Formation and maintenance of nitrogen fixing cell patterns in filamentous cyanobacteria

Javier Muñoz-García* and Saúl Ares†

**Departamento de Matemáticas and Grupo Interdisciplinar de Sistemas Complejos (GISC), Universidad Carlos III de Madrid, 28911 Leganés, Spain*

†GISC and Logic of Genomic Systems Laboratory, Centro Nacional de Biotecnología - CSIC, 28049 Madrid, Spain

In the study of the transition between unicellular and multicellular living forms, cyanobacteria forming one-dimensional filaments are important model organisms. Cyanobacteria were the first organisms to use oxygenic photosynthesis and are currently one of the most successful living groups, occupying a broad range of habitats across all latitudes and producing 20-30% of Earth's photosynthetic activity. These cyanobacteria may form colonies consisting of a one-dimensional filament composed under normal conditions only of vegetative cells. However, as a response to different environmental stresses they can differentiate into specialized cell types that perform important functions for the survival of the colony[1].

The genus *Anabaena* has received special interest because under nitrogen-limiting conditions, some cells of the filament differentiate into heterocysts, which lose the possibility to divide but are able to fix environmental nitrogen for the colony. These heterocysts form a quasi-regular pattern in the filament, representing a prototype of patterning and morphogenesis in prokaryotes. Here we will focus on the case of heterocyst differentiation. Heterocysts are specialized cells able to fix atmospheric nitrogen into a chemical form usable by vegetative cells. When external nitrogen sources are scarce heterocysts appear in regular patterns, with intervals of around 10 vegetative cells between consecutive heterocysts, representing a paradigmatic example in pattern formation of developing biological systems[2]. Since a continuous outer membrane covers the whole filament, the fixed nitrogen produced by heterocysts can diffuse through the periplasm and reach the vegetative cells. In turn, nutrients produced by photosynthesis in vegetative cells are also shared and reach the heterocysts.

The biology of this differentiation process has been the subject of several studies (for recent reviews see for example Refs. 1, 3). Most of these genetic studies have been focused on a particular species named Anabaena sp. PCC 7120 (also known as Nostoc sp. PCC 7120), which has become a prototypical organism in this field. However, theoretical models are scarce and the inclusion of recently discovered genetic regulations is still lacking.

In this study[4] we formulate a theoretical description of heterocyst pattern formation that includes the genetic regulations between the main genes identified in the process, such as hetR, patS, and hetN (see figure 1 for a diagram of the regulatory network and its interactions). This description has been coded using an object-oriented platform based on systems of stochastic reaction-diffusion differential equations for each cell, with variables representing the concentration of each molecular species. We reproduce qualitatively and quantitatively many important features of the observed differentiation process, including the appearance of heterocysts forming a quasi-regular pattern. Our results are in good agreement with experimental observations in wild type and mutants of Anabaena sp. PCC 7120, adding support for the regulatory relations proposed and allowing to make predictions on the role of recently described genes.

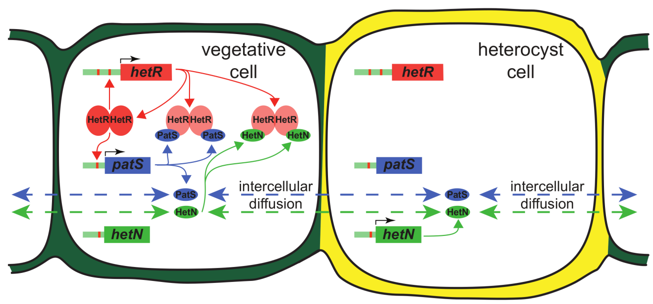

FIG. 1. Diagram of the regulatory network and its interactions. HetR dimers activate the expression of *hetR* and *patS*. *patS* is only expressed in vegetative cells, *hetN* is expressed constitutively in heterocystes. Active products of PatS and HetN can diffuse between cells in the filament and bind HetR, preventing it from binding DNA.

* javiermunozgarcia@gmail.com
`http://gisc.uc3m.es/~javier`

[1] E. Flores and A. Herrrero, *Nat. Rev. Microbiol.* **8**, 39 (2010).
[2] L. G. Morelli, K. Uriu, S. Ares, and A. C. Oates, *Science* **336**, 187 (2012).
[3] K. Kumar, R. A. Mella-Herrera, and J. W. Golden, *Cold Spring Harb. Perspect. Biol.* **2**, a000315 (2010).
[4] J. Muñoz-García and S. Ares, *preprint* (2014).