GENEESKUNDE & FARMACIE

INVITATION to the Public defence of

Jordy PEETERS

To obtain the academic degree of

'DOCTOR OF PHARMACEUTICAL SCIENCES'

Principles and Applications of Molecular Dynamics: Molecular understanding of the Serotonin-2A Receptor, Quantification of Chirality and Advancements in Nonbonded Potentials

Promotor

Prof. Dr. Kenno Vanommeslaeghe
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Chair

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Board of examiners

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The public defence will take place on

Monday, **22 December 2025 at 1 p.m.**

In Auditorium Piet Brouwer
VUB Health Campus
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

Summary of the dissertation

This thesis is centered around life science applications of Molecular Dynamics simulations (MD), which let us observe the movements of molecules at atomic resolution.

- The first application is related to serotonin, often called "the happy hormone". Serotonin is a chemical messenger that passes specific signals between nerve cells by binding to receptors. Most antidepressants amplify these particular signals, but classic psychedelics such as LSD, magic mushrooms, and ayahuasca also activate the same receptors. Indeed, clinical evidence suggests that psychedelics might bring rapid, long-lasting improvements in depression. However, psychedelic antidepressants are impractical, so developing non-psychedelic analogues would be advantageous. We used MD simulations to study how psychedelic and non-psychedelic compounds influence the so-called serotonin-2A receptor (5-HT_{2A}) at atomic resolution and found that psychedelics make it behave differently. We then propose a strategy to develop pharmaceuticals that may treat stubborn depression without causing hallucinations.

- The second application concerns chirality: the property of some molecules to exist in "left-handed" and "right-handed" forms, like a left and a right glove. Just like each glove fits only one hand, these mirror-image molecules can have vastly different effects on the body. We use MD simulations to map these differences and predict how each may interact with a given environment. This is important for the life sciences because many pharmaceuticals are chiral.

- Finally, our MD simulations represent molecules using mathematical models. These models are quite coarse because simulation speed is a common bottleneck in life science applications. We propose a new mathematical model to make MD simulations more accurate with only a small sacrifice in speed.

Curriculum Vitae

Jordy Peeters was born on June 16, 1994, in Antwerp, Belgium. He completed his secondary education in 2012 at P.I. Sint-Godelieve in the technical study program of Chemistry. He obtained his Bachelor's degree in Chemistry from the University of Antwerp and continued his studies at the Vrije Universiteit Brussel (VUB), where he earned his Master of Science in Chemistry.

As a Teaching Assistant, Jordy began his PhD journey in the research group of Analytical Chemistry, Applied Chemometrics and Molecular Modelling (FABI) under the supervision of Prof. Kenno Vanommeslaeghe. His doctoral research focuses on computational approaches to study proteins and identify novel pharmaceuticals. In addition, he contributed to interdisciplinary projects in analytical chemistry and chemometrics at FABI.

During his PhD, Jordy assisted in all first-year bachelor's chemistry courses in the Faculty of Medicine and Pharmacy and supervised three master's students during their thesis research.

His research has resulted in four publications in peer-reviewed journals, including two as first author and one as shared first author. He had the privilege to present his research, both orally and by poster, at several national and international conferences.