Supplementary Figure 1

Epistasis level vs. $W_{XY}$
**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 ($\varepsilon$) 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 $\varepsilon$ 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)