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Le Corps professoral de

Gembloux Agro-Bio Tech - Université de Liège vous prie

de lui faire l'honneur d'assister à la défense publique de la dissertation originale que

**Monsieur BAERT Jonathan,**

**Titulaire d'un diplôme de master bioingénieur : chimie et bioindustries,**
**à finalité spécialisée,**

présentera en vue de l'obtention du grade et du diplôme de

**DOCTEUR EN SCIENCES AGRONOMIQUES ET INGENIERIE BIOLOGIQUE,**

le 12 mars 2018, à 15 heures précises (personne ne sera admis après cette heure),

en l'auditorium CG ( Chimie Générale, bât. 8),

Passage des Déportés, 2, à 5030 GEMBLOUX.

Cette dissertation originale a pour titre :

« Single cell approaches for the characterization of microbial population dynamics in bioprocesses ».

**Le jury est composé comme suit :**

Présidente : Prof. M.-L. FAUCONNIER, Présidente du Département AGROBIOCHEM,
Membres : Prof. F. DELVIGNE (Promoteur), Prof. D. TOYE, Prof. B. JORIS, Prof. A. RICHEL, Prof. L. WILLEMS, Dr C. LEFEBVRE (Puratos, Andenne), Dr A. GRÜNBERGER (Forschungszentrum Jülich, Allemagne).

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**Summary**

Some evidences show that a clonal population of microbial cells exhibits variation at their physiological level. For this reason, several methods that allow cellular characterization with a single-cell resolution have been strongly developed this last decade. For instance, flow cytometry is a reliable analytic method to study the complex distribution of physiologies occurring among microbial populations. This so called "phenotypic heterogeneity" has been extensively discussed in the scientific literature and remains a hot topic for biotechnology development suggesting that clonal cells have not the same ability to synthesize a product of interest during bioprocesses course.

However, phenotypic heterogeneity patterns are not commonly interpreted in term of biological performances. Therefore, the current main challenges in single-cell techniques lies in an accurate understanding of the sources of biological inefficiency through a relevant interpretation of the phenotypic heterogeneity occurring in microbial populations. For this purpose, this work investigates the potentialities of both genetically encoded and exogenous biosensors to support the implementations of innovative optimization strategies considering biological traits of cell factories. Moreover, correlation between cell population heterogeneity and bioreactor heterogeneity has also been addressed by studying the response of biosensors under intensive culture conditions that occurs in industrial bioreactors. Thus, thanks to a deep analysis of biosensor signals, this work point out the added value brought by the single-cell concepts and make possible a better understanding of microbial physiology in bioprocesses conditions. Additionally, in parallel with an extended experimental strategy, this work proposed an original formalism in order to valorize the different component of single-cell technology and to facilitate its transfer towards industrial applications.

Finally, beside challenges in link with biosensors signals interpretation, flow cytometry analysis leads to the high-throughput characterization of cell suspension and then, provides thousands of data. This high information diversity compels to cope with strong data management challenges. Actually, the question is: "How structure and treat single-cell data to improve their interpretations accuracy?". In this frame, this study demonstrates the potential of single-cell distribution statistical treatment to rationally discriminate cellular samples which present different biological traits. In that way, we shown experimentally that the higher performant biological system can also be the more heterogeneous which is in opposite to the paradigm stating that only homogenous population are attractive for bioprocess applications. In a nutshell, this work set up the basis to study the relation between phenotypic heterogeneity and biological performance through the discussion of serval fundamental and applied concepts. That supports the proposal of rational optimization strategies while considering biological inputs and ensuring the valorization of single-cell concept as a response to current major industrial challenges.