Modeling the Mechanism of Postantibiotic Effect

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Abstract

Models for the emergence and spread of resistance have many challenges. In this paper we look at the specific problem of modeling the postantibiotic effect (PAE), the delayed regrowth of the bacteria after complete removal of an antibiotic.

A stochastic model for describing one of the possible underlying biological mechanisms of PAE is formulated. The model is based on the theory of penicillin binding proteins (PBPs), where the PAE is the time required by the bacteria to synthesize new PBPs before growth. Newly synthesized PBPs are unsaturated and becomes saturated under antibiotic pressure and eventually removed due to death.

The model assumes that unsaturated PBPs are attached (synthesized) to a bacterium according to a Poisson process and that these in turn are saturated with an intensity proportional to the antibiotic concentration of the treatment. The calculations and results are divided into three simplifying steps toward a more realistic approach. At first, we assume constant antibiotic concentration and no initial PBPs. Secondly, we assume constant antibiotic concentration, but with an initial set of unsaturated PBPs (no saturated PBPs). Thirdly, we assume exponentially declining antibiotic concentration and the same initial set of unsaturated PBPs.

The stochastic models are solved using a set of Kolmogorov equations and exact solutions with interesting properties can be derived for all three steps. The results are useful for giving a better understanding of the time properties of PAE.