

Supplementary Tables

Table S1 – Density of sign epistasis and mutational additivity in published datasets^a

System	Assay	Density of sign epistasis ^b	R^2 for mutational additivity ^c	Data source
Avian lysozyme mutants	Melting temperature	0/12	0.99	(Malcolm et al. 1990)
<i>E. coli</i> dihydrofolate reductase mutants	<i>in vitro</i> enzymatic activity	0/12	0.95	(Aita and Husimi 1996)
<i>A. niger</i> visible mutants	Growth rate	17/80	0.71	(de Visser et al. 1997, Franke et al. 2011)
<i>D. melanogaster</i> visible mutants	Fecundity and survival	18/80	0.61	(Whitlock and Bourguet 2000)
“	Male mating success	21/80	0.48	“
<i>E. coli</i> isopropyl malate dehydrogenase mutants	Growth rate	372/2304	0.50	(Lunzer et al. 2005)
<i>E. coli</i> β-lactamase mutants	MIC against cefotaxime at 35° C	21/80	0.92	(Weinreich et al. 2006)
“	MIC against piperacillin with inhibitor	15/80	0.94	(Tan et al. 2011)
“	MIC against cefotaxime at 25° C	18/80	0.97	Knies et al, in prep.
“	k_{cat}/K_M	11/32	0.94	This study

“	T_m	2/32	0.99	“
Mammalian glucocorticoid receptor mutants	Cortisol binding	11/32	0.63	(Bridgham et al. 2007)
Solinaceae sesquiterpene mutants	5-EA synthesis	69/192	0.27	(O'Maille et al. 2008)
<i>P. falciparum</i> dihydrofolate reductase mutants	IC ₅₀ against pyrimethamine in <i>E. coli</i>	9/32	0.57	(Lozovsky et al. 2009)
“	MIC against pyrimethamine in <i>S. cerevisiae</i>	2/12	0.90	(Brown et al. 2010)
“	IC ₅₀ against cycloguanil in <i>S. cerevisiae</i>	4/12	0.86	(Costanzo et al. 2011)
<i>S. cerevisiae</i> visible mutations	Haploid growth rate	70/192	0.81	(Hall et al. 2010)
“	Diploid growth rate	58/192	0.80	“
HIV glycoprotein mutants	<i>in vitro</i> infectivity	22/80	0.62	(da Silva et al. 2010)
<i>Metholobacterium extorquens</i> beneficial mutations in novel metabolic pathway	Growth rate	0/32	0.99	(Chou et al. 2011)
<i>E. coli</i> visible mutations	Growth rate	7/80	0.94	(Khan et al. 2011)

^a Independent datasets with $R^2 > 0.80$ shown in bold.

^b See methods.

^c In each case, linear regressions were performed on both raw and log-transformed data; the larger R^2 value is reported here.