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In-vivo Breakpoint Estimation Accounting for Variability in Drug Intake

Pharmacokinetic and pharmacodynamic (PK/PD) indices are increasingly being used in the microbiological field to assess efficacy of a dosing regimen. Contrary to methods using MIC, PK-PD-based methods reflect the in vivo conditions and are more predictive of efficacy. Unfortunately, these methods are based on the use of one static pharmacokinetic value such as AUC or Cmax and may thus lead to biased efficiency information when inter- or intra-individual variability exists.

In this work I will discuss the opportunity to evaluate the efficacy of a treatment by adjusting classical breakpoints estimation methods to the situation of variable PK profile. We propose here a logical generalisation of the classic AUC methods by introducing the weighted efficacy function. We will formulate these methods for both antibiotic classes: concentration-dependent and time-dependent. Using two drug models, we will illustrate how the newly introduced method can be applied to accurately estimate breakpoints.

This is a joint work with D. Gogore Bi and F. Nekka.