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Model for Gene Expression Tuning and Synthetic Gene Circuit Construction

Genetic circuit engineering has played an important role in many forms of synthetic biology. Based on a large collection of well characterized biological components, complex gene circuits with designed functions can be wired using established biological principles. Currently circuit assembly has two main strategies: one is monocistronic construct, in which one promoter drives one gene expression; the other is polycistronic construct, in which one promoter transcribes multiple genes (operon) into a single messenger RNA but is translated into individual products. To further the understanding of determinants of gene expression in synthetic circuits and accelerate circuit design and assembly, there needs to be a better understanding of how gene expression is impacted by adjacent genes/non-coding regions in a polycistronic operon, termed adjacent transcriptional regions (ATR).

Researchers at Arizona State University have developed a novel model of gene expression and generated a metric that takes into account ATRs in synthetic gene circuits. This method and system is able to provide quantitative guidance to the rational design and optimization of gene expression for large genetic circuits. The metric was used to design and construct logic gates with low basal expression and high sensitivity and nonlinearity. Further, 5'ATRs were designed with different GC content and sizes to tune protein expression levels over a 300-fold range which were then used to build synthetic toggle switches with varying basal expression and degrees of bistability.

This predictive model and gene expression metric provide solutions for facilitating future engineering of more complex synthetic genetic circuits for a number of synthetic biology applications.

Potential Applications

- Model and gene expression metric for predicting and tuning gene expression of complex synthetic gene circuits for:
 - o Drug development
 - o Pathogen detection
 - o Nitrogen fixation and environmental bioremediation

- o In vivo delivery
- o Chemical production of biofuels and other commodities
- o Gene therapy

Benefits and Advantages

- Facilitates engineering of more complex synthetic genetic circuits
- Saves researchers time and resources in screening and testing module combinations
- Helps understand how protein expression is affected by adjacent genes/non-coding regions and local mRNA secondary structures
- Highlights the positive correlation of ATR GC content with protein expression
- Highlights the negative correlation of ATR size and local free energy with protein expression
- Enables fine tuning of gene expression in synthetic circuits
- o Can avoid the production of unwanted peptides and reduce metabolic burden
- o Could be used to 'program' metabolic loads and fitness of a cell simultaneously

For more information about the inventor(s) and their research, please see [Dr. Wang's laboratory webpage](#)

For more information about this opportunity, please see [Wu et al - Cell Syst - 2018](#)