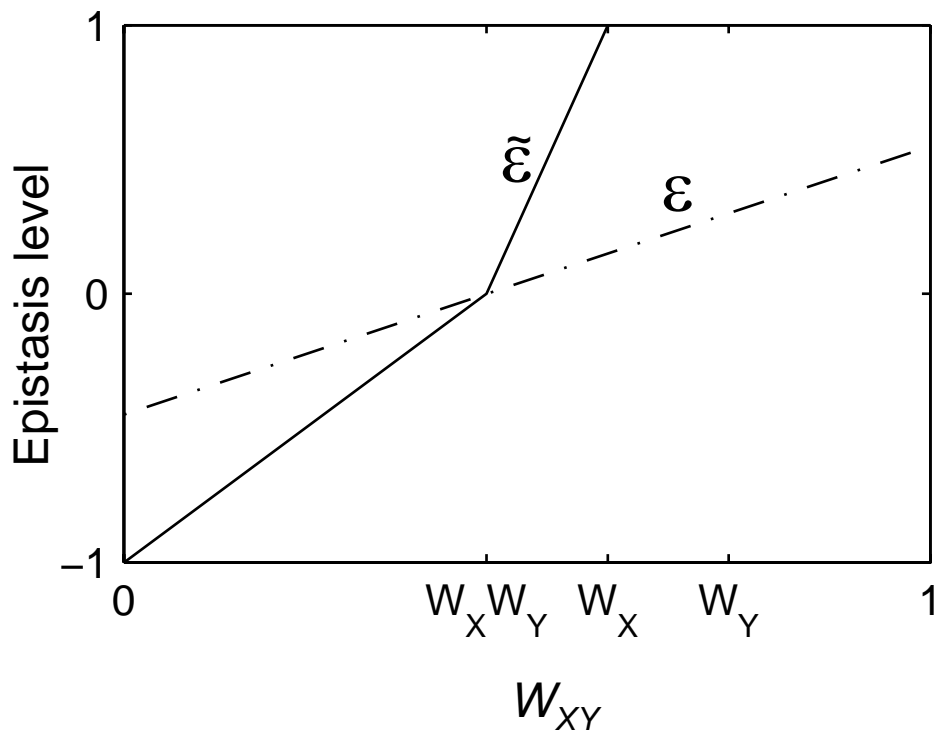


Supplementary Figure 1



Supplementary Fig. 1: The epistasis scale captures the strength of the epistasis effect relative to natural extreme values. The scaled ($\tilde{\varepsilon}$) and non-scaled (ε) epistasis shown as a function of the fitness W_{XY} of a double mutant for fixed fitness values W_X and W_Y of the corresponding single mutants (see **Table 1**; for other epistasis scales see Refs. ^{34,35}). To understand the motivation for the definition of $\tilde{\varepsilon}$, consider the two following cases: (I) $W_X=0.7$, $W_Y=0.7$, $W_{XY}=0.54$ and (II) $W_X=0.54$, $W_Y=0.91$, $W_{XY}=0.54$. In both cases $W_X \cdot W_Y=0.49$. The non-scaled epistasis ε would therefore be the same in both cases. However, the scaled epistasis value is 0.23 in case (I) compared to 1 in case (II). This reflects the fact that in case (II), but not in case (I), one of the mutations completely buffers the effect of the other.

(For references, see **Supplementary References** online)