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A CASE-BASED REASONING SYSTEM FOR THE DIAGNOSIS OF INDIVIDUAL SENSITIVITY TO STRESS IN PSYCHOPHYSIOLOGY

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Abstract

Stress is an increasing problem in our present world. Especially negative stress could cause serious health problems if it remains undiagnosed/misdiagnosed and untreated. In stress medicine, clinicians' measure blood pressure, ECG, finger temperature and breathing rate during a number of exercises to diagnose stress-related disorders. One of the physiological parameters for quantifying stress levels is the finger temperature measurement which helps the clinicians in diagnosis and treatment of stress. However, in practice, it is difficult and tedious for a clinician to understand, interpret and analyze complex, lengthy sequential sensor signals. There are only few experts who are able to diagnose and predict stress-related problems. A system that can help the clinician in diagnosing stress is important, but the large individual variations make it difficult to build such a system.

This research work has investigated several artificial Intelligence techniques for the purpose of developing an intelligent, integrated sensor system for establishing diagnosis and treatment plan in the psychophysiological domain. To diagnose individual sensitivity to stress, case-based reasoning is applied as a core technique to facilitate experience reuse by retrieving previous similar cases. Furthermore, fuzzy techniques are also employed and incorporated into the case-based reasoning system to handle vagueness, uncertainty inherently existing in clinicians reasoning process. The validation of the approach is based on close collaboration with experts and measurements from twenty four persons used as reference.

39 time series from these 24 persons have been used to evaluate the approach (in terms of the matching algorithms) and an expert has ranked and estimated the similarity. The result shows that the system reaches a level of performance close to an expert. The proposed system could be used as an expert for a less experienced clinician or as a second option for an experienced clinician to their decision making process in stress diagnosis.

Sammanfattning

Den ökande stressnivån i vårt samhälle med allt högre krav och högt tempo har ett högt pris. Stressrelaterade problem och sjukdom är en stor samhällskostnad och speciellt om negativ stress förblir oupptäckt, eller ej korrekt identifierad/diagnostiserad och obehandlad under en längre tid kan den få alvarliga hälsoeffekter för individen vilket kan leda till långvarig sjukskrivning. Inom stressmedicinen mäter kliniker blodtryck, EKG, fingertemperatur och andning under olika situationer för att diagnostisera stress. Stressdiagnos baserat fingertemperaturen (FT) är något som en skicklig klinker kan utföra vilket stämmer med forskningen inom klinisk psykofysiologi. Emellertid i praktiken är det mycket svårt, och mödosamt för att en kliniker att i detalj följa och analysera långa serier av mätvärden och det finns endast mycket få experter som är kompetent att diagnostisera och/eller förutsäga stressproblem. Därför är ett system, som kan hjälpa kliniker i diagnostisering av stress, viktig. Men de stora individvariationerna och bristen av precisa diagnosregler gör det svårt att använda ett datorbaserat system.

Detta forskningsarbete har tittat på flera tekniker och metoder inom artificiell intelligens för att hitta en väg fram till ett intelligent sensorbaserat system för diagnos och utformning av behandlingsplaner inom stressområdet. För att diagnostisera individuell stress har fallbaserat resonerande visat sig framgångsrikt, en teknik som gör det möjligt att återanvända erfarenhet, förklara beslut, genom att hämta tidigare liknande fingertemperaturprofilerar. Vidare används ”fuzzy logic”, luddig logik så att systemet kan hantera de inneboende vagheter i domänen. Metoder och algoritmer har utvecklats för detta. Valideringen av ansatsen baseras på nära samarbete med experter och mätningar från tjugofyra användare.

Trettionio tidserier från dessa 24 personer har varit basen för utvärderingen av ansatsen, och en erfaren kliniker har klassificerat alla fall och systemet har visat sig producera resultat nära en expert. Det föreslagna systemet kan användas som ett referens för en mindre erfaren kliniker eller som ett ”second opinion” för en erfaren kliniker i deras beslutsprocess. Dessutom har finger temperatur visat sig passa bra för användning i hemmet vid träning eller kontroll vilket blir möjligt med ett datorbaserat stressklassificeringssystem på exempelvis en PC med en USB fingertemperaturmätare.

Acknowledgement

I would like to express my sincere gratitude to my main supervisor, Peter Funk, for his valuable guidance and helping me with his intuitive ideas. Without his help I would have never even begun this thesis work. I am really fortunate for having opportunity to work with him. I would like to thank to my assistant supervisor, Ning Xiong, for his fruitful discussion and cooperation in writing the papers. I am thankful to my assistant supervisor, Bo von Schéele, who has always been helpful in proving the domain knowledge to make this research possible. I wish to thank to my assistant supervisor, Mia Folke, who has provided much encouragement and suggestions to complete the work. A special thank to Maria Lindén, for her support and cooperation. Many thanks are also forwarded to the staff at the department of IDT, Mälardalen University for always being helpful. I would like to acknowledge the funding companies, specially the PBM Stressmedicine AB and the Swedish Knowledge Foundation (KKS) for funding the project. Also I want to acknowledge my teachers in Dalarna University at the department of Computer Science and Engineering for their encouragement to start my research work. Finally, and most importantly, I want to thank and acknowledge my family: my parents, my husband and my son who have inspired me and supported me always in many ways.

List of Publications

Papers included in this thesis

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. Submitted to the *International Journal of Computational Intelligent Systems*.

Paper B. A Case-Based Decision Support System for Individual Stress Diagnosis Using Fuzzy Similarity Matching. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Bo von Schéele (PBMStressMedicine AB). In the *Journal of Computational Intelligence*, Blackwell Publishing, in press, 2009.

Paper C. Classify and Diagnose Individual Stress Using Calibration and Fuzzy Case-Based Reasoning. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Bo von Schéele (PBMStressMedicine AB). In proceedings of the *7th International Conference on Case-Based Reasoning*, Springer, pages Belfast, Northern Ireland, August, 2007

Paper D. Using Calibration and Fuzzification of Cases for Improved Diagnosis and Treatment of Stress. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Bo von Schéele. In the proceedings of *8th European Conference on Case-based Reasoning workshop proceedings*, p 113-122, Turkey 2006, Editor(s):M. Minor, September, 2006

Additional publications, not included in this thesis

Similarity of Medical Cases in Health Care Using Cosine Similarity and Ontology. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Bo von Schéele. International conference on *Case-Based Reasoning (ICCBR-07) proceedings of the 5th Workshop on CBR in the Health Sciences*, Springer LNCS, Belfast, Northern Ireland, August, 2007

Individualized Stress Diagnosis Using Calibration and Case-Based Reasoning. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Bo von Schéele. In Proceedings of the *24th annual workshop of the Swedish Artificial Intelligence Society*, p 59-69, Borås, Sweden, Editor(s): Löfström et al., May, 2007

Induction of an Adaptive Neuro-Fuzzy Inference System for Investigating Fluctuation in Parkinson´s Disease. Shahina Begum, Jerker Westin (Högskolan Dalarna), Peter Funk, Mark Dougherty (Högskolan Dalarna). In proceedings of the *24th annual workshop of the Swedish Artificial Intelligence Society (SAIS)* 2006, p 67-72, Umeå, Editor(s): P. Eklund, M. Minock, H. Lindgren, May, 2006.

A computer-based system for the assessment and diagnosis of individual sensitivity to stress in Psychophysiology. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Mia Folke, Bo von Schéele. Abstract published in *Riksstämman, Medicinsk teknik och fysik*, Stockholm 2007

A Three Phase Computer Assisted Biofeedback Training System Using Case-Based Reasoning. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong, Bo von Schéele. In proceedings of the *9th European Conference on Case-based Reasoning workshop proceedings*, Trier, Germany, August, 2008

Fuzzy Rule-Based Classification to Build Initial Case Library for Case-Based Stress Diagnosis**.** Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong, Bo von Schéele. In the *international conference on Artificial Intelligence and Applications (AIA)* 2009

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. *In the International Journal Transactions on Case-Based Reasoning on Multimedia Data*, vol 1, Number 1, IBaI Publishing, ISSN: 1864-9734, October, 2008.

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 of Artificial Intelligence in Medicine*, 2009

Multi-modal and multi-purpose case-based reasoning in the health sciences. Mobyen Uddin Ahmed, Shahina Begum, Peter Funk, Ning Xiong, *8th WSEAS International Conference on Artificial Intelligence, Knowledge Engineering and Data Bases (AIKED 2009),* February 21-23, 2009, Cambridge, UK.

An Overview on Recent Medical Case-Based Reasoning Systems. Shahina Begum, Mobyen Uddin Ahmed, Peter Funk, Ning Xiong, Bo von Schéele. In *25th annual workshop of the Swedish Artificial Intelligence Society*, Linköping, 27 May 2009.

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List of Abbreviations

ACTH	Adrenocorticotropin Hormone
AI	Artificial Intelligence
AIM	Artificial Intelligence in Medicine
CBR	Case-Based Reasoning
CRF	Corticotropin-Releasing Factor
DSS	Decision Support System
EEG	Electroencephalography
ECG	Electrocardiography
EMG	Electromyography
$ETCO_2$	End-Tidal Carbon dioxide
FT	Finger Temperature
FL	Fuzzy Logic
HR	Heart Rate
HRV	Heart Rate Variability
IPOS	Integrated Personal Health Optimizing System
RBR	Rule-Based Reasoning
RSA	Respiratory Sinus Arrhythmia

Table of Content

PART 1

Thesis

Chapter 1

This chapter presents an introduction and outline of the thesis work. A short background, research questions and the research contributions are also discussed here.

Introduction

Medical knowledge is today expanding rapidly making computer-aided diagnostic system desirable. Such system can give a clinician a second opinion. Recent advances in Artificial Intelligence (AI) offer methods and techniques with the potential of solving tasks previously difficult to solve with computer-based systems in medical domains. Research worldwide is focusing on the new applications in the medical field and particularly in diagnosis. This thesis is especially concerned with the diagnosis of stress-related dysfunctions. Since there are large individual variations between individual persons when looking at sensor signals, this is a worthy challenge. The thesis is mainly based on the research project Integrated Personal Health Optimizing System (IPOS) funded by the Swedish Knowledge Foundation (Kunskap och Kompetens Stiftelsen, KKS)[1].

A procedure for diagnosing stress-related disorders has been put forward by Nilsson et al. [32] under the Artificial Intelligence in Medical Application (AIM) project at Mälardalen University, Sweden. According to which stress-related disorders are diagnosed by classifying the heart rate patterns analyzing both cardio and pulmonary signals, i.e. physiological time series and used as a research tool in psychophysiological medicine. This was an initial attempt to use a decision support system (DSS) in a previously unexplored domain e.g. psycho-physiological medicine. This tool is more suitable to use in clinical environment.

The dissertation is divided into two parts. The Part-I includes chapter 1 '*Introduction*' which presents a background, motivation, research questions

[1] http://www.kks.se/

and research contributions. In chapter 2 '*Background*' the pertinent theoretical background of the methods and techniques and a short description of the application domain of my research work are described. Chapter 3 '*Stress diagnosis*' analyzes the nature of the research and justifies the choice of the methodological approach for this domain. Chapter 4 '*Research contributions'* summarizes the papers included in this thesis. Chapter 5 '*Related work*' considers related work in the area of case-based systems in medicine. Chapter 6 '*Conclusions and future work*' concludes the first part of the thesis and proposes future work. The Part-II of this thesis contains chapter 6, chapter 7, chapter 8 and chapter 9 which present the complete versions of the paper A, paper B, paper C and paper D respectively.

1.1 Motivation and aim

Today, everyday life for many people contains many situations that may trigger stress or result in an individual living on an increased stress level under long time. It is known that high level of stress may cause serious health problems. Different treatments and exercises can reduce this stress. Since one of the effects of stress is that the awareness of the body decreases, it is easy to miss signals such as high tension in muscles, unnatural breathing, blood-sugar fluctuations and cardiovascular functionality etc. It may take many weeks or months to become aware of the increased stress level, and once it is noticed, the effects and unaligned processes, e.g. of the metabolic processes, may need long and active behavioural treatment to revert to a normal state [43]. For patients with high blood pressure and heart problems high stress levels may be directly life-endangered. A system determining a person's stress profile and potential health problems would be valuable both in a clinical environment as second opinion or at home environment as part of a stress management program.

Clinical studies show that the finger temperature (FT), in general, decreases with stress. The pattern of variation within a finger temperature signal could help to determine stress-related disorders. For the other conventional methods such as respiration (e.g. end-tidal carbon dioxide ($ETCO_2$)), heart rate (e.g. calculating the respiratory sinus arrhythmia (RSA)) and heart rate variability (HRV) etc. used clinically, the diagnosis often expensive and require equipment (often using many sensors) not suitable for use in non - clinical environment and without experienced clinical staff. Finger temperature measurement can be collected using a sensor (comparatively low in cost) and used as a supplementary convenient tool to diagnose and control stress at home and working places by a general user. However, the finger temperature sensor signal is so individual and interpreting a particular curve and diagnosing stress level is difficult even for experts in the domain. In practice, it is difficult and tedious for a clinician, and particularly less experienced clinicians to understand, interpret and analyze complex, lengthy sequential measurements in order to make a diagnosis and treatment plan. Therefore, this thesis work is mainly motivated by a desire to develop a computer-based stress diagnosis system that can be used by people who need to monitor their stress level during everyday situations e.g. at home and in work environment for health reasons. This can also be used by the clinician as a second option.

In summary, the research aim of the thesis is to:

- Develop a method and technique able to classify slowly changing sensor signals e.g. such as finger temperature or $ETCO_2$.
- Handle classification of sensor signals despite large individual variations.
- Develop a classification method and technique able to classify stress with low cost sensor/sensors.

1.2 Problem discussion

In this research project, the following research questions have been formulated based on the motivation and aim of the work presented in the previous section.

- *What methods/ techniques can be used for diagnosing stress in non-clinical environment i.e. at home and in working places and are acceptable by the clinicians?*

The first question addresses the need of a diagnostic system that not only supports in assisting the clinicians in the clinical environment but also could be possible to use by the users in their daily life. The answer to this first question requires literature review and domain knowledge as there are many parameters e.g. Finger Temperature (FT), Respiratory Sinus Arrhythmia (RSA), End-Tidal Carbon Dioxide ($ETCO_2$), Electromyogram (EMG) etc. that can help in different ways in identifying stress. The psychophysiological parameter helpful in daily use and the appropriate AI methods to be applied have to be identified.

- *What is needed for enabling autonomous system able to identify individual's stress levels?*

The second research question has indicated the need of the appropriate methods or techniques that could help in developing an automated system in diagnosing individual stress utilizing the finger temperature sensor signal. The pattern of the FT signal is very individual which makes it difficult to use it in a computerized system. So there is a need to find out a technique to measure personalized parameters to identify individual stress levels.

- *How can we classify individual stress levels when there are no clear guidelines to do so and the domain knowledge is weak?*

The third research question deals with a method/ technique for the computer-based classification of stress level based on the FT sensor signal. The complex pattern of the individual FT measurements and the lack of general set of rules make this classification tasks even a difficult task for the expert of the domain.

- *How to extract the essential features from a slowly changing signals such as finger temperature?*

The fourth research question addresses the feature extraction and selection from the FT sensor signal. Feature extraction is becoming complicated in recent medical systems due to the complex data format where data is coming from sensors, images, in a form of time series or in free text format etc. such as in this Psychophysiological domain. Hidden key features may effect on the retrieval performance [16]. Also, feature selection and weighting is another important issue for which many systems depend on the expert's knowledge. Selecting an appropriate feature extraction approach able to extract for the diagnosis essential features is a key to success; a less suitable feature extraction leads to undetected features of importance and to inferior performance.

1.3 Research contributions

The contributions of this licentiate thesis work have been described briefly in the included research papers. In this research work, a combined approach based on a calibration phase and case-based reasoning to provide assistance in diagnosing stress is proposed, using data from the finger temperature sensor readings. The calibration phase helps to establish a number of individual parameters. The system uses a case-based reasoning approach to facilitate experience reuse and decision explanation by retrieving previous similar temperature profiles. Further, fuzzy technique is also incorporated into the case-based reasoning system to handle vagueness, uncertainty inherently existing in clinicians reasoning. This case-based system may help the clinician to make a diagnosis, classification and treatment plan. The case may also be used to follow the treatment progress. The individual cases including calibration may also be used in an autonomous system at home or in work environment for treatment programs for individuals often under high stress.

The main contributions of this thesis can be summarized as follows and the related paper(s) for each contribution are also mentioned here.

- Methods for identifying features from finger temperature measurements i.e. automatic feature extraction from the sensor signal. [paper D and paper C]

- A calibration phase to establish a number of individual parameters to diagnose individual stress-related disorders in a computer-aided system [paper C and paper B].
- Methods for the computer-based classification of the individual's stress level i.e. finger temperature measurement classification [paper C].
- Implement a new system that allows a clinician to use it in clinical environment and a general user to use it at home and in working places for diagnosing stress [paper A and paper B].

Chapter 2

This chapter describes the theoretical background upon which the research is based on. It begins with a discussion about the case-based reasoning and fuzzy logic. Next, a short description of the problem domain is presented.

Background

Even today diagnosis and treatment of individual patient in the medical domain is mostly manual and rarely aided by the computerized system. In this research project, case-based approach help the clinician to make computer-based stress diagnosis and fuzzy set theory is integrated to compose efficient matching between old cases and a new case. This chapter gives a theoretical overview of the methods and medical aspects of the research which will help to provide a better understanding of the next chapters to the readers.

2.1 Case-based reasoning

Case-based reasoning is inspired by the way human's reasoning e.g. solve a new problem by applying previous experiences adapted to the current situation. An experience (a case) normally contains a problem, a diagnosis/classification, a solution and its results. For a new problem case, a CBR system matches the problem part of the case against cases in the so called case library and retrieves the solutions of the most similar cases that are suggested as solution after adapting it to the current situation.

The origin of the CBR stems from the work of Schank and Abelson in 1977 [39] at Yale University. According to Schank [40], "remembering is at the root of how we understand... at the root of how we learn." They have explored that the new experiences reminds us the previous situation (i.e. case) or the situation pattern. CYRUS [21, 22] developed by Janet Colodner, is the first CBR system. She employed knowledge as cases and use the indexed memory structure. Many of the early CBR systems such as CASEY [23], and MEDIATOR [42] were implemented based on the CYRUS's work. The early work exploiting CBR in the medical domains are done by Konton [23], and Braeiss [4, 47] in the late 1980's.

2.1.1 CBR in medicine

CBR is suitable in the medical domain especially for its cognitively adequate model, facility to integrate different types of knowledge and its case representation which is possible to get from the patients records [18]. In particular, diagnosis of a patient in the medical domain depends on the experience. Historically, CBR diagnosis systems have most commonly been used in the medical domain. A clinician/physician may start his/her practice with some initial experience (solved cases), then try to utilize this past experience to solve a new problem and simultaneously increases his/her experiences (i.e. case base). So, this method is getting increasing attention from the medical domain since it is a reasoning process that also is medically accepted. CBR has shown to be successful in a number of different medical applications [5, 18, 33]. The advantages of CBR in medical domain have been identified in several research works i.e. in [5, 18, 31].

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

- *Feature extraction*- Feature extraction is becoming complicated in recent medical CBR systems due to the complex data format where data is coming from sensors and images or in a form of time series or free text. Feature selection and weighting is another important factor for which many CBR systems depends on the expert's knowledge. Cases with hidden key features may effect on the retrieval performance.

- *Limited number of available cases in the initial phase of a medical CBR system*- There are often a limited number of cases available, which may reduce the performance of the system. If past cases are missing or very sparse in some areas the accuracy is reduced.

- Adaptation in medical domain often performed manually by the expert of the domain. A number of problems such as, complexity in medical domain, rapid change in medical knowledge, large number of features, and also risk analysis for an automatic adaptation strategy lead to avoid adaptation steps in many medical CBR systems [31].

CBR is applied in a wide variety of medical scenarios and tasks such as diagnosis, classification, tutoring, treatment planning, as well as knowledge acquisition/management. Also hybrid CBR systems are frequent where CBR combined with other AI methods and techniques such as rule-based reasoning, data mining, fuzzy logic, as well as probabilistic and statistical computing. This enables the adoption of CBR for solving problems previously complex to solve with one single method.

2.1.2 CBR cycle

A case represents a piece of knowledge as experience and plays an important role in the reasoning process. Cases can be presented in different ways [19]. To provide solution of a new case, the cases can be represented as problem and solution structure. For the evaluation of a current case, cases can also contain outcome/result (Figure 1).

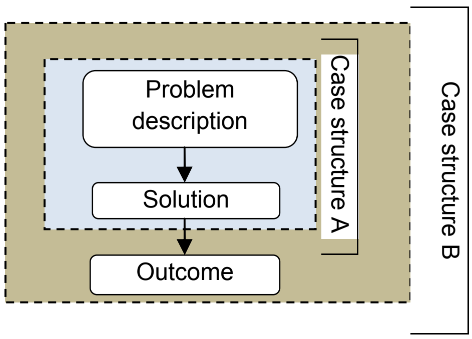

Figure 1. Cases can contain problem description and solution only or may include the result/outcome as a case structure in medical domain [58].

Prior to the case representation many CBR system depends on the feature extraction because of the complex data format in some domain. The case comprises the unique features to describe a problem. Aamodt and Plaza has introduced a life cycle of CBR [2] which is a four-step model with four Re-s, as shown in Figure 2. The four Re-s, Retrieve, Reuse, Revise and Retain present key tasks to implement such kind of cognitive model. These steps are described here focusing the issues in the medical CBR systems although they are most often designed based on the particular application at hand.

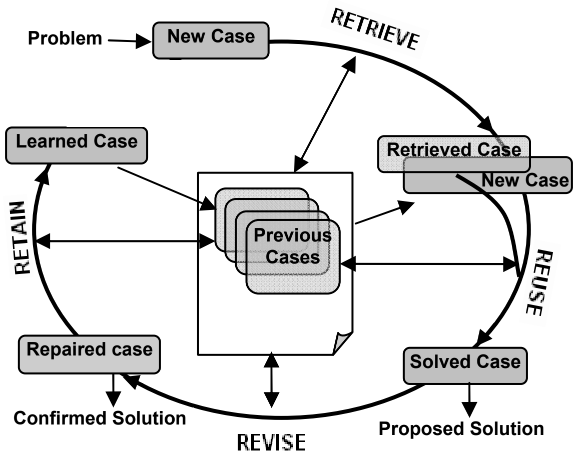

Figure 2. CBR cycle. The figure is introduced by Aamodt and Plaza [2].

Retrieve: Case retrieval is a major phase in CBR cycle where matching between two cases plays a vital role. The retrieval step is essential especially in medical applications since missing similar cases may lead to less informed decision. The reliability and accuracy of the diagnosis systems depend on the storage of cases/experiences and on the retrieval of all relevant cases and their ranking. The new retrieved cases are ranked on the basis of their similarity in matching and often propose the highest ranked case as the solution of a current situation at hand. In the medical domains, the domain knowledge is often not well understood as in circumstances of diagnosing stress related to psychophysiological issues. Therefore, retrieving a single matching case as a proposed solution may not be sufficient for the decision support system in this domain. The comparison of a new case with the old cases from the case base could be carried out applying different similarity matching algorithms. One of the commonly used similarity measurement techniques is the Nearest-neighbour algorithm [19, 41]. A standard equation (equation 1) for the nearest-neighbour is

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

Where C is a current/target case, S is a stored case in the case base, w is the normalized weight, 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. Generally there are two ways to specify the values of weights for individual features. One way is to define weights by experts in terms of the domain knowledge, while the other is to learn or optimize weights using the case library as information source. Fuzzy similarity matching algorithm, another retrieval technique, is presented in chapter 3.

Reuse and revise: The new retrieved cases are sending to the reuse step (see Figure 2) where the solution of a past case often adapts to find a suitable solution for a new case. A user can adapt solutions i.e. it could be a combination of two solutions from the list of retrieved and ranked cases in order to develop a solution to the problem in a new case. This adaptation could be done by clinicians in the domain. The clinician/expert determines if it is plausible solution to the problem and he/she could modify the solution before approved. Then the case is sent to the revision step where the solution is verified manually for the correctness and presented as a confirmed solution to the new problem case. In the medical system, there is not much adaptation, especially in a decision support system where the best cases are proposed to the clinician as suggestions of solutions and when the domain knowledge is not clear enough [19].

Retain: Finally, this new solved case is added to the case base functioning as a learning process in the CBR cycle and allows the user to solve a future problem by using this solved case, which is commonly termed as retain. Retaining of a new solved case could be done manually based on clinician or expert's decision.

2.2 Fuzzy logic

Fuzzy set theory has successfully been applied in handling uncertainties in various application domains [20] including medical domain. Fuzzy logic was introduced by Lotfi Zadeh, a professor at the University of California at Berkley in 1965[48]. The use of fuzzy logic in medical informatics has begun in the early 1970s.

The concept of fuzzy logic has been formulated from the fact that human reasoning particularly, common sense reasoning is approximate in nature. So, it is possible to define inexact medical entities as fuzzy sets. Fuzzy logic is designed to handle partial truth i.e. truth values between completely true and completely false. For instance, Fuzzy logic allows both a person is young and old to be partly true. It explains fuzziness existing in a human thinking process using fuzzy values instead of using a crisp or binary value. It is a superset of classical Boolean logic (see detail in section 2.2.1 and 2.2.2). In fuzzy logic, exact reasoning is treated as a special case of approximate reasoning. Everything in fuzzy logic appears as a matter of some degree i.e. degrees of membership function or degrees of truth.

For example, Monica is tall because her height is 181 cm (Table 1). In Boolean logic if we draw a crisp boundary at 180 cm (Figure 3), we find that Jerry, who is 179 cm, is small. At the same time, in fuzzy set all men are "tall", but their degrees of membership depend on their height.

Table 1. The classical 'tall men' example using Crisp and Fuzzy values

Name	Height, cm	Degree of membership	
		Boolean	Fuzzy
John	208	1	1.00
Monica	181	1	0.82
Jerry	179	0	0.78
Roger	167	0	0.15
Sofia	155	0	0.00

So for instance, if we consider Jerry is tall we can say the degree of truth of the statement 'Jerry is tall' is 0.78. The graph of the example interpreted as a degree of membership is given in Figure 4:

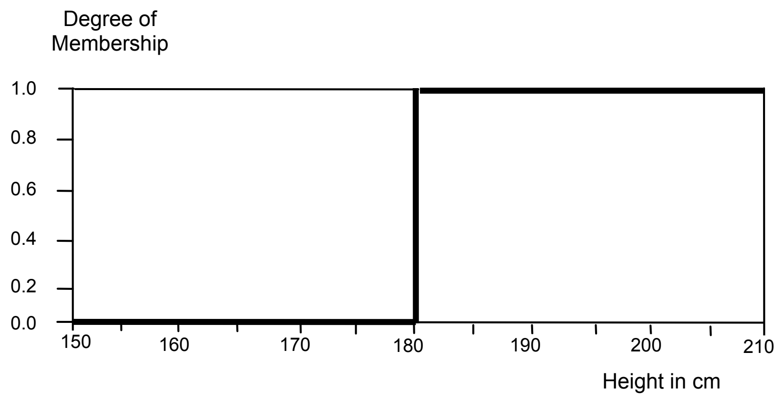

Figure 3. Example presented in crisp set.

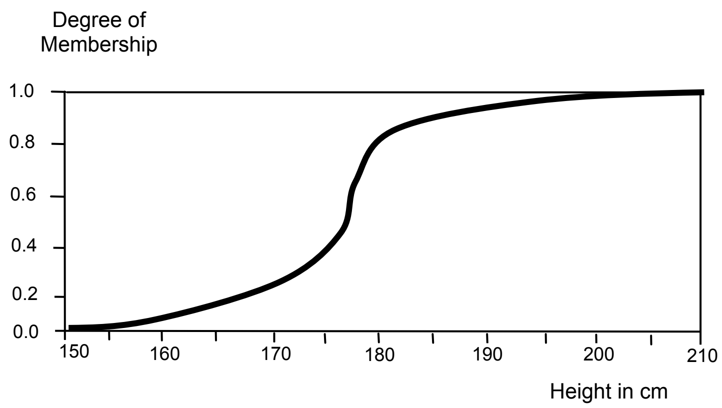

Figure 4. Example presented in fuzzy set.

Where, X-axis is the universe of discourse which shows the range of all possible values for an input variable i.e. men's heights. Y-axis represents the degree of membership function i.e. the fuzzy set of tall men maps height values into corresponding membership values (Figure 4).

2.2.1 Classical set theory

In classical set theory, a point x belongs to a set A if and only if $\varphi_A(x)$=1. i.e.

$$\varphi_A(x) = \begin{cases} 0, & x \notin A \\ 1, & x \in A \end{cases}$$

Where, $\varphi_A(x)$ is a characteristic function, mapping from any universal set X to the binary set $\{0,1\}$.

2.2.2 Fuzzy set theory

A fuzzy set A is defined as any set that allows its members to have different degrees of membership i.e. membership function $\mu_A(x)$ mapping from the universal set X to the interval [0, 1].

$$\mu_A(x): X \to \{0,1\}, \text{Where, } \mu_A(x) = 1; \text{ if x is totally in A}$$
$$\mu_A(x) = 0; \text{ if x is not in A}$$
$$0 < \mu_A(x) < 1; \text{ if x is partially in A}$$

The characteristic function of classical set $\varphi_A(x)$ is a special case of the membership function $\mu_A(x)$ of fuzzy set theory. Thus the fuzzy set is a generalization of the classical set theory.

The set operations (union, intersection, complement etc.) in terms of this membership function are:
Union: Union is the largest membership value of the element in either set (Figure 5). The union of two fuzzy sets A and B on universe X can be given as: $\mu_{A\cup B}(x) = \max(\mu_A(x), \mu_B(x))$,

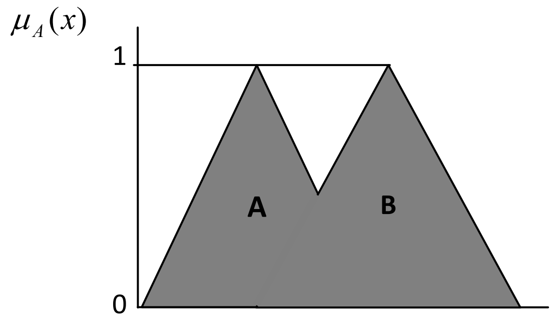

Figure 5. Example of fuzzy union.

Intersection: intersection is the lower membership in both sets of each element (Figure 6). The intersection of two fuzzy sets *A* and *B* on universe of discourse X can be given as: $\mu_{A \cap B}(x) = \min(\mu_A(x), \mu_B(x))$

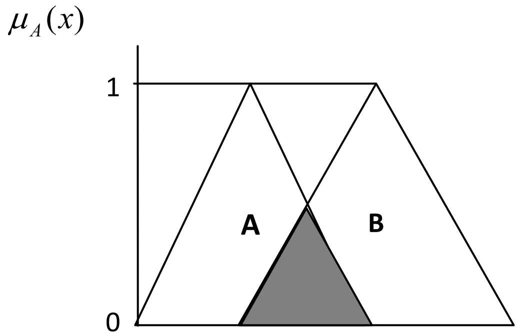

Figure 6. Example of fuzzy intersection.

Complement: The complement of a set is an opposite of that set (Figure 7). For a fuzzy set A the complement is: $\mu_{notA}(x) = 1 - \mu_A(x)$

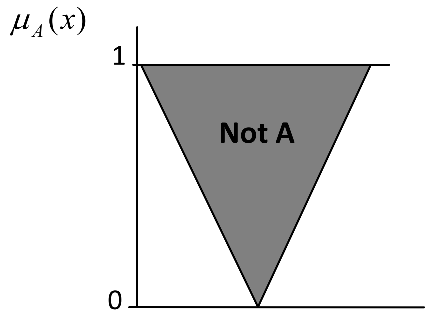

Figure 7. Example of fuzzy complement.

2.3 Stress

The term ‘stress’ was first introduced by Hans Selye in the 1950s who has noticed that patients suffering physically due to not only their disease or medical condition. He defined stress as "non-specific response of the body to any demand" [52]. Stress is our body’s response to any threat to defend the body from its potential harm. Another definition of stress by Lazarus is "stress occurs when an individual perceives that the demands of an external situation are beyond his or her perceived ability to cope with them" [59]. Individual response to a situation/thing can be varied and depends on one’s coping capability. For example, a person might take a huge work load without being worried and the same amount of work could make another person worried thinking how to cope with that situation. So, individuals’ mental state and way to appraise determine whether stress occurs or not. In our everyday life 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. This is called the “fight-or-flight” reaction, or the stress response.

Human nervous system is divided into two main parts, the voluntary system and autonomic system. The automatic nervous system is divided into two parts: sympathetic and the parasympathetic nervous system.

The sympathetic nervous system (SNS) works to protect our body against threat 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, increase blood pressure, decrease digestions and constricting (narrowing) blood vessels i.e. vasoconstriction which slow down the flow of blood etc. Sympathetic nervous system is thus activates the body for the fight-or-flight (fight or run) response to stress. The parasympathetic nervous systems counteracts to fight-or-flight response to return the body to the normal state. It stimulates the digestion, the immune and eliminative organs. As a result increase digestion, decrease heart rate, relaxing muscles etc. to rebuild the body [60].

2.3.1 Physiology of the stress response

When our brain appraises stress, the sympathetic nervous system, initiate in hypothalamus, prepares human brain to response to stress (see Figure 8). SNS stimulates the adrenal gland to release the hormone *Adrenaline* into the blood supply. It also releases *Noradrenaline* at the nerve endings and activates various smooth muscles. These hormones decrease digestions, increase the heart rate, increase in metabolic rate, dilates blood vessels in the heart and other muscles and constrict the skin blood vessels e.g. decrease skin temperature etc.

The Hypothalamus also releases *Corticotropin-releasing hormone* (CRH) which activates the pituitary gland to release the *Adrenocorticotropin hormone* (ACTH). ACTH then travels through the blood supply and stimulates the adrenal glands to release *Cortisol* into the blood supply.

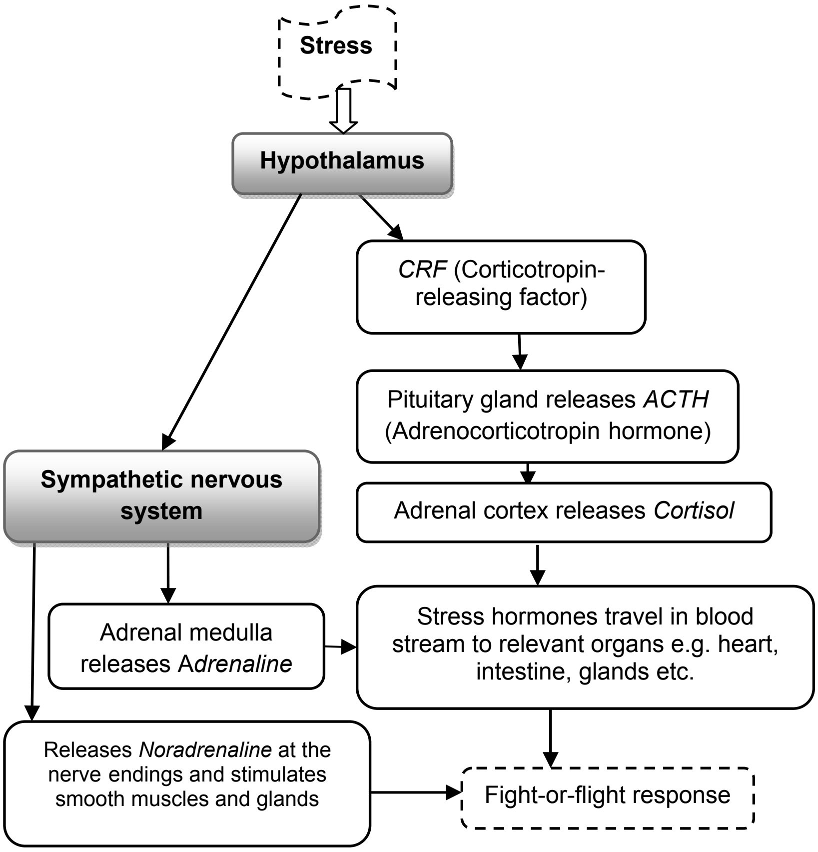

Figure 8. Physiology of the stress response [53].

Thus the human body supply energy and oxygen, and provide stimulation to the heart, other muscles, the brain, and other organs to help in response to stress [53]. When the brain receives the information that the stressed situation is over, parasympathetic nervous system helps to return the hormones in the baseline levels. Thus, the sympathetic nervous system activates during stress and helps to release the stored energy. On the other hand, parasympathetic nervous system works opposite i.e. tends to return the level as the normal state. So, due to stress response body releases large amount of energy immediately and this reaction to stress can affect many physiological mechanisms. To diagnose psychophysiological dysfunctions such as stress, clinicians often consider the balance between the activities in the sympathetic and parasympathetic nervous systems. A general overview of stress activity to our body is given in Figure 9.

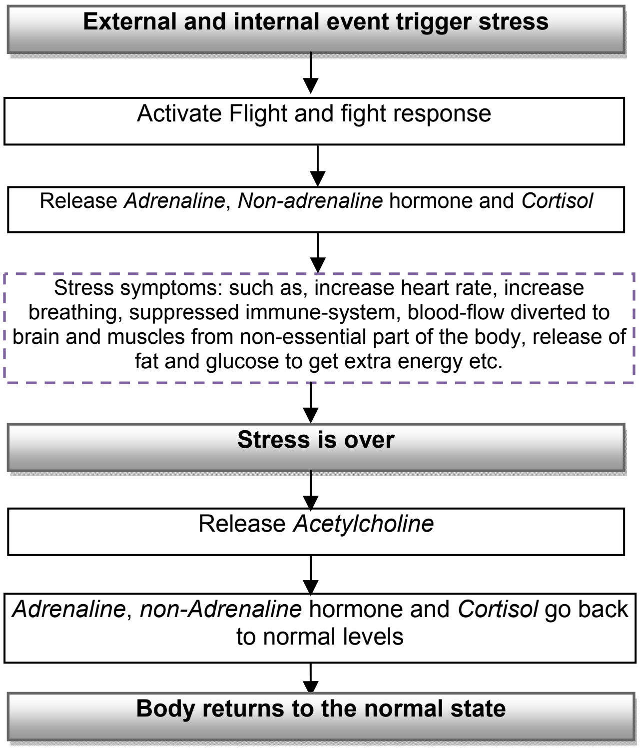

Figure 9. General overview of the stress response.

Small amount of stress is good for us. It can prepare to meet difficult challenges in life. On the other hand, long-term exposure to stress i.e. when the emergency stress response keeps ‘on’ i.e. out of its functional context the most of the time it may in worst case cause severe mental and physical problems that are often related to psychosomatic disorders, coronary heart disease etc. Symptoms of stress can be experienced in different ways such as anxiety, muscle tensions/cramp, depression and other bodily symptoms which in turn can further influences our sympathetic nervous system. There are several stress management techniques, such as relaxation, exercise, and cognitive-behavioural stress management etc.

2.3.2 Psychophysiology

Psychophysiology is a branch of psychology. It addresses the relation between ‘Psychology’ and ‘Physiology’. Psychophysiology is defined as the study of relations between psychological and physiological systems and their interactions. Andreassi [50] defined Psychophysiology as “the study of relations between psychological manipulations and resulting physiological responses, measured in the living organism, to promote understanding of the relation between mental and bodily processes”. There is an interaction between physical body and mind so for instance, a physical disease can be treated psychologically or vice-versa. If a person is informed about this mind-body connection, he/she can utilize this knowledge and control psychophysiologic activity and could improve health [51]. Physiological parameters commonly measured using skin conductance, skin temperature, respiration e.g. end-tidal carbon dioxide ($ETCO_2$), 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. Stress medicine is a branch of Psychophysiology where the treatment of stress-related dysfunctions is studied. Psychophysiologists investigate scientific ways to control body functions to prevent health problems i.e. in stress medicine prevent stress-related dysfunctions for individual. Skin temperature is one of the physiological parameters that can be used to measure stress. Also other parameters such as cardiovascular parameters i.e. heart rate, heart rate variability (HRV) can be used to quantify stress.

2.3.3 Biofeedback

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 psychophysical problems [1, 25]. The basic purpose of biofeedback is that the patient gets feedback in a clear way (patient observes the graph and knows from preceding education how it should change) and with this feedback can behaviourally train the body and/or mind to biologically respond in a different better way. Biofeedback often focuses on relaxation and how the patient can practice relaxation while observing, e.g. the changes in skin temperature. A temperature sensor can be used to collect finger temperature by attaching it to the finger.

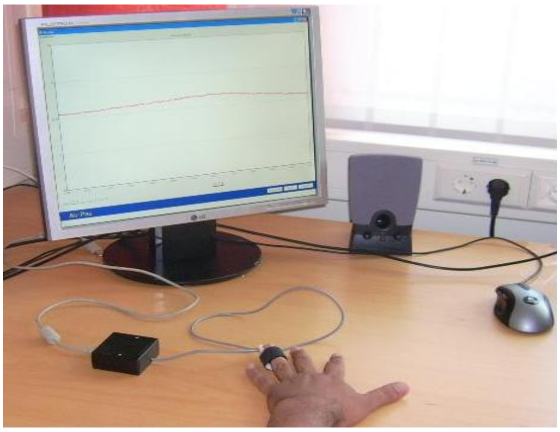

Figure 10. Biofeedback training using finger temperature measurement.

This finger temperature measurement taking using a temperature sensor during different stress and relaxed conditions is possible to monitor as electronic signal on the computer screen as shown in Figure 10. Thus the pattern of the finger temperature measurement observed from this signal can support biofeedback training for the management of stress-related dysfunctions. However, different patients with very different physical reactions to stress and relaxation make stress a complex area to apply biofeedback. A clinician is commonly supervising patients in the application of biofeedback in stress area and makes together with the patient adjustment to the individual based on observed dysfunctions and results from behaviour training.

Chapter 3

This chapter explains the choice of methods for the thesis work. First the nature of the research is presented and then the choice of methodological approach is discussed.

Diagnosis of stress

It is known today that high levels of stress may cause serious health problems. A system that notifies when stress levels are rising or too high (i.e. activity of SNS is increasing) is valuable in many situations, both in clinical environment and in other environments, e.g. the patients home and work environment. In clinical psychophysiology, diagnosis of stress is difficult even for an experienced clinician. Large individual variations and the absence of more specific rules make it difficult to diagnose stress and the risk of stress-related health problems. A clinician learns from education and with experience how to interpret the different symptoms and their interactions.

3.1 Finger temperature (FT) and stress

In general, finger temperature decreases when a person is stressed and increases during relaxation or in a non-stressed situation. This relates to mainly sympathetic intervention of the alpha-receptor in the vascular bed. When relaxation occurs, sympathetic nervous system activity decreases as well as the intervention of the alpha receptors, which leads to increased diameters in blood vessels and increase the blood flows and temperature [43]. Reverse situation occurs during stress i.e. the sympathetic nervous system activates causing a decrease in peripheral circulation which leads to decrease skin temperature. Thus the blood flow in the finger temperature responds also to change in emotional state. In clinical practice, the activity of automatic nervous system i.e. balances between the sympathetic and parasympathetic nervous systems are monitored as a part of diagnosis of psychophysiological dysfunctions. Therefore, the rise and fall of finger temperature as illustrated in figure 11 can help to diagnose stress-related dysfunctions or dysfunctional behaviours. However, the behaviour of the finger temperature is different for different individuals due to health factors, metabolic activity etc.

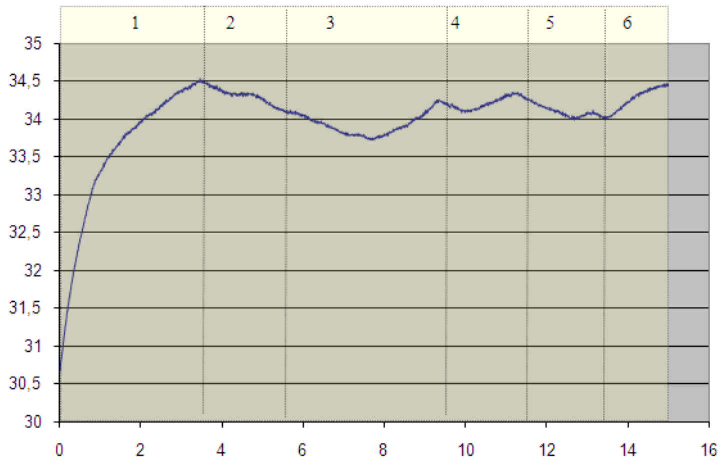

Figure 11. Variations on finger temperature measurement with stress in the different test phases

3.1.1 Diagnosis of stress using FT

In clinical practice, finger skin temperature has been used as one of the parameters in diagnosing patients with stress; also it is an effective parameter for the patients with Raynaud's syndrome [61]. One of the advantage of using FT in diagnosing stress is that the other conventional methods such as, respiration e.g. end-tidal carbon dioxide ($ETCO_2$), heart rate e.g. calculating the respiratory sinus arrhythmia (RSA) and heart rate variability (HRV) etc. used clinically, the diagnosis and biofeedback training is often expensive. These also require equipment not suitable for use in non-clinical environment and without experienced clinical staff. Since it is not always possible to provide clinical staff with a lab measuring many parameters (often using many sensors) a supplementary convenient tool that can be used any time at any place to diagnose and control stress for general user is important. A temperature sensor can be used to collect finger temperature by attaching it to the finger. The FT signals from the sensor readings during different stress and relaxed conditions can be possible to transmit as electronic signal on the computer screen. Thus it can serve as a convenient method to diagnose and treatment i.e. biofeedback to normalize stress-related dysfunctions at home and at working places for general user. Also it can be used as an auxiliary medical system for the clinical treatment.

3.1.2 Analysis of FT

The correlation between FT and stress reactions is a well known factor, but individual differences make it difficult to use in automatic systems since there are no absolute values of skin temperature in relation to stress levels. An example of the finger temperature measurement is shown in Figure 11 which can demonstrate the variations on finger temperature related with stress. The finger temperature is measured using a temperature sensor which is connected to a computer through an A/D converter. The temperature is then observed during different conditions i.e. in 6 steps (baseline, deep breath, verbal stress, relax, math stress, relax) as described in Table 2 [paper C]. This calibration phase helps to establish an individual stress profile and is used by us as a standard protocol in clinical environment for patients with stress-related dysfunctions. An experienced clinician evaluates these measurements during the different test conditions to make an initial diagnosis. This diagnosis is complex and based on long experience [37].

Table 2. Measurement procedure used to create an individual stress profile.

Test step	Observation time	Conditions	Finger temp	Notes
1.	3 min	Base Line		
2.	2 min	Deep Breath		
3.	2+2 min	Verbal Stress		
4.	2 min	Relax		
5.	2 min	Math stress		
6.	2 min	Relax		

The purpose of s*tep1* is to establish a representative level for an individual when he/she is neither under strong stress nor in a relax state. Sometimes clinicians let the person read a neutral text during this step. A clinician not only identifies an individual's basic finger temperature, but also notes fluctuations and other effects, e.g. disturbances in the environment or observes person's behaviour. During *step2* the person breaths deeply which under guidance normally causes a relax state. Also how quickly the changes occur during this step is relevant and record together with observed fluctuations. *Step3* is initiated with letting a person tell about some stressful events they experienced in life. It is important for the clinician to make sure that this really is a stressful event, since some persons instead select some more neutral event or tell about a challenge they were excited to solve. During the second half of the step a person thinks about some negative stressful events in his/her life. In *step4*, the person may be instructed to think of something positive, either a moment in life when he was very happy or a future event he looks forward to experiencing (this step may be difficult for a depressed person and adjusted accordingly by the clinicians). *Step5* is the math stress step; it 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 or person's capacity to relax.

3.1.3 Example of some interesting FT observations

We observe three situations while collecting the FT measurement *a.* finger temperature decreases with increasing stress which is the most common situation (Figure 11), *b.* finger temperature increases with increasing stress i.e. paradoxal relation (Figure 12) and *c.* little or no changes i.e., remains in the stable situation when a person is experienced with stress, this is exceptional but might happened for some persons. In such cases the clinical expertise is important.

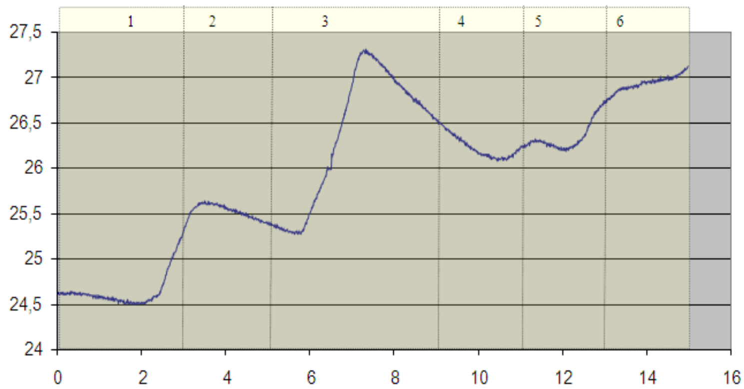

Figure 12. FT vs. paradoxal relation (increase of FT in stress situations). Y-axis: temperature in degree Celsius and X-axis: time in minutes.

Ideally the temperature is monitored repeatedly in short occasions during a longer period, i.e. a week, to determine the temperature consistency or pattern for the person. And it varies for different persons, e.g. some may have representative temperature of 27° C as her/his lowest temperature while for other person 32° C may be the lowest. An example of different representative temperature is illustrated in Figure 13 and 14 for two different persons (e.g. Individual A and Individual B).

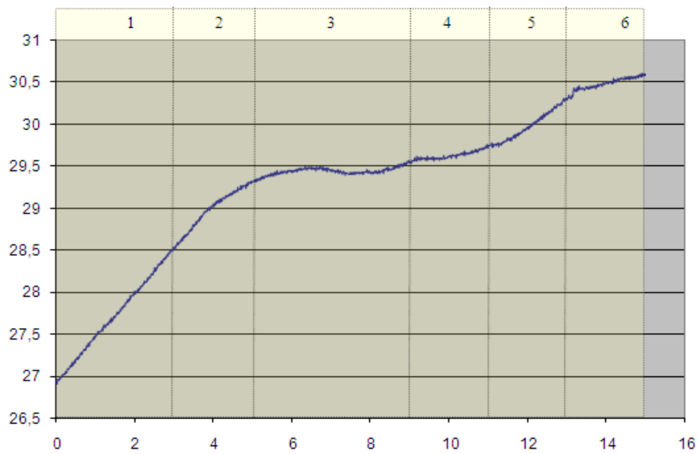

Figure 13. Individual A. Variations on the representative temperature depend on individual person. Y-axis: temperature in degree Celsius and X-axis: time in minutes

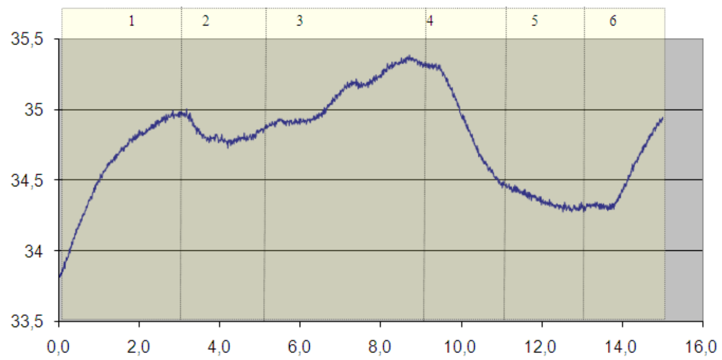

Figure 14. Individual B. Variations on the representative temperatures depend on individual person. Y-axis: temperature in degree Celsius and X-axis: time in minutes

Changes in temperature before and after meal can be pronounced in some individuals as shown in Figure 15.

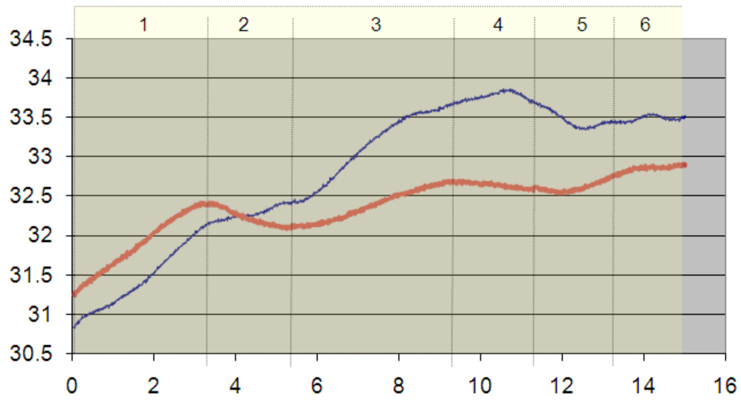

Figure 15. Finger temperature for a person before (orange) and after lunch (blue). Y-axis: temperature in degree Celsius and X-axis: time in minutes.

Stress response is different for different person and also the coping capability is very individual. Reactivity time is important to identify stress levels and to make an individual treatment plan. For instance, in Figure 16 the person cannot cease to think about the stressful events until the next stages. So this person might need longer time to recover from stress.

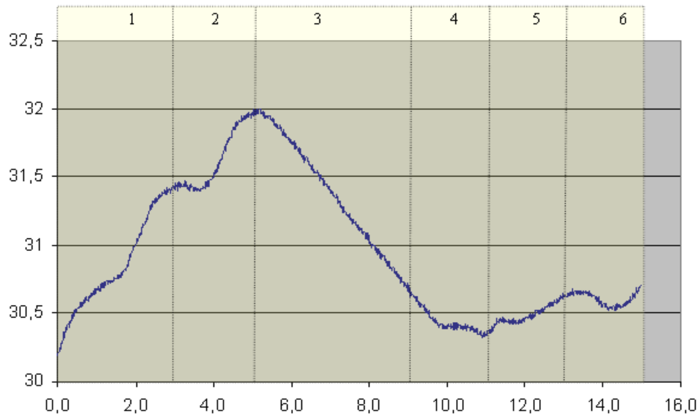

Figure 16. The person cannot remove thinking the stressful events until the next stages. Y-axis: temperature in degree Celsius and X-axis: time in minutes.

Finger temperature measurement in Figure 17 for a student before his master's thesis presentation explains that he was so much stressed before the presentation and could not recover from the stress in the next stages.

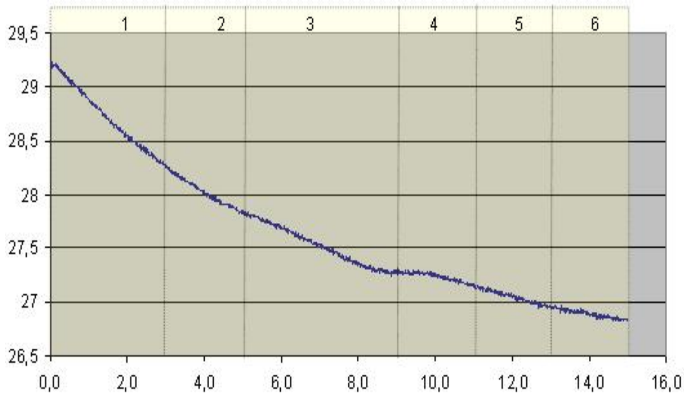

Figure 17. A student before the thesis presentation. Y-axis: temperature in degree Celsius and X-axis: time in minutes.

3.2 Feature extraction from FT sensor signal

During diagnosis, when done manually, an experienced clinician often classify FT signal without being pointed out intentionally all the features he/she uses in the classification. However, extracting appropriate features is of great importance in performing accurate classification in a computer-aided system. After the test during calibration phase, a person is requested to answer some questions for instance, when he/she had his/her meal, food habit, food allergy and so on because these could also affect the FT measurement [paper C]. The FT sensor measurements are recorded using software which provides filtered data to the system. This signal data and answer to the questions from the calibration phase are then stored in a file. From the exported file, system retrieves 15 minutes finger temperature measurements (time, temperature) in 1800 samples, together with other numeric (age, room-temperature, hours since meal, etc) and symbolic (gender, food and drink taken, sleep at night, etc) features.

3.2.1 Calculating the slopes

As can be seen in section 3.1 after analyzing a number of finger temperature signals, the temperature is rising and falling against time and after an initial increase, finger temperature decreases in stress condition (step 3) and increases in relax condition (step 4). Our opinion is that either mean value or standard deviation of the FT measurement might not be indicative for stress. For instance, consider two signals one is increasing from 20° C to 30° C, the other decreasing from 30° C to 20° C, and then both have same mean/standard deviation value in the duration, but indicate opposite for stress levels. As alternative way, the mean of the slope value might be a feasible feature to convey relation with stress. If the mean slope is sufficiently positive, it will be a clear indication that the activity of SNS is decreasing e.g. relax, otherwise an indication of stress. But if the mean slope is around zero, it shows a situation with high uncertainty for decision or weak decision. Then according to closer discussion with clinicians on the interpretation of such graph, it is concluded that in general, the finger temperature could decrease with stress and increase in relax state and the changes between the steps are also of importance for the clinicians. A standardization of the slope that is using negative and positive angles makes it more visualise and gives a terminology to a clinician for reasoning about stress. Therefore, we calculate the derivative of each step to introduce “degree of changes” as a measurement of the finger temperature changes.

A low angle value, e.g. zero or close to zero indicates no change or stable in finger temperature. A high positive angle value indicates rising finger temperature, while a negative angle, e.g. -20° indicates falling finger temperature. Usually, the purpose of the *step1* (baseline) is to stabilize the finger temperature before starting the test hence this step has not been considered and the clinician also agreed on this point.

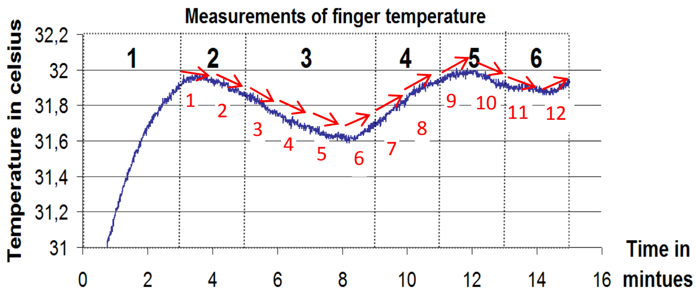

Figure 18. Changes in FT data against time during different stress and non-stress condition.

Each step is divided by one minute time interval (4 minutes step3 is extracted as 4 features) and each feature contains 120 sample data (time, temperature). Thus 12 features are extracted from the 5 steps (step 2 to 6) and named as *Step2_Part1*, *Step2_Part2*, *Step3_Part1*, ………, *Step6_Part1*, *Step6_Part2* as shown in Figure 18, for detail description see [paper B]. Five other features which have also been extracted from the sensor signal are *start temperature* and *end temperature* from step2 to step6, *minimum temperature* of step3 and step5, *maximum temperature* of step4 and step6, and *difference between ceiling and floor*. Finally, 17 (12+5) features are extracted (Table 3) automatically from the fifteen minutes (1800 samples) FT sensor signal data.

Table 3. List of features extracted from the FT sensor signal.

No	Feature
1	Step2_part1
2	Step2_part2
3	Step3_part1
4	Step3_part2
5	Step3_part3
6	Step3_part4
7	Step4_part1
8	Step4_part2
9	Step5_part1
10	Step5_part2
11	Step6_part1
12	Step6_part2
13	Start_temperature
14	End_temperature
15	Maximum_ temperature
16	Minimum_ temperature
17	Diff_ceiling/floor

Classification of individual sensitivity to stress based on “degree of change” as a measurement for finger temperature changes is available in paper C section 4.1. A low value, e.g. zero or close to zero is no change or stable in finger temperature. A high value indicating a steep slope upwards indicates a fast increase in finger temperature, while a negative angle, e.g. -20° shows a steep decline. The proposal is that the X-axis in minutes and the Y-axis in degrees Celsius, hence a change during 1 minute of 1 degree gives a “degree of change” of 45° see Figure 19.

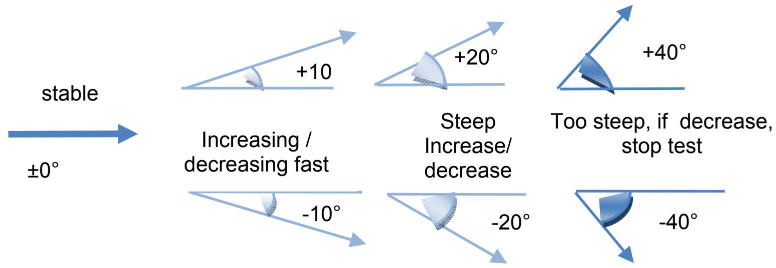

Figure 19. Example of visualizations of temperature change, X-axis minutes, Y-axis in degree Celsius.

3.3 Artificial intelligence (AI) for decision-support in stress diagnosis

The term decision support system (DSS) is defined by Little as "model-based set of procedures for processing data and judgments to assists a manager in his decision making" [54]. Medical decision-support system (DSS) has been defined by many people in many different ways. According to Shortliffe a medical DSS is "any computer program designed to help health professionals make clinical decisions [55]." The early AI systems in medical decision making emerged around 1950s' mainly build using decision trees or truth tables. After that, different methods or algorithms have been introduced to implement medical decision support system such as, Bayesian statistics, decision-analytical model, symbolic reasoning, neural-networks, rule-based reasoning, fuzzy logic, case-based reasoning etc.

3.3.1 Why Case-based reasoning?

Since the implementation of MYCIN [56] many of the early AI systems were attempted to apply rule-based system in developing computer based diagnosis system. However, for a broad and complex medical domain the effort of applying rule-based system has encountered several problems. Some of the preliminary criteria for implementing a rule-based system are that the problem domain should be well understood, and constant over time and the domain theory should be strong enough [45]. In psychophysiology, diagnosis of stress is difficult that even an experienced clinician might have difficulty in expressing his knowledge explicitly. Large individual variations and the absence of general rules make it difficult to diagnose stress and the risk of stress-related health problems. For that reason, in this research project, case-based reasoning (CBR) is chosen since it works well in such domains where the domain knowledge is not clear enough i.e. weak domain theory. Furthermore, CBR system can learn automatically which is very important as the medical domain is evolving with time. Rule-based system cannot learn automatically, new rules are usually inserted manually. Statistical techniques are also applied successfully in medical systems. But to apply statistical model we need usually a large amount of data at hand to investigate a hypothesis which is also not available in our application domain.

Several motivation of applying CBR in stress diagnosis can be identified:

1. CBR [2, 19] method can work in a way close to human reasoning i.e. solves a new problem applying previous experiences. This reasoning process is also medically accepted and the experts in diagnosing stress too rely heavily on their past memory to solve a new case. This is our prime reason why we prefer to use CBR.

2. Knowledge elicitation is another problem in diagnosing stress, as human behaviour or response to stress is not always predictable. Even an experienced clinician in this domain might have difficulty to articulate his knowledge explicitly. Sometimes they make assumptions and predictions based on experiences or old cases. To overcome this knowledge elicitation bottleneck we use the CBR because in CBR, this elicitation can be performed with the previous cases in the case base.

3. For diagnosing stress we use finger temperature sensor signals. By analysing this biomedical signal we identified large individual variations which make it difficult to define in a model or using a set of rules. Other AI systems such as, rule-based reasoning or model

based reasoning is not appropriate in this context. CBR can be used when there are no sets of rules or a model [57].

4. To implement a case-based reasoning system in this domain we need to identify the features from the FT sensor signal which would allow a clinician to identify features for the success or failure of a case. This would help to reduce the repetition of mistakes in the future.

5. The knowledge in the domain is growing with time so it is important that the system can learn new knowledge. Many of the AI systems failed to continue because of the lack of this type of maintenance. CBR system can learn by adding new cases into the case base.

6. The cases in the case base can be used for the follow up of the treatment for an individual and also for the training purposes of the less experienced clinicians.

3.3.2 Why Fuzzy similarity matching?

Fuzzy techniques are incorporated into our CBR system to better accommodate uncertainty in clinicians reasoning. Many crisp values both from the FT measurements and given by a clinician are known to have a possibility distribution often known by experts and used in their reasoning. We propose that this dimension and domain knowledge is represented by fuzzy similarity, a concept well received by clinical experts. Representation of a similarity value using a matrix [paper B] often shows a sharp distinction which may provide an unreliable solution in domains where it is known that these values are less exact. Fuzzy similarity matching reduces this sharp distinction and handles the underlying uncertainty existing in the reasoning process.

3.3.3 Stress diagnosis system

A decision support system for diagnosing individual stress-condition based on finger temperature measurements works in several stages as illustrated in Figure 20.

The first stage is the Calibration phase [paper D] where the finger temperature measurement is taken using a temperature sensor to establish an individual stress profile.

Feature extraction [paper C] is the second stage described in section 3.1.2 where relevant features are extracted automatically from the outcome of the calibration phase.

Then a new case is formulated with 19 features in total stored in a vector with 12 extracted features (Section 3.2 Table 3), to which *hours since last meal* and *gender* are also added. Finally, this new case is passed to the case-based reasoning cycle.

The new case is then matched using different matching algorithms including *modified distance function*, *similarity matrix* and *fuzzy similarity matching*, see details in paper B. The DSS can provide matching outcome in a sorted list of best matching cases according to their similarity values in three circumstances: when a new problem case is matched with all the solved cases in a case base (between subject and class), within a class where the class information is provided by the user and also within a subject.

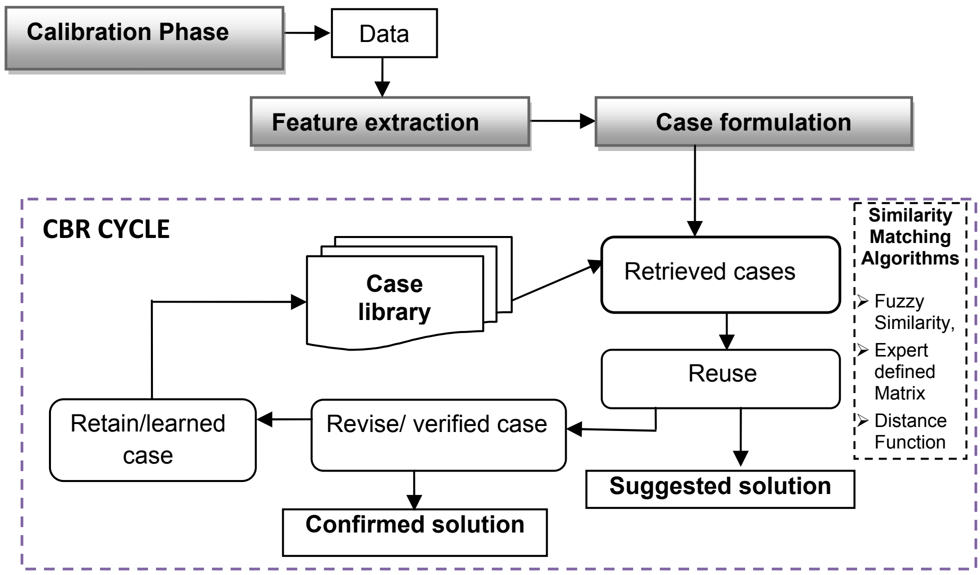

Figure 20. General overview of a decision support system for stress diagnosis.

A clinician thereafter revises the best matching cases and approves a case to solve the new problem case by using the solution of this old case; this confirmed solution is then prescribed to the patient. However, often an adjustment to the solution of the old case may be required since a new problem case may not always be as same as an old retrieved case. However, there is no adaptation of the cases in the proposed system. This adaptation, in our system could be done by clinicians in the domain. In many other medical systems, automatic adaptation is rare, especially in a decision support system where the best cases are proposed to the clinician as suggestions of solutions and when the domain knowledge is not clear enough [45]. Finally, this new solved case is added to the case base functioning as a learning process in the CBR cycle and allows the user to solve a future problem by using this solved case, which is commonly termed as retain. Retaining of a new solved case could be done manually based on clinician or expert's decision.

The decision support system is currently implemented as a prototype in Java so it is platform independent. An evaluation of the system performance compared to a domain expert/clinician is presented in paper B. The evaluation process is designed for the three algorithms including *distance function*, *similarity matrix*, and *fuzzy matching*, used in the system. The System performance in terms of accuracy has been compared with experts in the domain where the main goal is to see how close the system could work compared to an expert. The case base is initialized with 39 reference cases classified by the domain expert and the classification of sensitivity to stress has been denoted as *Very Relaxed*, *Relaxed*, *Normal/Stable*, *Stressed* and *Very Stressed*. Both in ranking and in similarity performance, fuzzy similarity matching algorithm shows better result than the other algorithms (i.e. distance function and similarity matrix) compared with the expert's opinion.

3.3.4 Fuzzy similarity matching

Similarity matching plays an important role in Case-based reasoning systems. Different matching algorithm or measurements approaches can be applied to calculate the similarity between the feature values of a current case and an old case. Fuzzy sets can be used as a similarity measurement technique in CBR systems [10, 15, 44]. A discussion about the relationship between the similarity concept and several other uncertainty formalisms including fuzzy sets can be found in [38]. Fuzzy CBR matches the cases in terms of degrees of similarities between attribute values of previous cases and a new case instead the traditional Boolean matching.

One of the fuzzy similarity matching techniques [15] using equation 2 is described in Figure 21. The similarity between an old cases and a new case is calculated using the overlapping areas between the two fuzzy values in their membership functions. The similarity equation is defined as-

$$S_{m_1 m_2} = \min(om/m_1, om/m_2) \text{ ------------------ } (2)$$

Here m_1 is the area of one attribute value with one membership function and m_2 is associated with the second membership function and the overlapping area is denoted as om.

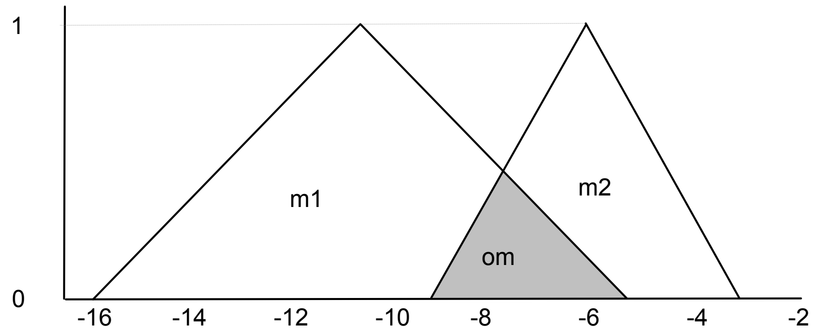

Figure 21. Fuzzy similarity using triangular membership functions. X-axis denotes the feature values and Y-axis degrees of membership functions.

For example, the attribute '*S'* of a current case and an old case have the values -6.3 and -10.9 respectively. Here, the weight of the membership function (*mf*) is fuzzified with 50 % in each side as shown in Figure 21. This fuzzification can be done by a trial and error process based on the application domain. For the current case, the input value -6.3 is represented with the *mf* grade of 1 and the lower and upper bounds are -9.45 and -3.15 represented with an *mf* of grade 0. For the old case the input is -10.9 represented with an *mf* grade of 1 and shows the lower and upper bounds -16.35 and -5.45 with an *mf* grade of 0.

From Figure 21, m_1=5.45 and m_2=3.15 where area is defined by the equation area=(1/2) x base x height. For *om*=0.92, height is defined from the intersection point of the two fuzzy membership functions. So from equation 2, the local similarity is *min (0.17, 0.29)=0.17* and *max* is 0.29. If the *mf*s are considered as 100 % fuzzified then minimum local similarity will be 0.34 and maximum will be 0.58. In this way a user has option both for tuning the *mf*s and choosing the min/max values for the similarity function depending on the requirements. When the overlapping areas become bigger, then the similarity between the two features will also increase, and for completely matched features similarity will be 1.

Chapter 4

This chapter summarises the thesis contributions. A short summary for each included paper is presented here.

Research contributions

The contributions of this research work have been described in the included four research papers. The connections between the research questions and the contributions can be seen from Figure 22. The contribution of paper A is to make a comprehensive survey on the recent (2004 - 2008) CBR systems in medicine to investigate the current trends in this domain based on some system properties.

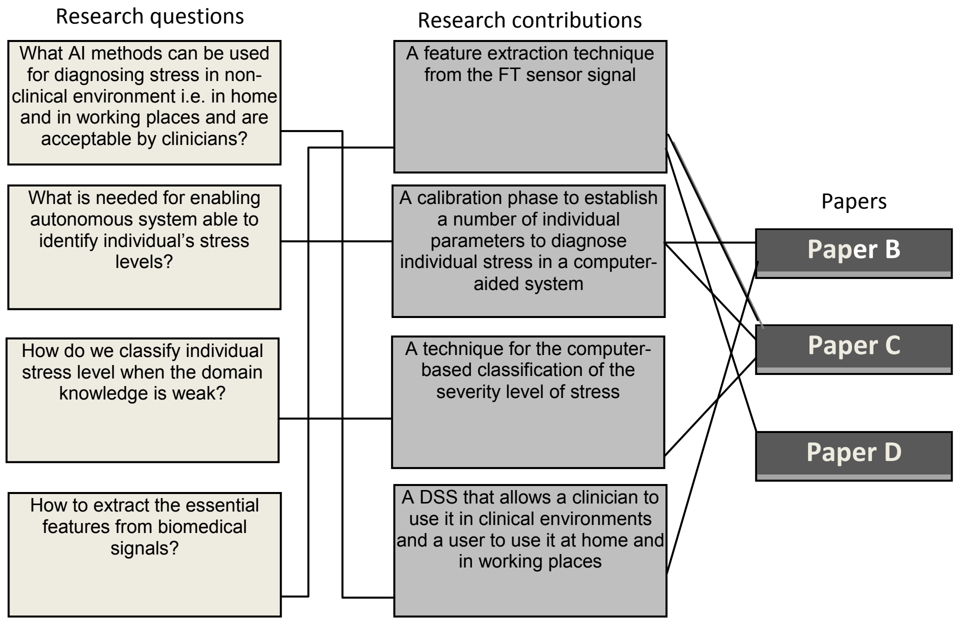

Figure 22. Connections between the research questions and contributions

4.1 Summary of the appended papers

This section shortly summarizes the contributions from each paper. The full versions of these papers are presented at the end (Part II) of this thesis report.

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

I am the main author of the paper and contributing in systems studies, literature reviews, and analysis of the systems properties, result and result discussion.

This paper presents a comprehensive survey of applied research of CBR in medical domains. A number of recent medical CBR systems are analyzed deeply in terms of not only their functionalities but also the techniques adopted for system construction. In particular we outline a variety of methods and approaches that have been used for case matching and retrieval which play a key role in these medical CBR systems. It is demonstrated from our survey that CBR has been a powerful methodology applied in many medical scenarios for various tasks such as diagnosis, classification, tutoring, treatment planning, as well as knowledge acquisition/management. It also leaves us with the awareness that hybridization of CBR with other AI techniques such as ontology, rule-based reasoning, data mining, fuzzy logic, neural network, as well as probabilistic and statistical computing would create promising opportunities to enhance CBR systems to scale up to increasingly large, complex, and uncertain data and information in clinical environments.

4.1.2 Paper B: A Case-Based Decision Support System for Individual Stress Diagnosis Using Fuzzy Similarity Matching.

For this journal paper I work as a main author and involved in writing the chapters' method and system overview, related work, features extraction and case formulation, case retrieval and matching and fifty percent of the evaluation chapter.

The paper addresses a decision support system using case-based reasoning in combination with other artificial intelligent (AI) techniques. Case-based reasoning is applied as the main methodology to facilitate experience reuse and decision explanation by retrieving previous similar temperature profiles. Furthermore, fuzzy techniques are also employed and incorporated into the case-based reasoning system to handle vagueness, uncertainty inherently existing in clinicians reasoning as well as imprecision of feature values. The paper shows that a fuzzy matching algorithm in combination with case-based reasoning is a valuable approach in domains where the fuzzy matching model similarity and case preference is consistent with the views of domain expert. This combination is also valuable where domain experts are aware that the crisp values they use have a possibility distribution that can be estimated by the expert and is used when experienced experts reason about similarity. This is the case in the psycho-physiological domain and experienced experts can estimate this distribution of feature values and use them in their reasoning and explanation process. In this system fuzzy similarity matching is applied in CBR-retrieval. In addition, in extracting features from signal data we have considered step 2 to step 6 of the calibration phase. The paper presents a result of the evaluation of a computer-aided stress diagnosis system in comparison to a domain expert/clinician.

4.1.3 Paper C: Classify and Diagnose Individual Stress Using Calibration and Fuzzy Case-Based Reasoning

As a main author for this paper I am involved in writing the chapters' classification, fuzzy case-based reasoning, similarity matching, reliability of the test and background.

In this research paper we have demonstrated a system for classifying and diagnosing stress level, exploiting finger temperature graphs and other features. This system relies on CBR as well as on fuzzy sets theory. During calibration a number of individual parameters are established. The system uses fuzzy logic to incorporating the imprecise characteristics of the domain. In extracting features from FT signal we have considered step 3, 4 and 5 (calibration phase, see paper D) and investigated the temperature variation of these steps. These cases are also useful for the individual treatment process and transfer experience between clinicians. The validation of the approach is based on close collaboration with experts and measurements from 24 persons used as reference.

4.1.4 Paper D: Using Calibration and Fuzzification of Cases for Improved Diagnosis and Treatment of Stress.

I am the main author for this initial paper and have written the chapters establishing a person's stress profile, related work, data collection and analysis, preparing data for the case- based system, case representation and matching.

In this paper a stress diagnosing system using CBR has been designed based only on the variation of the finger temperature measurements. This paper proposes a combined approach based on a calibration phase and case-based reasoning to provide assistance in diagnosing stress, using data from the finger. But this previous research does not address whether any other factors that could also be used in diagnosing individual stress level. A 6 step (i.e. Base line, Deep breath, Verbal stress, Relax, Math stress and Relax) calibration phase is described here for establishing a person’s stress profile based on a number of individual parameters. The individual cases including calibration and fuzzy membership functions show promising result to be used in an autonomous stress diagnosis system for individuals often under high stress.

Chapter 5

This chapter gives the reader an overview of the related work on case-based reasoning systems in the health sciences. A survey of the recent medical CBR systems is provided here.

Related work

Case-based reasoning has been demonstrated as a powerful methodology widely applied in medical scenarios for decision support including diagnosis, classification, tutoring, treatment planning, as well as knowledge acquisition and management. The focus in the construction of the medical CBR system has also been changed in recent years i.e. not based only on the CBR technique. Hybridization of CBR with other AI techniques such as rule-based reasoning, data mining, fuzzy logic, as well as probabilistic and statistical computing becoming a common practice to enhance CBR systems to scale up to increasingly large, complex, and uncertain data in cases in clinical environments. The construction of multi-purposed and multi-modal medical systems is becoming a hot topic in current applied CBR research. Also notable that many systems/projects that are not on an early stage aim at commercialization or are commercialized today which shows a big advancement in recent years. Some systems/projects [6, 13] are also address more advanced issues such as standardization of CBR systems and cases, i.e. formalizing case representation, reasoning procedures etc. to exchange or share among the systems.

The following section shortly narrates a number of close related CBR systems/projects in the health sciences.

5.1 System/project descriptions

The system's/project's name is given in the header and systems/projects without any formal names are presented with their authors' name. All systems in this section are created or reported after about the year 2003. A description of the earlier medical CBR systems are addressed by Gierl and Schmidt 1998 [18] and Nilsson and Sollenborn 2004 [33].

5.1.1 RHENE

RHENE [29, 30] is a case-based system in the domain of nephrology for the management of end stage renal disease patients treated with hemodialysis. The system performs the classification, planning, knowledge acquisition/ management tasks. It mainly concentrates on the retrieval of patterns of failure over time and allows the physician to analyze the solution within and between the patients. RHENE assists to look for the consistency of a prescribed therapy plan to a proposed dialysis session and provides an assessment of the treatment efficacy. Each dialysis session is represented as a case in which static features characterize a patient and dynamic features are collected from the time series measurement. A case-based architecture is further described in [26] for parameter configuration of temporal abstractions on time-series data to reduce the dimensionality of the feature and is exploited into the RHENE system. CBR is applied as a dominating technique and to feature dimensionality reduction purposes temporal abstractions is used here.

5.1.2 SOMNUS

SOMNUS [24] is a prototype implemented in the domain of Obstructive Sleep Apnea (OSA) to support in diagnosis, planning, and tutoring tasks. OSA is a respiratory disorder that causes sleeping problems in patients. The intention is to assist the respiratory therapy students in the sleep disorders clinic at the University College of the Cariboo. The students can analyze diagnosis and treatment process on a case by retrieving cases similar to a current case. The case base comprises three types of cases: individual cases- extracted from 37 OSA patients, prototypical and exceptional cases - collected manually with the help of a sleep specialist. Somnus is constructed as a combined framework in which fuzzy logic is applied for modelling of the case features and semiotic approach is used for the modelling of their measurements.

5.1.3 Marling et al.

Marling et al. describes a case-based decision support system assisting daily management in patients with Type 1 diabetes on insulin pump therapy [28]. It considers real-time monitor of patients' blood glucose level along with their life-style factors in adjusting patient-specific insulin dosage. It reduces the cumbersome manual review process for a physician in proving individual therapeutic recommendations. The best matching case is retrieved in two steps. First a subset with potential relevant cases is retrieved and then, from this subset, the most useful similar cases are retrieved using a standard Nearest- metric. An evaluation of the prototypical decision support system in the clinical context with 50 cases from the 20 patients articulates the potential applicability of CBR in managing diabetes on insulin pump therapy.

5.1.4 O'Sullivan et al.

O'Sullivan et al. [34] develops a case-based decision support system exploiting patients' electronic health records delivered by the wireless networks. It allows a user to electronically input and compare the patient records. The system facilitates knowledge sharing in the domain and allows 'remote-access health-care'. Cases are represented as multimedia data format containing patient information i.e. medical images, annotations, endoscopies, and physician's dictations. Contextual expert knowledge for the relevant cases is also stored into the case base of encapsulated patient cases. Cases contain the textual features and textual indices generated from each of the constituent features are used in the matching process. The system is evaluated using a dataset from 100 encapsulated patient profiles in the dermatology domain.

5.1.5 Brien et al.

Brien et al. [11] attempt to classify Attention-Deficit Hyperactivity disorder (ADHD) patients in the neuropsychiatric domain. The system is classifying a patient based on a hypothesis that the eye movement of a person i.e. altered control of saccadic eye movements contains significant information to diagnose ADHD which has not yet been established clinically. Nevertheless, the intention is to assist as a second option for the clinicians who have currently employed multi-source system to diagnose ADHD. The paper exploits an iterative refinement strategy during the knowledge acquisition step to achieve a satisfactory performance in terms of the case description and similarity assessment which can be applicable across other domains.

5.1.6 Doyle et al.

Doyle et al. [14] present a decision support system for Bronchiolitis treatment focusing on the necessity of the explanation in decision making tasks. It assists in classification and tutoring tasks. Whether to Discharge /Admit patient with Bronchiolitis is classified by the system. The recommendations are provided based on the precedent cases, besides this, explanatory text imparts the supporting and non-supporting aspects of a selected case as well as indicates the level of confidence in the prediction. This CBR system also takes benefits of the backup rules to prevent certain situations not covered by the cases. The CBR system is evaluated at the Kern Medical Center and the result shows that the recommendation with explanation is rather useful for the medical professionals in making decision.

5.1.7 Fungi-PAD

Fungi-PAD [35, 36] describes an object recognition method applying image processing and case-based reasoning to detect biomedical objects i.e. airborne fungal spores in a digital microscopic image. The appearance of fungal spores cannot be generalized to a model due to the large biological variation. The system uses a set of cases to explain the appearance of each object. It compares an object in the image to the original object. This original object is generated using a template which is a prototypical case produced by a semi-automatic process.

5.1.8 SISAIH

SISAIH [27] is a decision support tool to assist in decision making process to the hospital admission authorities in the Brazilian health public system. The system attempts to manage admission of patients in hospital, handles patients billing error and medical procedures i.e. in general, managerial job. Expert knowledge to solve a problem i.e. an evaluation of hospital admission authorization (HAA) which decides whether to accept or reject a current HAA, is stored in each case. It assists to find frauds in the health care system SISAIH simplifies the problematic manual knowledge acquisition process and utilizes the resources in a cost-effective way which in turn speeds-up and makes the process more accurate.

5.1.9 KASIMIR

The KASIMIR project [13], is an effort to provide decision support for the breast cancer treatment based on a protocol in Oncology. It performs multi tasks like, diagnosis, classification, and knowledge acquisition/ management. KASIMIR is a hybrid system including technologies from knowledge representation and reasoning, semantic web technologies (OWL, C-OWL), knowledge acquisition and discovery technology, belief revision theory, fuzzy reasoning technology, and ergonomy. The adaptation of the protocol is an important issue handled here to provide therapeutic decisions for the cases those are out of the protocol. It matches source (general) cases with the target case using adaptation knowledge (Figure 23).

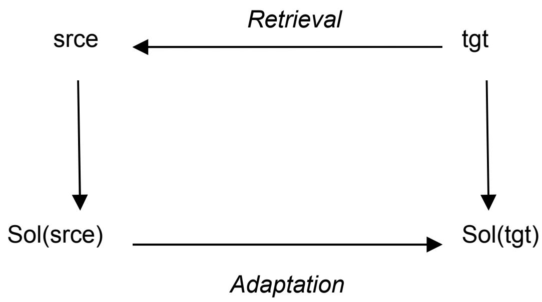

Figure 23. The CBR in KASIMIR. A source case (srce,Sol(srce)) similar to tgt is retrieved from the case base and adapted to solve tgt.

The system [12] stresses particularly on the importance of the proper management of domain knowledge to avoid wrong decisions. The analysis of failure adds as a new dimension of knowledge into the domain knowledge enabling automatic evolution of this knowledge. Conservative protocol adaptation to a new case, depending on a revision operator provides a consistency between the domain knowledge and the target case.

5.1.10 Mémoire

The Mémoire Project [6], at the University of Washington, offers a framework to exchange case bases and the CBR systems in biology and medicine. It is an effort to apply semantic web approach in biomedical domain. The Me´moire archetecture is described in Figure 24.

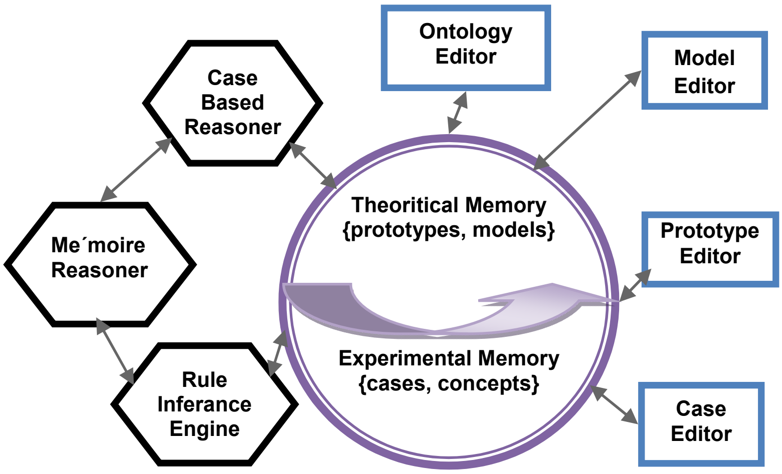

Figure 24. Me´moire architecture. Right: memory acquisition tools, left: reasoning components. Adapted from [6].

Mémoire uses OWL representation language to make the case bases interoperable. It assists in diagnosis, planning, knowledge acquisition/ management, tutoring and research tool. A number of researches have been taken place [7, 9] in the Mémoire project to validate the different roles of prototypical cases. In [8] the author deals particularly with the prototypical cases, where the prototypical cases act as maintenance cases by keeping the knowledge up-to-date with the rapid development in the biomedical domain. The author argues that this maintenance prototypical case can be generated by mining from the medical literatures which could in turn lead to building and maintaining of case bases in an autonomous way in the medical domain. The project explores prototypical cases and how they can serve in various ways in a CBR system for example, maintenance of memory, maintenance of knowledge, management of reasoning and bootstrapping a case base. Bichindaritz have developed several other systems that addresses the issues related to prototypical cases in the biomedical domain such as, ProCaseMiner [7] automatically builds initial case base.

Chapter 6

A conclusion drawn from the research work is presented in this chapter. It also discusses the research issues that remain to be solved.

Conclusions

During the research, four research questions have been formulated:

- *What methods/ techniques can be used for diagnosing stress in non-clinical environment i.e. in home and in working places and are acceptable by clinicians?*
- *What is needed for enabling autonomous system able to identify individual's stress levels?*
- *How do we classify individual stress level when the domain knowledge is weak?*
- *How to extract the essentials features from biomedical signals?*

During the research, these research questions are addressed and different solutions complement each other and contribute to an overall accomplishment of the thesis work. The nature of the research area is also analyzed to be able to make an appropriate choose of the methods and strategy. To diagnose stress the method of case-based reasoning is employed comparing previous similar cases in terms of features extracted. Also the calibration phase is introduced to estimate individual parameters in diagnosing individual stress levels. Moreover, fuzzy techniques are incorporated into our CBR system to better accommodate uncertainty in clinicians reasoning as well as decision analysis.
The fulfilment of the research questions lead to the following main contributions:

- *A feature extraction technique from the FT sensor signal.*

- *A calibration phase to establish a number of individual parameters to diagnose individual stress in a computer-aided system.*
- *A technique for the computer-based classification of the severity level of stress.*
- *A decision support system combining CBR and fuzzy logic that allows a user to use it at home and in working places for diagnosing individual stress.*

The contributions are presented in detail in the included papers. In short, the major findings of this research can be pointed out as follows: it provides a feature extraction method that can identify automatically essential features from the finger temperature sensor data, the individual stress profiling is also accomplished by introducing a calibration phase, and proposes a better similarity matching algorithm that works close to an expert compare to traditional similarity algorithm. The evaluation of the work shows a level of performance close to an experienced expert; on an average the calculated goodness-of-fit for the system (using fuzzy matching algorithm) is 90 % in ranking and 81 % in similarity estimation see details in [paper B]. Thus from the research work we could conclude that using FT sensor signal the system could serve as a convenient tool to diagnose stress-related dysfunctions at home and in working places without the supervision of a clinical staff. Also it can be used as an auxiliary system for the clinical environment.

One of the limitations of this research work is the performance of the system due to insufficient cases in the case library. CBR method has this constraint that the performance of the system depends on its case library. Often medical CBR system does not contain enough reference cases in the initial period and the system decreases the performance. A supplementary method that can help to build initial case library by creating artificial cases to reach enough cases into the case library can be introduced to overcome this problem. The system has no option for automatic adaptation today this is function manually by the clinician but our plan is to include adaptability into the system. Ongoing research is looking at automatic adaptation strategy. Although the system is still in the research phase, it aims to be developed for day-to-day use.

6.1 Future research

Several research topics could be investigated further on the basis of the work presented in this licentiate thesis. Some of the possible research directions are the following:

First, the proposed system is now tested with 39 cases in the current case library; in future it could be evaluated with large number of real cases to investigate the reliability of the system. User level evaluation of the DSS is important to be able to implement it in the day-to-day clinical use.

Automatic feature weighting and adaptation are important issues in medical CBR systems that could be investigated in our system. An algorithm for the automatic weighting of the feature values instead of manual weighting is described in [17].

Today the system is based on one physiological parameter i.e. finger temperature sensor signal. In future (towards completing my doctoral dissertation), several other parameters such as heart rate variability, breathing rate etc. could be investigated as a reference of the work for the more reliable and efficient decision support in stress management.

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PART 2

Included papers

Chapter 7

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. Submitted to the *International Journal of Computational Intelligent Systems*.

Abstract

With over 50 case-based reasoning(CBR) systems in the area of health sciences, and more than 20 systems and project ongoing shows that health sciences is one of the major application areas for CBR today. The survey is based on e-mail questionnaire and the majority of the researchers returned it. Some clear trends have been identified, such as multipurpose systems, not even mentioned in a recent survey from 2004. Today 73% of the systems address more than one task, e.g. a combination of classification and knowledge acquisition/management. Planning is also a fast emerging area in CBR for health sciences. A big change since the last survey made 2004 is that half of the projects/systems that are not on an early stage aim at commercialization or are commercialized today.

7.1 Introduction

CBR for health science is today both a recognized and well established method. The health science domain offers researchers in the CBR community worthy challenges driving the research area of CBR forward and at the same time enable researchers to develop methods and techniques in the medical domain previously difficult to solve with other methods and approaches.

A number of interesting publications are looking at a CBR in health science and also number of influential CBR systems in health science (Gierl, and Schmidt, 1998; Schmidt et al. 2001; Holt et al. 2006; Bichindaritz and Marling 2006; Bichindaritz 2006; Montani 2008; Bichindaritz 2008).

Due to the area's fast and successful development and progress we recognize the need for a systematic survey capturing and indentifying recent trends in CBR for health science and following the same approach as (Nilsson and Sollenborn 2004) with a through literature search followed by an e-mail survey to the authors of the systems and the paper contains a comprehensive survey and investigation of CBR in medical domains between 2004 and 2008. We outline a number of medical CBR systems' recent development followed by analysis of properties and functionalities of such systems. The survey shows clearly that CBR is a powerful methodology applied in many medical scenarios for various tasks such as diagnosis, classification, tutoring, treatment planning, as well as knowledge acquisition and management. Also hybridization of CBR with other AI techniques such as rule-based reasoning, data mining, fuzzy logic, as well as probabilistic and statistical computing exhibits are explored and show promising opportunities to enhance CBR systems to scale up to increasingly large, complex, and uncertain data in cases in clinical environments. It is also notable that recent CBR systems plan for commercialization.

Before going into the survey results we give a short summary and references of the systems included in the survey. If you are familiar with the area you may prefer to read the following section *Assessment of Current*

Trends and use the following section *Recent CBR Systems in the Health Sciences* as reference section.

7.2 Recent CBR Systems in the Health Sciences

An effort has been made to include all of today's active systems in the area and considerable time has been spent on searching journals, conferences and workshops. Our aim is that this section gives sufficient information to trigger interest to systems not familiar to the reader and lead to exploration of the original publications. Some systems with many purposes have been given longer explanations. In some system descriptions we also included brief summaries of issues not dealt with further in this survey but of interest out of a trend perspective, e.g. standardization efforts.

An overview and status of medical CBR systems from 1999 to 2003 was done by Nilsson and Sollenborn (Nilsson and Sollenborn 2004) and before 1998 (Gierl and Schmidt 1998) published an overview. This overview paper surveys systems developed between 2004 to date. The focus is on progress and changes in CBR systems in the health sciences area. We selected a number of specific prosperities, particularly the use of CBR systems and their changes in construction made to date. The following chapter narrates a number of major CBR systems/projects in the health sciences with the aim of assessing recent trends in CBR for health science. We have ranked the systems/projects' name in alphabetic order and then systems/projects (without name) are listed with their authors' name. The purpose of the systems follows the categories earlier identified by Gierl and Schmidt 1998 and Nilsson and Sollenborn 2004. The purpose *Knowledge acquisition/management* is used accordingly to (Watson 2001) where knowledge acquisition is labeled as a one of the activities of knowledge management. In medical domain *planning* generally refers to treatment planning or therapy support. For instance, the RHENE system (Montani et al. 2006) provides planning expertise for the End Stage Renal Disease patients by monitoring and adjusting the treatment over time.

1. **CaseBook** (McSherry 2007) [*Purpose: Diagnosis, Classification*] is a hypothetico-deductive CBR system for classification and diagnosis that applies hypothetico-deductive reasoning (HDR) in conversational CBR systems. HDR facilitates to find the significant hypothesis or to rule out a hypothesis proposed by a system or user while minimizing the number of tests required. The strategy is exemplified in recommending type of contact lenses in the contact lenses classification domain.

2. **ExpressionCBR** (De Paz et al. 2008) [*Purpose: Diagnosis, Classification*], is a decision support system for cancer diagnosis. The system classifies the Leukemia patients automatically from Exon array data and helps in diagnosis of patients with various cancer types. It uses a data filtering algorithm that deals with the dimensionality problem in data sets. Besides, a clustering algorithm for classification approach speeds up the process.

3. **Fungi-PAD** (Perner et al. 2006, Perner and Bühring 2004) [*Purpose: Classification, Knowledge acquisition/ management*] describes an object recognition method applying image processing and case-based reasoning to detect biomedical objects i.e. airborne fungal spores in a digital microscopic image. The appearance of fungal spores cannot be generalized to a model due to the large biological variation. The system uses a set of cases to explain the appearance of each object. It compares an object in the image to the original object. This original object is generated using a template which is a prototypical case produced by a semi-automatic process.

4. **FrakaS** (Cordier et al. 2007) [*Purpose: Diagnosis, Knowledge acquisition/ management*] is a prototype build in the domain of oncology using CBR. The paper emphasizes on the proper management of the domain knowledge to avoid wrong decisions in medical decision support system. Evolution of the domain knowledge is highlighted into the paper in a way when inconsistency between the domain and the expert knowledge is added as a new

knowledge. These authors propose a conservative adaptation strategy for knowledge acquisition from experts.

5. **GerAmi** (Corchado, Bajo, and Abraham 2008) [*Purpose: Planning, Knowledge acquisition/ management*] '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 included CBR system to provide case-based planning mechanism. This helps to optimize work schedules and provide up-to-date patient data. The prototype system has been implemented at a care facility for Alzheimer patients in geriatric residences.

6. **geneCBR** (Glez-Peña et al. 2005; Díaz, Fdez-Riverola, and Corchado 2006) [*Purpose: Diagnosis, Classification*] is focusing on the classification of cancer, based on gene expression profile of microarray data. Each case contains 22,283 features. 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. Several AI techniques are combined to optimize the classification accuracy. Cases are represented using fuzzy sets, and fuzzy-prototype based retrieval is applied in the case retrieval. A set of rules helps to present an explanation of the provided solution. The patients are clustered into group of genetically similar patients using neural networks.

7. **HEp2-PAD** (Plata et al. 2008; Perner 2006a; Perner 1999) [*Purpose: Classification, Knowledge acquisition/ management*] addresses a novel case-based method for image segmentation in medical image diagnosis. The system combines CBR, image processing, feature extraction and data mining techniques to optimize image segmentation at low level unit. CBR performs the segmentation parameter selection mechanism based on current image characteristics. Cases are represented with image and non-image information. Similarity value is calculated from both the

image and non-image information. This provides an image interpretation close to a human expert.

8. In the **ISOR** (Schmidt and Vorobieva 2006) [*Purpose: Diagnosis, Planning*], the authors address particularly the endocrine domain. The system identifies the causes of ineffective therapies and advises better recommendations to avoid inefficacy to support in long-term therapies. The system is exemplified in diagnosis and therapy recommendations of Hypothyroidism patients treated with hormonal therapy. The system is not only based on the case base but also on other knowledge components such as a knowledge base that represents the domain theory in a tree structure, prototypes i.e. generalized cases and medical histories of a patient. Information of these containers worked in a form of dialogue and key words are used for the case retrieval.

9. The **IPOS** (Begum et al. 2008) [*Purpose: Diagnosis*] project aims at proving a case-based decision support system to assist clinicians in diagnosing individual stress condition based on finger temperature measurements. The system uses calibration phase to generate an individual stress profile. Case-based reasoning is applied as the key methodology to facilitate experience reuse and decision explanation by retrieving previous similar temperature profiles. Further, fuzzy technique is incorporated into the CBR system to handle vagueness, uncertainty inherently existing in clinicians reasoning as well as imprecision of feature values. In addition, a hybrid CBR system is illustrated in (Ahmed et al. 2008a) dealing with combined time series signals and unstructured textual information for clinical decision support in stress medicine. The time series measurements and textual data capture different yet complementary aspects of a subject and they are desired to be tackled simultaneously for more comprehensive situation awareness and thereby more reliable diagnoses and decisions.

10. The **KASIMIR** project (D'Aquin, Lieber, and Napoli 2006) [*Purpose: Diagnosis, Classification, Knowledge acquisition/*

management], is an effort to provide decision support for the breast cancer treatment based on a protocol in Oncology. The adaptation of the protocol is an important issue handled here to provide therapeutic decisions for the cases those are out of the protocol. The system (Cordier et al. 2007) stresses particularly on the importance of the proper management of domain knowledge to avoid wrong decisions. The analysis of failure adds as a new dimension of knowledge into the domain knowledge enabling automatic evolution of this knowledge. Conservative protocol adaptation to a new case, depending on a revision operator provides a consistency between the domain knowledge and the target case.

11. The **Mémoire Project** (Bichindaritz 2006a) [*Purpose: Diagnosis, Planning, Knowledge acquisition/ management, Tutoring*], at the University of Washington, offers a framework to exchange case bases and the CBR systems in biology and medicine. It is an effort to apply semantic web approach in biomedical domain. Mémoire uses OWL representation language to make the case bases interoperable. A number of researches have been taken place (Bichindaritz 2008a; Bichindaritz 2007) in the Mémoire project to validate the different roles of prototypical cases. In (Bichindaritz 2007a) the author deals particularly with the prototypical cases, where the prototypical cases act as maintenance cases by keeping the knowledge up-to-date with the rapid development in the biomedical domain. The author argues that this maintenance prototypical case can be generated by mining from the medical literatures which could in turn lead to building and maintaining of case bases in an autonomous way in the medical domain. The project explores prototypical cases and how they can serve in various ways in a CBR system for example, maintenance of memory, maintenance of knowledge, management of reasoning and bootstrapping a case base. Bichindaritz have developed several other systems that addresses the issues related to prototypical cases in the biomedical domain such as, ProCaseMiner (Bichindaritz 2007) automatically builds initial case base.

12. **RHENE** (Montani et al. 2006; Montani et al. 2006a) [*Purpose: Classification, Planning, Knowledge acquisition/ management*], is a case-based system in the domain of nephrology for the management of end stage renal disease patients treated with hemodialysis. It mainly concentrates on the retrieval of patterns of failure over time and allows the physician to analyze the solution within and between the patients. RHENE assists to look for the consistency of a prescribed therapy plan to a proposed dialysis session and provides an assessment of the treatment efficacy. Each dialysis session is represented as a case in which static features characterize a patient and dynamic features are collected from the time series measurement. A case-based architecture is further described in (Leonardi et al. 2007) for parameter configuration of temporal abstractions on time-series data to reduce the dimensionality of the feature and is exploited into the RHENE system.

13. **Somnus** (Kwiatkowska and Atkins 2004) [*Purpose: Diagnosis, Planning, Tutoring*], is a prototype implemented in the domain of Obstructive Sleep Apnea (OSA). OSA is a respiratory disorder that causes sleeping problems in patients. The intention is to assist the respiratory therapy students in the sleep disorders clinic at the University College of the Cariboo. The students can analyze diagnosis and treatment process on a case by retrieving cases similar to a current case. The case base comprises three types of cases: *individual cases*- extracted from 37 OSA patients, *prototypical* and *exceptional cases* - collected manually with the help of a sleep specialist. Somnus is constructed as a combined framework in which fuzzy logic is applied for modeling of the case features and semiotic approach is used for the modeling of their measurements.

14. **SISAIH** (Lorenzi, Abel, and Ricci 2004) [*Purpose: Diagnosis*], is a decision support tool to assist in decision making process to the hospital admission authorities in the Brazilian health public system. The system attempts to manage admission of patients in hospital, handles patients billing error and medical procedures i.e. in general, managerial job. Expert knowledge to solve a problem i.e. an

evaluation of hospital admission authorization (HAA) which decides whether to accept or reject a current HAA, is stored in each case. SISAIH simplifies the problematic manual knowledge acquisition process and utilizes the resources in a cost-effective way which in turn speeds-up and makes the process more accurate.

15. **SIDSTOU** (Ochoa et al. 2006) [*Purpose: Diagnosis, Planning, Tutoring*], is an intelligent tutoring CBR system for providing medical education on Tourette syndrome. It works as a tool for diagnosing Tourette syndrome and could minimize the need of Psychiatrist or Neurologist at the initial stage. The system can also learn automatically based on a number of defined predicting characteristics. An evaluation of the system comparing with the expert in the domain presents the reliability of the system.

16. Ahmed et al. (Ahmed 2008) [*Purpose: Planning*], proposes a three phase computer assisted sensor-based biofeedback decision support system to provide treatment for stress-related disorders. A CBR framework is deployed to classify a patient, estimate initial parameters and to make recommendations for biofeedback training. Fuzzy techniques are incorporated into the system to better accommodate uncertainty in clinicians reasoning as well as decision analysis. Biofeedback training is mostly guided by an experienced clinician and the results largely rely on the clinician's competence. The intention of the system is to enable a patient to train himself/herself without particular supervision.

17. Brien et al. (Brien 2005) [*Purpose: Classification, Knowledge acquisition/ management*], attempt to classify Attention-Deficit Hyperactivity disorder (ADHD) patients in the neuropsychiatric domain. The system is classifying a patient based on a hypothesis that the eye movement of a person i.e. altered control of saccadic eye movements contains significant information to diagnose ADHD which has not yet been established clinically. Nevertheless, the intention is to assist as a second option for the clinicians who have currently employed multi-source system to diagnose ADHD. The

paper exploits an iterative refinement strategy during the knowledge acquisition step to achieve a satisfactory performance in terms of the case description and similarity assessment which can be applicable across other domains.

18. Doyle et al. (Doyle, Cunningham, and Walsh 2006) [*Purpose: Classification, Tutoring*], present a decision support system for Bronchiolitis treatment focusing on the explanation in decision making. The system provides recommendations based on precedent cases, beside this, explanatory text imparts the supporting and non-supporting aspects of a selected case as well as indicates the level of confidence in the prediction. The CBR system is evaluated at the Kern Medical Center and the result shows that the recommendation with explanation is rather useful for the medical professionals in making decision.

19. O'Sullivan et al. (O'Sullivan, Bertolotto, and Wilson 2006) [*Purpose: Diagnosis*], develops a case-based decision support system exploiting patients' electronic health records delivered by the wireless networks. It allows a user to electronically input and compare the patient records. The system facilitates knowledge sharing in the domain and allows 'remote-access health-care'. Cases are represented as multimedia data format containing patient information i.e. medical images, annotations, endoscopies, and physician's dictations. Contextual expert knowledge for the relevant cases is also stored into the case base of encapsulated patient cases. Cases contain the textual features and textual indices generated from each of the constituent features are used in the matching process. The system is evaluated using a dataset from 100 encapsulated patient profiles in the dermatology domain.

20. Marling et al. [*Purpose: Planning*], describes a case-based decision support system assisting daily management in patients with Type 1 diabetes on insulin pump therapy (Marling, Shubrook, and Schwartz 2008). It considers real-time monitor of patients' blood glucose level along with their life-style factors in adjusting patient-specific insulin dosage. It reduces the cumbersome manual review process for a physician in proving individual therapeutic recommendations. The best matching case is retrieved in two steps. First a subset with potential relevant cases is retrieved and then, from this subset, the most useful similar cases are retrieved using a standard nearest neighbor metric. An evaluation of the prototypical decision support system in the clinical context with 50 cases from the 20 patients articulates the potential applicability of CBR in managing diabetes on insulin pump therapy.

21. Song et al. [*Purpose: Planning*], proposes a system in radiotherapy for dose planning in prostate cancer (Song, Petrovic, and Sundar 2007). Their system is able to adjust the appropriate radiotherapy doses for an individual while, at the same time, 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. The matching between cases applies the fuzzy similarity measurement to incorporate the experts' knowledge in retrieving past similar experiences. Dempster-Shafer theory is introduced to fuse multiple cases to recommend a dose plan for a case, when in a real-world situation several retrieved similar cases provide different treatment solutions.

22. Wu et al. (Wu, Weber, and Abramson 2004) [*Purpose: Knowledge acquisition/ management, Planning*], present a CBR framework based on NutriGenomics knowledge considering person's genetic variation i.e. individual gene expression to provide personalized dietary counseling. Genetic variation of a person has an impact on person's response to diet. The system proposes a dietary strategy that influences individual gene expression and, as a consequence, facilitates to maintain health and prevent diseases. The NutriGenomics knowledge is collected applying the data mining technique and represented in form of ontologies. A distributed case base allows the system to save this knowledge, and generates new cases automatically if necessary, using a Case Builder based on this stored knowledge.

7.3 Assessment of Current Trends

A survey has been done by email and all authors were asked to answer a questionnaire about the system properties. The system properties are divided into two parts: purpose-oriented and construction-oriented properties. We have interpreted the purpose- properties as diagnosis, classification, tutoring, planning, based on previous surveys (Nilsson and Sollenborn 2004; Gierl and Schmidt 1998). Knowledge acquisition/management is one added purpose-oriented properties. Construction-oriented properties according to (Nilsson and Sollenborn 2004) are further investigated for the recent medical CBR systems (table 2). According to our survey, numerous systems are multipurpose-oriented. A matrix illustrated in table 1, presents CBR systems with their purpose-oriented properties and application domain. From table 1 it can also be seen that several other techniques are integrated into the CBR systems such as- Hypothetico-deductive reasoning (HDR), Rule-based reasoning (RBR), Knowledge management (KM) technique, Neural network (NN), Data mining etc.

No	Author/ system	Purpose-oriented properties	CBR & other techniques	Application domain /context
1	McSherry/ CaseBook	Diagnosis & Classification	CBR & HDR	Contact Lenses
2	De Paz /ExpressionCBR	Diagnosis & classification	CBR,NN & Statistic	Cancer diagnosis
3	Perner/ Fungi-PAD	Classification, Knowledge acquisition/ management	CBR & Image processing	Object recognition
4	Cordier/ FrakaS	Diagnosis, Knowledge acquisition/ management	CBR	Oncology
5	Corchado/ GerAmi	Planning, Knowledge acquisition/ management	CBR & Variational calculus	Alzheimer patients
6	Glez-Peña / geneCBR	Diagnosis & Classification	CBR, RBR & Fuzzy logic	Cancer classification
7	Perner/ HEp2-PAD	Classification, Knowledge acquisition/ management	CBR, Image processing & data mining	Image Classifier
8	Schmidt/ ISOR	Diagnosis & planning	CBR & Statistic	Endocrine
9	Begum/ IPOS	Diagnosis	CBR & Fuzzy Logic	Stress diagnosis
10	D'Aquin/ KASIMIR	Diagnosis, classification, Knowledge acquisition/	CBR, semantic web, belief revision theory,	Breast Cancer

		management	fuzzy logic & ergonomy	
11	Bichindaritz / Mémoire	Diagnosis, planning , tutoring, Knowledge acquisition/ management	CBR, RBR, Data mining & Statistic	Biology & medicine
12	Montani/ RHENE	Classification, planning, Knowledge acquisition/ management	CBR & Temporal abstractions	Hemodialysis
13	Kwiatkowska/Somnus	Diagnosis, planning and tutoring	CBR & Fuzzy logic	Obstructive sleep apnea
14	Lorenzi / SISAIH	Diagnosis	CBR	Fraud detection in health care
15	Ochoa /SIDSTOU	Diagnosis, planning & Tutoring	CBR & Data mining	Tourette syndrome
16	Ahmed ./Biofeedback	Planning	CBR & Fuzzy logic	Stress management
17	Brien/ADHD	Classification, Knowledge acquisition/ management	CBR	Neuropsychiatric
18	Doyle/ Bronchiolitis	Classification and tutoring	CBR & RBR	Bronchiolitis
19	O'Sullivan/ Dermatology	Diagnosis	CBR, KM & image processing	Dermatology
20	Marling/ Type-1diabetes	Planning	CBR & RBR	Diabetes
21	Song/ radiotherapy planning	Planning	CBR, Fuzzy logic, Dempster-Shafer theory & Simulated annealing	Prostate Cancer
22	Wu/ Dietary counseling	Planning & Knowledge acquisition/ management	CBR, Data mining & Ontology	Dietary counselling

Table 1: Property matrix, CBR systems and their application domains.

An interesting observation is how the purpose-oriented properties have changed and how they are combined in different systems. In figure 1 we see that beside a new category, knowledge acquisition/management, more systems address diagnosis and planning than in 2004. Few systems address tutoring and the increase of classification systems is moderate. Nearly half of the system address planning and four systems are single purpose systems only addressing planning. This may be interpreted as planning in the medical domain offers interesting challenges to case based reasoning researcher and/or being an application where the case-based reasoning methodology may offer valuable progress and commercial applications (more than half of the systems in table 2 are aim at commercialization).

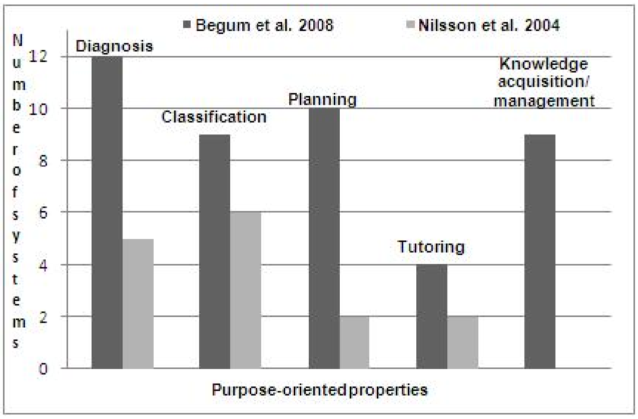

Figure 1: Number of systems belonging to each purpose-oriented category.

Another interesting observation is that in 2004 only 2 (13%) of the evaluated systems where multipurpose systems while today 73% have two or more purposes (figure 2). Note that, Nilsson et al. investigated 15 CBR systems yet did not explicitly mention overlapping among their purpose-oriented properties.

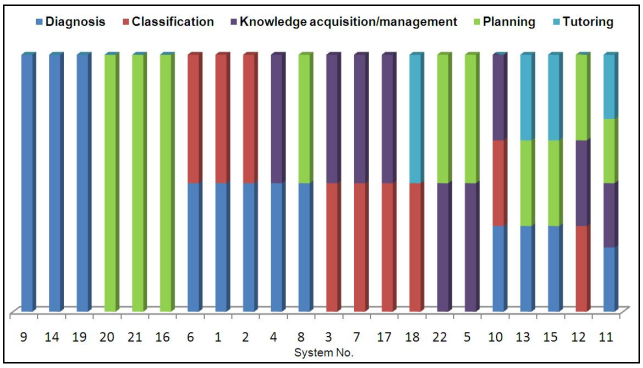

Figure 2: Overlapping areas among several purpose-oriented properties. X axis denotes the systems no according to table 1.

In figure 2 the systems are displayed in order of the number of purposes, the first 6 being single purpose systems. Every purpose is given a colour, but the size/area of the colour has no significance since we don't know the balance in the system between the different purposes. The order of the multi-purpose systems is set by the order of the purpose (hence system 6, 1, 2, 4, 8, are first in the category of two-purpose systems, all addressing diagnosis as one of their purpose category). An interesting observation is that, it is popular to combine classification and knowledge acquisition/management, five of 16 multipurpose systems.

System no.	Author/ System	Subject	No. of cases	Case type	Prototype	Adaptivity	Hybridity	Autonomy	Commerc-ialization	Clinical use	Reliability
21	Song/ radiotherapy planning	6	72	real case	some extent	Yes	yes	highly	planned	in progress	87% of Cases
20	Marling/ Type-1diabetes	20	50	real case	yes	planned	yes	some extent	planned	planned	testing underway
18	Doyle /Bronchiolitis	400	40	real case	yes	some extent	yes	some extent	no	Clinical eval.	Clinician
15	Ochoa / SIDSTOU	47	100	real case	yes	some extent	yes	some extent	planned	Clinical eval.	Clinician
14	Lorenzi/ SISAIH	5	70	real case	yes	No	pure cbr	highly	no	no	expert level
13	Kwiatkowska/ Somnus	37	37	real case	some extent	No	yes	some extent	no	no	not relevant
12	Montani/ RHENE	37	1476	real case	no	Yes	some extent	no	planned	planned	not tested
11	Bichindaritz / Mémoire	simulator	122	real,prototypical	yes	Yes	yes	highly	no	planned	expert level
10	D'Aquin/ KASIMIR	not relevant	100	real, generic	some extent	Yes	yes	some extent	no	clinical eval	expert level
9	Begum/ IPOS	24	39	prototypical case	yes	No	yes	some extent	planned	clinical eval.	expert level
7	Perner/ HEp2-PAD	10	300	real case	yes	No	yes	highly	yes	day-to-day use,	expert level
6	Glez-Peña/ geneCBR	7	43	real case	yes	No	yes	highly	no	clinical eval.	expert level
5	Corchado/ GerAmi	20	4000	real case	yes	Yes	yes	highly	yes	day-to-day use	always right
4	Cordier/ FrakaS	not relevant	10	prototypical case	yes	Yes	no	some extent	no	no	not relevant

3	Perner/ Fungi-PAD	8	400	real,prot otypical	yes	No	yes	highly	planned	clinical eval.	expert level
2	De Paz/ ExpressionCB R	212	212	real case	yes	Yes	yes	highly	no	clinical eval.	Clinician

Table 2: Construction-oriented property matrix. Survey results on CBR system in health science.

In terms of constriction-oriented properties, answer to the questionnaire of the survey is used to formulate a matrix presented in table 2. A few systems not completed or on an early stage are not included in the matrix, e.g. Ahmed et al. 2008. In terms of system construction, 37 as minimum and 4000 as maximum numbers of cases are involved in the described systems. Majority of the systems appears with both prototypes and real cases. Only few systems use automatic adaptation strategies but the majority of systems/projects in table 2 include adaptation. Most of the systems are multi-modal or hybrid and few of them developed apply pure CBR. A larger part of the systems also address user interaction and a few of them are commercialized until now. In terms of reliability, most of the systems are operational secure in some degree of expert level, others are on earlier stages. A few system address standardization of CBR systems and cases, that is formalizing case representation, reasoning procedures etc. to exchange or share among the systems, e.g. in the Memoire project by Bichindariz (Bichindariz 2006).

7.3.1 Overall Trends

The majority of the recent CBR systems address more than one purpose-oriented category. The systems are not only concentrating on the diagnostics and treatment tasks as the early CBR systems. Recent CBR systems tend to support in other complex tasks in the health care domain. In particular, we can observe the use of CBR systems in Knowledge acquisition/management has attained increasing attention in recent years.

The wide range of application areas and a number of successfully implemented systems have proved that the interest of applying CBR in the health sciences is increasing. There is also an indication that the interest for applying CBR in the bioinformatics domain is increasing.

Majority of the health care domain requires pre-processing of datasets which leads to feature extraction or feature mining prior to the case representation. Also some of the systems/projects have successfully extracted features from multimedia data i.e. time series and images in a separate phase. Feature mining from multimedia data is a notable trend in health science domain which helps to represent cases with original implicit and complex features. Example of system focusing on feature mining is the dietary counseling system by Wu et al. 2004.

One of the identifiable achievements made in the medical CBR systems is that almost all that participated in the survey implemented their systems in a form of prototype. Only a few medical systems i.e. Perner 2006a and Corchado et al. 2008 showed successful commercialization of their systems. Several other projects which still are in the research phase, aim at commercial systems in future. Many of the systems have been successfully evaluated in a clinical environment. But day-to-day use in clinical setting is not common.

Adaptation is often a challenging issue in the medical domain. Nevertheless, the survey shows that a number of recent medical CBR systems adopt and explore different automatic and semi-automatic adaptation strategies.

Indeed few systems depend only on CBR today; almost all medical CBR systems are combined more than one method and technique. In fact the multi-faced and complex nature of the medical domain leads to designing such multi-modal systems (Montani 2007; Nilsson and Sollenborn 2004). Integration of CBR and RBR was common in past CBR systems such as in CASEY (Koton 1988), FLORENCE (Bradburn 1994). Recent trends in hybrid CBR systems today are data mining, fuzzy logic and statistics.

7.4 Conclusions

This paper presents a comprehensive survey of investigations of CBR in medical domains. We outline a number of medical CBR systems developed recently followed by analysis of properties and functionalities of such systems. It is demonstrated in our survey that CBR has been a powerful methodology applied in many medical scenarios for various tasks such as diagnosis, classification, tutoring, treatment planning, as well as knowledge acquisition/ management. We also point out that hybridization of CBR with other AI techniques such as rule-based reasoning, data mining, fuzzy logic, as well as probabilistic and statistical computing exhibits promising opportunities to enhance CBR systems to scale up to increasingly large, complex, and uncertain data and information in clinical environments.

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Chapter 8

Paper B:
A Case-Based Decision Support System for Individual Stress Diagnosis Using Fuzzy Similarity Matching

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Abstract

Stress diagnosis based on finger temperature signals is receiving increasing interest in the psycho-physiological domain. However, in practice, it is difficult and tedious for a clinician and particularly less experienced clinicians to understand, interpret and analyze complex, lengthy sequential measurements in order to make a diagnosis and treatment plan. The paper presents a case-based decision support system to assist clinicians in performing such tasks. Case-based reasoning is applied as the main methodology to facilitate experience reuse and decision explanation by retrieving previous similar temperature profiles. Further fuzzy techniques are also employed and incorporated into the case-based reasoning system to handle vagueness, uncertainty inherently existing in clinicians reasoning as well as imprecision of feature values. Thirty nine time series from 24 patients have been used to evaluate the approach (matching algorithms) and an expert has ranked and estimated similarity. On average goodness-of-fit for the fuzzy matching algorithm is 90% in ranking and 81% in similarity estimation which shows a level of performance close to an experienced expert. Therefore, we have suggested that a fuzzy matching algorithm in combination with case-based reasoning is a valuable approach in domains where the fuzzy matching model similarity and case preference is consistent with the views of domain expert. This combination is also valuable where domain experts are aware that the crisp values they use have a possibility distribution that can be estimated by the expert and is used when experienced experts reason about similarity. This is the case in the psycho-physiological domain and experienced experts can estimate this distribution of feature values and use them in their reasoning and explanation process.

Keywords: case-based reasoning, fuzzy logic, decision support system, classification, diagnosis.

8.1 Introduction

Stress is a common problem for many people in today's modern society. It is well known that increased stress level can lead to serious health problems. Stress has a side effect of reducing awareness of bodily symptoms and people often on a heightened level of stress may not be aware of it and first notice it weeks or months later when the stress is causing more serious stress related effects in the body and health (Von Schéele and Von Schéele 1999). Severe stress during long periods is highly risky or even life-endangering for patients with e.g. heart disease or high blood pressure. A computer-aided system that helps early detection of potential stress problems would bring vital benefits for treatment and recovery in both clinical and home environments.

Medical investigations have identified that finger temperature has a strong correlation with stress status for most people. Interpreting and analyzing finger temperature profiles for diagnosing severity of stress and other related dysfunctions is receiving increasing significance within the psycho-physiological domain. In doing this, clinicians are required to carefully inspect lengthy streams of measurements for capturing indicative characteristics and recognizing any possible disorders. It is a time-consuming and tedious task for humans to carry out. Further, understanding large variations of measurements from diverse patients requires knowledge and experience and without adequate support, errors of judgment could be made by a less experienced staff.

In this paper we present an approach to provide decision support for clinicians in analyzing and classifying finger temperature measurements. The aim of this research work is to help clinicians to diagnose individual stress level of a patient. The main approach is based on the use of case-based reasoning, a methodology receiving increased attention in the medical and psychological domain, e.g. as in (Bichindaritz 1996; Perner et al. 2003, Schmidt et al. 2006, and Nilsson et al. 2006). The approach enables reuse of experience from previous cases with analyzed temperature and stress profiles. Three similarity matching functions have been established for this purpose to assess case similarity and relevance in this application scenario.

The comparative performance of these three similarity functions have been evaluated empirically. 39 Measurements from 24 people have been collected and used in evaluations where the clinical expert has ranked and estimated their similarity. In order to verify the system, goodness-of-fit and absolute mean difference are calculated where the main goal of the evaluation is to see its performance in comparison to an expert's estimations. In this evaluation the suggested fuzzy similarity matching method yields the best performance concerning the rank of retrieved cases, i.e. producing a rank that is most consistent with domain expert opinions.

Fuzzy logic in combination with case-based reasoning shows some interesting features and may be of value in similar medical applications. Fuzzy theory has proved a powerful tool for representing and dealing with imprecision, vagueness and ambiguity arising from measurements, judgments and concepts. By using fuzzy set theory we can achieve more soft distinctions for making decisions that have a closer accordance with the experts' results. In (Burkhard and Richter 2000) it was identified that the central notion of similarity in CBR could be treated as fuzzy relation and a composite similarity measure could be constructed via fuzzy operations. Currently we have integrated fuzzy techniques into our system in such aspect where every crisp case index is fuzzified into a set of fuzzy sets for fuzzy matching, which makes similarity assessment more robust against known possibility distributions in values given by humans, noise and measurement errors.

The paper is organized as follows; section 2 gives an overview of our system being developed together with relevant background knowledge. Related work is outlined in section 3. Then in section 4 we explain the details of feature extraction from finger temperature signals. Section 5 presents three matching functions for retrieving and ranking similar cases, which is followed by reuse and retain schemes in section 6. The relative performance of three matching function is then evaluated and presented in section 7. Finally the paper is concluded by section 8 with summary and discussion.

8.2 Method and System Overview

Clinical studies show that finger temperature (FT) generally decreases with stress; however this effect of changes is very individual. The pattern of variation within a finger temperature signal could help to determine stress-related disorder. However, interpreting a particular curve and diagnosing stress level is difficult even for experts in the domain. In the proposed system, we use Case-based Reasoning (CBR) as it works well in such domain where the domain knowledge is not clear enough as in the psycho-physiological domain where even an experienced clinician might have difficulty expressing his knowledge explicitly. A fuzzy set theory is used to compose efficient matching method for finding most relevant cases by calculating similarities between cases. So, combinations of all such artificial intelligent techniques help us to build a computer-aided decision support system for diagnosing stress-related disorder and severity level of the disorder.

8.2.1 Case-Based Reasoning

A case-based reasoning (CBR) (Aamodt and Plaza 1994; Watson 1997) method can work in a way close to human reasoning e.g. solves a new problem applying previous experiences. A clinician/doctor may start his/her practice with some initial experience (solved cases), then try to utilize this past experience to solve a new problem and simultaneously increases his/her case base. So, this method is getting increasing attention from the medical domain since it is a reasoning process that also is medically accepted. CBR has shown to be successful in a number of different medical applications (Nilsson and Sollenborn 2004). Aamodt and Plaza has introduced a life cycle of CBR (Aamodt and Plaza 1994) with four main steps as shown in Figure 1. Retrieve, Reuse, Revise and Retain present key tasks to implement such kind of cognitive model.

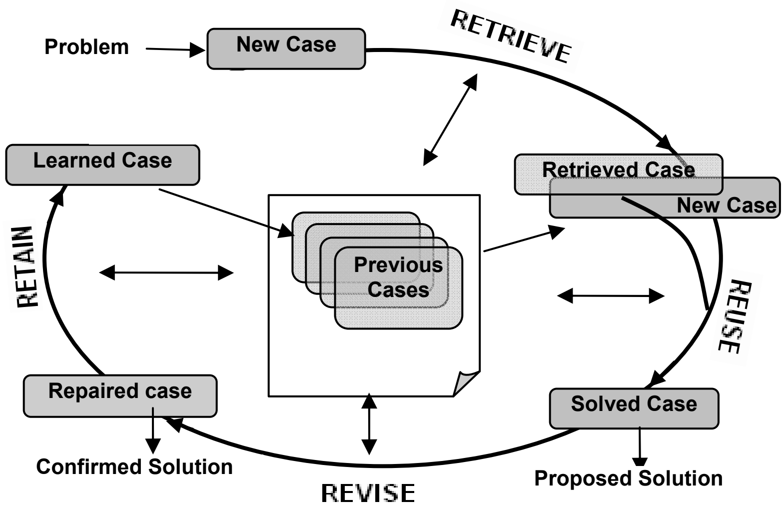


FIGURE 1. CBR cycle. The Figure is introduced by Aamodt and Plaza (Aamodt and Plaza 1994)

In the retrieval step, for any new problem the system tries to retrieve the most similar case(s) by matching previous cases from a case base. If it finds any suitable case that is close to a current problem then the solution is reused (after some adaptation and revision if necessary). A clinician may revise the selected case with solution and retain this solution along with the new problem into the case base. The CBR method in the proposed system is used to suggest recommendations for diagnosis of stress-related disorder for a new case by retrieving and matching previously solved similar problems from the case base.

8.2.2 Fuzzy Logic and Case-Based Reasoning

Fuzzy set theory has successfully been applied in handling uncertainties in various application domains (Jang, Sun, and Mizutani. 1997) including medical domain. Inexact medical entities can be defined using fuzzy sets. Fuzzy set theory was developed by Zadeh in 1965. It explains fuzziness existing in a human thinking process using fuzzy values instead of using a crisp or binary value. Use of fuzzy logic in medical informatics has begun in the early 1970s. In fuzzy CBR, fuzzy sets can be used in similarity measure (Bonissone and Cheetham 1998; Dvir, Langholz and Schneider 1999; Wang 1997). A discussion about the relationship between the similarity concept and several other uncertainty formalisms including fuzzy sets can be found in (Richter 2006). In the proposed application, fuzzy set theory is used for matching similarities between existing cases and a current case to model imprecise expert's knowledge in the psycho-physiological domain. It matches cases in terms of degrees of similarities [0-1] between attribute values of previous cases and a new case.

8.2.3 System Overview

A decision support system for diagnosing individual stress-condition based on finger temperature measurements works in several stages as illustrated in Figure 2. The first stage is the Calibration phase (Begum et al. 2006a) where the finger temperature measurement is taken using a temperature sensor to establish an individual stress profile. Feature extraction is the second stage described in section 4 where relevant features are extracted automatically from the outcome of the calibration phase. Finally, these extracted features thereafter help to formulate a new problem case and passed to the case-based reasoning cycle. The new case is then matched using different matching algorithms including modified distance function, similarity matrix and fuzzy similarity match, see details in section 5. The DSS can provide matching outcome in a sorted list of best matching cases according to their similarity values in three circumstances: when a new problem case is matched with all the solved cases in a case base (between subject and class), within a class where the class information is provided by the user and also within a subject, see more details in section 6.

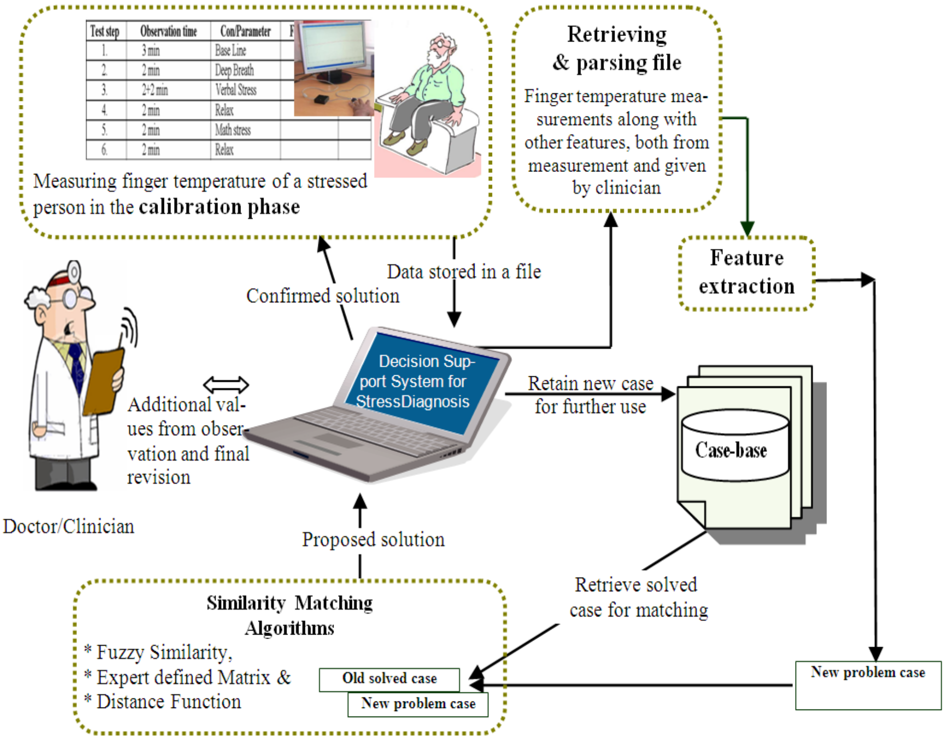


FIGURE 2. System overview of a decision support system for stress diagnosis

A clinician thereafter revises the best matching cases and approves a case to solve a new problem case by using the solution of this old case; this confirmed solution is then prescribed to the patient. However, often an adjustment to the solution of the old case may require since a new problem case may not always be as same as an old retrieved case. However, there is no adaptation of the cases in the proposed system. This adaptation could be done by clinicians in the domain. In the medical system, there is not much adaptation, especially in a decision support system where the best cases are proposed to the clinician as suggestions of solutions and when the domain knowledge is not clear enough (Watson 1997). Finally, this new solved case is added to the case base functioning as a learning process in the CBR cycle and allows the user to solve a future problem by using this solved case, which is commonly termed as retain. Retaining of a new solved case could be done manually based on clinician or expert's decision. The decision support system is currently implemented as a prototype in Java so it is platform independent. An evaluation of the system performance compared to a domain expert/clinician is presented in section 7.

8.3 Related Work

A procedure for diagnosing stress-related disorders has been put forward by Nilsson et al. (2006) according to which stress-related disorders are diagnosed by classifying the heart rate patterns analyzing both cardio and pulmonary signals, i.e., physiological time series and used as a research tool in psycho-physiological medicine. This was an initial attempt to use a DSS in a previously unexplored domain e.g. psycho-physiological medicine. This tool is more suitable to use in clinical environment whereas the DSS, diagnosing stress-related disorder analyzing the finger temperature signal, proposed in this paper can be developed as a tool to be used by people who need to monitor their stress level during everyday situations e.g. in home and in work environment for health reasons.

In our previous work (Begum et al. 2006a), a stress diagnosing system using CBR has been designed based only on the variation of the finger temperature measurements, but this previous research does not addressed whether any other factors that could also be used in diagnosing individual stress level. In the earlier research (Begum et al. 2007) we have further demonstrated a system for classifying and diagnosing stress level, exploiting finger temperature graphs and other features. This system relies on CBR as well as on fuzzy sets theory. In extracting features from FT signal we have considered step 3, 4 and 5 (calibration phase, see Begum et al. 2006a) and investigated the temperature variation of these steps. The current paper presents a result of the evaluation of a computer-aided stress diagnosis system in comparison to a domain expert/clinician. In this system fuzzy similarity matching is applied in CBR-retrieval. In addition, in extracting features from signal data we have considered step 2 to step 6 of the calibration phase.

Apart from the psycho-physiological domain, CBR has been applied in several others diagnosis/classification tasks in the medical domain. Montani et al. (2001) has combined case-based reasoning, rule-based reasoning (RBR), and model-based reasoning to support therapy for diabetic patients. Auguste (Marling and Whitehouse 2001) project has been developed for diagnosis and treatment planning in Alzheimer's disease. This is a hybrid system that combines CBR and RBR. MNAOMIA (Bichindaritz 1996) has been developed for the domain of psychiatry. CARE-PARTNER (Bichindaritz, Kansu and Sullivan 1998) is a decision support system developed in stem cell transplantation. The system uses a multi modal reasoning framework combining CBR and RBR. BOLERO (Lopez and Plaza 1993) is a successfully applied medical CBR diagnosis system in diagnosing pneumonias applies fuzzy set theory for representing uncertain and imprecise values. A CBR technique with fuzzy theory has been used for the assessment of coronary heart disease risk in (Schuster 1997). A CBR approach to dose planning in Radiotheraphy has been proposed by Song et al. in (2007) where fuzzy set theory is applied for measuring the similarity. A CBR system for cancer diagnosis has been proposed by (Diaz, Florentino, and Corchado 2006) which combine fuzzy case representation, a neural network to cluster the cases and a set of rules for the classification. All these projects and others (Gierl 1993, Schmidt and Gierl 2002, and Perner et al.2003) show significant evidence of successful implementations of the CBR techniques in the medical domain. Nevertheless, the application of CBR in the psycho-physiological domain has been limited so far. Therefore, to our knowledge, research work addressed in this paper for providing decision-support to clinicians in the psycho-physiological medicine is of great significance in applying CBR and other artificial intelligence techniques in medical domain.

8.4 Features Extraction and Case Formulation

Extracting appropriate features is of great importance in performing accurate classification in a computer-aided system whereas in manual process an experienced clinician often classify FT signal without being pointed out intentionally all the features he/she uses in the classification. A standard procedure followed by clinicians to establish a person's stress profile has already been discussed concerning the calibration phase (Begum et al. 2006a) whereby an experienced clinician manually evaluates the FT measurements during different stress conditions as well as in non-stressed (relaxed) conditions to make an initial diagnosis. In this phase, the finger temperature is measured using a temperature sensor connected to a computer and the temperature is observed in 6 steps (1. Baseline, 2. Deep-breath, 3. Verbal-stress, 4. Relax with positive thinking, 5. Math-stress and 6. Relax). After the test, a person is requested to answer some questions for instance, when he/she had his/her meal, food habit, food allergy and so on. The output from the calibration phase is then used in extracting significant features and afterwards a new case is formulated employing these extracted features.

The FT sensor measurements are recorded using software which provides filtered data to the system. This signal data and answer to the questions from the calibration phase are then stored in a file in the local device and exported to the DSS. From the exported file, system retrieves 15 minutes finger temperature measurements (time, temperature) in 1800 samples, together with other numeric (age, room-temperature, hours since meal, etc) and symbolic (gender, food and drink taken, sleep at night, etc) features. In fact, dealing with sensor signal is more complex than human designed features such as age, gender, room temperature etc.

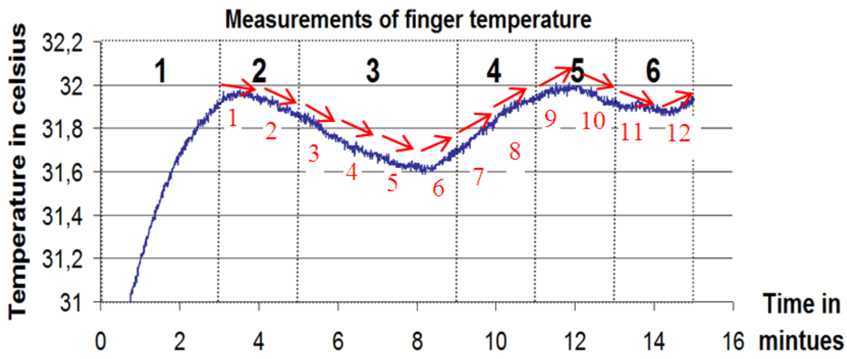


FIGURE 3. Changes in FT data against time during different stress and non-stress condition

Figure 3 displays skin temperature of the finger during both the stress and non-stress conditions. As can be seen, after analyzing a number of finger temperature signals, the temperature is rising and falling against time and after an initial increase, finger temperature decreases in stress condition (step 3) and increases in relax condition (step 4). According to closer discussion with clinicians on the interpretation of such graph, it is concluded that in general, the finger temperature could decrease with stress and increase in relax state and the changes between the steps are also of importance for the clinicians. A standardization of the slope that is using negative and positive angles makes it more visualise and gives a terminology to a clinician for reasoning about stress.

Therefore, we calculate the derivative of each step to introduce “degree of changes” as a measurement of the finger temperature changes. A low angle value, e.g. zero or close to zero indicates no change or stable in finger temperature. A high positive angle value indicates rising finger temperature, while a negative angle, e.g. -20° indicates falling finger temperature. Step1 (baseline) is used normally to stabilize the finger temperature before starting the test hence this step has not been considered and the clinician also agreed on this point. Each step is divided by one minute time interval (4 minutes step3 is extracted as 4 features) and each feature contains 120 sample data (time, temperature). Thus 12 features are extracted from the 5 steps (step 2 to 6) and named as Step2_Part1, Step2_Part2, Step3_Part1, ………, Step6_Part1, Step6_Part2 as shown in Figure 3. First, a slope of the linear regression line has been calculated through the data points, as y is temperature (in Celsius) and x is time (in minute) by equation 1 for each extracted feature from the measurement.

$$slope_f = \frac{\sum_{i=0}^{n}(x-\bar{x})(y-\bar{y})}{\sum_{i=0}^{n}(x-\bar{x})^2} \tag{1}$$

Where f denotes the number of features (1 to 12 see Figure 4), i is the number of samples (1 to 120) and $\bar{x},\bar{y}$ is average of the samples. Then this slope value is converted to arctangent as a value of angle in radians (-pi/2 to +pi/2) and finally expressed arctangent value in degrees by multiplying 180/PI. The converting function from radians to degree is described in equation 2 where PI is 3.14 as a standard value. So these 12 features contain degree values comprising 120 sample data (time, temperature). Instead of keeping the sample data these degree values are used or represented as features.

$$\mathrm{deg}ree_f = \left[\tan^{-1}(slope_f)\right] * \frac{180}{PI} \tag{2}$$

Five other features which have also been extracted from the sensor signal are start temperature and end temperature from step2 to step6, minimum temperature of step3 and step5, maximum temperature of step4 and step6, and difference between ceiling and floor. Finally, 17 (12+5) features are extracted automatically from the fifteen minutes (1800 samples) FT measurements signal data. Then a new case is formulated with 19 features as a total keeping in a vector above 12 features and adding hours since last meal and gender.

The DSS thereafter formulates a new problem case combining this generated extracted features and human defined features. This new formulated case is then applied in diagnosing stress and making treatment plan by using the CBR cycle.

8.5 Case Retrieval and Matching

Case retrieval is the major phase in CBR cycle where matching between two cases plays vital role because near-most or most relevant solved cases could be retrieved if a superior matching algorithm exists. To be more cautious, the proposed DSS used three different matching algorithms and in three different matching prospects. The retrieval step is essential especially in medical applications since missing similar cases may lead to less informed decision. The reliability and accuracy of the diagnosis systems depend on the storage of cases/experiences and on the retrieval of all relevant cases and their ranking. To solve and store a new case the DSS used 19 features in total. Of which 12 features are Step2_Part1, Step2_Part2, Step3_Part1, ………, Step6_Part1, Step6_Part2 and 7 other features are start temperature and end temperature from step2 to step6, minimum temperature of step3 and step5, maximum temperature of step4 and step5, difference between ceiling and floor, Hours since last meal and gender.

In the DSS three implemented matching algorithms are 1) modified distance function for calculating similarity where distance between two cases are used as similarity value 2) similarity matrices defined by the expert where distance between two cases are converted into similarity values using matrices and 3) fuzzy set theory to calculate similarity between two cases. Similarity measurement is taken to assess the degrees of matching and create the ranked list containing the most similar cases retrieved by equation 3

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

Where C is a current/target case, S is a stored case in the case base, w is the 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 (Cf,, Sf) is the local similarity function (see sections 6.1, 6.2 and 6.3) for attribute f in cases C and S.

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

Here, the Local weight (lw) defined by experts, assumed to be a quantity reflecting importance of the corresponding feature, Normalized weight (w) is calculated by equation 4. Generally there are two ways to specify the values of weights for individual features. One way is to define weights by experts in terms of domain knowledge, while the other is to learn or optimize weights using the case library as information source. In this project, both of these approaches have been implemented to create suitable weight values. The performance of both expert weights and automatic weights (learnt from the case base) in similarity evaluation will be evaluated in section 7.

8.5.1 Modified Distance Function

Distance between the features of two cases (C, S) can be calculated by one dimensional Euclidean distance function. 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). However, we normalized the distance values from 0 to 1 using equation 5, where 1 indicates no distance and 0 far away (largest distance).

$$sim(C_f, S_f) = 1 - \frac{abs(C_f - S_f)}{Max(C_f, S_f) - Min(C_f, S_f)} \tag{5}$$

Function sim (Cf , Sf) in equation 5 represents local similarity and function abs is used to get an absolute value of (Cf - Sf). Max retrieves the maximum feature value for a feature f between the whole case base and a query case C and Min retrieves the minimum feature value for a feature f between the whole case base and a query case C.

8.5.2 Similarity Matrix

For the numeric features, distance between two features is calculated through the one dimensional Euclidean distance function. After calculating the distance, this value is converted using the local similarity values as depicted in Table 1 where the similarity values for different features are defined by a domain expert. But the similarity between two symbolic features is calculated directly using matrix without calculating the distance. For example, similarity between same genders is defined as 1 otherwise 0.5, as can be seen from Table 1.

TABLE 1. Example of the expert defined matrices used to calculate similarity

Similarity for step		Similarity for ceiling/floor		Hours since last meal						Similarity for gender		
Distance	sim		sim	T/S	0	1	2	3	>4		m	f
0-2 degree	1	<0.3	1	0	1	0.8	0.6	0.4	0	m	1	0.5
>2 and <4	0.8	0.3-0.5	0.8	1	0.8	1	0.8	0.6	0.4	f	0.5	1
>4 and <6	0.6	0.5-0.7	0.6	2	0.6	0.8	1	0.8	0.6			
>6 and <8	0.4	0.7-0.9	0.4	3	0.4	0.6	0.8	1	0.8			
>8 and <10	0.2	0.9-1.1	0.2	>4	0	0.4	0.6	0.8	1			
>10	0	> 1.1	0									

8.5.3 Fuzzy Similarity

Many crisp values both from measurements and given by a clinician are known to have a possibility distribution often known by experts and used in their reasoning. We propose that this dimension and domain knowledge is represented by fuzzy similarity, a concept well received by clinical experts. Representation of a similarity value using a matrix as shown in Table 1 often shows a sharp distinction which may provide an unreliable solution in domains where it is known that these values are less exact. Fuzzy similarity matching reduces this sharp distinction. After discussions with clinical experts a triangular membership function (*mf*) replaces the crisp input feature with a membership grade of 1. For instance, as shown in Figure 4 a current case has the lower and upper bounds 2.5 and 7.5 represented by an mf of grade 0 and an input value 5 is represented by an mf grade of 1 (fuzzy set *m1*). Again an old case has the lower and upper bounds -1.5 and 4.5 represented by an mf grade of 0 and an input value 3 is represented by an mf grade of 1 (fuzzy set *m2*). In both cases, the width of the mf is fuzzified by 50% in each side. Then by applying fuzzy intersection between the two fuzzy sets *m1* and *m2* we get a new fuzzy set *om* which represents the overlapping area between *m1* and *m2*.

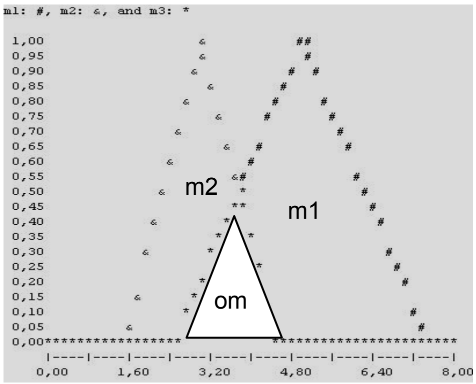


FIGURE 4. Fuzzy similarity using triangular membership functions

Similarity between the old case and the new case is now calculated using equation 6 where area of each fuzzy set (*m1*, *m2* and *om*) is calculated. The similarity equation according to (Dvir et al. 1999) is defined as-

$$sim(C_f, S_f) = s_f(m1, m2) = \max(om/m1, om/m2) \quad (6)$$

Where, s_f (*m1*, *m2*) calculates similarity between two features f of new and old cases. When the overlapping area (*om*) is bigger then the similarity between two features will also increase and for two identical fuzzy sets the similarity will reach unity.

8.6 Reuse and Retain

The objective of this implemented system is the diagnosis of an individual's stress condition where the main functionality lies in solving a new problem case by using solution of past solved cases. However, solution of a past case often requires adaptation to find a suitable solution for the new case. This adaptation might often be a combination of two or more solutions of cases from the retrieved cases. Specially, in medical domains the domain knowledge is often not well understood as in circumstances of diagnosing stress related to psycho-physiological issues. Therefore, retrieving a single matching case as a proposed solution may not be sufficient for the DSS in this domain. So, the proposed system retrieved a list of ranked cases in three matching circumstances shown by the indicators 1, 2 and 3 in Figure 5. The three yielded matching circumstances are: 1) a ranked list by the system for a current/new case matching with all the other cases in a case base 2) a sorted list of matched cases that matches a current/new case with the same subjects'/patients' cases and 3) presented best matched cases when a new problem case is matched with the solved cases in the same class where case-class is given by the user. In all the circumstances ranked list of cases are presented on the basis of their similarity value and the identified class. The solution for a retrieved old case, that is diagnosis and treatment suggestions, are also shown using indicator 5 in Figure 5. Indicator 6 shows comparison of FT measurement between a new case and old case where FT values are plotted through line chart and user can use different matching algorithms by selecting specific method shown by indicator 7. It can be seen using indicator 4 in Figure 5, details of the matching information for a new case with an old case is displayed thereby clinicians/users get an opportunity to see more details of the matching cases which may help to determine if the solution is reusable or require an adaptation for a new problem.

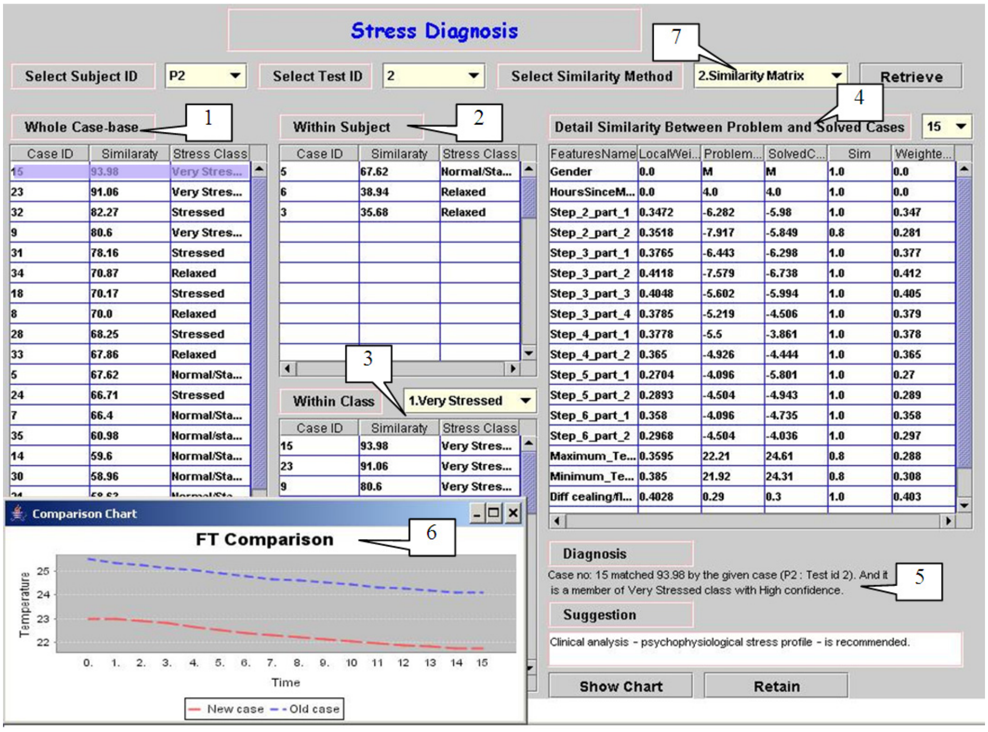


FIGURE 5. A screenshot of the stress diagnosis system.

Users can adapt solutions i.e. it could be a combination of two solutions from the list of retrieved and ranked cases in order to develop a solution to the problem in the new case. Then clinician/expert determines if it is plausible solution to the problem and he/she could modify the solution before approved. Then the case is sent to the revision step where the solution is verified manually for the 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 a new knowledge.

8.7 Evaluation

After implementing the proposed DSS, performance of the system has been evaluated where the evaluation is conducted on the similarity matching. System performance in terms of accuracy has been compared with experts in the domain where the main goal is to see how close the system could work compared to an expert. The accuracy of the system as compared to the expert is calculated using a statistics square of the correlation coefficient or Goodness-of-fit (R^2) (Carol 2002). Absolute mean difference is also calculated to determine the deviation between expert and the system. The case base is initialized with 39 reference cases classified by the domain expert and the classification of sensitivity to stress has been denotes as Very Relaxed, Relaxed, Normal/Stable, Stressed and Very Stressed.

8.7.1 Similarity Matching

We have discussed in the earlier section (section 5) about the three matching algorithms implemented in this system and now the performance of these algorithms is evaluated in this section. For the evaluation we have chosen randomly three subsets of cases and three query cases, the subsets are as follows: 1) Set A: {7 cases} with query case id 4, 2) Set B: {11 cases} with query case id 16 and 3) Set C: {10 cases} with query case id 28. All the three sets have been sorted according to the similarity with the query case decided by a domain expert (human reasoning). The sorted cases are then converted to the rank numbers, i.e., the position of a case in the ranking. Likewise, the evaluation process is designed for the three algorithms including distance, matrix, and fuzzy matching (see details in section 6), used in the system. Top six cases from each set according to the expert's ranking are used as standard for the evaluation process where both the similarity values and the ranking numbers are considered; one example evaluation result for case Set A is shown in Table 2.

TABLE 2. Similarity matching for Set A with case id 4 in comparison with a clinical expert

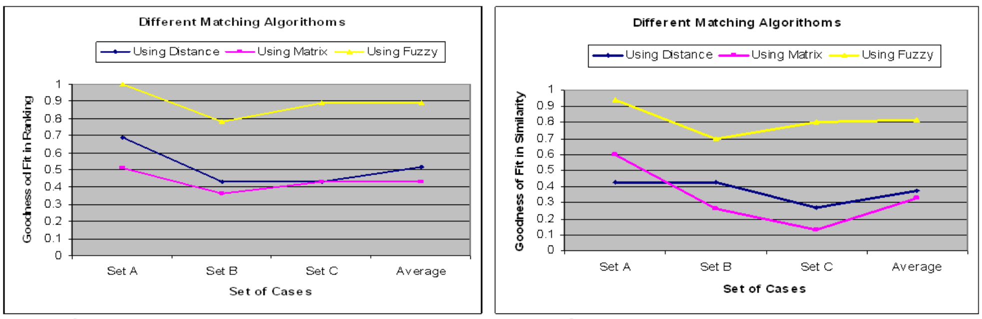
Matching (Query, Set A)	Expert		Modified Distance		Similarity Matrix		Fuzzy Similarity	
	Ranking	Similarity (%)	Ranking	Similarity (%)	Ranking	Similarity (%)	Ranking	Similarity (%)
4, 15	1	96	1	95	1	93	1	94
4, 23	2	95	2	94	2	90	2	89
4, 9	3	94	4	87	4	79	3	84
4, 24	4	75	5	84	6	65	4	74
4, 31	5	70	3	92	3	80	5	70
4, 7	6	65	6	80	5	67	6	65
Goodness-of-fit			0.69	0.43	0.51	0.60	1.00	0.94
Absolute Mean Difference			0.67	9	1.00	8	0	3

In the table above, the 1st column describes identification of two matching cases (Query and Set A). For instance query case id 4 is matched with case id 15 in Set A. Gray coloured columns represent the position of each case ranked by the expert and other three algorithms. The rest of the columns display the similarity value of each case both by the expert and the system using the three algorithms. Last two rows show the value of goodness-of-fit (R^2) and absolute (ABS) mean difference, calculated on the basis of the ranking and similarity values identified by the expert and the system. According to the R^2 value and absolute mean difference both in ranking and in similarity, fuzzy similarity matching algorithm shows better performance than the other algorithms on the example Set A compared with the expert's opinion.

TABLE 3. Average Goodness-of-fit and absolute mean difference for three matching algorithms

Similarity Algorithms in Average (Set A, B and C)	Goodness-of-fit		Absolute Mean Difference	
	Ranking	Similarity (%)	Ranking	Similarity (%)
Modified Distance	0.52	0.38	1.00	9.33
Similarity Matrix	0.43	0.33	1.00	8.00
Fuzzy Similarity	0.90	0.81	0.33	11.67

Table 3 shows the average outcome across the three subsets: Set A, Set B and Set C in terms of the goodness-of-fit (R^2) and absolute mean difference for evaluating three algorithms (Using distance, matrix and fuzzy-logic), comparing expert's ranked cases with the cases ranked by the system and with their similarity value as well. As can be seen from Table 3, similarity matching algorithm using fuzzy logic seems to be reliable both in similarity and ranking value and it outperforms the other two matching algorithms. According to the calculated average R^2 between the yielded (using fuzzy-logic) and the desired values (using domain expert) for the ranking and similarity assessments across three case subsets, it is showed that the fuzzy matching can yield results coinciding with expert suggestions with 90% in ranking and 81% in similarity evaluations. Regarding the average absolute mean difference on the three sets (A, B and C) fuzzy-logic has lower error (i.e. 0.33) in ranking compared to others although the error in similarity (i.e. 11.67) is higher than the others. The error may be due to the fact that the fuzzy similarity matching algorithm depends on the width of the fuzzy set membership functions (*mf*) and in our system the width of the *mf* is fuzzified by 50% in each side. Overall, using fuzzy logic the proposed system can retrieve more relevant cases which have been chosen by an expert/clinician comparing the other two algorithms.



a) R^2 in ranking value b) R^2 in similarity value

FIGURE 6. Comparison among three different matching algorithms.

Comparison charts of the three matching algorithms using the three sets according to their goodness-of-fit (R^2) is presented in Figure 6, where a) shows calculated R^2 for ranking values and b) shows R^2 for similarity values.

Until now all the results we have discussed are based on weights defined by domain expert. As another alternative we also attempted to discover proper weight values by learning from the case base. The basic idea followed is to distinguish individual features in terms of discriminating powers (Funk and xiong 2007) on the discritized universes of features. The weight of an individual feature is simply defined to equal the metric of discriminating power, which further can be estimated using samples in the case base. The performance of such automatic learnt weights is demonstrated in Table 4 as compared to expert results in similarity evaluation and case ranking using fuzzy similarity matching algorithm.

TABLE 4. Performance of automatic weighting.

Similarity (Query, Case Sets)	Goodness-of-fit in Ranking	Goodness of Fit in Similarity	Absolute Mean Difference in Ranking	Absolute Mean Difference in Similarity (%)
4, Set A	0.89	0.92	0.33	4
16, Set B	0.60	0.55	1.00	21
28, Set C	0.79	0.58	0.67	18
Average	0.84	0.68	0.67	14.67

We see from table above that, with 14.67% as the mean difference in similarity and 0.67 as the mean position error in ranking, the automatic weights are satisfying by producing good results close to expert evaluations. This also indicates that weight learning from the case base is a feasible solution that would help when domain knowledge is not available.

8.8 Summary and Discussion

This paper presents a computer-aided decision support system for analyzing and diagnosing stress-related disorders based upon finger temperature signals. Our work to date features three main points, namely feature extraction from time series data, case-based reasoning, and fuzzy information processing. Feature extraction is tasked to “dig out” key characteristics from original signals to reach a concise yet sufficient description of problems. The success for this heavily relies on domain knowledge and 19 time-based features have been identified and confirmed through cooperation with domain experts. The method of case-based reasoning is employed to make recommendations for stress diagnosis by retrieving and comparing with previous similar cases in terms of features extracted. Moreover, fuzzy techniques are incorporated into our CBR system to better accommodate uncertainty in clinicians reasoning as well as imprecision in case indexes. All such ideas have been implemented and validated in a prototypical system.

Feature weighting is another important issue under investigation in our project. With available test data we have recognized that the extracted features have different importance and proper weightings for them plays a crucial role for system performance.

So far we have two sets of weight values, both of which offered acceptable system performance in evaluation. One of such weight sets was exclusively defined by an experienced domain expert, and the other set was learnt from the case base by applying the so called discriminating power (Funk and Xiong 2007) on discretized universes of individual features. The automatic learnt weights have shown to perform sufficiently close to an expert in identifying similar cases, sufficiently good bearing in mind that different expert have different opinions and that there is no exact answer. We conjecture there would be two reasons for this inferiority. The first lies in the fact that there are merely 39 cases in the current case library and this low number of samples may degrade the reliability of weights achieved. The second and possibly more important is the lack of expert preference information in the case base. One of our future research directions will be optimization of feature weights by directly utilizing case preferences of expert as learning signals.

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Chapter 9

Paper C:

Classify and Diagnose Individual Stress Using Calibration and Fuzzy Case-Based Reasoning

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Abstract

Increased exposure to stress may cause health problems. An experienced clinician is able to diagnose a person’s stress level based on sensor readings. Large individual variations and absence of general rules make it difficult to diagnose stress and the risk of stress-related health problems. A decision support system providing clinicians with a second opinion would be valuable. We propose a novel solution combining case-based reasoning and fuzzy logic along with a calibration phase to diagnose individual stress. During calibration a number of individual parameters are established. The system also considers the feedback from the patient on how well the test was performed. The system uses fuzzy logic to incorporating the imprecise characteristics of the domain. The cases are also used for the individual treatment process and transfer experience between clinicians. The validation of the approach is based on close collaboration with experts and measurements from 24 persons used as reference.

9.1 Introduction

Today everyday life for many people contain many situations that may trigger stress or result in an individual living on an increased stress level under long time. It is known that high level of stress may cause serious health problems. Different treatments and exercises can reduce this stress. Since one of the effects of stress is that the awareness of the body decreases, it is easy to miss signals such as high tension in muscles, unnatural breathing, blood-sugar fluctuations and cardiovascular functionality. It may take many weeks or months to become aware of the increased stress level, and once it is noticed, the effects and unaligned processes, e.g. of the metabolic processes, may need long and active behavioural treatment to revert to a normal state [25]. For patients with high blood pressure and heart problems high stress levels may be directly life-endangered. A system determining a person's stress profile and potential health problems would be valuable both in a clinical environment as second opinion or in a home environment as part of a stress management program.

A well known fact is that finger temperature has a correlation with stress for most people, but large individual fluctuations make it difficult to use a traditional diagnosis system. In this paper we propose a system that uses case-based reasoning (CBR) and fuzzy logic along with a calibration phase. CBR [1, 9] is a method based on learning from similar cases and since this is spread practiced in clinical work, it is a method readily accepted by many clinicians. The calibration phase helps to determine a number of parameters that are important inputs both for a clinician to make the final diagnosis and treatment plan and also for the following system to classify the severity of the current stress level and makes a prognosis of its development so counter measures and treatment can be chosen.

9.2 Background

9.2.1 Stress medicine

Psycho-physiology addresses the relation between psychology and physiology. Stress medicine is a branch of Psycho-physiology where the treatment of stress-related dysfunctions is studied. In psychology stress is defined as a condition caused by different factors in which human beings are inclining to change the existing normal stable state. When we react to certain events or facts it may produce stress. Stress may in worst case cause severe mental and physical problems that are often related to psychosomatic disorders, coronary heart disease etc. [24].

9.2.2 Establishing a person's stress profile

We will give a brief description of the standard procedure followed by the clinicians to establish a person's stress profile without going into clinical details, and only give a general understanding of the test procedure. Measurement of the finger temperature is taken using a temperature sensor connected to a computer during stress conditions as well as in non-stressed (relaxed) conditions as shown in fig.1.

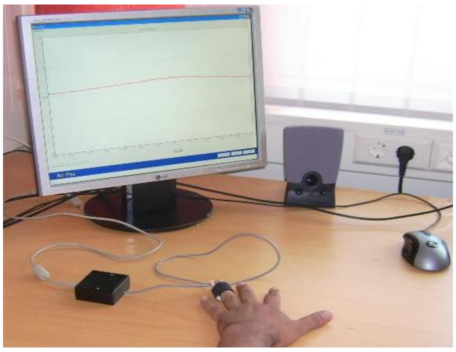

Fig. 1. Taking finger temperature measurement using a temperature sensor

Adjustments before starting the test conditions are achieved under the base-line measurement conditions, by securing a stable room temperature and allowing time for a person to adjust from the outdoor temperature (if the person has been outside recently). Thus it allows a person to stabilize the hand temperature and then temperatures are measured following a standard procedure (table 1).

Table 4. Measurement procedure used to create an individual stress profile

Test step	Observation time	Con/Parameter	Finger temp	Notes
1.	3 min	Base Line		
2.	2 min	Deep Breath		
3.	2+2 min	Verbal Stress		
4.	2 min	Relax		
5.	2 min	Math stress		
6.	2 min	Relax		

Step1 may be seen as indicating the representative level for the individual when he/she is neither under strong stress nor in a relax state. Sometimes clinicians let the person to read a neutral text during this step. A clinician not only identifies an individual's basic finger temperature, but also notes fluctuations and other effects, e.g. disturbances in the environment or observes person's behaviour.

During step2 the person breaths deeply which under guidance normally causes a relax state. Also how quickly the changes occur during this step is relevant and recorded together with observed fluctuations.

Step3 is initiated with letting a person tell about some stressful events they experienced in life. It is important for the clinician to make sure that this really is a stressful event, since some persons instead select some more neutral event or tell about a challenge they were excited to solve. During the second half of the step a person thinks about some negative stressful events in his/her life.

In step4, the person may be instructed to think of something positive, either a moment in life when he was very happy or a future event he looks forward to experiencing (this step may be difficult for a depressed person and adjusted accordingly by the clinicians).

Step5 is the math stress step; it 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.

9.3 Materials and methods

Finger temperature is measured by attaching a temperature sensor to the little finger. The signal from the sensor contains the pattern of the finger temperature during different stress and relaxed conditions. An example of the finger temperature measurements is shown in fig. 2 demonstrating the variations on finger temperature.

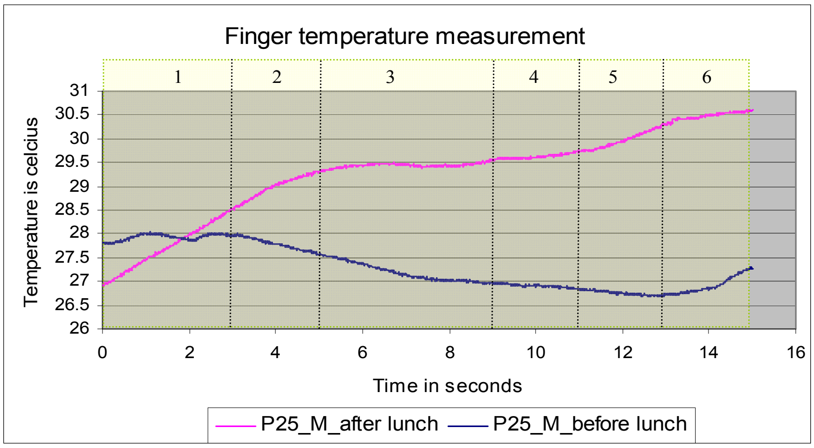

Fig. 2. Variations on finger temperature before and after lunch

Clinical studies show that when talking about any stressful events/experience finger temperature decreases and in extreme cases it decreases up to 5 to 10 degrees of Celsius. Recalling a minor misunderstanding could even decrease the temperature by 1 degree [13]. However, this effect of changes varies for different persons. Ideally the temperature is monitored repeatedly during a longer period, e.g. a week, to determine the temperature consistency or pattern for the person. This pattern could be different for different persons, e.g. some may have lowest representative temperature at 22C while for another person 28C may be the lowest. Changes in temperature before and after meal can be pronounced in some individuals, but for persons with some food allergy no changes or a decrease may occur. In general, temperature associated with stress may vary from 15.5 degree Celsius to 37.2 degree Celsius in a normal room temperature (20C to 23C).

The procedure described above for establishing a person's stress profile is used as a standard procedure in the clinical work in patients with stress related dysfunctions and an experienced clinician evaluates these measurements during the different test conditions to make an initial diagnosis. This diagnosis is complex and based on long experience and tacit knowledge [19]. The approach proposed here is based on feature extraction from temperature signals and case-based reasoning to detect appearance of stress and fuzzy set theory to tackle imprecision of input given by patient or clinician as well as imprecision of the domain.

9.3.1 Fuzzy logic and case-based reasoning

Fuzzy case-based reasoning is useful for some applications in representing cases where the information is imprecise [17, 18]. It is possible to define inexact medical entities as fuzzy sets. For a fuzzy set, the idea of fuzziness is initiated by the assignment of an indicator function (membership function) that may range from values 0-1. Also in retrieving cases fuzzy set theory can be useful for matching similarities between the existing cases and the current case. Fuzzy CBR matches the cases in terms of degrees of similarities between attribute values of previous cases and a new case instead the traditional Boolean matching. Several matching algorithms have been proposed [5, 26 and 7] to retrieve cases in fuzzy CBR systems.

9.4 Related work

CBR has been applied in the psycho-physiological domain in several studies. For example, a procedure using CBR for diagnosing stress-related disorder was put forwarded by Nilsson et al. [15] where stress-related disorders were diagnosed by classifying the heart rate patterns. A CBR system was outlined in [2] where the cases were fuzzified depends on finger temperature changes for diagnosing stress in the psycho-physiological domain, but it is not sufficient to depend on only the temperature changes for classifying individual sensitivity to stress. Apart from the psycho physiological domain, CBR techniques were applied in several others diagnosis/classification tasks in the medical domain. Montani et al. [23] combines case-based reasoning, rule-based reasoning, and model-based reasoning to support therapy for diabetic patients. AUGUSTE [14] project was developed for diagnosis and treatment planning in Alzheimer's disease. MNAOMIA [3] was developed for the domain of psychiatry. CARE-PARTNER [4] was used in stem cell transplantation. BOLERO [12] is a successfully applied medical CBR diagnosis system in diagnosing pneumonias using fuzzy set theory for representing uncertain and imprecise values. A CBR technique with fuzzy theory is used for the assessment of coronary heart disease risk [22]. All these projects and others [8, 21, and 16] show significant evidence of successful application of CBR techniques in the medical domain.

9.5 Classification

Before defining the severity of stress for a person we consider the variation of the finger temperature with stress and define three categories such as: a. finger temperature decreases with increasing stress which is the most common situation, b. finger temperature increases with increasing stress and c. little or no changes i.e., remains in the stable situation when a person is experienced with stress which is exceptional but might happened for some persons. In such cases the clinical expertise is important, and also similar cases in a case library may give important clues on explaining the result. As the treatment advised for the different groups would be different this categorization provides valuable information for selecting the treatment procedure for each individual.

9.5.1 Classify individual sensitivity to stress

According to the clinical experts step 3 and step 4 (table 1) are the most significant steps to classify a person's sensitivity to stress. Step 3, verbal stress is defined as reactions during lab stress conditions and step 4 which is a relaxation step soon after finishing the stress condition in step 3, is to see how quickly a person recover or cope with stress. We find that different persons behave differently in step 3, (talking about and thinking about a negative event) some have a very sharp drop in finger temperature, others a slow drop, a few have no drop in temperature (i.e. after lunch). Also some persons quickly recover in phase 4 (thinking positive event) others have slow increase in temperature, a few just continue dropping. According to the clinicians the later may be an indication of being more sensitive to stress, but in some cases there are normal explanations for these cases (i.e. a person having an exam after the test or being very hungry) and they are probably not needing treatment, but if this pattern is repeatedly consistent, then there may be a problem that need some treatment. Also a stressed person may not reach a stable or relaxed state if the body is misadjusted. This can be caused by different illnesses or by long periods of increased stress. One indication of such an increased stress level may be that the difference between a stressed state (step 3) and a relaxed state (step 4) is small. The time it takes for a person to switch from one state to another state is relevant information for a clinician, e.g. a person who still has a finger temperature level that corresponds to stressed state after spending time on relaxation exercises may need a different treatment than a person quickly reaching a finger temperature corresponding to a relaxed state. This kind of reasoning is what clinicians often doing, weighting different information. Therefore, the shape or 'behaviour' in step 3 and 4 are significant to classify a person's sensitivity to stress.

We propose to introduce "degree of change" as a measurement for finger temperature change. A low value, e.g. zero or close to zero is no change or stable in finger temperature. A high value indicating a steep slope upwards indicates a fast increase in finger temperature, while a negative angle, e.g. -20° indicates a steep decline. Together with clinicians we have agreed on a standardisation of the slope to make changes visible and patients and situations easier to compare. The proposal is that the X axis in minutes and the Y axis in degrees Celsius, hence a change during 1 minute of 1 degree gives a "degree of change" of 45° see fig.3.

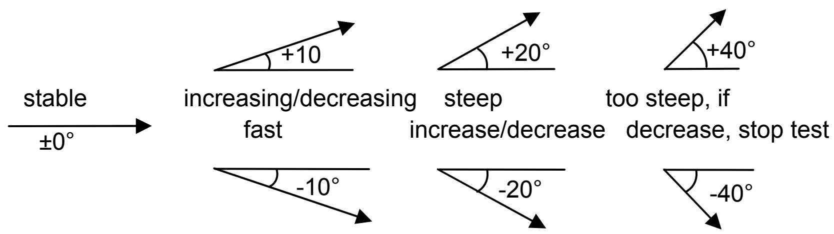

Fig. 3. Example of visualisations of temperature change, X axis minutes, Y axis 0.5 degree Celsius and clinicians response.

Decrease of temperature may be an indication of stress and how steep the change is also of importance for the clinicians. Using negative angles make this more obvious and give the clinician a terminology to reason about change. This is shown in figure 4 as text under the arrows.

If a clinician classifies temperature change we have to be aware that this also is context dependent, e.g. -17° decline may be classified "decreasing fast" for one patient and "steep decrease" for another. This is important e.g. when explaining a case to a clinician or explaining the differences and similarities between two cases.

In a test step both the average drop and the steepest drop during a time frame are relevant. The first step in the decision support system is to translate the curves into relevant sections of interest and calculate their angles as illustrated for step 3 in fig.4.

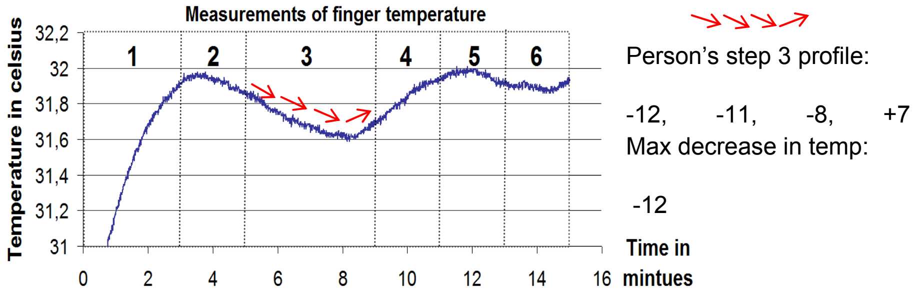

Fig. 4. The visualisations of temperature change and clinician's response

This notation makes it also easier to compare different person's differences and similarities during the test cycle, despite that their finger temperature differs widely.

9.5.2 Fuzzy classification

Furthermore, improved classification is possible by using fuzzification of these angles. Instead of using the sharp distinction we can use the fuzzy membership function (mf) because this change of finger temperature in step 3 and step 4 is highly individual and difficult to make any sharp boundaries among the classified regions. For example in step 3, 10 degrees of changes in temperature towards the negative direction can be classified as '*fast decreasing*' but in real life a person who has the 13 degrees of changes in temperature in the same direction can be classified as the same level of severity (*fast decreasing*) by the clinician. An experienced clinician does this with his own judgment. So the sharp distinction to classify individual sensitivity to stress might not always provide us the accurate result. The fuzzy membership functions are applied to generate a more smooth distinction among the sensitivity levels to classify stress. By doing this a person can be diagnosed as having multiple severity levels of stress simultaneously whereas with different degrees.

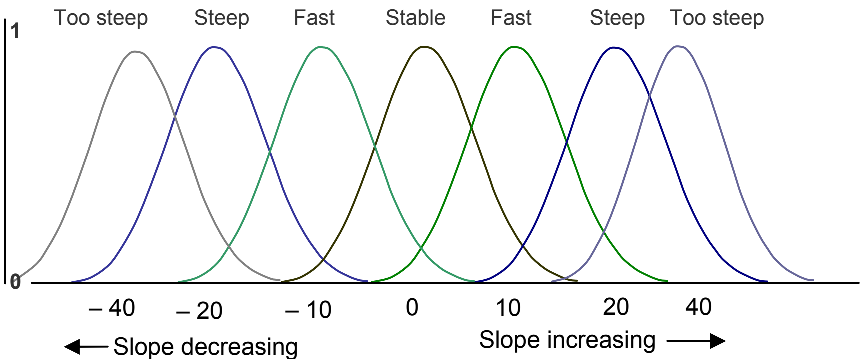

Fig. 5. Membership functions for different levels of sensitivity of stress for the similar individuals

In figure 5 an example is shown where the levels of severity of stress are defined (linguistic classifications) as too steep, steep, fast increasing/decreasing and stable depend on the 'degrees of changes' of the finger temperature in both positive and negative directions (i.e. -45 degree to +45 degree) with a set of fuzzy membership functions.

9.6 Fuzzy case-based reasoning

Initial case library was build using some reference cases from the experts then the new cases are adapted and retained manually by the expert. The output from the calibration phase is used to create an individual case. This case will contain the derivative values of various important steps. We consider the temperature from step 3 to step 5 because these are the most significant steps to determine the sensitivity to stress according to the expert. Each step is divided in one minute time interval (4 minutes step 3 is divided into four time windows) and the derivative is calculated for each window. These values along with other attributes (gender, different between ceiling and floor temperature, etc) are stored into the case library with different weight values.

9.6.1 Similarity matching

The retrieval step is especially essential in medical applications since missed similar cases may lead to less informed decision. The reliability and accuracy of the diagnosis systems depend on the storage of cases/experiences and on the retrieval of all relevant cases and their ranking. Similarity measurement is taken to assess the degrees of matching and create the ranked list containing the most similar cases retrieved by equation 1

$$Similarity\ (C, S) = \sum_{f=1}^{n} w_f * sim\ (C_f, S_f) \qquad \textbf{(7)}$$

Where; C is the current case, *S* is a stored case in the case library, *w* is the normalized weight, *n* is the number of the attributes in each case, *f* is the index for an individual attribute and *sim* is the local similarity function for attribute *f* in case *C* and *S*.

For the numeric attribute values, the distances between two attributes values are calculated through the Euclidean distance shown in equation 2.

$$sim\ (C_f, S_f) = \left| C_f - S_f \right| \qquad \textbf{(2)}$$

After calculating the distance, this value is compared with the similarity values as depicted in table 2 where the similarity values for different matrices are defined by the expert.

Table 2. Different matrices for the similarity values

Similarity for step	
Distance	*sim*
0-2 degree	1
>2 and <4	0.8
>4 and <6	0.6
>6 and <8	0.4
>8 and <10	0.2
>10	0

Similarity for ceil-ing/floor	
	sim
<0,3	1
0,3 -0,5	0.8
0,5-0,7	0.4
>0,7	0

Hours since last meal					
T/S	0	1	2	3	>4
0	1	0.8	0.6	0.4	0
1	0.8	1	0.8	0.6	0.4
2	0.6	0.8	1	0.8	0.6
3	0.4	0.6	0.8	1	0.8
>4	0	0.4	0.6	0.8	1

Similarity for gender		
	m	f
m	1	0.5
f	0.5	1

So, finally the global similarity is calculated as a weighted sum of local similarities. An example is shown in table 3 where a current case is compared with two other stored cases (C_92 and C_115) in the case library.

Table 3. Similarity matching between cases

Attributes	Local weight	Normalized weight	Current case	Stored case C_92	Similarity Function	Weighted similarity	Stored case C_115	Similarity function	Weighted similarity
Gender	5	0.05	M	M	1.00	0.05	F	0.50	0.03
Hours since last meal	10	0.11	1	3	0.60	0.07	1	1.00	0.11
Room Temp	7	0.08	20	21	1.00	0.08	21.00	1.00	0.08
Step_3_part_1	7	0.08	-17.09	-1.39	0.00	0.00	-14.39	0.60	0.05
Step_3_part_2	7	0.08	-6.38	-10.91	0.60	0.05	-8.11	1.00	0.08
Step_3_part_3	7	0.08	-7.62	-7.55	1.00	0.08	-7.55	1.00	0.08
Step_3_part_4	7	0.08	1.52	3.15	1.00	0.08	3.15	1.00	0.08
Step_4_part_1	7	0.08	16.58	1.08	0.00	0.00	5.08	0.00	0.00
Step_4_part_2	7	0.08	8.34	6.34	1.00	0.08	7.13	1.00	0.08
Step_5_part_1	6	0.07	-8.66	-2.17	0.40	0.03	-6.17	0.40	0.03
Step_5_part_2	6	0.07	-9.44	-1.77	0.40	0.03	-1.77	0.80	0.05
Diff cealing /floor	9	0.10	0.75	0.59	1.00	0.10	0.59	1.00	0.10
					Global Similarity for C_92	**0.67**		**Global Similarity for C_115**	**0.80**

Here, the *Local weight (LW)* is defined by the experts, *Normalized weight (NW)* is calculated by the equation 3 where i=1 to n number of attributes, *Similarity function* calculates the similarity between attributes of the current case and the stored cases using the equation 2 and comparing the similarity values from the table 3, *Weighted similarity* for each attribute is defined by the normalized weight multiply the output of the similarity function, *Global similarity* between the cases are calculated as weighted sum of local similarities using the equation 1.

$$NW_i = \frac{LW_i}{\sum_{i=1}^{n} LW_i} \qquad (3)$$

In table 3 the global similarity between the current case and case C_92 is 67% and current case and case C_115 is 80%.

9.6.2 Fuzzy matching

The representation of a similarity value using a matrix as shown in table 2 often shows a sharp distinction which often provides an unrealistic solution. Moreover, multiple if-then rules are needed to implement the matrices. Fuzzy similarity matching is used to reduce this sharp distinction which also helps to avoid multiple rules. A triangular membership function replaces the crisp input attribute with the membership grade of 1. The width of the membership functions (*mf*) are provided by the expert's of the domain.

For example, in table 3 the attribute '*Step3_part2'* of the current case and the old case have the values -6.3 and -10.9 respectively. The weight of the *mf* is fuzzified with 50% in each side as shown in fig.6. For the current case the lower and upper bounds are -9.45 and -3.15 represented with an *mf* of grade 0. The input value is -6.3 with the *mf* grade of 1. The old case has the lower and upper bounds -16.35 and -5.45 with an *mf* grade of 0 and the input is -10.9 with an *mf* grade of 1.

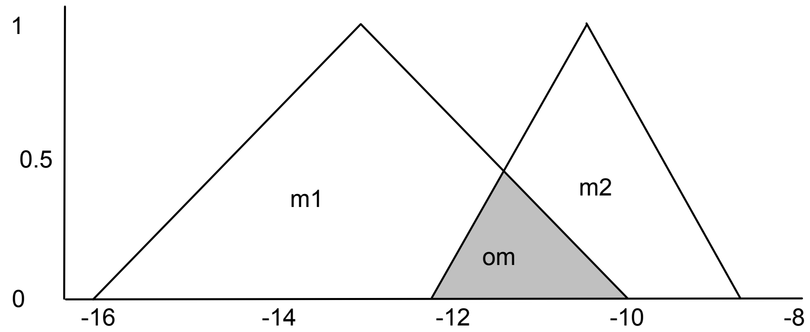

Fig. 6. Similarity matching using membership functions

The similarity between the old cases and the new case is calculated using the overlapping areas between the two fuzzy values in their membership functions [6]. The similarity equation is defined as-

$$S_{m_1 m_2} = \min(om/m_1, om/m_2) \tag{4}$$

Here m_1 is the area of one attribute value with one membership function and m_2 is associated with the second membership function and the overlapping area is denoted as om. In fig.6, m_1=5.45, m_2 =3.15 and om=0.92 where height is defined from the intersection point of the two fuzzy membership functions. So from the equation 4, the local similarity is *min (0.17, 0.29) =0.17* and *max* is 0.29. If the *mf*s are considered as 100% fuzzified then minimum local similarity will be 0.34 and maximum will be 0.58 which is close to the value of table 3. In this way the user has option both for tuning the *mf*s and choosing the min/max in the similarity function depends on the requirements. When the overlapping areas become bigger then the similarity between the two attributes will also increase and for a completely matched attributes similarity will be 1.

The system returns a ranked list with the most similar cases. Cases are sorted according to the percentage where 100% means the perfect match and represented the solution with the classification shown in the previous section. From the table 3, case C_115 has higher rank than C_92 that is the current case is more similar to the case C_115. A threshold value can be defined and modified by the user to get a list of similar cases and this list of cases are treated as candidate cases. From these candidate cases a case can be proposed by the user as an acceptable case and that can be reused to solve the new problem. If necessary, the solution for this acceptable case is revised by the expert that is often important in the medical domain. Finally, the current problem with confirmed solution is retained as a new case and added to the case library. In terms of adaptation any changes can be done by the expert before adding it into the case library and this could be done manually.

9.6.3 Reliability of the test

Once the decision support system suggests a number of similar cases it is important for the clinician to know how reliable the similarity estimate is. One valuable indication of reliability in diagnosing stress is how well the person succeeded in doing the different test assignments or how sure a clinician is on a given value or judgment. Such input will make the foundation of a confidence factor [7] for a case.

A person can grade the severity of a stressful event (step 3) he/she was thinking by using a Visual Analogue Scale (-5 to +5) where +5 is very severe traumatic memory while 0 is not stressful and -5 is extremely positive. Discussing with the clinical experts and analysing the grade and measurement from the 24 persons it is clear that they are aware of their success rate in the specific step. But the grading does not have a high accuracy and needs to be fuzzified due to many factors such as humans tend to give a precise answer without really having a basis for this “preciseness”. The value is fuzzified using two membership functions (Fig. 7). The left linear mf (from -2 to +5) represents the fuzzy values for the negative range (rate of failure in test) and the right linear mf (from -5 to +2) represents the positive range (success in test) in the universe of discourse (-5 to +5) for the fuzzy variable scale. This will give a value for the success rate in some degrees of mf instead of just a precise value and also reduce the number of rules to one.

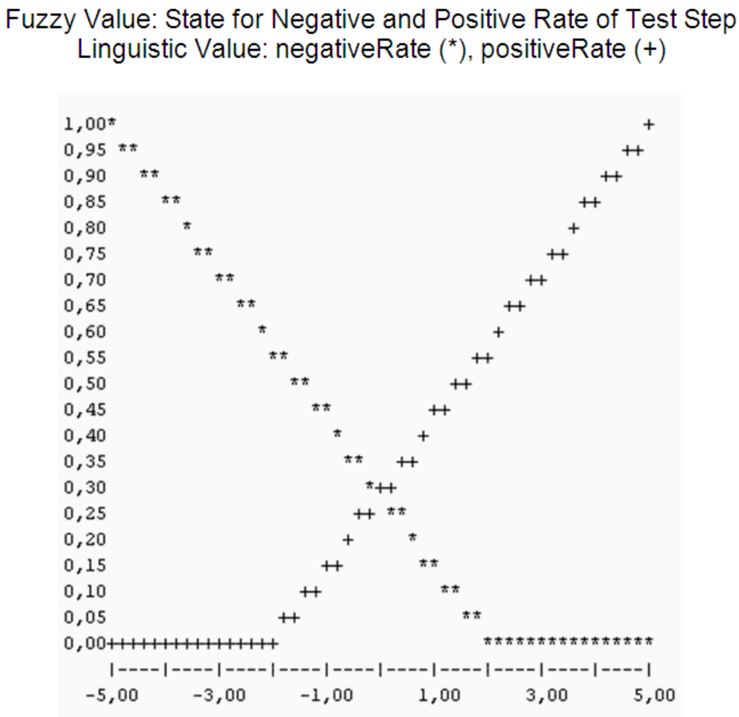

Fig. 7. Membership function of the positive and negative success rate of test

For example in table 3, the current case (CC) and case C_92 and C_115 have the success rate for the test step 3,4, and 5 are CC(7,3,6), C_92(5,6,5) and C_115(8,4,3) respectively. On an average the differences in success rate between CC and C_92 is 2 and CC and C_115 is 1.6. Suppose the global similarity between CC and other two cases are same then according to their rating of success the case C_92 will get more preference. Besides the same global similarities, this rating helps the clinician able to take a closer look at the suggested cases when the global similarities among them are different.

9.7 Summary and conclusions

We have presented a decision support system based on a case-based method using a calibration procedure and fuzzy membership functions. Integration of CBR with fuzzy set theory enables the system to handle impreciseness in input features and domain knowledge in a way understood and accepted by the clinicians. The calibration phase also assists to individualize the system. The system extracts key features from the finger temperature signal and classifies individual sensitivity to stress. This provides important information to the clinician to make a decision about individual treatment plan. One of the strengths of the method is that it bears similarities with how the clinicians work manually and when clinicians are confronted with the concepts and functionality of the decision support system it is readily accepted by them. This support is valuable since clinicians are willing to participate actively in the project and validate the results. Our hope is that the classification system can be developed to a tool used by people that need to monitor their stress level during every day situations for health reasons. Such a system may be used in different ways: to monitor stress levels that are reported back to clinicians for analysis used in relaxation exercises or actively notify a person, in some suitable way, that stress levels are increased and counter measures are advisable and this may be important for patients with increased risk of stroke or heart problems.

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Chapter 10

Paper D:
Using Calibration and Fuzzification of Cases for Improved Diagnosis and Treatment of Stress

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Abstract

In the medical literature there are a number of physiological reactions related to cognitive activities. Psychosocial and psychophysiological stress is such activities reflected in physiological reactions. Stress related symptoms are highly individual, but decreased hands temperature is the common for most individuals. A clinician learns with experience how to interpret the different symptoms but there is no adaptive diagnostic system for diagnosing stress. Decision support systems (DSS) for stress diagnosis would be valuable both for junior clinicians and as second opinion for experts. Due to the large individual variations and no general set of rules, DSS are difficult to build for this task. The proposed solution combines a calibration phase with case-based reasoning approach and fuzzification of cases. During the calibration phase a number of individual parameters and case specific fuzzy membership functions are established. This case-based approach may help the clinician to make a diagnosis, classification and treatment plan. The case may also be used to follow the treatment progress. This may be done using the proposed system. Initial tests show promising results. The individual cases including calibration and fuzzy membership functions may also be used in an autonomous system in home environment for treatment programs for individuals often under high stress.

10.1 Introduction

Stress is an increasing problem in our society. High levels of stress puts a high strain on the body, shut and prepare the body for fight or flight. After a stress reaction the body needs time to recover and restore normal functionality. If short periods of stress occur this recovery does not leave any permanent damages to the body. Today every day life for many people contains many situations that may trigger stress or results in an individual to live on an increased stress level under long time. It is known today that high levels of stress may cause serious health problems.

It is known that different treatments and exercises can reduce the stress. Since one of the effects of stress is that the awareness of the body decreases, it is easy to miss signals such as high tension in muscles, unnatural breathing, blood-sugar fluctuations and cardiovascular functionality. It may take many weeks or months to become aware (perhaps first when symptoms reach a handicapping or dramatic level) of how high the stress has been, and once notified, the effects and unaligned processes, e.g. metabolic processes, may need long and active behavioural treatment to revert to a normal state [von Schéele and von Schéele, 1999]. For patients with high blood pressure and heart problems high stress levels may be directly life endangering. A system that notifies when stress levels are rising or too high is valuable in many situations, both in clinical environment and in other environments, e.g. the patients home and work environment.

A well known fact is that finger temperature has a correlation with stress for many persons, but individual fluctuations make it difficult to use in automatic systems since there are no absolute values of temperature with relation to stress levels. We propose a case-based system used in a calibration phase to determine a set of initial parameters and hypotheses that can be used as decision support for clinicians.

In this paper we will outline the case-based calibration method and fuzzification of cases to determine a number of parameters that are important input both for a clinician to make the final diagnosis and treatment plan and also for the following system to classify the severity of the current stress level and make a prognosis of its development so counter measures and treatment can be chosen.

10.2 Related Work

Case-based reasoning (CBR) is getting increasing attention from the medical domain since it is a reasoning process that also is medically accepted. Some applications of CBR in the psycho physiological domain are: A procedure for diagnosing stress related disorder by Nilsson et al. [Nilsson et al. 2006] where stress related disorders were diagnosed by classifying the heart rate patterns analyzing both cardio- and pulmonary signals, i.e., physiological time series and used as a research tool in psycho physiological medicine. The classifier, HR3Modul uses CBR approach with a wavelet based method to retrieve features from the signals. Moreover a second subsystem, the pattern identifier was introduced to find out the familiar patterns from the classified signals. A system was proposed in [Andrén and Funk 2005] that monitors a person's stress level using biometrical data such as keystroke dynamics. This applies CBR approach to determine individual patient's stress level within the keystroke patterns. Apart from the psycho physiological domain, CBR techniques were applied in several other diagnosis/classification tasks in medical domain. Montani et al. [Montani et al. 2001] combines case-based reasoning, rule-based reasoning, and model-based reasoning to support therapy for diabetic patients. AUGUSTE [Marling and Whitehouse 2001] project was developed to diagnosis and treatment planning in Alzheimer's disease. MNAOMIA [Bichindaritz 1996] was developed for the domain of psychiatry which helps in diagnosis, treatment planning, clinical research assistance. CARE-PARTNER [Bichindaritz et al. 1998] was used in stem cell transplantation. It facilitates the diagnosis and treatment planning using a multimodal framework for reasoning. BOLERO [Lopez and Plaza 1993] is a successfully applied medical CBR diagnosis system in diagnosing pneumonias using fuzzy set theory for representing uncertain and imprecise values. A CBR technique with fuzzy theory is used for the assessment of coronary heart disease risk [Schuster 1997]. All these projects and others [Koton 1988, Gierl 1993, Gierl and Schmidt 2002, Perner et al. 2003] show significant evidence of successfully applying CBR techniques in medical domain. It seems that not so much work has yet been done using CBR in psycho physiological domain.

10.3 Establishing a Person's Stress Profile

If people feel stress, which can be experienced in different ways such as anxiety, muscle tensions/cramp and even panic. This influences SNS (Sympathetic nervous system). In general, temperature of the finger decreases when the person is stressed and increases during relaxation or in a non stressed situation. This relates to Sympathetic intervention of the alpha-receptor in the vascular bed. When relaxation occurs, SNS activity decreases as well as the intervention of the alpha receptors, which lead to increased diameters in blood vessels and increase the blood flows and the temperature. In Post Traumatic Stress Disorders reverse reactions are observed.

The procedure described below is used as standard procedure in clinical work with patients with stress related dysfunctions and an experienced clinician is evaluating the measurements during the different test conditions to make an initial diagnosis. The diagnosis is complex and based on long experience and tacit knowledge [Polanyi 1976].

We will give a brief description of the procedure without going into clinical details, and only give a general understanding of the test procedure.

A temperature sensor is attached for measuring skin temperature of the finger. Data are collected from the sensor readings during stress conditions as well as in non stressed (relaxed) conditions. Adjustment before starting test conditions is achieved under the base-line measurement conditions, which is to secure stable room temperature and enable time for person to adjust from outdoor temperature (if the person has been outside recently). For example, during cold seasons hand temperatures tend to decrease which might bias the result, taking drinks like coffee also could bias the result. So try to keep away from other hot or cold contacts such as hot drinks or outdoor exposure in connection with finger temperature (FT) measurements. Base line period allows the persons to stabilize hand temperature and then temperatures are measured following a standard procedure (table 1).

Step1 may be seen as indicating the representative level for the individual when neither under strong stress nor in a relaxed state. Sometimes clinicians let the person to read a neutral text during this step. A clinician not only identifies an individual's basic finger temperature, but also notes fluctuations and other effects, e.g. disturbances in the environment or observations of person's behaviours. Some changes in FT might also be related to inactivation, during sitting. If temperature does not reach a plateau level, this step may be extended in time.

During *step2* the person breaths deeply which under guidance normally causes a relaxed state. Also how quickly the changes occur during this step is relevant and recorded together with observed fluctuations.

Table 1: Measurements procedure used to create an individual stress profile

Test step	Observation time	Con/Parameter	Finger temp	Notes
1.	3 min	Base Line		
2.	2 min	Deep Breath		
3.	2+2 min	Verbal Stress		
4.	2 min	Relax		
5.	2 min	Math stress		
6.	2 min	Relax		

Step 3 is initiated with letting the person tell about some stressful event they experienced. It is important for the clinician to make sure this really is a stressful event, since some persons instead select some more neutral event or tell about a challenge they were excited about to solve. During the *second half* of the step the person thinks about the negative and stressful event.

In *step 4*: *relaxation part,* the person may be instructed to think of something positive, either a moment in life when he was very happy or a future event he looks forward to experiencing (this step may be difficult for a depressed person and adjusted accordingly by the clinicians).

Step 5 is the *math stress* step, it tests the person's reaction to direct induced stress by the clinician where person is requested to count backwards.
Final *relaxation step* tests if and how quickly the person recovers from the stress.

Clinical studies show that when talking about the stressful events experience finger temperature decreases, in extreme cases up to 5 to 10 degrees Celsius, and even to recall a minor misunderstanding could decrease the temperature by 1 degree [Lowenstein 1995]. However, this effect of changes varies between different persons. Ideally the temperature is monitored repeatedly during a longer period, e.g. a week, to determine the temperature consistency or pattern for the person. And it varies for different persons, e.g. some may have representative temperature of 22C as her/his lowest temperature while for other person 28C may be the lowest. Changes in temperature before and after meal can be pronounced in some individuals, but in persons with some food allergy no changes or a decrease may occur. Stress related temperature can vary from 15.5C (60 F) degrees Celsius to 37.2C (99F) degrees Celsius in persons in a normal room temperature (20C to 23C).

10.4 Preparing Data for the Case-Based Classification System

Finger temperature is measured using the sensor attached with the little finger of the non-dominant hand of a person. The signal from the sensor contains the pattern for the parameters of the finger temperature for different stress and relaxed conditions. These time series data [see Fig 1] could contain many redundant and noisy information such as in finger temperature data might be noisy with the loss of connection of the sensor or with the room temperature, so not all time points would contain the necessary information. Therefore, it is necessary to carefully reduce time series to extract the selected features that influence the whole series or a part of the series. Discrete Fourier Transform (DFT) and later also Discrete

Wavelet Transform (DWT) have been used successfully in medical applications, e.g. in Nilsson's work [Nilsson et al 2006]. Wavelet Transform is an extension of Fourier Transform. DWT measures frequency at different time resolutions and locations. For the DWT the coefficients are inclined by the sub-series of different sizes. Wavelet packet analysis is the same as the wavelet analysis but it gives more flexibility to represent the signal [Coifman et al 1992]. To find the wavelet packet table which contains the wavelet coefficients, fast splitting algorithm [Bruce and Gao 1992] is used and this is an adaptation of the pyramid algorithm [Mallat 1989].

The basis function is

$$\psi_{j,b,k}(t) = 2^{j/2}\psi_b\left(2^j t - k\right) \quad \textbf{(1)}$$

Where, j is the resolution level, b is the number of oscillations, k is the translation shift. A signal f (t) is represented as a sum of wavelet packet functions and different scales.

$$f(t) \approx \sum_j \sum_b \sum_k c_{j,b,k}\psi_{j,b,k}(t) \quad \textbf{(2)}$$

Where, $c_{j,b,k}$ represents the wavelet packet coefficient

Feature extraction is done by the best basis algorithm [Coifman et. al. 1992] which selects optimal transforms from the wavelet packet tables.

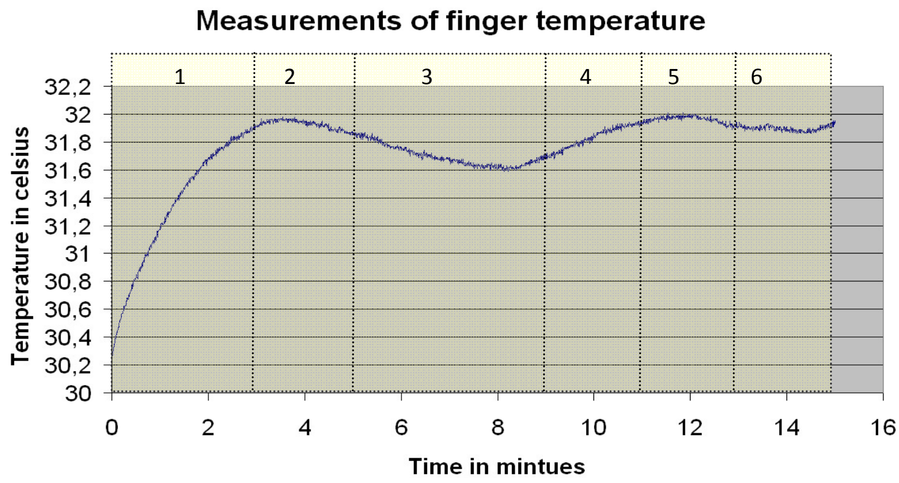

Fig 1: An example of measurements of finger temperature during the 6 steps in Table 1

10.5 Fuzzy Cases Capturing Variations and Probabilities

A specific finger temperature pattern is associated with a specific stress/relaxation level, but the correlation also depends on a number of other factors which will be discussed later. But if we look at the current situation without knowledge of any other influencing factors, we can use fuzzy set theory to determine the correlation between temperature and the different levels of stress. Later on we can make further adjustments when more information will be available about the current situation.

Fuzzy logic provides reasoning methods for approximate inference [Linkens 1988]. Fuzzy set theory, which was developed by Zadeh in 1965, instead of crisp or binary value, is used to explain the fuzziness existing in human's thinking. It is possible to define inexact medical entities as fuzzy sets. For a fuzzy set, the idea of fuzziness is initiated by the assignment of an indicator function (membership function) that may range on values 0-1. When the boundaries between different classes are not clear in such cases fuzzy set theory can be applicable. Fuzzy logic allows defining cases with vague attributes [Plaza and Lopez 1990, Jaczynski 1994]. It gives the linguistic representation of patterns. Features vectors from DWT are given as the input in the fuzzy classifier where they are fuzzified and classified using the rules defined by the expert of the domain.

The general membership function cannot be used directly for an individual, but data collected from the calibration phase provide the values needed to individualize the membership functions for an individual. After the calibration phase it should ideally not have other influencing factors, such as unusual room temperature, measured during unusual conditions etc.

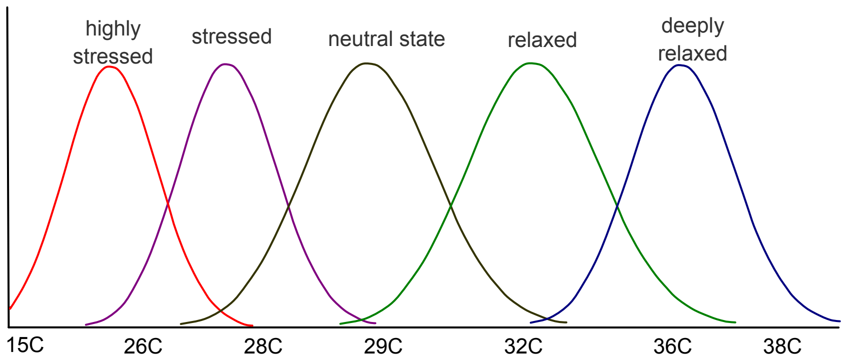

Fig 2: General membership function for the different levels of finger temperature for person belonging to category a

Considering the variation of temperature with stress three categories are defined such as: a. persons finger temperature decreases during the stress condition which is a general situation, b. finger temperature increases with stress and c. little or no changes i.e., remains in the stable situation when the person is experienced with stress which is exceptional but might happen for some persons. In such cases the clinical expertise is important, and also similar cases in the case library may give important clues on explaining the result.

Different levels of stress for individual persons depend on how much the temperature changes which is highly individual, so difficult to make any boundary between different regions. In this case, the levels of temperature are defined (linguistic classifications) as highly stressed, stressed, neutral state, relaxed, and deeply relaxed with a set of fuzzy membership functions. By doing this a person can be diagnosed as having multiple stress levels simultaneously whereas with different degrees. These fuzzy values are initially chosen with the help of the experts' knowledge in the domain. In representing cases, the fuzzy membership functions corresponding to the regions are stored as cases. It is also possible to use a Neuro-fuzzy system to tune the parameters of the membership function but this would require a large dataset for training [Begum et al. 2006].This would be possible once sufficiently many cases have been collected in the case library.

10.6 Case Representation and Matching

The output from the calibration phase is used to create an individual case. This case will contain the individualization parameters for the membership functions. The easiest level to determine is the stressed level, which is the temperature from *step 3* and *5*. But a stressed person may not reach a neutral or relaxed state since the body is misadjusted. This can be caused by different illnesses or by long periods of increased stress. One indication of such an increased stress level may be that the difference between a stressed state and a neutral or relaxed state is small. Also the time it takes for a person to transfer from one state to another state is relevant information for a clinician, e.g. a person that still has a finger temperature level that corresponds to stressed state after spending time on relaxation exercises may need a different treatment than a person quickly reaching a finger temperature corresponding to a relaxed state.

These parameters are set by the clinician based on experience and feedback from the persons and stored in the person's case. This is a "New Calibration Case", and since we add other relevant information important for diagnosis and treatment we call it "New Case" in the following. The new case can be used in a variety of situations, e.g. to assess the effect of treatment and recovery or to identify dangerous stress levels, e.g. on patients with increased risk for strokes.

Figure 3 contains an outline of the case-based method that identifies similar patient to help the clinician to diagnose the patient and select a treatment plan. The combination of fuzzy set theory and CBR systems supports two different tasks: 1) defining classes for indicating the levels of stress and 2) Selection of the matching cases from the previous experience. Case retrieval is made using a similarity measure based on these membership functions.

The proposed system consists of 6 steps: calibration, pre-processing including fuzzification, retrieval, reuse, revise and retain.

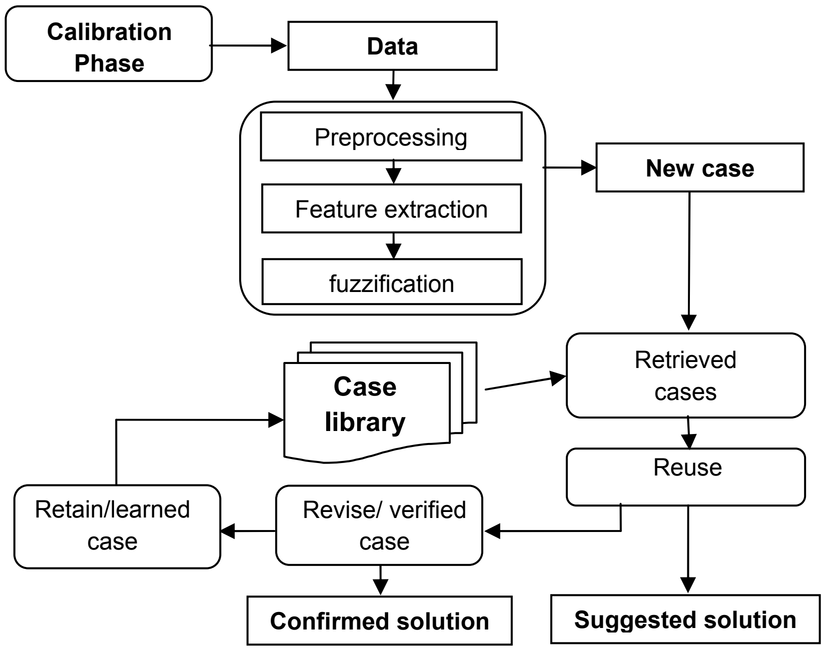

Fig 3: Case-based method to determine a person's stress level

The CBR systems include the essential steps such as retrieval, reuse, revise, and retain. The retrieval step is the most important step where proper similarity measurements should be done to retrieve the best matching one. Reliable and accurate function of the diagnosis systems depends on the storage of cases or experiences and on retrieving the most appropriate one for the current problem definition. But comparing each case stored in the case library to retrieve the similar one is a time-consuming task. Fuzzy set theory is applied to evaluate the similarity between the stored cases and the new case. The general matching approaches would require a large number of cases in the case library to cover all the given input queries. The fuzzy set theory applied makes it accurate and faster.

For matching cases, similarity measurement is done by fuzzy matching. A Gaussian membership function will be formed to replace the crisp attribute value for the similarity matching. Experts of the domain will define the membership function. The similarity of the old cases to the new case is calculated using the overlapping areas between two fuzzy values in their membership functions [Dvir et al. 1999].

In the reuse step the retrieved cases are reused to solve the new case. If necessary, the solution is revised. Finally, the current problem with corresponding final solutions is retained as a new case and added into the case library.

10.7 Summary and Conclusions

We have in this paper outlined a decision support system based on a case-based method using a calibration procedure and fuzzy membership functions. The method bears similarities with how clinicians work manually and when clinicians are confronted with the concepts and functionality of the decision support system it is readily accepted by them. This support is valuable since clinicians are willing to participate actively in the project. Initial evaluations show that using the calibration phase and individualized fuzzification also improves performance, but this needs to be confirmed and larger trails and measurements are ongoing. Representing fuzzy cases also enables following a patient's treatment progress and would enable self treatment if the person would have access to such a system and the calibration case produced under clinical conditions.

The method is also resistant to large variations since the fuzzification parameters are individual for each case. Once such a case library grows in size with cases it becomes a valuable clinical tool to discover causal relations that may be medically interesting and enable progress in diagnosis and treatment.

Our hope is that the classification system can be developed to a tool used by people that need to monitor their stress level during every day situations for health reasons. Such a system may be used in two ways, either just to monitor levels that are reported back to clinicians for analysis, or used actively to notify person, in some suitable way, that stress levels are increased and counter measures are advisable. This may be important in patients with e.g. increased risk of stroke or heart problems.

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