Noise in analogous circuits affects adaptability

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Short Abstract — **Phenotypic variability in a population is determined by genetic network architecture and affects fitness. *Bacillus subtilis* is a model bacterium that is used study the impact of stochastic gene expression upon phenotypic and dynamic variability in differentiation across a population of cells. Here we compare how analogous competence differentiation circuits in *B. subtilis* respond dynamically to increasing stressful stimuli. Previous work has shown that a synthetic competence circuit can match the median duration of the natural competence duration while differing in noise. We now further explore the adaptability and fitness of the underlying synthetic network architecture in stressful environments.**

Keywords — **Noise, differentiation, dynamics, adaptation, fitness, stochastic model, probabilistic model, competence, *Bacillus subtilis***

I. Purpose

THE variability of phenotypes in a clonal population of bacterial cells in a single environment has significant consequences for how well the organisms can adapt to their environment. Heterogeneity in phenotypes allows cells to account for uncertainty in future environmental conditions [1,2]. Homogeneity in phenotypes, however, may allow for cells to take advantage of certain optimal conditions.

Bacillus subtilis is a gram positive bacterium that undergoes a natural and transient differentiation event that allows the organism to incorporate exogenous genes into its genome while under stress. The duration of competence is naturally variable, but an analogous, synthetic circuit, SynEx, has been developed that is less variable [1]. This synthetic circuit is still physiologically functional but is more specialized for a smaller range of DNA concentrations in the environment.

The reduction of noise in the SynEx circuit is due to a permutation of repression and activation as compared to the natural circuit [3,4]. We now examine how this change affects the dynamic response of this circuit to different levels of stressful stimuli and investigate how this may affect the fitness of this synthetic strain versus the natural strain.

II. Results

In order to study the dynamics of the competence circuits precisely, we introduced a lactose-inducible promoter, Phyperspank, into both the natural and synthetic competence circuits in order to control the transcriptional expression of main competence regulatory peptide, ComK. This effectively allows us to simulate stress directly by changing the amount of a lactose analogue, IPTG, in the environment rather than using physiological stress that may themselves induce variable responses.

A. Stress Induction

With increasing stress induction, the frequency of competence is known to increase [3]. Furthermore, at moderate levels of induction the natural competence circuit can reenter and exit competence in succession before remaining stably in the competence state at high levels of induction. In contrast, we find that the synthetic circuit enters a permanent competence state starting at moderate levels of IPTG induction and does not experience oscillatory dynamics with increasing artificial stress.

B. Mathematical Modeling

Using stochastic simulations and probabilistic models [5] we examine both the dynamics of individual organisms and the population distributions to better understand differences between the analogous competence circuits. The models support the experimental findings that the synthetic circuit differs in response to moderate stress.

C. Fitness evaluation

We now examine the relative fitness of bacteria containing either the natural or synthetic competence circuits in different environments. We control environmental conditions in time using microfluidics, experimentally, or dynamic simulations, computationally.

III. Conclusion

Different noise characteristics in analogous competence genetic circuits are coupled to changes in environmental adaptability at higher levels of induced stress. Changing variability in one aspect of a circuit's response also affects the adaptability of the organism to different environments.

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