Title of the PhD thesis:
Towards multivariant pathogenicity predictions: using machine-learning to directly predict and explore disease-causing oligogenic variant combinations

Nathaniel Vincent Mon Père (1991) obtained his master’s degree in physics with high honors from the University of Antwerp in 2016. He began his PhD research under the supervision of Tom Lenaerts at the Interuniversity Institute of Bioinformatics in Brussels (IB2, ULB) under a grant from Télévie, and later entered a joint PhD with VUB under Sophie de Buyl at the Applied Physics Research Group (APHY). He has collaborated internationally with researchers at Universidade do Minho (Portugal), Princeton University (USA), and Queen Mary University of London (UK).

Promotor:
Prof. dr. Sophie De Buyl

Co-promotor:
Prof. dr. Tom Lenaerts

The defense will take place on
Friday, November 27, 2020 at 16h00

The defense can be followed through a live stream. Contact Nathaniel.Mon.Pere@vub.be for more information

Members of the jury
Prof. dr. Dominique Maes (VUB, chair)
Prof. dr. Bortolo Mognetti (ULB, secretary)
Prof. dr. ir. Lendert Gelens (Gelens Lab, KUL)
Dr. Benjamin Werner (Barts Cancer Institute, Queen Mary University of London, UK)

Abstract of the PhD research

Cell populations in the human body form highly complex systems, their behavior driven by countless processes within the cells themselves as well as their interactions with each other and their environment. A mathematical approach to describing their emergent phenomena on the tissue level typically requires abstractions of these underlying systems in order to obtain tractable and interpretable models, which in turn often leads to descriptions involving stochastic processes.

In this doctoral thesis two such cellular systems are investigated. The first is the human hematopoietic system: the machinery by which precursor cells of the blood are cultivated and matured in the bone marrow. This process is essential to enable mammalian physiology, from providing oxygen-carrying erythrocytes to ensuring regular upkeep and preservation of the immune system. Obtaining a quantitative understanding of key aspects of this system can provide valuable insights and testable predictions concerning the origin and dynamics of various blood-related diseases, however, in vivo studies of maturing blood cells pose significant challenges and in vitro studies provide only limited predictive power. The system’s hierarchical architecture is on the other hand well fit to the application of mathematical techniques relying only on a few basic assumptions and parameters. This research aims to contribute to two broader questions concerning hematopoiesis, the first being “What is the shape of this system?” and the second “How does it behave?”. Both questions must be answered sufficiently before quantitative models can be developed with enough predictive power to aid in clinical research and applications.

The second project stems from questions in oncology concerning the locomotive capabilities of various cancerous cell types, but ultimately poses these in a broader context, attempting to understand cell motion in the context of a growing but spatially restricted population. Drawing from the domain of non-equilibrium statistical mechanics applied to actively moving particles, an important goal is to understand the effects of heightened proliferation on the collective motion.

Curriculum vitae

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