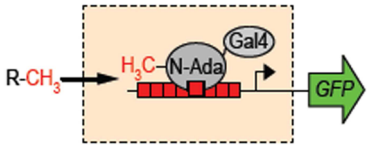
ACS SyntheticBiology

In This Issue

pubs.acs.org/synthbio

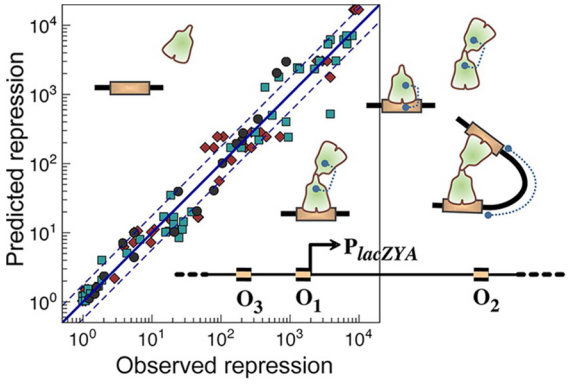
GENETIC SENSOR FOR STRONG METHYLATING COMPOUNDS



Methylating chemicals are common in industry and agriculture and are often toxic, partly due to their propensity to methylate DNA. The *Escherichia coli* Ada protein detects methylating compounds by sensing aberrant methyl adducts on the phosphoester backbone of DNA. Here, Moser and Horwitz et al. (DOI: 10.1021/sb400086p) characterize and expand the function of the Ada protein in *E. coli* as a sensor for strong methylating agents.

The authors also moved this sensor into *Saccharomyces cerevisiae* and demonstrated that it retains much of its native function, making it the only known sensor for DNA methyl phosphotriester adducts in eukaryotes. They show that this sensor is useful for screening assays and detecting strong methylating agents in complex environmental samples, making this paper of interest to synthetic biologists seeking novel sensors for genetic programs and applications.

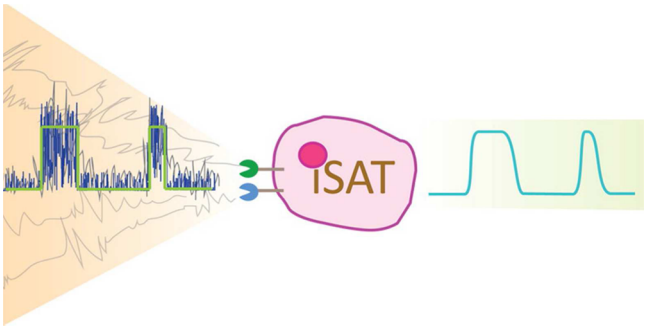
RELIABLE PREDICTION OF COMPLEX PHENOTYPES



Understanding how a system's underlying molecular complexity shapes it and controls its cellular behavior is of utmost importance in synthetic biology applications. Here, Vilar and Saiz (DOI: 10.1021/sb400013w) provide an exceptionally efficient computational approach to integrate the prototypical complexity of the control of gene expression into a few-parameter model to accurately predict system behavior from a few simple rules to connect the parts.

The authors show that, for the lac operon, it is possible to use just six experimental points to calibrate the model without fitting. This allowed the capture, for the first time, of the full range of regulation of the lac operon over a 10 000-fold range for 21 different operator setups, different repressor concentrations, and tetrameric and dimeric forms of the repressor.

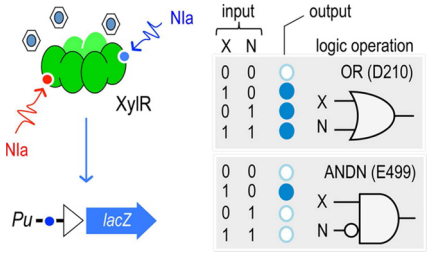
NOISE ATTENUATION IN BIOLOGICAL SWITCHES



Biological signaling systems are subject to various fluctuations in the environment, and they have to make reliable switches between ON and OFF states. In this manuscript, Chen et al. (DOI: 10.1021/sb400044g) present a novel method to evaluate noise buffering in both these states, and we report an interesting trade-off in noise buffering when both ON and OFF states are considered.

The authors describe input associated Signed Activation Time (iSAT), a new parameter that provides a concise description of how a circuit may response to input noise. The analysis of iSAT helps to reveal the noise properties of biological networks and to design robust switches that buffer noise at both the ON and the OFF states.

EXPANDING THE BOOLEAN LOGIC OF PROKARYOTIC XYLR

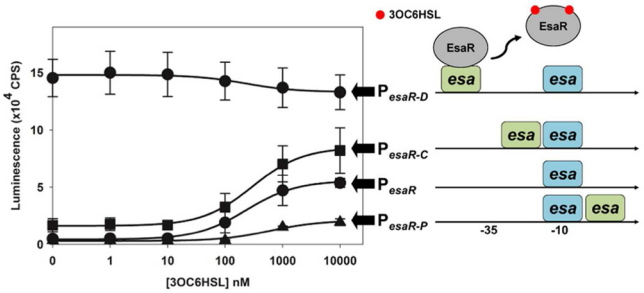


Promoters are the basic molecular devices that initiate transcription of specific DNA sequences into mRNA. Regulation of these promoters is carried out by transcription factors. One such promoter, Pu, is activated by the σ-54 prokaryotic transcription factor, XylR, in the presence of the aromatic effector m-xylene. Here, Calles and de Lorenzo (DOI: 10.1021/sb400050k) detail a mechanism to regulate XylR activity by either terminating it or generating an effector-independent, constitutive transcription factor.

The authors inserted a target site for the viral protease NIa in permissive protein locations that once cleaved *in vivo*. This resulted in NIa-sensitive XylR specimens allowed the design of novel regulatory nodes. This approach promises to facilitate the functionalization of transcription factors and other proteins with new traits, especially in the absence of structural data.

Received: September 26, 2013
Published: October 18, 2013

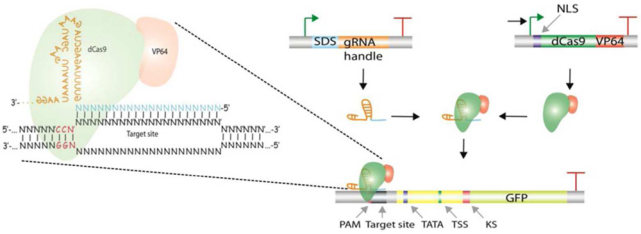
ENGINEERING THE *ESAR* PROMOTER



The development of new tools for density-dependent gene expression is important because these biological parts and systems can reduce the need to add exogenous inducers to turn on gene expression. Here, Shong and Collins (DOI: 10.1021/sb4000433) describe the generation and characterization of a new set of promoters that are regulated by the quorum-sensing regulator EsaR, which can function as a repressor or activator.

The authors show that the position of a second regulator-binding site added to the native *esaR* promoter leads to changes in gene expression levels and signal sensitivity. By adding endogenous quorum-sensing signal production, the authors also demonstrate that the new promoters, in combination with engineered EsaR regulator proteins, can be used to tune the timing and levels of expression observed in response to cell density.

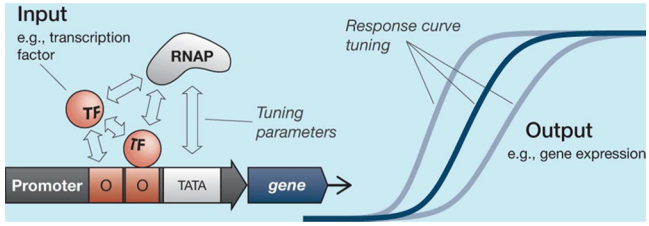
TUNABLE AND MULTIFUNCTIONAL EUKARYOTIC TRANSCRIPTION FACTORS



The regulation of gene expression in eukaryotic cells is primarily achieved through the combinatorial effects of regulatory factors that act on promoters of individual genes. In order to understand these effects in natural systems or to build upon them in synthetic networks, one needs scalable and simple tools for transcriptional regulation. Now, Farzadfard et al. (DOI: 10.1021/sb400081r) describe an engineered bacterial CRISPR/Cas system to function as a tunable universal transcriptional regulation platform for eukaryotes.

In this system, a single transcription factor can be targeted to different loci *in vivo* simply by expressing guide RNAs complementary to those loci. It greatly simplifies the process for building new transcriptional regulators and could also reduce the overall metabolic load imposed on the cells for large-scale transcriptional networks.

TUNING BIOLOGICAL RESPONSE CURVES



Recent years have seen an explosion in explorations of tuning in synthetic biology, along with its key importance in the development of the field as an engineering discipline.

In this review article, Ang et al. (DOI: 10.1021/sb4000564) address the experimentally demonstrated methods of tuning the shape of the rate-of-response curves in biological systems at transcriptional, post-transcriptional, and post-translational levels.

dx.doi.org/10.1021/sb400148y | *ACS Synth. Biol.* 2013, 2, 542−543