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### 3D individual based model for simultaneous growth and interaction of *L. Monocytogenes* and lactic acid bacteria

G. Desmeulles<sup>\*1,3</sup>, F. Harrouet<sup>1,3</sup>, D. Thuault<sup>4</sup>, V. Huchet<sup>4</sup>, P. Redou<sup>1,3</sup>, L. Gaubert<sup>1,3</sup>, G. Longelin Péron<sup>1</sup>, P. Ballet<sup>1,2</sup>, V. Rodin<sup>1</sup>

<sup>1</sup>UMR CNRS 6285, Lab-STICC, IHSEV, France, <sup>2</sup>University of Brest, France, <sup>3</sup>CERV ENIB, France, <sup>4</sup>ADRIA Développement, France

#### Objectives

By interacting with pathogens, lactic acid bacteria (LAB) are able to contribute to food safety. By means of their lactic acid production which induces pH decrease, LAB influence the growth of pathogens. The aim of this study is to model and simulate lactic acid production, pH evolution, according to carbohydrate concentration in media, temperature, water activity and ratio of both population.

#### Methods

To address the challenges related to the interdisciplinary context of this study, we have used a method based on two modeling steps.

*In virtuo* modeling relied on the Virtual Reality principle. RéISCOP software aim is to interactively model and simulate complex dynamical systems (1). We built models of *Carnobacterium piscicola* and *Listeria monocytogenes* interacting on a petri dish (2,3). Bacteria shapes are 3D capsules that have mechanical interactions. Bacteria feed on glucose and divide themselves over the time, depending on the parameters of their local environment. *Carnobacteria* produce lactate. The substrate was modeled as a simple 3D discretized reaction-diffusion system in which glucose and lactate diffuse. We made use of Unity3D to handle the graphical user interface that made possible to see, experiment and modify the model during the simulation. This *in virtuo* model was a toolbox to design an individual-based model from the cardinal populational data and model (2,3).

*In silico* optimized predictive model: based on this *in virtuo* modeling, we used the Transprog C library (4), so as to develop an optimized and parallelized model. Simplifications were made to allow simulation of hundred millions of cells (spherical shapes, only one bacteria layer in colony). Our validation process includes theoretical and experimental phases. For a single colony growth, we compare individual-based results and validated populational results. Secondly, with regards to the growth of two colonies in competition, we compare individual based models and experimental data.

#### Results

The first result of this study is the development of two softwares that can be easily re-used for other studies (we are trying 5). We have a virtual lab in which non-IT biologists can quite easily design models without coding. Furthermore, we have an optimized software to simulate various bacteria on a whole petri dish (  $10^7$  bacteria individuals in real time on an ordinary PC).

Regarding the results of modeling, we are, at this time, calibrating and validating the models for three single colonies growing on a substrate: *Listeria*, *Lactis* and *Carnobacterium*. Experimental data for validation are already produced.

#### Conclusions

Data for validation have been collected and will be discussed. Validations remain to be achieved.

Individual-based model was a modeling key to study competition between colonies. We would like to be able to study the 3D colony shape and we envisage to model more complex food substrate.

In this study, using “virtual lab” was a methodological key to make us (biologists, computer scientists and mathematicians) be able to understand each other. We hope that this approach allows us to offer biologists new modeling techniques like individual-based model.

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