



Figure S1 (Caption next page.)

Figure S1 (Previous page.) Median net F2 hybrid misregulation in relation to population size and the evolutionary rate of the directionally selected trait (ΔP_{opt}), for pleiotropic (clear boxes) and two-domain (gray boxes) models. Populations evolved from $n = 24$ to zero mismatched bits in the positively selected regulatory interaction over the course of 2000 to 40,000 generations, under population sizes ranging from 25 to 400. (A) Misregulation of the directionally selected trait. Pleiotropy constrained misregulation overall, especially when populations were large and selection was gradual. Missing data in the first column is due to population extinction. (B) Misregulation of the conserved trait. In the pleiotropic model, selection produced moderate change in the pleiotropic locus, in turn favoring a compensatory response at the *cis*-regulated locus of the conserved trait, resulting in interpopulation divergence and hybrid misregulation there. In the two-domain model, divergence occurred mainly due to neutral compensatory evolution between the conserved *cis*-regulated locus and the *trans*-regulating domain upstream of it. With pleiotropy, divergence in the conserved interaction occurred in a shorter time and at larger population sizes. Missing data in the first column is due to population extinction. Box plots show median, quartiles and full ranges.