy sets "SingletonFuzzySet" on the universe of discourse of Stress_Condition class. The basic structure of fuzzy logic expert systems, commonly known as a fuzzy inference system (FIS) is shown in Fig. 17.

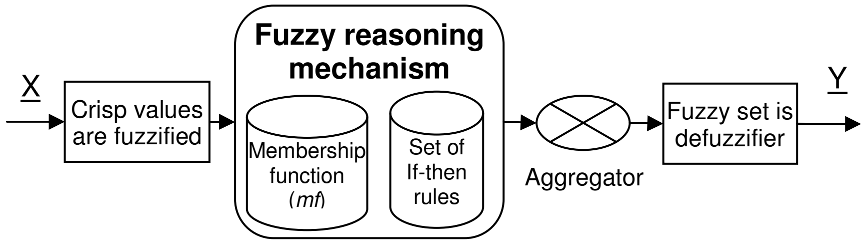

Figure 17. A block diagram of a fuzzy inference system [30].

A rule-based system consisting of three conceptual components: a rule base that consists of a collection of fuzzy IF–THEN rules; a database that defines the Membership Functions (*mf*) used in the fuzzy rules; and a reasoning mechanism that combines these rules into a mapping routine from the inputs to the outputs of a system to derive a reasonable conclusion as output. X is the crisp value inputted for fuzzificaiton. The fuzzy reasoning mechanism takes the fuzzified inputs and applies them to the antecedent part of the fuzzy rules. The value or firing strength from each rule represents the result of the antecedent's evaluation. After that this number is applied to generate consequent MFs. All the output MFs are combined into a single fuzzy set through the aggregator. Finally, defuzzification determines a crisp value from the output membership function as the solution which is Y.

4.1.3 Textual Information Retrieval

Unlike measurement-based experience, human perceptions are usually expressed in an informal and natural language format, and they are provided important information for diagnosis. Furthermore, contextual awareness is essential for decision support in diagnostics and treatment plans in the medical domain which is often conveyed in relevant notes or reports. Therefore, capturing perception-based experience coming from human observations and feelings and utilising contextual awareness in a medical CBR system can provide more reliable and effective experience reuse.

In fact, when diagnosing an individual's stress level, clinicians also consider other factors such as the patient's feelings, behaviour, social factors, working environment and lifestyle. Such information can be presented by a patient using a natural text format and a visual analogue scale. Thus, the textual data of patients capture important indications not contained in measurements and also provide useful supplementary information. Therefore, the system adds textual features in a case vector which helps to better interpret and understand the sensor readings and transfer valuable experience between clinicians [PAPER C]. To enable similarity matching on less structured cases containing text, this research contributes with a proposal which combines cosine similarity with synonyms and ontology. [PAPER C] presents a hybrid model that considers textual information besides FT sensor signal readings. For textual cases, the *tf-idf* (term frequency–inverse document frequency) [88] weighting scheme is used in a vector space model [87] together with cosine similarity to determine the similarity between two cases. Additional domain information that often improves results, i.e. a list of words and their synonyms or a dictionary provides comparable words and relationship within the words using classes and subclasses are also included. It uses domain specific ontology that represents specific knowledge, i.e. the relationship between words. The different steps in retrieval of similar cases in the system are described in Fig. 18.

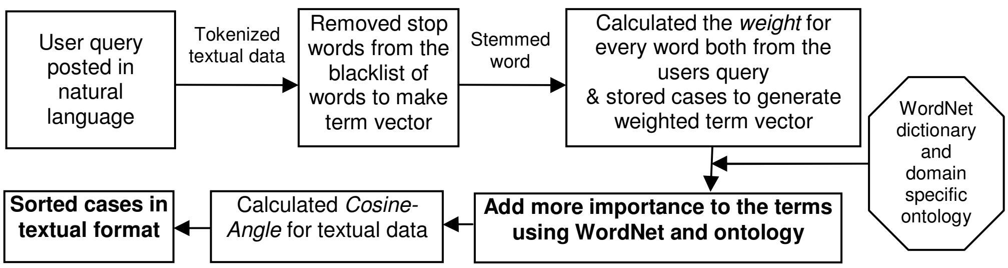

Figure 18. The different steps for case retrieval.

The text tokenize algorithm decomposes the textual information into sentences, and then into individual words. Due to a huge amount of words a filtering step is required to improve the retrieval efficiency. The following three steps are applied to extract important textual features:

1. Remove the stop-words and special characters, blacklisted from both the users' query and patients' record.
2. A list of synonyms of words is used to reduce the number of terms. The Porter stemming algorithm helps to stem the words and provide ways of finding morphological variants of a search term. After calculating a weight for each word, these words are represented as terms in a vector space.
3. Improve the importance assessments of candidate terms before measuring the cosine similarity value for the textual information between the stored case and user's query case by using domain specific ontology.

The *tf-idf* [88] weighting scheme is used for this system where the word "document" is treated as a case. The weight of a term is computed as a function $W_{i,j}$, that calculates the weight of each term or word in the stored cases and in the query case as illustrated in Equation 5. Here, $W_{i,j}$ is the weight of a term T_j in a case C_i, $tf_{i,j}$ is the frequency of a term T_j in a case C_i and idf_j is the inverse case frequency where N is the number of cases in a case library and df_j is the number of cases where term T_j occurs at least once.

$$W_{i,j} = tf_{i,j} * idf_j = tf_{i,j} * \log_2(\frac{N}{df_j}) \quad \textbf{(5)}$$

Equation 5 is modified slightly to give more emphasis to the terms, an adaptation of $tf_{i,j}$ based on the frequency of the instances in each case is computed in Equation 6 where $max_k(tf_{j,k})$ is the frequency of the most repeated instance tf_k in C.

$$tf_{i,j} = \frac{tf_{i,j}}{\max_k(tf_{j,k})} \quad \textbf{(6)}$$

In a traditional VSM model, term vectors are generated by ordering terms in a case vector according to their occurrence in the case i.e. by a normalised *tf-idf* score where synonyms or the relation of words are not used. However, the implemented system uses a WordNet dictionary to provide the necessary information about the relation by employing synonyms, hyponyms and hypernyms of words. Therefore, it is necessary to alter a term vector to a new vector. In this term vector, previous terms are re-weighted and/or new terms are added on the basis of different conditions. The function for re-weighting a term is shown in Equation 7.

$$W'_{i,j} = W_{i,j} + \sum_{sim(j,k) \geq T}^{j \neq k} W_{i,j}\, sim(j,k) \tag{7}$$

Where $W'_{i,j}$ is the new weighting function for a term *j* of a case vector *i,* adjusted by similar terms *k* within the same vector. *T* is a user defined threshold, we use *T*=0.8; that means each term in a vector will match with other terms in the same vector and the terms who have a similarity value more than 0.8 will be added by multiplying their original weight. The source term can obtain several related terms employing synonyms, hyponyms and hypernyms which means a term can be related with other terms that already exist in the case term vector. Now all the terms with a similarity value greater than a threshold value (*T=0.9*) will be considered as new terms and are added to the case term vector. These new terms are then weighted according to the similarity values of the terms in the case vector. If a related term already exists in the vector then only the similarity value of that term will be added with the original weight of the source term. Thus, the system identifies and gives higher preferences to these key terms compared to other terms in order to match a source case with query cases.

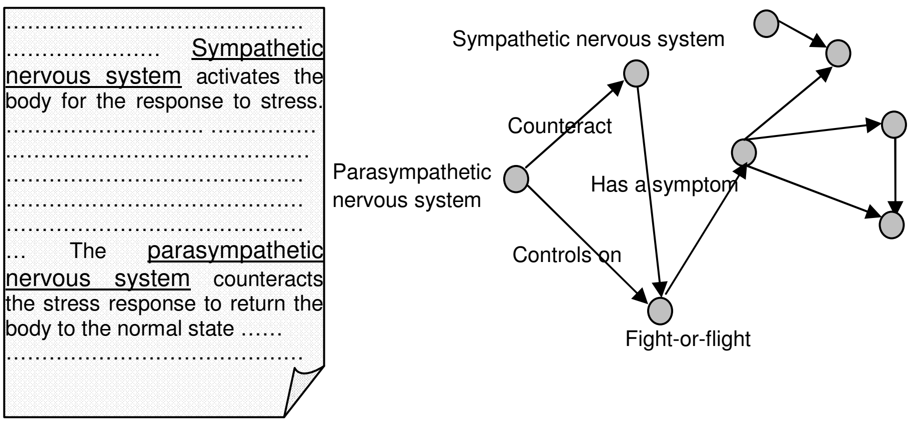

Figure 19. Weighting the term vector using ontology.

A domain specific ontology or user defined ontology represents specific domain knowledge, i.e. the relation between words. The terms of a case can be compared with other cases by exact matching or synonym matching or using a co-occurrence. However, some words or terms can have a complex relationship (for example, the term “sympathetic nervous system” and “parasympathetic nervous system”), the weight of such terms can be increased automatically using a domain specific ontology defined by an expert. An example is shown in Fig. 19 of how the ontology helps to improve the weight vector.

From Fig. 19 "sympathetic nervous system" is a term that appears both in the case text and in the ontology. It also has a relation with another term "fight-or-flight" in the ontology but the term does not exist in the case text, so the term "fight-or-flight" is important for this case. Again the term "parasympathetic nervous system" and "sympathetic nervous system" both already exist in the case text and has a relation to the ontology, so the value of the strength of their relationship for those two terms will increase the weights of their importance. The terms "parasympathetic nervous system" and "sympathetic nervous system" are related with another term "fight-or-flight" in the ontology so the term "fight-or-flight" will receive greater importance.

The similarity between the stored case vector C_i and a new case as a query vector Q is calculated using a cosine similarity function [41, 87, and 104] where the cases deal with textual information. This ratio is defined as the cosine of the angle between the vectors, within the values between 0 and 1 and can be calculated by Equation 8.

$$Cos\theta_{C_i} = Sim(Q, C_i) = \frac{Q \bullet C_i}{\|Q\|\|C_i\|} = \frac{\sum_j w_{q,j} w_{i,j}}{\sqrt{\sum_j w_{q,j}^2}\sqrt{\sum_j w_{i,j}^2}} \tag{8}$$

Where $Cos\theta_{C_i}$ is the *cosine of the angle* between a stored case and query case which is defined as the similarity function *Sim(Q, C$_i$)*. The dot product of a stored case and a query case is $Q^{\bullet}C_i$ where the zero products are ignored; and $w_{i,j}$ and $w_{q,j}$ are the weight of vector length.

4.1.4 Biofeedback Treatment

The basis of a biofeedback system is that a patient gets feedback in a clear way (a patient observes a graph and knows from prior education how it should change). The feedback can behaviourally train the body and mind in a better way with a biological response. After discussions with clinicians it can be seen that most of the sensor-based biofeedback applications comprise of three phases illustrated in Fig. 20, 1) analyse and classify a patient and make a risk assessment, 2) determine individual levels and parameters, and finally 3) adapt and start the biofeedback training. If the clinician only uses sensor readings shown on a screen then the classification is highly experience-based. [PAPER D] addresses this issue through the research contribution added in part 2 (included in the paper section) of this thesis.

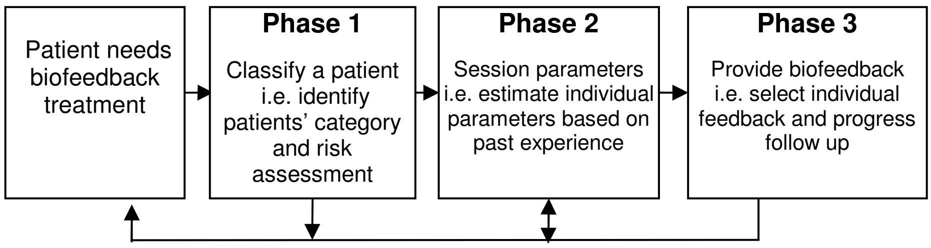

Figure 20. General architecture of a three-phase biofeedback system.

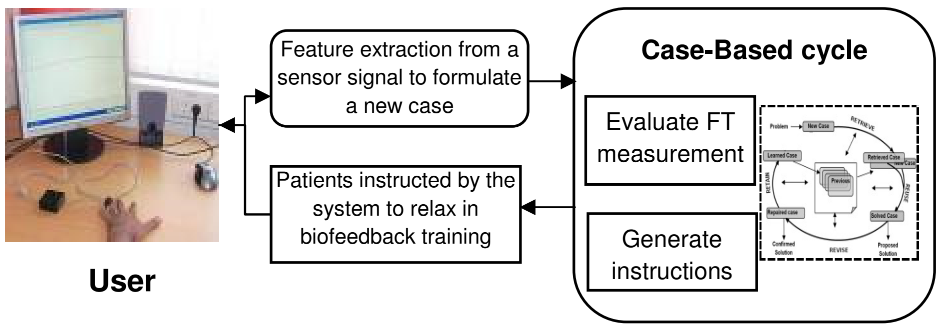

Figure 21. A schematic diagram of the steps in the biofeedback treatment cycle.

In this cycle shown in Fig. 21, a user connects a sensor to their finger and can see the changes of FT during several instructions in relaxation training. The FT measurements are performed in real time and every 2 minutes the system evaluates the last 2 minutes measurement and if necessary generates instructions for the patient. A CBR cycle is applied for the biofeedback training in stress management; this training time is flexible, which means a patient can choose the duration of their training between 6 minutes (as minimum) to 20 minutes (as maximum). Nevertheless, the system generates feedback with appropriate suggestions after every 2 minutes if necessary. Thus, for each individual, the biofeedback cases are formulated with a feature vector from a biomedical signal (i.e. with 2 minutes FT measurement) in the conditional part and a suggestion for relaxation in the solution part. A new biofeedback case is compared to previously solved cases applying a fuzzy similarity matching algorithm and displays the outcome as feedback. Here, the feedback is defined with a pair i.e. it presents an evaluation of the FT measurement and a recommendation for the next training. This generated feedback is then presented to a clinician as a proposed solution. The clinician thereafter reviews the proposed cases and takes a final decision to suggest a treatment to the patient. Thus the system assists a clinician, as a second option, to improve the patient's physical and psychological condition.

4.2 CDSS in Post-Operative Pain Treatment

Approximately 40 million patients are undergoing minor to major surgical operations every year in Europe[2]. At least half of these patients from children to elderly suffered with a moderate or severe amount of post-operative pain. The degree of post-operative pain differs for various patients depending on operation site and the type of operation. For example, an operation of the thorax and upper abdomen are more painful than the lower abdomen. Pain is considered to be an obstacle of recovery and also requires significant health care resources to manage. A number of factors such as clinical, local and patient-related questions are asked to the patient by the healthcare provider before and after the operation to decide on a proper treatment plan in pain relief. In practice, the clinician makes a pain treatment plan using guidelines (follows a standard protocol) and an evidence-based approach before the operation and observations afterwards. However, approximate 30% of the population does not conform to recommended procedures due to individual factors and unusual or exceptional clinical situations. Physicians might have experience with unusual or exceptional situations but may not remember them at the point of care due to large amounts of regular situations. Thus, the quality improvement of individual postoperative-pain treatment has become an important issue. A computer-aided intelligent Decision Support System (DSS) that generates alarms by presenting both regular and rare situations is by many physicians seen as a beneficial tool in their decision making tasks in post-operative pain treatment (according to informal discussions with physicians in the Pain-out project).

Human experience is a valuable asset and could be even more valuable if stored and reused in an efficient way. Physicians have experience collected over

[2] http://pain-out.med.uni-jena.de/index.php/about-pain-out/research

many years of both successful solutions as well as unsuccessful solutions. This opens up new possibilities for experience reuse. The aim of this research is to investigate how to develop a dynamic computer-based system that can act as an “intelligent” Clinical Decision Support System (CDSS) for experience reuse in post-operative pain treatment. The system can be described as “intelligent” as it not only retrieves the latest innovative clinical findings on patient healthcare but also identifies and retrieves cases, knowledge, expertise and statistics directly relevant for the patient at hand. This will help physicians and care givers to make more informed decisions and provide better care, reduce healthcare costs and effectively disseminate latest clinical results, comments and findings. The problems are addressed as below:

1. Traditional computer-based methods do not adequately enable experience reuse, dynamic performance improvement and efficient decision support in post-operative pain treatment.
2. Today, there is no system designed for post-operative pain treatment that identifies rare (i.e. exceptional and unusual) cases in order to enable experience reuse for the clinicians.

The research focuses on the development of a computer-based system that is able to address current problems faced by the healthcare industry by using CBR, knowledge discovery (i.e. clustering) and identification of rare cases. Therefore, the system combines case-based retrieval with knowledge discovery in terms of clustering and outlier detection in order to enable experience reuse by identifying rare cases. One of the advantages of Case-Based Reasoning (CBR) is that it facilitates experience reuse by retrieving similar cases and reuses the previous solutions to solve a current situation so it is worth applying CBR for implementing such an intelligent DSS for post-operative pain treatment where experience reuse is an important issue.

4.2.1 Vision and Overview of the System

Experience can be represented as a contextualised piece of knowledge in a case. A case can be constructed in traditional ways with symptoms and a solution (treatment) and added outcome (recovery success) in an innovative way (discussed in [PAPER F]).

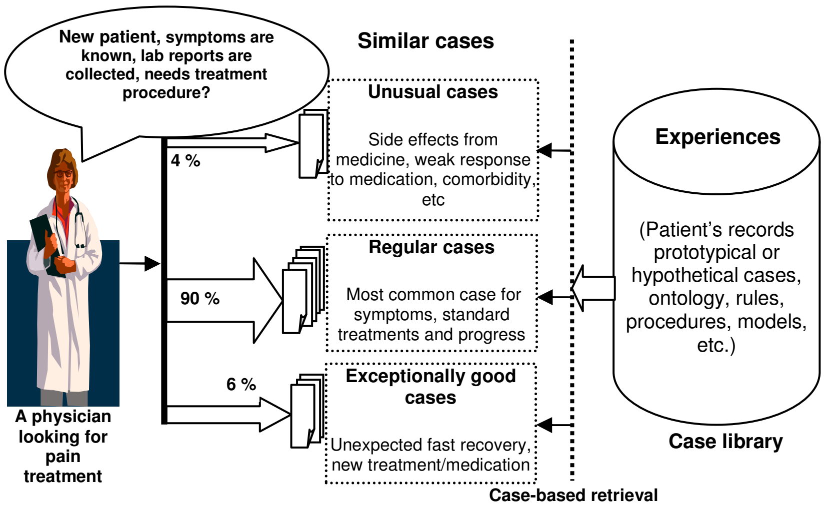

Figure 22. An example of an experience reusing system.

In this article cases that do not follow any standard protocol are regarded as outliers and classified in the "rare case" group. The "rare case" group contains exceptionally good cases and/or unusually bad cases. In the medical domain, these relatively rare cases can be particularly valued for their uncommonness and more interesting than frequently occurring ones (e.g. meningitis is a comparatively rare case often with similar symptoms as flu). Fig. 22 illustrates a scenario of the experience reuse in the context of medical (both regular and rare) cases using the system.

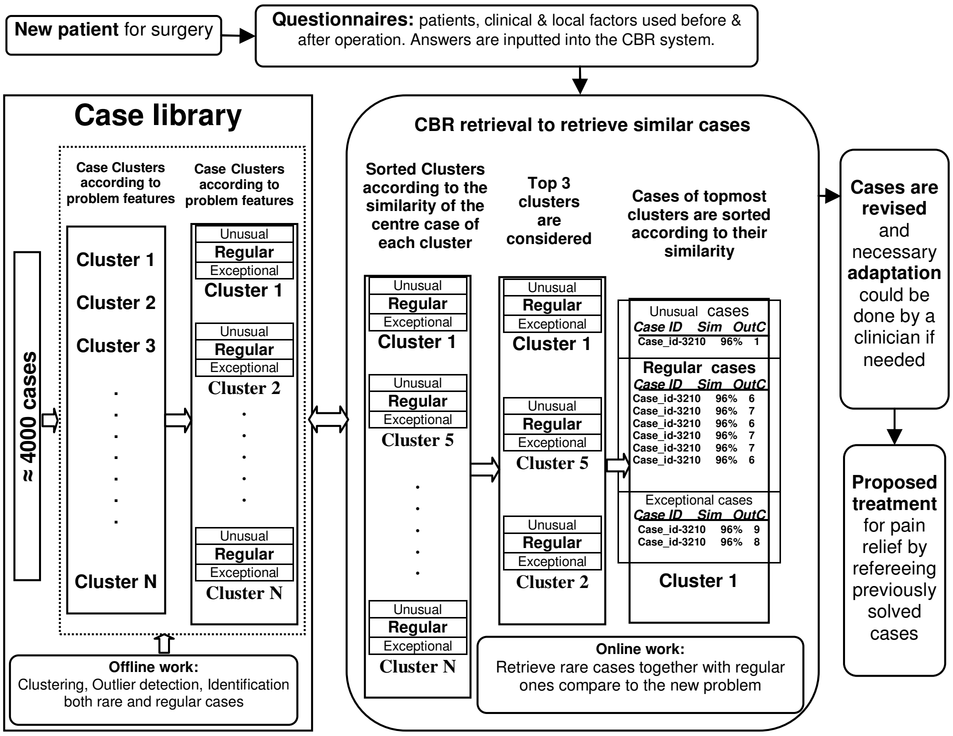

Figure 23. Schematic diagram of the system's work flow

When a physician is presented with a new patient they might start to analyse the whole situation according to different symptoms and lab reports. Here, to diagnose the source of the disease, the physician uses the experience reusing system. The system applies CBR with thousands of real patient cases as experiences. It provides similar cases e.g., regular, and/or rare (i.e., exceptional and/or unusual cases) compared to the situation (i.e. symptoms and lab reports) for the new patient. As an example, in Fig. 22, the physician finds 90% of the regular cases with treatment and outcome (a new structure is used in post-operative pain treatment) similar to the new problem. However, 10% of the similar cases are presented as rare, some cases among them have severe outcomes (i.e. 4%) and defined as unusual, on the other hand some have a (6%) better outcome than expected (may use a new medication) and are presented as exceptional cases. Thus, the information presented by the system will assists a physician to make a more informed decision for the patient. It also helps to take into account the experience from rare cases and situations while making decisions on pain treatment. Therefore, the CDSS using CBR approach with a case-library containing both regular and rare cases will support a physician in experience reuse for post-operative pain treatment. As a consequence, it will provide better healthcare by generating alarms to raise awareness and assist in decision making tasks.

A clinician confronted with an unknown case may be able to save the patient's life by remembering just one similar case and what was done to cure the patient. In this post-operative pain treatment context, it could be assumed that there may be some patients with rare conditions who have been treated successfully outside any standard protocol. The detailed information of such patients can be created as a case and these cases are then collected and stored to build a case library. A case is represented with a feature vector in the conditional part where the patient's contextual information, habits, site and nature of the surgery are considered. The solution part of the case consists of prescribed medication, and the outcome part of the case could contain pain assessment in a Numerical Visual Analog Scale (NVAS). The outcome explains the intention of using the solution and the potentiality of the solution to solve the problem. The retrieval step of the CBR cycle [1] can retrieve the best matching cases (rare and regular cases) with solutions and outcomes from the case library. A schematic diagram of the proposed system is illustrated in Fig. 23. The three main components of the proposed decision support system are:

1. A library for knowledge and methods: a case library which contain around 4000 records of previous cases where all the cases are clustered off-line. The clustering has been conducted in 2 steps; firstly cases are clustered according to their problem description, and secondly each clustered case is clustered again according to their outcome.
2. An inference engine: CBR retrieval: an inference engine that employs the reasoning methodology to retrieves similar cases. In this system, the retrieval mechanism is conducted in two steps, firstly a new problem case will be compared with the center case of each cluster and the clusters are sorted accordingly, and then the top 3 clusters are considered for final comparison. Here, all the cases from the top most clusters are compared with the new one and sorted according to their similarity values.
3. An efficient and interactive user interface: provide a friendly 'look and feel' user interface for the doctors to revise, reuse and retain a case.

The design detail of the system starts during the admission of a surgical patient in a clinic, where the patient's general, contextual, surgical, and habitual information is collected. This information is used in CBR systems to formulate a new problem case and to represent cases in the case library. In this CBR system, a new problem case is matched with selected cases from the case library and depends on the most similar clusters. The following tasks could be performed to implement the case-based system:

- Given a new problem case (new patient), the system will measure its similarity by comparing the feature vectors of a new problem case and center cases from each cluster, then sort the clusters accordingly. Finally, the system will retrieve similar cases from similar clusters in order to select the proper medication for a new patient.
- The physician could see regular and rare cases (i.e., exceptional and unusual cases) close to the new case to make a decision. The physician might reuse the same treatment or could revise the cases to adapt previous solutions to the new patient and advise on patient-specific medication for treatment.
- The physician could save the new problem case with the solution i.e. prescribed treatment and outcome as new knowledge for future use.

4.2.2 Identification of Rare Cases by means of clustering

Rare cases are often interesting for health professionals, physicians, researchers and clinicians in order to reuse experience in professional healthcare systems. In the medical domain, identifying relatively rare diseases, for instance, breast cancer for a male patient is one typical example where a rare case is interesting and critical than a more frequently occurring one. A common case belongs to a region in any search space where the characteristics and/or features of the cases are somewhat similar and provide significance with respect to any domain. A rare case is a case that covers a small region or may belong to several outliers of the research space, relatively few in number and different from the common characteristics. A traditional example is, an ostrich or penguin are non-flying bird which can be classified as rare cases with respect to the class 'birds', since very few birds do not fly.

In fact, finding rare cases is a difficult problem and especially true in the context of case mining, where one often wants to uncover subtle patterns that may be hidden in massive amounts of data. So, there is a need to develop mechanisms to identify these rare cases. One common and easy way is to cluster all the cases in a case library and then identify the rare cases. In this system, the rare case identification is done offline in two steps: 1) all cases in the case library are clustered using a Fuzzy C-Means Clustering (FCM) algorithm and 2) the cases from each cluster are again grouped by applying the Hierarchical algorithm. Fig. 24. illustrates the steps that are taken into consideration while searching the rare cases.

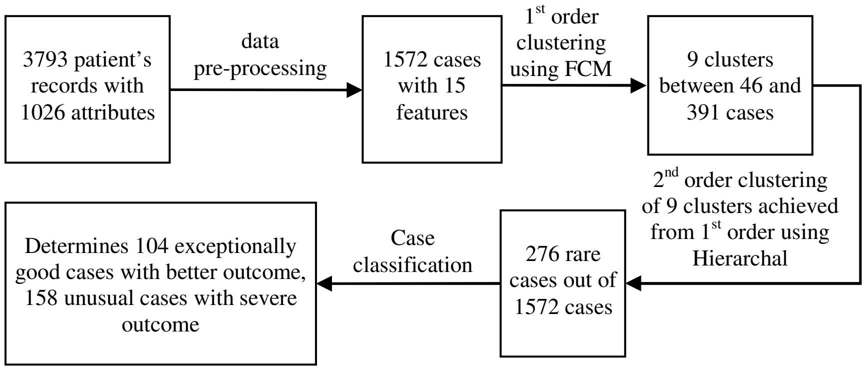

Figure 24. Steps of the approach in order to identify rare cases.

A data pre-processing step including feature abstraction step is performed on the 3793 records of post-operative pain patients. In total 1572 cases with 17 features (1 for case ID, 15 for *problems* and 1 for *outcomes*) are obtained after the data preprocessing step and is discussed in [PAPER G]. However, only 15 features in the *problems* part of the cases were used in clustering. All the clustering algorithms and the user interface to identify rare cases are developed in MATLAB and applied MATLAB build-in clustering functions.

The 1st order clustering has been done using a FCM algorithm on the *problems* part of the cases. The detailed FCM method is presented in [PAPER G] and in [CHAPTER 3]. FCM is applied as a multi-variant clustering where 15 features are involved excluding ID. The main goal of this stage is partitioning, i.e. all the cases should be divided into several small groups with a similar frequency. Here, the percentage of average variance (i.e. the algorithm runs 10 times for each k) is used as a function to determine the number of clusters. The lowest percentage of average variance is achieved when the number of clusters is 9. The detailed information is presented in [PAPER G].

In the 2nd order, these 9 clusters are used and the Hierarchical clustering algorithm is applied in each cluster. The details of the algorithm are presented in [PAPER G] and in [CHAPTER 3]. In Hierarchical clustering, the distance between pairs of objects is calculated using Euclidean distance as a default parameter of the MATLAB function 'pdist'. The linkage function applies 'single' (i.e. shortage distance) as a default parameter which determines the objects in the data set that should be grouped into clusters. Finally, a cluster function is applied to group the sample data set into clusters by specifying the cluster's number. Here, the cluster's number is determined by observing the percentage of the case frequency. That is, the algorithm continues its iteration by increasing the number of clusters as long as at least two clusters obtained more than 10% of whole cases. Then, the clusters with small sizes (i.e. less than 10 %) are selected as the rare case cluster and thus the approach has achieved 17.60% (i.e. 276 out of 1572) as rare cases.

The last step in Fig. 23, determines the 232 cases whether they are *exceptionally* good (0-3.9) or *unusual* bad (6-10) according to the pain outcome (the threshold for good/bad may be changed). The attribute outcome is the average value of the pain measurement for each case. A clinician may be most interested in the extreme cases first (0/10) when looking for similar cases among the rare cases. Thus, the approach obtained 158 cases as unusually bad and 104 cases as exceptionally good. Only 14 cases with the outcome value between 4 and 5 exist among the set of rare cases.

4.2.3 Case-Based Decision Support System

A case-based system mainly depends on cases, their types and how they should be represented. The case comprises unique features to describe a problem. Cases can be presented in different ways; in the post-operative pain treatment application domain the case structure contains three parts: 1) problem, 2) solution and 3) outcome. The cases could be defined differently on the basis of their use, manner and nature. Different DSSs might have different requirements on which type of cases are to be handled. For this project we have proposed different types of cases namely regular cases and rare cases which is a more user-friendly format for physicians. Further, these cases are also authorised and tagged by the case owner. A short description of the different types of cases used in the system is presented in [PAPER F]. As the cases in this project are formulated in three parts, the 'problem description' part contains around 278 attributes, and 'treatment' as a solution consists of 685 attributes, while ‘outcome’ as a recovery measure has 19 attributes. However, to formulate a case, feature abstraction has been done only considering the problem description and outcome information, which has been further mapped with the solution. So, out of 278 attributes only 15 features are extructed in the *problem* part and only 1 from 19 attributes were extracted from the *outcome* part. Deatailed information about feature abastruction is presented in [PAPER F]. Note that, the solution part of the cases remains unchanged since this data contains important medicine information which might modify during abstraction.

Retrieval is essential in medical applications since missed similar cases may lead to less informed decisions. Two of the factors which the reliability and accuracy of the system depends on are: 1) which cases are stored in the case library i.e. quality of the cases; 2) the retrieval of the relevant cases and their ranking. In this CBR system, similarity measurements are used to assess the degrees of matching by applying the standard Nearest Neighbour method as a global similarity algorithm. However, the similarity calculation has been done in two steps:

- Step 1: a new problem case is compared with the centre case of each cluster (note, all the clustering and outlier detection has been made on offline) and all the clusters are then sorted according to their similarity value.
- Step 2: the new problem case is compared again with all the cases belonging to each cluster. Hence, the system only considers the top three nearest clusters to the new problem case.

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All cases stored in the database

ID	D12aText	Outcome
321	dekompression	2.37
382	partial gastrectomy with bypass gastrogastrostomy	5.68
402	anterior resection of rectum	3.17
423	total hip replacement	7.17
425	pfn gamma nail	5.17
426	hemrrhoidectomy	1.72
461	fundoplication	2.71
462	laparoscopic resection of rectum	5.00
463	revision of ileostomy	3.63
466	total laparoscopic cholecystectomy	4.82
467	femoropliteal bypass	2.61
468	aspiration of skin and subcutaneous tissue	2.79
481	partial hepatectomy	4.35
502	unilateral repair of femoral hernia with graft	2.67
521	total laparoscopic cholecystectomy	4.33
522	total laparoscopic cholecystectomy	3.44
527	excision of hemorrhoids	6.00
529	other open incisional hernia repair with graft or prothesis	4.78
531	total laparoscopic cholecystectomy	1.16

Figure 25. A screen shot of the DSS presents all stored cases with pain outcomes.

The CBR retrieval approach was developed using the PHP programming language and the case library was built using a MySQL database. In Fig. 25, a screen shot of the DSS presents all stored cases from the case library along with their average outcome. Two cases are compared using different local similarity algorithms including *modified distance function*; *similarity matrix* and *fuzzy similarity matching* [8] [PAPER C]. The local weight defined by the case author or owner for each stored case, is assumed to be a quantity reflecting the importance of the corresponding feature individually. The reason to use individual case weighting is to combine several clinicians and experts knowledge into the system. The average weight of each feature and user defined threshold are presented in Fig. 26.

Weight feature description

IDs	Feature Names	Weights
s1	inclusion_criteria	7
d6	language	4
s2	sleep_or_sedation_level	4
d1	gender	6
d3	weight	7
d2	age	7
d8	comorbidities	8
d9	existing_state	3
d10	chronic_pain	5
d11	opioid_before_admission	6
m1	pre-medication	8
m2	non-opioids_pre-medication	4
m3	opioids_pre-medication	6
d12	number_of_surgical_procedure	7
d12a	major_surgical_procedure	3
thc	threshold	50
cls	cluster_numbers	9
nuc	number_of_cases	20
thclu	threshold_cluster	40

Figure 26. A screen shot of the DSS presenting features and average weight of the stored cases in the case library.

The verification of the proposed approach performed in a prototypical system involves a close collaboration with doctors, nurses and clinics. The performance of the matching function in CBR is verified by whether the system can retrieve best similar cases with suitable solutions to provide proper treatment for a new case. The most similar cases are compared to a new problem case are retrieved and presented in 9 different clusters as shown in Fig. 27.

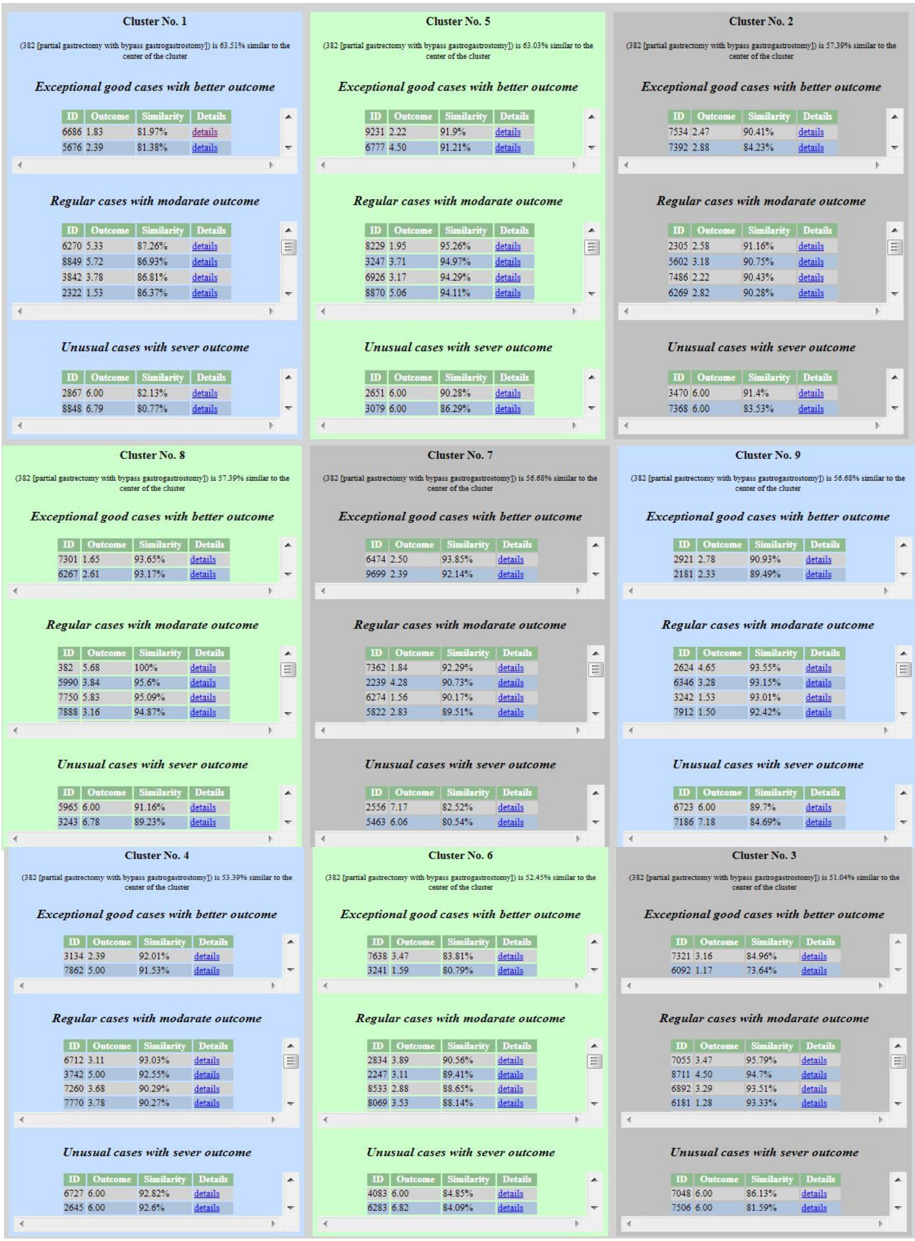

Figure 27. A screen shot of the CBR system presenting the most similar cases both with rare cases (exceptional and/or unusual) and regular outcomes in different clusters.

Here, cases are presented in different clusters based on the problem description and outcome. A case outcome has a value between 0 and 10, where "0" defines no pain at all and "10" defines severe pain. Note that, in the domain of post-operative pain treatment, similar solutions have different outcomes.

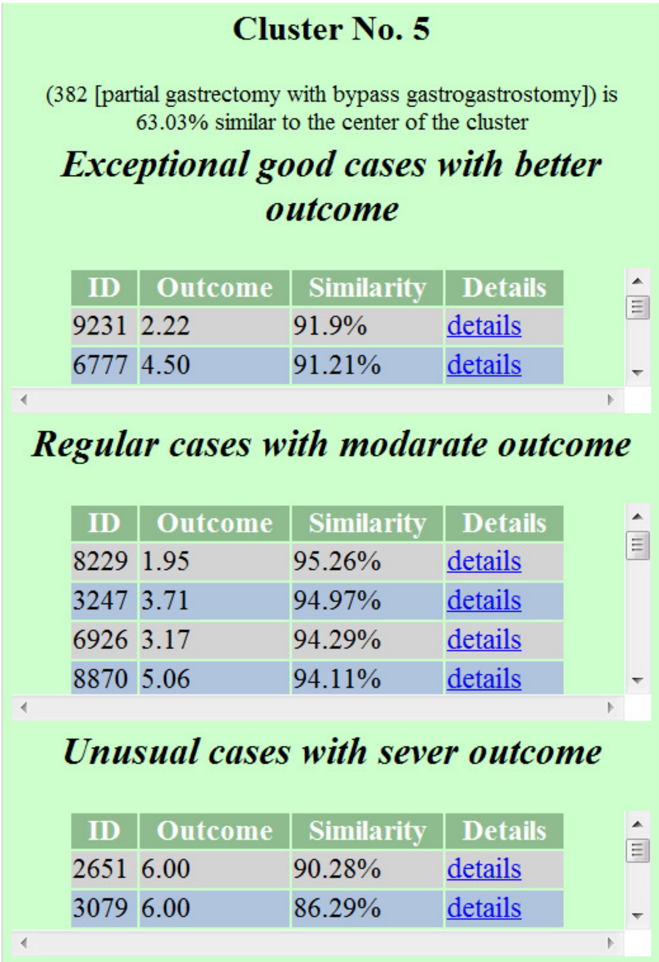

Figure 28. A screen shot of Cluster 5, where most similar cases are presented both in rare and regular.

For example, cases in cluster 5 (in Fig. 28) are presented as rare (exceptional and unusual) and regular cases based on the case outcome. A doctor can look at the details and revise the case and thereafter make the decision. Thus, the doctor can reuse the solution from the previous case or may adjust a new solution for the pain treatment. This new problem case, the associated solution and the outcome in 24 hours could be stored in the case base for further use.

15
source: (382) partial gastrectomy with bypass gastrogastrostomy
target: (6777) laparoscopic excision of retroperitoneal tumor

feature	source	target	sim	wight	norm_w	sim*norm_w
S1	0.60	0.60	100	7	0.08	8.24
S2	1	1	100	4	0.05	4.71
D1	1	1	100	6	0.07	7.06
D2	33	25	75.76	7	0.08	6.24
D3	102	80	78.43	7	0.08	6.46
D6	1	1	100	4	0.05	4.71
D8	1	1	100	8	0.09	9.41
D9	0	0	100	3	0.04	3.53
D10	0	0	100	5	0.06	5.88
D11	0	0	100	6	0.07	7.06
M1	1	1	100	8	0.09	9.41
M2	0	0	100	4	0.05	4.71
M3	0	0	100	6	0.07	7.06
D12	2	1	50	7	0.08	4.12
D12a	4389	5900	74.39	3	0.04	2.63
Total				**85~85**		**91.23**

Figure 29. A screen shot of the DSS presents the overall similarity calculation between two cases.

In Fig. 29, the overall calculations for similarity measurement of two cases are presented, where cases are 'source' i.e. stored case (id=382) from the case library and 'target' i.e. a new problem case that needs to be solved. Here, the weight of each feature is determined by calculating the average of all the weights of that feature and the weights are then normalised. The calculation shows the similarity between these two cases are 91.23, i.e. 91% the cases are similar. As we discussed earlier (in Fig. 23), the overall system works both offline and online, so the system has been tested according to 2 criterions: 1) clustering and identification of rare cases and 2) case-based retrieval. Both the evaluations are presented in [PAPER F] and in [PAPER G].

4.3 Programming Languages and Tools

Both the CDSSs (mainly CBR approaches) are web-based and developed using the PHP programming language while the case libraries were built using a MySQL database. The main goal is to evaluate the functionalities of the systems therefore they are prototype systems. In stress management, the client user interface that collects FT measurements is developed using the JAVA programming language. However, reference cases are collected using third party software, together with sensors named cStress provided by the company PBM Stressmedicine AB. In post-operative pain treatment the clustering approaches are conducted in a MATLAB environment. All the evaluations and experimental works are conducted using MS-Excel and its built-in functions.

Chapter 5.

Summary of Included Papers

This chapter presents the research contributions and author's contributions through a short summary of each included paper.

TO ANSWER the research questions presented in the introduction chapter, the research contributions of this PhD thesis includes 3 journal articles, 3 international conference papers and 1 international workshop paper. In [PAPER A], 34 projects/systems have been studied in order to understand the recent developments and state of the art. It has been seen that a CBR approach is used on all of projects as a core technique and other AI methods are also included due to application needs. In [PAPER B], the DSS in stress management was evaluated and the obtained sensitivity, specificity and overall accuracy compared to an expert were 92%, 86% and 88% respectively. [PAPER C] presented a hybrid framework that is capable of handling multi-media data in stress diagnosis. Similarly, [PAPER D] addressed a three-phase biofeedback system for stress treatment, here, one case study of the evaluation shows that the DSS outperforms trainee clinicians based on a case library of cases authorised by an expert. [PAPER E] presented a supplementary method of a CBR approach that helps to initiate a case library by generating artificial cases. The evaluation result demonstrated that the system improved the performance up to 22% when the case library is doubled by combining both artificial cases and reference cases from an expert. [PAPER F] presented a retrieval system in post-operative pain treatment using a CBR approach. Here, the research introduced a two-layer case structure i.e. 'solution' is the first layer and 'outcome' is the second layer that better suits this medical application. Moreover, the CDSS was built with a case-library containing both regular and rare cases to support a physician in experience reuse for post-operative pain treatment. The rare cases are automatically identified using a cluster-based approach which is presented in [PAPER G]. According to the results, this novel approach has identified 18% of cases from the whole population as rare.

The following sub-chapters highlight the summary of each included paper and the full versions of the papers are attached at the end of the thesis in "Part 2". A block diagram that shows the link between the overall goal and the contributions through the included papers is illustrated in Fig. 30.

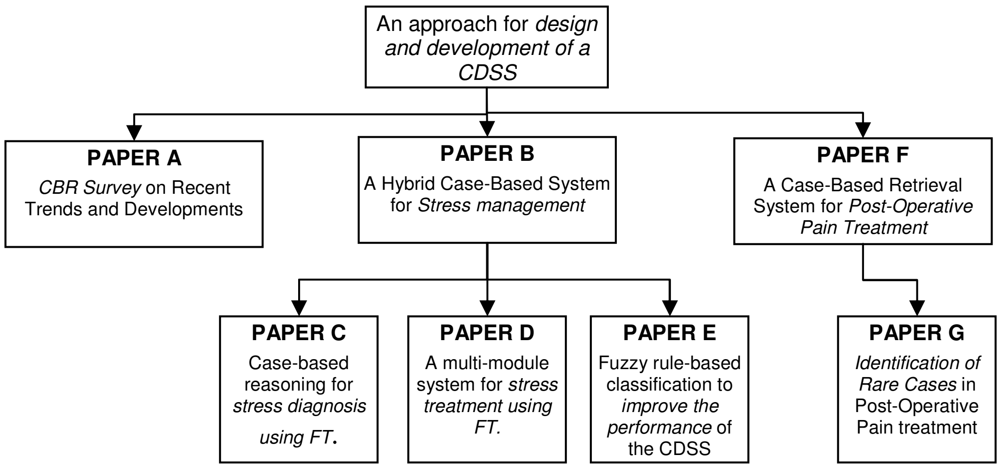

Figure 30. Linkages between the overall research goal and research contributions through the included papers

5.1 Paper A: Case-Based Reasoning Systems in the Health Sciences: A Survey on Recent Trends and Developments

This paper is published in the international journal "IEEE Transactions on Systems, Man, and Cybernetics-Part C: Applications and Reviews", Volume 41, Number 4, 2011, pp 421-434.

It is a journal paper where I was the main co-author. Here, a literature study and system review was conducted on 34 systems and I have studied 16 out of 34 systems. The analysis of the systems' properties, email questionnaires and analysing the survey results was performed by me in order to identify the recent trends and developments.

In this paper, some of the recent medical CBR systems are studied (based on literature review) along with a survey (e-mail questionnaire to the corresponding authors) between the year 2004 and 2009, investigating the current trends and developments. The article makes an in-depth study of the issues and challenges of applied CBR researches in the medical domain. Recent CBR systems were outlined in terms of not only their functionality but also the various key techniques that support such systems. In particular it was highlighted that a current hot trend in CBR applications is to build multi-modal and multi-purpose CBR systems to tackle the underlying complexity in medical domains.

5.2 Paper B: A Hybrid Case-Based System in Stress Diagnosis and Treatment

The paper is accepted in the IEEE-EMBS International Conference on Biomedical and Health Informatics (BHI2012), 2012.

I am the main author of this paper and the overall idea was proposed by me. I was responsible for writing the whole paper and also designing and implementing the experimental work. The other authors contributed by discussing ideas and giving comments and suggestions to improve and finalise the paper.

In this paper, a hybrid case-based system that supports a clinician in a number of complex tasks in stress management is proposed. Here, several artificial intelligence methods and techniques are explored and investigated where CBR is applied as the core method. It also combines case-based reasoning, textual information retrieval, rule-based reasoning, and fuzzy logic to enable a more reliable diagnosis and treatment of stress. The proposed hybrid case-based approach has been validated by implementing a prototype in close collaboration with leading experts in stress diagnosis. The obtained sensitivity, specificity and overall accuracy compared to an expert are 92%, 86% and 88% respectively. The system is valuable both for less experienced clinicians and experienced clinicians by aiding the planning process for diagnosis and treatment.

5.3 Paper C: Case-Based Reasoning for Diagnosis of Stress using Enhanced Cosine and Fuzzy Similarity

The paper is published in the international journal "Transactions on Case-Based Reasoning on Multimedia Data" by the IBaI Publishing; October, Volume 1, Number 1, 2008, pp 3-19.

As the main author of this journal paper I contributed by writing a system overview, a method for extracting features from textual information, a matching algorithm for textual case retrieval, evaluation and related work. In addition, a prototype of the implemented system was developed to evaluate the approach, system framework and its functionality.

This paper proposes a method for a hybrid case-based reasoning system to diagnose stress which is capable of coping with both numerical signals and textual data at the same time. The total case index consists of two sub-parts corresponding to signal and textual data respectively. For matching of cases on the signal data, we present a fuzzy similarity matching metric to accommodate and tackle the imprecision and uncertainty in sensor measurements. A preliminary evaluation has revealed that the fuzzy matching algorithm leads to a more accurate similarity estimate for improved case ranking and retrieval compared with a traditional distance-based matching criterion. For evaluation of similarity based on the textual data an enhanced cosine matching function augmented with related domain knowledge is proposed. This is implemented by incorporating WordNet and domain specific ontology into the textual case-based reasoning process for refining weights of terms according to available knowledge encoded therein. Such knowledge-based reasoning for matching of textual cases has empirically shown its merit in improving both precision and recall of retrieved cases with our initial medical databases.

5.4 Paper D: A Multi-Module Case-Based Biofeedback System for Stress Treatment

This paper is published in the international journal "Artificial Intelligence in Medicine", Volume 51, Issue 2, Publisher: Elsevier B.V., 2010, pp 107-115.

This is another journal paper included in the thesis where I am the main author and the basic idea of the designed framework is introduced by me. I contributed by writing the introduction, related work, and biofeedback system for stress treatment, experimental results and discussion chapters. I was also responsible for the evaluation part of the paper.

This paper presents a computer-based decision support system for biofeedback training in health care. The system aims to facilitate experience sharing and reuse among clinicians by utilising the CBR methodology from artificial intelligence. The main contribution of this research is a three-module system architecture enabling decision support to clinicians carrying out biofeedback. The classification and parameter estimation also deals with biofeedback training. The approaches have been validated in a case study related to stress diagnosis and treatment. The results of the case study reveal that our case-based system for biofeedback training outperforms novice clinicians in patient diagnosis and performs close to senior experts in the underlying domain. Clinicians and experts say that our developed system will be a valuable tool to help less experienced clinicians to make more accurate and prompt decisions as well as to offer useful second opinions for experts in dealing with complex situations. Future work will focus on the interaction among the three modules in the existing system and also investigate ways to further improve the overall performance of the system.

5.5 Paper E: Fuzzy Rule-Based Classification to Build an Initial Case Library for Case-Based Stress Diagnosis

This is a conference paper published in the proceedings of the 9th international conference on "Artificial Intelligence and Applications (AIA), 2009", Austria February, 2009, pp 225-230.

I contributed as the main author of this paper and the idea of the proposed method was introduced by me. I was responsible for writing the related works section, fuzzy rule-based classification, rule induction with a generalised feature section and the experimental results. I was also responsible for writing the evaluation part of the paper.

This paper proposes a fuzzy rule-based classification scheme which is introduced into the existing CBR system to improve performance of stress diagnosis tasks. In the initial phase of a CBR system there are often a limited number of cases available which reduces the performance of the system. If past cases are missing or are very sparse in some areas the accuracy of the system is reduced. Experimental results show that a CBR system using the enhanced case library can correctly classify 83% of the cases, whereas previously the correctness of the classification was 61%. Consequently the proposed system has an improved performance of 22% in terms of accuracy. In terms of the discrepancy in classification compared to an expert, the goodness-of-fit value of the test results is on average 87%. Thus, by employing fuzzy rule-based classification, the new hybrid system can generate artificial cases to enhance the case library. Furthermore, it can classify new problem cases previously not classified by the system.

5.6 Paper F: A Case-Based Retrieval System for Post-Operative Pain Treatment

This is a workshop paper published in the proceedings of the "International Workshop on Case-Based Reasoning CBR 2011", IBaI, Germany, New York/ USA, Editor(s): Petra Perner and Georg Rub, pp 30-41, September, 2011.

I contributed as the main author of this paper and the idea of the proposed method was introduced by me. I was responsible for writing the whole paper; however other co-author also participated by discussing the idea, reviewing the paper and making suggestions for improvements.

This paper presents a clinical decision support system based on case-based retrieval approach to assist physicians in post-operative pain treatment. Here, the cases are formulated by combining regular features with features using a Numerical Visual Analogue Scale (NVAS) through a questionnaire. Feature abstraction is done both in the problem and outcome description of a case in order to reduce the number of attributes. The system retrieves the most similar cases together with their outcomes. The outcome of each case brings benefits for physicians since it presents both the severity and speed of recovery of the applied treatment in post-operative patients. In the system, the solution presents the treatment and the outcome containing recovery information of a patient, as physicians are often interested in the risks, complications and side effects of a treatment. Therefore, we have introduced a two-layer case structure i.e. the solution is the first layer and outcome is the second layer, which better suits this medical application.

5.7 Paper G: Mining Rare Cases in Post-Operative Pain by Means of Outlier Detection

This is a conference paper accepted in the "IEEE International Symposium on Signal Processing and Information Technology, ISSPIT'11", 2011.

I contributed as the main author of this paper and the idea of the approach was introduced by me. I was responsible for writing all the section of the paper. The co-author contributed by discussing the idea and suggesting improvements to the paper.

The results of this paper are used as an input for the CBR CDSS in post-operative pain domain. In this paper, a number of well-known clustering algorithms are investigated and finally a novel method "2nd order clustering" approach has been applied by combining the Fuzzy C-means algorithm with the Hierarchical algorithm. The approach is used in order to identify rare cases from 1572 patient cases in the domain of post-operative pain treatment. The results show that the approach enables an automatic identification of rare cases in the domain of post-operative pain treatment. Here, 18% of the cases are identified as rare cases.

Chapter 6.

Discussion, Conclusions and Future Work

This chapter presents a summary of the thesis contributions and discusses the issues related to justification of using the methods chosen and results of the research. Conclusions drawn from the research work are presented in this chapter together with the limitations and future direction of this research.

THIS RESEARCH mainly focuses on the investigation of methods and techniques in order to design and develop Clinical Decision Support Systems (CDSSs). Several Artificial Intelligence (AI) methods, techniques and approaches have been investigated and applied to develop the CDSSs. Here, the researcher had the opportunity to work with two medical domains which were 1) stress management and 2) post-operative pain treatment. Literature studies, interviews and discussions with clinicians and experts have been conducted in order to understand the clinical knowledge and content of the domains. During the research, several research questions and sub-questions were addressed and at the same time several solutions with novel results have been achieved. Although the CBR approach is applied as a core technique for both of the domains, other AI methods were also combined and applied. A prototypical CBR system has been developed for both the domains considering the purpose of the system and its data formats. The functionality of both of the systems is validated through close collaboration of expert in the domains.

6.1 Main Research Results

The main goal of the research work is to investigate an approach that can be used in the design and development of CDSSs in order to assist clinicians in their decision making tasks such as diagnosis, classification and treatment. In order to attain the goal the research was split into several research questions and sub-questions as formulated and presented in chapter 1. Several results have been achieved to answer the questions and presented as research contributions through the included papers [PAPERS A-G]. Recalling the research questions, the answers to them through the achieved results are summarised below:

RQ 1. What ***approaches, methods and techniques*** can be used to design and develop CDSSs where the domain knowledge is weak e.g. stress management and post-operative pain treatment.

To answer the question several investigations have been conducted and the key results are as below:

- A literature study has been done (i.e. presented in section 2.1 and 2.2 [CHAPTER 2]) for both the domains to understand the content of the domain and how the diagnosis and treatment have been conducted in a real and clinical environment.
- A close collaboration with the experts and doctors of each domain in order to better understating the content, diagnose and treatment tasks. Several interviews, meetings and seminars/workshops have been conducted during the research period.
- A literature study on related work about the design and development of Decision Support Systems (DSSs) or intelligent systems in some medical domains, in stress management and in post-operative paint treatment has been conducted and presented in section 2.3 [CHAPTER 2]. Moreover, a comprehensive survey has been done through [PAPER A], which investigates the current trends and developments of CBR system in medical domain. There 34 projects/systems are considered out of 50 for the study and survey and the result demonstrates that the CBR approach is increasingly used in complex medical applications. Most of them applied only a CBR approach and others have added other AI techniques due to the nature of the application and requirements.

RQ 2. How can a CDSS be ***designed, developed and validated*** for complex medical decision making tasks (i.e. diagnosis/classification and treatment) in stress management using FT measurement?

The general answer is to use a multimodal approach which considers a combination of several AI techniques and methods (presented in [PAPER B]) in order to design, develop and validate the CDSS in stress management using FT measurement. Here, the percentage of the total correctly classified cases in terms of the system's accuracy was obtained as 88% and only 12% of the total cases are misclassified. The Goodness-of-fit (R^2) value was almost the same for both the senior clinician and the system i.e. 82% and 88%. The second research question has three sub-question and they are:

RQ 2. 1. How can a computer-based system provide more reliable solutions in the stress diagnosis task? In particular, could the CDSS framework handle textual information capturing e.g. human perceptions and feelings and use these with biomedical signals e.g. FT measurements to support the diagnosis of stress?

- Upon a close discussion with the expert of the domain and a literature study it was found that the human perceptions, feelings and contextual information of a patient also captured important information and which is not available in the FT sensor measurements. So, a hybrid system is required to address this issue.
- The research addresses the design and evaluation of such a hybrid diagnosis system through [PAPER C] that is capable of handling multimedia data i.e. human perceptions, feelings and contextual information of a patient using textual format and FT measurements using sensor signal.

RQ 2. 2. What ***methods and techniques*** can be used to design a system to assist in treatment e.g. bio-feedback training in stress management using FT sensor signals?

- Here, the research investigates a novel framework of a DSS for sensor-based biofeedback training using FT measurement. According to [PAPER D], it is a three-module architecture that enabling a decision support to clinicians carrying out patient classification, individual parameter estimation and biofeedback training using FT measurement.

RQ 2. 3. How can the CDSS be useful from the start even if there are a limited number of cases available?

- It was observed, evaluated and identified that the proposed DSS's performance in the initial stages was diminished since in initial stage the case library in the CBR system contained only few cases.
- In this research, a method is explored through [PAPER E] to overcome this problem a set of fuzzy rules is used to generate hypothetical cases in regions where limited number of cases are available.

RQ 4. How can the proposed multimodal approach be enriched to fit other medical domains such as post-operative pain treatment?

The overall goal of this issue is that the applied approach in stress management is also suitable to apply in post-operative pain treatment domain and how much adaptation is needed. To answer this question the following investigation has been conducted.

- A CDSS is developed in post-operative treatment where the same multimodal approach is applied and little adaptation and enhancement is done. For example, in this domain a CBR approach is combined with a clustering approach which is presented in [CHAPTER 4.2].
- For the CDSS in [PAPER F], the feature abstraction and feature weighting approach is slightly different than the stress management domain. Moreover, cases are formulated by combining problem, solution and outcome which is also different from a structural point of view.
- A novel clustering based approach is proposed (presented in [PAPER G]) in order to identify rare cases in the post-operative pain domain which will be further used in the CBR system to retrieve and present the most similar regular and rare cases. Here, 18% of cases are identified as rare using the automatic approach.

From an overall observation of the results, a multimodal approach is proposed in order to design and develop a CDSS for the complex medical domains. Here, a CBR approach is found suitable to apply as a core or base technique and other AI methods such as rule-based reasoning, fuzzy-logic, textual information retrieval and clustering approach are combined with CBR as tools in order to optimize the performance of the CDSSs.

6.2 Research Related Issues

Several related issues are considered during this research and they are also formulated as research questions presented in section 1.3 [CHAPTER 1]. The research is initiated by studying literature and interviewing experts from the stress management domain. The main goal was to understand the domain knowledge that is human stress, good vs bad stress, stress diagnosis and treatment and physiological parameters related to stress and so on. The background knowledge about the application domains (i.e. stress management and post-operative pain treatment) is presented in section 2.1 and 2.2 [CHAPTER 2]. The next issue is to identify proper AI methods, techniques and approaches which will help to design and develop a CDSS for stress diagnosis and treatment. Another literature study has been conducted where CDSS or DSS in several medical application domains including both stress management and post-operative pain treatment have been investigated. The main goal was to identify the current research progress on developing DSS in medical applications especially what has been done in stress management and in postoperative pain treatment. The summary of this detail study has been presented in section 2.3 [CHAPTER 2]. After studying several AI methods (presented in [CHAPTER 3]) and close discussions with my supervisors, it was found that the CBR approach fit well within the stress management domain. However, the research also investigated several (i.e. 34) CBR systems in the medical domain which is presented in included in [PAPER A]. In this paper, a study on the recent medical CBR systems and a survey (e-mail questionnaire to the corresponding authors) between the year 2004 and 2009 have been done. The main goal was to investigate the current trends and developments as well as identify the issues and challenges of applied CBR researches in the medical domains. The following section of this chapter presented a summary of the reason behind the applied methods, techniques and approaches. Moreover, the reason behind the selection of FT as a physiological parameter is also discussed.

6.2.1 CBR Approach Applied as a Core Technique

When the domain knowledge of any medical application is complex or not well defined such as stress management or post-operative pain treatment, it is very difficult to build a CDSS. Many of early CDSSs attempted to apply pure rule-based reasoning (i.e. IF-THEN rules), for example MYCIN [17] uses a knowledge base of ~600 rules. In order to define these 600 rules, one need to very detailed knowledge about the domain. The domain theory should be strong and well defined and this is complex and time consuming [101]. In the stress management domain, the knowledge is not well defined and there is large variation within and between patients. There is no general straight forward rule for diagnosis and treatment of stress and sometimes it is very difficult even for an experienced clinician [PAPER C][PAPER D]. In these situations the CBR approach works well as a CDSS since it provides the clinician with past similar cases to help them make more informed solutions. Moreover, the system can learn by acquiring new cases which can be done without modification to the system, [101]. However, in this research, both CBR as well as RBR approaches are applied. To some extent, when the domain knowledge is well-defined the RBR can work, for example, when FT increases the patient is in a relaxed state and when FT is decreasing it is usually a sign of a stressed state. These simple rules can be used and in this research they are used only to create artificial cases [PAPER E]. On the other hand when the domain knowledge is less well-defined i.e. when FT is oscillating then it is very difficult to say whether the measurement is stressed or relaxed.

The CBR approach is much better compared to Neural Network (NN) when data source is multi-media, i.e. not purely a numerical data format rather a mixture of symbolic, textual and numeric data formats. At the same time, NN requires a large data set since it divides the whole data set into three parts, training, validation and testing. Whereas a CBR system can use its whole data set in order to build and evaluate. Thus a CBR system can start its functionality with a few cases. In the stress management domain, the NN was not used due to too few cases (i.e. only 68) and the data format is not purely numeric. Although the research could apply NN in the post-operative pain treatment domain since it has more than 1500 complete cases. However, a major disadvantage of NN is that it functions as a 'black box'. The output from an NN is a utility of the weighted vectors of its neurons [101]. It cannot give any explanation or justification about the output. Moreover, it is very difficult for clinician's to trust the system in this domain as clinicians are not likely to accept any solution without an explanation. In the CBR approach the most similar cases are retrieved and presented to the clinicians to enable them to make a more informed decision. This was one of the key reasons for the clinicians in the Pain-Out project to accept the CBR approach and this is why this research applied the CBR approach for post-operative pain treatment [PAPER F].

The research could use other techniques such as machine learning or statistics but again they require a large volume of data. The data set should be well-understood, the knowledge/hypothesis should be well-defined, there should be generalizable rules and they should be actable by rule-trace [101]. The research applied CBR as the core technique for both the application domains since CBR has process similarity i.e. it is inspired by human reasoning [1, 101]. The reasoning process is also medically accepted since doctors quite often used previous experience to solve a problem. Using CBR, an expert can directly apply their knowledge by choosing related features and their importance, for example a patient's weight is more important than a shoe size. Moreover, they can also let the system know about the similarity of two features, considering gender as a feature, a male and female may differ in similarity in e.g. choice of medication. Maintenance of a CBR system is much simpler since new knowledge can be inserted by adding new cases and the cases in case library can be used by trainee clinicians. Another interesting observation is that the CBR approach is compatible with other AI methods and thus the system can take advantage of other techniques in order to improve its performance [PAPER B] [CHAPTER 4.2].

6.2.2 Others AI Techniques Applied as Tools

Besides the CBR approach, the research also has investigated and applied several AI technologies and approaches. The other AI technologies have been used as tools that help to fine tune the CBR approach in order to obtain the complete benefit of the CBR systems. The combination of several AI techniques depends on the nature of the domain, data format, complexity and performance. For both the application domains, fuzzy logic is applied in the similarity measurement of the CBR approach since it helps to accommodate uncertainty. Moreover, fuzzy similarity matching presented in [PAPER C] reduces the sharp distinction which is obtained in similarity matrix [9] formulated by an expert. In [PAPER B] section 3.1, comparisons of three local similarities are presented and it shows that when using fuzzy similarity the system can achieve a better performance. The information retrieval approach i.e. mainly vector space modeling (VSM) is applied together with a WordNet dictionary and domain specific ontology in order to retrieve textual cases presented in [PAPER C]. Here, the system did not combine textual cases and FT cases in order to provide a combined solution rather the most similar textual cases are presented. These textual cases provide information regarding patients' contextual feelings, behaviors, social facts, working environments, lifestyle and other additional information which enhances the reliability of the CDSS. Thus, the CDSS for stress management provides support to clinicians in their decision making tasks by only retrieving the most similar cases (both textual cases and FT measurements cases simultaneously) rather than providing any combined direct solution. Again, in the stress management domain, fuzzy rule-based reasoning is used together with a CBR approach in order to improve the system's performance since there are very few reference cases in the case library. In [PAPER B] section 3.2, the result shows that the CDSS succeed to improve its performance by 22% by using a bigger case library initiated both by using reference cases and cases created by fuzzy rules. The details of the fuzzy rule-based reasoning scheme and related experimental works are presented in [PAPER E]. On the other hand, in post-operative pain treatment, there were more than 1500 reference cases in case library, so the clustering approach [PAPER F] is used in order to identify rare cases from the regular ones. Here, 4 frequently used clustering methods (i.e. K-means, Fuzzy C-means (FCM), Gaussian mixer model and Hierarchical) are studied and a summary of these are presented in section 3.4[CHAPER 3]. According to the evaluation in [PAPER G], it was observed that none of them was individually suitable to identify rare cases. For example, the k-means/fuzzy c-means works better in partitioning cases and hierarchical works better in identifying outliers. However, in a large data set the hierarchical algorithm was not sufficient to identify maximum outliers. So, the research in [PAPER G] proposed a novel combination of the FCM and Hierarchical clustering which was able to identify 18% of cases as rare cases. Moreover, using this approach all the case are grouped into several groups and the retrieval function only considers the most similar groups which reduced retrieval time [CHAPTER 4.2].

6.2.3 FT used as a Physiological Parameter

The CDSS in stress management only used FT as a physiological parameter since the intention of the research was to design and develop a CDSS both for diagnosis [PAPER C] and treatment [PAPER D] which should be simple, inexpensive and easy to use. Although the research could use some other parameters such as Heart Rate (HR), Respiratory Rate (RR), Electroencephalography (EEG) and so on, however including more parameters the system will be complex, expensive and special training is needed in order to use the system. FT measurement is an effective parameter [45, 71] for self-regulation training (i.e. biofeedback) since it is directly related to the sympathetic and parasympathetic nervous system. That means FT decreases with the response of stress while the Sympathetic Nervous System (SNS) is activated and FT increases with relax state when Parasympathetic Nervous System (PSNS) is activated. By only using heart rate or heart rate variability it is more difficult than the FT to classify a patient's stress level since it contains the information about both the sympathetic and parasympathetic nervous systems. Moreover, using HR the diagnosis is more expensive than FT since it often requires more than one sensor and the sensors are not easy to use and training is required. In this research, for the experimental work presented in [PAPER B], the measurements have been collected using different parameters (e.g. heart rate, skin conductance, respiration rate, CO2/ETCO2) together with finger temperature (FT) and the expert classification was also done by considering all of the measurements. Finally, the comparisons are done where the system classifies patients using only FT measurements and the expert classifies patients using all the parameters (mentioned above). Thus the overall accuracy of 0.88 has been achieved, i.e. the system is 88% similar to the expert in classification.

6.3 Conclusion and Future Work

CDSSs have proven to be able to extend the capability of clinicians in their decision making tasks. But reliability is often a concern in clinical applications. The research presented in this thesis, explores an approach for a clinician to support diagnosis, classification and treatment tasks both in stress management and post-operative pain treatment. Here, several artificial intelligence methods and techniques are applied as in a multimodal approach for both the domains. Moreover, the proposed approach facilities a framework that is able to use data in multimedia format. In the stress management domain, the approach combines more than one AI technique (i.e. fuzzy logic, rule-based reasoning and textual information retrieval) where CBR is applied as the core technique of the CDSS. Reliability of the clinical system based on sensor readings increased by providing contextual information supporting the reasoning tasks. Therefore, the system considers additional information in textual format applying textual information retrieval with ontology. Here, it is also illustrated that it is possible to increased accuracy in the classification task, by extending the case library with artificial cases by applying fuzzy rule-based reasoning. The experiment results (mainly in [PAPER B]) show that the system reaches a level of performance close to the expert and better than the senior and trainee clinicians. Thus, according to results, the CDSS can be useful for an expert as a second option or opinion for trainee clinicians. Similarly, in post-operative pain treatment, the approach combines CBR retrieval with a clustering approach in order to retrieve and present rare cases together with regular ones. Here, the automatic approach identifies 276 cases out of 1572 as rare cases. Moreover, according to the results [PAPER G] among the rare cases (i.e. 276), around 57.25% of the cases are classified as unusually bad since the average pain outcome value is greater or equal to 5 on the NVAS scale 0 to 10.

Although the experimental work in stress management shows promising results, there are still some limitations. First of all, the reference cases used here were collected neither from a hospital nor from any real patient. They are from voluntary participants; however, some of them were really stressed during the measurement was taken. The measurement of a student before his M.Sc thesis presentation is one example. For the textual feature, the experiment has been conducted with the artificial cases and very limited ontology. The number of the reference cases is still limited even though the research contributions included a supplementary method to address this issue. Moreover, today the system is based on one physiological parameter i.e. finger temperature sensor signal. In future, several other parameters such as RSA i.e. heart rate together with respiration rate could be investigated. Even though in the post-operative pain treatment domain, the cases are collected from hospitals and the case's subjects are real post-operative patients but it is necessary to verify the rare cases (which are automatically identified by the clustering approach) whether they are very rare. Also, the clinical findings are an ongoing part of the PAIN-OUT project. In future, the researcher would like to apply other techniques and methods such as machine learning and statistics in this application domain and the main intention is to perform a comparison between CBR and other approaches. Since both CDSSs applied a CBR approach as the core technique, automatic adaptation and automatic feature weighting are two important issues which could be investigated in future. In addition, in terms of user-level evaluation, both the CDSSs need to be verified in a clinical environment. Beside this, the integration of the CDSSs into a clinical environment is also an important issue. With the intention to deploy it in a day-to-day clinical practice the evaluation process needs to be done on a large scale.

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PART 2

Included Papers