16.1 INTRODUCTION

Most of our current knowledge regarding bacterial physiology and development is based on in vitro single pure culture experiments. However, bacteria in nature rarely exist in isolation. In nature, most bacteria: (1) are members of complex micro- and macrocommunities; and (2) predominantly exist in surface-associated, highly ordered microbial communities embedded in a biofilm matrix (see Chapter 6). Often, the survival of a bacterial species is dependent on the ability of individual bacterial cells within a population to communicate among themselves and/or between themselves and other organisms. These other organisms can be unrelated bacteria, organisms that share the same ecological niche, or eucaryotic hosts.

The environments that bacteria inhabit are complex and subject to change. In order to be successful, bacteria must be able to sense changes in their environment and respond rapidly to these changes by altering the expression of specific genes and metabolic pathways. It is becoming increasingly apparent that most bacteria also produce signals that allow communication between cells. Fundamentally, cells communicate by emitting specific chemicals, known as cell-to-cell signals, into a particular environment inhabited by other organisms. When, or if, the concentration of the signal reaches a critical threshold, other cells recognize the signal and gene expression of all organisms present may become modified. Communication appears to be important for coordinating gene expression within a single population of bacteria (intraspecies communication), between bacterial populations (interspecies communication), and between bacteria and other organisms (interkingdom communication) (Fig. 16.1).

Communication signals consist of a wide variety of chemical structures. The primary requirements for cell-to-cell signals are that they are small, they can be released from cells either by passive diffusion or by active transport, and that other cells recognize them and alter behavioral patterns in response to their presence. Because these signals are known to alter bacterial behaviors, they have been referred to as bacterial pheromones. Scientists are only beginning to appreciate the world of bacteria–bacteria and bacteria–host communication. This chapter discusses the current understanding of bacterial communication using
examples of communication systems with focus on communication in gram-negative bacteria via quorum sensing with N-acyl homoserine lactones and communication in gram-positive bacteria via γ-butyryl lactones and small peptide signals. In addition, several communication systems are introduced, including universal communication via the signal Autoinducer-2 (AI-2), interkingdom signaling via Autoinducer-3, and recent mechanisms involved in communication interference and signal breakdown.

16.2 COMMUNICATION VIA QUORUM SENSING IN GRAM-NEGATIVE BACTERIA

Quorum sensing is the regulation of gene expression in response to fluctuations in cell population density; that is, a sufficient number of cells or a quorum must be present in order for gene expression to occur (Fuqua et al., 2001). Specifically, quorum sensing bacteria produce and release chemical signal molecules or autoinducers that ultimately control gene expression of the whole bacterial population. Both gram-positive and gram-negative bacteria use quorum sensing systems, utilizing different chemical signals to control different target genes.

16.2.1 N-Acyl Homoserine Lactones (AHLs)

In gram-negative bacteria, the best studied diffusible signals are the N-acyl homoserine lactones (AHLs) (Table 16.1). To date, over 50 bacterial species have been shown

![FIGURE 16.1 Examples of cell-cell signaling interactions in nature. (1) Signaling within a single bacterial population. Signals such as AHLs (gram-negative) and γ-butyryl lactones (gram-positive) are commonly used in bacterial communication within a population. (2) Signaling also occurs between unrelated bacteria. The AHLs have been shown to also participate in communication between different bacteria, as has the universal autoinducer AI-2. (3) It is increasingly being recognized that signaling occurs between bacteria and eukaryotic hosts such as plants.](image-url)
to produce AHL signals (Scott et al., 2006). This signal class consists of a conserved homoserine lactone ring moiety connected to a fatty acyl side chain (Dong and Zhang, 2005). Specificity of AHL signals is determined by the length of the fatty acyl side chain as well as the types and number of side chain modifications. AHL-mediated regulation of gene expression is a well-known example of quorum sensing.

An excellent example of a quorum sensing system is that of the bioluminescent marine bacterium Vibrio fischeri. This bacterium exists in a symbiotic association with the marine squid Euprymna scolopes (Nealson et al., 1970). This tiny nocturnal squid contains specialized organs called light organelles that are colonized only by V. fischeri, which is ubiquitous in the ocean at low cell densities. Immature Euprymna scolopes have ciliated “arms” that collect seawater and pass it over the empty light organelles. When V. fischeri comes in contact with the light organelles, it colonizes the organs and is supplied nutrients by the host. Colonization by V. fischeri induces the loss of the squid’s ciliated arms by apoptosis (organized cell-mediated cell death) and also causes the bacteria to lose their flagella and reduce their cell size, indicating a true symbiosis. The eucaryotic squid host provides the host with light that is possibly used for several purposes including: attracting a mate and/or an antipredation strategy in which it counterilluminates itself using the light from V. fischeri. This counterillumination is aimed downward, and enables the squid to avoid casting a shadow beneath it on nights when light from the stars and moon penetrates the seawater, thus allowing the squid to be invisible to predators beneath it.

Light emission is correlated with the cell population density of the bacteria in the host. As the population of bacterial cells increases it produces and releases an AHL into the extracellular environment, which is the eucaryotic light organ. Here the concentration of the AHL increases and hence acts as a signal that communicates to the bacteria that they are inside the host as opposed to outside in the seawater. The AHL also initiates a signaling cascade that results in the emission of light (Information Box 16.1).

The simplest model for quorum sensing regulation involves two proteins. The first is an AHL synthase, encoded by a gene commonly referred to as an I gene (luxI, phzI, tral, lasI, etc.), that converts cellular precursors into one or more AHL signals. The second is an AHL-responsive regulatory protein (R protein), encoded by a gene referred to as an R gene (luxR, phzR, trcR, lasR, etc.), required for the activation (or in some cases, the repression) of specific genes. At low cell densities, the AHL signal either diffuses out of the cell following a concentration gradient or is actively transported out of the cell. As cell density increases, the concentration of AHL signal accumulates within the cell. On reaching a threshold level, the AHL interacts with the R protein, resulting in dimerization of the R protein. This causes the R protein dimer to bind to a specific sequence in the promoter of the quorum sensing–regulated gene(s), which recruits RNA polymerase and activates gene expression (Information Box 16.1).

Many gram-negative bacteria have been shown to utilize quorum sensing to regulate the expression of diverse traits. In all cases, increasing cell numbers result in increased AHL signal concentration, resulting in interaction with the R protein that alters the binding affinity of the R protein for a specific sequence located within the promoter regions for genes under quorum sensing control (Dunlap, 1999; Qin et al., 2000; Zhu and Winans, 1999). Although this form of regulation was given the name quorum sensing because in many cases the population of bacteria is recognizing its own AHL signal, in reality a single bacterial cell will activate quorum sensing–regulated genes in the presence of sufficient AHL signal. Thus, it is the concentration of AHL, not the number of bacteria per se, that determines gene expression patterns. This has important implications regarding the effect of AHL signaling on bacterial behaviors in single or mixed species populations. Quorum sensing originally was termed “autoinduction” as it was identified first and studied in a single species of bacteria. It has become apparent that communication via AHL signals occurs between related and unrelated bacterial populations, and between bacteria and their eucaryotic hosts.

### 16.2.2 Quorum Sensing in Agrobacterium tumefaciens, a Ubiquitous Plant Pathogen

Agrobacterium tumefaciens is a common soilborne plant pathogenic bacterium with an extremely wide host range (>140 plant genera). A. tumefaciens causes crown gall disease of plants, so named because the symptoms usually occur at the soil surface, or crown of the plant (Fig. 16.2). Typical disease symptoms include the development of galls, tumor-like growths representative of unrestricted plant cell division at the site of infection. The disease is induced in a variety of dicotyledonous plants, particularly stone fruits, roses, and grapes. The majority of the bacterial genes necessary to induce the disease are plasmid borne. Most of the genes necessary for tumor induction are located on a large 180-kb plasmid called the Ti plasmid (Fig. 16.3). This plasmid contains the virulence (vir) genes that are required for the processing and transfer of specific plasmid DNA known as T-DNA to the plant. The vir genes themselves consist of about 35 kb of DNA and are essential for tumor formation, although they are not transferred into the plant. The induction of the vir genes occurs following exposure to plant signal molecules, which are synthesized by the plant on wounding. This explains why crops that rely on root cuttings are particularly susceptible to crown gall disease. One of the signal molecules has been identified as the phenolic compound acetosyringone. This molecule plus sugar monomers, which are precursors of the plant cell
Quorum sensing was first discovered in the late 1960s during studies on a light-producing marine squid, *Euprymna scolopes* (see top left figure). This tiny nocturnal squid contains specialized organs called light organelles that are colonized by a single luminescent bacterium, *Vibrio fischeri*. The ability of *Vibrio fischeri* to luminesce is contained on an operon (the *lux* operon) that encodes enzymatic machinery that results in the release of photons of light (see signaling pathway figure below right). The first gene in the operon, *luxI*, encodes for an AHL synthase (LuxI) that converts cellular precursors into the AHL signal C6-HSL. Upstream of the *lux* operon is *luxR*, which encodes the transcriptional protein (LuxR) required for activation of high levels of expression of the *lux* operon. In the absence of AHL signal, LuxR is inactive.

At low cell densities, the AHL signals generated by LuxI diffuse passively out of the cell following a concentration gradient. Thus, the *lux* operon is not expressed. As the bacterial population size increases, the number of C6-HSL signals accumulates in the light organelle and thus within each bacterial cell. When a sufficient concentration of C6-HSL is reached within the bacterial cell, it interacts with the LuxR protein, causing LuxR to dimerize. Dimerization of LuxR allows it to bind to the *lux* operon promoter region and increase expression of the *lux* operon. Note that expression of the operon results in increased levels of LuxI, resulting in even more C6-HSL signal production and ensuring a rapid onset of light production.

Interestingly, the squid can control the amount of light produced by *V. fischeri* in the light organelles either by covering the light organelle with its black ink sac or by reducing the *V. fischeri* population in the light organelle by flushing out excess bacteria with seawater.

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**Information Box 16.1 Quorum Sensing in a Marine Squid**

**Euprymna scolopes**, a bioluminescent squid. From the National Science Foundation, 2005a.

**Colonies of *Vibrio fischeri***. (Left) Photo taken under light source. (Right) Photo taken in the dark showing the bacteria luminescing. From the National Science Foundation, 2005b.
quorum sensing strategy to ensure that the plasmid is maintained in the population. This is based on maintaining rapid rates of plasmid transfer via conjugation to any cells that may have lost the plasmid (Fig. 16.4). Thus, activation of plasmid conjugation by opine-induced quorum sensing control serves to ensure that all members of the *A. tumefaciens* community contain a copy of the Ti plasmid and are able to utilize opines for growth (Piper et al., 1993).

### 16.2.3 Quorum Sensing and Cross-Talk

The ability of AHL signals to serve as a means for communication between unrelated bacteria (cross-communication or cross-talk) is now recognized as widespread. One of the first demonstrations of cross-communication utilized the beneficial root-colonizing rhizosphere bacterium *Pseudomonas chlororaphis* (aureofaciens) strain 30–84 (Pierson et al., 1998b). *P. chlororaphis* produces three pigmented antibiotics called phenazines. Phenazines are nitrogen-containing broad-spectrum compounds synthesized by the products of the phenazine operon (*phzXYFABCDO*) (Mavrodi et al., 1998). Phenazine production is regulated, in part, by the PhzR/PhzI quorum sensing system. PhzI is an AHL synthase that produces the AHL C6-HSL and PhzR is the transcriptional regulator that responds to the AHL signal.

To demonstrate quorum sensing, a library of 800 culturable bacterial strains from the rhizosphere (the zone surrounding the plant root) of wheat plants from different U.S. geographic regions was individually spotted onto a lawn of a *phzI* mutant of strain 30–84 that did not produce phenazines because it could not produce the quorum sensing signal. Approximately 8% of the library strains restored phenazine production to the *phzI* mutant as indicated by restoration of orange pigmentation in the lawn, a phenomenon termed positive cross-communication (Fig. 16.5). Of even greater importance, cross-communication between various rhizosphere strains was demonstrated *in situ* on wheat roots using a *phzI*-, *phzB::inaZ* reporter of strain 30–84 (Pierson et al., 1998a). This nomenclature indicates that the reporter does not produce phenazine as it is defective in the PhzI AHL synthase and that it has a reporter gene encoding ice nucleation activity inserted within the *phzB* biosynthetic gene (*phzB::inaZ*). For further explanation of reporter genes, see Section 13.9. Thus, this reporter expresses ice nucleation activity only when phenazine is produced. However, since the reporter’s *phzI* gene is defective, it does not produce phenazine and so has a 1000-fold decrease in ice nucleation activity as compared to the wild-type *phzI* strain.

When the *phzI*-, *phzB::inaZ* reporter was grown with several of the rhizosphere strains from the library, ice nucleation activity by the reporter strain was restored to wild-type levels on roots in soil, demonstrating that quorum sensing was required for phenazine production on roots, and that communication occurred between different bacterial...
populations via AHL signals! This exciting result was one of the first demonstrations that quorum sensing actually occurs in a natural environment (the wheat rhizosphere). A large number of diverse gram-negative bacteria have been shown to utilize quorum sensing as a key regulatory mechanism. Additionally, many currently unculturable bacteria also appear to produce quorum sensing signals or related compounds as detected by a number of different quorum sensing reporter bacteria. This widespread occurrence of quorum sensing in bacteria indicates that quorum sensing has evolved to play important roles in bacterial ecology. It is difficult to obtain direct evidence for the ecological roles of quorum sensing. The best examples to date include the demonstration that bacterial pathogen mutants defective in quorum sensing are reduced in their ability to cause disease and that mutants of beneficial bacteria such as _P. chlororaphis_ defective in quorum sensing are impaired in their ability to prevent disease. Some of the many possible ecological roles of quorum sensing include the following: (1) coordination of gene expression within a single bacterial population; (2) coordination of gene expression and bacterial behavior among multiple populations; (3) avoidance of host defense responses; and (4) as we will see shortly, direct communication between the bacterium and the host organism.

16.3 SIGNALING IN GRAM-POSITIVE BACTERIA

Gram-positive bacteria do not contain classic AHL-mediated quorum sensing communication systems. One possible reason is that gram-positive bacteria lack a porous outer membrane and instead contain a thick peptidoglycan layer that may restrict diffusion of the AHL signals through the cell wall. Instead, some gram-positive bacteria utilize \( \gamma \)-butyrolactones,

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**FIGURE 16.3** The plant-_A. tumefaciens_ interaction that results in crown gall formation. In soil, _A. tumefaciens_ is attracted to plant roots due to their release of root exudates. Wounded plant roots release additional phenolic compounds such as acetosyringone (step 1). Acetosyringone is recognized by a two-component regulatory system (VirA/VirG) encoded by the Ti plasmid as a signal that a plant wound is present (step 2). This recognition induces the expression of a complex region of the Ti plasmid called the _vir_ region (for virulence) (step 3). The _vir_ region encodes several proteins that interact with a 25-kb T-DNA region on the Ti plasmid. Some of the _vir_ gene products are responsible for excising a copy of the T-DNA (step 4) while others encode a type four secretory system (T4SS) that is involved in transferring the copy of the T-DNA across the bacterial and plant cell walls and into the plant cell cytoplasm (steps 5 and 6). The end result is the random insertion of the T-DNA into one of the plant chromosomes (step 7). The integrated T-DNA contains genes that encode for the production of plant hormones and genes that encode enzymes for the production of opines, unusual amino acid derivatives, by the plant cells (step 8). The T-DNA–directed production of opines provides a unique carbon and nitrogen food source for the growth of _A. tumefaciens_. The T-DNA–directed production of growth hormones results in uncontrolled cell division and the development of the symptoms typical of _A. tumefaciens_ infection, plant galls.
molecules that are structurally related to AHLs, to regulate specific gene expression in a cell density-dependent manner. However, the majority of gram-positive bacteria utilize small peptides as their primary communication molecules.

16.3.1 γ-Butyrolactones

The first bacterial communication signals discovered in the 1960s were the gamma-butyrolactones (γ-butyrolactones) produced by Streptomyces spp. Streptomyces are actinomycetes or gram-positive soil bacteria that undergo cellular differentiation and are known to produce many secondary metabolites. In fact, many antibiotics in use today are derived from Streptomyces spp. A handful of γ-butyrolactones have been purified from different Streptomyces species. These signaling compounds superficially resemble AHLs, and analogous to AHLs they differ in stereochemistry, the length of their fatty acid side chains, and side branch number. Both γ-butyrolactones and AHLs are biologically active at extremely low concentrations, that is, at the nano- to micromolar level. However, despite the similarity, AHL receptors do not respond to γ-butyrolactones and vice versa, indicating that each sensory system is specific to its own signal type. Recall that most AHLs activate target gene expression by altering the affinity of a transcriptional regulatory protein that binds to a promoter region and recruits RNA polymerase to stimulate gene expression. In contrast, γ-butyrolactones usually act by derepressing gene expression. In other words, they cause a repressor protein to dissociate from the promoter region of the target gene(s), thus allowing gene expression to proceed.

The compound A-factor (2-isocapryloyl-3R-hydroxy-methyl-γ-butyrolactone) made by the soil bacterium Streptomyces griseus was the first γ-butyrolactone identified and is the best known example of this type of cell density-dependent signaling. A-factor stimulates aerial mycelium formation and production of the antibiotic streptomycin by regulating the expression of the transcriptional activator AdpA (Fig. 16.6).

FIGURE 16.4 Quorum sensing control of A. tumefaciens infection. A. tumefaciens needs to maintain the Ti plasmid during the plant infection process. Therefore, the Ti plasmid contains genes (tra genes for transfer) involved in conjugation and transfer of the Ti plasmid back into A. tumefaciens cells that may have lost the plasmid. Conjugation is regulated by the TraR/TraI quorum sensing system, a classic quorum sensing regulatory system in which TraR is stimulated by the AHL C8-HSL signal produced by TraI. Uniquely, the TraR/TraI system is only active in the presence of plant-provided opines. In the absence of opines, a repressor protein, AccR, binds within the opine promoter regions, blocking the expression of the genes required for uptake and catabolism of opines. When opines are present, however, they bind to AccR (step 1), causing it to dissociate from the promoters and allowing expression of the opine uptake and catabolic regions (step 2). The traR promoter region also contains an AccR-binding sequence (step 2). The consequence of this is that TraR is produced only when opines are present. When present, TraR recognizes the A. tumefaciens AHL signal and activates bacterial conjugation (step 3).

16.3.2 Peptide Signaling

Most gram-positive bacteria utilize a variation of a quorum sensing system that incorporates a two-component regulatory system (see Information Box 16.2). This combined regulatory system has been termed a three-component quorum sensing system. This three-component quorum sensing system consists of a cell membrane-localized histidine kinase (HSK) sensor protein and a cytoplasmic response regulator protein (RR). Coupled to this two-component system is an autoinducing peptide (AIP) secreted by the producing cell (Lyon and Novick, 2004).

The ubiquity of this type of signaling is exemplified by the gram-positive foodborne pathogen Staphylococcus aureus. This microbe’s genome contains approximately 17 putative two-component systems (Rasmussen et al., 2000), all of which are believed to be involved in bacteria–bacteria or bacteria–environment signaling! Perhaps the best studied three-component quorum sensing system is the regulation of exotoxin production by S. aureus. These heat-stable exotoxins, including toxic shock syndrome toxin 1 (TSST-1), cause illness in animals and humans (Diggle et al., 2003). As shown in Figure 16.7, S. aureus utilizes a cell density-sensing mechanism to activate virulence gene (exotoxin) expression while simultaneously repressing surface factors to avoid host detection.

A second example of gram-positive cell–cell signaling includes a group of bacteria known as probiotics. Probiotics are intestinal bacteria that exert positive effects on the health of the human or animal host by interfering with the ability of deleterious bacteria to colonize (Guarnier and Schaafsma, 1998). Probiotic bacteria inhibit colonization via the production of extracellular peptides known as bacteriocins (Riley and Wertz, 2002). Lactobacillus salivarius UCC118 is an example of a well-studied probiotic that colonizes the human intestine and produces a broad-spectrum bacteriocin effective against a number of foodborne and medically
16.4 OTHER TYPES OF SIGNALING

16.4.1 Autoinducers-2 and -3

In 1997 a novel type of universal bacterial signal was reported that is quite different from AHL (gram-negative) and peptide (gram-positive) signals (Bassler et al., 1997). This new class of signal, termed Autoinducer-2 (AI-2), is a family of related furanosyl-borate diester molecules that is produced by over 55 gram-positive and gram-negative bacteria (Table 16.1). Scientists have just begun to explore the AI-2 signal. So far, it is known that AI-2 plays a role in signaling in two species, *Salmonella enterica* serovar Typhimurium and *Vibrio harveyi* (see Information Box 16.3) (reviewed in Vendeville et al., 2005). A second potential universal bacterial signal, Autoinducer-3 (AI-3), was reported in 2003 (Sperandio et al., 2003). AI-3 is chemically distinct from AI-2, although its exact structure is not yet known.

16.4.2 Eavesdropping on the Party Line

Although many bacteria have been shown to produce communication signals, many other bacteria that do not
Two-component regulatory systems comprise a sensor protein and a response-regulator (RR) protein. The sensor protein is normally located within the cell’s outer membrane and can detect changes in the external environment surrounding the cell. The sensor protein then communicates these changes to the response-regulator protein inside the cell. The response-regulator protein in turn regulates the expression of key genes to allow an appropriate response to the external stimulus. Communication between the sensor protein and the response-regulator protein is via phosphorylation–dephosphorylation reactions.

AbpT/AbpD

AbpK (HSK)

P

Abp

abp

abpIM

abpK

abpR

abpT

abpD

AbpR-P

AIP

AIP

H9251

H9252

RNA III

AGR

AgrA-P

AgrB

P2

P3

Production and secretion of virulence factors

FIGURE 16.7 Regulation of S. aureus exotoxin synthesis utilizes an autoinducing peptide (AIP) signal. The agr locus encodes four proteins (AgrA, AgrB, AgrC, and AgrD). The AgrD protein is an AIP that is processed and secreted by AgrB, a membrane-associated protease. As the bacterial cell density increases, the AIP concentration accumulates. When AIP reaches a critical level, it binds to the AgrC/AgrA two-component regulatory system. AgrC is a cell membrane-localized histidine sensor kinase (HSK) that, when bound to AIP, transfers a phosphate group to AgrA, a cytoplasmically localized response regulator (RR). Phosphorylated AgrA (AgrA-PO4) activates transcription from a promoter (P3) that expresses a small noncoding regulatory RNA (RNA III). RNA III plays a role in the activation of a number of virulence genes, including those involved in production and secretion of several exoproteins, enterotoxins, exfoliatins, hemolysins, leukocidins, and lipases. Additionally, AgrA-PO4 serves to repress the expression of several bacterial surface proteins. Because cell surface components are often the triggers for host defense responses, the repression of expression of these surface proteins might assist the bacterium in evading recognition by the host.

16.4.3 Bacterial Communication Interference

Communication among bacterial populations appears to be widespread and integral for many essential bacterial processes. For some bacteria, the result of this quorum sensing-controlled expression benefits the health of the microbial community or the host. In pathogenic bacteria, quorum sensing often regulates the production of products detrimental to the community and the host. Therefore, the ability of other members of the community or the host to recognize various communication signals may be advantageous. Additionally, the ability to respond to, or interfere with, this communication may also have important consequences. Several examples of signal interference have been discovered including active degradation of signals in the environment. This interference can alter the expression of traits is appropriate. For example, there is evidence that Pseudomonas aeruginosa listens in on the microbial community to aid the infection process. P. aeruginosa is an opportunistic pathogen and the primary cause of morbidity and mortality in patients suffering from cystic fibrosis, a hereditary life-threatening childhood disease. This ubiquitous gram-negative bacterium primarily colonizes the lungs in cystic fibrosis patients, where it exacerbates mucus formation.
The bioluminescent bacterium *Vibrio harveyi* has a well-characterized AI-2 regulatory system. Similar to *V. fischeri*, *V. harveyi* can colonize a number of marine organisms and also produces light via a bioluminescence operon (lux operon). *V. harveyi* also can exist in high numbers in a free-living state. Fascinatingly, *V. harveyi* has been implicated as the causative agent of milky seas, a phenomenon in which *V. harveyi*-generated bioluminescence can cover areas of the ocean the size of Connecticut. These milky seas have been observed by merchant vessels and are visible from space (see figure on left, from Miller *et al.*, 2005). However, *V. harveyi* regulates light production much differently than *V. fischeri* (Information Box 16.1). *V. harveyi* contains a LuxR regulatory protein required for lux operon activation, but the LuxR protein does not require an AHL signal. Instead, in *V. harveyi*, there is a reversible phosphorylation cascade involving four proteins, LuxP, LuxQ, LuxU, and LuxO. In the absence of AI-2, there is an induction of a signal cascade mechanism from the periplasmic protein LuxP to the cytoplasmic proteins LuxQ, LuxU, and LuxO. Phosphorylated LuxO (LuxO-P), in conjunction with the sigma factor RpoN (σ^54_), results in activation of a small noncoding regulatory RNA (sRNA) that results in the degradation of the luxR mRNA and therefore no luminescence. Alternatively, when sufficient AI-2 is present, it causes the phosphorylation cascade to go from LuxO to LuxQ, resulting in dephosphorylation of LuxO. In this instance, LuxO is inactive and the luxR mRNA transcript is protected, resulting in production of luminescence.

16.4.4 Interkingdom Communication

It was first believed that quorum sensing allowed a population of bacteria to coordinate group-specific behaviors such as colonization, light production, and pathogenicity by controlling gene expression in response to specific signals (intraspecies communication). Next it was shown that unrelated bacteria could cross-talk with each other and that some bacteria eavesdropped on these conversations (interspecies communication). It is now recognized that this signaling communication can occur between bacteria and their eucaryotic hosts, a phenomenon known as interkingdom communication. This interkingdom communication can result in: (1) the ability of bacteria to eavesdrop on the host via host signals (Mathesius *et al.*, 2003); (2) interference of bacterial signaling pathways
via host-produced signals (Teplitzki et al., 2000); or (3) recognition of bacterial signals by the host resulting in altered host gene expression.

### 16.4.5 Host–Bacterial Communication

Communication between plants and bacteria has been studied extensively in the *Rhizobium* spp.–legume symbiotic association (see Information Box 14.1) (reviewed in Brensic and Winans, 2005). Studies have documented the exquisite signal communication that occurs by both the bacteria and plant, resulting in colonization, infection, nodule development, and nitrogen fixation. Communication between the plant pathogen *Agrobacterium tumefaciens* and its hosts also has been studied extensively (Brensic and Winans, 2005). However, both of these plant-associated bacteria interact with their hosts by invading tissues, whereas the majority of plant-associated bacteria remain on the surface of the plant. Work suggests that interkingdom communication between hosts and associated microbes is both widespread and appears to occur bidirectionally.

### 16.5 SUMMARY AND CORE CONCEPTS

Originally bacteria were thought to be single-celled organisms that sensed and responded to environmental inputs individually. However, bacteria are now believed to be able to communicate among themselves both within a single population and between unrelated populations to essentially behave analogously to multicellular organisms. This communication is dependent on a combination of characterized and uncharacterized signals. Communication between microbes and their hosts is known to directly affect the expression of bacterial genes that encode functions critical to all aspects of bacterial survival, bacterial–bacterial, and bacterial–host interactions, including (1) coordination of gene expression within a single population; (2) coordination of gene expression among unrelated populations; (3) avoidance of host defense responses; (4) coordination of virulence gene expression; (5) inhibition of a competitor’s gene expression; and (6) inhibition or stimulation of host colonization.

Besides allowing communication between bacterial populations, quorum sensing signals have been shown to facilitate communication between bacteria and eucaryotic hosts such as fungi, algae, plants, and animals. This signal-dependent communication appears to be a two-way street in that the eucaryotic host can produce quorum sensing signal mimics that directly influence the expression of bacterial genes involved in host–microbe interactions and bacterial quorum sensing signals can also influence eucaryotic host gene expression patterns. These communication networks represent key ecological control points that directly determine the outcome of host–microbe interactions.

Understanding these communication networks may facilitate large-scale improvements in bacterial–host interactions, pathogen suppression, bioremediation, and water and waste treatment.

### QUESTIONS AND PROBLEMS

1. Compare the benefits and limitations of AHL-mediated quorum sensing to peptide-mediated quorum sensing.
2. Design an experiment to determine the effect of bypassing quorum sensing control (i.e., making target gene expression constitutive) on the ability of a human pathogenic bacterium to infect its host.
3. Since higher organisms evolved in the presence of bacteria, it makes inherent sense that these diverse organisms can communicate with each other. What processes can you think of that might require bacterial–host cooperation?
4. We have seen examples of both positive cross-talk and negative cross-talk (signal interference) between bacteria and between bacteria and hosts. Are these forms of cross-talk communitywide, or could selected subpopulations be differentially affected? Can you devise an experiment to test this idea?

### REFERENCES AND RECOMMENDED READINGS


