

EPISTASIS BETWEEN ANTIBIOTIC RESISTANCE MUTATIONS

Sandra Trindade^{1,2}, Ana Sousa¹, Francisco Dionísio², Isabel Gordo¹

¹*Instituto Gulbenkian de Ciência, Oeiras, Portugal*

²*Faculdade de Ciências da Universidade de Lisboa, Departamento de Biologia Vegetal & Centro de Biologia Ambiental, Lisboa, Portugal*

strindade@igc.gulbenkian.pt

Genetic interactions between genes are extremely important in several features of biology. The importance of epistasis in evolution has led to conflicting views of adaptation in natural populations (especially between Wright and Fisher). In fact epistasis is key in Wright's shifting balance theory, Bateson-Dobzhansky-Muller incompatibility model of speciation, Kondrashov's mutational deterministic hypothesis for the evolution of sex and many other evolutionary important features. Here we take the first steps towards understanding the level of epistatic interactions between alleles at different loci. Unlike others who have asked about pairwise interactions when genes are absent, or epistasis between mutations caused by transposon insertions, we ask about interactions between the most common types of mutations that are the fuel of evolution: single nucleotide changes. We find a distribution of interactions where both, positive and negative epistasis exist, with significant positive average in *Escherichia coli*. Surprisingly we also found evidences of sign epistasis such that some resistant mutations can partially compensate for the cost of resistance in other loci. This implies that there is pervasive buffering between deleterious mutations, which is compatible with low levels of recombination in this bacterial species, and pinpoints the difficulties in eradicating multi-resistant bacteria.