SCIENCES & BIOENGINEERING SCIENCES

The Research Group

General Chemistry

has the honor to invite you to the public defense of the PhD thesis of

Johannes L. TEUNISSEN

to obtain the degree of Doctor of Sciences

Title of the PhD thesis:

Inverse Molecular Design: Optimization and Application of Categorical and Stochastic Approaches

Promotors:

Prof. dr. Frank De Proft (promotor, VUB)
Dr. ir. Freija De Vleeschouwer (promotor, VUB)

The defense will take place on

Wednesday 11 September 2019 at 16:00h

in Auditorium D.0.08 at the Campus Humanities, Sciences and Engineering of the Vrije Universiteit Brussel, Pleinlaan 2 - 1050 Elsene, and will be followed by a reception.

Members of the jury:

Prof. dr. Steven Ballet (chairman, VUB)
Prof. dr. Marc Elskens (secretary, VUB)
Prof. dr. Mercedes Alonso (VUB)
Prof. dr. Ann Dooms (VUB)
Prof. dr. Emilie Cauët (ULB)
Dr. Julia Contreras-Garcia (Sorbonne Univ., Fr.)
Prof. dr. David N. Beratan (Duke Univ., USA)

Curriculum vitae

In 2014 Johannes (Jos) Teunissen obtained his master degree in the Top Master Program of Nanoscience at the University of Groningen (NL).

During his PhD at the VUB, he optimized several inverse molecular design strategies, as well as learning new strategies during a research stay at Duke University (USA).

Currently two first-author papers are published while three others are in preparation. Finally, this PhD involved teaching duties encompassing the supervision of two bachelor and three master students.

Abstract of the PhD research

One estimates that the number of stable molecules that can be constructed from only C, N, O, H and S atoms amounts to more than 10^{60}, of which only a tiny fraction is known. This astronomically large set of compounds spans the so-called chemical compound space (CCS). When one searches for novel molecules exhibiting some desired characteristics, one needs to screen the CCS until new, suitable and improved molecular structures are found. This resembles finding a needle in a haystack unless one applies clever search strategies.

The research described in this thesis focuses on Inverse Molecular Design strategies. Instead of starting from a (newly proposed) molecule and investigating its properties, we let the desired property guide the search by optimizing it as a function of the chemical structure. This inverse approach could deliver an important aid in the discovery of new valuable compounds, as such reducing the timescale of drug and materials development. More specifically, this PhD is oriented towards the optimization, acceleration and application of different inverse design methods.

Two general inverse design strategies are exploited. The first strategy concentrates on relatively small-sized chemical spaces defined by a fixed molecular framework on which certain chemical fragments can be substituted by others.
Finding the best combination of structural fragments for this molecular framework is an optimization problem that can be solved effectively by discrete optimization algorithms, in particular the Best First Search (BFS) algorithm. In this work, several aspects of these algorithms are optimized to avoid local optima and to reduce the computational cost.
The improved algorithms were applied to diamondoids (nano-diamonds) and pentacene derivatives, both having potential as semiconductors.

The second strategy is to search through chemical space by a stochastic method that samples much larger regions of CCS, as such removing the constraint of a fixed molecular framework.
We used the ACSESS algorithm, which inversely designs molecules by an iterative procedure of repeatedly making random mutations and selecting the best and most diverse subset.
The property-optimizing ACSESS method was finally applied to find highly redox-active molecules for aqueous organic flow batteries using either quinone derivatives or stable radicals.
As a result, quinone derivatives with high reduction potentials were designed showing large aromatic stabilization of the reduced form and also a method to efficiently assess the radical stabilities was devised.