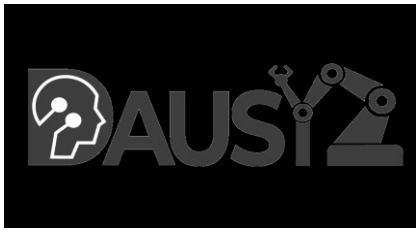

NATIONAL PH.D. PROGRAM IN AUTONOMOUS SYSTEMS

Title of the research

Advanced learning and control methods for life science applications

Ph.D. candidate

Pierluigi Francesco DE PAOLA

Cycle

XXXVIII

Tutors

Fabrizio Dabbene (CNR-IEIIT)

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1. Description of the research program

The research program is aimed at defining new solutions in terms of systems and control methods and machine learning (ML) techniques for the individualized prediction and prevention of chronic diseases, with particular reference to type-2 diabetes mellitus (T2DM).
The focus is to develop tools aimed at providing combined short-term and long-term prediction of the risk associated to patients and consequently aimed at controlling it.
Researches have already been carried out to evaluate the application of ML models useful for predicting the onset of diabetes 2 or aimed at classifying potential patients in different risk categories.
In particular, recently new proposals have been made in T2DM risk prediction through artificial intelligence techniques called counterfactuals, which are some of the most valuable types of explanation machine learning techniques. A counterfactual explanation reveals what should have been different in an instance to observe a diverse outcome: in the field of disease prediction and prevention, outcomes are usually associated with high or low risk of developing the disease [1].
In this context, a very challenging aspect that the research intends to pursue is to try to overcome the limitations in black-box ML predictive models, through the combination of mathematical and control models and explainable AI.
In this sense, the research is aimed at defining controllers relying on dynamical models that would map the evolution of the different biomarkers (fasting blood sugar, systolic blood pressure, body mass index, high and low density lipoproteins, triglycerides, total cholesterol) [2] that contribute to the definition of counterfactuals, thus defining a dynamical approach to the control of each of the features of the ML algorithm. To extend the study of the conditions that can increase or reduce the risks associated with diabetes, the research also intends to focus on identifying and modeling the long-term effects of physical activity, to carry out a comprehensive and open analysis of each scenario [3][4].
A combined analysis, obtained by the integration of control methods and learning techniques, would even suggest the possibility of developing control algorithms that could in turn contribute to the interpretability and explainability of the machine learning methods.
Moreover, a such control method would even let the possibility to investigate the robustness of the classification induced by the single counterfactual associated with the single individual.
The importance of giving a realistic representation of both short-term and long-term physiological conditions, in terms of mathematical model, is of crucial importance in this application, thus the research will focus even on existing maximal models (Cobelli, Hovorka, Sorensen, Castiglione) [4][5] to inspire the methodology for further implementations associated with the research project.
Leveraging the so defined combined control and learning approach, it would be possible to reach a quasi-real-time prediction and control of the prediabetic risk of a patient.
For the sake of completeness, it should be noted that here T2DM is taken as a methodological reference, while this approach could be performed for prediction and risk control of other chronic diseases.

[1] Lenatti M, Carlevaro A, Guergachi A, Keshavjee Karim, Mongelli M, Paglialonga A. Individualized minimum viable recommendations for Type 2 Diabetes prevention using counterfactual explanations. Plos One, 2022.

[2] Lenatti M, Carlevaro A, Mongelli M, Paglialonga A. Counterfactual Building and Evaluation via eXplainable Support Vector Data Description. IEEE Access, 2022.

[3] Bird S, Hawley J. Update on the effects of physical activity on insulin sensitivity in humans. BMJ Open Sport & Exercise Medicine, 2016.

[4] Palumbo M, Morettini M, Tieri P, Fasma D, Sacchetti M, Castiglione F. Personalizing physical exercise in a computational model of fuel homeostasis. Plos Computational Biology, 2018.

[5] Pompa M, Panunzi S, Borri A, De Gaetano A. A comparison among three maximal mathematical models of the glucose-insulin system. Plos One, 2021.

2. Schedule of the research activities

First academic year (planned)

	Description	Period	Activity abroad
Research in the state of the art	Research on the state-of-the-art literature to identify improvements and new approaches in the field of learning and control methods for chronic disease prevention.	1-6	NO
Study and design of new learning and control techniques	Design of new approaches to learning and control methods for chronic disease prevention, analysis of arising issues	7-12	NO

Second academic year (planned)

	Description	Period	Activity abroad
Design of new learning and control techniques	Implementation and refinement of the identified solutions	1-6	NO
Implementation of new learning and control techniques	Implementation and refinement of the identified solutions, identification of possible scenarios to test solutions	7-12	NO

Third academic year (planned)

	Description	Period	Activity abroad
Further developments	Design of tools for the analysis of the solutions proposed.	1-6	YES
Final results	Implementation of tools for testing solutions and writing of the PhD thesis.	7-12	NO

3. Training and research activities plan

First academic year (planned)

	Description	Period	Final Exam	ECTS
A. Ph.D. courses	Modeling and simulation of biological and medical systems	January/June 2023	Yes	3
	Stochastic approaches in Systems Biology	January/February 2023	Yes	1.5
	Linear Algebra for control applications	Spring 2023	Yes	2
	Linear and nonlinear Kalman filtering: theory and applications	January/February 2023	Yes	1.5
	Mathematical introduction to control and optimal control problems		Yes	3
	Nonlinear and data-driven model predictive control EECI	March 2023	Yes	3

	Dealing with uncertainty in data based learning (Politecnico di Milano PhD course offer)	June/July 2023	Yes	5
	SIDRA school courses		No	4
B. Master's degree courses				
C. Soft skill courses				
D. Participation to seminars				
	Complex Networks: Theory, Methods, and Applications spring school	May 2023		5
E. Participation to international congresses or workshops	Participation to at least two seminars/workshops according to availability			2
F. Presentation of research products at international congresses or workshops				
	TOTAL OF ECTS FOR TRAINING ACTIVITIES			30
G. Individual research activity	Individual research on the topics relating advanced learning and control techniques for chronic disease prediction and prevention (including T2DM)	1-12		22
H. Supervision of students	Supervision of students under the guidance of the tutors	1-12		4
I. Integrative teaching activities				
J. Preparation of manuscripts for conferences or journals	Presentation of the results obtained in papers for conferences and/or journals	6-12		4
	TOTAL OF ECTS FOR RESEARCH ACTIVITIES			30
	TOTAL OF ECTS			**60**

Second academic year (planned)

	Description	**Period**	**Final Exam**	**ECTS**
A. Ph.D. courses	Phd course about interpretability and explainability in machine learning to be defined	1-6	No	3
	PhD course about Partial Differential Equations to be defined	1-6	No	3
B. Master's degree courses				
C. Soft skill courses				
D. Participation to seminars				
E. Participation to international congresses or workshops	Participation to at least two seminars/workshops according to availability.	1-12		8

F. Presentation of research products at international congresses or workshops	Presentation of the research and results obtained to at least two international workshops	1-12		4
	TOTAL OF ECTS FOR TRAINING ACTIVITIES			18
G. Individual research activity	Individual research on the topics relating advanced learning and control techniques for T2DM	1-12		26
H. Supervision of students	Supervision of students under the guidance of the tutors	1-12		7
I. Integrative teaching activities	Integrative didactic activities to be carried out under the supervision of the tutors	1-12		3
J. Preparation of manuscripts for conferences or journals	Presentation of the research and results obtained to at least two international workshops	6-12		6
	TOTAL OF ECTS FOR RESEARCH ACTIVITIES			42
	TOTAL OF ECTS			**60**

Third academic year (planned)

	Description	**Period**	**Final Exam**	**ECTS**
A. Ph.D. courses				
B. Master's degree courses				
C. Soft skill courses				
D. Participation to seminars				
E. Participation to international congresses or workshops	Participation to at least three seminars/workshops according to availability.	1-12		6
F. Presentation of research products at international congresses or workshops	Presentation of the research and results obtained to at least three international workshops	1-12		6
	TOTAL OF ECTS FOR TRAINING ACTIVITIES			12
G. Individual research activity	Individual research on the topics relating advanced learning and control techniques for T2DM	1-12		25
H. Supervision of students	Supervision of students under the guidance of the tutors	1-12		6
I. Integrative teaching activities	Integrative didactic activities to be carried out under the supervision of the tutors	1-12		5
J. Preparation of manuscripts for conferences or journals	Presentation of the results obtained in papers for conferences and/or journals	1-12		12
	TOTAL OF ECTS FOR RESEARCH ACTIVITIES			48
	TOTAL OF ECTS			**60**

4. List of the publications written by the candidate in the triennium