

# The Paradoxical Effects of Allelic Recombination on Fitness

David P. Parsons<sup>1,3</sup>, Carole Knibbe<sup>2,3</sup> and Guillaume Beslon<sup>1,3</sup>

<sup>1</sup>Université de Lyon, CNRS, INRIA, INSA-Lyon, LIRIS, UMR5205, F-69621, France

<sup>2</sup>Université de Lyon, CNRS, INRIA, Université Lyon 1, LIRIS, UMR5205, F-69622, France

<sup>3</sup>IXXI, Institut Rhône-Alpin des Systèmes Complexes, Lyon, F-69007, France  
guillaume.beslon@liris.cnrs.fr

## Extended Abstract

### Introduction

Horizontal transfer (HT) plays a major role in bacterial evolution, providing a way for bacteria to take advantage of beneficial mutations found by other bacteria, possibly from other species. Within a given species, horizontal transfers allow bacteria to evade the clonal interference phenomenon (Hill and Robertson, 1966) through allelic recombination: when two different beneficial mutations are found concomitantly in two different lineages, horizontal transfer allows both mutations to be assembled into a single organism, thus speeding up evolution. Transfer also enables the isolation of the “ruby in the rubbish” (Peck, 1994): beneficial mutations being very rare compared to deleterious ones, it is likely that deleterious mutations will happen at the same time as a beneficial one, thus overwhelming the benefits of the latter. Transfer however, allows to solve this problem by breaking the linkage between the affected alleles.

In this work, focusing on transfer involving recombination rather than simple plasmid exchange, we used the Aevol model to study the influence of HT on the evolution of both fitness and genomic architecture. The Aevol model is a digital genetics model which is realistic at the level of the genome but abstract at the phenotypic level: each individual has a double stranded genome upon which genes are detected through signal sequences and a transcription-translation process. These genes are then interpreted in a mathematical formalism and combined to solve a curve-fitting task (Knibbe et al., 2007).

### Experiments

We let 105 populations of 1,000 individuals evolve independently for 50,000 generations with the same curve-fitting task. Each population was seeded with a random binary sequence of 5,000 bp containing at least one “good” gene. At each replication, the genome could undergo point mutations, indels (up to 6 bp) and chromosomal rearrangements (duplications, deletions, translocations and inversions) with random breakpoints (7 rates tested, from  $10^{-6}$  to  $10^{-4}$  per base). In addition, we tested 3 different schemes of HT, thus forming 3 groups of simulations. In group A, at each

replication, a transfer attempt was conducted with probability 0.1. A transfer attempt consists in trying to replace a sequence of the form  $(end1)(anysequence)(end2)$  in the (replicating) recipient genome by a sequence with similar ends  $(\sim end1)(anysequence)(\sim end2)$  from the (randomly chosen) donor genome. Note that because the regions that need to be similar are limited to the sequences around the breakpoints and not the whole sequence, the transferred and the replaced sequences may differ greatly in length and content. A simple match/mismatch scoring function (no gaps) was used: highly similar sequences ( $score > 30$ ) were given a high probability of leading to a transfer event (homologous recombination) while regions of low similarity were only assigned a low, although not null, probability (nonhomologous recombination). This model of HT is similar to the homology driven chromosomal rearrangement model described in (Parsons et al., 2011). In the second group of simulations (HT scheme B), transfers were deterministically triggered between random points at the same rate as that effectively observed in group A. Finally, in group C, transfer was completely disabled.

### Results

We analysed the transfer events that occurred during the whole evolution and found that the sensitivity to sequence similarity proves to favour those transfers whose involved segments (transferred and replaced segments) are of roughly the same size (figure 2). It appears that many transfers consist in replacing a given sequence by another sequence of exactly the same size. We also observe that there are more transfers involving sequences that differ by only one to six bases in length than there are with greater differences. This is of particular interest since in these experiments, the maximum size of an indel is of precisely six. This strongly suggests that both sequences are homologous, having undergone only point mutations and at most one indel. It hence appears that alignment driven transfer does indeed promote allelic recombination.

The distribution of the scores of the alignments that lead to either beneficial, neutral or deleterious transfers in group

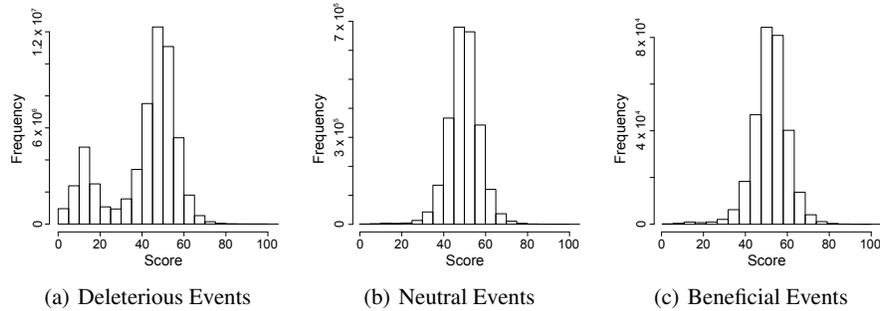


Figure 1: Distribution of the score of the alignments that lead to a **(a)**: deleterious, **(b)**: neutral and **(c)**: beneficial transfer.

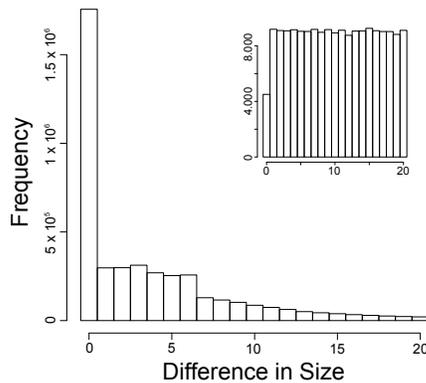


Figure 2: Distribution of the difference in size between the transferred and the replaced sequence for alignment driven transfer (group A). Inset: distribution for random point transfer (group B).

A (figure 1) is of great interest: almost all the replications involving transfer that either improved the fitness or were neutral correspond to the exchange of segments with highly similar ends ( $score > 30$ ) while most of the exchanges with weakly similar ends had deleterious effects. As a matter of fact, the proportion of both neutral and beneficial replications among those involving transfer was higher by up to two orders of magnitude in the case of homology driven transfer (group A) than in the case of random point transfer (group B – data not shown).

Surprisingly, even though homology driven transfer has proved to allow for allelic recombination, and despite all the theoretical benefits it could confer, there seems to be very little (if any) differences in the fitness of the evolved organisms between the different groups of simulations. We conducted a statistical analysis (multiple linear regression with Student's t-tests on the coefficients, Kruskal-Wallis test) of the fitnesses of the final best organism of each population. These tests show that the HT scheme has no significant effect on fitness after 50,000 generations. Actually, the only parameter that significantly affects fitness is the rearrangement rate, which supports our previous results (Knibbe et al., 2007) on the impact of rearrangement rates on evolution.

This lack of effect of transfer on the outcome of evolution in terms of fitness comes as a paradox when considered in the light of the apparent benefit of allelic transfer at the individual level. Indeed, it could be expected that group A would benefit from transfer since it was shown to allow for fitness improvements. The fact that this fails to happen could be explained by different hypotheses: the coalescence time in these experiments seems to be very short, which suggests a regime of successive rather than parallel mutations. This means that clonal interference might be very rare in these experiments. Also, even though transfer is beneficial more frequently when alignments are involved, it remains mostly deleterious. Given that in our experiments, transfers are rare, it is clear that beneficial transfers are very rare and might not make any difference in the long term.

Future experiments will thus aim at assessing under which conditions transfer can be beneficial on the population level.

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