AAP Contrats doctoraux en Intelligence artificielle

ARRHYTHM.IA : Artificial intelligence for Arrythmia diagnosis

1. DESCRIPTION OF THE PHD THESIS PROJECT (UP TO 4 PAGES)

1.1 OBJECTIVES OF THE PROJECT BASED ON THE CURRENT STATE OF THE ART

Neuro-cardio-vascular diseases are the first cause of death in the world (17,5 million/year, i.e. 31% of all deaths). Stroke is the second most common cause of mortality world-wide (5.54 million/year) and the third most common in more developed countries. Up to 80% of strokes are attributed to brain ischemia with 30% of cardioembolic origin, atrial fibrillation (AF) being the most frequent and a major modifiable factor associated with a 5- fold increased risk especially in elderly. AF diagnosis is not obvious because of silent (asymptomatic) and mostly paroxysmal AF clinical forms in stroke patients. Current international recommendations are to use 24 hours Holter electrocardiogram (ECG) monitoring to detect occult AF when suspected but diagnosis rate is weak. Improving new AF diagnosis is medically necessary and technologically challenging. The longer or the more frequent ECG monitoring, the higher AF detection rate. Then it has been shown that serial 30s ECG significantly improve detection of AF 3-fold[1]. Academic researchers and industrials rely on technology advances to provide automatic tools that could facilitate physicians' work throught computing cardiology. Most of AF automatic detection techniques focus on high[2], and/or irregular[3] heart rate identification. But dealing with only heart rate and irregularity is insufficient. Since whole ECG signals include all necessary information to classify heart rhythm, instead of extracting and analysing multivariate time series from ECG singularities and their dynamics, more sophisticated computing methods including machine learning and deep learning are used with success on non-noisy signals. This “blind” and "brute-force like" approach seems to be efficient with standards ECG recordings but could misfit with nomadic devices use for at least two reasons : first, reliability of signals is weaker than from standard ECG devices, and second, intermittence of ECG documentation introduces a superimposed sampling challenge. Only few works are available on this focus[4,5]. Similarly to other scientific fields that have benefited of dynamical complex systems and deep learning approaches, such as particle or high energy physics, the possibility and then the

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[1] Douen et al. Serial electrocardiographic assessments significantly improve detection of atrial fibrillation 2.6-fold in patients with acute stroke, Stroke 39 480-482. 2008

[2] Tison et al. Passive Detection of Atrial Fibrillation Using a Commercially Available Smartwatch. JAMA Cardiol. May 1;3(5):409-416. 2018

[3] Haddi et al. Automatic atrial fibrillation detection using univariate and multivariate data analysis: Review. *Submitted*. 2018

[4] Xia et al. Detecting atrial fibrillation by deep convolutional neural networks. Comput Biol Med. Feb 1;93:84-92. 2018

[5] Kamaleswaran et al. A robust deep convolutional neural network for the classification of abnormal cardiac rhythm using single lead electrocardiograms of variable length. Physiol Meas. Mar 27;39(3):035006. 2018

capacity to mathematically describe and predict the cardiac electrical behaviour will be revolutionary to diagnose, treat, and prevent neuro-cardio-vascular diseases.

The aim of this thesis work will be to study and develop a set of effective tools to automatically classify cardiac rhythm states and predict the occurrence of arrhythmias from ECG. We will focus on the so-called embologenic rhythm disturbances, that is to say at the origin of clots which can migrate and obstruct the arteries (at the origin for example of ischemic strokes). These mainly include atrial fibrillation, atrial flutter, and numerous ectopias.

1.2 METHODOLOGY

To provide some generic and personalized models of ECG dynamics, a heart rhythm ECG classifier algorithm based on machine learning (neural networks and deep learning), and finally a medical decision making support software prototype we will process according to the methodology described below.

Several steps will be considered, including the design (models, architectures, and learning strategies) of efficient and portable classifier tools from existing collected data (specialized public databases, internal databases), the design of specific methods in order to adapt the models learned to clinical data related to ECG recordings, and an exploratory analysis in order to optimize the protocol for acquiring ECGs from patients explored for suspected embologenic arrhythmias. The work will therefore be carried out first on retrospective data, then on prospective data as part of a dedicated clinical trial.

Prediction and classification tools. We will design the most effective prediction and classification tools in view of the targeted and available data (ECG 1 derivation of 30s annotated from potentially discriminating related clinical data). Although the state of the art in machine learning and deep learning is well established, we will test and compare several convolutional and recurrent architectures. The models will be taught on the ECG data. We will use previous knowledge of the field (including the dynamics of heart rate) and the data studied to design architecture as was done for example in high energy physics[6]. For this we will use the existing mathematical models and those developed by our teams *(see section 2)*. In order to ensure the portability of the tools developed, we will explore the most promising strategies that have been proposed to obtain inexpensive resource implementations, including L1 regularization[7], compression of the layers of neural networks by low-ranking tensorial decomposition methods[8], and distillation[9].

Domain adaptation. We will have to take into account the potential gap between the data available in the development phase of the learning models, from traditional ECG recording conditions (resting

[6] Louppe et al. QCD-Aware Recursive Neural Networks for Jet Physics, Arxiv 2017.
[7] Cheng et al. A Survey of Model Compression and Acceleration for Deep Neural Networks, arxiv, 2017.
[8] Novikov et al. Tensorizing Neural Networks. NIPS 2015.
[9] Hinton et al. Distilling the Knowledge in a Neural Network, Arxiv 2015.

supine), and the data from nomadic devices on which our models are intended to be used. This is a domain adaptation problem (transfer learning). It will then be necessary to compare blind learning (that is to say without a priori knowledge of the noise generated by the nomadic ECG acquiring conditions) with alternative solutions proposing a specific domain adaptation with adversarial constraints or strategies[10,11,12,13]. We will increase transferability by integrating prior knowledge of the noise induced by the targeted ECG recording conditions.

Optimization of the acquisition. The study of the transition phenomena between the normal heart rhythm (sinus) and the targeted arrhythmias (in particular atrial fibrillation) should make it possible to propose a strategy of personalized and adaptive rhythm documentation encouraging the patient to carry out ECG recordings during more periods. high probability of arrhythmia. We will study and solve this problem by budgeted learning and sequential decision methods[14].

1.3 WORK PLAN

The methodology described above suggests splitting the project into five tasks. Below we provide some additional details about these tasks.

Task 1 *[T0-T6]*: State of the art review on both deep learning and on computational cardiology focusing on heart rhtyhm dynamics analysis and heart rhythm automatic classification.

Task 2 *[T0-T6]*: Creation of the dataset. Queries will need to be sent to the data warehouse of the medical service of the Assistance Publique – Hôpitaux de Marseille (AP-HM). This will require regulatory process including the authorization to use health data from the AP-HM univeristy hospital for research purposes and from the CNIL Health Data Access Commission, as well as generation an anonymization procedure.

Task 3 *[T6-T18]*: Prediction and classification tools, see methodology section.

Task 4 *[T18-T30]*: Domain adaptation and Optimization of the acquisition, see methodology section.

Task 5 *[T28-T36]*: Clinical trial, exploitation of results.

We plan to organize these tasks according to the following Gantt chart :

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[10] Long et al. Learning transferable features with deep adaptation networks. In Proceedings of the 32nd International Conference on International Conference on Machine Learning - Volume 37 (ICML'15), Francis Bach and David Blei (Eds.), Vol. 37. JMLR.org 97-105, 2015.
[11] Long et al. Deep Transfer Learning with Joint Adaptation Networks, International Conference on Machine Learning (ICML), 2017.
[12] Ganin et al. Unsupervised domain adaptation by backpropagation. In Proceedings of the 32nd International Conference on International Conference on Machine Learning - Volume 37 (ICML'15), Francis Bach and David Blei (Eds.), Vol. 37. JMLR.org 1180-1189.
[13] Goodfellow et al. Generative Adversarial Nets. NIPS 2014: 2672-2680.
[14] Contardo et al. Recurrent Neural Networks for Adaptive Feature Acquisition. ICONIP (3) 2016.

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Task 1	■	■	■	■	■	■																														
Task 2	■	■	■	■	■	■																														
Task 3							■	■	■	■	■	■	■	■	■	■	■	■																		
Task 4																			■	■	■	■	■	■	■	■	■	■	■	■						
Task 5																													■	■	■	■	■	■	■	■

1.4 SUPERVISOR AND RESEARCH GROUP DESCRIPTION

This research project will be supervised by Mustapha Ouladsine (PhD, see profile below) and Stéphane Delliaux (MD-PhD, see profile below). The medical knowledge including heart rhythm dynamics and electrogenesis aspects will be carried out by Stéphane Delliaux while computational and deep learning aspects will be devoted to Mustapha Ouladsine. Both have worked together from 2015 on automatic heart rhythm classification strategies and have several common research papers and patents (see recent publications section below). A collaboration has been established specifically for this project with Thierry Artières, international expert in deep learning and Pr Jean-Claude Deharo (head of the rhythmology department of Marseille university hospital) for the clinical trial.

The project is neither supported by other research funds nor is part of a larger research programme.

2. RECENT PUBLICATIONS

T. Youssef, Bouchra Ananou, Mustapha Ouladsine. An Advanced Arrhythmia Recognition Methodology Based on R-waves Time-Series Derivatives and Benchmarking Machine-Learning Algorithms. *European Control Conference (ECC 2020)*, May 2020, Saint Petersburg, Russia.

Z. Haddi, B. Ananou, Y. Trardi, J-F. Pons, S. Delliaux, M. Ouladsine, and J-C. Deharo, *Relevance Vector Machine as Data-Driven Method for Medical Decision Making,* European Control Conference, 1011-1016, 2019

Delliaux et al. Mental Workload Alters Heart Rate Variability, Lowering Non-linear Dynamics. Front Physiol. 2019 May 14;10:565.

Youssef Trardi*, Bouchra Ananou, Zouhair Haddi, Mustapha Ouladsine. An Effective Data-Driven Diagnostic Strategy for Cardiac Pathology Screening. 15th European Workshop on Advanced Control and Diagnosis, ACD'19. Bologna, Italy, 21-22 November 2019

Y. Trardi ; B. Ananou ; Z. Haddi ; M. Ouladsine , Multi-Dynamics Analysis of QRS Complex for Atrial Fibrillation Diagnosis . *5th IEEE International Conference on Control, Decision and Information Technologies (CoDIT 2018)* Page s: 1067 – 1072. April 10-13, 2018 Thessaloniki, Greece.

Y. Trardi ; B. Ananou ; Z. Haddi ; M. Ouladsine A Novel Method to Identify Relevant Features for Automatic Detection of Atrial Fibrillation. 2018 *26th IEEE Mediterranean Conference on Control and Automation (IEEE MED)*. Zadar, Croati, June 19-22, 2018

Zouhair Haddi, Bouchra Ananou, Youssef Trardi, Jean-François Pons, Stéphane Delliaux, Mustapha Ouladsine, Jean-Claude Deharo, *An Efficient Pattern Recognition Kernel-Based Method for Atrial Fibrillation Diagnosis,* Computing in Cardiology, vol. 45, 1–4, 2018.

Zouhair Haddi, Jean-François Pons, Stéphane Delliaux, Bouchra Ananou, Jean-Claude Deharo, Ahmed Charaï, Rachid Bouchakour, Mustapha Ouladsine, *A Robust Detection Method of Short Atrial Fibrillation Episodes,* Computing in Cardiology, vol. 44, 1–4, 2017.

Jean-François Pons, Zouhair Haddi, Jean-Claude Deharo, Ahmed Charaï, Rachid Bouchakour, Mustapha Ouladsine, Stéphane Delliaux, *Heart rhythm characterization through induced physiological variables,* Scientific Reports, 7:5059, 1–13, 2017

Zouhair Haddi, Stephane Delliaux, Jean-Francois Pons, Ismail Kechaf, Jean-Claude Deharo, Mustapha Ouladsine, *Multivariate Data Analysis for Automatic Atrial Fibrillation Detection, accepted for Oral presentation in 18th International Conference on Telecare and Telemedicine, Miami, USA, December* 05-06, 2016

3. EXPECTED PROFILE OF THE CANDIDATE

We are looking for a highly motivated candidate with a solid background in mathematics and computer science. He/she must have recently obtained a master's degree or be about to complete it. The candidate must have an interest in life sciences and more specifically in medicine, as the project aims to apply his/her fundamental knowledge in the medical field. He/she will need to have a strong interaction with physicians. The candidate will also need to demonstrate good programming skills, including MATLAB, Python and C++. Knowledge of statistical data processing and analysis, neural networks and machine learning and diagnostics will be appreciated.

Depending on the interdisciplinary orientation of the project and the team, the candidate should also be open-minded, curious, able to learn a little more about human functioning and medical knowledge, and able to adapt to his/her comfortable environment.

4. SUPERVISORS' PROFILE

- *Data sciences and Machine learning supervisor*

Mustapha Ouladsine received his PhD in automation from the University Henri Poincarré, Nancy, France in 1993. He is currently full professor at the University of Aix-Marseille (AMU) in France. He is Professor of Data Science, Neural Networks and Diagnostics at AMU. He has served as editor of some IEEE conferences. His research focuses on health monitoring of dynamic systems. He is the author of several international publications and books on fault detection and isolation in dynamic systems. He has supervised more than 22 PhDs and is currently supervising 4. Since 2016, he is interested in the use of artificial intelligence and more specifically in competitive learning by neural networks for health diagnosis.

- *Medical supervisor*

Stéphane Delliaux is assistant professor - full lecturer in physiology at Aix-Marseille University. He is an intensivist medical doctor (MD, 2003) and physiologist (PhD, 2006). He is in charge of the cardiorespiratory and exercise physiological tests at the North Hospital university hospital of Marseille (AP-HM). He is also researcher in the Dysoxia Team of the joint INSERM - AMU team that is the C2VN (Center for CardioVascular and Nutrition research, Aix - Marseille University). He focuses on physiological and medical states modeling and particularly focuses on hearth rhythm dynamics research. He co-leads the creation of a federal structure merging numerical sciences and artificial intelligence forces to target health and medical challenges. He is currently preparing his leading research habilitation and he is not supervising any PhD student.

VISA DU RESPONSABLE DE L'INSTITUT ET DU DIRECTEUR DE LABORATOIRE CONCERNÉS

Visa du responsable de l'institut,
NOM Prénom

Fait à Marseille, le

Signature

Visa du directeur du laboratoire,
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Fait à Marseille, le 14 mai 2020

Signature

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