UNIVERSITÀ DI TRENTO
Dipartimento di Matematica

DOTTORATO

CYCLE 35th
ORAL DEFENCE OF THE PHD THESIS

Monday 23 October 2023 – at 2.00 pm

Department of Mathematics
Seminar Room 1
The event will take place in presence and online through the ZOOM platform.
To get the access codes please contact the secretary office

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PhD Student in Mathematics

Hybrid modeling techniques to support drug-development and post-market analysis of anti-infectives

Abstract:
Nowadays, decision-making processes are highly assisted by computational predictive platforms in any discipline. In drug development and global health fields, massive use of *in silico* tools deals with the anticipation of plausible scenarios, which overall inform on best therapeutic options. The thesis exemplifies this model-based contribution by addressing two practical open questions within the anti-infective pipeline. The first case-study regards the support of a novel granuloma-centric approach to anti-tuberculosis (TB) regimen design through the quantification of site-of-action pharmacokinetic attainments of any anti-TB compound to come. In a step-wise manner, an *in vivo* minimal physiologically-based pharmacokinetic (mPBPK) platform for anti-TB drug disposition was derived from a full-body version and enriched with an innovative intra-granuloma module described via ODE-based passive diffusion mechanisms. The simultaneous support of several anti-TB agents and successful validation step provided strong indications of the design quality and universality. Afterwards, under a data augmentation paradigm, mPBPK model-based simulations of granuloma-to-plasma partition coefficients in rabbits were used to supplement non-compartmental approaches and aid the training of a minimal signature machine learning (ML) predictive tool. Sitting at the early stage of the drug development, the ML model was developed to require easy-accessible and animal-testing free descriptors of a molecule to forecast its granuloma PK scores and consequent profile. Although the reduced size of the training set, results from the cross-validation endorsed the use of the ML model to close the gap from bench to bed. The second part of the thesis covers model-based post-market therapeutic evaluations with an application coming from the anti-flu vaccine area. A natural history decision tree was applied upon simulations of a multi-group and age-structured SEIR (Susceptible-Exposed-Infected-Recovered) epidemiological model to reconstruct economical tolls of a novel vaccination strategy. In particular, the cost-benefit scenario of the introduction of the adjuvanted QIV (aQIV) vaccine in the elderly Spanish population (65+ years) was analyzed, leveraging specific real data from demographic, viral, and event cost scales. To complement the population-level section, modeling efforts on the COVID-19 pandemic are presented as ancillary activity to endorse the parallel role of non-pharmaceutical interventions in limiting an infection spread.

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CONTATTI
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