necessary to kill a pigeon-sized bird", whereas mimetic tropical butterflies are often merely described as 'distasteful'.

Truly nasty Müllerian mimics are found in the tropics — poison arrow frogs are clearly a little more than 'distasteful' [9] and pitvipers are, after all, best avoided [12] — but perhaps nearer the equator mimicry can also evolve more easily among less well defended species. The diversity of predators is much greater in the tropics, and there are more insectivores specialising on flying insects such as butterflies, so mimicry may be favored for signalling to particular predators. The great diversity of potential prey may also increase the selection pressure for mimicry, as predators are unlikely to be capable of learning a vast diversity of suitable prey in tropical communities [5]. Additionally, birds, often implicated as the 'predator' in mimicry systems, are known to live longer in the tropics, offering greater opportunity for learning [13].

A recent review of warning coloration and mimicry recommends that "more experimental field studies, especially with non-lepidopteran groups" are needed to better understand the phenomenon [7]. The Appalachian millipedes offer a great opportunity to study poorly understood aspects of Müllerian mimicry, such as predator discrimination and perception, the strength of selection for mimicry and the reasons for geographical heterogeneity in mimicry signals. Overall, however, this is an elegant new example of Müllerian mimicry, an evolutionary phenomenon that remains one of the most compelling examples of natural selection, 130 years after its first discovery.

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DOI: 10.1016/j.cub.2009.07.008

Microbial Interactions: Bacteria Talk to (Some of) Their Neighbors

A recent study reports that *Bacillus subtilis* biofilm formation depends upon paracrine signaling where the signal-producing and target-responsive cells are different.

Ishita M. Shah and Jonathan Dworkin

Bacteria rely on precisely coordinated signaling mechanisms to ensure efficient and accurate transmission of chemical messages within a population. During bacterial differentiation, this signaling has been thought to be autocrine — that is, all cells produce and respond to the same signal. However, in a recent paper in *Genes and Development*, Lopez *et al.* [1] report that biofilm formation in *Bacillus subtilis* involves paracrine signaling. Specifically, they found that, while most cells within the population produce a prenylated peptide, this molecule triggers the production of another signaling molecule — surfactin — only in a small subset of cells. As a consequence, a subpopulation of cells not capable of producing surfactin responds to surfactin to produce the extracellular matrix component of the biofilm.

In autocrine signaling the same cells both produce and respond to a signal, whereas in paracrine signaling the producing and receiving cells are different. While paracrine signaling controls eukaryotic processes dependent on cell–cell signaling, such as neurotransmission, blood clotting, angiogenesis, and embryonic differentiation, cell–cell communication in bacteria has been thought to be autocrine. For example, the phenomenon of quorum sensing involves the detection of a threshold concentration of a signaling molecule by bacteria that also produce these signals (Figure 1A) [2]. In the case of quorum sensing in *Vibrio* species, AHL autoinducers are detected by cytoplasmic proteins like LuxR, which activate transcription of quorum-sensing genes upon binding to their partner autoinducers [3]. Similarly, the *B. subtilis* genetic competence regulator ComX is recognized by a sensor histidine kinase that triggers phosphorylation events necessary for proper target gene expression [4].

While these responses can occur over distances within bacterial populations, signaling that requires cells to be in close proximity to one another can also occur. For example, during fruiting body formation in *Myxococcus xanthus*, a signal protein is displayed on the surface and interacts with a receptor on an adjacent cell to transmit signal. Both cells express the signaling molecule as well as the receptor (Figure 1B) [5]. Another

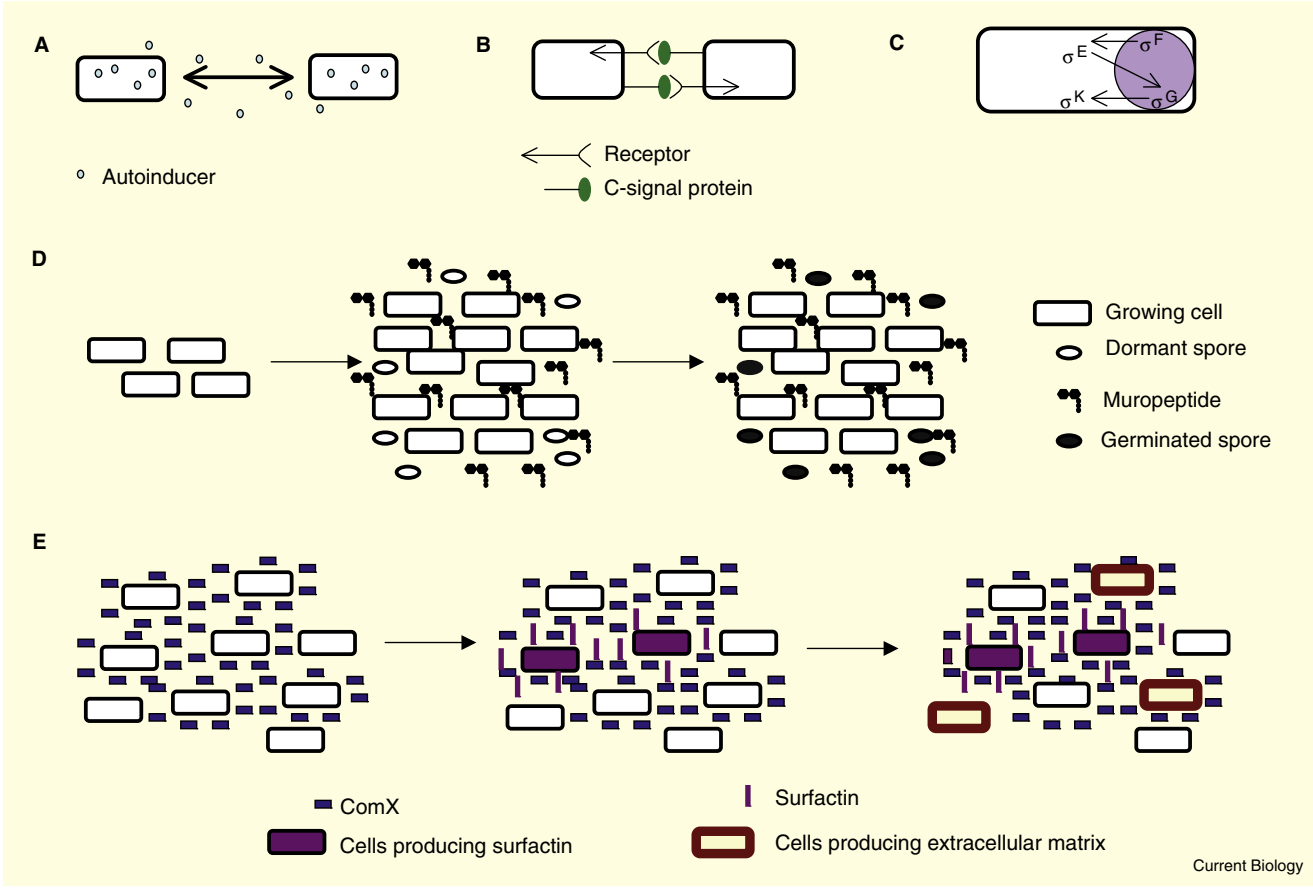

Figure 1. Cell–cell communication in bacteria.

(A) Quorum-sensing bacteria produce and respond to extracellular signaling molecules called autoinducers. (B) During fruiting body formation in *M. xanthus,* adjacent cells interact via the surface-displayed C-signal protein of one cell with a hypothetical receptor of the other cell. (C) The forespore and the mother cell within a two-compartment sporulating cell of *B. subtilis* communicate via secreted signaling proteins generated in response to the activation of specific sigma factors in each compartment. (D) Growing cells generate large quantities of muropeptides in the extracellular milieu. These molecules are detected by a receptor kinase in the dormant spores, causing them to germinate and resume growth. (E) During biofilm formation in *B. subtilis*, most cells produce and secrete ComX. A subset of these cells becomes surfactin producers and secretes surfactin and a distinct population that does not itself synthesize surfactin responds to this surfactin and generates the extracellular matrix. (A, B, and C adapted from [14].)

example is the criss-cross signaling between the mother cell and the forespore during sporulation in *B. subtilis* where cell–cell communication occurs between cells that are in intimate contact (Figure 1C) [6].

Other inter-bacterial signals have been described whereby growing cells release muropeptides derived from the cell wall that trigger a developmental switch in dormant cells that are not producing this molecule. Since both populations express the receptor for the muropeptide, the growing cells can, in theory, respond to the signal. However, this signal does not lead to changes in the physiological state of the growing cells, in contrast with dormant cells that exit dormancy in response to the signal. Thus, this system can be viewed as autocrine and paracrine [7] (Figure 1D).

Unlike the situation in eukaryotic cells whereby developmental processes result in many co-existing cell types, bacterial populations are often thought to consist of singular cell types. However, there is increasing evidence that bacteria have qualities of multicellular organisms — for example, the mycelial structures observed in streptomycetes [8], fruiting bodies in myxobacteria [9] or contact-dependent inhibition in *Escherichia coli* [10]. Biofilm formation in bacteria involves genetically identical cells that undergo differentiation into different types with only a fraction synthesizing the extracellular matrix necessary for the formation of the mature biofilm [11,12].

How this differentiation is generated has been a mystery since most cells generate and respond to ComX, the prenylated peptide that operates extracellularly and stimulates production of the cyclic lipopeptide surfactin [4]. An important clue arose from the observation that surfactin also acted as a signaling molecule capable of inducing a subpopulation of *B. subtilis* cells within a developing biofilm to become matrix producers [13]. An hypothesis following from this observation was that surfactin-producing cells were unable to respond to surfactin. To examine this possibility, Lopez *et al.* [1] monitored gene expression in individual cells that carried transcriptional reporters (P_{comQ}-*yfp*, P_{srfAA}-*yfp* and P_{yqxM}-*cfp*) distinguishable using flow cytometry to identify cells producing ComX, surfactin and the matrix, respectively. As expected, most of the cells in

the biofilm expressed genes involved in ComX production, and a small fraction of the population responded to ComX by producing surfactin. Furthermore, expression of the matrix protein operon was observed only in a subpopulation of cells. Importantly, however, surfactin-producing and matrix-producing cells were found as distinct populations, an observation that was confirmed by direct microscopy. Thus, Lopez *et al.* [1] concluded that surfactin producers are not capable of responding to the surfactin that they themselves generate and thereby provided a plausible explanation for the source of heterogeneity observed in the production of matrix.

As matrix producers do not become surfactin producers, the authors explored the possibility that the extracellular matrix physically prevents ComX action on the matrix producers. Lopez *et al.* [1] used different genetic backgrounds to manipulate the synthesis of the extracellular matrix and found that the levels of a ComX reporter were increased in the absence of extracellular matrix. They suggested that the matrix interferes with the ability of ComX to activate ComP, a kinase that phosphorylates a transcription factor required for surfactin production. They tested this interpretation using mutants lacking SinR, a repressor of matrix gene expression, which constitutively produce matrix. As expected, these cells did not produce surfactin, but they did produce functionally active ComX, as cleverly assayed using a heterologous strain that reports ComX activity but cannot synthesize ComX. Therefore, the defect in surfactin signaling does not lie in an inability to make ComX, but, consistent with the hypothesis, the matrix must somehow interfere with the ability of ComX to activate ComP and prevent the production of surfactin in matrix producers.

Thus, Lopez *et al.* [1] demonstrate that distinct populations of cells co-exist during *B. subtilis* biofilm formation, resulting in the formation of multicellular communities composed of genetically identical cells that are signal producers, signal responders or neither (Figure 1E). Surfactin-producing cells may become cells capable of genetic competence, whereas the matrix producers ultimately differentiate to become dormant spores. How these fates are determined by their prior developmental state remains unknown. In addition, an important question is how surfactin producers develop immunity to surfactin. The authors speculate that ComS, a protein produced by all surfactin-producing cells, may indirectly inactivate the transcription factor Spo0A that is required for the response to surfactin.

Cell–cell communication is central to a variety of developmental processes in bacteria. This signaling can be either between species or within species or between organisms that are in close proximity or between organisms that are in communities in which the signal-generating cell may be distant from the receiving cell. Further research will undoubtedly illuminate how these signaling events lead to genome-wide alterations in expression and provide genetically identical bacteria with the capability to exhibit individual phenotypic and communal properties.

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DOI: 10.1016/j.cub.2009.07.010

Visual Perception: Larger Is Faster

A recent study has shown that neurons in the inferior temporal cortex of the macaque monkey brain show earlier selectivity to global and large shapes than to local and small ones, which may underlie the faster behavioral responses to global aspects of a scene.

Rufin Vogels

A visual scene, for example of a forest, can be conceptualized as having different hierarchical levels of structure: from the global configuration, the forest, to its local elements, the trees. The results of decades of research suggest that humans analyse the global aspect of a visual scene before the local elements — the forest before its trees [1,2]. This issue has been investigated using, for example, Navon stimuli, named after their inventor David Navon [3]: these hierarchical stimuli consist of a global shape that is defined by the configuration of smaller, local shapes. The shapes of the global configuration and local elements can be manipulated independently (Figure 1), allowing the researchers to assess the degree to which the behavior of the subject is