PROBABILISTIC SAFETY AND OPTIMAL CONTROL FOR SURVIVAL ANALYSIS OF BACILLUS SUBTILIS

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The investigation of the stress response network of *Bacillus Subtilis* ATCC 6633 offers a detailed explanation of how the bacterium reacts to competitive environmental conditions, among the many options, by producing the antibiotic *subtilin* in order to directly suppress other cells while getting immunized. The mechanisms of this generation are fairly well understood and described by a genetic and protein pathway that involves some non-deterministic interplay between the involved quantities: in particular, the presence of switching modes exhibits the activation/deactivation of certain genes and the production of proteins; these transitions in turn depend non-linearly on the above quantities.

According to the general principles of evolution, we may postulate that the way this pathway functions is according to certain criteria and levels of optimality; in this context optimality is intended as a measure of personal fitness or, in the particular instance, of own survival. In particular, one would expect that the switches in the network happen `optimally’ in the above sense.

In this work, we look at a recently developed dynamical model for the genetic network describing the production of subtilin and propose modifications for the model to bring it in line with other evidence reported in the literature. We obtain a system that presents partially decoupled high-level dynamics (those dealing with the population size and the nutrient level) and low-level ones (those describing the mechanism of generation of subtilin by the single cell). The high-level model is non-linear and deterministic, while the low-level one is piecewise-affine, hybrid and stochastic.

The new model allows one to reinterpret the survival analysis for the single *B. subtilis* cell and study it as a probabilistic, decentralized safety specification problem over a short time horizon; it is `probabilistic’ because of the certainly stochastic dynamics, as well as according to possible `trembling’ features of the actions; it is `over a short time horizon’ because of the greedy nature of the survival games that are played at this level; it is naturally `decentralized’ because each entity, while optimizing for its own fitness (which depends on global information), does not communicate with the competitors, nor has knowledge of their actions; furthermore, we motivate that the solution of the problem may not be globally optimal.

Using recently developed techniques for probabilistic verification in a stochastic hybrid systems setting, we reinterpret the above probabilistic safety problem as a (stochastic) optimal control one, where the controls are (possibly randomized) functions of the state-space that encode the switches in the network. Finally, the solution of this short-time-horizon, stochastic and decentralized optimal control problem yields the structure of the switching behaviors under study. Matching these outcomes with the data in the literature allows concluding that the corresponding mechanisms in the subtilin production network function with a degree of optimality, according to certain survival criteria.