

# Individual-Based Modeling of Bacterial Foraging with Quorum Sensing in a Time-Varying Environment

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**Abstract.** “Quorum sensing” has been described as “the most consequential molecular microbiology story of the last decade” [1][2]. The purpose of this paper is to study the mechanism of quorum sensing, in order to obtain a deeper understanding of how and when this mechanism works. Our study focuses on the use of an Individual-based Modeling (IbM) method to simulate this phenomenon of “cell-to-cell communication” incorporated in bacterial foraging behavior, in both intracellular and population scales. The simulation results show that this IbM approach can reflect the bacterial behaviors and population evolution in time-varying environments, and provide plausible answers to the emerging question regarding to the significance of this phenomenon of bacterial foraging behaviors.

## 1 Introduction

Systems biology has been proposed in the past a few years to overcome the existing barriers in biology, as a result, computerized analysis of biological models is investigated. Individual-based Modeling (IbM) is one of the emerging approaches [3] to this problem. The basic idea of IbM is to simulate the behavior or dynamics of an individual which interacts with the others synchronously or asynchronously in a same or different living patterns. IbM is commonly based on cellular automation models, explaining qualitatively colonial pattern formations for different nutritional regimes [4]. An essential capability of an IbM enables the description of all the states, inputs and outputs of an individual and their relationship with that of the other individuals which are living in a same population. In contrast to the population-based model (PbM), the IbM should possess a more flexible and robust capability for simulating a complex system where there are a large number of individuals which have their own behaviors dynamics influenced by the other individuals and the environment.

It is well recognized that bacterial diseases such as cholera, meningitis, *E.coli* infection and many others are among the deadliest in the world. However, it has

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been reported recently that bacteria can cause an illness only when there are a sufficient number of them. A cell-to-cell signal is involved in the development of bacterial communities, such as biofilms [5]. This communication between bacteria is often referred as “quorum sensing”, which is widespread in nature. It also controls the processes of bacterial behavior, especially those that are usually unproductive when undertaken by an individual bacterium but become effective in a group. For instance, bioluminescence, secretion of virulence factors, sporulation and conjugation are believed to have relationship with quorum sensing. In this sense, bacteria are able to function as multi-cellular organisms with this underlying mechanism.

In the past a few years, quorum sensing has been the research topic addressing a broad audience. Ward *et al.* [6] introduced a general mathematical model of quorum sensing in bacteria. Dockery *et al.* [7] presented a mathematical model of quorum sensing in *P.aeruginosa*, to show how quorum sensing works using a biochemical switch. A number of biologically realistic mechanisms, such as “quorum sensing”, have been considered in [8], to study the pattern forming properties of bacteria. A stochastic model to connect intracellular and population scales of the quorum sensing phenomenon has been proposed in [9] to demonstrate that the transition to quorum sensing in an *Agrobacterium* population in liquid medium requires a much higher threshold cell density than in biofilm. Muller *et al.* [10] investigated and analyzed a spatially structured model for a cell population, including a detailed discussion of the regulatory network and its bistable behavior. The modeling approaches done by You [11] and Garcia-Ojalvo [12] also revealed a number of important properties of quorum sensing.

However, all the work discussed above are based on differential equations, which share the same drawbacks, *e.g.*, the parameters of these models have to be determined from the experimental data. Moreover, they are not able to be generalized for analysis of various events of the biological system from which the data were collected. With the aim of systematic approach, it is rare that these models could be able to describe the whole evolution process of biological colonies.

To demonstrate the effectiveness of IbM based models in solving the problems in Systems Biology, we have previously presented a Varying Environment Bacterial Modeling (VEBAM), which is an individual based model of bacterial foraging incorporating mechanisms of chemotactic behaviors [13]. In this paper, we consider a novel VEBAM based approach by which quorum sensing can also utilize biologically realistic mechanisms, including the employment of cell density sensing mechanisms.

This paper is organized as follows: Section 2 introduces the framework and basic components of the previously presented model, VEBAM. Section 3 describes the phenomenon and its underlying mechanism of quorum sensing in detail, then the modeling of quorum sensing based on VEBAM is presented. The bacterial behaviors with and without quorum sensing mechanism are simulated, and the numerical difference between them with a wide variety of intrinsic and extrinsic