Proceedings of the 2nd
International Workshop on
Artificial Intelligence
and NetMedicine

In conjunction with
IJCAI 2013
Table of Contents

Preface ........................................................................................................................................... iv
Invited talk - The Promise and Challenges of “Smart” Health Information Technology .... vii
John S. Baras, University of Maryland
Program Committee .................................................................................................................. viii
Recognizing Physical Activities by Wearable Computing ........................................................ 1
Ali Mehmood Khan and Michael Lawo
Unobtrusive Low Cost Pupil Size Measurements using Web cameras ................................... 9
Sergios Petridis, Theodoros Giannakopoulos and Constantine D. Spyropoulos
Virtual Carer: A BDI Agent System for Ambient Assisted Living ........................................ 21
Paolo Sernani, Luca Palazzo, Andrea Claudi, Gianluca Dolcini,
Gianluigi Biancucci, Guglielmo Trentalange and Aldo Franco Dragoni
Electrocardiography Recognition Based on Wavelet Filter and EMAlogorithms .................... 31
Xingjia Lu, Yong Lin and Jianbo Fan
A Multi-Agent Architecture for Health Information Systems .............................................. 41
Luca Palazzo, Paolo Sernani, Andrea Claudi, Gianluca Dolcini,
Gianluigi Biancucci and Aldo Franco Dragoni
Towards Evidence-Based Decision Support Systems ......................................................... 51
Raphael Bahati and Femida Gwadry-Sridhar
Discovering and disseminating interesting patterns from imbalanced clinical data - a case study ........................................................................................................................................ 61
A. Fazel Famili, Sieu Phan and Ziying Liu
ORC: an Ontology Reasoning Component for Diabetes ...................................................... 71
Özgür Kafali, Michal Sindlar, Tom van der Weide and Kostas Stathis
Preface

This volume collects the proceedings of the second “International Workshop on Artificial Intelligence in NetMedicine” (NetMed’13), organized this year as satellite workshop of the “International Joint Conference on Artificial Intelligence” (IJCAI’13).

The aim of the workshop is that of bringing together scholars from AI-driven Health Informatics to address some new topics that are emerging in what we call "NetMedicine", i.e. "every Health-related activity which is carried on through the Internet".

Perhaps the 50-years old term “Telemedicine” nowadays sounds almost outmoded since it does not reflect the two most important technological breakthroughs in our modern society, i.e.:

1. the digitalization of the information (in our case of the diagnostic examinations and data)

2. the advent of the Internet.

The term “Telemedicine” recalls of pioneering point-to-point communication episodes, between one patient and one doctor, performed through analogical channels (mostly RF), but fails completely to address the contemporary digital format of the data, the communication protocols that enable them to be exchanged and, mostly important, the fact that the practice of Medicine is often performed in a collaborative manner as a teamwork over a net (the Internet exactly). Medical tele-reporting and second-opinion over the Internet are nowadays cost-effective and widely adopted practices. Physicians and general practitioners make daily use of tele-consultation over the WEB, VOIP, chat and digital video-conferencing. Furthermore, social networking favors the constitution of large communities of members sharing similar medical interests.

Having this revolution in mind, the main idea that moved us in organizing this workshop was the intuition that after more than 40 years of AI servicing the Medicine, nowadays AI
could called back to arms to serve the NetMedicine, either as squadron of veterans or as battalion of young soldiers recruited for this new battle.

To represent concretely what we have in mind, think for instance of:

- semantically interpreting and filtering diagnostic data
- automatically classifying and conveying medical information
- fostering interoperability between different healthcare information systems
- virtualizing nurses and hospital lanes to reduce the costs of healthcare.

In 1984 Clancey and Shortliffe defined “medical artificial intelligence” as “AI programs that perform diagnosis and make therapy recommendations”. “Medical AI programs” were based, from the beginning, on symbolic models of disease entities and their relationship to patient factors and clinical manifestations.

During the 90’s there has been an increasing disillusion with the potential for such systems (notwithstanding with the fact that they actually have proven their reliability and accuracy). Perhaps that was because of the poor way in which they have fitted into clinical practice, and that was probably for two main reasons:

1. logical problem solving was not clearly perceived to be an issue

2. such medical expert systems tended to impose changes in the way clinicians worked, or, worse, tended to reduce the areas of decision of doctors.

Of course, we know that when medical AI programs fill an appropriately role, they do indeed offer significant benefits, and those aspects of medical practice that are best suited to be approached by AI systems have been characterise accurately.

Nowadays, the advent of the Internet in Medicine, i.e. the advent of the NetMedicine, opened other important problems / questions / opportunities, for instance:
• retrieving medical information all over the globe

• performing correctly Internet-based *clinical* services

• performing correctly internet-based *administrative* services

• providing immediate access to every patient information

• producing proactive notification systems (agents?) for critical events

• providing a universal common user interface

• offering extremely low cost medical consultations and health services

It is for these reasons that we decided to organize such a workshop, thus hoping to contribute to fill a gap in current research on AI-related techniques in Medicine.

And what about the further future? Will we be alive when someone will organize a scientific conference about how Artificial Intelligence will be contributing to make a single, universally expert, “Big Doctor” available through the Internet?

Aldo Franco Dragoni

Università Politecnica delle Marche, Italy

Co-chair of NetMed'13
Invited Talk

The Promise and Challenges of “Smart” Health Information Technology

John S. Baras
Institute for Systems Research and
Electrical and Computer Engineering Department
Fischell Department of Bioengineering
Applied Mathematics, Statistics and Scientific Computation Program
University of Maryland College Park

Abstract

Health Information Technology has been spreading recently as the most promising solution to the global grand challenge of providing high quality health care to everyone and at the same time controlling and reducing the fast rising costs. In this lecture we will review several recent initiatives and promising advances in Health IT and the challenges they present from the combined economic-technological-social-behavioral perspective. We will address four major areas: the creation, management and availability of large databases of anonymized medical data; The development of intelligent software systems to facilitate and enhance the communication between physicians and patients; The security and privacy issues associate with Health IT; The overarching challenge of developing an integrative systems engineering modeling, synthesis and performance analysis frameworks for Health IT systems. We will provide as an example our development of a management system for Intensive Care Units (ICU) and will use to illustrate the challenges we faced and how we resolved them. I will close with a brief description of promising directions of future research.

Short Bio

John S. Baras, Lockheed Martin Chair in Systems Engineering. B.S. in Electrical Eng. from the Nat. Techn. Univ. of Athens, Greece, 1970; M.S. and Ph.D. in Applied Math. from Harvard Univ. 1971, 1973. Since 1973 with the Electrical and Computer Engineering Department, and the Applied Mathematics Faculty, at the University of Maryland College Park. Since 2000 faculty member in the Fischell Department of Bioengineering. Founding Director of the Institute for Systems Research (ISR) from 1985 to 1991. Since 1991, has been the Director of the Maryland Center for Hybrid Networks (HYNET). Fellow of the IEEE and a Foreign Member of the Royal Swedish Academy of Engineering Sciences. Received the 1980 George Axelby Prize from the IEEE Control Systems Society and the 2006 Leonard Abraham Prize from the IEEE Communications Society. Professor Baras' research interests include control, communication and computing systems.

Email: baras@umd.edu  Web page: http://www.isr.umd.edu/~baras/
Program Committee

Program Chairs
Aldo Franco Dragoni – Università Politecnica delle Marche, Italy
Constantine D. Spyropoulos – NCSR “Demokritos”, Greece
Femida Gwadry-Sridhar – University of Western Ontario, Canada
Lucio Tommaso de Paolis – Università del Salento, Italy

Program committee
Henrik Eriksson – Linköping University, Sweden
Peter Lucas – Radboud University Nijmegen, The Netherlands
Rainer Schmidt – Universität Rostock, Germany
Paola Mello – Università di Bologna, Italy
Siriwan Suebnukarn – Thammasat University, Thailand
Amparo Alonso-Betanzos – University of La Coruña, Spain
María Taboada Iglesias – Universidade de Santiago de Compostela, Spain
Andrea Claudi – Università Politecnica delle Marche, Italy
Catherine Garbay – French National Centre for Scientific Research, France
Domenico Massimo Pisanelli – Consiglio Nazionale delle Ricerche, Italy
Sergios Petridis – NCSR “Demokritos”, Greece

Associate reviewers
Anna Montesanto, Università Politecnica delle Marche, Italy
Fabrizio Riguzzi, Università di Bologna, Italy
Veronica Bolon Canedo, University of La Coruña
Recognizing Physical Activities by Wearable Computing

Ali Mehmood Khan, Michael Lawo
{akhan,mlawo}@tzi.de
Tzi-Universität Bremen
Bremen, Germany

Abstract

One of the major scientific undertakings over the past few years has been exploring the interaction between humans and machines in mobile environments. Physical activity is a major part of a user’s context for wearable computing applications. The system should be able to acquire the user’s physical activities by using body worn sensors. We want to develop a personal activity recognition system that is practical, reliable, and can be used for health-care related applications. We propose to use the axivity device [1] which is a ready-made, light weight, small and easy to use device for identifying physical activities like lying, walking, running, sitting, standing, cycling, ascending stairs, descending stairs, strength training and swimming using decision tree classifier. In this paper, we present an approach to build a system that exhibits this property and provides evidence based on data for 10 different activities collected from 32 different subjects. Our results indicate that the system has a good accuracy rate.

Keywords

Physical activities, 3D accelerometer sensor, machine learning classifiers

Introduction

Human activity recognition by using body worn sensors has received attention in recent years. Activity recognition systems in health care support especially in elder care, long-term health/fitness monitoring, and assisting those with cognitive disorders [1, 2, 3] has been demanded. Therefore, recognizing human physical activities with body worn sensors is not a new research field; much research has already been done in this area. We can identify users’ physical movements using a body movement suit [2]. We also have other research projects where researchers identify the users’ physical activities using some sensors like [3, 4, 5, 6, 7, 8 and 9].
In some diseases like diabetes, heart problems, mentally disabled persons, elder patients are required to perform some physical activities in order to make them physically fit. Similarly, in some cases patients need to be monitored by nurses which is very time consuming and expensive.

According to paper [12], medical experts think that following physical activities can influence heart rate i.e. lying, walking, running, sitting, standing, cycling, ascending, descending stairs, strength training and swimming. Physical activities and emotion states are also required along with the physiological information for doctors in order to examine their patient's conditions when he is away from the doctor's clinic [12]. Physical activities and emotion states [19] can be recognized by AI techniques using wearable devices and physiological data can be measured using physiological devices, then information (physical activities, emotion states and physiological data) can be transmitted to a doctor's clinic through internet so that doctor could assess patients' health condition. In this research, we want to address problems related to physical activities from paper [12] in order to provide a solution. We want to develop a physical activity recognition system using a minimum amount of sensors which should be able to identify the needed physical activities i.e. lying, walking, running, sitting, standing, cycling, ascending stairs, descending stairs, strength training and swimming.

In our research we want to prove that it is possible to identify the aforementioned activities for a specific user by using a 3D accelerometer. In the next chapter, “related work” will be discussed, “hypothesis and research question” will be discussed in the 3rd chapter, “experimental methodology” will be discussed in the 4th chapter, “evaluation” will be discussed in the 5th chapter and “conclusion and future work” will be in the last.

Related work

Researchers have identified various physical activities using wearable sensors like sitting [3,6,7,8], standing [3,6,7,8], lying [6], walking [3,4,5,6,7,8], climbing stairs [3,4,6,7,8], running [5,7,8], cycling [5,8], strength training [8], etc. However, for their recognition system they have used more than one sensor.

Researchers also identified a few physical activities and strength-training techniques using 3D accelerometer sensor [9, 13 and 14]. Researchers also have identified different swimming styles by using wearable devices [15, 16, 17 and 18].

In our work, we want to develop a single system for recognizing few physical activities (i.e. lying, walking, running, sitting, standing, cycling, ascending stairs, descending stairs, strength training and swimming) which can influence heart rate level. These activities are already indentified (except strength training and swimming) by using a 3D accelerometer [13] but we found following drawbacks:

a) Data was not pre-processed before applying machine learning algorithms.

b) Only two Machine learning algorithms were used.
c) It is stated that "For every user, the system needs to be trained with the sensor data so that it would be able to predict the physical activities using axivity device" [13].

In this work, we want to pre-process our data before applying any machine learning algorithms, we want to use neural network and SVM algorithms and we also want to develop a generic system and we want to recognize strength training and swimming too.

We also want to develop a single system for recognizing sports activities (i.e. strength-training and swimming).

Physical training exercises are already identified by using a 3D accelerometer [14] but we found following drawbacks:

a) Data was not pre-processed before applying machine learning algorithms.

b) Only two Machine learning algorithms were used.

c) It is stated that "For every user, the system needs to be trained with the sensor data so that it would be able to predict physical training exercises using the axivity device" [14].

In this work, we want to pre-process our data before applying any machine learning algorithms, additionally we want to use neural network and we also want to develop a generic system for recognizing both activities (physical training exercise and swimming).

Hypothesis and research question

The acceleration measured by a 3 axis accelerometer (X,Y,Z) at a specific point, indicates which activity the person is performing (lying, sitting, walking, standing, cycling, running, ascending, descending stairs, strength-training and swimming), using classifier algorithms (J48, AODE, Neural network (multilayer perceptron) and Support Vector Machine).

In this paper, we investigate some practical aspects of creating an automatic, personal activity recognition system. Through our experiments, we want to find the answers of the following questions:

a) Is it possible to identify which activity the person is performing (lying, sitting, walking, standing, cycling, running, ascending, descending stairs and swimming) by using a 3D wearable accelerometer sensor on participants' backbone with better accuracy?

b) Is it possible to identify which activity the person is performing (strength-training and swimming) by using a 3D wearable accelerometer sensor on participants' backbone with better accuracy?
Experimental Methodology

We used AX3 data logger [1] in order to identify physical activities (as shown in Figure: 1).

![Figure 1: Axivity device](image)

The AX3 data logger contains 3-axis of accelerometer with flash memory and clock. This device is small and easy to use, its dimensions are 6x21.5x31.5 mm and its weight is 9 grams. The device comes with pre-installed software with the possibility to configure its settings. For example, we can configure sample rate, gravity etc. It continuously logs contextual information (time; hh:mm:ss and axis; X, Y, Z) to its internal memory. We can also set the duration for logging this information. There is also a possibility to export the logged data from the device to a computer in CSV format.

We implemented an application for ‘Pocket PC’ where we can state the starting and ending time for each physical activity during experiments. This application generates text files with this information for each physical activity for training data. It also stores the participants’ personal information i.e. age, gender, height and weight. We implemented another application in Java for analysis. This application requires two input files: training data from ‘Pocket PC’ as well as the CSV file from the axivity device. Firstly, it filters needed data from the CSV file based on the time stamp from the files from the ‘Pocket PC’ for each physical activity and generates training data files in ARFF format. Later, it preprocesses the data (which is described below) and then we applied machine learning algorithms (J48, AODE, neural network and SVM algorithms) on training data in order to get results from all mentioned algorithms as shown in Figure 2.

Data collection from Axivity device

We conducted three user studies in order to prove our hypothesis. One was for identifying physical activities, one was for physical training exercises and another one was for identifying different swimming styles.

For identifying physical activities, we recruited 12 testers (7 males, 5 females) for our experiment setup. The range of participants’ age was from 20 to 30 and ranged in BMI (body mass index) [10] from 18.7 to 28.7 (mean 23.1, SD 2.98). Participants performed
each physical activity (Lying, Sitting, Standing, Walking, Running, Cycling, Ascending and Descending stairs) for a minute. In order to attach this device on the participants’ back, we used sticky tape which was directly placed on the skin as shown in Figure 3.

For identifying physical training exercises, we recruited 14 participants (9 males, 5 females) for our experiment setup. The range of participants’ age was from 20 to 41 (mean 29.14, SD 10.11) and ranged in BMI (body mass index) from 19.6 to 27.8 (mean 23.03, SD 2.39). They performed four different physical training exercises (using elliptical trainer, butterfly, bench-press and pull down) for a minute. In order to attach this device on the participants’ arms, we used sticky tape which was directly placed on the skin as shown in Figure 4.

For identifying different swimming styles, we recruited 6 participants (5 males, 1 female) for our experiment setup. The range of participants’ age was from 19 to 42 (mean 29.17, SD 19.58) and ranged in BMI (body mass index) from 19 to 24.8 (mean 21.48, SD 2.16). They were required to swim 30 meters in each swimming style. Our participants had different swimming levels, some of them were beginners and some of them were expert in swimming. Our participants did it twice; once axivity device was attached on their arms and once it was attached on their backs as shown in Figure 3 and Figure 4.

We logged continuous data with 8G and the sample rate was 100 Hz. At the end we collected data from 32 participants out of all studies (physical activities, physical exercise activities and swimming styles).

**Ground truth**

Participants’ were continuously observed during experiments. An observer was stating starting/ending time of each activity.

**Feature computation**

Each window represents a data of 5 seconds and it contains correlation of \((X, Y)\), correlation of \((Y, X)\), correlation of \((Z, X)\), average of \(X\), average of \(Y\) and average of \(Z\).
Classifications

The 10-fold cross-validation is used to evaluate the J48, AODE, Neural network (Multilayer perceptron) and Support Vector Machine models. We used WEKA toolkit [11] for evaluating our results.

![Figure 3: Backbone’s location](image1)

![Figure 4: Arm’s location](image2)

Evaluation

<table>
<thead>
<tr>
<th></th>
<th>Lying</th>
<th>Walking</th>
<th>Running</th>
<th>Sitting</th>
<th>Standing</th>
<th>Cycling</th>
<th>Ascending stairs</th>
<th>Descending stairs</th>
<th>Swimming</th>
</tr>
</thead>
<tbody>
<tr>
<td>J48</td>
<td>99.39%</td>
<td>78.18%</td>
<td>73.17%</td>
<td>82.55%</td>
<td>88.82%</td>
<td>67.86%</td>
<td>68.34%</td>
<td>71.11%</td>
<td>98.85%</td>
</tr>
<tr>
<td>AODE</td>
<td>100%</td>
<td>52.12%</td>
<td>52.44%</td>
<td>64.43%</td>
<td>37.27%</td>
<td>23.57%</td>
<td>26.62%</td>
<td>28.89%</td>
<td>96.55%</td>
</tr>
<tr>
<td>Neural network</td>
<td>53.13%</td>
<td>63.03%</td>
<td>53.05%</td>
<td>67.79%</td>
<td>52.8%</td>
<td>37.86%</td>
<td>53.96%</td>
<td>42.22%</td>
<td>40.23%</td>
</tr>
<tr>
<td>SVM</td>
<td>74.85%</td>
<td>36.36%</td>
<td>62.2%</td>
<td>67.79%</td>
<td>52.8%</td>
<td>37.86%</td>
<td>53.96%</td>
<td>42.22%</td>
<td>40.23%</td>
</tr>
</tbody>
</table>

Table 1: Results from backbones

Our results (Table 1) show that 'Laying’ activity was predicted with an accuracy of 100% by the AODE classifier but J48 was able to predict all other physical activities like 'Walking', 'Running', 'Sitting', 'Standing', 'Cycling', 'Ascending stairs', 'Descending stairs' and 'Swimming' with better accuracy than other algorithms.
Our results (Table 2) show that sports activities (i.e. ‘Strength-training’ and ‘Swimming’) were predicted with an accuracy of 100% by the SVM classifier. Other classifiers were also able to recognize ‘Strength-training’ with high accuracy. Our results also show that placing a 3D sensor on participants’ arms can be better instead of placing it on their backs for recognizing “swimming” activity.

### Conclusion and future work

Our system is able to recognize a high percentage of the needed activities with the help of the J48 (decision tree) classifier. Results have shown that one 3D accelerometer sensor is enough for identifying required physical activities (lying, sitting, walking, standing, cycling, running, ascending stairs, descending stairs and swimming) and sports activities (strength-training, swimming). This prototype is only a "proof of concept" and our results show that a single 3D accelerometer sensor can identify the above mentioned physical activities independent of BMI (body mass index) and age group. The accelerometer sensor has to be fixed properly on the participants’ skin in order to predict their movements successfully. To conclude our discussion we can safely lay claim to being able to identify the aforementioned physical activities by using a 3D wearable accelerometer sensor. We will put the accelerometer sensor on other parts of the body in order to identify some other physical activities and we will use it for online machine learning.

### Acknowledgement

This research is supported by USEFIL (www.usefil.eu).

### References


Unobtrusive Low Cost Pupil Size Measurements using Web cameras

Sergios Petridis, Theodoros Giannakopoulos and Constantine D. Spyropoulos
National Center for Scientific Research “Demokritos”
{petridis,tyianak,costass}@iit.demokritos.gr

Abstract

Unobtrusive every day health monitoring can be of important use for the elderly population. In particular, pupil size may be a valuable source of information, since, apart from pathological cases, it can reveal the emotional state, the fatigue and the ageing. To allow for unobtrusive monitoring to gain acceptance, one should seek for efficient methods of monitoring using common low-cost hardware. This paper describes a method for monitoring pupil sizes using a common web camera in real time. Our method works by first detecting the face and the eyes area. Subsequently, optimal iris and sclera location and radius, modelled as ellipses, are found using efficient filtering. Finally, the pupil center and radius is estimated by optimal filtering within the area of the iris. Experimental result show both the efficiency and the effectiveness of our approach.

Keywords

video analysis, eye tracking, pupil size estimation, physiological measurements

Motivation

Unobtrusive every day health monitoring can be of important use for the elderly population. In particular, pupil size may be a valuable source of information, since, apart from pathological cases, it can reveal the emotional state, the fatigue and the ageing. To allow for unobtrusive monitoring to gain acceptance, one should seek for efficient methods of monitoring using common low-cost hardware. A low cost camera that monitors the user while in front of a laptop or behind a mirror (Poh, McDuff, & Picard, 2011) falls into this scenario. Detecting pupils and pupil sizes in this context is of great importance. Namely, pupil sizes may be a valuable source of information, since, apart from pathological cases, it can reveal the emotional state (Partala & Surakka, 2003), the fatigue (Morad, Lemberg,
Yofe, & Dagan, 2000) and the ageing (Winn, Whitaker, Elliott, & Phillips, 1994) of the subject under monitoring.

Towards this end, this work presents a method for detecting iris and pupils, including both their centers and sizes, from low resolution visible-spectrum images, using a robust unsupervised filter-based approach. Iris detection performance outperforms most state of the art methods compared, and is competitive to few others. With respect to pupil detection, to our knowledge, detecting pupil sizes detection is not reported elsewhere in the related literature. Using a dataset compiled in particular for this purpose, we show that our method is accurate enough to provide significant information for everyday long-term monitoring.

**Relevant Work**

The task of detecting eyes in images or videos is crucial and challenging in many computer vision applications. First, eye detection is a vital component of most face recognition systems, where eyes are used for feature extraction, alignment, face normalization, etc. In addition, eye tracking is widely used in human computer interaction (gaze tracking). Eye detection systems can be categorized according to the adopted data acquisition method in (a) visible imaging and (b) infrared imaging. According to the first (Jesorsky, Kirchberg, & Frischholz, 2001a; Zhou, 2004; Asteriadis, Nikolaidis, Hajdu, & Pitas, 2006; Hassaballah, Murakami, & Ido, 2011; Valenti & Gevers, 2008; Cristinacce, Cootes, & Scott, 2004; Hamouz et al., 2005), ambient light reflected from the eye area is captured, hence the task is rather difficult, due to the fact that captured information can contain multiple specular and diffuse components (Li, Iowa State University Human Computer Interaction Program.). On the other hand, infrared-based approaches (Li, Iowa State University Human Computer Interaction Program.; Li, Winfield, & Parkhurst, 2005; Villanueva et al., 2009) manage to eliminate specular reflections and lead to a better and accurate pupil detection. Another discrimination between eye detection approaches is based on the distance of the recording device: (a) head-mounted and (b) remote systems. Needless to say, head-mounted approaches can lead to more accurate systems. However, under particular requirements of low cost and low level of obstruction, remote sensing is the only acceptable solution.

**Method**

**Preprocessing**

The overall scheme of the proposed method is presented in Figure 1. At a first stage, the face is detected. Face detection is a well studied problem in machine vision (Viola & Jones, 2001) and there exist now several commercial tools that achieve high accuracy with high speed. For our purposes, we have used SHORE™ which achieves face detection at a

---

1SHORE™: Sophisticated High-speed Object Recognition Engine, Fraunhofer IIS
frame rate greater than 50fps.
The same engine, also provides directly as a rough estimate of the two eyes area, which we have used to initiate iris and pupil detection.

![Sample eye area image](image)

**Figure 2: Sample eye area image**

### Sclera and Iris detection

The sclera/iris detection method aims at determining the coordinates \((e_L^x, e_L^y), (e_R^x, e_R^y)\) and the radii \(e_L^r, e_R^r\) of the left and right irises, considered as circular disks\(^2\). Detection is done independently in each eye and is achieved by maximizing that output of a scoring process, while applying a specialized bank of linear filters parametrized by the radius of the iris, within the rough area of the eye. Therefore, this process results in both the estimation of the center of iris and its radius. The overall score is evaluated as a sum of three scores, based on luminosity, saturation and symmetry, whose definitions are given below.

### Detection based on luminosity

Denoting the luminosity pixels of the eye rough area as \(I_L\) and the set of applied masks as \([M^L_r]\), the luminosity score is defined as:

\[
  l(e_x, e_y, e_r) = I_L[x, y, r] \cdot M^L_r
\]

\(^2\)The left (respectively right) eye is denoted by subscript L (respectively R)
where \( \cdot \) above denotes element by element multiplication and \( I_L[x, y, r] \) is the luminosity values of an image region centered at \((x, y)\) and with size equal to the size of mask \( M_L^r \).

The motivation here is that the iris can be located as a region darker than the surrounding sclera. To that end, we have used a mask with three regions, as depicted in Figure 3, where the elements of each region all share the same value. In particular:

- **iris** a circle centered at the center of mask, where elements have the same negative value
- **sclera** a region defined as the difference of the above circle and the co-centered ellipse of equal radius along the vertical axis and double radius along the horizontal axis, where elements have the same positive value
- **skin** a region define as the difference of the above ellipse and a co-center rectangular region, where the elements have zero value

The mask values are normalized such that they sum up to zero.

**Detection based on saturation**

To detect the sclera and the iris, it is useful to observe that the sclera is typically much less saturated than both the iris and the surrounding skin. To that end we apply the same method as above using a set of masks \( M_S^r \). These masks are similar to the ones used for detection based on luminosity, in that they are composed of the same regions. The difference lie in the value of pixel within each region. Namely, for the iris and skin elements share the same positive value whereas for the sclera the same negative value. As for luminosity, the mask values are normalized such that they sum up to zero. The score based on saturation is then evaluated as

\[
s(e_x, e_y, e_r) = I_S[x, y, r] \cdot M_S^r
\]

where \( I_S \) is the saturation values of the eye rough area considered.

Note that, as a practical approximation, our method actually uses the \( V \) channel of the \( YUV \) format to approximate saturation.
Detection based on symmetry

A further observation to boost the accuracy of sclera and iris detection is that these regions show a significant symmetry. In particular, we have experimentally found that checking for horizontal symmetry inside the iris and sclera regions significantly removes false eye detections.

In particular, by denoting with superscript H an image region obtain by horizontal flipping, we evaluate the symmetry score as

\[ h(e_x, e_y, e_r) = (|l_L[x, y, r] - l_H^L[x, y, r]| + |l_S[x, y, r] - l_H^S[x, y, r]|) \cdot M^H_r \]  

Note that both luminance and saturation values are used here. The mask \( M^H_r \) is of similar structure to \( M_L^r \), though with negative elements inside the sclera and iris and zero elements within the skin area.

Overall Score

The overall score for each candidate iris center and radius is evaluated as a sum over the respective luminance, saturation and symmetry scores.

\[ c(e_x, e_y, e_r) = l(e_x, e_y, e_r) + s(e_x, e_y, e_r) + h(e_x, e_y, e_r) \]  

and the final choice is made by exhaustively searching over the rough eye area found during preprocessing.

\[ (\hat{e}_x, \hat{e}_y, \hat{e}_r) = \arg \max_{e_x, e_y, e_r} c(e_x, e_y, e_r) \]

Pupil Detection and measurement

As soon as the disk that defines the iris area for each eye has been estimated, the pupil is detected as a circle within the iris that optimal satisfies a gradient-based criterion. Candidate pupils are circles with center \((p_x, p_y)\) in the close neighborhood of the iris center \((e_x, e_y)\), with radius such that they fall strictly inside the iris area.

The gradient criterion is evaluated as the difference between the average luminosity of the pixel defining the perimeter of the candidate circle with the average luminosity of the immediate outer pixels of the circle. The greater the difference, the greater the possibility that the circle corresponds to the pupil. Note that the sign of the difference is important here.

Though this approach is conceptually simple, it has shown that it is quite accurate, even in the presence of light reflections, which may degrade the performance of a non-gradient method.
Optimal Frame

The procedure outlined for detecting the iris and the pupil is repeated for every frame obtained from the camera, for both eyes. Since the ultimate goal is to measure the pupil size, and given that pupil size does not change from frame to frame\(^3\), it is not needed to measure the pupil on each frame, but rather on a frame where it can be measured with higher confidence. To that end, we describe now a method that evaluates the optimal frame based on which detecting the pupil and measuring its size can be attempted.

Namely, for every frame, we compute an overall confidence score, as the product of the following measures:

- left eye iris detection score
- right eye iris detection score
- \(e^L_y\) and \(e^R_y\) equality based score
- \(e^L_y\) and \(e^R_y\) equality based score
- \(p^L_y\) and \(p^R_y\) equality based score

Regarding the first two items of the above list are directly given through Eq 4. The equality based scores are evaluated based on the generic formula

\[
s = \frac{|l - r|}{\max\{l, r\}}
\]

where \(l\) (respectively \(r\)) is a measured obtained from the left (respectively right) eye.

Therefore, as the video is streaming, we evaluate the overall confidence score and compare it to the one that has been obtained so far. In case it is greater, the less confident value is discarded and the new one is kept as the optimal one. In this way, the latest results are always based on the more confident frames. The procedure is repeated until the person under monitoring is stopped from being tracked, or after the end of a predefined time duration. In both case, the confidence score is reset and the procedure is repeated again.

Complexity Analysis

A main concern in the development of the proposed method has been to keep low the overall complexity. This has been important for two reasons. The first one relates to low resources that the method should be needing. Either running as a background process on a tablet, or as a process on a dedicated hardware, detecting and measuring pupils should take as few resources as possible, given that the same hardware may be hosting other

\(^3\)we assume here that lighting conditions stay the same
processes too. The second one relates to the speed of execution. Even though pupil size measurement is not critical, and therefore latency is affordable, the need of video recording should nevertheless be avoided to address users’ privacy concerns. Overall, our goal has been to measuring pupils in at least real time given limited processing resources and no storage.

**One-pass iteration**

The method that has been described in this paper does achieve this goal. In particular, a significant speed up has been achieved by allowing scores involving iterations over pixels to be computed with a single pass over the respective image region. This has been possible, since all masks share the same structure and therefore scores are simultaneously updated by iterating over the region pixels. Moreover, since mask elements have no more than three values for each mask, the computation requires a number of additions equal to the number of pixel in the region. Multiplications are only constant with respect to image region size.

**Pupil Scores**

In the same direction, we also stress that candidate pupil scores are evaluated within the same iteration. To achieve this, the value of the mask element within the iris is used. In particular, notice that while the sign of the elements can be used to identify that they belong to the iris, the value is of non particular importance when evaluating the luminance and saturation values, since, as noted above, a plain summation of the values within the iris is performed, followed by a normalization using a pre-calculated normalization factor. Therefore, the value of the elements have been used to tag the distance from the mask center, as depicted in Figure 4. In this way, while iterating over the mask elements, an array indexed by the distance from the center, progressively accumulates the sum of the values with the same distance from the center. After iterating over all elements, this array will contain, in each element (index), the sum of luminance values for the given index.
Parallelization

Note also that our method can be graciously parallelized in many cores — one instruction processing architecture which would allow a further speedup on the execution. Such a solution is highly desirable in cases which one wishes to make the most out of a dedicated hardware including both CPU and GPU. Actually, the authors are currently implementing the method using the CUDA programming language, such that it can be executed on a low energy consumption nettop (Zotac Z-BOX ID84 PLUS) featuring a Intel Atom D2550 1.86 GHz Dual-Core CPU and NVIDIA GeForce GT 520M (512 MB) GPU.

Tuning the frame rate

We further notice that in case the method needs to be implemented in a lower processing capabilities hardware, real time analysis can be guaranteed by lowering down the video frame rate per second. Of course, in this case, a lower accuracy may be noticed, given that frames containing clearer pupil sizes may have been missed. The frame rate achieved in the Zotac Z-BOX ID84 PLUS using only CPU has been 5 frames per second, whereas a frame rate above 30 has been achieve for a PC feature an Intel Core i5-2500 CPU @ 3.30GHz.

Results

Our evaluation had two purposes. First, to evaluate the performance of the iris detection module. In this case, we are only interested in estimating the iris center (not its size), since most of the related publicly available datasets only have center annotations (e.g., (Jesorsky, Kirchberg, & Frischholz, 2001b)). Second, to evaluate the performance of pupil detection. Here, we are interested in estimating the exact pupil area (center and radius). Towards this end, we have built a dataset with pupil-related annotations.

Iris center localization performance

The proposed method has been evaluated against nine state of the art methods. Two of them are provided by the MATLAB Vision Toolbox (Shiqi, n.d.; Castrillón, Déniz, Guerra, & Hernández, 2007), namely (a) CART (Shiqi, n.d.) and (b) HAAR (Castrillón et al., 2007), and allowed an in depth comparison using several performance measures. The others have been compared using reported results in (Jesorsky et al., 2001a; Zhou, 2004; Asteriadis et al., 2006; Hassaballah et al., 2011; Valentí & Gevers, 2008; Cristinacce et al., 2004; Hamouz et al., 2005). Furthermore, a "Rough" estimation has been used as baseline based on setting the estimated iris center as the center of the initial individual eye areas, which are extracted as explained in Section . In some cases only the results of MATLAB-related methods are shown, since these are reproducible, while all compared methods are only shown for the
Table 1: Iris Detection Average Relative Error (left, right and overall) results (MATLAB-related methods compared)

<table>
<thead>
<tr>
<th>Method</th>
<th>$E_l$</th>
<th>$E_r$</th>
<th>$E$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAAR</td>
<td>0.052</td>
<td>0.040</td>
<td>0.046</td>
</tr>
<tr>
<td>CART</td>
<td>0.060</td>
<td>0.057</td>
<td>0.058</td>
</tr>
<tr>
<td>Rough</td>
<td>0.054</td>
<td>0.053</td>
<td>0.053</td>
</tr>
<tr>
<td>Proposed</td>
<td>0.035</td>
<td>0.021</td>
<td>0.028</td>
</tr>
</tbody>
</table>

The performance measures involved in this evaluation are defined as follows. First, let $d_l$ (respectively $d_r$) be the euclidean distance between the detected and manually annotated left (respectively right) iris centers. Also, let $d_{lr}$ be the distance between the manually annotated left and right iris centers. The relative errors for the two detected irises are evaluated as $e_l = \frac{d_l}{d_{lr}}$ and $e_r = \frac{d_r}{d_{lr}}$, whereas the relative error over both eyes as $e = (e_l + e_r)/2$. The respective error measures over the dataset are naturally defined as average errors over all dataset samples: $E_l = \frac{1}{N} \sum_{i=1}^{N} e_l(i)$, $E_r = \frac{1}{N} \sum_{i=1}^{N} e_r(i)$ and $E = \frac{1}{2}(E_l + E_r)$, where $N$ is the total number of samples in the testing set. Table 1 shows the average iris detection errors for the compared MATLAB-related methods. The proposed method outperforms all compared methods.

Furthermore, we have compared our method against an tolerance-based accuracy measure widely used in the literature (Jesorsky et al., 2001a; Zhou, 2004; Asteriadis et al., 2006; Hassaballah et al., 2011; Valenti & Gevers, 2008; Cristinacce et al., 2004; Hamouz et al., 2005). Namely, given an error tolerance $T$, an eye detection result is considered as successful if both errors $e_l$ and $e_r$ are less than $T$: 

$$A_T = \frac{\sum_{i \in \text{max}(e_l(i), e_r(i)) \leq T} 1}{N}$$

Using this measure, it has been possible to compare the proposed method against (Jesorsky et al., 2001a; Zhou, 2004; Asteriadis et al., 2006; Hassaballah et al., 2011; Valenti & Gevers, 2008; Cristinacce et al., 2004; Hamouz et al., 2005) as well, using the corresponding reported results. A typical value for the threshold is $T = 0.25$, because it corresponds to an accuracy of about half the width of an eye in the image, while $T = 0.1$ has also been used (Zhou, 2004; Jesorsky et al., 2001b; Asteriadis et al., 2006). In Table 2 the tolerance-based accuracy for three different tolerance thresholds is presented. The proposed method outperforms most of the compared methods, except for the case of $T = 0.05$.

Pupil size estimation performance
Table 2: Iris detection tolerance-based accuracy results for three different tolerance values (all methods compared)

<table>
<thead>
<tr>
<th>Method</th>
<th>$T$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>HAAR</td>
<td>22</td>
</tr>
<tr>
<td>CART</td>
<td>8</td>
</tr>
<tr>
<td>Rough</td>
<td>15</td>
</tr>
<tr>
<td>(Jesorsky et al., 2001a)</td>
<td>40</td>
</tr>
<tr>
<td>(Zhou, 2004)</td>
<td>-</td>
</tr>
<tr>
<td>(Asteriadis et al., 2006)</td>
<td>50</td>
</tr>
<tr>
<td>(Hassaballah et al., 2011)</td>
<td>45</td>
</tr>
<tr>
<td>(Valenti &amp; Gevers, 2008)</td>
<td>84</td>
</tr>
<tr>
<td>(Cristinacce et al., 2004)</td>
<td>56</td>
</tr>
<tr>
<td>(Hamouz et al., 2005)</td>
<td>59</td>
</tr>
<tr>
<td>Proposed</td>
<td>47</td>
</tr>
</tbody>
</table>

Pupils size estimation evaluation needs a different setting from the one described above. To begin with, annotations of the pupil’s whole area, not just its center, is needed. To our knowledge, there is no available dataset with such annotations. Therefore, we have built a manually annotated dataset of pupil area. Three humans annotated the irises and pupils, to estimate an inter-annotator agreement level. Final pupil annotations have been considered as the average areas of all annotators. The compiled dataset consists of 50 1280x960 resolution face images of 10 different humans.

With respect to the performance measures, we have used the recall, precision and F1 measures over the pupil areas. In particular, let $A_a$ be the area of the manually annotated pupil, $A_e$ be the area of the estimated pupil and $A_c$ be the area of their intersection. The recall, precision and $F_1$ rates are defined as $R = \frac{A_c}{A_a}$, $P = \frac{A_c}{A_e}$ and $F1 = \frac{2 \cdot R \cdot P}{R + P}$ respectively.

These same measures have also been used for evaluating the inter-annotator agreement. The results of the evaluation are displayed in Table 3. Note that the inter-annotation agreement scores are relatively low, revealing the difficulty even for a human in annotating the pupil area, especially for dark and brown eyes.

In terms of average $F_1$ measure, the proposed pupil detection method is 12% less accurate than the human annotation performance. In terms of pupil diameter size estimation, our method achieves on average 85% accuracy. This means that for an average 6mm pupil diameter, average error is 0.9mm, which is much lower than the threshold of 2mm indicated for significant pupil differentiations (Partala & Surakka, 2003; Winn et al., 1994).

A specific benchmark dataset containing such cases would nevertheless be needed to explicitly verify this conclusion.
<table>
<thead>
<tr>
<th></th>
<th>Precision</th>
<th>Recall</th>
<th>F1</th>
</tr>
</thead>
<tbody>
<tr>
<td>i-a.a</td>
<td>82</td>
<td>84</td>
<td>79</td>
</tr>
<tr>
<td>Proposed Method</td>
<td>66</td>
<td>68</td>
<td>67</td>
</tr>
</tbody>
</table>

Table 3: Pupil detection performance and comparison to inter-annotator agreement (i-a.a).

Discussion

A method for iris and pupil detection, including their sizes, has been presented, based on a robust unsupervised recursive filtering technique. Evaluation on iris center detection has shown that the proposed method outperforms most of related algorithms. Pupil size estimation was evaluated on a separate dataset which also contains annotations regarding not only pupils position but their sizes as well. The final pupil detection performance results showed that the proposed method’s accuracy is accurate enough to be considered as a low cost pupillometry for long-term monitoring. Further results on video should be presented to show the utility of the confidence of the result based on frame sequences.

Acknowledgments

The research leading to these results has been funded by the European Union’s Seventh Framework Programme (FP7/2007-2013) under grant agreement no 288532. For more details, please see http://www.usefil.eu.

References


Abstract

Population ageing is a phenomenon occurring, with different degrees and paces, in almost every country in the world, and it is becoming a major problem in Europe, Japan and USA, due to the high dependency ratio of these countries. Research in the fields of Ambient Assisted Living (AAL) and Ambient Intelligence (AmI) is thus gaining great attention. To cope with the changing needs that characterize the life of people with chronic diseases, it seems necessary to combine AAL and AmI with Artificial Intelligence and develop intelligent systems that can adapt to the changing conditions of the patient. This paper presents the Virtual Carer (VC), a Multi-Agent System (MAS) based on the Belief-Desire-Intention (BDI) paradigm. The main goal of the system is to help an elderly patient in his daily activities, while his health conditions are monitored in order to ensure his security.

Keywords

Virtual Carer, Multi-Agent Systems, BDI, AAL, Ambient Intelligence.

Introduction

Population ageing is a shift in the distribution of a country’s population towards older ages. This demographic shift is ongoing in almost every country in the world, to the point that the world has never seen as aged a population as currently exists globally. Due to their higher dependency ratio (i.e. the ratio between the number of people over 65 years old and those of working age), this is becoming a major problem in Europe, USA and Japan (United Nations, 2002; Christensen, Doblhammer, Rau, & Vaupel, 2009).
The increasing median age of the population has significant social and economic implications. For example, it results in a rise in the number of chronic diseases which in turn cause the increasing of health-related emergencies and an increase in the health care spending (Kleinberger, Becker, Ras, Holzinger, & Müller, 2007). Ambient Assisted Living (AAL) focuses on these themes and aims at extending the time older people can live in their home environment, assisting them with the activities of daily living, promoting the use of intelligent products and Information Technology (IT) tools to provide remote care services (Sun, De Florio, Gui, & Blondia, 2009).

Through the AAL Joint Programme, the European Union aims to foster the emergence of AAL services and systems for ageing well at home, in the community, and at work (AAL EUROPE). The AAL Joint Programme defines these key objectives for AAL:

- to extend the time people can live in their preferred environment by increasing their autonomy, self-confidence and mobility;
- to support maintaining health and functional capability of the elderly individuals;
- to promote a better and healthier lifestyle for individuals at risk;
- to enhance the security, to prevent social isolation and to support maintaining the multifunctional network around the individual;
- to support carers, families and care organizations;
- to increase the efficiency and productivity of used resources in the ageing societies.

Every AAL system is based on pervasive devices typically used in Home Automation systems, and on Ambient Intelligence (AmI) technologies to integrate devices and build a safe environment for the assisted person (Sun et al., 2009). The main goal of AmI is to help people in their daily activities, building around them an unobtrusive, interconnected, adaptable, dynamic, embedded, and intelligent environment (Sadri, 2011). Humans can interact with AmI-based systems using natural user interfaces like speech and gestures. One of the goals of AmI is to allow the user to interact with an AmI system like it would do with any other human (Kleinberger et al., 2007).

AAL and AmI systems have to adapt themselves over time to cope with the changing needs and health conditions of the assisted person. Moreover, they need to perceive variation in habits that can signal health-related problems or stressful situations. Applying Artificial Intelligence techniques on this domain seems to be a promising direction for research (Pollack, 2005; Cook, Augusto, & Jakkula, 2009; O’Grady, Muldoon, Dragone, Tynan, & O’Hare, 2010).

In this paper we present Virtual Carer, a Multi-Agent System (MAS) based on the Belief-Desire-Intention (BDI) paradigm, which models, integrates and manages the typical services of an AAL system.
The Virtual Carer manages a distributed sensor network formed by ambient and biometric sensors. To increase modularity and reliability of the system, each sensor is associated with an agent; thus the system is resilient to sensor failures and disconnections. Depending on the complexity of the system to be managed, one or more BDI agents are used to form the Virtual Carer Agency (VCA). The main goal of VCA is to model logical structures, reasoning and behaviours similar to those of a human caregiver, transforming data from sensor agents in logical predicates representing its knowledge base. To perform actions on the monitored ambient and interact with the assisted person, VCA can collaborate with agents controlling actuators. Thus the system can monitor the health conditions of the assisted person and facilitate his daily activities.

The rest of the paper is organized as follows. The next section deals with some related works on MAS and AAL; then the core of the proposed system is described. A simple simulation scenario highlights some features of the Virtual Carer. In the end some conclusions are drawn and future work suggested.

Related Works

As stated in (Russell & Norvig, 2009), an agent is an entity that can perceive the environment through sensors and act on the environment through actuators. In (Wooldridge & Jennings, 1995) the main properties of an agent are outlined: autonomy, social ability, reactivity and pro-activeness indicate that agents operate without external intervention, interact with other agents using some kind of Agent Communication Language (ACL), perceive the environment answering to changes and are able to autonomously exhibit goal-directed behaviours.

MAS are capable to autonomously adapt to context changes resulting from user activity, device failures, and the addition or removal of devices and services. Hence, they meet the requirements on modularity and adaptability of AAL systems (Ayala, Amor, & Fuentes, 2012). BDI agents act on the basis of practical reasoning (Bratman, 1987): their intentions, i.e. the set of actions that an agent can perform, originate from the intersection between beliefs, i.e. the agent knowledge about the environment, and desires, i.e. the set of states representing the environment as desired by the agent. MAS and BDI agents with an appropriate knowledge base can meet the guidelines of AAL and AmI, indicating the need of unobtrusive, adaptable and dynamic intelligent environments (Sadri, 2011) and requiring technical solutions that are flexible and adaptable to individual and changing needs (Wolf et al., 2010).

MAS applications in the AAL domain are proposed in several scientific contribution. (Nefti, Manzoor, & Manzoor, 2010) presents a system to monitor patients suffering from dementia, in which a Risk Assessment Agent, using its knowledge base and information provided by agents responsible for various ambient sensors, applies a method based on fuzzy logic to predict risk situations and to trigger proper alarms. In the system described in (Borowczyk, Gawinecki, & Paprzycki, 2008), instead, each agent cooperates with other
agents to carry out specific tasks, uses its own knowledge base to trigger an alarm if needed, and can alert the medical staff in dangerous situations. In (McNaull, Augusto, Mulvenna, & McCullagh, 2011) the focus is on the interaction with the user rather than on monitoring. The work in (Reinisch & Kastner, 2011) is based on Home Automation and describes a small society of BDI agents able to cope with energy efficiency issues when different devices are available.

A different research area is focused on Internet of Things scenarios for AAL and remote healthcare (Dohr, Modre-Opsrian, Drobics, Hayn, & Schreier, 2010). Here, the main problem is interoperability between different devices and sensors. The multi-agent paradigm offers a way to integrate such information sources in a manageable knowledge base, thus allowing for a better use of resources.

The Virtual Carer Architecture

The Virtual Carer is a MAS modelling a distributed, reliable and modular sensor network composed by biometric and ambient sensors, and integrating a BDI core agent (Virtual Carer Agency, VCA). The Virtual Carer is an IT system able to communicate with an assisted person, to monitor his health conditions and to control the environment around him. To cope with a highly variable environment, and following the BDI paradigm, VCA models reasoning mechanisms and behaviours similar to those of a human being. The large amount of information used by VCA is represented by logical predicates, forming its Knowledge Base (KB). VCA chooses the right actions to perform on the environment with an inference engine applied on its KB. The VCA works as follows:

- it analyzes data provided by sensors and devices forming the system (i.e. by agents controlling them) and updates its KB;
- when its KB is updated, VCA generates new knowledge using its inference engine;
- with backward reasoning rules applied on its KB, VCA selects the main goal and chooses (through backtracking) the plan to satisfy it;
- VCA carries out the actions of chosen plan, collaborating with agents responsible for actuators, in order to directly act on the environment.

Figure 1 shows the basic architecture of the system. The system is composed by the BDI Virtual Carer Agent, a Register Agent and a number Actuator Agents and Sensor Agents. The Actuator Agents are responsible for the activation and deactivation of the devices composing the system, like speakers, lights, monitors and so on. They must be able to receive requests from other agents and to execute on/off commands on the devices. The Register Agent is responsible for the database storage of all the information provided by sensors and of the anomalies detected by the VCA.
Sensor Agents can be distinguished in two types: Ambient Agents and Health Agents. Ambient Agents are responsible for reading the value of ambient sensors, for example the temperature of a specific room. They check if the recorded values are in a predetermined range: if the value is outside of the range, the Ambient Agent communicates the anomaly to the VCA. Presence sensors are managed by Ambient Agents, too. For example, we can consider a Passive Infrared (PIR) sensor: the Ambient Agent controlling it merely informs the VCA about the presence of someone in the monitored room.

Health Agents, instead, manage sensors measuring values related to the health conditions of the assisted person. For example, a Health Agent can control a heartbeat sensor.

The arrows in Figure 1 highlight the information flow characterizing the system. The VCA receives alarms from Sensor Agents when a value is out of the predetermined range; in addition, the VCA can directly require to read a value, for example because the chosen plan requires data to satisfy the goal. The Register Agent receives and store in a database values from Sensor Agents and warning and anomalies report from the VCA. The VCA can require values from the database to the Register Agent. The VCA sends request to the Actuator Agents in order to execute actions corresponding to the adopted plan. For example the VCA can send a request to turn on the light in the living room because the PIR agent detects the presence of the assisted person.

Sensor and Actuator Agents are implemented using the JADE framework (Bellifemine, Caire, & Greenwood, 2007) whilst the BDI agent representing the VCA and the Register Agent are implemented using JASON and the AgentSpeak language (Bordini, Hübner, & Wooldridge, 2007). It is important to notice that the use of JADE framework allows the communication between agents with FIPA-ACL messages, ensuring the modularity of the system: different devices can be added anytime simply integrating more agents. JASON
is used for the BDI agents composing the VCA, in order to apply the BDI paradigm, and for the Register Agent, allowing to store beliefs directly in the database.

![Home map for the implemented simulation scenario](image)

**Simulation Scenario**

In order to test the proposed architecture, a preliminary simulation was carried out. The system was complemented by a BDI agent, the Elderly Agent, modelling behaviours and activities of the person assisted by the Virtual Carer System. For simulation reasons the Elderly Agent is able to send messages to other agents of the system: for example, it informs the PIR agent when it moves in the controlled room, and sends requests to the Health Sensors to know the value of specific health parameters.

Figure 2 shows the fictional home map we used in the simulation scenario, highlighting the arrangement of the available devices in the environment.

There are 4 rooms: the bedroom (room 1), the hallway (room 2), the bathroom (room 3) and the living room (room 4). For each one, a temperature sensor (T1, T2, T3, T4), a PIR sensor (PIR1, PIR2, PIR3, PIR4) and a device to turn on/off the light (AL1, AL2, AL3, AL4) are provided. In addition there are a speaker (SP1, SP2, SP3) for each one of the first three rooms, and a monitor to visually communicate with the assisted person in room 4. Pressure sensors are supposed to be in each place where the person can sit or lie down (e.g. couch, bed, seats), and contact sensors are supposed to be placed on every door and window, to monitor their open/close state. Body sensors are used to monitor the vital parameters (e.g. heartbeat, body temperature) of the assisted person. For each sensor and device in the described scenario the proper Ambient, Health and Actuator Agents are created.
In this simulation, the VCA agent has two emergency plans: the first, shown in figure 3, is executed when an Ambient Agent, responsible for a temperature sensor, read a value out of the predetermined range. In this case the VCA communicates the anomaly to the Register Agent and activates the plan `notify` in order to evaluate if the monitored person has to be notified with some alarms.

```prolog
/* Piano Emergenza Temperatura stanza*/
+emergency1(V)[source(A)] : true <-
        .print("Ricevuto Parametro Temperatura fuori norma");
        .print("dal sensore ", A);
        .print("con valore", V);
        .time(H,M,S);
        .send(register,tell,anomaly(A,V,H,M,S));
        .print("Info inviata a Agent Register");
        +em1(N);
        New = N + 1;
    -+em1(New);
    !notify;
    !canc.
```

Figure 3: Emergency plan for room temperature

The plan in figure 4 is activated when the body temperature of the assisted person is out of a security range. This plan is similar to the previous one.

```prolog
/* Piano Emergenza Temperatura Corporea*/
+emergency2(V)[source(A)] : true <-
        .print("Ricevuto Parametro Temperatura corporea fuori norma");
        .print("dal sensore ", A);
        .print("con valore", V);
        .time(H,M,S);
        .send(register,tell,anomaly(A,V,H,M,S));
        .print("Info inviata a Agent Register");
        +em2(N);
        New = N + 1;
    -+em2(New);
    !notify;
    !canc2.
```

Figure 4: Emergency plan for body temperature

To simulate the different behaviours of the assisted person, the Elderly Agent was provided with different plans. Figure 5 shows a plan including the transition from the hallway to the bedroom, and the request of the body temperature value.

In a first simulation scenario, we modelled the situation in which the assisted person goes to bed and measures its body temperature. The simulation works as follows. At first, the Elderly Agent initializes the VCA Agent, providing it the information about its initial position; then, after 5 seconds (i.e. the time necessary to get to bedroom), it informs the PIR Agent of its presence in the final position. The PIR Agent controlling the bedroom notifies
the VCA about the presence of a person in the bedroom; thus VCA has a new belief (i.e. the presence of the assisted person in room 1), and activates the plan to turn on the light in the bedroom and to turn it off in the hallway. Finally, the Elderly Agent send a message to the VCA to know its body temperature value. VCA activates a plan that includes all the actions necessary to require the data from the proper Health Agent and to communicate it to the Elderly Agent.

Beside plans similar to the one just described, we simulated plans without an explicit request by the Elderly Agent, in which the Virtual Carer had to infer the right actions. For example, when a window remains open in the bedroom and the assisted person is sleeping, the decreasing of room and body temperature should activate the plan to wake up the person and ask him to close the window. In this scenario, the Ambient Agent associated to the bedroom window informs the VCA that the window state is "open". At a later stage the Ambient Agent responsible for T1 sensor communicates to the VC Agent that the detected value is out of the predetermined range; a similar message is sent by Health Agent. VCA updates its KB with these new beliefs and activates a plan ending with a message to the Elderly Agent, asking it to close the window.

Of course, the ideal test for the proposed approach should include an AAL scenario with sensors and devices deployed in a real home environment. However, the simulations we carried out are adequate to underline that MAS and BDI paradigm are useful when applied to AAL contexts: the MAS approach guarantees modularity to the system, in order to cope with the addition or removal of devices, while the BDI paradigm allows to quickly respond to changes in a dynamic environment.

Conclusions

We described a MAS approach to AAL to deal with a dynamic environment, monitoring the health conditions of an elderly or disable person. The core of the system is a BDI agent representing a Virtual Carer. The Virtual Carer collaborates with other agents modelling various sensors and devices to simplify the daily activities of the assisted person and to trigger alarms when something is wrong with parameters regarding his health conditions. The JADE framework guarantees the communication through FIPA-ACL messages, ensuring the flexibility of the system: new devices can be added simply integrating agents in the proposed platform. We tested the system considering several simulation scenarios.

Figure 5: Elderly Agent example plan

```prolog
+!scenario5 : true <-
  .wait(60000);
  .send(badante,tell,init(corridoio));
  .wait(10000);
  .send(pir1,tell,at);
  .send(badante,achieve,queryP(tempB)).
```

We described a MAS approach to AAL to deal with a dynamic environment, monitoring the health conditions of an elderly or disable person. The core of the system is a BDI agent representing a Virtual Carer. The Virtual Carer collaborates with other agents modelling various sensors and devices to simplify the daily activities of the assisted person and to trigger alarms when something is wrong with parameters regarding his health conditions. The JADE framework guarantees the communication through FIPA-ACL messages, ensuring the flexibility of the system: new devices can be added simply integrating agents in the proposed platform. We tested the system considering several simulation scenarios.
and representing the assisted person using another BDI agent. Several plans was taken into account, modelling different actions performed by the Elderly Agents (e.g., movements, direct requests, changing of health parameters). Tests confirm that MAS and BDI paradigm improves modularity and adaptability of AAL and AmI systems. The Multi-Agent approach guarantees the modularity of the system, whilst the BDI paradigm permits to respond to changes in the environment and in the needs of the assisted person.

As future work more insightful tests have to be conducted: a real AAL scenario, i.e. a daily-used home environment equipped with devices and sensors, where an assisted person can live, is beyond our possibilities at this stage of the work, but is the only way to fully validate the proposed approach. The next step could be towards the integration of more technologies in the Virtual Carer system: for example those for video surveillance described in (Claudi, Di Benedetto, Dolcini, Palazzo, & Dragoni, 2012) could be useful with the purpose of monitoring the conditions of the assisted person, ensuring its security. Furthermore the interface with the Virtual Carer could be improved, considering Automatic Speech Recognition (ASR) and Text-To-Speech (TTS) technologies.

Acknowledgments

The work reported in this paper is supported, in part, by OPENMOB srl.

References


Electrocardiography Recognition Based on Wavelet Filter and EM Algorithms

Xingjia Lu¹ Yong Lin¹ and Jianbo Fan¹

School of Sciences, Ningbo University of Technology, Ningbo, 315016, P.R.China.
Shlxj800@gmail.com

Abstract. In this paper, we proposed a heart disease recognition approach which was based on wavelet transform and EM (Expectation Maximization) algorithm using ECG (Electrocardiography) signals. In order to overcome the effect of the traditional Fourier transform, wavelet transform which reserved the features of ECG in different solutions was used to extract the features of ECG. Then, EM algorithm was used to recognize the heart diseases by the features of ECG signals. In the experiments, European ST-T database, Multilead CSE database and MIT-BIH database were trained and tested. The results obtained show that the new approach can improve heart disease recognition and ischemia detection.

1 Introduction

Heart diseases are one of the mortality factors in the developing countries and developed countries recently. Electrocardiography (ECG) is a simple way of obtaining information without invasive methods, which is a series of biomedical signals originating from the actions of the human heart[1]. The human heart operates cyclically pumping blood into the arterial system, which causes bioelectrical variations detectable from human skin. The whole ECG recording consists of several consecutive cardiac cycles, which includes periodic waves and peaks corresponding to the consecutive phases of the heart’s action. Fig.1 displays the cardiac cycle of an ECG signal which includes a QRS complex as its primary and most dominant sub-pattern. Before the QRS complex, there is a P wave in the ECG, and after the QRS complex, there is a T wave which is larger than the P wave. Flat segments between the above-mentioned components are PQ, ST and TP segments. A RR interval is the delay between two consecutive QRS complexes, and the features of ECG give us useful information about the action of the heart[2]. The most important features for the cardiologists are the durations and the amplitudes of the above-mentioned sub-patterns. All of these sub-patterns originate from the specific action of the heart. The P wave of the cardiac cycle corresponds to the depolarization of the atria, the QRS complex to the depolarization of the ventricles and the T wave to the repolarization of the ventricles. By analyzing these sub-patterns, cardiologists can obtain information about the defects of the heart. For instance, if the contraction of the atria is slower than normal, the PQ segments become longer and the duration of the QRS complex becomes wider. By examining RR intervals too low, too high or
too irregular, heart pulse rate can be found. The ECG have much noise with the human body background, changes in the size of the T wave, the deformations of T wave shape and ST slope can be associated with arrhythmia and cardiac infarcts.

ECG signal analysis have been studied by several methods, including HMM training method, Gaussian mixture model and generalized orthogonal forward regression. In such methods, HMM has been applied to ECG analysis, HMM also has been applied successfully to a variety of problems such as gene sequence analysis, speech recognition, computer vision as well as gesture recognition. In this paper, wavelet filter and EM algorithm are proposed to extract wave features and estimate heart diseases through the ECG wave parameters.

![Cardiac Cycle Signal](image1)

**Fig. 1. Cardiac Cycle Signal**

![Atrial Fibrillation](image2)

**Fig. 2. Atrial Fibrillation**
2 Materials and Methods

In heart disease, atrial fibrillation is an irregular heart rate that commonly causes poor blood flow to the body. During atrial fibrillation, the heart’s two upper chambers (the atria) beat chaotically and irregularly out of coordination with the two lower chambers (the ventricles) of the heart (Fig.2).

Atrial fibrillation symptoms include heart palpitations, shortness of breath and weakness. Ventricular tachyarrhythmias include a number of different rhythms, which arise in a number of different clinical situations. The ventricular tachyarrhythmias are fast heart rhythms that arise entirely within the lower chambers of the heart (the ventricles). They are faster than 100 beats per minute by definition. Generally, the tachyarrhythmias can be characterized as either monomorphic ventricular tachycardia or polymorphic ventricular tachycardia.

2.1 Wavelet Transform

Wavelet transform is a time frequency analysis method which differs from traditional short time Fourier transform (STFT) by allowing arbitrarily high localization in time of high frequency signal features[7]. Wavelet transform of a continuous time signal $x(t)$ is defined as:

$$T(a, b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{+\infty} x(t) \Psi^*(t) \psi\left(\frac{t-b}{a}\right) dt$$

where $\Psi^*(t)$ is the complex conjugate of the analysing wavelet function $\Psi(t)$, $a$ is the dilation parameter of the wavelet and $b$ is the location parameter of the wavelet. In order to be classified as a wavelet, a function must satisfy certain mathematical criteria. These are:

(a) It must have finite energy:

$$E = \int_{-\infty}^{+\infty} |\Psi(t)|^2 dt < \infty$$

(b) If $\hat{\Psi}(f)$ is the Fourier transform of $\Psi(t)$, i.e.

$$\hat{\Psi}(f) = \int_{-\infty}^{+\infty} |\Psi(t)| e^{-i(2\pi ft)} dt$$

then the following condition must hold:

$$C_g = \int_{0}^{+\infty} \frac{\hat{\Psi}(f)^2}{f} df < \infty$$

$\Psi(t)$ implies that the wavelet has no zero-frequency component, i.e. $\hat{\Psi}(0) = 0$, or to put it another way, it must have a zero mean. Equation (4) is known as the admissibility condition and $C_g$ is named the admissibility constant. The value of $C_g$ depends on the chosen wavelet.
(c) For complex (or analytic) wavelets, the Fourier transform must be both real and vanish for negative frequencies.

\[ E(a, b) = |T(a, b)|^2 \]  

In practice, all functions which differ from \(|T(a, b)|^2\) by only a constant multiplicative factor are also called scalograms. The important factor to select wavelet refers to the simplicity of the computed wavelet transform coefficients, while having the appropriate and sufficient data about the ECG signal. In this paper Haar wavelet has been selected for feature extraction and analysis shows that extracted features from ECG signal by using the Haar mother wavelet would be suitable and appropriate for the data classification and the computed coefficients can represent morphological differences very well.

In order to compute wavelet coefficient of ECG signals in a specific range of scales, we select haar wavelet to compute coefficient of ECG. The analysis shows that computing coefficient of signals in the range of scales from \(a = 2\) to \(a = 32\), the level of wavelet coefficient have 16 levels. Both noise of signals and the effect of morphological differences can be analyzed and the extracted features would be useful for classification of the signals. Using this range of scales has two advantages: First, by computing wavelet coefficient in the range of \(a = 2\) through \(a = 24\), the ECG signal can be analyzed in detail; Second, by using range of \(a = 12\) through \(a = 16\), the general morphology of the signal and its differences with other types of ECG signals can be highlighted (Fig. 3).

\[ \text{Fig. 3. Wavelet Transform of ECG} \]
2.2 Expectation Maximization

Expectation maximization (EM) algorithm is an iterative method for finding maximum likelihood or maximum a posteriori (MAP) estimation of parameters in statistical models, the model depends on unobserved latent variables. The EM iteration alternates between performing an expectation (E) step, and a maximization (M) step. E step creates a function for the expectation of the log-likelihood evaluated using the current estimate for the parameters and M setp computes parameters maximizing the expected log-likelihood found on the E step. Then, these parameter-estimates are used to determine the distribution of the latent variables in the next E step.

In order to classify the type of heart diseases, we define a stochastic finite state automata, which is a tuple sets \( \lambda = (\pi, A, B) \), where \( \pi \) is a state transition probability, \( A \) is the initial state probability and \( B \) presents the emission probability density function of each state. EM algorithm is used to compute the probability of observing sequence \( O = O_1, O_2, ..., O_T \), \( P(O|\lambda) \) to find the corresponding state sequence that maximizes the probability of the input sequence \( P(Q|O, \lambda) \), and in order to induce the model that maximizes the probability of a given sequence \( P(O|\lambda') > P(O|\lambda) \). ECG signal recognition with EM algorithm require the robust estimation of the transition and emission probabilities distribution parameters. EM algorithm is very sensitive to initialization and also leads to meaningless parameters estimation when the EM converge to the boundary of the parameter space (where the likelihood is unbounded)[8].Using train samples, the parameter values are usually estimated by means of variant of EM algorithm[9].

\[
\gamma_t(i) = P(q_t = s_i | O, \lambda) \quad (6)
\]

\[
\xi_t(i, j) = P(q_t = s_i, q_t + 1 = s_j | O, \lambda) \quad (7)
\]

\[
\xi_t(i, j) = \frac{a_t(i)a_{t+1}b_jO_{t+1}\beta_{t+1}(j)}{P(O|\lambda)} \quad (8)
\]

In equation (6), \( \gamma_t(i) \) represents the conditional probability of the observation and classification, and \( \xi_t(i, j) \) represents the latent variable transform matrix in \( O \) and \( \lambda \) condition. HMMs are established serving as statistical models for distinct pattern classifications, and they have to be evaluated when classifying sequences of observations(Fig-4), \( \lambda \) represents the classification of heart diseases, state sequence is latent variable, and \( O \) represents observation sequence. Using the backward algorithm, the prior probability \( P(O|\lambda) \) of a HMM \( \lambda \) producing the given sequence \( O \) can be calculated. More common is the deployment of the Baum-Welch algorithm, which additionally decodes the most probable state-sequence chosen producing the observations[10]. By means of the technique above, HMM can be estimated and evaluated very efficiently for various applications in different domains.
2.3 Hidden Markov Model

The problem of segmenting an ECG signal with straight-line segments could be stated as a problem of finding the best approximation of an original signal with a continuous broken line[11]. The assumption underlying our method of clustering is that all of the sequences that belong to a cluster are generated by the HMM method and have high probabilities under this HMM. Each cluster is therefore presented by one HMM model, then HMM uses the approach of Baum-Welch to train sample data, producing high probability of observation sequence, all steps follow in equation (9-11).

\[
\gamma_t(i) = \frac{a_t(i)\beta_t(i)}{P(O|\lambda)} = \frac{a_t(i)\beta_t(i)}{\sum_{i=1}^{N} a_t(i)\beta_t(i)} \tag{9}
\]

\[
\gamma_t(i) = \sum_{i=1}^{N} \xi_t(i, j) \tag{10}
\]

\[
Wf(n, j) = \sum_{m=0}^{M-1} f(m) \times \bar{\psi}_j[m - n] \tag{11}
\]

The Wavelet filter EM approach, which is depicted by the following algorithm:

step 1. Training HMM for each sequence \(O_j\), in sample set \(O\), the HMMs are identified by \(\lambda_i\).

step 2. Evaluating model probability to generate the sequence \(O_j\) obtaining a measure matrix \(W_s = P(O|\lambda)\).

step 3. Estimating system states transfer matrix and emission matrix based on observation sequence and states sequence.
HMM exploits the measure which is defined by similarity of expresses between two observation sequences[12]. Through the use of HMM, we are able to recognize a ECG sequence.

3 Experiments

The system is evaluated by using European ST-T database, the multilead CSE database and the MIT-BIH database, each sampling frequency used is 250Hz, 500Hz or 360Hz. The proposed algorithm has been developed by Matlab 7.0. The algorithm is performed on Pentium 4 2.0 Ghz PC computer. In order to examine the effectiveness of the new approach, we compare its performance with that of HMM in terms of error rate. Picking up ECG signal Character by Wavelet method, the experiments pick up the QRS wave after ECG signal pretreatment and inspect the P wave and T wave.

3.1 Evaluation

Evaluating the implementation of the algorithm in Matlab has been verified in terms of sensitivity, specificity, and overall accuracy. The Wavelet filter EM algorithm is following three steps: The first step employ the ECG database. It contains 250 two-channel records of 10 min ECG, at the sampling frequency of 250 Hz. The first channel of all recordings is used to evaluate waveform detection, since the database provides at least 3000 labels of each waveform made by a cardiologist. The second step is ischemia detection, which is performed on a subset of 48 two-channel records from the ST-T database. Each record is 2 hours long, with a sampling frequency of 250 Hz frequency, and contains annotations of the ST and T episodes made manually by cardiologist team. The episodes are indicated according to the channel where they appear. The third step is multi-channel fusion, the episodes of each channel are merged through a Boolean logic operation, giving a total of 120 episodes. The performance of experiments is evaluated through three criteria: Sensitivity(Se)is related to the fraction of events correctly detected, which means

\[
Se = \frac{TP}{TP + FN} \tag{12}
\]

where TP (true positive) is the number of matched events and FN (false negative) is the number of events that are not detected by the approach. Specificity(Sp) gives the ability of detecting true events, and is defined as

\[
Sp = \frac{TP}{TP + FP} \tag{13}
\]

where FP (false positive) is the number of events detected by the approach and do not match with the manual labels. The overall accuracy is the the total number of ECG correctly recognize. The results are presented in terms of average statistics, in which every recording is assigned equal weights.
3.2 Results

The performances of algorithm corresponding to specificity, sensitivity and accuracy are presented in Tables 1 and 2 respectively. The results presented are associated to four different implementations: Non-adapted implementation, where the models are not adapted; Andreao, which corresponds to the adaptation scheme; Incremental EM and Wavelet transform EM, which are the approaches developed in this work and whose theoretical aspects are presented in the previous section.

### Table 1. Performance of Non-adapted and Adreao methods

<table>
<thead>
<tr>
<th></th>
<th>Non-adapted EM</th>
<th>Adreao</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity (%)</td>
<td>86.9</td>
<td>88.9</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>93.2</td>
<td>91.51</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>90.1</td>
<td>90.63</td>
</tr>
</tbody>
</table>

Results of Table 1 show that a meaningful performance improvement when comparing the adapted approaches to the non-adapted, as expected. In addition, in some cases the performance of the approach named Andreao is equivalent to, or even a little better than, those corresponding to the incremental approaches, although being a non-incremental one.

### Table 2. Performance of Incremental EM and Wavelet filter EM methods

<table>
<thead>
<tr>
<th></th>
<th>Incremental EM</th>
<th>Wavelet filter EM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity (%)</td>
<td>84.03</td>
<td>89.7</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>93.62</td>
<td>95.6</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>92.17</td>
<td>93.3</td>
</tr>
</tbody>
</table>

To see the heart diseases recognition results, we compare the receiver operating characteristics (ROC) curve to four kinds of ECG recognition[13]. Area under an ROC curve (AUC) is a common method to calculate the integration of ROC curve, because the AUC is a portion of the area of unit squares, its value will always between 0 and 1.0. Fig.5 shows ROC curve of four ECG signal recognize method. Wavelet transform EM algorithm performance have bigger area than other methods.

4 Conclusion

In this paper, we recognized ECG signals with wavelet transform and EM algorithm, and found that a suitable number of states. We are able to classify from
training data accurately. The key ideas is to use Haar wavelet to extract features to increase numbers of sample, as well as to increase prediction accuracy. The algorithm solves the major problems of the heart disease pattern recognition: Firstly, the ECG signals can be trained without the use of prior information; Secondly, algorithm produces probability values of heart disease. Finally, we use ROC curve to measure algorithm’s sensitivity and specificity, and use AUC to measure recognized results, which gives more accurate ratio than binary decision. Compared with other three methods, the approach proposed in the paper has better specificity and sensitivity. However, if wavelet coefficient between two distribution is very near to each other, the algorithm does not discriminate the signal well. In the condition of low probability, we may increase the training data set, which can increase the algorithm accurately.

5 Acknowledgments

This work is supported by NingBo Natural Science Foundation (Funding No.2012A610020), Scientific Research Fund of Zhejiang Provincial Education Department (Funding No.Y201225208).

References


A Multi-Agent Architecture for Health Information Systems

Luca Palazzo, Paolo Sernani, Andrea Claudi, Gianluca Dolcini, Gianluigi Biancucci, Aldo Franco Dragoni
{l.palazzo, p.sernani, a.claudi, g.dolcini, g.biancucci, a.f.dragoni}@univpm.it
Dipartimento di Ingneria dell’Informazione (DII)
Università Politecnica delle Marche
Via Brecce Bianche 60131 Ancona, Italy

Abstract

The healthcare domain is wide and characterized by system and data herogeneity. To achieve high quality and efficiency standards, interoperability between different information systems is strongly required. The aim of this paper is to propose an agent oriented architecture to address this kind of issues, which is compliant with the European Union (EU) guidelines and with requirements issued by the Italian Ministry of Health. To validate and to show the capabilities of our system, we developed on such architecture a typical emergency-response scenario, where a first aid medical staff urgently needs to retrieve, through mobile devices, the Patient Summary (PS) of a citizen, which is part of his Electronic Health Record (EHR).

Keywords

Health Information Systems, Interoperability, Multi-Agent Systems, Patient Summary (PS), Electronic Health Record (EHR), HL7 CDA.

Introduction

The healthcare domain is facing a growing number of challenges. The incidence of medical errors is rising; many medical facilities are understaffed, and serve increasingly large areas; healthcare costs are rising more and more. The healthcare budgets are shrinking in many countries, and healthcare facilities are under pressure to provide better services with less resources (Varshney, 2003). Health Information Systems (HIS) are at the heart of all these challenges. They can provide a better coordination among medical professionals and facilities, thus reducing the number and incidence of medical errors. In the same time, they can reduce healthcare costs and may provide a means to improve the management of hospitals (Haux, 2006). Unfortunately, due to the inherent complexity of their application domain, HIS are fragmented in various systems that hardly make use of communication standards, process definition protocols and homogeneous data representations. Much of the research in this field is aimed to address these problems, and different solutions have been proposed during the last years.
Related Works

In recent years, two different technologies have been the subject of much of the research relating to HIS: cloud computing and multi-agent systems. A mobile system that enables electronic healthcare data storage, update and retrieval using Cloud Computing is proposed in (Doukas, Pliakas, & Maglogiannis, 2010), in which a mobile application based on an Android client enables the users to retrieve remotely health information and images. In (Rolim et al., 2010) a wireless sensor network is used to automate the data collection process. The collected information are distributed through a Cloud Computing solution to medical staff. An alternative approach is proposed in (Koufi, Malamateniou, & Vassilacopoulos, 2009), where data and service interoperability is obtained through a distributed and agent-oriented system. Finally, (Capozzi & Lanzola, 2010) and (Lyell & Liu, 2012) use the multi-agent system technology to support the home-care monitoring and treatment of patients.

Our Contribution

In this paper we propose an agent oriented architecture capable to access geographically distributed data to allow health professionals to retrieve/update any patient's record efficiently and reliably. Such architecture meets the interoperability requirements among different health facilities and, at the same time, integrates with existing legacy systems (including local databases), being a new software layer on top of existing ones: this allows to protect the investments made by facilities and institutions as required by ministerial directives (Ferronato, Lotti, & Berardi, 2006), in addition to address interoperability issues.

The main advantages of such architecture are:

- **Distribution.** A key concept of agent technology is flexibility: the complex issues of interoperability and integration with existing systems is broken down to minor tasks assigned to individual agents: cooperation is the solution to the original question. Retrieving data is possible from any point in the territory just through communication of distributed agents, and expensive infrastructures - as happens with Cloud solutions - are not required.

- **High modularity.** Thanks to standardization activities made by the multi-agent systems (MAS) community - FIPA IEEE -, simply adding new agents in the architecture (registering their services and sharing the same ontology) is enough in order to extend the capabilities of the system.

- **Robustness.** An agent oriented infrastructure provides many recovery techniques to better achieve fault tolerance goals.

- **Integration with existing systems.** With the aid of wrapper agents, each one designed for a particular instance of legacy information systems, the architecture represents a higher fully interoperable software layer. Communication at this level is readily able to use well established standard ontologies for messaging.
(HL7), definition of clinical documents (HL7 CDA), scheduled workflows (IHE) and health care terminologies (such as LOINC and SNOMED CT).

Paper Structure

The rest of this paper is organized as follow: next section details the multi-agent system architecture; then an implementation related to an emergency-response scenario is illustrated; in conclusion the results are discussed.

Infrastructure

The agent oriented architecture is expressed by three levels of abstraction, named local platform, district platform and client platform (Fig. 1-2): each one is characterized by its specific agents and resources as described in the next subsections. The discriminating factor between the first two layers is of administrative nature: there is a local platform for each health facilities in the territory (e.g., a hospital); facilities refers to administrative districts, which constitute the second layer of the architecture; finally, the client level is represented by any software agent which needs to login to the infrastructure to retrieve documents or insert/update a patient’s health record.

![Diagram of Infrastructure](image)

**Figure 1.** The global architecture is structured in three logic layers.

Local Platform

There is a local platform (Fig. 3) for each health facility. It has the role to interface with any information system, currently present in the structure, committed to the management of clinical documents (create, edit, search, access) and the scheduling of different departments in the facility. Every local platform needs to know the address of its referring district platform in order to have access to the entire agent infrastructure.

**LocalDBWrapper.** The task of such agents is to interface with the databases of a certain local healthcare institution. The advantages in the use of wrapping agents are the following:
Figure 2. Relation between local platforms and their referring district platform.

- All the legacy systems would not be modified or replaced, but in fact encapsulated within such agents. In this way, any external agent, which needs to access to data contained by a local database, will be able to obtain them simply by communicating with the referring LocalDBWrapper agent, thus avoiding direct interaction with legacy systems.

- It makes possible to abstract the actual data representation within the different information systems available in the various facilities. With this solution, we don't need to address issues like information conflicts (such as homonymy and synonymy) or data schema inconsistencies by burdensome techniques of renaming, restructuring or even system redesign; it is sufficient to design a wrapping agent for each different legacy system able to translate the internal data representation in the ontology shared by all the agents in the infrastructure.

In order to add a local platform to the entire agent oriented architecture, the LocalDBWrapper agents must register to DF_Intra-District agent of their referring district platform: this makes it available from distributed and remote agents, which need to retrieve data contained by the local structure.
**DocumentHandler.** This kind of agents are able to access the content of a specific clinical document produced within the facility, such as clinical reports, laboratory tests, prescriptions, etc. In general, a DocumentHandler is contacted by a client agent to get health records managed by it: the DocumentHandler agent locates the requested document through its unique identifier, obtains it from the clinical repository and translates the information in an outgoing message towards the requesting client agent. Hence, the latter will be able to get the contents of clinical data requested.

**Service Agents.** This set consists of agents for the management of different departments of the healthcare structure (e.g., radiology, cardiology, analysis laboratory, etc.). This paper does not provide further information on this field, but it is possible to find details about an agent oriented implementation of the Radiology Scheduled Workflow provided by Integrated the Healthcare Enterprise (IHE) consortium in (Palazzo, Dragoni, Claudi, & Dolcini, 2012).

**District Platform**

The main task of a district platform (Fig. 4) is to encapsulate all the local platforms that administratively belong to it. Basically, the district platforms represent the logic layer which composes the final architecture and allows to achieve the interoperability goal of our distributed system: every district platforms, therefore, must know each other their address.

**DistrictDBWrapper.** These agents have similar functions with local wrappers: they manage data within district databases. The gateway agent contacts wrappers in order to store or retrieve any reference to a patient's clinical records, which have been produced by every local platform in the territory or by general practitioners.

**DocumentHandler.** DocumentHandler agents manage those kind of documents which are of administrative competence of a district, such as EHR and Patient Summary (Ciampi, De Pietro, Esposito, Sicuranza, & Donzelli, 2012). They may refer to health records which are distributed in different local platforms: the Gateway agent has the role to look for and gather this information.
Gateway. The Gateway agent catches the client requests and makes queries to local and district wrappers to retrieve data about any distributed health record of a citizen (Fig. 5). It returns the addresses of DocumentHandler agents which the client must contact to get the required documents. To accomplish this task, the gateway performs two basic activities:

- When it retrieves the distributed data required to fulfill a client request, it must integrate them into a data structure, so that the client can handle a single dataset.

- When a clinical record is produced within a district for a patient belonging to another district, the former gateway must inform the latter one to make its referring DistrictDBWrapper agent register such event in its own district database.

Init. During the starting phase of the district platform, the Init agent registers the same platform Gateway to all the active DF_Inter-district agents of the remote district platforms in the territory.

DF_Inter-district. As we just said, it is the Directory Facilitator in which all the remote Gateways are registered. This allows a single Gateway to communicate with any other distributed gateway in the entire infrastructure.

DF_Intra-district. This Directory Facilitator contains all the LocalDBWrapper agents registrations of the local platforms belonging to the same district.
Figure 5. The Gateway agent retrieves the ubication of health records within the system.
**LoginServer.** Its task is to establish a secure connection with the client that wants to access to the infrastructure to retrieve data in a specified district.

**Client Platform**

This logic platform contains client applications, which may be any agent oriented software that is able, after a login phase, to access data through the connection with a district gateway agent. Examples of client applications could be: software to access Electronic Health Record (EHR), both by medical staff and citizens, mobile applications to retrieve the Patient Summary for emergency situations, software to update health records by general practitioners, etc.

**Scenario**

To show the capabilities of this architecture we assumed a scenario where an emergency doctor urgently needs to consult a patient's health records, in particular his patient summary. According to the EU definition, a patient summary is a clinical document that is digitally stored in repositories with cumulative indexing systems and secure access by authorised people. It is an HL7 CDA compliant document, contained in the patient's EHR, whose purpose is to summarize a patient's clinical history and his current situation.

In short, the main Patient Summary's use cases can be summed up in (Italian Health Ministry, 2010):

- Emergency situations in which the patient may not give an exhaustive description about his clinical history (problems, allergies, current medicines, etc.).
- Reliability of the information flows between family doctor and health facilities.
- Patients affected by chronic deseases managed by several specialists or elderly in home care regime.
- Diagnostic process support, telemedicine, etc.

Finally, the Patient Summary contains both mandatory and optional fields, and it is expressed through XML markup language.

To build such scenario we used:

- Jade Framework  (Bellifemine, Caire, & Greenwood, 2007) to develop local and district agents in some desktop computers.
- An android smartphone application to simulate the client agent, developed with Jade Leap addon.
Ministerial directives to compose a Patient Summary for our experiment, an XML parser and an agent ontology based on HL7 concepts.

The operating mode is very simple (Fig. 6). First of all, the mobile client application log in to the district platform entering its username and password: a secure connection is established with the platform using TSL protocol to ensure secure access to patients' personal and sensitive data. Then, the client asks for a citizen's Patient Summary and its relative health records by typing his tax code: the Gateway agent will query the different distributed entities to find the ubication of required data and inform the client where it can retrieve health records. Finally, the client application gather this data asking directly to DocumentHandler agents of the platforms which hold the patient's records.

Figure 6. The client agent queries the infrastructure for a citizen's health records.

Conclusion

In health information systems, the importance of addressing interoperability issues among existing systems is widely recognized. A crucial aspect is to allow health professionals to get any information they need about a patient in a pervasive and reliable way, even if these data are distributed in technically and geographically different health information systems.

To meet these requirements, in this paper we proposed an architecture based on multi-agent systems technology that takes advantage of the adoption of established standards for the management of clinical documents. Our goal was to show how MAS features can improve HIS in terms of interoperability, reliability, modularity and robustness; and
how health professionals - and thus citizens - could benefit from this efficient distributed system.

References


Towards Evidence-Based Decision Support Systems

Raphael Bahati
Raphael.Bahati@lawsonresearch.com
I-THINK Research, Lawson Health Research Institute

Femida Gwadry-Sridhar
Femida.Gwadry-Sridhar@lhsc.on.ca
I-THINK Research, Lawson Health Research Institute

Abstract

Patients with diabetes continue to encounter ongoing morbidity and diminished health-related quality of life despite the advances in evidence-based therapies. One of the reasons for this diminished benefit from therapy is medication non-adherence. Considerable evidence has shown that a combination of therapeutic lifestyle changes (increased exercise and diet modification) and drug treatment can control and, if detected early enough, even prevent the development of diabetes and its harmful effects on health. Understanding the influential factors in diabetes is one way to address the problem.

This paper presents an approach utilizing both data analytics and visualization to help diabetes patients improve adherence to medication. Patient engagement has been shown to help improve adherence. Visualization is one such way of facilitating patient engagement. Our approach has two core building blocks: (1) Data analytics combining several statistical and machine learning models, founded under different principles and clinical assumptions, into a single meta-model for predicting adherence. The aim is to create superior models for behavior prediction — knowledge that can help preempt non-adherence. (2) Incorporating data analysis and visualization into decision support tools that can intelligently interact with participants by alerting them to important data correlations. Such tools could provide useful patient feedback, either directly to the patient or a health care provider, where risks for medication non-adherence are visualized and interpreted. The benefit of these types of targeted approaches is that appropriate resources can be directed to those who need adherence support the most.
Keywords

Type 2 diabetes, adherence to medication, machine learning, artificial neural networks, evidence-based system, visualization tools

1 Introduction

Diabetes is an epidemic affecting a projected 366 million people by 2030 (Wild, 2004). In the U.S. alone, diabetes affects 25.8 million people (CDC, 2011). Diabetes is a major cause of heart disease and stroke, and is the leading cause of kidney failure and non-traumatic lower limb amputations among American adults (CDC, 2011). Despite the fact that type 2 diabetes is treatable and reversible with appropriate management, medication non-adherence remains a spanner in the works for diabetes treatment. In order to be clinically effective, diabetes - for which 95% of care is self-management by patients - requires constant adherence to treatment strategies (Funnell, 2000). These treatment strategies include physical exercise, healthy diet, low alcohol intake, medication, no smoking, and glucose monitoring (Cramer, 2004). Current evidence shows patient blood glucose and HbA1c control rates are less than ideal (Scott, 2004; Ralston, 2004). Research on diabetes treatment adherence is crucial as improved adherence was found to be associated with improved glycemic control and decreased health care resource utilization (Asche, 2011).

Adherence refers to the degree to which a patient follows medical advice on how to take diabetes medication. Medication possession ratio (MPR), which calculates the percentage of time a patient has access to medication, is often used to measure adherence behavior. According to guidelines (Cramer, 2008), on average an MPR < 80% is considered non-adherence. The importance of adherence stems from the relationship between maintenance of HbA1c levels, progression of disease, and adverse health outcomes. Multiple factors have been said to influence diabetes medication adherence. These range from intentional non-adherence behavior to non-intentional behavior. Regardless of patient’s intention to take medication, data suggest that patients who are non-adhering to medication use are influenced by either non-modifiable factors such as age, gender and ethnicity or by modifiable factors such as social support, health literacy, comorbid conditions, duration of disease, complexity of treatment, socio-economic status, and/or social prejudice (Cramer, 2004; Fukunaga, 2011). While studies have been done that measured physiological and demographic determinants, rarely have they investigated the dynamic interplay of candidate influences (those with direct and indirect effect) on diabetes.

Feedback through information visualization has been shown to promote behavior changes (Shneiderman, 2013). Visualization enables users to engage while exploring and learning about their environment. In this paper, we present an approach leveraging the power of analytics and visualization to help patients improve adherence. We begin in Section 2 with a description of the analytical approach, which make use of patients’ demographic, history of medication use, and other treatment characteristics to derive
meta-models for predicting adherence. In Section 3, we present the results of the analysis examining 6,878 patients prescribed medication to treat type 2 diabetes. Section 4 outlines how, through visualization, these results could be translated into patient-centered decision-support tools.

2 Analytical Approach

In this section, we present an approach utilizing machine-learning techniques to determine predictors of adherence/non-adherence behavior among patients prescribed diabetes medication. A variety of computer models exist in the area of machine learning and statistics that can be used to predict clinical outcomes. In this paper, our focus is on the use of Clustering and Artificial Neural Networks (ANN) models, which have been shown to be useful tools in the medical domain (Kanner, 2009; Hamou, 2010). It has been shown that the predictive accuracy of each model tends to vary significantly from one dataset to another. For example, while the ANN model may outperform a regression model in one setting, the latter could be more accurate in predicting adherence in another setting. It is this inconsistency that illustrates the main motivation for the approach proposed in this paper; i.e., how to aggregate the predictive power of multiple models into a single model.

Our approach consisted of the following key steps. Firstly, we utilized data clustering techniques to assign patients to subgroups (or clusters), each consisting of patients with similar characteristics. This enabled us to examine the accuracy of the different approaches for predicting adherence within each group, revealing additional insights into the effectiveness and limitations of each methodology. Secondly, we modelled the influence of patients’ demographic and treatment characteristics using a meta-model derived from ANN and Logistic Regression approaches to help identify predictors of adherence/non-adherence behavior.

Data Source

In this study, we analyzed data from 6,878 patients from US who were prescribed medication to treat type 2 diabetes. We created the dataset by merging cohort (demographics information), US Census information (such as ethnicity and education attainment on Zip code level), baseline (patient characteristics and pharmacy-related characteristics, co-morbidity indicators), and outcomes (adherence and persistence of medication). The mean age (SD) of patients was 59.53 (11.24), with 56.59% male, and an overall adherence rate (MPR $\geq 80\%$) of 60.51\%.

Modelling Adherence

An ANN is a mathematical model designed to mimic the functionality of the brain (Anderson, 2001). It can be thought of as an adaptive parallel distributed processor capable of modelling non-linear relationships between input and output parameters. In
the context of the current study, the different demographic, treatment, and patient medication usage characteristics would constitute input parameters whereas medication adherence behavior (i.e., adherence versus non-adherence to medication) would constitute output parameters. Many different types and architectures of neural networks, each with different approaches to learning, exist (Basheer, 2000; Penny, 1996). In the simplest form, an ANN model consists of an interconnected set of nodes (neurons) comprising of an input layer, a hidden layer, and an output layer as illustrated in Figure 1. The hidden layer, in particular, is necessary to handle problems with nonlinearity and complexity. Though a model could have multiple hidden layers, one is often sufficient to handle complex problems. This is the architecture adopted for this study.

Figure 1. A neural network model for adherence: modelling variables' impact on adherence to prescription medication.

We also utilized the Expectation Maximization (EM) clustering algorithm (Dempster, 1977) to assign patients to groups based on demographics, medication utilization, and adherence information. EM utilizes Gaussian mixture components as a basis for the models. In this paper, a v-fold cross-validation technique was used to estimate $k$; i.e., the optimal number of groups (or clusters) in the sample. Research has shown that this technique is very accurate at evaluating how results from the analysis of a sample could be generalized to an independent data set. In our previous work, for example, we successfully demonstrated how data clustering techniques can be utilized to model and predict disease outcomes, which have shown great potential in assessing disease progression in Alzheimer’s (Hamou, 2010). In the sections that follow, we demonstrate how the results from clustering could also help devise patient-centered strategies for improving medication adherence for diabetes patients.
3 Analysis Results

Table 2 summarizes the results of EM clustering across the predictors of medication adherence (see Figure 2). A logistic regression model and a neural network model (fixed learning rate = 0.3, momentum = 0.2, iterations = 2000) with 38 input parameters, 21 hidden nodes, and MPR as output parameters (see Figure 1) were applied to each cluster. Of the 6 clusters, the ANN model was consistently more accurate (i.e., had higher ROC Area) than the regression model in predicting adherence behavior among diabetes patients. Note, however, that while the ANN model outperformed the regression model in Cluster3, the latter was more accurate in prediction adherence behavior (MPR≥80). It is this inconsistency that illustrates the main motivation for the approach proposed next.

Our strategy involved developing a meta-model that aggregates the predictive power of both the Regression and the ANN model to help predict adherence/non-adherence behavior. The approach, in particular, utilizes prediction probabilities of both models in classifying patients as either adhering or non-adhering in computing an aggregate weight to be used for classification. Our strategy for prediction was based on the following:

- In the simplest case where both the regression and the ANN model predicted the same outcome for a particular patient, our meta-model also predicted the same outcome.

- In the case that the two models predicted different outcomes for the same patient, we applied prediction weights of each model to determine which outcome provided the most accurate prediction.

Sensitivity analysis was then performed to identify variables with significant impact on the meta-model’s accuracy. Briefly, the process involved the following steps: First, input variables were removed from the model, one at a time, while observing their impact on the model’s error. This process was repeated for all input variables while recording the classification output. Second, variables were ranked according to importance, with those having an impact greater than the initial model error identified as predictors of adherence/non-adherence behavior.

The results of the sensitivity analysis are summarized in Figure 2. The analysis confirms that age, gender, and race are significant predictors of adherence. The level of education also ranked relatively high in sensitivity analysis. Finally, other factors including previous use of diabetes medication, whether a patient is insured or not, and distance to a pharmacy were significant predictors of adherence to medication. These findings are aligned with the literature (Cramer, 2004; Fukunaga, 2011).
Figure 2. Factors affecting medication adherence; y-axis measures the classification error when a variable is omitted.

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Cluster0</th>
<th>Cluster1</th>
<th>Cluster2</th>
<th>Cluster3</th>
<th>Cluster4</th>
<th>Cluster5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Demographic and patient treatment characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>3919</td>
<td>618</td>
<td>804</td>
<td>724</td>
<td>444</td>
<td>369</td>
</tr>
<tr>
<td>Age: mean (SD)</td>
<td>59.39 (10.22)</td>
<td>59.95 (10.99)</td>
<td>56.40 (12.31)</td>
<td>55.16 (8.87)</td>
<td>58.16 (10.73)</td>
<td>77.39 (6.48)</td>
</tr>
<tr>
<td>Gender: (M/F)</td>
<td>61.98%</td>
<td>57.28%</td>
<td>45.90%</td>
<td>61.33%</td>
<td>72.75%</td>
<td>17.34%</td>
</tr>
<tr>
<td>Percentage Race: mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>6.59 (0)</td>
<td>7.35 (0)</td>
<td>30.41 (0)</td>
<td>8.54 (2.94)</td>
<td>16.82 (5.05)</td>
<td>6.59 (0)</td>
</tr>
<tr>
<td>Indian</td>
<td>0.53 (0)</td>
<td>0.83 (0)</td>
<td>0.99 (0)</td>
<td>0.47 (0.39)</td>
<td>0.42 (0.04)</td>
<td>0.53 (0)</td>
</tr>
<tr>
<td>Pharmacy Access: mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miles to the pharmacy</td>
<td>2.10 (2.37)</td>
<td>2.13 (2.61)</td>
<td>1.35 (1.74)</td>
<td>1.46 (1.81)</td>
<td>1.86 (2.43)</td>
<td>1.26 (1.63)</td>
</tr>
<tr>
<td>Pharmacy count within 15 miles</td>
<td>136.98 (158.49)</td>
<td>130.09 (104.95)</td>
<td>159.12 (204.80)</td>
<td>137.78 (107.48)</td>
<td>474.09 (721.50)</td>
<td>225.20 (198.25)</td>
</tr>
<tr>
<td>Pharmacy Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>42.20%</td>
<td>27.51%</td>
<td>32.59%</td>
<td>24.31%</td>
<td>31.08%</td>
<td>45.26%</td>
</tr>
<tr>
<td>Chain</td>
<td>53.35%</td>
<td>67.64%</td>
<td>61.69%</td>
<td>67.96%</td>
<td>67.79%</td>
<td>49.86%</td>
</tr>
<tr>
<td>Franchise</td>
<td>3.29%</td>
<td>0%</td>
<td>0.62%</td>
<td>0.14%</td>
<td>0.45%</td>
<td>4.34%</td>
</tr>
<tr>
<td>Government</td>
<td>0.08%</td>
<td>0.32%</td>
<td>2.86%</td>
<td>3.45%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Alternative</td>
<td>1.07%</td>
<td>4.53%</td>
<td>2.24%</td>
<td>4.14%</td>
<td>0.68%</td>
<td>0.54%</td>
</tr>
<tr>
<td>Specialty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Practice</td>
<td>45.90%</td>
<td>53.55%</td>
<td>64.77%</td>
<td>29.70%</td>
<td>28.82%</td>
<td>28.18%</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>31.28%</td>
<td>26.86%</td>
<td>23.63%</td>
<td>29.14%</td>
<td>37.39%</td>
<td>44.99%</td>
</tr>
<tr>
<td>Endocrinology</td>
<td>2.67%</td>
<td>4.21%</td>
<td>3.11%</td>
<td>10.77%</td>
<td>3.83%</td>
<td>2.98%</td>
</tr>
<tr>
<td>Emergency Medicine</td>
<td>2.24%</td>
<td>2.43%</td>
<td>3.11%</td>
<td>1.80%</td>
<td>4.28%</td>
<td>2.17%</td>
</tr>
<tr>
<td>Other</td>
<td>14.31%</td>
<td>11.49%</td>
<td>16.29%</td>
<td>23.07%</td>
<td>16.67%</td>
<td>16.53%</td>
</tr>
<tr>
<td>Unknown</td>
<td>3.57%</td>
<td>1.46%</td>
<td>7.09%</td>
<td>5.52%</td>
<td>9.01%</td>
<td>5.15%</td>
</tr>
<tr>
<td>Percentage Education Attained: mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than grade 9</td>
<td>3.83 (0)</td>
<td>4.11 (0)</td>
<td>8.24 (0)</td>
<td>4.32 (0.24)</td>
<td>6.61 (0.80)</td>
<td>3.83 (0)</td>
</tr>
<tr>
<td>Professional Degree</td>
<td>5.53 (0)</td>
<td>5.33 (0)</td>
<td>5.03 (0)</td>
<td>7.67 (1.64)</td>
<td>5.48 (0.34)</td>
<td>5.53 (0)</td>
</tr>
</tbody>
</table>
### 2. Medication measures in 180-day baseline period

<table>
<thead>
<tr>
<th>Comorbid diseases</th>
<th>Infection (Yes)</th>
<th>Hypertension (Yes)</th>
<th>Lipid Irregularity (Yes)</th>
<th>Dermatology (Yes)</th>
<th>Previous patterns of diabetes medication use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>34.65%</td>
<td>82.65%</td>
<td>73.13%</td>
<td>12.93%</td>
<td>Naïve0</td>
</tr>
<tr>
<td></td>
<td>28.32%</td>
<td>84.14%</td>
<td>71.84%</td>
<td>11.33%</td>
<td>85.69%</td>
</tr>
<tr>
<td></td>
<td>31.71%</td>
<td>77.23%</td>
<td>65.17%</td>
<td>15.79%</td>
<td>86.41%</td>
</tr>
<tr>
<td></td>
<td>33.28%</td>
<td>75.82%</td>
<td>71.27%</td>
<td>16.30%</td>
<td>81.72%</td>
</tr>
<tr>
<td></td>
<td>33.56%</td>
<td>77.48%</td>
<td>65.77%</td>
<td>18.24%</td>
<td>87.85%</td>
</tr>
<tr>
<td></td>
<td>41.46%</td>
<td>93.50%</td>
<td>71.81%</td>
<td>27.91%</td>
<td>79.80%</td>
</tr>
<tr>
<td><strong>Infection (Yes)</strong></td>
<td><strong>34.65%</strong></td>
<td><strong>82.65%</strong></td>
<td><strong>73.13%</strong></td>
<td><strong>12.93%</strong></td>
<td><strong>85.69%</strong></td>
</tr>
<tr>
<td><strong>Hypertension (Yes)</strong></td>
<td><strong>28.32%</strong></td>
<td><strong>84.14%</strong></td>
<td><strong>71.84%</strong></td>
<td><strong>11.33%</strong></td>
<td><strong>86.41%</strong></td>
</tr>
<tr>
<td><strong>Lipid Irregularity (Yes)</strong></td>
<td><strong>31.71%</strong></td>
<td><strong>77.23%</strong></td>
<td><strong>65.17%</strong></td>
<td><strong>15.79%</strong></td>
<td><strong>81.72%</strong></td>
</tr>
<tr>
<td><strong>Dermatology (Yes)</strong></td>
<td><strong>33.28%</strong></td>
<td><strong>75.82%</strong></td>
<td><strong>71.27%</strong></td>
<td><strong>16.30%</strong></td>
<td><strong>87.85%</strong></td>
</tr>
<tr>
<td><strong>Previous patterns of diabetes medication use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>79.80%</strong></td>
</tr>
</tbody>
</table>

### 3. Utilization measures in the follow-up

| Behavioral Health (Yes) | 11.96%          | 8.57%             | 11.32%                   | 14.36%            | 10.36%                                      | 24.39%                                      |

### 4. Medication adherence

<table>
<thead>
<tr>
<th>Medication possession ratio (MPR)</th>
<th>Adherence: MPR ≥ 80%</th>
<th>Non-adherence: MPR&lt;80%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>63.69%</td>
<td>36.31%</td>
</tr>
<tr>
<td></td>
<td>66.02%</td>
<td>33.98%</td>
</tr>
<tr>
<td></td>
<td>49.25%</td>
<td>50.75%</td>
</tr>
<tr>
<td></td>
<td>60.08%</td>
<td>39.92%</td>
</tr>
<tr>
<td></td>
<td>50.90%</td>
<td>49.10%</td>
</tr>
<tr>
<td></td>
<td>54.47%</td>
<td>45.53%</td>
</tr>
</tbody>
</table>

### 5. Classification Accuracy

<table>
<thead>
<tr>
<th>Model</th>
<th>Adherence: MPR≥80%</th>
<th>Non-adherence: MPR&lt;80%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANN Model (ROC Area)</strong></td>
<td>0.972</td>
<td>99.3%</td>
</tr>
<tr>
<td></td>
<td>0.972</td>
<td>99.3%</td>
</tr>
<tr>
<td></td>
<td>0.965</td>
<td>86.9%</td>
</tr>
<tr>
<td></td>
<td>0.946</td>
<td>93.3%</td>
</tr>
<tr>
<td></td>
<td>0.991</td>
<td>99.6%</td>
</tr>
<tr>
<td></td>
<td>0.995</td>
<td>98%</td>
</tr>
<tr>
<td><strong>Log. Regression (ROC Area)</strong></td>
<td>0.654</td>
<td>85.7%</td>
</tr>
<tr>
<td></td>
<td>0.665</td>
<td>85.7%</td>
</tr>
<tr>
<td></td>
<td>0.679</td>
<td>93.1%</td>
</tr>
<tr>
<td></td>
<td>0.619</td>
<td>96.9%</td>
</tr>
<tr>
<td></td>
<td>0.711</td>
<td>98.2%</td>
</tr>
<tr>
<td></td>
<td>1.01</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model</th>
<th>Adherence: MPR≥80%</th>
<th>Non-adherence: MPR&lt;80%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANN Model (ROC Area)</strong></td>
<td>91.1%</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>93.4%</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td>66.4%</td>
<td>58.8%</td>
</tr>
<tr>
<td></td>
<td>97.3%</td>
<td>27.3%</td>
</tr>
<tr>
<td></td>
<td>74.3%</td>
<td>67.9%</td>
</tr>
<tr>
<td></td>
<td>89.1%</td>
<td>29.2%</td>
</tr>
</tbody>
</table>

### Table 1. EM Clustering with classification accuracy for Regression and ANN.

### 4 Personalized Feedback

We foresee using this approach in the development of visualization tools leveraging the power of mobile technologies to facilitate meaningful interactions between existing data and its users. The key promise is the opportunity for a timely discovery of relevant information where intelligent tools would simplify and accelerate the analysis of data collected from existing as well as new patients and intelligently interact with users by alerting them to any interesting correlations and relationships in the data. Figure 3 below illustrates how data analysis and visualization could be incorporated into patient-centered decision-support tools.

**Inputs:** The initial stage of the process involves data collection. Mobile devices such as smart phones and iPads could be used to collect relevant information during a doctor-patient interaction. In the context of medication adherence, this information may, for example, include demographic characteristics (i.e., gender, race, education), history of medication use, barriers to medication use and other relevant information, which could be used to classify patients based on risk factors. As such, the collected information forms the input of the decision-making component.

**Decision-Making:** The second stage involves using the information collected from the initial stage to predict patients’ adherence behavior. This process includes the following: (1) utilize the meta-model (derived from the existing dataset - see Section 3) to help
predict whether or not the patient is likely to adhere to medication; (2) use an ANN model trained to predict cluster assignments to determine which cluster (among the six clusters in Table 2) the current patient belongs. Unique patients’ characteristics within each cluster likely suggest that different intervention strategies might be needed to help preempt non-adherence behavior. Having models from the pre-processed datasets to work with would speed up this process, allowing for quick grouping of patients based on risk to non-adherence to medication.

Figure 3. A data flow model incorporating analytics and visualization into decision support tools.

**Outputs:** The final step in the process involves providing feedback to users through alerts and notifications. Visualization tools could provide feedback indicating, for example, a high-risk to medication non-adherence, as well as the most effective strategy for preempting the bad behavior, in which case appropriate resources could be directed to those who need help the most. In the context of the approach discussed in Section 2, adherence rates within clusters, for example, could help identify which groups of patients have higher likelihood of non-adherence to medication based on patients’ initial classification. Unique characteristics distinguishing one cluster from another (see highlighted features in Table 2) could also help devise a strategy for helping a patient improve his/her adherence behavior. For example, we know from the results of cluster analysis that a patient belonging to Cluster2 is likely to be least educated (8.24% with less than grade9 education) Hispanic individual (30.41%) with best access to a Family Practice (64.77%). On the other hand, a patient belonging to Cluster5 is likely to be an old (mean age, 77.39) female (82.66%) living closest to a pharmacy (mean miles to pharmacy, 1.26), has the worse history of comorbid diseases (41.46% Infection; 93.50% Hypertension; 27.91% Dermatology), has best access to an Internal Medicine specialty (44.99%), and utilizes the most behavioral health measures (24.39%). We foresee such information as critical to the development of intervention tools that can adapt based on specific needs of users.

5 Conclusions

A common trend in current data analyses approaches is the focus on using a single analysis model to examine the correlations among various parameters. What is lacking are approaches that combine multiple techniques to derive meta-models that can more
accurately predict future disease outcomes from baseline characteristics. Previous research has shown that these approaches generally achieve better performance than individual techniques (Xu, 1992; Dietterich, 1997). A key motivation of the approach proposed in this study is the recognition that the predictive power of individual models tends to vary significantly, even when dealing with the same dataset. This is due to various assumptions made by the different approaches about the data-generating process. As such, the analysis approach chosen offers greater precision and detection of nuances in the data enabling users to uncover hidden patterns in various test results that would otherwise be difficult to correlate.

In this paper, we also proposed an approach utilizing data analysis and visualization to help diabetes patients improve adherence to medication. The aim is to facilitate a more personalized interaction that recognizes the role of self-motivation as an important determinant of why people change behavior - or not. Studies show that effective communication between patients and physicians can help improve adherence. Having the ability to predict adherence behavior from baseline patient characteristics can not only facilitate effective communications but also help educate patients about the benefits of adherence to medication use. The approach proposed is both dynamic and can adapt across a wide variety of settings reflecting diverse adherence behavior of type 2 diabetes population. By using smart technologies that are patient-centric, the approach described in this paper offers personalized feedback in ways unique to individual patients, essentially helping preempt poor adherence behavior, ensuring continuous improvement in patients’ health and engaging patients as part of the solution, rather than the problem. We are currently in the process of developing intelligent tools to facilitate patient-driven mobile interfaces.

References


Discovering and disseminating interesting patterns from imbalanced clinical data - a case study

A. Fazel Famili, Sieu Phan and Ziying Liu

Knowledge Discovery Group, National Research Council Canada, 1200 Montreal Road, Ottawa, Ontario, K1A 0R6, Canada

Abstract

Search for patterns in analyzing imbalanced clinical data (e.g., gene expression) has become an interesting area of research. To properly identify models (e.g., informative genes) through analyzing gene expression data using techniques other than random sampling is the main objective of the research reported here. This study shows our attempt to identify informative genes from highly imbalanced data sets for the objective of identifying genes associated with Acute Myeloid Leukemia (AML) and therapy related-AML (t-AML). We also propose ideas on how the discovered and validated knowledge can be disseminated.

Keywords
Knowledge discovery, imbalanced clinical data, gene expression, t-AML/AML.

Introduction

Over the past 10-20 years many approaches have been proposed for efficient data warehousing and knowledge discovery, targeting all data rich environments, such as physical systems and life sciences. For life science data these approaches are in response to the substantial challenges posed by the quantity, diversity and complexity of clinical data. The data in this domain consists of various forms among which are: (i) meta data, (ii) genomics, (iii) proteomics, (iv) metabolomics, and (v) clinical reports. The data for three of these five categories, namely genomics, proteomics and metabolomics are mostly in granular form, while other types can also be decomposed into features. This granularity of data (being mostly in the form of high-throughput numeric set of
attributes or features) makes the data readily available for knowledge discovery and has been the prime motivation for so many case studies all targeting medical data mining where the results could be incorporated into intelligent medical information systems.

Medical data mining has challenges of its own among which are many situations where the available data is imbalanced. The class imbalance problem corresponds to situations where majority of samples belong to one class and a small minority belongs to the other, which in many cases is equally or even more important. Although we have not seen it explicitly stated anywhere, ratios of 5:1, 10:1, and 100:1 have often been used in experiments under the category of imbalanced data sets (He, 2003). So ratios of 2:1 or better will not be regarded as imbalanced by many. Most machine learning algorithms are overwhelmed by the majority class and ignore the minority class since the traditional classifiers focus more on minimizing the overall error rate instead of paying special attention to the minority class. This could result in classifying all the data into the majority class in order to achieve higher accuracy. As an example, decision trees tend to over-generalize the class that is represented by most of the examples in the data. This obviously creates a major problem.

Several approaches to deal with imbalanced data have been proposed in the past which are beyond the scope and space limitation of this paper (Blagus, 2010; Kerr 2009; Kubat, 1997; Li, 2008; Liu, 2009; Padmaja, 2007 and Van Hulse, 2007). Therefore we only briefly report a few of the related work in this section. Changing class distributions by under-sampling the majority class (Japkowicz, 2002; Joshi, 2001) or over-sampling the under-represented class (Chawla, 2009; Han, 2005; Kim, 2007) to make both classes balanced is one approach. In addition, there are several heuristics-based over-sampling methods mainly similar to SMOTE (Chawla, 2002; Han, 2005), which generate synthetic examples of the under-represented class in order to over-sample such a class. However it is reported that the under sampling could discard potential useful data that could be important for the classifier (Guo, 2008). Over-sampling may also increase the possibility of over-fitting since it makes exact copies of all the cases from the minority class. Treating imbalance data at the algorithmic level is another approach. For example, Provost and Fawcett (Provost, 2001) built a hybrid classifier by adjusting the costs of the various classes, the probabilistic estimate at the tree leaf (when building decision trees), and the decision threshold. Other researchers have also combined the above two methods to deal with imbalanced problem (Joshi, 2001). All of the above approaches are based on random sampling from the majority class and ignore the reality of data characteristics that in some domains such as life sciences could be an important factor. Yen and Lee (Yen, 2009) propose a cluster-based approach to select representative data from both majority and minority class combined. Similarly, Kim (Kim, 2007) proposes a Self-Organized Map (SOM) approach to identify subsets for under-sampling and combining with a minority class.

The remainder of this paper is divided into four sections. Section 2 is the problem statement and a brief description of our approach. Section 3 contains the information about public data sets used in our studies. Section 4 is the data analysis and results and in Section 5 we conclude.
Problem Statement and Our Approach

The classical approach to address the problem of imbalanced data for the purpose of building reasonable training sets is to randomly select samples from the majority class and combine selected samples with all or even subsets from the minority class to perform classification. This has been the preferred choice in just about any domain. Depending on the overall approach, this selection process may continue until certain criteria, such as a desired learning performance or selection of all possible subsets, is achieved. One of the issues with this approach is that it obviously does not take into account the inherent characteristics of the cases in the majority class, which is proven to be relevant in certain domains such as life sciences. An example is subsets that can normally be identified in a large patient data set, or group of objects that have relatively distinguished characteristics. This is the prime motivation for our research reported here.

To analyze an imbalanced data set, samples are selected from the majority class using an unsupervised machine learning approach. One may or may not take into account the labels in the majority class. Subsets are then combined with the minority class to be used as training data. This is the one of the differences between our approach and the one proposed by Yen and Lee (Yen, 2009) in which we perform unsupervised leaning only on the majority class while they use the entire data at this stage. Among unsupervised methods applied in our case studies are K-means and SOM which we use to identify subsets from our majority class and combine selected subsets with all the cases from the minority class.

Figure 1 shows a high-level representation of the data selection process in both random sampling and our approach. Let’s say the number of samples in the majority class is $N_{ma}$ and minority class $N_{mi}$, where $N_{ma} \gg N_{mi}$. To properly explain the data selection process, we divide the explanation into two sections: (a) Random sampling: in which samples in the majority class are randomly picked to form $\chi$ subgroups. The number of samples in each subgroup depends on several factors such as the sample size of $N_{ma}$ and $N_{mi}$. In our study, we randomly selected the number of samples close to the total number of samples in minority class for each group, where these subgroups could have overlapping elements. Each of these subgroups is combined with the minority class to be used as a training set for data mining. (b) Data characteristics sampling: where sampling is performed through an unsupervised machine learning (ML) approach. All samples in the majority class are clustered into $k$ clusters, and some form of cluster quality is applied to optimize $k$. Each of the selected clusters is then combined with the minority class to be used as a training set for data mining.
The Data and the scope of preliminary analysis

The two imbalanced data sets used in our earlier studies for analyzing imbalanced data based on random sampling consisted of: (i) 44 de novo AML with normal karyotype plus 4 therapy-related AML (t-AML), from Bullinger’s data, and (ii) 235 de novo AML plus 6 t-AML from Klein’s data, both reported and explained in (Famili, 2011). As evident from the above numbers (ratios of 44:4 and 235:6) our two data sets were quite imbalanced. The data used in this study also comes from Bullinger’s group (Kharas, 2010) and is available in Gene Expression Omnibus (www.ncbi.nlm.nih.gov/geo/, with accession number GSE 22778). The data was for a total of 436 patients of which 367 were AML, 40 secondary acute myeloid leukemia (s-AML), 28 t-AML, and one without label. This data came from nine datasets produced under nine different platforms. Our first task was to map each data set with each platform which was done according to their IMAGE IDs. Probe sets in majority class and minority class were ranked based on variance. The common probe sets between 40% of high ranking probe sets from majority class and 40% of low ranking probe sets from minority class (as shown in Figure 2) which are 1239 probe sets, were used for subsequent data analysis. This was based on the assumption that the minority class is more homogeneous than the majority class and the majority class is highly variable containing several groups. The high variance
features in the majority class are more informative to separate the samples into different groups. However, since the small minority class is more homogenous, the high variance features are likely attributed from noise. We therefore retain only the low variance features for the minority class.

To start our investigation, samples in the majority class were clustered into K clusters, using K-Means. In these experiments we varied K from 2 to 12, and used Manhattan distance as the distance measure. The qualities of each set of clusters obtained through this process were further evaluated using J48 classifier (with 10 fold cross validation). As shown in Figure 3 and Figure 4, clustering this data into 6 clusters produced a better sample distribution while the accuracy didn’t drop significantly.
Data analysis and learning patterns from imbalanced data

The main objective of our data preprocessing and preliminary analysis was first to obtain a good understanding of the data used in this study and also to properly select subsets through an unsupervised method. This would then help us to generate meaningful data sets for training. The following is a summary of all steps taken at this stage.

Step 1: Clustering: the majority class was first clustered applying K-means and SOM where Manhattan was used as the distance measure. Based on our preliminary results, we observed that the results from K-means were far better than SOM (reasonable number of clusters and their density). The results were then validated using supervised machine learning methods. We also noticed that the accuracy of the cluster sets dropped significantly if the entire data was sliced to more than 6 groups. We therefore decided on stopping at 6 clusters (as shown in Figure 3).

Step 2: Evaluating the contents of clusters – Of the six clusters generated from the total of 367 cases in the majority class, we observed one cluster contained only 2 cases (well below a meaningful number) while the remaining clusters contained between 54 and 100 cases. We therefore decided to continue our investigation with the contents of 5 clusters that contained an average of 73 cases (as shown in Figure 4).

Step 3: Combining clustering data with minority class and analyzing training sets. This was the most crucial step in our data analysis process where 5 training sets were created. The content of each set was the combination of selected 5 clusters with all 26 cases in minority class. A list of probe sets was discovered from the first run (J48 classifier) (Table 1). Three of the five training sets exceeded 75% accuracy. In addition, we further analyzed these three data sets based on our discover-and-mask approach (Famili, 2003) with the accuracy cut-off of 80%. A list of additional probe sets was discovered from the second run (Table 2). The idea behind the discover-and-mask approach is to analyze the training data using a standard machine learning algorithm (e.g., J48) and mask all attributes reported in the discovered models for the next round of analysis until one of following three criteria is met:

a. The accuracy in the discovered models drops below certain level (e.g., 75%),
b. A number of target attributes (e.g., genes) have been identified (e.g., top 20),
c. Certain a-priori target attributes (e.g., target genes) have been identified,
regardless of the accuracy of their associated models.
Here we decided on the first option (a above) for our data analysis with the accuracy
cut-off value of 75%. As a result, we only had to continue into a second run for 3 out of 5
data sets, for discovery of additional genes.
Step 4: Summarizing the results from the above runs. The first 5 runs resulted in
identifying a total of 21 genes (Table 1), all reported in models whose accuracy was
above 75%, while the second set of runs from 3 training sets produced an additional 18
genes (Table 2).

Discussion and future directions

The ultimate goal of this class of research is to identify the best method to search for
patterns in imbalanced data, given any data set of this nature. This is particularly
important if the data in majority class contains some inherent characteristics and
random sampling is not the best option. Our efforts in this study are towards this
direction where we think an alternative to random sampling from imbalanced data is to
search for meaningful and inherent characteristics in the majority class and identify
subsets to build training sets. Our experience to this end shows that there exist some
inherent characteristics in data that are interesting. This is especially true in clinical data
of this nature and one should take advantage of this phenomenon. Of course, the
ultimate objective should be to compare or complement the results of data
characteristics sampling with random sampling when it gets to clinical validation or
even dissemination of discovered knowledge. We would also like to emphasize that the
eventual goal of applying and disseminating our models would be to incorporate them
into architectures similar to the one proposed in Figure 5. That should allow us to
exploit the results of our discoveries through networks and internet and properly
disseminate them to all who would benefit from. This research is along the line of our
Bio-intelligence research program (Phan, 2008) which is our goal for exploring AI
methodologies to omics class of data to build better clinical predictors.
Table 1. Results from the **first** run

<table>
<thead>
<tr>
<th>K-Means Cluster No.</th>
<th>Accuracy</th>
<th># of probe set</th>
<th>Probe IDs &amp; corresponding Gene Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6</td>
<td>82.93%</td>
<td>3</td>
<td>IMAGE:431796 (PPIL1); IMAGE:1518890 (MTL5); IMAGE:823715 (SERTAD2);</td>
</tr>
<tr>
<td>C5</td>
<td>87.76%</td>
<td>2</td>
<td>IMAGE:265040 (SHPRH); IMAGE:768453 (WDR68)</td>
</tr>
<tr>
<td>C4</td>
<td>60.94%</td>
<td>7</td>
<td>IMAGE:126522 (GGT7); IMAGE:142248 (GBGT1); IMAGE:1636069 (MRPL12); IMAGE:1707680 (FBXO9); IMAGE:271038 (RGS5); IMAGE:306813 (ROSI1); IMAGE:530460 (S100PBP)</td>
</tr>
<tr>
<td>C3</td>
<td>72.16%</td>
<td>6</td>
<td>IMAGE:878253 (ZDHHC16); IMAGE:1523144; IMAGE:126522 (GGT7); IMAGE:593520 (SPG21)</td>
</tr>
<tr>
<td>C1</td>
<td>81%</td>
<td>4</td>
<td>IMAGE:1031918; IMAGE:1048601 (MGC39584); IMAGE:725392 (CCDC76); IMAGE:126239 (MRPL16); IMAGE:1899175; IMAGE:1931664; IMAGE:241787; IMAGE:246543; IMAGE:757242 (SLC30A6); IMAGE:814288 (CRYZL1); IMAGE:824219</td>
</tr>
</tbody>
</table>

Table 2. Results from the **Second** run

<table>
<thead>
<tr>
<th>K-Mean Cluster</th>
<th># of probe set</th>
<th>Probe IDs &amp; corresponding Gene Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6</td>
<td>0</td>
<td>IMAGE:1031918; IMAGE:1048601 (MGC39584); IMAGE:725392 (CCDC76); IMAGE:126239 (MRPL16); IMAGE:1899175; IMAGE:1931664; IMAGE:241787; IMAGE:246543; IMAGE:757242 (SLC30A6); IMAGE:814288 (CRYZL1); IMAGE:824219</td>
</tr>
<tr>
<td>C5</td>
<td>11</td>
<td>IMAGE:1031583; IMAGE:1908650 (UBE2W); IMAGE:306446 (C11orf24); IMAGE:591422 (GSTO2); IMAGE:726564; IMAGE:771254 (UBA6); IMAGE:811607 (STAMBPL); IMAGE:1899175</td>
</tr>
</tbody>
</table>

Note: Because the cut off accuracy is 80%, no genes were identified for C6 in the second run.
Figure 5. Bio-Intelligence conceptual architecture

References


\textit{O\textsc{r}C}: an \textit{O}ntology \textit{R}easoning \textit{C}omponent for Diabetes

Özgür Kafalı\textsuperscript{1}, Michal Sindlar\textsuperscript{2}, Tom van der Weide\textsuperscript{2} and Kostas Stathis\textsuperscript{1}

\textsuperscript{1} Department of Computer Science
Royal Holloway, University of London, Egham, TW20 0EX, UK
{ozgur.kafali,kostas.stathis}@rhul.ac.uk

\textsuperscript{2} Portavita B.V., 1000 BG Amsterdam, Netherlands
{m.sindlar,t.van.der.weide}@portavita.eu

Abstract

\textit{O\textsc{r}C} is an ontology reasoning component that builds upon existing ontology modelling tools and techniques to support the integration and interpretation of multimodal medical information. We show how to embed \textit{O\textsc{r}C} as a reasoning capability in reactive infrastructure agents that support intelligent agents operating in COMMODITY\textsubscript{12}, a personal health environment for diabetic patients and the medical professionals that treat them. The benefits of the approach are illustrated by showing how medical information for patient profiles at different sources can be included in COMMODITY\textsubscript{12}, thus extending the generality and potential of the resulting system. The approach also illustrates how ontologies can be combined with a variety of artificial intelligence tools and techniques to support e-Health activities on the Internet, thus contributing towards the vision of NetMedicine.

Introduction

The usefulness of medical data is greatly increased when data are available in formats that allow them to be integrated with other data. A well-known strategy for data integration, medical or otherwise, is through the annotation of multiple bodies of data using common controlled vocabularies or \textit{ontologies} (Guarino, 1998). However, the very success of this strategy in medical systems has led to a proliferation of medical ontologies, which itself creates obstacles to integration (Bodenreider, 2009). As a result, choosing or creating the right ontology, in combination with associated tools and techniques, can be a non-trivial task.

We are motivated by our participation in the COMMODITY\textsubscript{12} project (Kafalı et al., 2013), a personal health system (PHS) aiming to support diabetic patients and the medical professionals that treat them. Data integration in this project follows a mediator-based approach (Hernandez & Kambhampati, 2004). Mediator-based integration concentrates on data translation of existing information.
sources. In COMMODITY$_{12}$ these sources include information entered through a Web interface, sensor information coming from devices that monitor patients, information from databases with patient data, and decision support information provided by logic-based agents. However, the translation between components is done statically, i.e., when a new message type needs to be processed throughout the system, all the translators of the mediator should be updated manually to support the required information flow. The issue then becomes how to standardize the domain knowledge, so that this can be used systematically as if it was originating from a single source.

The aim of this paper is to study how to complement the translation process of the COMMODITY$_{12}$ mediator with ontologies and semantic reasoning support. Our objective is to identify the relevant architecture, tools and techniques to support the development of ontologies so that it can be integrated into our PHS. We are particularly interested in reasoning about information accessed from the patient database or sensor devices in general, and information regarding data exchanges relevant to the profile of a diabetic patient in particular.

To address the aim and objectives of the semantic reasoner for COMMODITY$_{12}$, we study how to embed such a reasoner as a reasoning capability in what we call infrastructure agents, viz., reactive agents deployed to support the smooth (inter)operation of components in a PHS, including support for semantic reasoning and ontologies. We also describe a diabetic patient profile using an ontology formalised in OWL, and we present SWRL rules to provide semantic reasoning on the ontology concepts. We instantiate the ontology with individuals coming from a patient database. We implement the semantic reasoner in Java, and use Protégé to develop the ontology. Moreover, we show how the infrastructure agents that perform semantic reasoning can be combined with the existing logic-based agents of COMMODITY$_{12}$ providing monitoring, advice and diagnosis.

In the remainder of the paper, we first present the COMMODITY$_{12}$ architecture specialised to contain ontology managing components in the form of infrastructure agents. These agents manipulate a diabetes ontology, the details of which we describe next. We then present an illustrative example where we demonstrate how our approach works on patient data. Finally, we conclude the paper by summarising our contribution, comparing it with existing literature, and outlining our plans for extending it in the future.

**COMMODITY$_{12}$ extended with Semantic Reasoning**

COMMODITY$_{12}$ (COntinuous Multi-parametric and Multi-layered analysis Of Dlabetes TYpe 1 & 2) aims to design, build, and validate an intelligent system for the analysis of multi-parametric medical data. It will uptake the existing cutting-edge technologies and extend these technologies by combining state-of-the-art networks, software interoperability, and artificial intelligence techniques in order to realize the concept of translational medicine by means of a PHS. A prototype PHS has been developed (Kafalı et al., 2013) that allows patients to take measurements of vital signals through a set of wearable sensors (e.g., heart rate and respiration rate), and enables doctors to input data about their patients via a web interface. This information is then processed to provide advice to the patients as well as alerts to the doctors. The main reasoning is provided by logic-based agents, built according to the LAMA agent model and deployed using the GOLEM agent platform (Bromuri & Stathis, 2008). The LAMA agents are developed using artificial intelligence tools and techniques combining deductive, hypothetical and temporal reasoning. An agent’s knowledge-base consists of logic rules formulated according to medical guidelines plus a set of facts describing the environment in which the agent is situated. The left part of Figure 1 demonstrates the COMMODITY$_{12}$ architecture.
Data integration in COMMODITY12 follows a mediator-based approach (Hernandez & Kambhampati, 2004) which concentrates on translation of data coming from different information sources. These sources feed valuable information to the system that include: (i) measurements from the patients via sensors, (ii) observations from doctors following patient visits, or (iii) profile information from the patient DB. Note that some of the arrows in Figure 1 are double-sided, representing flow of information to both sides, e.g., the doctor enters data about the patient which is sent to the LAMA agent for processing, and the resulting alert is displayed via the doctor’s screen.

One major problem regarding the current architecture of the system is that each translator is specialized in a specific part of the system, which makes the effort of adding new concepts harder. Consider the following scenario: a new rule is added to the LAMA agent that requires the concepts of the patient’s systolic blood pressure and living place to decide whether an e-consultation is justified. Because there are multiple code systems that use different codes for these concepts, the translator needs to map all the codes onto something that the translator understands. Consequently, the same functionality would be implemented in all translators, which makes maintenance and testing costly and inefficient. Adding an ontology reasoner would not only standardize the domain knowledge at a single source, thus reducing the effort of maintenance and introducing new concepts, but it also aids in disease management through the use of patient profiles and the new information that is inferred with the ontology. To address this need, we have developed the ORC agent. It is developed in Java, provides semantic reasoning and consists of the following components as shown in the right part of Figure 1:

---

1E-consultation means that a specialist logs into the system, looks into the patient’s health records, studies the patient’s observation values, and provides advice without the patient having to visit the specialist.
• an OWL\textsuperscript{2} ontology describing diabetes patient profiles and importing other relevant ontologies such as food and medical observations;
• patient data asserted to the ontology as OWL individuals, e.g., age, living place, blood pressure measurements;
• a set of SWRL\textsuperscript{3} rules that are used to infer new properties about existing individuals;
• a processing component that retrieves patient information and infers ontology properties.

Currently, \textit{ORC} agents are purely reactive in that they only respond to requests coming from \textit{LAMA} agents. When such a request comes regarding the retrieval of a specific patient profile information, \textit{ORC} first loads the ontology and retrieves relevant data from the patient DB. This data is then translated to OWL syntax and asserted to the ontology as individuals. The next step is to execute the SWRL rules to infer new properties about the individuals. These are then translated to logical terms and passed to the \textit{LAMA} agent that needs those terms for further reasoning.

```
advise_e_consultation(Patient, T):-
    has_age(Patient, Age, T), Age < 80,
    has_no_hospital_access(Patient, T),
    \+ consulted(Patient, internist, years, 1, T),
    has_systolic_bps(Patient, [MostRecent, SecondMostRecent|Rest], months, 6, T),
    MostRecent > 140, SecondMostRecent > 140.
```

Listing 1: Prolog rule for advising e-consultation in the case of high blood pressure.

Let us now explain the functionalities of each agent via a rule for determining whether the patient needs e-consultation, based on the blood pressure monitoring outcome as well as other profile information (Sluiter et al., 2012). The rule in Listing 1 is given in Prolog syntax in the form of conclusion holds (the head of the rule) if (represented by the :- symbol) conditions hold (the body of the rule). \(+\) is the negation-as-failure operator. A call of the form \(+P\) succeeds if all possible ways of solving \(P\) fail finitely. \(T\) represents the current time. The first two conditions check whether the patient is less than 80 years old and has no easy access to a hospital, respectively. Now, certain parts of this rule can be improved via semantic reasoning both in terms of (i) access to / inference on data and (ii) knowledge representation / development effort. For example, the second condition can be inferred by the \textit{ORC} agent by looking at the patient profile and checking whether the patient lives in a rural area or not (providing inference on data). The last two conditions check whether the patient has not consulted an internist in the last year, and her last two blood pressure measurements are higher than 140 mmHg in the last six months, respectively. Evaluating these two conditions requires temporal reasoning which is provided by the \textit{LAMA} agent. Observe that the rule uses negation-as-failure, which is acceptable here because the database holds complete knowledge of the data underlying the negated clauses. Systolic blood pressure can be measured as part of different examinations, which can result in relevant data being stored using different codes. However, the rule is only representing the generic concept, so that any type of systolic blood pressure measurement qualifies as a valid measurement for this rule. Coming back to the improvements provided by semantic reasoning, using an ontology with a class hierarchy for the systolic blood pressure concept, which offered by the \textit{ORC} agent, removes the need to describe the sub-class relations in the \textit{LAMA} agent (reducing development effort).

\textsuperscript{2}http://www.w3.org/TR/owl-ref/
\textsuperscript{3}http://www.w3.org/Submission/SWRL/
Figure 2. Class hierarchy in Protégé.

An Ontology for Diabetes Patient Profiles

In COMMODITY12, we are interested in using an ontology for diabetes management. We started with exploring the literature to find an ontology that was sufficient for our purposes. Unfortunately, our search was unsuccessful (see Discussion section). As a result, we are presenting here our consortium’s attempt to design such an ontology for diabetes management. Our approach is patient centric and aims to include only the necessary patient information so that different types of diabetes can be managed via a PHS. In other words, the schema defining the ontology is that of defining a patient profile.

To process information in profiles we embed ORC in infrastructure agents to support semantic reasoning given a taxonomy of diabetes concepts as well as the logical relations regarding those concepts. These will be represented in OWL, where concepts correspond to classes while the relations are given as either object or data properties (Guarino, 1998). On top of this design, individuals can be created to represent specific instances of classes. Moreover, logic rules described in SWRL allow inference of new properties for individuals. We identify the following classes to describe a patient profile based on the medical knowledge gained from the COMMODITY12 consortium:

- **GeneralInformation**: contains information about the patient’s age, gender and ethnicity;
- **LifeStyle**: describes the patient’s living conditions, exercise habits and alcohol intake;
- **Work**: contains information about the patient’s education and occupation;
- **Diet**: contains information about the patient’s eating habits and details on restricted food;
- **MedicalHistory**: contains the history of patient’s medical records and family history;
- **Observation**: contains the history of observations and measurements regarding the patient;
- **Genetics**: describes the patient’s genetic information.

Figure 2 shows part of the class hierarchy for our patient profiles as developed with the ontology development tool Protégé4. The highlighted class SystolicBloodPressureObservation on the left panel is a sub-class of Observation. Thus, it describes a more specific type of observation. Further details of the class are shown on the right panel. Figure 3 demonstrates the data properties for the classes, as well as rules formulated in SWRL. The panel on the left shows part of the data

---

4http://protege.stanford.edu/
properties defined in our ontology. The highlighted property hasObservationValue has the class Observation as its domain, and describes the measured value as an integer (bottom right panel). The properties of a particular class are inherited by its children (i.e., subclasses), so that all types of blood pressure observations have this property. The top right tab describes a simple SWRL rule.

Following our running example, the highlighted rule infers that a rural area has no access to a hospital. This kind of reasoning allows us to avoid describing in the LAMA agent’s knowledge-base whether a hospital is easily accessible for the patient. That is, the ORC agent provides this information via semantic reasoning. Lack of space does not allow us to provide the full details here, but we hope to report them in future work.

An Illustrative Example: The Portavita Patient Database

We have developed a prototype implementation for the ORC agent and we are in the process of integrating it with the COMMODITY system through the mediator interface. The current implementation as well as the OWL design for the ontology is available online. Here, we demonstrate the workings of our approach using the sample rule given in Listing 1 on patient data extracted from the Portavita database. Recall that one of the conditions in the rule is related to the concept systolic blood pressure. Measurements of systolic blood pressure can enter the database as part of multiple examinations performed by doctors, with a company-specific coding system used for classifying these measurements.

In order to unify the concepts for describing blood pressure with a standardized vocabulary, we have integrated the Portavita-specific ontology with the widespread SNOMED CT ontology. Figure 4 illustrates this integration. The lower part shows the class hierarchy for the Portavita ontology focusing on the systolic blood pressure concept, of which the class SystolicBloodPressureObservation is shown in more detail in Figure 2. The upper part demonstrates the relevant concepts from the SNOMED CT ontology. Note that SNOMED CT’s Systolic blood pressure (observable entity) is mapped to the ClinicalSystolicBloodPressureObservation class from the Portavita ontology, as illustrated by the arrow that crosses the dashed line. This denotes an OWL equivalence relation. Mapping a custom ontology onto a standardized one in such a way has the benefit of giving flexibility as to where equivalence or subclass relations are put; if one wishes to, e.g., re-
guard instances of Portavita’s SelfMeasuredBloodPressure concepts as instances of SNOMED CT’s concept of Systolic blood pressure, then it would suffice to “lift” the equivalence relation one level up in the Portavita ontology. Additionally, one could posit an equivalence relation between Sitting systolic blood pressure (observable entity) and SittingSystolicBloodPressureObservation.

It was noted before that systolic blood pressure is stored as part of several examinations, amongst which the Ankle Brachial Pressure Index (ABPI) and a generic blood pressure examination. A single code is used for storing generic blood pressure observations, along with an optional attribute that can be used to further specify whether the patient was lying, sitting, or standing. In this respect, the Portavita code system oversimplifies the blood pressure observation with respect to SNOMED CT, even though the measurement method (lying/sitting/standing) can be distinguished in a different way. In contrast, in Portavita’s ABPI examination the observations of systolic blood pressure at the left / right arms and ankles are stored with four separate codes, thus specializing the concept further than SNOMED CT does in this respect. Apart from enabling cross-relations with standardized ontologies, the definition of a custom ontology makes such matters explicit, and thereby can provide novel insights regarding the underlying data model.

We now consider the patient data in Table 1 with regards to the rule of Listing 1 to determine whether the patient applies for an e-consultation. In order to perform semantic reasoning on this data, first the ORC agent uses the data in Table 1 to assert the individuals regarding this patient to the ontology as illustrated by the pseudo-code in Listing 2. To relate codes to concepts, ORC consults the hasActCode property in the ontology to find concepts that have a given act code. For example, 8480-6 is translated to GenericSystolicBloodPressureObservation and Portavita714 to ClinicalSystolicBloodPressureObservation (see Figure 4).
<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Observation ID</th>
<th>Measurement Date</th>
<th>Code</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>82319</td>
<td>11783457</td>
<td>25-01-2013</td>
<td>8480-6</td>
<td>133</td>
</tr>
<tr>
<td>82319</td>
<td>11827346</td>
<td>15-02-2013</td>
<td>Portavita714</td>
<td>141</td>
</tr>
<tr>
<td>82319</td>
<td>12053457</td>
<td>01-04-2013</td>
<td>8480-6</td>
<td>157</td>
</tr>
</tbody>
</table>

Table 1

Information stored for patient with ID 82319: administrative data shown on the top table, observations shown on the bottom table with codes 8480-6 for generic systolic blood pressure and Portavita714 for systolic blood pressure in left ankle.

Listing 2: Pseudo-code to instantiate the ontology with data from the database.

After the individuals are created, the SWRL rules are executed to infer additional information about the individuals by refreshing the reasoner and realizing its knowledge-base. After this step, it follows from the knowledge-base that both types of systolic blood pressure observations in Table 1 are instances of ClinicalSystolicBloodPressureObservation. This greatly simplifies querying data for the rule of Listing 1, which pertains to systolic blood pressure in general.

Once the ontology reasoning is performed, the resulting individuals are translated to logical terms. Part of the output produced by the ORC agent is shown in Listing 3. Note that the predicate has_no_hospital_access is inferred since the patient lives in Lutjebroek, which is regarded as a rural area. Furthermore, to obtain all systolic blood pressure observations, ORC can now simply query for all individuals of type ClinicalSystolicBloodPressureObservation and translate those to the format that the LAMA agent requires. According to this data and the rule, the LAMA agent draws the conclusion that an e-consultation is suitable for the patient.

Listing 3: Output of ORC.
Discussion

We have presented ORC, an ontology reasoning component that builds upon existing ontology modelling tools and techniques to support the integration and interpretation of multimodal medical information. We have illustrated how to embed ORC as a reasoning capability in reactive infrastructure agents supporting intelligent agents operating in COMMODITY\textsubscript{12}, a personal health environment for diabetic patients and the medical professionals that treat them. The benefits of the approach have been exemplified by showing how medical information for patient profiles at different sources can be included in COMMODITY\textsubscript{12}, thus extending the generality and potential of the system. The approach also illustrates how ontologies can be combined with a variety of artificial intelligence tools and techniques to support e-Health activities on the Internet.

Approaches using ontologies and semantic reasoning in medical knowledge already exist (Bouamrane, Rector, & Hurrell, 2008; Cantais, Dominguez, Gigante, Laera, & Tamma, 2005; Curé, 2005; Latfi, Lefebvre, & Descheneaux, 2007; Li & Ko, 2007). However, as we are interested in the representation of ontologies for disease management in general and the management of diabetes in particular, we are going to avoid comparing our work with application of ontologies in telehealth environments such as smart homes for helping elderly people (Latfi et al., 2007), or similar frameworks.

We will focus on approaches that complement our work in the application context, for instance that of Cantais et al. (2005), who present a food ontology to help diabetic patients with their diet. Although our focus has been on more general coverage of a diabetic patient profile, we foresee that a food ontology could strengthen what we have presented here. Other approaches complement our work in terms of techniques. In (Bouamrane et al., 2008), an ontology-driven approach is used for medical history modelling to customise patient questionnaires. The system uses semantic reasoning to compute similarities among different illnesses so that it can generate further questions based on previous answers provided by the patient. This idea of similarity metrics can complement the way we process historical profile information and the conclusions we draw from such information, e.g., to detect patients with abnormal working hours which can be used to adapt the patient’s medication accordingly.

Another possible use of ontologies is presented by Curé (2005), who propose a self-medication system with the use of drug and symptom databases, and an electronic health record for patients. While such a work partly describes medical concepts about diabetes, we are not aware of any work that operates in the context of a personal health system like ours, i.e., starting from the retrieval of diabetic patient records from a medical database as well as aggregating information from a variety of sensors, to displaying the diagnosis to the doctor / patient using agent technology.

Semantic reasoning with ontologies in our work has been embedded as an agent capability for special types of agents that we have called infrastructure agents. These agents’ sole task is to reason about ontologies, and they are similar to ontology agents used in FIPA\textsuperscript{6}. The adoption of such agents in COMMODITY\textsubscript{12} not only allows us to support data integration in a systematic way but also enables semantic interoperability between agents that communicate with each other to provide monitoring, advice and diagnosis.

We are currently working towards extending the work presented here in three different directions: (i) We provided a generic ontology for diabetes patient profiles resulting from the medical knowledge gathered in the COMMODITY\textsubscript{12} consortium, and extended it with observations regard-

\textsuperscript{6}www.fipa.org
ing blood pressure concepts as described in Portavita and SNOMED CT. We plan to integrate other ontologies such as for food and alcohol, to enrich the concepts regarding a patient’s diet, e.g., calory values for meals, alcohol intake based on drink types. (ii) We created a prototype implementation for the ORC agent which consists of specialised translators to convert concepts among different components. We plan to provide generic translators based on a concept ontology such that they can be reused and updated from a single source. A sample translation from OWL to Prolog is given in (Samuel et al., 2008). (iii) We believe that the semantic reasoner component (ORC) improves the overall efficiency of the system by simplifying some of the agent reasoning performed by the temporal reasoner (LAMA). We plan to run experimental tests to evaluate our system using patient data from the clinical trials that are to be conducted as part of COMMODITY12.

Acknowledgements

This work was partially supported by the EU FP7 Project COMMODITY12 (www.commodity12.eu). We thank the medical doctors in the COMMODITY12 consortium for providing us with the information for describing a diabetic patient profile.

References