Mini-symposium
JOBIM 2024, Toulouse

Digital Twins for Human Health – The Role of Bioinformatics and Computational Biology

June 27, 2024 - 16h30 - 18h30

Digital twins are emerging in Life Sciences and medicine, with efforts to create virtual patients for decision-making in various fields. The need for robust bioinformatics pipelines is real and timely for building and calibrating high-performance models at the patient level. The mini-symposium aims to bring together bioinformatics, digital twin initiatives, and computational systems biology researchers to discuss the challenges of data integration, model personalisation, and sustainable simulation platforms. The symposium will be split into three sessions: short talks, a round table discussion, and an open discussion. It aims to attract scientists interested in medical Digital Twins initiatives and active in bioinformatics, single-cell technology, and computational modelling in healthcare. The organisers are committed to a gender-balanced symposium.

Digital Twins for Human Health – *The Role of Bioinformatics and Computational Biology* **June 27th afternoon, duration: 120 minutes in total (2h), 16h30 - 18h30**		
Session 1		
Time slot (10-minute talk and 5 minutes Q&A)	**Title talk**	**Speakers**
16h30 -16h40	**Opening comments**	**Organisers**
16h40 - 16h55	**Digital Twin in Oncology: Optimizing Immunotherapy with Multimodal Analysis**	**Emmanuel Barillot**
16h55 - 17h10	**One Digital Twin fits all? Building Digital Twins from Heterogeneous Datasets**	**Malvina Marku**
17h10 - 17h25	**TBA**	**Nicola Gaudenzio**
17h25 - 17h40	**Learning causal models in biology for discovering better patient treatments**	**Andrey Zinovyev**
17h40 - 17.55	**TBA**	**Christophe Lanneau**

Session 2		
17h55 - 18h15	**Round table: what's next**	**Speakers and organisers**
18h15 - 18h25	**Open discussion: challenges and realistic outputs**	**Speakers, organisers, and audience**
18h25 - 18h30	**Closing remarks**	**Organisers**

Programme - detailed version

16h30 - 16h40
Anna Niarakis, Arnau Montagud, Laurence Calzone
Introduction

16h40 - 16h55
Emmanuel Barillot - Institut Curie, Paris
Digital Twin in Oncology: Optimizing Immunotherapy with Multimodal Analysis
A Digital Twin in Health can be built from two perspectives: data-driven or model-driven. I will discuss both.
Data-driven: The survival of patients with metastatic non-small cell lung cancer (NSCLC) has been increasing with immunotherapy. However, efficient biomarkers are still needed to optimize patient care and guide therapeutic decisions. Multimodal machine learning approaches, integrating diverse data modalities to capture different aspects of the disease across different scales, show great promise but currently need more evidence to establish their superiority. I will present our results on a multimodal cohort of ~400 metastatic NSCLC patients treated with first-line immunotherapy. At baseline, we collected positron emission tomography images, digitized pathological slides, transcriptomic profiles, and other health record information. We explored the benefits of multimodal approaches to predict the outcome of patients undergoing immunotherapy using multiple machine-learning algorithms and integration strategies. Our study fosters the collection of large multimodal NSCLC cohorts to develop robust and powerful multimodal biomarkers for immunotherapy outcomes.
Model-driven: Another approach is to model explicitly the tumor heterogeneity, its microenvironment, and its spatial dimension. These three aspects are key for understanding tumor onset, evolution, drug response, and potential fragilities for new therapeutic strategies. They are accessible now with omics technologies. I will explain how we model their mechanisms and their biochemical and biophysical components using a combination of Boolean modeling and agent-based modeling.

16h55 - 17h10
Malvina Marku - Oncopole, INSERM, Toulouse
One Digital Twin fits all? Building Digital Twins from Heterogeneous Datasets
In the realm of growing efforts towards personalized medicine, Digital Twins (DT) represent enormous potential for shedding light on the complex interplay of multiple regulatory

processes on different scales. While building such DT requires implementing various types of data from large cohorts of patients, several challenges arise from the unavoidable patient variability, data harmonization, and their integration into computational models, which in turn should be elaborated enough to capture the enormous complexity of biological systems and allow personalizing them patient-specific in applications. Overcoming these challenges will unlock the full potential of DTs, revolutionizing healthcare by providing tailored, data-driven approaches for diagnosis, treatment, and prevention strategies, ultimately leading to improved patient outcomes and enhanced population health.
In this presentation, we will present our recent efforts in using experimental data to build dynamic models of gene regulation, which consist of one of the main building blocks of DTs. Using *in vitro* cultures from patient samples, we aim to study the functional processes determining the cellular interactions at the molecular level by investigating how regulatory interactions between genes characterize cellular phenotypes. Building on time-course bulk RNAseq datasets, we perform different analyses, including gene regulatory network (GRN) inference, differential gene expression analysis, and transcription factor activity analysis, to highlight important features of gene modules and their biological features. Then, following a similar data-driven approach, we aim to infer the dynamical models of GRNs and capture the temporal dynamics of gene regulation, thus better understanding cellular behavior and response to external stimuli.

17h10 - 17h25
Nicolas Gaudenzio - INFINITY, INSERM, Genoskin,Toulouse
TBA

17h25- 17h40
Andrei Zinovyev - Evotec, Toulouse
Learning causal models in biology for discovering better patient treatments
Distilling causality from correlations is essential in transforming drug discovery by efficiently utilizing molecular patient data. One promising method to tackle this significant challenge involves employing mechanistic mathematical modeling of various kinds to the existing knowledge, aiming to explain as much of the gathered observations as possible and infer new, yet unobserved, consequences from what we already know. What can be the right approach for learning causal models and connecting them to mechanistic modeling in biology? Can we orient the development of foundational models to focus on causality? I will share some thoughts and present a project to build a large DNA Damage Response regulation model for drug discovery in oncology.

17h40 - 17h55
Christophe Lanneau - Genopole, Evry
TBA

17h55 - 18h15
Round table: Speakers and organizers

18h15 - 18h25
Open discussion: Speakers, organizers, and audience

18h25-18h30
Closing remarks

List of organisers:

- Dr Anna Niarakis, Professor of Computational Systems Biology, Center of Integrative Biology (CBI), University of Toulouse III- Paul Sabatier; Lifeware, INRIA Saclay; anna.niaraki@univ-tlse3.fr
- Dr Laurence Calzone, Research scientist, Institut Curie (Institut Curie / U900 INSERM / Mines Paris Tech; France; Laurence.Calzone@curie.fr
- Dr Arnau Montagud, Researcher, Institute for Integrative Systems Biology (I2SysBio, CSIC-UV), Barcelona Supercomputing Center (BSC), Spain; arnau.montagud@csic.es

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