Licentiate Thesis Proposal

Artificial intelligence diagnostics in psychophysiological medicine

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Abstract

This is a proposal of the content of a licentiate degree in computer science at Mälardalen University, Sweden. The contents of this licentiate thesis are concerning the use of Artificial Intelligence (AI) for classification of complex measurements. Measurements targeted in this research have previously only been classified by domain specialists. The reason for this is the complexity of the classification process. A method has been developed to accomplish this classification. The method is mainly based on Case-Based Reasoning but uses a number of other techniques. Both AI methods and mathematical methods are used for feature identification. The system is classifying continuous non-stationary measurements, and has the capacity to improve performance with a growing number of solved cases. A system based on the proposed method is implemented for a clinical application (in psychophysiological medicine)[†] as proof of concept and for evaluation purposes.

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Contents

1 Introduction

Classification of complex measurements is essential in many diagnostic tasks. Correct classification of measurements may in fact be the most critical part of the diagnostic process. Diagnosing psychophysiological dysfunctions is a medical application where measurement classification is difficult and complex. See appendix A for further information on psychophysiology. Physicians use sensors to measure physiological parameters in order to diagnose and treat stress related psychophysiological dysfunctions. The physicians make a manual classification of the measurements before they can make a reliable diagnosis. This is difficult, even for experienced physicians. A system with an ability to automatically classify these measurements would ease the physicians work and increase the reliability of the diagnosis, especially for less experienced physicians. Case-based reasoning (CBR) is a concept that is recognized in medical domains and has been applied in a number of medical diagnostic projects [28], but not for direct classification of complex sensor readings from patients, as in this research.

1.1 Case-Based Reasoning

Case-Based Reasoning [15, 18] is an Artificial Intelligence (AI) method, which is partly based on cognitive psychological research. The CBR approach is psychological plausible as it has been shown in empirical studies that humans use specific past experience to solve new problems [1, 6].

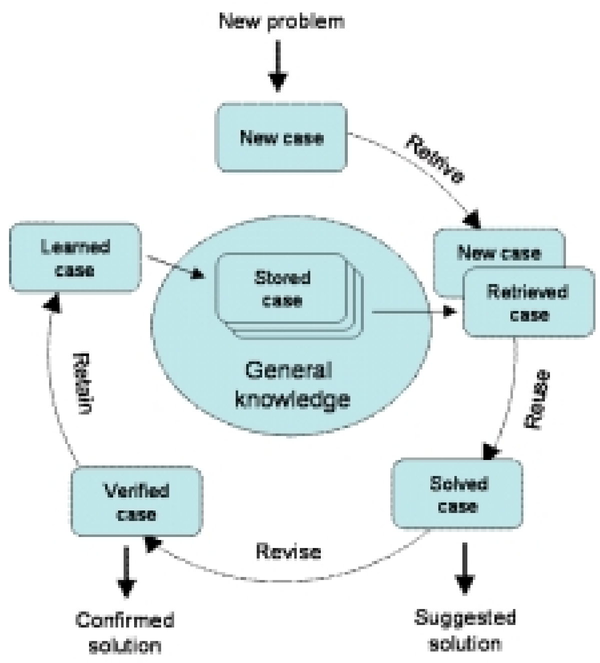

Figure 1: The four (Retrieve, Reuse, Retain, Revise) step Case-Based Reasoning model, adapted from Aamodt-Plaza [1].

CBR is based on a four step model. The four steps are Retrieve, Reuse, Revise and Retain (see figure 1). A CBR systems general knowledge is its previously stored experience. Experience is stored as cases. A case represents explicit, specific knowledge, often including a problem, the solution and the result of applying the solution. The cases are stored in a case library. CBR uses these cases in its decision process, hence the name Case-Based Reasoning. A new problem to solve is a partial case, it only contain the problem part.

The retrieve part tries to find already stored cases that resemble the new case. Matching techniques weight and compare the features in the cases. A search on the matched cases is used to rank and find the cases with the highest similarity to the new case, i.e. the problem. The retrieved cases plus the new case are sent to the reuse part, as seen on the right side in figure 1. The reuse part modifies, combines, adapts, etc. (if needed) the retrieved cases in order to find a solution to the problem, i.e. the new case. The CBR system will then suggest the solution for an external evaluation. The evaluator may for instance be a domain expert or another system. The solved case is then sent to the revise part, on the condition the evaluator has not objected to the solution (otherwise, the system returns to the retrieve part for another solution). The solved case is then verified for correctness by the revise part. If the solution is valid, it will be presented as a confirmed solution to the problem. The new case can be incorporated by the system if it is interesting enough, for instance cover new problems, or be an example of how to not solve a problem. This takes place in the retain step. Cases may also merge, if they cover similar problem areas.

1.2 Measurement classification

Classification of medical measurements is often vital for a correct patient diagnosis. Classification is often a manual process made by the diagnosing physician. There are of course exceptions, such as cancer recognition system using x-ray images as basis for diagnoses. Classification of complex measurements is not widely used in medical systems today. To make a reliable classification, interaction with the physician is needed. Such systems are difficult to build.

1.3 Motivation

A diagnosis, in the field of psychophysiology, is based on measurements measured from a patient. Today, physicians manually diagnose the patients. The physician diagnoses the patient by looking for familiar features in the measurements. Since this is a relatively small area in medicine, there are a limited number of experts working in this field. Hence, the knowledge on how to make a diagnose is not widely known. A general practitioner could possibly make basic diagnoses in physiological medicine if he/she had some sort of medical support system.

An AI system with a feature searching and a reasoning system [24, 23], using these features, would fit the requirements of an online decision support system in the field of psycho physiology. Various online systems for medical classification already exist. Those systems commonly use Artificial Neural Networks (ANN). ANNs are very useful if many good learning examples are available [9], which is not always the case. The lack of examples and the fact that features may be altered or added continuously make CBR a good candidate for a system used as a medical support system in psycho physiological medicine. A CBR system may also transfer experience to the user by referring to a similar successful case. This is more difficult for e.g. ANNs.

1.4 Related work

One of the first knowledge based medical systems is MYCIN [31, 32] by Shortliffe et al. MYCIN is a Rule-based system (RBR) which was developed in the 1970's. The system tries to find treatments on blood infections. MYCIN uses a backward chaining reasoning and heuristics to find a solution. The system interacts with the user of the system through a series of questions.

PROTOS [14] was developed in the late 1980's by Bareiss et al. The system is CBR based and diagnoses hearing disorders. PROTOS is learning like an apprentice from an expert, or teacher. When the system makes a mistake, an expert explains the mistake for the system like a teacher explains it for a novice.

Koton produced a system in the late 1980's called CASEY [17, 16]. Casey uses Case-based and causal reasoning techniques together with a model based expert system. The system deals with heart failure (cardiac disease) diagnosis. Casey makes therapy suggestions through a matching, evaluating and adaptation process.

Fault tolerance is important in medical applications. Limitations of CBR in medical systems are addressed by Schmidt and Gierl [29, 28] where they approach the difficult task of case adaptation. Atzmulluer *et al* [2] points out the issues of handling multiple faults, or diagnoses, in a medical system. Their solution is to decompose the problem part of a case into several smaller ones and find solutions to them instead. When the system comes up with solutions to the smaller problems they combine all solutions to solve the original problem.

Marling and Whitehouse [22] uses what they call a *master-slave* architecture. Their system is about the care of Alzheimer's disease patients. The system contains a CBR subsystem as a method of evaluating if neuroleptic drugs are to be given. If neuroleptics are to be given a RBR subsystem makes the recommendations on which specific drug to use.

Perner use CBR for image analysis and feature extraction [25, 26] on computed tomography (CT) scans of the brain. The system creates abstract representations of the images through a series of image interpretation layers [27]. The images pass feature extraction and symbolic interpretation before they can be interpreted.

CBR imaging techniques are also used by Balaa and Traphöner where they detect fetal malformations [3]. They utilise ultrasonographical examinations of uteruses to detect abnormal organs and extremities.

Jaulent *et al* [13] is diagnosing histopathology. A case is described with written natural language in a standardised report for pathology. A case undergoes both semantic and structural matches for similarity. The system has been restricted to breast tumour diagnosis. Further reading about CBR in medical systems and their applications can be found in [10].

1.5 Contribution

The contribution of this thesis is,

- The development of a novel method suitable for measurement classification. Traditional CBR methods are based on discrete features; the research enables the use of CBR for classification of complex analog measurements. This is important for a number of different application domains, e.g. in medical diagnosis.
- A method for feature identification of analog measurements based on an interaction with experts. The Program implementation uses agent based architecture for flexibility, where each agent is specialized on identifying specific features.
- The development of a hybrid system architecture using both CBR and agent technology.

2 Thesis outline

This section contains a sketch of the proposed contents of the licentiate thesis.

1. Introduction
   An introduction to the subject and the chapters in the thesis. The introduction contains a brief explanation of Case-Based Reasoning and to the targeted problem domain.
2. Paper summary
   A summary of the papers the thesis is based on. This section will also include a presentation of non-included papers. The non-included papers are out of scope for this thesis.
3. Motivation
   Definition of the underlying problems and why they need to be solved. This section will also contain what obstacles we have countered and how we solved them.
4. Conclusions
   Conclusions of the research from the included papers.
5. Related work
   A discussion of related work that has been done.
6. Future work
   This section will contain research topics not yet solved and list possible research topics for a doctoral degree.
7. Papers
   A section, which displays all, for this thesis, relevant papers I have written/co-written. The papers are mainly from conferences and workshops. Technical reports and similar work may also be included if they are suitable.

3 Time plan

A time plan for the licentiate degree. The first section is regarding already completed work and the following about work that is planned or already started.

3.1 Completed work

Already completed and credited work;

- Written and published a paper on classification of complex measurements using CBR. Published at the workshop on health sciences at the ICCBR intenational conference.
- Written and published a short paper/extended abstract on measurement classification in medical systems. Published at the SAIS-SSLS national workshop.
- Written a technical report regarding AI in medical systems.
- Completed courses;
  Research methodology for computer science and engineering (5p) ; Science planning for PhD students (5p) ; Wireless sensor technology (uncredited course) ; Distributed realtime systems (5p) ; Autonomous robotics (5p) ; Artificial intelligence (5p).
- A prototype on notch analysis on heart and respiratory measurements.

3.2 Remaining work

2003-09	Implement an Agent structure to be able to extract features from measurements (the PAUL project), 10p.
2003-10	Take a 5p course in psycho physiological medicine.
2003-11	Take a 5p course in CBR.
2004-01	Write a paper about the evaluation of the implementation of the feature searching Agents, 4p.
2004-02	Co-write a paper in a medical/physiological journal about the PAUL case, 3p(analysing)+3p(writing).
2004-03	Write a paper containing the CBR part of the signal classification part of the AIM project, 4p.
2004-04	The writing and submission of the licentiate thesis, 2p.

The estimated time of the remaining work is 36 weeks.

4 Future work

Some appealing areas for further research and consequently a doctoral thesis are;

- An interactive feature searching agent system where a simple language can describe an Agent and its behaviour.
- Can we make a system that automatically make changes to and identifies new features from the measurements while observing the physicians behaviour? That is to study the interaction the user (physician) has with the system.
- Is it possible to optimize the entire system down to a portable solution, like a handheld device? What kind of portable measurement sensors do we need etc.

References

[1] Agnar Aamodt and Enric Plaza. Case-based reasoning: Foundational issues, methodological variations, and system approaches. *AI Communications*, 7(1):39–59, 1994.

[2] Martin Atzmueller, Joachim Baumeister, and Frank Puppe. Evaluation of two strategies for case-based diagnosis handling multiple faults. 2nd German Workshop on Experience Management, April 2003.

[3] Ziad El Balaa and Ralph Traphöner. Case-based decision support and experience management for ultrasonography. 2nd German Workshop on Experience Management, April 2003.

[4] Gary G. Berntson, J.T. Bigger, D.L. Eckberg, P. Grossman, P.G. Kaufmann, M. Malik, H.N. Nagaraja, S.W. Porges, J.P. Saul, P.H. Stone, and M.W. van der Molen. Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology*, 34(6):623–648, 1997.

[5] Marie J. Cowan, Helen Kogan, Robert Burr, Sue Hendershot, and Lynne Buchanan. Power spectral analysis of heart rate variability after biofeedback training. *Journal of Electrocardiology*, 23:85–94, 1990.

[6] Padraig Cunningham and Barry Smyth. A comparison of model-based and incremental case-based approaches to electronic fault diagnosis. In *Proceedings of the Case-Based Reasoning Workshop*. American Association of Artificial Intelligence, 1994.

[7] Ingrid Daubechies. The wavelet transform, time-frequency localization and signal analysis. *IEEE Transactions on Information Theory*, 36(5):961–1005, September 1990.

[8] Tuan Pham Dinh, Helene Perrault, Pascale Calabrese, Andre Eberhard, and Gila Benchetrit. New statical method for detection and quantification of respiratory sinus arrhytmia. *IEEE Transactions on Biomedical Engineering*, 46(9):1161–1165, September 1999.

[9] Laurene Fausett. *Fundamentals of Neural Networks*. Prentice Hall, Upper Saddle River, New Jersey 07458, USA, 1994.

[10] Lothar Gierl, Mathias Bull, and Rainer Schmidt. Cbr in medicine. In *Case-Based Reasoning Technology: From Foundations to Applications*, pages 273–297. Lecture Notes in Artificial Intelligence, May 1998.

[11] P. Grossman, J. Van Beek, and et al. A comparison of three quantification methods for estimation of respiratory sinus arrhytmia. *Psychophysiology*, 27(6):702–714, November 1990.

[12] Ralph D. Hippenstiel. *Detection Theory*. CRC Press, 2000 N.W. Corporate Blvd., Boca Raton, Florida 33431, USA, 2002.

[13] Marie-Christine Jaulent, Christel Le Bozec, Eric Zapletal, and Patrice Degoulet. A case-based reasoning method for computer-assisted diagnosis in hisopathology. In *Artificial Intelligence in Medicine*, pages 239–242. Proceedings of the 6th Conference on Artificial Intelligence in Medicine Europe, March 1997.

[14] Ellis Raymond Bareiss jr. *PROTOS: A unified approach to concept representation, classification and learning*. UMI Dissertation Services, 300 North Zeeb Road, P.O. Box 1346, Ann Arbor, Michigan 48106-1346, USA, 1988.

[15] Janet Kolodner. *Case-based Reasoning*. Morgan Kaufmann Publishers Inc, 340 Pine St, 6th floor, San Fransisco, CA 94104, USA, 1993.

[16] Phyllis Koton. Reasoning about evidence in causal explanations. In *Proceedings of the DARPA Case-Based Reasoning Workshop*, pages 256–261. Seventh National Conference on Artificial Intelligence, 1988.

[17] Phyllis Koton. *Using Experience in Learning and Problem Solving*. MIT Press, 1988.

[18] David B. Leake. *Case-based Reasoning: Experiences, Lessons, and Future Directions*. MIT Press, 1996.

[19] Paul M. Lehrer, Alexander Smetankin, and et al. Respiratory sinus arrhytmia biofeedback therapy for asthma: A report of 20 unmedicated pediatric cases using the smetanikn method. *Applied Psychophysiology and Biofeedback*, 25(3):193–200, 2000.

[20] Paul M. Lehrer, Evgeny Vaschillo, and Bronya Vaschillo. Resonant frequency biofeedback training to increase cardiac variability: Rationale and manual for training. *Applied Psychophysiology and Biofeedback*, 25(3):177–191, 2000.

[21] Marek Malik, John Camm, and et al. Heart rate variability - standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, 17:354–381, March 1996.

[22] Cindy Marling and Peter Whitehouse. Case-based reasoning in the care od alzheimer's disease patients. In *Case-Based Research and Development*, pages 702–715. 4th International Conference on Case-Based Reasoning, July/August 2001.

[23] Markus Nilsson and Peter Funk. Classification of psycho-physiological measurements in medical systems. In *Proceedings of the SAIS-SSLS joint Workshop*. Swedish Artificial Intelligence Society and Swedish Society for Learning Systems, April 2003.

[24] Markus Nilsson, Peter Funk, and Mikael Sollenborn. Complex measurement classification in medical applications using a case-based approach. In *Case-Based Reasoning in the Health Sciences*. International Conference on Case-Based Reasoning, June 2003.

[25] Petra Perner. Using cbr learning for the low-level and high-level unit of an image interpretation system. In *Advances in Pattern Recognition*, pages 45–54, 1998.

[26] Petra Perner. An architecture for a cbr image segmentation system. In *Case-Based Reasoning Reasearch and Development*, pages 525–534. Third International Conference on Case-Based Reasoning, July 1999.

[27] Petra Perner. Why case-based reasoning is attractive for image interpretation. In *Case-Based Reasoning Reasearch and Development*, pages 27–43. Proceedings of the 4th International Conference on Case-Based Reasoning, July/August 2001.

[28] Rainer Schmidt and Lothar Gierl. Case-based reasoning for medical knowledge-based systems. XVI International Congress of the European Federation for Medical Informatics, 2000.

[29] Rainer Schmidt, Olga Vorobieva, and Lothar Gierl. Case-based adaptation problems in medicine. 2nd German Workshop on Experience Management, April 2003.

[30] Knut Sevre and Morten Rostrup. Undersokelser av hjertefrekvensvariabilitet og barorefleksensivitet. *Tidsskr Nor Laegeforen*, 26(121):3059–3064, 2001.

[31] E.H. Shortliffe, S.G. Axline, and et al. An artificial intelligence program to advise physicians regarding antimicrobial theraphy. *Computers and Biomedical Research*, 6:544–560, 1973.

[32] E.H. Shortliffe, F.S. Rhame, and et al. Mycin: A computer program providing antimicrobial theraphy recommendations. *Clinical Medicine*, 34, 1975.

[33] Samuel D. Stern. *Digital Signal Processing*. CRC Press, 2000 N.W. Corporate Blvd., Boca Raton, Florida 33431, USA, 2003.

[34] Karsten Sternickel. Automatic pattern recognition in ecg time series. *Computer Methods and Programs in Biomedicine*, 68:109–115, 2002.

[35] Jan van Dixhoorn. Cardiorespiratory effects of breathing and relaxation instruction in myocardial infarction patients. *Biological Psychology*, 49:123–135, 1998.

[36] Carl F. Weems. The evaluation of heart rate biofeedback using a multi-element design. *Journal of Behaviour Theraphy and Experimental Psyciatry*, 29:157–162, 1998.

Appendix

A Psychophysiology

Stress is a fuzzy and widely used word which invokes many different associations. When someone is referred to as a burnt out due to stress, it is more accurate to describe it as the individual is suffering from a psycho physiological dysfunction. Psycho physiology is not only about what is commonly call stressed individuals, it can for instance also incorporate torture victims having nightmares and anxiety attacks many years after they recuperated physically. Psycho physiology is about taking back physiological control of the body through psychological sessions combined with physiological exercises.

When reading this document we will talk about the different systems within the **Autonomic Nervous System (ANS)**, a good way is to visualise it as the *fight or flight* responses remaining from when man lived in caves. We will introduce two (out of three) parts of the ANS, the sympathetic and the parasympathetic nervous systems. The third part is the enteric nervous system.

A.1 Heart rate variability

Heart rate variability (HRV) [21, 5] can be view as the natural variability of the frequency of the heartbeat, or the hearts interbeat interval. HRV is often used to measure the balance between the sympathetic and the parasympathetic system [30], a part of the autonomic nervous system (ANS). The lower frequencies (LF,VLF and ULF) [1] houses the sympathetic part of the ANS which is an side effect of a weaker vagal tone/signal from the vagus nerve. The level of the vagal tone decides the activity level of the parasympathetic system. The parasympathetic system increases on a higher vagal tone. The vagus nerve becomes inhibited during an inhalation; this causes an increased sympathetic part in the sympathetic/parasympathetic balance causing an increase in the **Heartrate (HR)**. There are also other biological systems at work in lower frequency bands than the sympathetic system, for instance changes in body temperature during the diurnal rhythm [4]. In contrast, the high frequency variability (in the HF band, see section A.1.2) is only created by the parasympathetic system, but an important note is that the parasympathetic system is also at work in the lower frequencies. Sometimes we can isolate parasympathetic RR activity in the LF band, one such case is when someone is performing pacing. Pacing is a technique where a man do controlled breaths, if the **Respiratory Rate (RR)** is directed towards 0.1Hz a synergetic effect appears between the sympathetic and the parasympathetic system [20]. The RR is basically a measurement of the breath to breath interval and are normally calculated from **Carbon dioxide** (CO_2) level measurements.

A.1.1 Quantification

There exist a couple of methods to calculate, or more accurate, estimate the HRV.

- A common way is to compute a frequency spectrum analysis [21, 8]. There are numerous ways to compute the spectrum. What technique to use, is often application dependant. Fast Fourier Transformations (FFT) [12, 33] or similar techniques is often sufficient. But if we want a more accurate computation or a more detailed resolution on when and where different frequencies occur in time, a wavelet [7, 12, 33, 34] transformation is sometimes required. Wavelets use a dynamic function window instead of the static one in a discrete/short-time Fourier transformation. The function window expands in the time domain during lower frequencies while investigating the frequency domain closer, see [7] for further details.

- A HRV analysis can be achieved without a spectral analysis. The HRV is calculated directly in the time domain by either **(A)** Statistical methods or **(B)** Geometrical methods.
  A Statistical methods is more often used on measurements recorded from longer time periods, normally 24h [21]. HRV are calculated by either measuring the Normal-to-Normal (NN) heartbeat interval or the differences in the NN interval. There exist a couple of statistical methods, but they are basically the same since

[1] See section A.1.2 for an explanation of the frequency bands.

they are all based on standard derivations of the NN.
B Sample density distributions are used in geometric pattern methods. Calculations on NN histograms are a common ground for the geometric methods. They can for instance be interpolated by geometrical shapes or be mathematical equations. 24h recording periods are recommended for the geometrical methods.

A.1.2 Frequency bands in the HRV

Following subdivisions of the frequency bands are relevant for the HRV:

- *0.15Hz-0.4Hz* is the **High Frequency (HF)** band. HF is only affected by the parasympathetic system.
- In the **Low Frequency (LF)** band, at *0.04Hz-0.15Hz*, we can find both the sympathetic and the parasympathetic system at work.
- At *0.003Hz-0.04Hz* we have the **Very Low Frequency (VLF)** frequencies, whom are a good way to record changes in the diurnal rhythm. The parasympathetic has a lesser interference at these low frequencies.
- And finally at lower frequencies than *0.003Hz*, we got the **Ultra Low Frequeny (ULF)** band. To accurately detect VLF and ULF we need a 24h recording period instead of the 5 minute recommended in [21].

A.2 Respiratory sinus arrhythmia

Respiratory Sinus Arrhythmia (RSA) [11, 8, 20, 19] is often referred to as a non-invasive index of parasympathetic cardiac control [11]. The RSA is a form of high frequency variability found in the HR. RSA is an effect of the ever-changing state of the vagal tone caused by, among other things, the pulmonary system. The vagal tone changes for instance on a stroke of breath. RSA can be quantified with similar methods as used in quantifying the HRV. Quantification techniques are described in section A.1.1.

A.2.1 Quantification

Since RSA is closely connected to the HR, quantification techniques resemble those used on HRV. Nevertheless, there exist differences, since estimations uses the heart period variability [8, 11] to quantify the RSA some contamination from non respiratory related heart rate variations may occur. On the other hand, the spectral and statistical analyses seems to be both equally influenced by those interferences [11]. This implies choosing methods for RSA estimations is application dependant rather than method dependant.

A.3 Biofeedback

Biofeedback (BF) training [36, 5, 20, 19] is often used as a treatment method to conquer post traumatic stress, burnout syndromes and other psycho physiological dysfunctions. The biofeedback methods for psycho physiological dysfunctions are usually about respiration control. Other methods of treatments include relaxation and breathing techniques combined with regular exercise [35].