Quorum-sensing induced transitions between bistable steady-states for a cell-bulk ODE-PDE model with lux intracellular kinetics. (English) Zbl 07458803

Summary: Intercellular signaling and communication are used by bacteria to regulate a variety of behaviors. In a type of cell-cell communication known as quorum sensing (QS), which is mediated by a diffusible signaling molecule called an autoinducer, bacteria can undergo sudden changes in their behavior at a colony-wide level when the density of cells exceeds a critical threshold. In mathematical models of QS behavior, these changes can include the switch-like emergence of intracellular oscillations through a Hopf bifurcation, or sudden transitions between bistable steady-states as a result of a saddle-node bifurcation of equilibria. As an example of this latter type of QS transition, we formulate and analyze a cell-bulk ODE-PDE model in a 2-D spatial domain that incorporates the prototypical LuxI/LuxR QS system for a collection of stationary bacterial cells, as modeled by small circular disks of a common radius with a cell membrane that is permeable only to the autoinducer. By using the method of matched asymptotic expansions, it is shown that the steady-state solutions for the cell-bulk model exhibit a saddle-node bifurcation structure. The linear stability of these branches of equilibria are determined from the analysis of a nonlinear matrix eigenvalue problem, called the globally coupled eigenvalue problem. The key role on QS behavior of a bulk degradation of the autoinducer field, which arises from either a Robin boundary condition on the domain boundary or from a constant bulk decay, is highlighted. With bulk degradation, it is shown analytically that the effect of coupling identical bacterial cells to the bulk autoinducer diffusion field is to create an effective bifurcation parameter that depends on the population of the colony, the bulk diffusivity, the membrane permeabilities, and the cell radius. QS transitions occur when this effective parameter passes through a saddle-node bifurcation point of the Lux ODE kinetics for an isolated cell. In the limit of a large but finite bulk diffusivity, it is shown that the cell-bulk system is well-approximated by a simpler ODE-DAE system. This reduced system, which is used to study the effect of cell location on QS behavior, is easily implemented for a large number of cells. Predictions from the asymptotic theory for QS transitions between bistable states are favorably compared with full numerical solutions of the cell-bulk ODE-PDE system.

MSC:
35Q92 PDEs in connection with biology, chemistry and other natural sciences
35B25 Singular perturbations in context of PDEs
35P30 Nonlinear eigenvalue problems and nonlinear spectral theory for PDEs
92C05 Biophysics
93C15 Control/observation systems governed by ordinary differential equations

Keywords:
cell-bulk coupling; bulk diffusion; lux kinetics; quorum-sensing; bistable states; Green’s function; globally coupled eigenvalue problem

Full Text: DOI

References:
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