ISSN 0026-2617, Microbiology, 2021, Vol. 90, No. 1, pp. 20–36. © Pleiades Publishing, Ltd., 2021.
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REVIEWS

# Bistability and Formation of the Biofilm Matrix as Adaptive Mechanisms during the Stationary Phase of *Bacillus subtilis*

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Received February 25, 2020; revised July 1, 2020; accepted July 7, 2020

**Abstract**—*Bacilli* control behavioral reactions such as motility, biofilm formation, production of enzymes and metabolites, differentiation, and others by integrating a variety of environmental signals through a complex regulatory network. In the natural environment, *Bacillus subtilis* exists predominantly in the form of biofilms, which has made it an ideal model for studying the molecular strategy of biofilm formation. This paper systematizes information on the main regulatory systems responsible for the loss of mobility and the formation of *B. subtilis* biofilms, analyzes the behavior of bacteria within the biofilm population, leading to a state of bistability and differentiation into different types of subpopulations. It also evaluates the regulatory relationship between control systems responsible for the synthesis of structural components in the biofilm matrix. Particular emphasis is placed on data concerning signaling mechanisms that trigger the formation of a biofilm and its dispersion. In general, we summarize information about the latest discoveries in this area and their integration into the general idea of these complex microbial communities.

**Keywords**: *Bacillus subtilis*, biofilm, bistability, transcription regulators, repressors, antirepressors, metabolic regulation, signal mechanisms

**DOI:** 10.1134/S002626172006017X

During the stationary growth phase, bacilli can display various adaptive responses associated with changes in the expression of survival-promoting genes. Under natural conditions, biofilms represent the predominant lifestyle; their formation under nutrient limitation is a complex and tightly regulated process. The biofilm-synthesizing capacity is a prerequisite for completion of the life-cycle of most microorganisms and it is a part of a successful strategy for protecting bacteria from detrimental environmental factors. Therefore, the molecular basis of biofilm formation has received increasing attention in microbiology. Presently, various bacterial models are used for elucidating the molecular mechanisms of biofilm formation and operation. The biofilms of the soil-dwelling bacterium *Bacillus subtilis* are envisaged as ideal models for this purpose. They are characterized by unique architectural features that result from carrying out complex programs of cell specialization and cell-cell communication within the community (Ryan-Payseur and Freitag, 2018; Kovacs and Dragos, 2019). This research is aimed at investigating the evolution, biological role, morphological traits, and structure of biofilms, as well as the molecular mechanisms underlying cell differentiation within a microbial community. The regulatory and metabolic relationship between biofilm formation in bacilli and other stationary phase-related processes in their cells, such as sporulation, motility, and secretion of secondary metabolites and proteins, including lipopeptides and extracellular enzymes, e.g., proteinases is of special interest (Aktuganov et al., 2019; Pisithkul et al., 2019). *B. subtilis* biofilms were shown to contain proteinase-producing cells, which increase in number during biofilm development (Kobayashi and Ikemoto, 2019). Moreover, the genes that encode biofilm formation are involved products are implicated, in regulatory terms, in the synthesis and secretion of various extracellular metabolites and signal molecules that enable cooperative interactions within a microbial community (Martin et al., 2020). Based on recent information, a platform for creating artificial biofilms by 3D printing for goal-directed practical use has been developed (Huang et al., 2018; Balasubramanian et al., 2019). We place special emphasis on summing up new data on the formation, development, and dispersion of *B. subtilis* biofilms.

The goal of this work was to systematically analyze data on the formation and dispersal of *B. subtilis* biofilms in terms of their interaction with other physiological processes during the stationary phase of this bacterium.