

Pattern formation of nitrogen fixing cells in filamentous cyanobacteria

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In the study of the transition between unicellular and multicellular forms of life with differentiated cell types, an important model organism are cyanobacteria. 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 colony¹.

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. Bacteria and archaea are the only forms of life able to fix atmospheric N₂, making them crucial for all living forms on Earth. When external N-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 systems². 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 ex-

ample 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 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*. 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 some of the main 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 in our model and allowing to make predictions on the role of recently described genes.

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