



Figure 6 - figure supplement 2: In most cases, two enhancer models drive lower noise than the single enhancer model. To explore the behavior of CV in these different models, we use several approaches. A. We plot the mean expression level versus CV for the five models above and one set of parameters, $k = 1$, $p = 1$, $\gamma = 0.1$. The single enhancer model (dark purple) drives the highest CV, indicating that, under the assumptions of our models, adding an additional enhancer generally lowers intrinsic noise. Except for XOR model (yellow), all other models produce more mRNA than the single enhancer model. The other colors are: blue, OR model; green, additive model; brown, synergistic model. B. Here we plot the CV as a function of l , the rate of promoter-enhancer dissociation, for the five models above and vary l from 0.1 to 10 on a logarithmic scale with $k = 1$, $p = 1$, $\gamma = 0.1$. With the exception of the XOR model with low l , the single enhancer model drives a higher CV than the models with two enhancers for the same value of l . These results show that, under the simplifying assumptions that the production rates and on-off rates of enhancers are independent of the position and number of enhancers, the addition of a second enhancer generally lowers the predicted intrinsic noise. In our experimental data (Figure 6), we only observe a significant decrease in interallele noise for the shadow enhancer pair compared to the single distal or single proximal enhancer. Duplications of either the proximal or distal enhancer do not have significantly lower noise than their respective single enhancer constructs. Therefore, we expect that the simple addition of an identical enhancer likely does not fulfill the simplifying parameter assumptions used here and suggests that further investigation is needed to understand the complexity of the relationship between interallele noise and the numbers of enhancers controlling a promoter.