

# Robust pattern size control in engineered bacteria by a quasi-Turing mechanism

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**Short Abstract** — Formation of precise patterns is a salient property of a variety of developmental processes. Recent work has suggested a critical role for the interplay between gene expression, cell proliferation, and cell movement in pattern generation and robust size control. However, these processes are poorly understood. To gain insights into this issue, we have engineered the bacterium *Escherichia coli* to generate self-organized bullseye patterns in microcolonies by using a regulatory motif that is analogous to the Turing mechanism. These microcolonies exhibited robust control of pattern sizes over time and may have implications for understanding similar size-control processes in developmental systems.

Pattern formation is ubiquitous throughout the biosphere, driving such varied biological processes as slime mold aggregation [1], feather branching [2], and tissue stratification [3]. A critical feature of these self-organized pattern-forming systems is their ability to robustly control pattern size over time. While this characteristic is fundamental in any pattern-forming process, mechanisms for robust size control in self-organized pattern formation are not well understood. A growing body of experimental evidence supports a mechanism for size control which involves the regulation of cell growth and movement by diffusible molecules. Since pattern formation is often coupled with cell fate determination [4], the transient dynamics of morphogens can have important consequences regarding size control over time. Indeed, the transient effects of diffusible molecules can be perpetuated into permanent spatial patterns as in the cases of limb patterning and tissue stratification [5, 6]. Specifically, Verheyden et al. have shown evidence that chick and mouse limb bud size is determined by the temporal dynamics of diffusible morphogens, which is interrelated with cell proliferation [7]. Moreover, stratification of different cell types in the development of such varied tissues as the olfactory epithelium (OE) [3], the hair follicle [8], and the skeletal muscle [9] occurs due to the interplay between the temporal dynamics of diffusible factors and the proliferation of different cell types. The complex interactions between diffusible elements and cell

proliferation in each of these cases not only gives rise to self-organized pattern formation but also to robust control of the size of the resulting spatial pattern over time.

We have taken a synthetic-biology approach to examine self-organized pattern-formation dynamics in engineered bacteria. This approach is advantageous due to its clear mapping between modeling and experiments, which facilitates the investigation of how circuit dynamics are modulated by experimentally tractable parameters [10]. In addition, because of the interrelated roles of transient temporal gene expression dynamics and cell state in our synthetic system, the system is analogous in various respects to certain natural biological pattern-forming processes which implement precise size control, such as those involved in limb bud outgrowth and tissue stratification.

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