Abstract

Tran, Vu. Ph.D., Purdue University, May 2018. Transfer of Antibiotic Resistance in *Enterococcus Faecalis*. Modeling and Computational Study. Major Professor: Doraiswami Ramkrishna

Bacteria of the genus *Enterococcus*, commonly found in the intestinal tract, are the main cause of antibiotic-resistant infections that are acquired in hospitals. Donor cells that contain plasmid pCF10 have the ability to resist to antibiotics and are capable of transferring this plasmid to recipient cells. This transfer occurs via a rapid horizontal inducible conjugation regulated by peptide-mediated cell-cell signaling molecules (quorum sensing), known as cCF10 and iCF10. This quorum sensing system functions by producing low levels of an inducing substance that accumulates in the environments until a threshold is reached, at which point there is a change in cellular behavior. Cells of this type can either exist in the free floating form or in biofilms, which are composed of cells attached on biotic and abiotic surfaces. Complexity of the biofilm structure hinders and affects the exposures of cells to antibiotics and hence reduces treatment efficacy. Successful models of this mechanism can lead to useful techniques/methods in controlling or interfering with the plasmid transfer.

Several efforts to model this phenomenon have been initiated and developed by our group in recent years. Recently, the collaborative experimental group in University of Minnesota has discovered new mechanisms that are associated with the system. This discover invalidates previous assumptions and hence requires modifications on both reactions and modeling assumptions. Moreover, various variables in the system have shown stiff behaviors which are much more challenging to work with. Explicit SDE, used in previous system, can be no longer capable of obtaining accurate solutions. For these reasons, this thesis presents new updated strategies to capture the drug resistance transfer in both Planktonic and biofilm environments.

Since the two systems are inherently different in structure and physics, usage of varied modeling formulations for each environment is inevitable. Deterministic models are very simple and can be used to acquire a rough prediction of Planktonic environment. However, their simplicity also limits their capability of capturing large complex systems such as biofilms and other highly heterogeneous systems. Unfortunately, stochastic models can also carry a huge burden on CPU time. Therefore, another part of this thesis is dedicated to illustrate techniques, which can be used to reduce stochastic simulation time without losing accuracy. Successfully solving these two major problems together can potentially serve as a tool to gain knowledge about the system and eventually develop methods to treat/control this phenomenon.