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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).

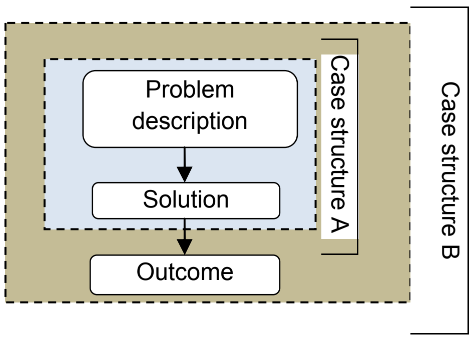

Figure 1. Cases can contain problem description and solution only or may include the result/outcome as a case structure in medical domain [58].

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.

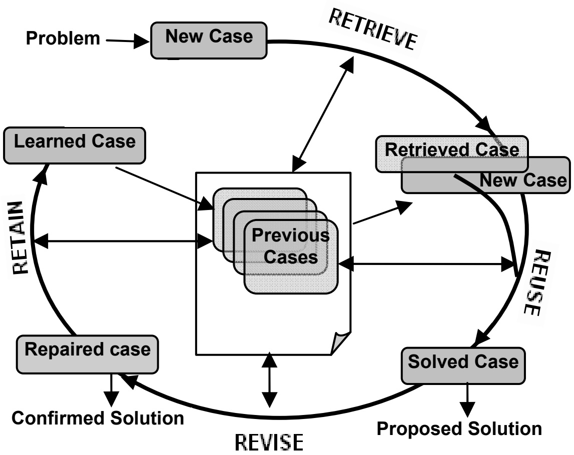

Figure 2. CBR cycle. The figure is introduced by Aamodt and Plaza [2].

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:

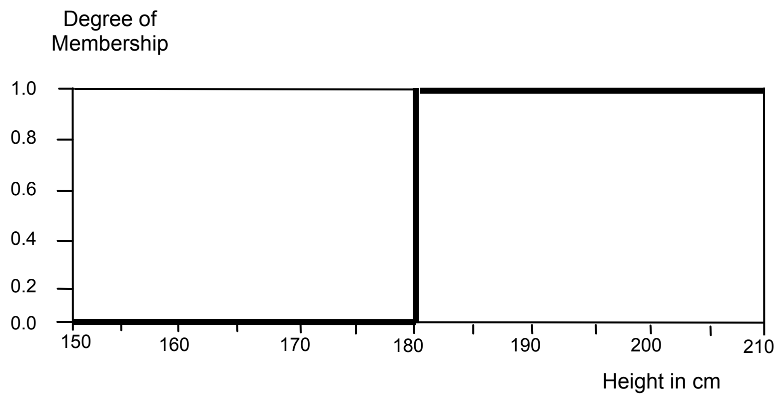

Figure 3. Example presented in crisp set.

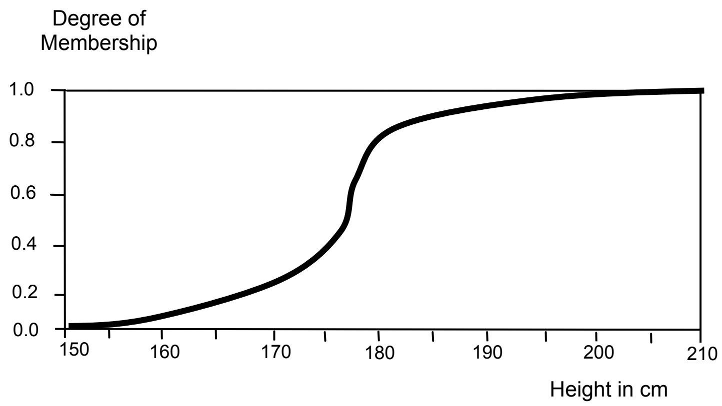

Figure 4. Example presented in fuzzy set.

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].

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

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: $\mu_{A\cup B}(x) = \max(\mu_A(x), \mu_B(x))$,

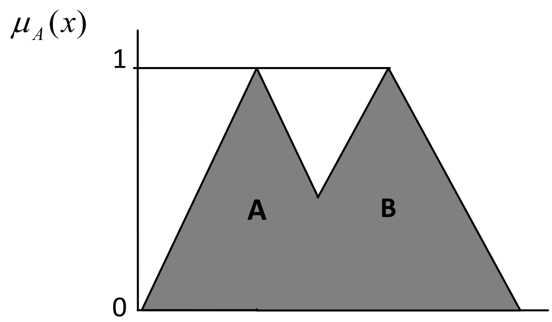

Figure 5. Example of fuzzy union.

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: $\mu_{A \cap B}(x) = \min(\mu_A(x), \mu_B(x))$

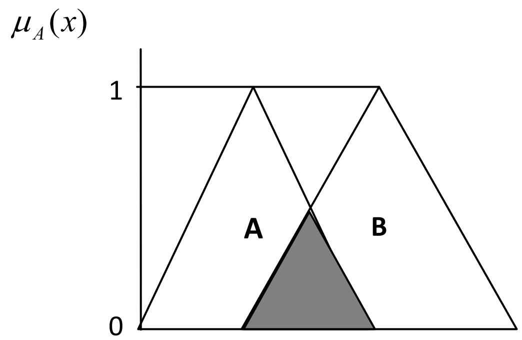

Figure 6. Example of fuzzy intersection.

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

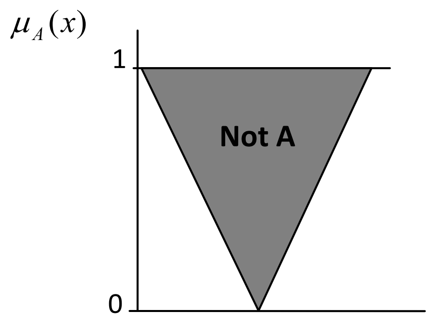

Figure 7. Example of fuzzy complement.

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.

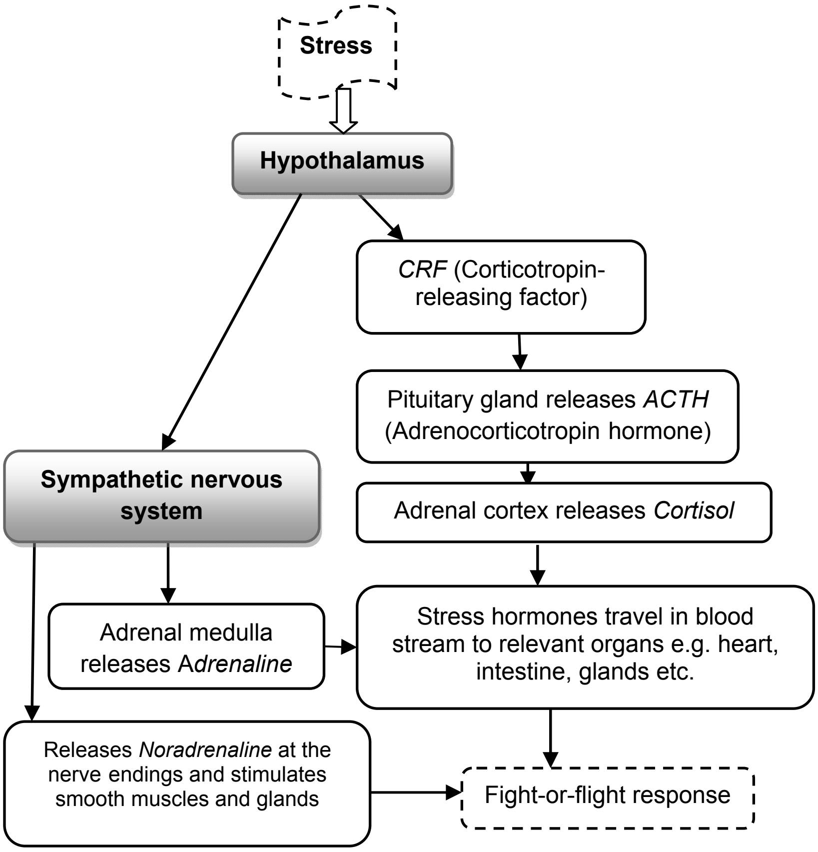

Figure 8. Physiology of the stress response [53].

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.

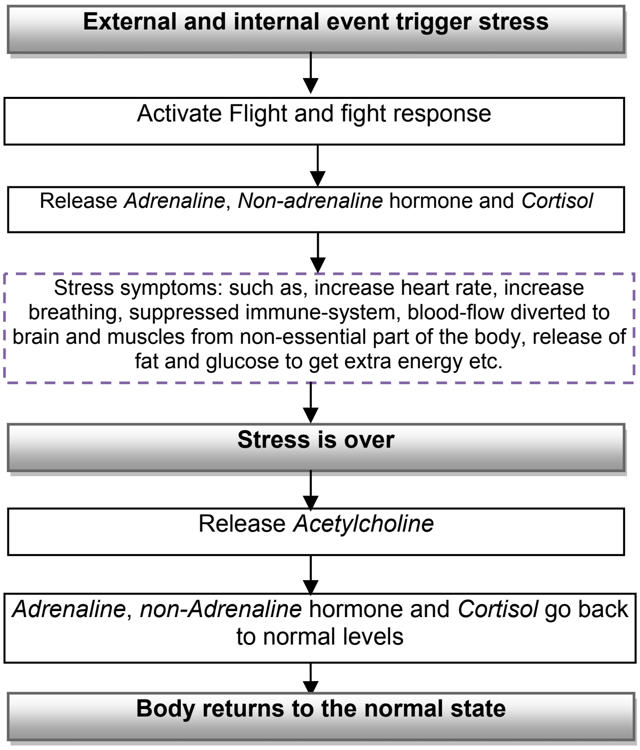

Figure 9. General overview of the stress response.

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.

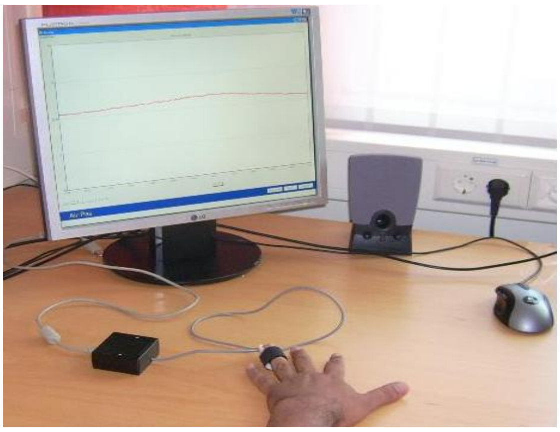

Figure 10. Biofeedback training using finger temperature measurement.

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.

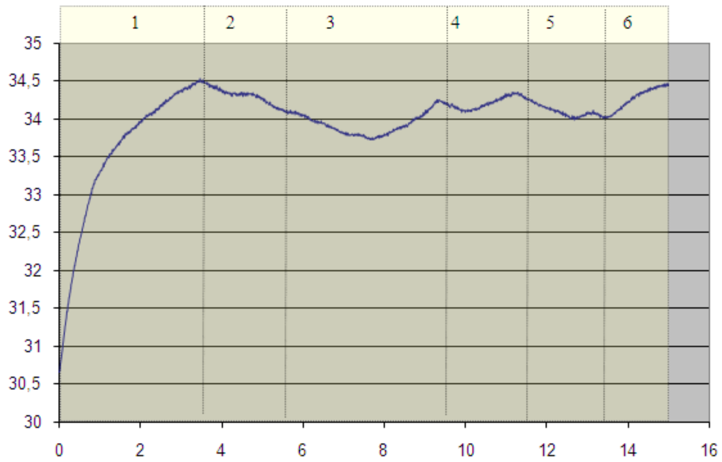

Figure 11. Variations on finger temperature measurement with stress in the different test phases

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.

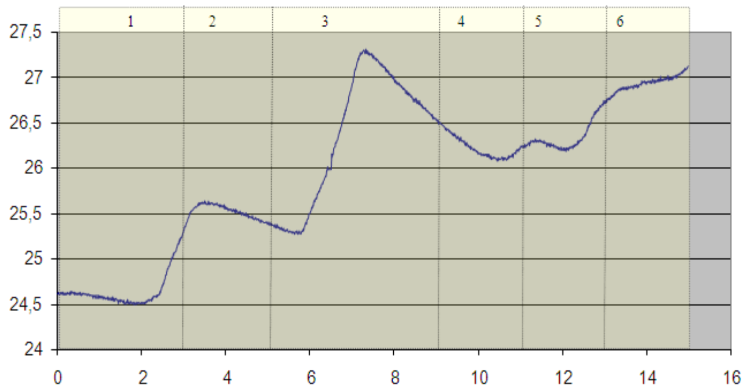

Figure 12. FT vs. paradoxal relation (increase of FT in stress situations). Y-axis: temperature in degree Celsius and X-axis: time in minutes.

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).

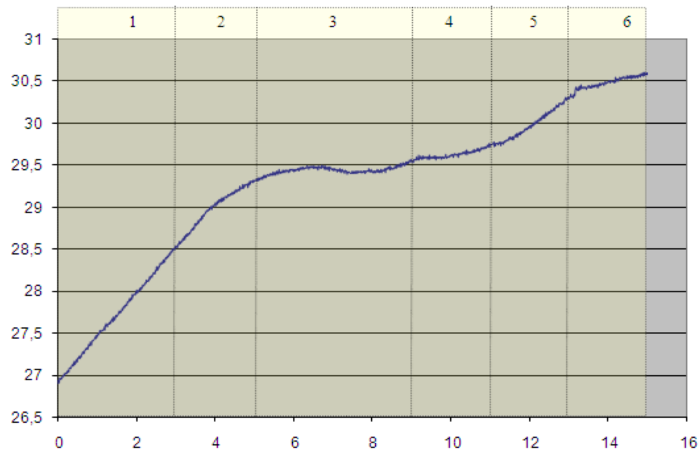

Figure 13. Individual A. Variations on the representative temperature depend on individual person. Y-axis: temperature in degree Celsius and X-axis: time in minutes

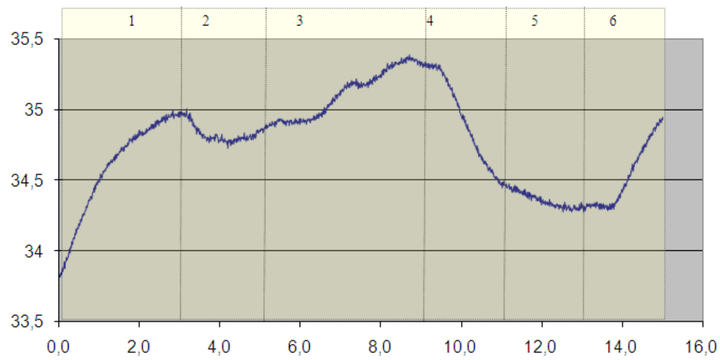

Figure 14. Individual B. Variations on the representative temperatures depend on individual person. Y-axis: temperature in degree Celsius and X-axis: time in minutes

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

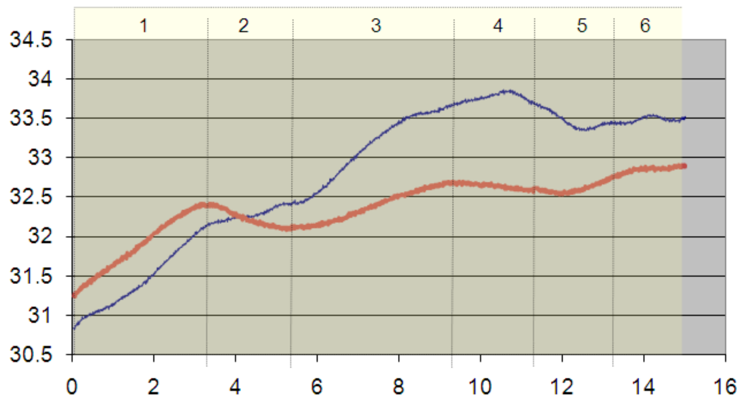

Figure 15. Finger temperature for a person before (orange) and after lunch (blue). Y-axis: temperature in degree Celsius and X-axis: time in minutes.

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.

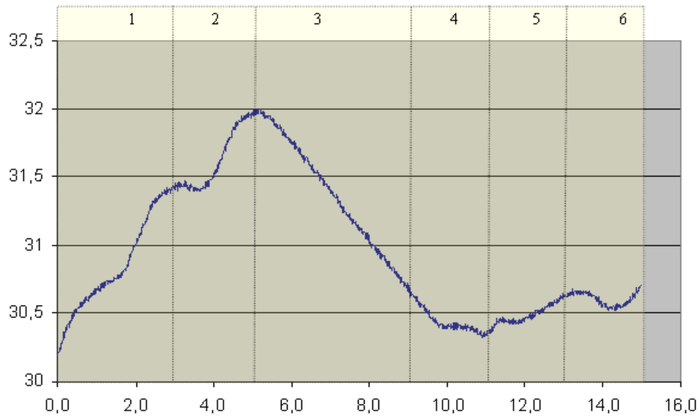

Figure 16. The person cannot remove thinking the stressful events until the next stages. Y-axis: temperature in degree Celsius and X-axis: time in minutes.

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.

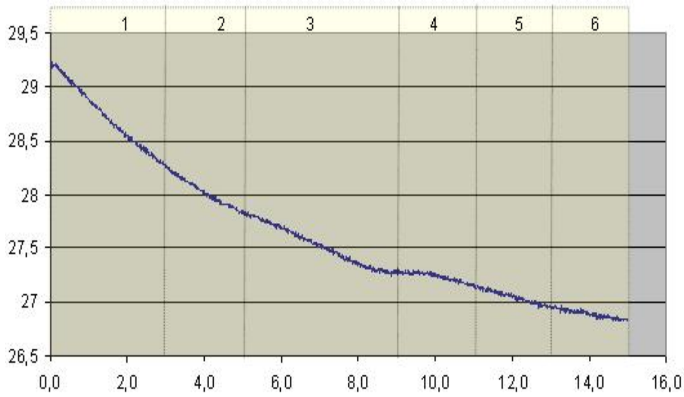

Figure 17. A student before the thesis presentation. Y-axis: temperature in degree Celsius and X-axis: time in minutes.

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.

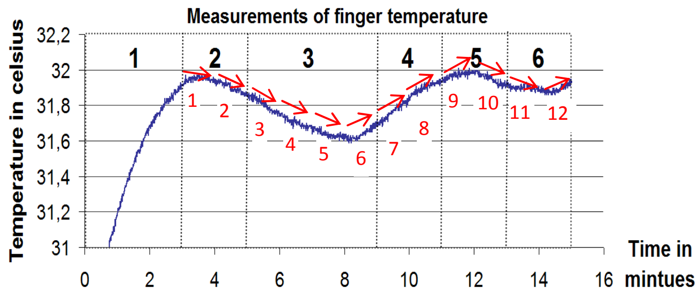

Figure 18. Changes in FT data against time during different stress and non-stress condition.

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.

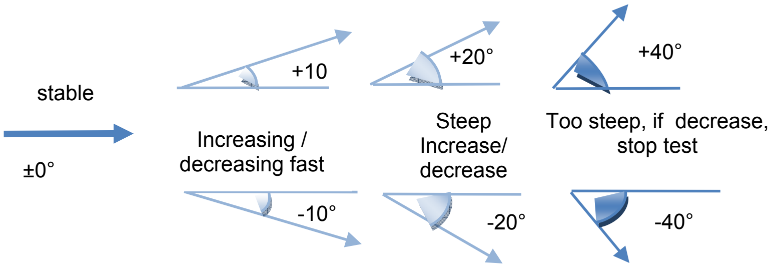

Figure 19. Example of visualizations of temperature change, X-axis minutes, Y-axis in degree Celsius.

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.

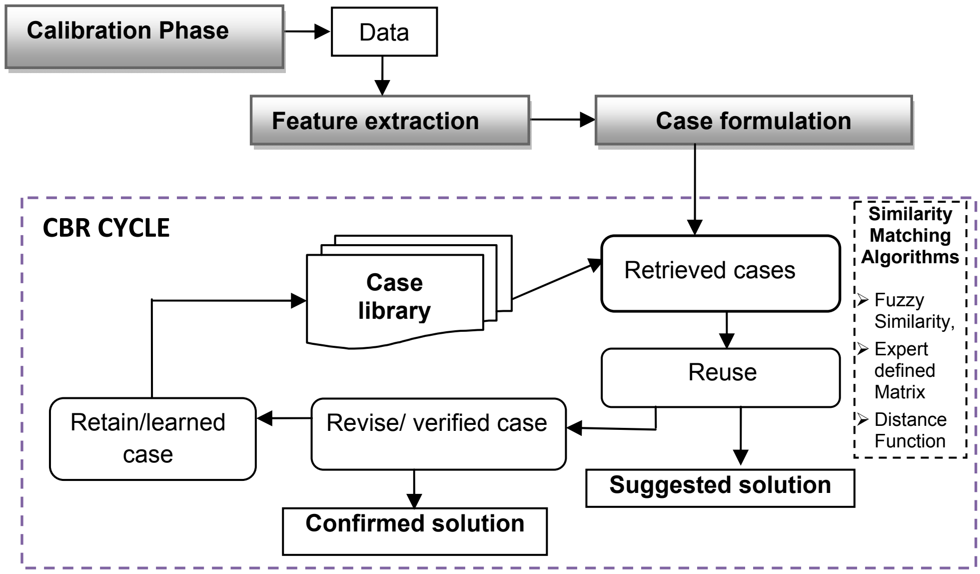

Figure 20. General overview of a decision support system for stress diagnosis.

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.

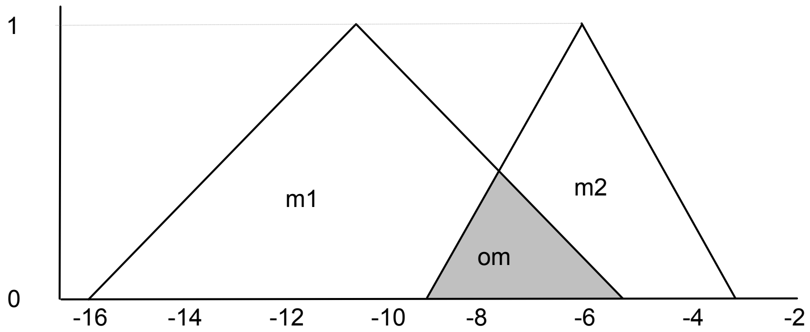

Figure 21. Fuzzy similarity using triangular membership functions. X-axis denotes the feature values and Y-axis degrees of membership functions.

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.

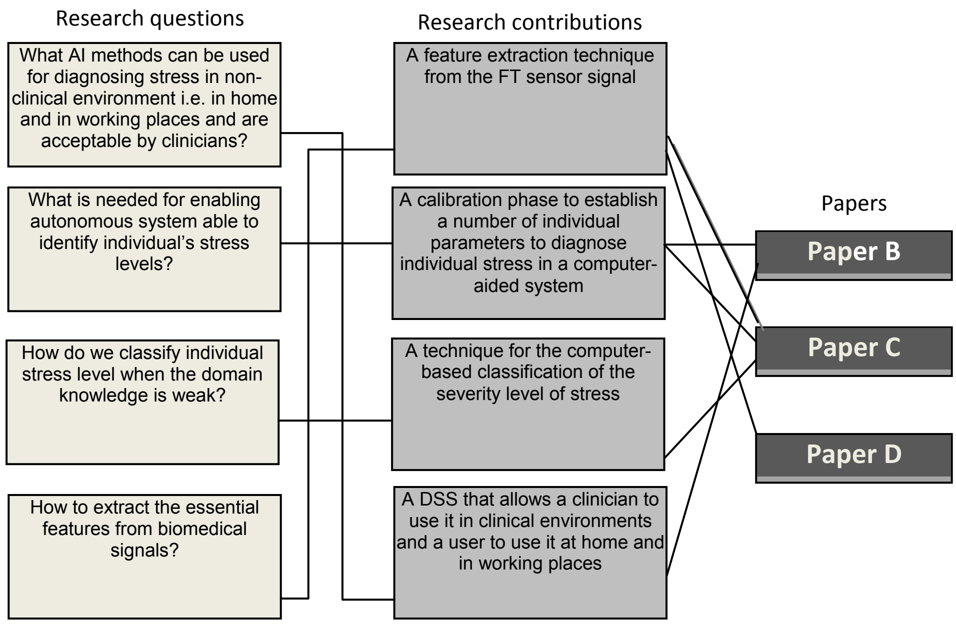

Figure 22. Connections between the research questions and contributions

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).

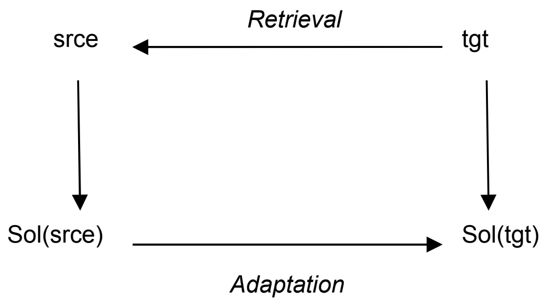

Figure 23. The CBR in KASIMIR. A source case (srce,Sol(srce)) similar to tgt is retrieved from the case base and adapted to solve tgt.

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.

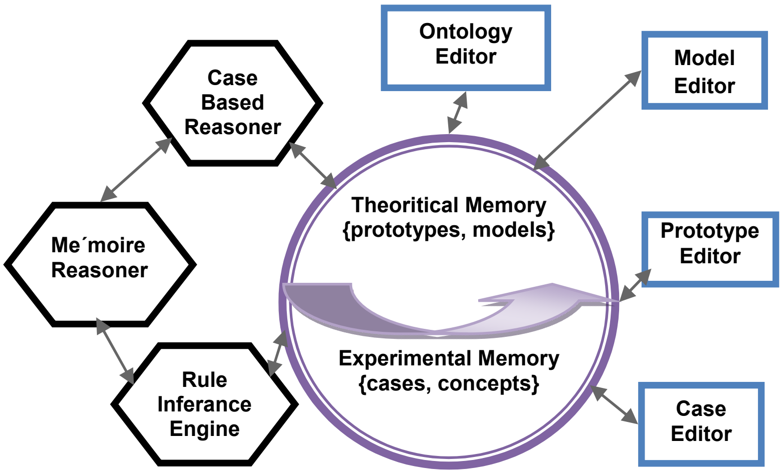

Figure 24. Me´moire architecture. Right: memory acquisition tools, left: reasoning components. Adapted from [6].

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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