# eXiT Research Group at the University of Girona: Artificial Intelligence and Machine Learning Applied to Medicine and Healthcare

Beatriz López, Natalia Mordvanyuck, Joaquim Massana, Ferran Torrent-Fontbona, Gerard Cáceres, Carles Pous
*eXiT research group*
*University of Girona*
{beatriz.lopez,natalia.mordvanyuk}@udg.edu,quim.massana@hotmail.com,
ferran.torrent@udg.edu,gerardgi96@gmail.com,carles.pous@udg.edu

***Abstract*—This paper describes the research activity of the eXiT research group at the Universitat of Girona and the main results achieved. The research is organized in four main groups: prognosis, clinical decision support systems, mHealth, and biosignal processing. The paper describes past, current and future research of the group.**

***Index Terms*—Case-based reasoning, Personalization, Patient monitoring, Resource optimization.**

## I. Introduction

Research group eXiT (Control Engineering and Intelligent Systems) focuses its work on decision support systems, case-based reasoning, machine learning and optimization. There are two main labs in the group and one of them, Medicine and Healthcare lab, is dedicated to Medicine and Healthcare and focuses on the incorporation of intelligent systems and biomedical engineering in health management and on the development of innovative medical technologies.

The research activity on eXiT Medicine and Healthcare lab (eXiT for short from now on) starts around 2005, when the Foundation Hospital Dr. Josep Trueta becomes a research institution and synergies between the hospital's researchers and the University staff pop up.

As a result of eXiT's research activity, several awards were conceded: Best Paper in the 2014 IMIA Yearbook of Medical Informatics for the work 'Enabling the use of hereditary information from pedigree tools in medical knowledge-based systems', ITEA Excellence Awards 2015 for the MEDIATE project, 2nd prize in the Vall d'Hebron Research Institute (VHIR) Innovation Healthcare Contest for the NoaH project, and the ITEA Vice-chairmans award for SME Success in the MOSHCA project. Moreover, eXiT has been awarded since 1995 by the regional government with quality labels (current label: 2017 SGR 1551). Another important outcome is the eXiT*CBR tool (http://exitcbr.udg.edu/), which is available to all of the researchers.

An overview of the different application domains in which eXiT has been working on is shown in Figure 1. In the next sections, the applications are described and grouped according to the problems addressed: prognosis (purple color in Figure 1), Clinical Decision Support Systems (CDSS, green), mHealth (blue), biomedical signal processing (orange) and healthcare services (garnet). Some future applications (black) are commented at the end of the paper.

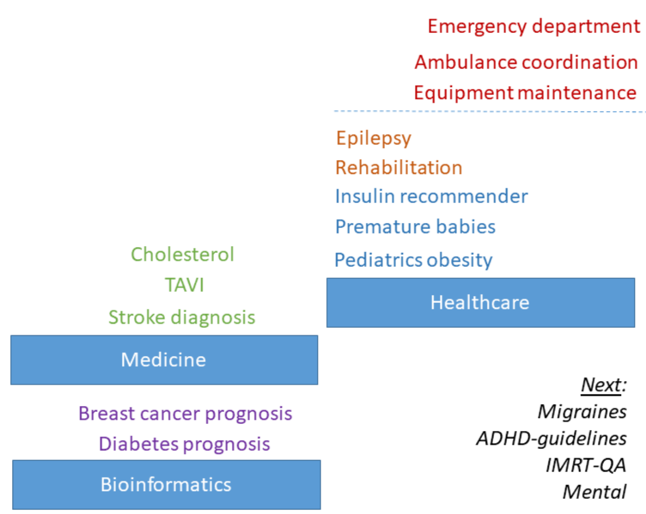


Fig. 1. Overview of application domains. Coloured applications described in this paper: Purple: Prognosis; Green: Clinical Decision Support Systems; Blue: mHealth; Orange: biomedical signal processing; Garnet: Healthcare services; Black: future research.

## II. Prognosis

Artificial Intelligence (AI) and Machine Learning (ML) methods have been applied to prognosis for two risk diseases: breast cancer and Type 2 Diabetes Mellitus (T2DM).

This project has received funding from the European Unions Horizon 2020 research and innovation programme under grant agreement No 689810 (PEPPER). Work developed with the support of the awarded distinction by the Generalitat de Catalunya 2017 SGR 1551, the MESC project funded by the Spanish MINECO (Ref. DPI2013-47450-C21-R), and the University of Girona grant to supporting research groups to improve their scientific productivity (MPCUdG2016).

### A. Breast Cancer

We were facing the following prognosis problem: generate a breast cancer risk model from a dataset of 871 cases (628 healthy women and 243 women with breast cancer). The core technology used was case-based reasoning (CBR, [1], [10]).

Instead of developing a dedicated system, we opted to build a generic tool, eXiT*CBR [15], [27], which provided some key features for Medicine, such as the importance of experiment repetition and the need to interact with clinicians showing the results in plots that were easy to interpret for them.

The main techniques used include the particular methods to implement the basic steps of the CBR methodology (i.e. similarity metrics, cases selection), as well as evaluation techniques (e.g. cross-validation), metrics (e.g precision, recall), and plots (e.g. ROC-plots). eXiT*CBR also includes some plug-ins and pre-processing steps, one of them related to the acquisition of inheritance data from families, which has been awarded by the International Medical Informatics (*IMIA Best paper in 2014*, [7]).

In a second stage, the need for improving the results of the first prototype led us to include additional features into the second version of eXiT*CBR: multi-agent management (enabling physicians in a joint prognosis) [23], multi-criteria decision making (as a consequence of the first one) [14], feature learning with the use of genetic algorithms [16], and subgroup discovery [11].

The medical research team of such joint research are members of the Catalan Institute of Oncology (Joan Brunet, Judith Sanz, Teresa Ramon y Cajal). The funding received for this research was provided by the Girona Biomedical Research Institute ("Family history as a model for evaluation breast cancer risk"), and the University of Girona (eXiTDM: Data Mining Platform).

### B. Type 2 Diabetes Mellitus

In this case, we dealt with the problem of building a model for T2DM prognosis. The starting point was 1074 subjects with and without T2DM, which included both, clinical data (IMC, sex, age) and up to 112 polymorphisms (insulin-like growth factor binding protein, CD36 antigen, adiponectin receptor 2, etc.).

The methods applied were dimensionality reduction with PCA, i.e. regular simplex PCA which is adequate for discrete data, and personalized prediction with CBR. The achieved success ratio was around 89% with 5 principal components [26].

The research was carried out with the endocrinologist Dr. J.M. Fernandez-Real of the Girona Biomedical Research Institute (IdiBGi). This work was made possible by the support of the Spanish MEC project DPI2005-08922-C02-02, the IdiBGi project GRCT41, and DURSI AGAUR SGR 00296 (AEDS).

## III. Clinical Decision Support Systems

One of the first works on CDSS developed by eXiT was for acute stroke classification. Acute strokes are medical emergencies that require from an expert neurologists in order to detect the illness in the appropriate therapeutic time window. Thanks to the development of new treatments, like the rt-Pa treatment, mortality rates have been descending in the last decades. However, the final diagnosis of the patients is often imprecise, and from it depends the administration of new treatments. That is, a patient can have a diagnosis of acute stroke, but the clinical category of it is often unknown. This situation has been detected by the Spanish Association of Neurologists, which has set up a repository of cases named Badisen. Using this database, we have designed a multi-agent case based system with the aim of giving support in the acute stroke diagnoses. An agent in the system keeps information of experiences in a single hospital, maintaining the particular decision criteria employed by the main physician. Agents collaborate in a lack of confidence in the initial diagnosis, thanks to a trust mechanism [17]. The medical team includes Dr. Serena from the Hospital Dr. Trueta of Girona.

The second problem addressed was a workflow-based CDSS designed to give case-specific assessment to clinicians during complex surgery or minimally invasive surgery. Following a perioperative workflow, the designed software uses the CBR methodology to retrieve similar past cases from a case base to provide support at any particular point of the process. The graphical user interface allows easy navigation through the whole support progress, from the initial configuration steps to the final results, organized as sets of experiments easily visualized in a user-friendly way. As a result, the eXiTCDSS tool was developed [5]. This work has been performed in the context of the MEDIATE European Project (Eureka ITEA 2 no 09039 -TSI-020400-2010-84) with several clinical teams involved and the key collaboration of *Hospital Clinic de Barcelona*.

Finally, we are currently finalizing HTE 3.0, a CDSS for lipid-lowering treatment and familial hypercholesterolemia detection [2]. In that case, the main AI technique used is rule based reasoning combined with a three-layer decision chain: risk analysis, treatment personalization, and safety and cost-effectiveness criteria. The work has been carried out with Dr. A. Zamora of the *Corporació de Salut del Maresme i La Selva*. HTE 3.0 has been registered at the Intellectual Property Register of Girona, ref UdG - Reg GI2532016 - Web CDSS HTE 3.0., and it has been sponsored by Sanofi.

## IV. mHealth: Monitoring and Personal Recommendations

One of the key challenges in modern Medicine is to provide individualized assessments to patients [3]. In this regard, precision Medicine is looking for genetics particularities in order to provide the appropriate treatment to patients. However, other ICT approaches that deal with personalized responses to the users, taking into account their particular history and context, are also dealing with such challenge. CBR has been proven to be a useful technique for providing adapted and personalized recommendations. eXiT*CBR has been used with this purpose in two case scenario: care of premature babies at home and insulin dose recommendations. Moreover, from the collaboration with a pediatric team, a project for promoting healthy habits in obese kids was developed.

### A. Premature Babies at Home

Nowadays women give birth to healthy babies, but sometimes premature due to their advanced age during pregnancy. That means many newborns should stay several weeks in the hospital intensive care units until they reach a safe weight. However, recent studies have shown that premature babies develop faster if they stay at home, in a familiar environment, instead of at the hospital. Thus, several hospitals have started to discharge babies at home, in special hospital programs, where a nurse attends once or twice per week the family by visiting the baby at home.

In order to improve the monitoring of such babies, reduce the stress of parents, and dedicate nursing personnel especially to critical cases, the NoaH platform was developed (see Figure 2). The medical team involved was headed by Dr. Abel López-Bermejo (pediatric doctor of Hospital Dr. Trueta of Girona) in cooperation with Dra. Eva Bargallo and Dra. Cristina Armero, both neonatologists, and supported by Dra. Judith Bassols. This work has been carried out in the context of the MOSCHA European project (EUREKA ITEA 2 n 11027 IPT-2012-0943-300000).

The NoaH platform has two main components: a mobile component and a server component. The mobile part is managed by the parents, and it is connected to a pulsi-oximeter used to read vital signs of the baby. Once a day parents place the sensor to the baby and input to a dedicated mobile application some other information such as baby's weight, number of intakes, depositions, sleep, etc. Thanks to a hybrid system composed by a rule-based system (with general medical knowledge) and a CBR system (with particular knowledge of baby's history), the parents receive an assessment about the child: normal, warning, alert. This information is sent through the NoaH platform to the clinical server, where the clinical staff revises it.

The CBR methodology helps to avoid false positives by considering information about the baby's history. For example, a rule could say that a baby should gain 10gr weight per day, but a baby is doing around 8gr per day. If the daily gain is consistent with her history, the system will not trigger any warning [12]. Furthermore, in order to take advantage of the computing capabilities of mobile phones, context aware reasoning was also considered [24].

The NoAH platform was tested in a controlled scenario (in hospital) with a successful feedback from users and it is in the process of being deployed in practice. Moreover, it was awarded in 2015 with the second prize in the Vall d'Hebron Research Institute (VHIR) Innovation Healthcare Contest and it has been finalist in the mHealth category of the Summer Competition of the Universite de la Sante, Castres, France.

### B. Insulin Bolus Recommender System

The burden of diabetes has led to dedicate a huge amount of research efforts to improve the quality of life of people that suffer the disease, as well as, to minimize the impact on healthcare systems. In this context, the PEPPER project [9] proposes the development of an ICT platform to follow up people with T1DM and recommending them the insulin dose to administer in ingests events with the use of a recommender mobile app. The platform has two main components: a mobile part and a server component. Analogous to NoaH, the mobile part is addressed to citizens, in this case people with T1DM, while the server component is designed to be managed by the clinical staff.

The mobile component is attached to two sensors: a continuous glucometer that measures the blood glucose level, and a wrist band that provides information about the physical activity of the user. Moreover, the outcome (insulin dose), could be sent to an insulin pump for its infusion. Thus, there are two scenarios considered in PEPPER: multiple daily injections with insulin pen (MDI architecture in Figure 3), and insulin pump (CSII architecture in Figure 3). In this latter case, after the system recommendation is validated by the user, the dose is automatically sent to the pump and administrated to the user.

Regarding the recommendations provided in the mobile component, the use of CBR enables a personal and adapted answer to the user throughout time. PEPPER CBR methodology has been implemented using eXiT*CBR, however, the following new functions were added to it to meet PEPPER requirements: numerical reuse, revise step and maintenance step, which includes retain, review and restore, capable of tackling concept drift. The first task addressed was the numeric reuse, as the solution of the CBR methodology is a numeric parameter used to calculate the needed insulin dose [29]. Second, the CBR methodology of eXiT*CBR was extended by including a revise step and a maintenance phase, as proposed in [19], in order to correct proposed solutions given their outcome and then analyze the convenience of incorporating new experiences to the knowledge base and deleting old ones. Thus, these steps enable the system to learn from its continuous use.

Maintenance methods, according to [19], include two additional stages in the CBR methodology: review and restore. In the review stage, the case base is analyzed looking for obsolete data, according to what is known as concept drift [6], [20]: changes in concepts. In the particular case of T1DM management, people can suffer physiological changes so that solutions that have been right two months ago, could not be longer valid. As a consequence, in the restore stage, cases no longer valid (or labeled to be discarded due some review metrics) are removed from the case base [30].

The medical team involved in the decisions made in the development of the new functions includes all the clinical staff of the PEPPER project (http://www.pepper.eu.com/).

Regarding the PEPPER insulin recommender system, it has been tested with the UVA/PADOVA simulator [21], achieving successful results as reported in [29] and [28]. It will be validated soon with real users in the context of the PEPPER project.

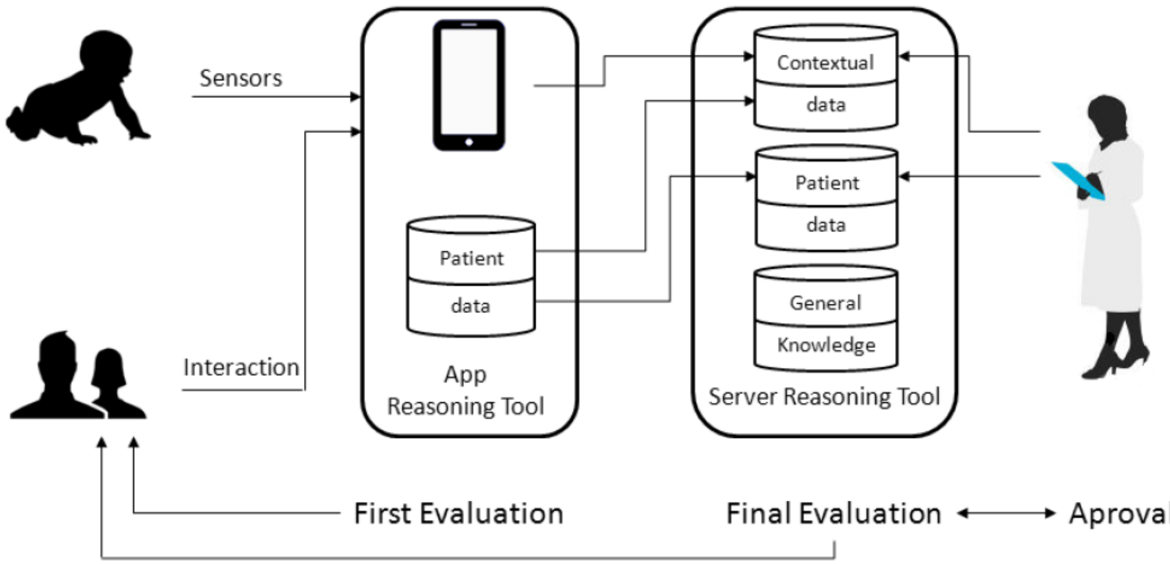


Fig. 2. Simplified architecture of NoaH from [24].

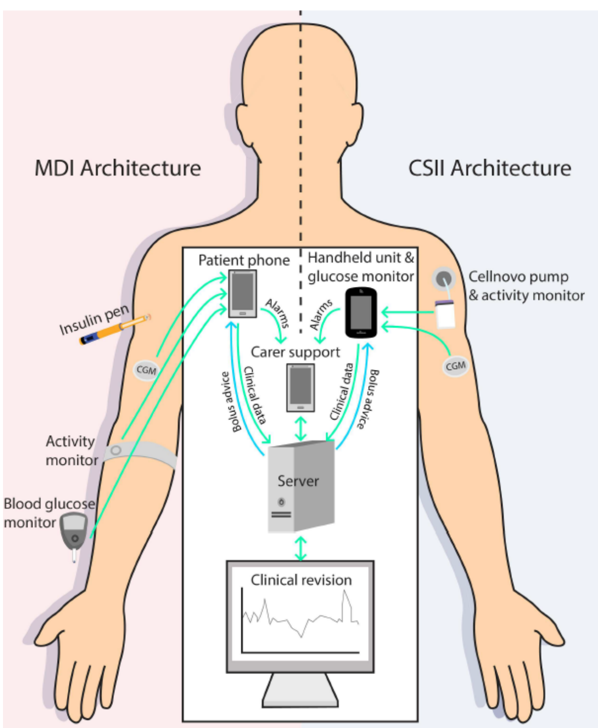


Fig. 3. Pepper architecture from [9].

*C. Healthy kids*

Having care of our kids today is the best bid we can make to have a healthy society tomorrow. However, three main diseases threaten kids' health: obesity, diabetes and asthma. While parents are conscious that diabetes and asthma are serious diseases, it seems that they are less aware about the harm of obesity. To address obesity issues, we develop MATCHuP, a tool to enhance good nutrition and exercise habits with the aim to reduce both, obesity and diabetes, known as metabolic diseases. MATCHuP platform is focused on people with metabolic diseases and their families to improve their education in the right habits. MATCHuP recommends actions connected to the patients' community using collaboration strategies to simplify input validation and competition incentives, to award the user with gaming. Dr. Abel Lpez-Bermejo from the Hospital Dr. Trueta of Girona supervised the research [18].

## V. Biosignal Processing

The appearance of new wearable and non-invasive sensors is providing new and disruptive solutions for the monitoring of patients, disease management and treatment adherence [22]. In fact, the mHealth applications described in the previous sections make use of wearables: NoaH uses a pulsi-oximeter, PEPPER uses a continuous glucometer and an activity wristband, and MATCHuP also uses wrist bands for monitoring kids' activity. However, there are new opportunities, new sensors that could be investigated for Medicine and Healthcare. This is the case of force sensors, for rehabilitation purposes, and portable EEG, for epilepsy seizure detection.

First, we worked in collaboration with the Evalan company in the context of the MOSCHA European project (EUREKA ITEA 2 n 11027 IPT-2012-0943-300000) and the Rehabilitation team of Dr. Herman R. Holstlag, Marco Raaben and Taco J. Blokhuis. The company developed sandal shoes with force sensors, in order to monitor patient gaits, In particular, people who have undergone hip surgery. The gait analysis provides information about the people who recovered in the expected time and people who had a slow recovery or never returned to a normal situation. Therefore, we dealt with a classification problem (good versus bad recovery). The input signal, first was processed with a bag-of-steps methodology, and then support vector machine and CBR were used for classification purposes [25].

A EEG wearable has been created by the MJN Neuroserveis company (http://mjn.cat/), and eXiT is studying the application of AI and ML techniques. This collaboration is subject to a confidential agreement.

## VI. Healthcare Services

In this section we have included the research related to the management of services, as ambulance coordination, medical equipment maintenance, and emergency attendance forecasting.

### A. Ambulance coordination

Ambulance services can be grouped in two main categories: emergency and programmed services. Regarding emergency services, they need to guarantee that persons with urgent treatment are attended in less than 15 minutes, independently of the distance to the nearest medical centre they are. To that end, we developed a multi-agent system, which includes fuzzy filters [13]. The system has been tested with the data provided in the Girona region, in collaboration with Quim Llorella and Rosa Prez (SEM services) who share with us the details of the real emergency transportation service. The work has been supported by the Spanish MEC (Ministerio de Educacin y Ciencia) project TIN2004-06354-C02-02.

Regarding the second category, programmed patient transport, the problem consists on providing, in a daily basis, a 24h scheduling to non-urgent ambulances in regard to their task of moving patients from home (or residences) to hospitals in order to receive a particular treatment; and next, provide an on-line scheduling to return them back home. To that end, we develop an ambulance coordination software module which has been transferred to the Lafcarr company under the name IrisAmb.

It is interesting to highlight that the research activity developed on ambulance coordination, especially on optimization methods, led to the creation, in 2011, of Newronia S.L., an spin-off company (http://en.newronia.com/). It is devoted to provide AI based solutions to optimize resources related to transportation and logistics.

### B. Medical Equipment Maintenance

Hospitals are having a growing burden on the management of medical equipment. To support them, two works have been carried out by eXiT: workflow monitoring for equipment repair, and fault prediction of complex medical equipment. First, workflow monitoring was proposed to follow-up the equipment repair status: expensive equipment had always the highest priority, and causes that less expensive one be never repaired. To implement the solution, we used Petri nets for workflow modeling and complex event processing (CEP) for workflow monitoring to predict possible delays [8]. The research was conducted inside the AIMES European project (Eureka ITEA2 07017, TSI-020400-2008-047) in collaboration with the University Hospital Magdeburg.

In the second case, we were dealing with a complex equipment, with several components that provide individual log reports. The aim was to predict the global, complex equipment failures as a combination of the information provided in the different individual logs. Therefore, we were dealing with longitudinal data. We use sequence learning methods to learnt sequential patterns, and next apply CBR for failure forecasting [4]. The work has been carried out under a confidential contract with a multinational company.

### C. Emergency attendance forecasting

Hospital patient waiting times and length of stay are indicators of the quality of emergency department (ED) services. It is necessary to accurately estimate ED patient arrivals in order to manage resources effectively. In the particular case of a Tourist region, this estimation is difficult due to the population variability. To that end, we collaborated with the ED of the Hospital of Palamós, placed in a tourist region, with a high population variability. We have tested several regression methods for attendance forecasting at different time horizons, and using some exogenous variables as calendar and weather data [1].

## VII. Conclusions

The eXiT research group has a long track of works in the Biomedical and Healthcare fields. This paper summarizes the main activities in these fields during the last years.

Future research include new application domains. First, regarding CDSS, we have been recently awarded with a project regarding attention-deficit hyperactivity disorder treatment recommendations, which is headed by Dr. D. Serrano and Dr. X. Castells. Second, concerning mHealth, we have an agreement with a private company to work with patients suffering migraines. Third, about biosignal processing, we are initiating some research on mental diseases. And finally, in regard to healthcare services, a PhD work is being conducted about improving the optimization of the plans for intensity-modulated radiotherapy.

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[1] Publication is under review

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