2nd Newsletter- August 2021 View online

PersonalizeAF Second Newsletter

Welcome to the second newsletter of the PersonalizeAF! The objective of this bianual publication is to keep all our public updated with all information and main ongoing activities while our project is under way. Today, we are launching the second edition of, in which we will sum up all the interesting results about our ESRs and their projects, together with their secondments plans, training, scientific results, events,...

Do not miss it and stay tuned for all this information! And suscribe to receive all the news!

PersonalizeAF, the project bringing universities, hospitals and companies from all over Europe together to tackle Atrial Fibrillation

What is Atrial Fibrillation?

Atrial fibrillation (AF) is a condition that causes an irregular and often abnormally fast heart rate. With different manifestations in each patient, it causes a worsening quality of life and a drastic reduction in life expectancy. Today, it is the most common cardiac arrhythmia, affecting more than 6 million Europeans and its prevalence is expected to double in the next forty years. Moreover, its cost exceeds 1% of European healthcare budgets (13.5 billion per year).

To reverse these figures - or at least reduce them - experts agree on the need to promote individualised patient management by personalising cardiovascular therapies.

What does PersonalizeAF network do?

PersonalizeAF addresses this challenge by delivering an innovative multinational, multi-sectorial, and multidisciplinary research and training programme in new technologies and novel strategies for individualized characterization of AF substrate to and increase treatments' efficiency.

This initiative involves European universities, hospitals and companies researching atrial fibrillation from different fields. Using artificial intelligence, signal processing and stem cell research, PersonalizeAF brings together engineers, clinicians and biologists to improve treatments, develop new diagnostic methods and optimise patient management.

From the research point of view, PersonalizeAF will integrate data and knowledge from in-vitro, in silico, ex vivo and in vivo animal and human models to:

1) generate an individual description of the state of the atrial muscle identifying the disease mechanisms and characteristics;

2) understanding the potential effect that different therapies have on different atrial substrates; and

3) combining this information to generate a specific profile of the patient and the best therapy for each patient.

With this purpose, PersonalizeAF partnership aggregates relevant scientific staff from the academic and clinical world with highly specialised biomedical companies which will be involved in a high-level personalised training programme that will train a new generation of highly skilled professionals and guarantee ESRs and future PhD students outstanding Career Opportunities in the biomedical engineering, cardiology services and medical devices sectors.

PersonalizeAF project updates

Our ESRs 15 and their research projects

Now, our 15 ESRs are working full-time in their projects around all Europe and different sectors: academic, clinical and industry. Each of them is working in their individual PhD, but work also collaboratively with the same purpose, improving the diagnosis and treatment of

Atrial Fibrillation patients in Europe. This, with the objective of improving the quality of life of all this patients.

In the first Newsletter, they shared some words about their expectations at their project, and now they will give an update on their work and how it has evolved after some months working as Early Stage Researchers, since the start of #PersonalizeAF project.

- **ESR1**: **Mariú Casini,** Instituto de Investigación Sanitaria la Fe (Spain):

"As some of you could already know, my project is mainly focused on building an in vitro model of atrial fibrillation to test the molecular and physiological effect of different drugs. Hopefully, this project will help clinicians for the drug decision process and researchers to understand other possible drug targets. But before working on the drug screening… I need a model! For this reason, what I have been doing so far is to differentiate human induced pluripotent stem cells (hiPSCs) into cardiomyocytes, not general cardiomyocytes, but the atrial ones. Because we want to test specific atrial fibrillation drugs and I need a population with a high percentage of only atrial cardiomyocytes. To reach this goal I spent my first 6 months of the project in cell culture to test different protocols on three hiPSC lines to get the atrial cardiomyocytes cells and start with the experiments."

- **ESR2: Carmen Martínez Antón:** Karlsruhe Institute of Technology (Germany)

"Regarding my simulations, I am setting up a 3D model of the MiFi catheter from Boston Scientific and one of the most used sheaths from Merit Medical to introduce it. This catheter in particular has three ring electrodes and three mini electrodes close to the tip, as well as the possibility of flushing NaCl through the tip. With this flushing is possible to control the temperature of the tissue during the ablation and be sure that it is not completely burn and creates an undesired scar, which is possible by heating the tissue in a better uniform distributed way.

So, giving different conductivity values to the different parts, we can set a tissue patch, a "vein", a catheter with its different conductive or isolated parts, a sheath that can be more or less overlapping with the catheter and the NaCl flushing. With all of them together inside of a "blood box", the goal is to perform in silico simulations in order to detect which factors can affect real performances."

- **ESR3**: **Eric Invers Rubio -**Institut d'Investigacions Biomèdiques August Pi I Sunyer(Spain)

" *In IDIBAPS we are starting to collect information from patients with AF that undergo an ablation procedure. For these patients we are collecting data from three different techniques: electrocardiographic imaging (ECGi), electroanatomical mapping and late-gadolinium enhancement MRI (LGE-MRI). We are collaborating with the group in UPV in order to compare the data from these three techniques and we are currently focusing on the analysis of reentries found with ECGi and fibrosis detected with LGE-MRI. We are planning to add the sinus rhythm information captured with ECGi and the electroanatomical data soon. "*

- **ESR4: Sachal Hussain-** Università di Bologna (Italy):

"My work is related to the image processing of AF patients. Initially, I am working on the segmentation of left atrium. For this purpose, I am acquiring and testing three dimensional echocardiographic data (3D Echo) of AF patients. Then I am studying and analyzing different approaches to dynamically segment left atrium using the acquired 3D Echo data of AF patients."

- **ESR5: Ozan Ozgul, -** Maastricht University (The Netherlands)

"During the first phase of my doctoral studies, my work focused on repetitive atrial activation pattern detection and quantification. I have proposed a framework for high coverage and high density atrial activation maps called composite maps. Apart from implementation and optimization of this technique, I have also tested it on various AF datasets -human and animal models of AF. A comprehensive paper exhibiting my works on composite maps is being prepared at the moment. Apart from composite maps, I have spent some time on development of additional computational tools that can be utilized during the generation of composite maps. One of these tools is an activation time annotation-free recurrence plot generation technique for intracardiac signals. I have proposed three techniques, each accepting raw electrograms as input and reconstructing phase space trajectories that can be utilized to characterize AF complexity and generate composite maps. Each of these techniques was observed to perform well on human AF datasets."

- **ESR6**, **Teresa Schiatti** at Universitaets-Klinikum Freiburg (Germany):

"Just to briefly recap, my projects aims at investigating how mechanics tunes cell coupling. To do so I am currently working on two main models: single cardiac cells and tissue slices (multicellular preparations). The first allows one to get an insight in how the bulk cell type of the cardiac tissue works, the second allows to study an integrated behaviour which is a bit closer to what is likely to happen in the native heart. I am currently characterizing a this slice culture model which is incredibly exciting - just thinking about the journey that the tissue does from the patient to when I put it in culture is astonishing. Concerning the single cells experiments, I have started to stretch this cells to investigate how this mechanical change affects calcium handling within the cell. Looking forward to see the results!"

- **ESR7: Cristian Barrios Espinosa -** Karlsruhe Institute of Technology (Germany):

"During the first 9 months of the project, a new Eikonal model capable of reproduce reentry has been in development. At the beginning, a literature review was done to better understand the field. Then, the most common Eikonal models were implemented in the state of the art. In the last three months a new algorithm has been introduced in the openCARP code for cardiac model simulations. This algorithm contains new ideas that renders reentry possible in this kind of model. At the moment, the last details before having a working model are being fixed. Once the model is producing results, it will be tested and compared with the biophysical model in different settings and clinical data.

In parallel with the main research, side projects related to conduction velocity influences produced by tissue geometry and wave-front shape have been created. Conduction velocity is the most important input in the Eikonal model. In these projects, regression models, based on parameters such as the wall thickness, curvature and distance to the boundary of the tissue, are being created based on bidomain simulations. Up until now, a regression model of the geometrical properties of the tissue has been implemented. Moreover, these results allowed successfully to reproduce in the Eikonal model the qualitative behavior observed in the bidomain model."

- **ESR8**: **Tomas Hutschalik-** NCARDIA, The Netherlands:

"Differentiating induced pluripotent stem cells into atrial cardiomyocytes turned out to be a success so far. The cells are beating and the many assays trying to look into their characteristics seem preliminarily fine as well.

Working on an in vitro model for atrial fibrillation using these cells has so far been fruitful as well. With my primary focus currently being to establish a coculture with other differentiated cells, I ended up with some interesting cell combinations that gave me some electrophysiology data to analyse for the coming days. Hopefully some exciting insights into were to move further with the model in the future are up ahead."

- **ESR9: Albert Dasì i Martìnez-** University of Oxford (United Kingdom):

"My main research project is focused on the personalization of drug therapies for improving the pharmacological management of atrial fibrillation.

The choice of an antiarrhythmic drug is based on the patient clinical profile, namely: type and severity of associated cardiovascular disease. However, a large proportion of young patients suffering from atrial fibrillation are free structural/functional heart disorders. These patients have no therapeutic procedure restriction, so the drug choice is made according to the cardioversion time of the available drugs (i.e., time from drug administration to recovery of the normal sinus rhythm). Priority is given to those drugs that produce a fast cardioversion.

However, since pharmacological agents target specific ionic currents and individuals present natural inter-subject variability in channel density, different subjects might respond differently to the same drug. Therefore, I hypothesize that pharmacological cardioversion rates would considerably increase if the drug choice was also made according to the electrophysiological profile of each subject.

In order to test my hypothesis, I have generated a population of virtual whole-atria human models that differ in their ionic current distribution. Atrial fibrillation has been induced using this population of 3D models, leading to more than 200 episodes of sustained fibrillation. After induction, drug administration has been modeled for a number of pharmacological compounds. Those episodes of atrial fibrillation that are cardioverted by the same drug are group together and compared against the episodes cardioverted by

other drugs. The electrophysiological profiles of the 3D model are then assessed to find relationships between drug success and specific ionic current distributions."

- **ESR10**: **Narimane Gassa-** University of Bordeaux (France)

"Our first concern is to build a cardiac electrophysiology model that is easy to calibrate and suitable for clinical use in terms of time computation with an accurate description of heart arrhythmia. We developed an eikonal model able to stimulate spiral waves that will appear in the FIMH 2021 conference. For this, We enhance the conduction velocity adapted eikonal mode presented in the work of Corrado and Zemzemi with a time-varying parametric function that describes the diffusive current. A potential advantage of this approach is the rapid simulations that can be performed. In fact, we have also reduced the computation time with an offline resolution of the ionic model. In our future work, we would like to use the eikonal model to improve solving the ECGI problem in atrial fibrillation conditions."

- **ESR11: Carlos Fambuena Santos** Universitat Politècnica de València (Spain)

"During this last months I have developed a rotor detection algorithm based on ECGI phase maps. I have created a platform in MATLAB to label patients data in order to test the accuracy of the algorithm and study the potential clinical prediction of phase singularities detected the algorithm. This last task was done using data recorded from AF patients who underwent pulmonary vein ablation.

Other than this, I have been working on introducing new atrial geometries in our AF simulation platform. I hope in the near future I can use these new geometries to simulate not only AF, but also different ablation strategies in order to test algorithms also from a treatment point of view."

- **ESR12**: **Patricia Martínez Díaz-** Karlsruhe Institute of Technology (Germany):

"During these past 8 months since the start of my PhD I have been working on the quantification of atrial fibrillation vulnerability. In order to do that, I generated a virtual model from a patient and tried to identify the points that could induce a reentry. The protocol I am using to induce a reentry is described in the paper by Azzolin L. et al. 2021.

The general ideal is to pace at different locations in the atria, especially close the vulnerable timing (e.g. after the end of the refractory period). Then the number of inducing points will be quantified, so at the end we could measure how vulnerable the model is. In addition, the model parameters have been modified in order to simulate two different mutations of the hERG gene: N588K and L532P as described in Loewe A., et al., 2014.

Recently I held my first scientific presentation at the Institute of Biomedical Engineering, where I described in more detail my research questions and possible modelling approaches to answer them. "

- **ESR13**: **Sergio Nabil Gadur-** SIMULA (Norway)

"During the first three months working as a researcher in the PersonalizeAF project, I have been simulating the blood flow in simple left atrium geometries. In order to obtain more realistic CFD simulations of the blood flow, taking into account that blood is a non-Newtonian fluid, I have performed a sensitive analysis and studied the influence of the non-Newtonian rheology models, simulating a single cardiac cycle and the flow rates at peak systole. All of these tasks represent a great progress in the study of atrial flows. However, the previous models were performed using rigid walls which is not reflective of the real problem: the movement of the heart walls during sinus rhythm and the atrial fibrillation condition. Thus, the next step will be to implement a prescribed motion technique in my model, introduce patient-specific medical images as input to my simulations, and run individual blood clot formation."

- **ESR14: Victor Gonzalves Marqués** - Maastricht University (Netherlands):

"My project has been focusing on two main areas: the first involves the improvement of the 3D atrial model we use for our simulations, including adjusting the anatomy to be more realistic, updating visualization algorithms, and obtaining electrogram AF signals with virtual catheters in the modeled atria. The second area is related to the signal processing, detecting phase singularities on the simulations, and relating them to the patterns observed in recurrence analysis applied on the AF electrograms."

- **ESR15: Alexander Lacki** - Universitat Politècnica de València (Spain)

"The first 9 months have passed, and we have made great progress, including submitting an abstract to the Computing in Cardiology conference. Tackling this difficult topic with my amazing colleagues is a great experience that is allowing me to grow and develop intellectually, as well as personally. I am excited to see what the future holds for us, and I am beyond optimistic that together we can change the paradigm in atrial fibrillation treatment."

If you want to get to know the Early Stage Researchers way better and they pathway, stories and experiences, click here

Some Photos of ESR11, ESR12, ESR9, ESR1, ESR4, ESR10, ESR14 and ESR2

Some Photos of ESR6, ESR5, ESR7, ESR8, ESR15, ESR4 and ESR13

Videoblogs in YouTube

In PersonalizeAF project we are committed to bring closer science to society, which is related to the H2020 objective of contributing to Open Science and research.

That’s why the 15 Early Stage Researchers part of this multidisciplinar and international network are contributing to this challenge staring their own videoblogs' project.

Sharing a common YouTube channel and social networks, they have started a project of Videoblogs, in which we will be able to know periodically the results of their research in #Afib, their activities, but we will also learn about clinical perspective, stem cells, artificial intelligence, signal processing, echocardiography, etc.

Don’t miss their videos, that will be launched every 6 months, and subscribe to their channel to stay tunned!

PersonalizeAF Youtube Channel

Computing in Cardiology 2021- 6 ESRs will be participating

We can proudly say that some of the ESRs working at PersonalizeAF network have submitted their papers to Computing and Cardiology Conference, which will be held at Brno, Czech Republic in 2021, 12-15 September. Computing in Cardiology is an international scientific conference that has been held annually since 1974, providing a forum to discuss current research in topics such as **computing in clinical cardiology** and **cardiovascular physiology**. Here the titles of the interventions they will be presenting:

ESR5: "*State Space Embedding of Atrial Electrograms to Detect Repetitive Conduction Patterns During Atrial Fibrillation"*

ESR9: "*Atrial Fibrillation in the Absence of Structural Inhomogeneities: Role of ionic current up-/down-regulation on fibrillation inducibility"*

ESR10: "*Cardiac EGM Automatic Screening of egmstransmitted by Implantable Electronic Devices"*

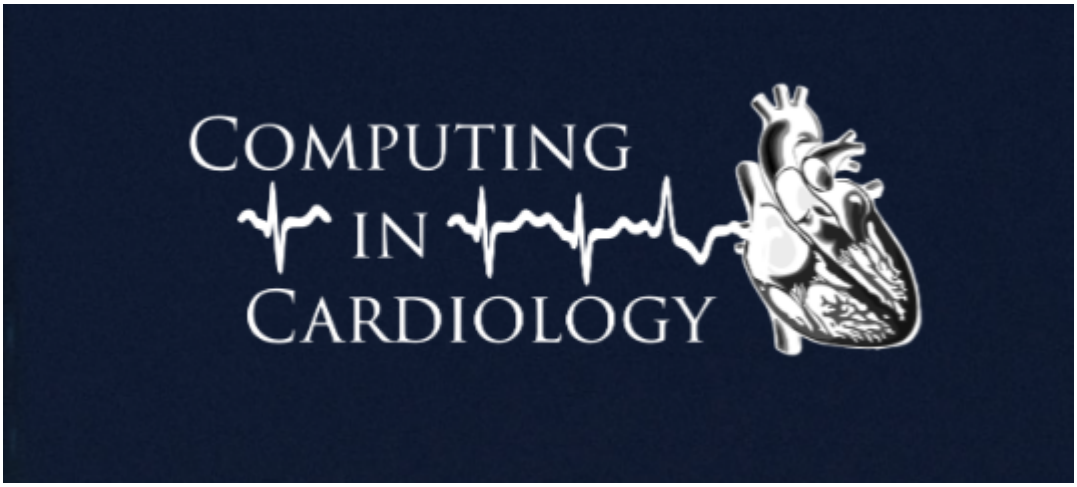
ESR11: "*An evaluation on the clinical outcome prediction of rotor detection in non-invasive phase maps."*

ESR14: "*Spatial Relationship Between Atrial Fibrillation Drivers and the Presence of Repetitive Conduction Patterns Using Recurrence Analysis on In-Silico Models"*

ESR15: "*ECGI Periodicity Unraveled: A Deep Learning ap-proach for the Visualization of Periodic Spatiotem-poral Patterns in Atrial Fibrillation Patients*"

Furthermore, ESR11 has been nominated to the Rosanna Degani Young Investigator Finals, and he we will be also opening the congress.

Congratulations to all our excellent researchers!



Events and training courses

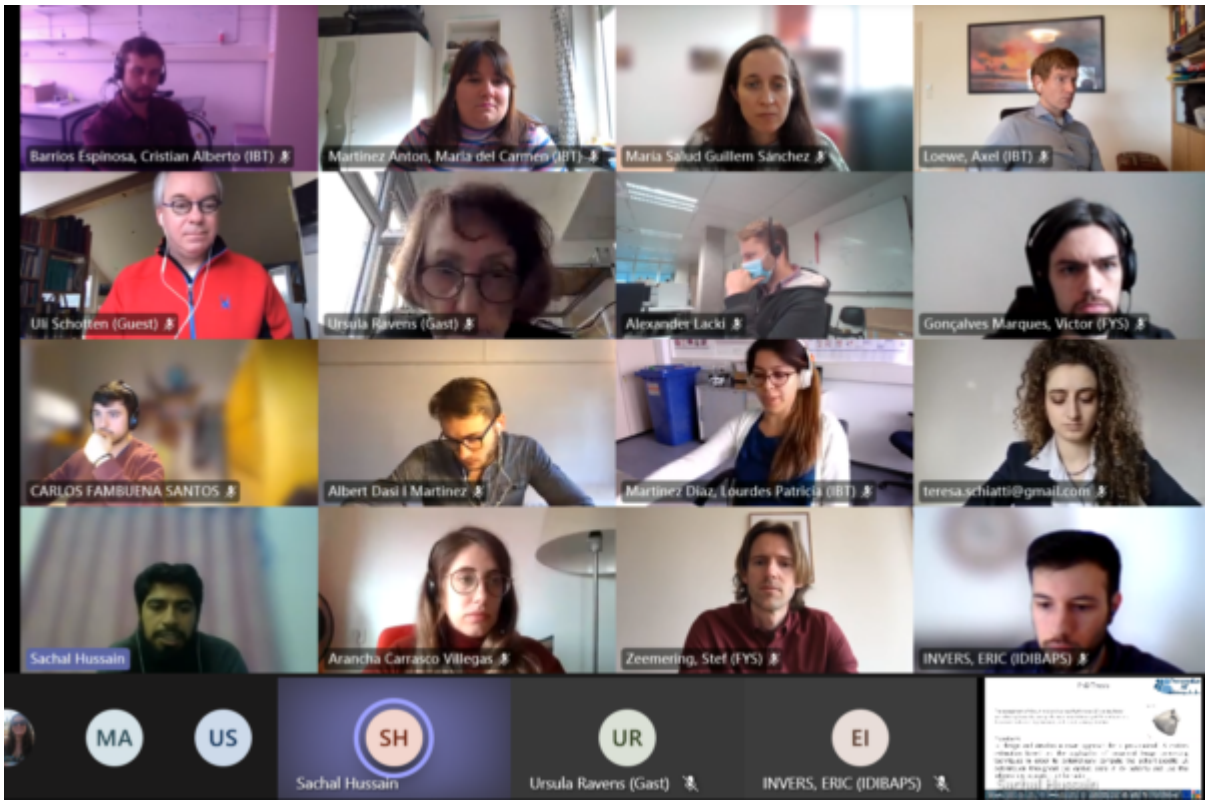
Second and Third Consortium Meeting of the Network

10th/11th March and 28th/29th June 2021, the 2nd and 3rd consortium meetings were held, respectively, in a fully online format.

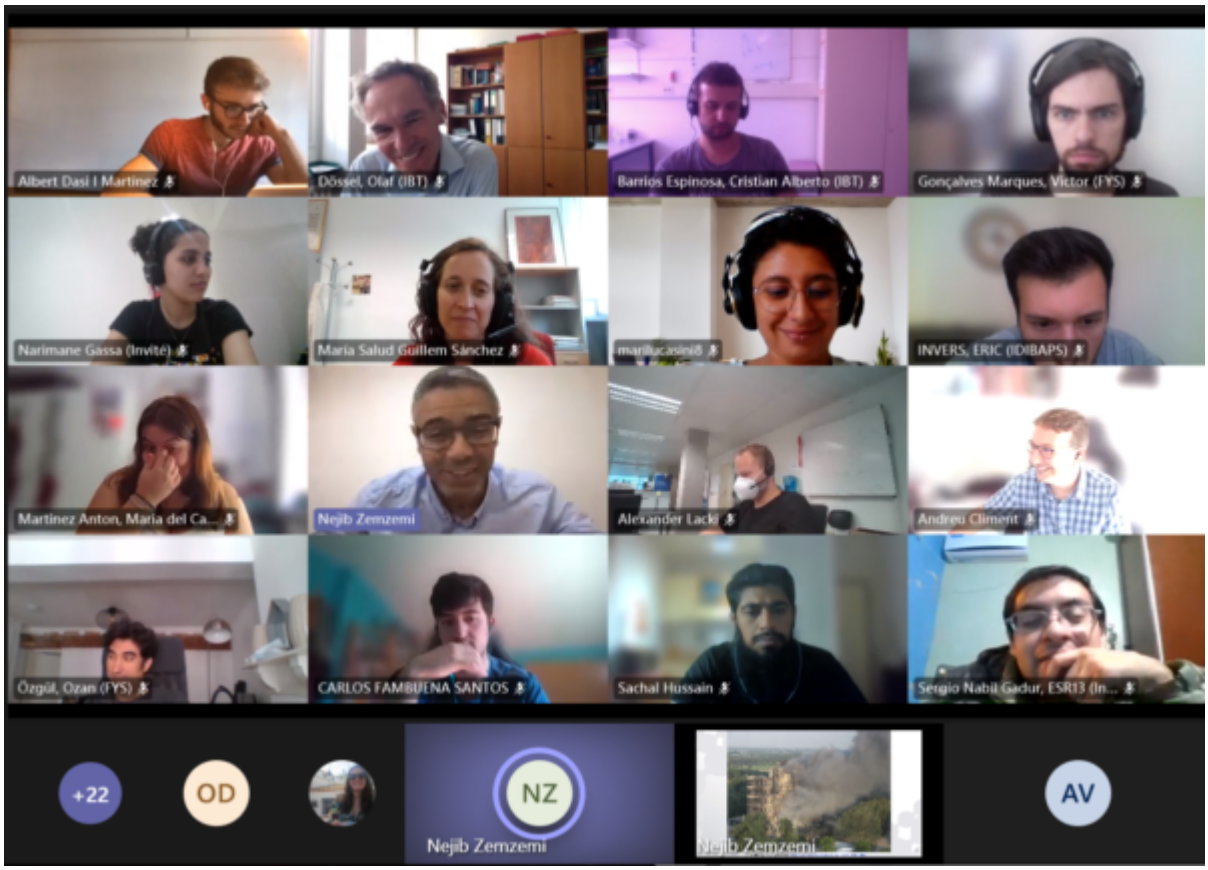
In these meetings, all ESRs presented their progress in their individual research projects, and could hear the feedback of their colleagues and supervisors.

Also, the different updates in the Work Packages were presented, such as the results in disseminations and communication, publications, participation in congresses, social media and website, training programs, ethics and GDPR… The ESRs also had the opportunity to talk with the Equal Opportunity Champion and Ethics misconduct delegate, and to join in the Student Committee.

Thanks to everyone for attending!



Some of the participants in the second meeting



PersonalizeAF members in the 3rd meeting

Meetings with Experts

During both meetings, the ESRs had the opportunity to meet with some experts: they presented their work and had inspiring conversations con **José Jalife**- Distinguished Senior Scientist at the Spanish National Cardiovascular Research Center (CNIC)- **Rob MacLeod** - Ph.D. Professor of Biomedical Engineering and Medicine at SCI Utah-, and **Natalia Trayanova**, Murray B Sachs Professor in the Department of Biomedical Engineering at Johns Hopkins University.

The impressions, both for the ESRs and the experts were highly positive. All the ESRs had the opportunity to learn from lead experts from different backgrounds and topics, and to include different perspective in their research plans.

In addition, we were honoured to host two talks for researchers by two members of the consortium: **Gernot Plank,** member of the Advisory Board, with his lecture “Automating workflows for creating high-fidelity digital twins of cardiac electro-mechanic function”, and **Barbara Casadei**, supervisor from University of Oxford, who presented the audience with a key reading called “Atrial Fibrillation: where are the gaps?”.

Screenshot of the Keynote lecture given by Barbara Casadei

Advanced signal and image processing school, organised by Maastricht University held online in April-May 2021.

In April-May 2021, Maastricht University organized the second PersonalizeAF course targeted to the 15 ESRs but also open to other newly researchers. The ESRs tell us what they learnt in this multidisciplinary course:

- **Systems in Biology** "*we learned about the different levels of AF research and review publications from each one: Transcriptomics and large scale histology, Mechanistic computer models of AF and Signal analysis*"
- **Advanced signal processing** " *we learned techniques for time-frequency representation of signals, blind source separation and complexity measures*".
- **Diversity in research**: "*Our personal impression of the professional performance of men vs women was test at the beginning of the course with a well designed experiment. We then had the chance to analyse the results. The conversation also included diversity management from a cultural point of view*."

- **Time Management:** "*We worked on a time management plan at different time scales, from a weekly plan to a long term project plan our thesis*."
- **Best teaching practices module:** "*Thanks to Janine and Pauline we understood how essential is the creative thinking process for communicating science. The course was made mainly of practical exercises to improve our teaching and communication skills.*"
- **Advanced Signal Processing module**:"*In the course of Advanced Signal Processing we learnt how to take the most advantage of different physiological signals with Stef and Pietro. In small groups, we presented a Miniproject at the end of the course, putting into practise different techniques such as PCA, or entropy measurements*."

Mid-term Check meeting

Last 7th May 2021, representatives from the different organizations which take part in the , together with the ESRs, held a full-day meeting with the Project Officer of the project. The meeting was held with the objective of reviewing the work done so far, and the plans for the future.

The Project Officer congratulated the consortium because of the interdiscilplinarity of the participants and the work done so far, and provide with some feedback to improve future work.

Next Events

4th Consosrtium meeting and "Clinical management of AF and bioengineering" workshop, January 2022 in Valencia (Spain)

Next January, and if the sanitary situation allows it, the PersonalizeAF consortium will be meeting in person in Valencia. The occasion will be the fourth meeting of the network, and will be organized by Hospital La Fe. The dates will be confirmed soon.

After the meeting has finished, the ESRs will attend their fourth training course, at La Fe premises. This course, named “Clinical management of AF and bioengineering workshop” will include the following trainings:

Scientific Modules: Cell culturing and stem cells differentiation module, Transcriptomic and proteomic analysis module, Next Generation Sequencing Technologies module, Clinical management of atrial fibrillation module

Transferable skills modules: Ethics in research module and Public engagement module.

Are you interested in the course? We will share more information soon, but if you want to be informed about this course, you can reach us in personalizeaf@itaca.upv.es

Atrial Signals Conference

Atrial Signals Conference will be held in Karlsrhue (Germany), between 23th -25th September which comprises more than 60 invited talks by renowned experts in the field. This conference will have sessions such as The Arrhythmogenic Substrate, Atrial Signals – Novel Technologies, or Depolarization Patterns of AFlut and AFib.

PersonalizeAF network will be presented there by María Guillem, our coordinator. Moreover, several of the researchers participating in PersonalizeAF will be taking part on it, such as Olaf Dössel, Ulrich Schotten or Blanca Rodríguez. Check the agenda and don't miss their interventions!

Gordon Conference

GRC is committed to our mission to advance the frontiers of science and provide an international forum for the presentation and discussion of frontier research in the biological, chemical, physical and engineering sciences, and their interface.

ESR6 will be presenting a poster in this conference. Congratulations!

FIMH2021 Conference

The FIMH2021 Conference created to discuss the latest in cardiac and cardiovascular imaging, electrophysiology, computational modeling, and translational applications.

Our ESR10 will be presenting her contribution in this conference with: "*Spiral Waves Generation Using an Eikonal-reaction Cardiac Electrophysiology Model*". Congratulations!

We recommend: Papers addressing Atrial Fibrillation

In this section, the consortium wants to share some of the Papers addressing Atrial Fibrillation and other arrythmias with were considered of interest and inspiring for our work. Check them out in order to learn more about Atrial Fibrillation, stem cells, image processing, 3rd printing cardiac modelling, etc!

"Geometrical Patterning and Constituent Cell Heterogeneity Facilitate Electrical Conduction Disturbances in a Human Induced Pluripotent Stem Cell-Based Platform: An In vitro Disease Model of Atrial Arrhythmias" by Hiroyuki Nakanishi J.L. et al

"The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz" by S Gabriel et al

"Slow whole left atrial conduction velocity after pulmonary vein isolation predicts atrial fibrillation recurrence" by Kurata, N., Masuda M. et al

"Making three-dimensional echocardiography more tangible: a workflow for three-dimensional printing with echocardiographic data" by Azad Mashari et al

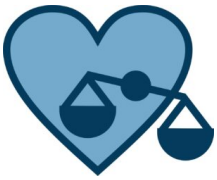
"Geometrical Patterning and Constituent Cell Heterogeneity Facilitate Electrical Conduction Disturbances in a Human Induced Pluripotent Stem Cell-Based Platform: An In vitro Disease Model of Atrial Arrhythmias" by Hiroyuki Nakanishi et al

"Molecular Basis of Atrial Fibrillation Pathophysiology and Therapy: A Translational Perspective" by Stanley Nattel et al

"Dynamics of Atrial Fibrillation Mechanisms and Comorbidities" by Jordi Heijman et al

Last blog entries and News

Once a month, our researchers are sharing their latest updates about their research pathway. Do you want to learn more about Atrial Fibrillation? About how researchers life is? Check their articles and follow them on Social media!

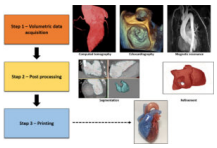


July 21, 2021

Decision-making under Uncertainty: Heuristics and Biases

Decision-making under Uncertainty: Heuristics and Biases Happy readers, Today I would like to discuss with you a paper by Amos Tversky and Daniel Kahneman [*] about the heuristics that used…

Read more...



July 19, 2021

Application of 3D printing in cardiology and Atrial fibrillation:

Application of 3D printing in Cardiology and Atrial fibrillation: This post explains the importance and application of modern manufacturing technology “3D printing” in cardiology to better understand cardiac models. 3D…

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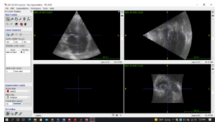

July 9, 2021

Echocardiography and Atrial fibrillation

Echocardiography and Atrial fibrillation This post is about echocardiography and its application in atrial fibrillation An echocardiogram (echo) is a test that uses high frequency sound waves (ultrasound) to make…

Read more...

July 8, 2021

Cells from Cells from Cells - The (never)ending cycle of life

Cells from Cells from Cells – The (never)ending cycle of life Prometheus being attacked by an eagle, depicted in a sculpture by Nicolas-Sébastien Adam, 1762 (Louvre) In a tale of…

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