



Figure S4: A decreasing proportion of genes is incorrectly 'on' as f^O increases. Each panel shows the excess of incorrectly on genes, i.e., $\Delta_m = f_{01} - f_{10}$, as a function of the strength of selection against incorrectly on genes (horizontal axis) and incorrectly off genes (color legend). **A)** $f^O = G_{on}/G = 0.25$; **B)** $f^O = G_{on}/G = 0.5$; **C)** $f^O = G_{on}/G = 0.75$. Horizontal bars ('empirical') indicate the strength of selection supported by empirical data (Kim et al. 2009; Mustonen and Lassig 2005; Mustonen et al. 2008; Hahn et al. 2003). All simulations are based on populations with $N_e = 10^3$ individuals, $p_B = 0.25$, $G = 1500$ loci, 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 zero misregulation ($f_{10} = f_{10} = 0$), 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. This average is the value shown in each bar chart. Error bars correspond to one standard deviation over these 100 generations, and are too small to be visible for most data points.