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Quorum Sensing Systems in Microorganisms and Their Potential Applications

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Abstract: Quorum sensing (QS) is an important communication mechanism between microorganisms and can affect their own metabolic functions. At present, the research on microbial QS mainly focuses on the potential hazards of pathogenicity and drug resistance of pathogens, but the application value of QS in various fields of human production and life is relatively little understood. This article systematically sorts out the QS systems of major microorganisms, introduces their application prospects in environmental protection, food industry, human health and bioengineering, and provides a certain reference for the efficient use of microbial QS.

Keywords: Quorum Sensing; Signaling Molecules; Applications.

1. Introduction

In the past, people believed that intercellular communication only existed between multicellular organisms. However, studies have shown that bacteria can synthesize and release signal molecules related to population density, thereby regulating their own physiological behaviors (Spacapan, Bez, & Venturi, 2023). However, there are also some zebrafish, mouse and human cells whose aromatic hydrocarbon receptors AhR regulate their own immune responses by recognizing QS signal molecules of *Pseudomonas aeruginosa* (Moura-Alves et al., 2019). Currently, the regulation and application of QS systems have become a research hotspot in the fields of medicine, food, and environment.

2. Quorum Sensing

In 1994, Fuqua et al. (Fuqua, Winans, & Greenberg, 1994) first proposed the concept of "quorum sensing" based on the luminescence phenomenon of *Vibrio fischeri*, that is, during the growth process, bacteria will synthesize and release an auto-inducing factor whose concentration increases with the population density. When the concentration of this signal molecule reaches a threshold, it can regulate the expression of its own genes. However, there is an important problem with this theory, that is, the concentration of signal molecules is easily affected by the external environment. For example, in an environment with a low diffusion rate but a high concentration of signal molecules, a single cell may also trigger QS. In response to this problem, Moreno-Gámez et al. (Moreno-Gámez, Hochberg, & van Doorn, 2023) proposed a new theory, that is, bacteria sense the state of the environment in a social interactive way by releasing and sensing signal molecules, thereby regulating gene expression. At present, QS can be divided into the following types according to different microbial species.

2.1. Quorum Sensing in Bacteria

2.1.1. AHLs-mediated Quorum Sensing of Gram-negative Bacteria

The QS system is widely present in Gram-negative bacteria. The LuxI-LuxR system is a typical representative and usually consists of three parts (Chu & Yang, 2024): (1) the autoinducing synthase LuxI, which is responsible for synthesizing the signal molecule N-acylhomoserinelactones (AHLs); (2) the regulatory protein LuxR, which can bind to AHLs and regulate gene expression; (3) AHLs and their analogs, which are small molecules that can diffuse freely outside the cell and accumulate in the surrounding environment. When the concentration of AHLs reaches a threshold, they can enter the cell and bind to LuxR to form a complex, activating the expression of downstream genes. In addition, although some bacteria cannot synthesize AHLs, they can still perceive exogenous signal molecules through the protein SdiA homologous to LuxR and regulate their own QS-related genes (Escobar-Muciño, Arenas-Hernández, & Luna-Guevara, 2022).

2.1.2. AIPs-mediated Quorum Sensing of Gram-positive Bacteria

The QS system of Gram-positive bacteria is mainly composed of the ABC transport system and the signal transduction system. Its signal molecules are autoinducing peptides (AIPs), which are formed by the leader peptide after being modified by specific enzymes. AIPs cannot freely penetrate the cell membrane. They rely on the transport system or membrane channel protein on the membrane to be released outside the cell. When the concentration of AIPs reaches the threshold, they will be specifically recognized by the receptors on the cell membrane, thereby regulating a series of physiological behaviors (Li & Zhao, 2020). At present, the research on the Agr quorum sensing system of *Staphylococcus aureus* is relatively in-depth. This system has been found in many Gram-positive bacteria, but its function and regulatory mechanism vary among different bacteria (Polaske et al., 2023).

2.1.3. AI-2-mediated Quorum Sensing

Unlike AHLs and AIPs, which are highly specific to bacteria, furanone boronate diester (Autoinducer-2, AI-2) is a universal signaling molecule widely present in microorganisms. Therefore, it can serve as a medium for cross-species communication, helping bacteria perceive different types of bacteria in the environment and regulate their own physiological behaviors. In addition, AI-2 also plays an important role in the signal transduction process in an environment where multiple bacteria coexist, and is

closely related to the formation of mixed biofilms and the expression of related genes (Roy, Adams, & Bentley, 2011). Current studies have shown that AI-2 is an intermediate product in the metabolic process of the S-adenosylmethionine cycle, and its synthesis depends on the synergistic action of multiple enzymes (Chu & Yang, 2024).

2.1.4. Bacterial Quorum Sensing Mediated by other Signal Molecules

The AI-3-mediated QS system can be synthesized in some Enterobacteriaceae and can recognize signal molecules such as norepinephrine and epinephrine, thereby regulating the physiological behavior of bacteria. Although the specific structure of AI-3 is not yet fully understood, studies have shown that AI-3 is a small molecule 3,6-DPO derived from the threonine metabolic pathway (Chu & Yang, 2024).

In addition to the above common quorum sensing signal molecules, bacteria can also synthesize and utilize a variety of other types of signal molecules. For example, *Xanthomonas campestris* can produce diffusible signal factors DSFs to regulate group behavior; the diketopiperazine compounds DKPs synthesized by *Xanthomonas* campestris are considered to be the key signal molecules of its QS system (Li & Zhao, 2020).

2.2. Quorum Sensing in Fungi

Since the first discovery of the bacterial-like QS phenomenon in *Histoplasmosis capsulati*, more and more studies have shown that QS plays an important role in regulating the biological behaviors of fungi. At present, the QS system of *Candida albicans* has been studied in depth. This fungus can switch between the yeast state and the hyphae state, and this morphological change is regulated by cell density (Li & Zhao, 2020). Two key QS signaling molecules have been identified in *Candida albicans*: (1) farnesol, which regulates the activity of drug efflux pump proteins; and (2) tyrosol, which promotes the transition from the yeast state to the hyphae state and enhances the ability of hyphae to form hyphae. It is worth noting that the QS system of fungi can not only regulate its own behaviors, but also inhibit the growth of competing microorganisms. For example, farnesol can inhibit the PQS quorum sensing system of *Pseudomonas aeruginosa*, thereby inhibiting its growth (Cugini et al., 2007). This shows that the QS mechanism of fungi can not only maintain its own ecological niche, but also affect the structure of microbial communities through interactions between microorganisms.

2.3. Quorum Sensing in Archaea

Bacteria and archaea coexist extensively in the natural environment and can communicate with fungi and bacteriophages through quorum sensing, which suggests that similar QS systems may also exist in archaea (Thompson, Busetti, & Gilmore, 2023). In recent years, researchers have gradually revealed some evidence of quorum sensing in archaea. For example, a study by Thomas et al. (Thompson et al., 2023) showed that the supernatant of the halophilic archaeon *Halorubrum saccharovorum* CSM52 could induce the expression of multiple AHL-dependent genes in *Pseudomonas aeruginosa*, indicating that cross-domain information exchange may exist between archaea and bacteria. Further analysis found that the signaling molecules contained in the supernatant were chemically modified AHLs or DKPs, which could not only interact with the bacterial QS pathway, but also affect the formation of the archaea's own biofilm.

2.4. Quorum Sensing in Viruses

Viruses also have quorum sensing systems similar to those of bacteria and fungi, and can coordinate or manipulate the QS pathways of host bacteria to regulate their own lysis and lysogenic conversion processes (Maxwell, 2019). This mechanism not only helps the virus survive and spread in the host, but may also affect the dynamic balance of the microbial community. For example, after the bacteriophage *phi3T* infects Bacillus bacteria, it produces a signal peptide AimP, which can bind to the bacteriophage receptor AimR, activate the expression of downstream target genes, and promote host cell lysis. However, when the concentration of AimP accumulates to a threshold, it will inhibit the activity of AimR, prompting the phage to enter the lysogenic cycle (Duddy & Bassler, 2021). Bacteriophage *VP882* carries a homolog of the Vibrio cholerae QS regulatory protein VqmA, which enables *VP882* to interact with the host's QS system and regulate host gene expression (Maxwell, 2019).

At present, research on viral QS is still in its infancy, and further exploration of viruses with QS functions and their effects on host QS regulatory mechanisms is needed in the future.

3. Applications of Quorum Sensing

As an important information exchange mechanism among microorganisms, quorum sensing plays a key role in biogeochemical cycles, species evolution and ecosystem stability, and profoundly affects many fields such as biosynthesis and degradation, food quality and safety, and human health. How to deeply analyze and effectively utilize this mechanism to optimize microbial functions and enhance the value of industrial applications remains an important direction for future research.

3.1. Application of Quorum Sensing in Environmental Protection

In the past few decades, the rapid development of the chemical industry and the intensification of human activities have led to the aggravation of global environmental pollution, which seriously threatens human health. Bacteria have shown great potential in pollution control due to their strong adaptability, genetic diversity and functional characteristics. For example, microbial biofilms in soil play an important role in addressing these challenges. They can use a series of physical and chemical pathways and cellular metabolic processes as a medium for the migration and transformation of these pollutants, fix heavy metals in the soil or degrade organic pollutants (G. L. Wang et al., 2024).

3.2. Application of Quorum Sensing in the Food Industry

The flavor formation of fermented foods is closely related to microbial activity. The microbial population and its abundance change continuously at different fermentation stages, giving fermented foods a unique flavor. Studies have shown that the microorganisms in the production process of various fermented foods are regulated by QS (Johansen & Jespersen, 2017). For example, *Debaryomyces hansenii* can synthesize aromatic alcohols, phenylethanol and tyrosol through the QS system, affecting the flavor of cheese; AI-2 activity has also been detected in *Lactobacillus plantarum* and *Lactobacillus sakei* in fermented meat products (Johansen & Jespersen, 2017). Although the potential value

of QS in the food industry has been confirmed, its specific mechanism of action still needs further study.

3.3. Application of Quorum Sensing in Human Health

There are various microbial communities in various parts of the human body, including both pathogenic bacteria and probiotics. Lactic *acid bacteria*, as important probiotics for the human body, can maintain the balance of intestinal flora, promote digestion and absorption, and enhance immune function. Its physiological activity is regulated by AI-2 quorum sensing (Meng, Zhao, & Lu, 2022). Fengmycin produced by edible probiotic *Bacillus* can bind to the QS receptor AgrC of *Staphylococcus aureus*, blocking the signal transduction of the pathogen and reducing its colonization and infection risk in the intestine (Piewngam et al., 2018). Using QS to regulate the gene expression of *Salmonella* and selectively release therapeutic proteins in tumors can minimize damage to healthy tissues (Liu, Lu, Li, Pang, & Gao, 2025). These studies have shown that QS plays an important role in the survival, function and antagonism of probiotics and pathogens in the human body.

3.4. Application of Quorum Sensing in Bioengineering

Bioengineering has been widely used in many fields due to its unique advantages, and maintaining the vitality of microorganisms is crucial. Viable but non-culture (VBNC) microorganisms are potential biological resources, and their recovery is affected by QS. Wang et al. (Y. H. Wang et al., 2021) used Rpf protein for cell recovery and successfully isolated two rare *Actinomycetes*. In terms of metabolic engineering, Honjo et al. (Honjo et al., 2019) designed a microbial community composed of *Escherichia coli* TA4222 strain and TA4179 strain, and achieved the synergistic conversion of cellobiose to isopropanol. These studies show that influencing the recovery and metabolic optimization of VBNC bacteria through QS can provide broader application prospects for bioengineering and metabolic engineering.

3.5. Application of Quorum Sensing Inhibitors

Nowadays, drug-resistant bacteria are prevalent in people's daily lives. Therefore, quorum sensing inhibitors (QSIs) targeting microbial QS have become a research hotspot and have shown broad application prospects. The following briefly introduces some application scenarios of QSI: (1) Human health: QSIs can be used as an innovative bacterial treatment to protect human health. For example, *Pseudomonas aeruginosa* is a common foodborne pathogen that seriously endangers human health. Benzoic acid as a QSI can significantly inhibit the formation of *Pseudomonas aeruginosa* biofilm and reduce its pathogenicity (Li & Zhao, 2020); (2) Aquaculture: *Vibrio harveyi* is a major marine pathogen that poses a potential threat to aquaculture. The use of furanone compounds can effectively inhibit the QS function of *Vibrio harveyi*, reduce its damage to aquaculture organisms, and increase the yield of aquatic products (Liu et al., 2025); (3) Food preservation: QS regulates various metabolic activities of bacteria and is closely related to food spoilage. For example, *Erwinia carotovora* can cause potatos black spot and soft rot, and pieridin A and glucosyl pieridin can significantly reduce the concentration of AHLs and inhibit the expression of virulence (Liu et al., 2025). In addition to the above QSIs, there are still many potential inhibitors to be explored, providing broader application prospects in the fields of antimicrobial treatment and food safety.

4. Conclusion and Outlook

Quorum sensing is a cell-to-cell communication mechanism widely found in microorganisms, and is involved in a variety of important physiological processes. At present, there has been a relatively in-depth explanation of the inhibition of quorum sensing of pathogens to reduce their harm to human production and life, and a variety of QSIs have been developed to deal with this harm. However, research on QSIs for fungi, viruses, and archaea is still in its infancy.

On the other hand, there is still a lack of systematic understanding of how to effectively use QS to promote the function of beneficial microorganisms and thus realize their application in the fields of food industry and environmental remediation. In-depth exploration in this field will help optimize the development and utilization of microbial resources. In the future, synthetic biology methods can be used to construct engineered strains that can regulate QS to optimize the function of probiotics, improve the quality of fermented foods, or enhance the degradation capacity of microorganisms in environmental pollution control, providing new solutions for the industrial and medical fields.

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