



Figure S4 Schematic illustrating tests to distinguish between second- and higher-order epistasis. Red indicates the ORE genetic background; blue indicates the SAM genetic background; grey indicates the genetic background of the deletion strain; white indicates a chromosomal deletion; and the light blue bar on the X chromosome indicates the sd^{E3} allele and the genetic background in which it was originally generated. The genotypes and phenotypes on the left illustrate that this particular deletion enhances the sd^{E3} phenotype in an ORE background, i.e., results in even smaller wings. On the right, however, this deletion suppresses the sd^{E3} phenotype in a short-wing introgression background (i.e., results in larger wings). However, because the short-wing and ORE flies both carry the same genetic background (ORE) opposite the deletion, this background dependence must be due to other loci elsewhere in the genome (in this case, illustrated by the SAM alleles elsewhere in the genome), indicating higher-order epistasis.