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Mathematical modeling and theoretical analysis for the quantitative control of the target gene expression of synthetic genetic circuit

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In recent years, synthetic genetic circuits have been developed as a gene expression regulatory system in expectation of biotechnological applications. For practical applications of them, quantitative control of target genes expression is necessary. For this purpose, various parameters, such as promoter or RBS strength and copy number of genes, should be adjusted properly according to characteristics of the circuit. Development of mathematical modeling on the basis of the experimental results *in vivo* is important for the efficient and deliberate construction of desired circuits. In this study, we designed a simple inducible switch which is composed of two gene expression modules ($P_L$tetO_1::*gene1* and $P_L$lacO_1::*tetR* (repressor) *gene2*) and a constitutive source of LacI repressor (P*lacI*^{q}::*lacI*). The switching of expression from *gene1* to *gene2* should be induced by addition of IPTG.

At first, we experimentally evaluated promoter strength of the two P_L promoters by monitoring expression level of GFP in *Escherichia coli*. Next, we built two stochastic models of each module and fitted their parameters to the results of the *in vivo* experiment. The desired switching behavior was realized by integrating two stochastic models above. Furthermore, the expression level of *gene1* and *gene2* showed a positive and a negative correlation with the increase in the copy number of P*lacI*^{q}::*lacI*, respectively. Based on these results, we constructed the genetic switch and examine its dynamic behavior *in vivo*. As the results, we obtained the desired switching and observed the predicted correlation between the copy number of *lacI* and target genes expression. For quantitative control of target genes expression, other parameters such as promoter strength or RBS strength can be adjusted in future work.

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