S4 Text. Weak promoter limit

We have so far usually worked in the weak promoter limit, i.e. \( \lambda_P x_P \ll 1 \). Where the regulatory architecture leads to activation, this assumption on its own is not enough to make the fold-change independent of RNAP fugacity. For that reason, we have invoked the assumption that \( \lambda_P x_P \ll \Sigma_0/\Sigma_P \), with \( \Sigma_0, \Sigma_P \) defined above, where, conveniently enough, it proves to be the case that this fraction is equal to \( 1/\text{fold-change} \), provided that we may actually make this assumption. The fold-change calculated thus provides us with a convenient tool to check a posteriori whether this assumption is justified.

A typical binding energy of RNAP to a promoter is \( \epsilon_P \sim -2.9k_B T \) (\( E. coli \) RNAP to \( lac \) promoter). In \( E. coli \), there are typically \( \sim 1000 \) RNAP molecules in a single cell, leading to an RNAP fugacity of \( \lambda_P \approx P/N_{ns} \sim 10^{-4} \). This means that typically, \( \lambda_P x_P \sim 2 \times 10^{-3} \). In order for the assumption to hold, we need to have \( \Sigma_P/\Sigma_0 \ll 5 \times 10^2 \). If not, then the assumption breaks down and the RNAP fugacity needs to be calculated explicitly in order to calculate an accurate fold-change.

In Fig. 10 is plotted the fold-change of the \( E. coli \) \( lac \) operon as a function of the total number of CRP (activators) and \( lac \) repressors. We see that the fold-change never exceeds \( 10^2 \), even for very high number of activators. The activator binding sites are essentially saturated with activators. In this regime, \( \Sigma_P/\Sigma_0 \) remains lower than \( 5 \times 10^2 \), although it does come close. This situation, however, only occurs when close to no repressors are present in the cell. When just over a single repressor is present, the fold-change drops dramatically to well below 1. In those circumstances, the assumption that \( \lambda_P x_P \ll \Sigma_0/\Sigma_P \) is already taken care of by the weak promoter limit.