Efficient pattern formation in nitrogen-fixing cyanobacteria

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Cyanobacteria produce an important fraction of oxygen on Earth and, together with archaea, fix atmospheric nitrogen used by all other organisms. Some types live in colonies with specialized cells that perform different functions. In particular, the genus *Anabaena* forms filaments in which some cells differentiate into a nitrogen fixing form called heterocyst, forming patterns to effectively provide nitrogen for the colony. We have recently presented a theory combining genetic, metabolic, and morphological aspects to understand this prokaryotic example of multicellularity. Our results quantitatively reproduced the appearance and dynamics of this pattern and we used them to learn how different aspects, like fixed-nitrogen diffusion, cell division, or stochasticity, affect it [1].

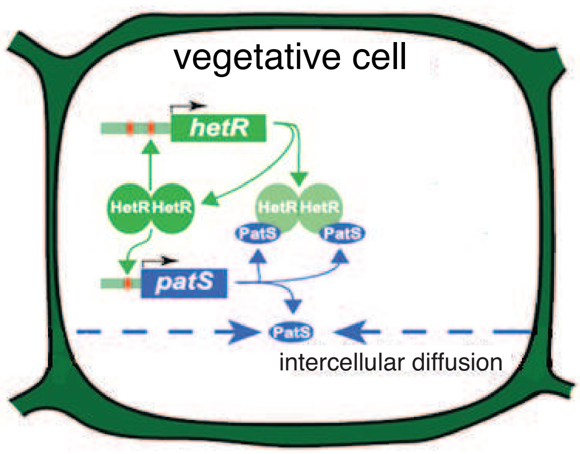

Figure 1: Model for the regulation of early differentiation in *Anabaena* cells after nitrogen deprivation.

Here we present a bifurcation analysis of the different parameters of a simplified version of our theory. This simple version only models the appearance of nitrogen fixing cells, but not its maintenance after the initial pattern is formed. We have restricted our analysis to a system of only two cells. HetR is a gene that acts as the master regulator of differentiation, activating its own expression and that of PatS. PatS is a protein whose product can diffuse along the filament of cells and inhibit differentiation. This inhibition works forming a complex with the activator that cannot bind to the regulatory regions of the DNA, see Fig. 1. Bifurcation diagrams for parameters of this theory typically look like Fig. 2.

The pattern forming region, characterized by coexisting high and low concentration solutions, appears and disappears through subcritical pitchfork bifurcations where it coexists with homogeneous solutions, represented by intermediate stable concentrations. Strikingly, for all the parameters of the model, wild type values determined previously [1] are very close to a bifurcation point, always to the one with lower concentration of activator and inhibitor. This finding suggests that evolution may have tuned this pattern forming process to occur efficiently at a working point where the concentrations of proteins needed to attain a heterogeneous state are close to the minimal possible. This might be an example of a more general biological principle of *energy minimization*.

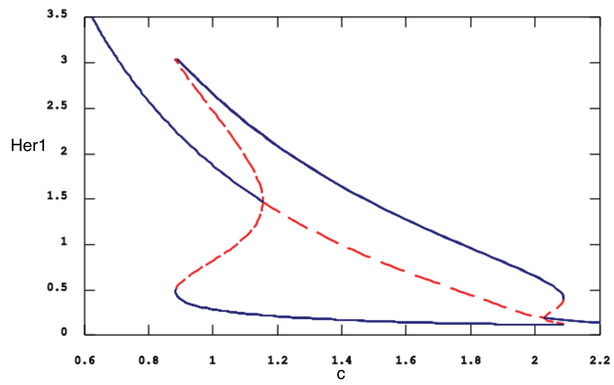

Figure 2: Bifurcation diagram for activator (Her1) concentration, as a function of activator degradation rate, c. Continuous lines denote stable steady states and dashed lines unstable steady states. Wild type parameter is $c = 2$.

[1] J. Muñoz-García and S. Ares, Proc. Natl. Acad. Sci. USA **113**, 6218 (2016).

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