International 2nd level Master in *In Silico* Trials

Presentation of the programme

In Silico Trials: a breakthrough innovation

All analysts agree that the cost of development and regulatory certification of medical products has been growing exponentially in the last years: to bring a new drug on the market, companies spent on average US$ 413m in the 80s, US$ 1,044m in the 90s, and US$ 2,558m in the 2000s (Source: J Health Econ. 2016 May; 47:20-33).

This is primarily due to the fairly obsolete methods in use; other industrial sectors with similar problems were able to dramatically shorten the time-to-market and their product development and certification costs by adopting **computer modelling & simulation**.

While in the past it was possible to provide regulatory evidences almost exclusively by mean of experimentation, since 2016 regulatory agencies are becoming more interested in considering evidences obtained by modelling & simulation, the so called **In Silico Trials**.

So far, the adoption of in silico technologies has been quite slow: the qualification of "first in kind" methods is challenging, and neither companies nor regulatory agencies have in house the necessary skills to pursue it. All recent reports indicate the lack of **specialised workforce** as the main barrier to the adoption of In Silico Trials.

Training new professionals: the master

The *International Master on In Silico Trials* is a 2nd level master programme that aims at filling this gap by providing new professional figures that will build expertise around in silico technologies.

The master is open to **students with a master's degree in engineering, physics, mathematics, or computer science**, and it will train up to 30 specialists in In Silico Trials per year starting from the Academic Year 2020-2021.

The programme is led by three professors of the Alma Mater Studiorum: Prof Marco Viceconti, Prof Lorenzo Chiari, and Prof Luca Cristofolini.

The programme includes 210 hours of frontal teaching, 16 hours of workshops, and 600 hours of internship at a company, research hospital, or regulatory agency.

During the internship, the development or deployment of In Silico Trials technologies will constitute the final project, which will constitute the final report (100 hours) each student has to submit before graduation. In total, the programme involves 936 hours, equivalent of 60 European Credit Transfer and Accumulation System (ECTS) credits.

The master has been designed to allow **working students** to attend, in order to receive a professional re-training. The training will be compressed into six full-immersion weeks, one month apart one to each other, for a weekly total of 35 hours of both frontal teaching and laboratory practice. Each week will be dedicated to a specific module:

- **Introduction to In Silico Medicine**: during this first module we will present the master programme, provide an introduction to the general concept of modelling the physical reality and to computational medicine, introduce some general concepts on regulatory

affairs in general and in relation to in silico method, and specifically the problem of assessing the credibility of predictive models.

- **Modelling the neuromusculoskeletal diseases**: in the second module we will introduce a series of modelling techniques to predict orthopaedic devices performance, skeletal strength, musculoarticular forces in neurodegenerative diseases, etc. We will introduce the concept of risk modelling and the design of in silico trials for paediatric orphan diseases.
- **Modelling the cardiovascular and respiratory diseases**: full immersion in the development of cardiovascular models, sub-cellular, cellular, and whole heart. Prediction of neurovascular hemodynamics and circulation, stenting outcome, etc.
- **Modelling cancer, transmissible, and metabolic diseases**: models of the sugar metabolism, of the immune system, prediction of physiology-based pharmacokinetics, molecular affinity binding, growth of solid tumours. Neurocomputational models.
- **Assessing the credibility of in silico technologies**: Fundamentals: legislation, quality assurance, risk assessment. Certification of in silico medicine solutions. Credibility of in silico trials methods, and of molecular dynamics models. Qualification of in silico methods to assess medical devices or medicinal products.
- **Industrial and regulatory perspective**: in silico trials for medicinal products and for medical devices. The role of consulting firms, software developers, and of software-as-a-service portals.

Each module will be taught by an international faculty of absolute prestige, assisted by a local group of teaching assistants and with the availability of a computer lab fully equipped with state-of-the-art modelling & simulation software packages, both Open Source and commercial.

Some of the world-class experts that will contribute to this programme are:

- Prof Francesco Migliavacca (Politecnico Milano)
- Dr Jan De Backer (Fluidda, BE)
- Dr Andrea Beccari (Dompè, IT)
- Prof Francesco Pappalardo (Università di Catania, IT)
- Prof Claudio Cobelli (Università di Padova, IT)
- Dr Mark Palmer (Medtronic, USA)
- Prof Mauro Ursino (Università di Bologna, IT)
- Dr François-Henri Boissel (Nova Discovery, FR)
- Dr Thierry Marchal (Ansys Europe, BE)
- Dr Luca Emili (In Silico Trials, IT)

The faculty also includes Dr Tina Morrison, in charge of In Silico methods for medical devices at the USA Food and Drug Administration, and Dr Flora Mutsuamba, co-director of the Modelling and Simulation Working Party of the European Medicine Agency.

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The programme

The Master programme provides 60 CFU, equivalent to 60 ECTS Credits. These are divided in 30 CFU of frontal teaching, 24 CFU for the mandatory stage with project, 4 CFU for the final examination (report of the project), and 2 CFU for other activities (workshops and stage search events).

We expect this master to interesting not only for newly graduated students seeking a specialisation, but also for professionals already working in biomedical industries, research hospitals, regulatory agencies, etc. to the purpose we designed the timetable to be sustainable also by working students. The frontal teaching is organised in six modules, each worth 5 CFU, and involving 35 contact hours spread over 6 days:

1. Introduction to In Silico Medicine
2. Modelling the neuromusculoskeletal diseases
3. Modelling the cardiovascular and respiratory diseases
4. Modelling cancer, transmissible, and metabolic diseases
5. Assessing the credibility of in silico technologies
6. Industrial and regulatory perspective

Each module starts on Monday morning, with six hours of contact per day until Friday, plus five hours contact on Saturday. Each day there will be a combination of frontal teaching and hands-on laboratories in the computer lab, so as to provide the students also with transferable skills on the use important software tools and methods. The first module will start on Monday September 7th, 2020, followed by a module per month, with the last in early March.

The stage will be done at university research labs, biomedical industries, research hospitals, Contract Research Organisations, or regulatory agencies. In principle it could be possible to arrange the stage of a working student within the organisation where they work, if pertinent. During the stage each student will develop a full deployment project for a specific solution for *in silico* trials, relevant for the host organisation. At the end of the stage the student will write a project report, that will have to be submitted in August; this will terminate the master activities. The Graduation ceremony will take place in September.

About the Director

Marco Viceconti is full professor of Computational Bioengineering in the department of Industrial Engineering of the Alma Mater Studiorum – University of Bologna, Italy. He is also the Director of the Medical Technology Lab of the Rizzoli Orthopaedic Institute. Until 2018 he was the Director of the Insigneo Institute, the largest research institute entirely dedicated to in silico medicine in Europe.

Prof Viceconti is one of the top experts of In Silico Medicine worldwide. Co-author of the 2005 white paper[1] that defined the Virtual Physiological Human, coordinator of the two key

[1] https://www.vph-institute.org/upload/file517569145f61b.pdf

research roadmaps in the field (STEP[2] and Avicenna[3]), he was the President of the VPH Institute[4], an international no-profit organisation that coordinates this research community, and is Board member of the Avicenna Alliance[5], which represent the biomedical industry interests in this domain.

Logistics and infrastructure

The first and the fifth modules will be held in the city of Bologna, at the new Bertalia Campus of the faculty of Engineering. Brand new teaching rooms and computer labs will provide the necessary infrastructure. The site is served by public transportation and is a 15 min ride to the train station and the city centre. The city is well served with hotels, B&B and short-term rental apartments. However, being Bologna a fairly touristic town, we recommend you book your accommodation with plenty of advance time.

All the other modules will be held at the University Residential Centre[6] at Bertinoro. Placed in a breath-taking location, the centre offers a full-immersion residential experience. It takes about one hour and half to reach the centre from Bologna. You can rent accommodation in the centre, which also offers full catering. The centre is equipped with various teaching rooms and a well-equipped computer lab, perfectly suited for our activities.

[2] https://www.vph-institute.org/upload/step-vph-roadmap-printed-3_5192459539f3c.pdf
[3] https://www.researchgate.net/publication/302776762_In_silico_clinical_trials_how_computer_simulation_will_transform_the_biomedical_industry
[4] https://www.vph-institute.org
[5] https://avicenna-alliance.com
[6] https://ceub.it/?lang=en