



Figure S5: Four ways in which misregulation can affect adaptive gene expression in a new state or environment. (Analogous to Figure 3 but for $p_B = 0.05$, $f^O = G_{on}/G = 0.5$.) The four panels show contour plots of four different quantities as a function of the fraction f^N of genes that must be expressed for optimal adaptation in the new state (horizontal axes), and as a function of the expression correlation c between the old and new state (vertical axes). These quantities are **A)** the change in the fraction Δf_{11}^m (eq. 2) of correctly 'on' genes under misregulation; **B)** the change in the fraction Δf_{00}^m (eq. 3) of correctly 'off' genes under misregulation; **C)** the change in the fraction $\Delta f_{00}^m + \Delta f_{11}^m$ (eq. 4) of all correctly expressed genes under misregulation; **D)** the change in mean fitness in the new state under misregulation, expressed as $r_w - 1 = (w^N/w^N|_{m-}) - 1$ (eq. 5). These quantities do not only depend on f^N and c , but also on the excess $\Delta_m = f_{01}^O - f_{10}^O$ of incorrectly on genes in the old state, which I obtained through computer simulations of the evolutionary dynamics of misregulation (Methods). These simulations are based on populations with $N_e = 10^3$ individuals, $G = 1500$ loci, $G_{on} = 750$ and thus $f^O = G_{on}/G = 0.5$, $p_B = 0.05$, $s_{01} = 0.1/N_e$, $s_{10} = 10/N_e$, as estimated from empirical data (Kim et al. 2009; Mustonen and Lassig 2005; Mustonen et al. 2008; Hahn et al. 2003), a mutation rate per nucleotide of $\mu = 10^{-5}$, and an incidence of mutations leading to the destruction or creation of binding sites estimated from mouse PBM data, as described in Methods. I initialized populations with no misregulation for each individual ($f_{01} = f_{10} = 0$), and continued the simulations for $1/\mu$ generations, because preliminary simulations (not shown) had indicated that populations reach equilibrium by then. After $1/\mu$ generations, I calculated the population average of f_{01} and f_{10} over 100 generations. I used this average to compute $\Delta_m = f_{01}^O - f_{10}^O$ for all panels.