SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Structural Biology Brussels

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

Mauricio MACOSSAY CASTILLO

to obtain the degree of Doctor of Bio-Engineering Sciences

Title of the PhD thesis:

The interplay between multifunctionality and protein intrinsic disorder

Promoter:

Prof. dr. Peter Tompa
Prof. dr. Shoshana Wodak (co-promoter)

The defense will take place on

February 28, 2020 at 16h

in Auditorium D2.01 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. Wim Vranken (chairman)
Prof. Inge Van Molle (secretary)
Prof. Damya Laoui
Prof. Kim Roelants
Prof. Emmanuel Levy (Weizmann Inst. of Science)
Prof. Lennart Maertens (VIB-UGent)

Curriculum vitae

In 2013, Mauricio Macossay Castillo earned a Master of Science degree in Molecular Biology, with the grade of Great Distinction at the VUB. Immediately after this, he undertook his doctoral studies. His PhD research focused on the systematic study of the relationship between intrinsic protein disorder and the multifunctional nature of proteins. This led to the publication of three articles in international peer-reviewed journals that represent his Thesis. Additionally, his work was presented in several congresses and academic meetings.

Abstract of the PhD research

Many biological macromolecules (DNA, RNA or protein) carry out more than one biological function that has been selected for by evolution. This allows living cells and organisms to accomplish more with limited resources. It is reasonable to assume that such multifunctional character would be associated with the degree to which the macromolecule can adapt to accommodate different functions in a sustainable way. However, the mechanisms by which such adaption occurs are poorly understood, and furthermore, there is little consensus on how multifunctionality should be defined.

Proteins carry out their function by forming specific associations with other macromolecules or small molecules in the cell. For a category of proteins, the so-called globular proteins, these associations and subsequent functional events critically depend on the protein adopting a well-defined sufficiently stable tertiary (3D) structure. Another category of proteins and protein regions, termed intrinsically disordered proteins or regions (IDP/Rs), has been attracting significant attention in recent years due to its lack of well-defined 3D structures; nevertheless, IDP/Rs are involved in a diverse set of biological functions and represent a significant fraction of cellular proteins.

In this Thesis, we investigate the relationship between IDP/Rs, and their different properties, with different aspects of multifunctionality on proteome and genome levels. First, we examine the relationship between protein intrinsic disorder and multifunctionality at the protein level, e.g. in proteins observed to carry out multiple cellular or molecular functions, as defined by their annotations in databases. Next, we analyze the propensity of proteins with intrinsic disorder to acquire additional functions due to translational readthrough (TR)-derived extensions. Lastly, we investigate links between IDP/Rs and biological functions at both the protein and nucleic acid level, which are associated with synonymous constraint elements (SCEs) of DNA, which likely encode functions at the DNA or RNA level, in addition to their protein-coding role.

Results from the three studies indicate a significant link between different manifestations of multifunctionality and IDP/Rs, suggesting that protein intrinsic disorder may be a feature that favors the evolution of multiple functions at the protein, DNA or RNA level. Our analyses also provide insights into the particular physical chemical properties of IDP/Rs, and other characteristics, such as their low level of sequence conservation, their lack of well-defined 3D structure, and the type of interactions they form with other proteins, which may enable these proteins to readily evolve multiple functions.