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Evolutionary Analysis of Quorum Sensing Systems among Bacterial Strains

Abeer Mahmood Faraj[1*], Amina thanoon hamid[2*]
[1]M.Sc. Northern Technical University Medical Technical Institute- Mosul \ Department of Pharmacy Technologies.
2 M.ScNinavah university Medicine collage

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ABSTRACT
A basic and extensively conserved bacterial communication mechanism, quorum sensing (QS) allows for precise gene expression coordinating in response to cell population density. The creation, release, accumulation, and detection of particular signaling molecules called autoinducers mediate this control. Once a threshold concentration is achieved, these molecules cause behavioral changes in the entire population. Here, we provide a thorough evolutionary analysis of QS systems in a wide range of bacterial taxa, including archaeal, Gram-positive, and Gram-negative lineages.We clarify the evolutionary origins, diversification paths, and adaptive adaptations that have molded QS networks by an integrated approach that combines comparative genomic research, phylogenetic reconstruction, and functional characterization. With significant heterogeneity in gene content, signaling circuits, and autoinducer usage among strains, the results show that both vertical inheritance and horizontal gene transfer are important factors in the distribution of QS genes. These changes are a result of ecological adaptation to various settings that are impacted by QS-inhibitory chemicals, temperature, pH, nutrition availability, and interspecies interactions.The evolutionary dynamics and structural and functional variety of QS systems are demonstrated by in-depth case studies of Vibrio harveyi, Staphylococcus aureus, and Pseudomonas aeruginosa. Clinical evidence supports QS's potential as a target for next-generation anti-infective treatments by demonstrating that it regulates virulence, biofilm formation, and antibiotic resistance. Furthermore, QS modulation has promising biotechnological uses in microbial engineering, synthetic biology, food safety, and agriculture. All things considered, this work gives an evolutionary framework for comprehending bacterial QS systems and insights into how to use them for both industrial advancements and medicinal interventions.

Keywords: quorum sensing, bacterial communication,, horizontal gene transfer,, pathogenesis, biofilm, antimicrobial targets

I. INTRODUCTION

Quorum sensing (QS) serves as a vital microbial gene regulation mechanism that significantly responds to changes in population density. The process involves the secretion of autoinducer molecules into the surrounding environment, which, as time progresses, accumulate within a local population of bacteria. This accumulation ultimately regulates gene expression in a coordinated and synchronous manner among the bacterial community. When the concentration of these specific signaling molecules reaches a critical threshold limit, a well-organized cellular response is initiated, which plays a crucial role in regulating a variety of phenotypic expressions. An evolutionary analysis focusing on QS systems across a wide variety of bacterial strains delves into how QS genes have been inherited among the diverse lineages over time. This exploration offers invaluable insights into the historical processes that have shaped the current diversity and functionality of QS systems in the complex and dynamic microbial world we observe today. [1][2]

II. BACKGROUND ON QUORUM SENSING

Quorum sensing (QS) is a chemical signaling discovery spanning over 60 years of microbiology research. Multiple systems exist where molecules called autoinducers are synthesized and exported to the external environment in response to environmental changes [2]. Services allow a particular bacterium to regulate gene expression over population-density changes and then alter cell physiology [3].QS systems have been identified in many Gram-positive and -negative bacteria and Archaea. Several types of signals are used in QS. These include acylated homoserine lactones (AHLs), fatty acid methyl esters, 2-alkyl-4-quinolones (AQs), and peptides [4]

QS is a cell–cell communication method that triggers coordinated gene expression among bacteria at a critical density. The process is used by Gram-negative bacteria to monitor the environmental tone through specific signaling molecules. Secreted proteins and products in large quantities are made only when enough bacteria are present, with products such as bioluminescence genes, antibiotics, and other materials. Bacterial growth promotion, virulence factor creation, plasmid transfer, and other activities that can be distributed from one bacterium to another. Gram-negative bacteria produce and use small specific signal molecules known as autoinducers. The signal molecules are released to the medium and can be detected either inside the cell or on the cell surface of a single quorum sensing strain. Gram-positive bacteria create, release, and use short peptides or 'autoinducing peptides' to monitor modifications in culture density. Control over the production of cleavage-liberated or exported peptide signals is maintained by two-component signal transduction systems, often accompanied by an alternative sigma factor.[5].

2.1. Definition and Mechanism

Quorum sensing (QS) is a cell-to-cell communication system that activates various physiological processes in response to bacterial population density [6]. Unique QS genes are widely distributed across bacterial genomes with several distinct QS systems often found in a single bacterial strain. According to the current evolutionary classification, the corresponding cognate QS kinases and regulators form a monophyletic clade but the autoinducer-synthases belong to different evolutionary groups. An evolutionary analysis of QS genes across bacterial strains shows that the QS systems of a given strain are neither distributed in a random manner nor formed by genes with common evolutionary history. Instead, the QS systems of a strain appear to share a common evolutionary background and are acquired through frequent horizontal gene transfer events.

Many bacteria regulate their gene expression by measuring their population density with signal molecules termed autoinducers that accumulate in the growth medium. With sufficient density, autoinducers stimulate the expression of genes affecting a wide range of physiological activities, including luminescence, plasmid transfer, production of antibiotics, toxin secretion, biofilm formation, and sporulation. While the regulatory circuits vary widely, they all share the same two central features: the production of a signal molecule, and the detection of a threshold concentration of that signal to coordinate behaviour. Gram-negative bacteria generally use acylated homoserine lactones as autoinducers,

whereas Gram-positive species utilize processed oligo-peptides, which are recognized by a two-component histidine kinase cascade; species of identified Archaea also use quorum sensing [7].

2.2. Types of Quorum Sensing

Bacteria integrate external information by recognition of signal molecules such as autoinducer 1 (AI-1), autoinducer 2 (AI-2), and hormones, among others, to regulate community-wide gene expression. Filamentous phages infecting scant aerobic bacteria when transportation and transfer of environmental nutrients become challenging. Quorum sensing (QS) is a cell-to-cell communication mechanism that controls bacterial social behavior such as bioluminescence, biofilm formation, sporulation, genetic competence, and the secretion of virulence factors by coordinating actions at the population level [6]. Bacteria can also use multiple QS signals in order to deduce their social (density) and physical (mass-transfer) environment. Bacteria have greatly altered physiology and gene expression at defined cell-population thresholds of signal molecules [4].QS has evolved to control gene expression in bacteria by regulating protein secretion, nutrient acquisition, antibiotic resistance, genetic competence, biofilm development, and virulence at the population level of multiple bacterial species. Study further showed that effective expression of secreted factors occurs only in high-density and low mass-transfer environments with secretome genes in bacteria preferentially controlled by synergistic "AND-gate" responses to multiple signal inputs.

Bacteria produce and detect extracellular signaling molecules called autoinducers (AIs) to coordinate gene expression in response to fluctuations in cell population. The accumulation of AIs and subsequent interaction with intracellular receptors leads to changes in gene transcription in a process called quorum sensing (QS). QS is an integral component of bacterial signaling and behavior that influences competence, virulence, antibiotic production, sporulation, biofilm formation, and motility. Bacteria use QS systems for interspecies and interkingdom communication and carry out social as well as physiological functions. Despite the wide knowledge and

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occurrence of bacterial QS, this form of cell-to-cell communication remains understudied.[8].

2.3. Significance in Bacterial Communication

The evolutionary significance of quorum sensing (QS) systems is highlighted by the phylogenetic analysis of genes encoding QS and associated proteins in various bacterial strains. Relationships among these genes clearly indicate that QS systems such as type I autoinducers and oligopeptides do not share common evolutionary origins. Extensive horizontal transfer of QS genes is observed among closely related bacteria from different species, and interspecies transfer is predicted in certain cases. Such horizontal transfer is likely to influence the evolutionary dynamics of biological signaling networks and represents an important factor in the development of the QS system. Diversity within the QS systems suggests that they are not absolutely essential to bacterial life and that there is considerable strain-to-strain variation in their ability to regulate specific targets [6]. Functionally conserved responses to identical signals may evolve independently in different species and ancestors of Gram-negative and Gram-positive bacteria. ● All of these analyses support the hypothesis that QS systems have spread primarily through transfer among related lineages and have evolved partly through changes in the genes for synthases and sensors, possibly by duplication and divergence

III. QUORUM SENSING SYSTEMS IN BACTERIA

Bacteria communicate using quorum sensing (QS) systems that encompass the production and detection of extracellular signal molecules [6]. Chemical-based quorum sensing systems occur in both gram-negative and gram-positive bacteria; a few occur in archaea. QS often regulates the expression of a wide range of important bacterial functions. For instance, the gram-negative pathogen Pseudomonas aeruginosa responds to cell-population density with a system that consists of a signal generator and a signal receptor. This mechanism involves the production and detection of signal molecules, which accumulate as a function of the local bacterial density. Certain virulence factors are expressed only at sufficiently high cell-population densities in a manner that depends upon these signal molecules. On the other hand, kin groups of the gram-positive pathogen Staphylococcus aureus use QS to regulate the expression of several toxins, enzymes, and molecules that influence the host immune system. Archaea appear to have functional QS systems in place as well. Although the only QS system so far characterized is luxS, there is at least one additional QS mechanism. QS systems nevertheless exhibit significant differences from the canonical proteobacterial QS architectures and appear to have been shaped by a complex evolutionary process linked to the diversification of archaea [3].

3.1. Gram-Positive Bacteria

Gram-positive bacteria typically utilize oligopeptides as their primary autoinducers, which play a critical role in communication between bacterial cells. These oligopeptides operate in conjunction with two components of a sophisticated two-component phosphorelay system that allows for effective signal transduction. The synthesis of these signaling peptides is highly reliant on the growth phase of the bacterial cells, meaning that the capability to produce them varies as the bacteria mature and multiply. Furthermore, the concentration of these extracellular peptides increases in direct proportion to the density of the bacterial population. When this concentration reaches a specific threshold that is crucial for activation, certain histidine-protein kinases undergo autophosphorylation. This autophosphorylation process enables them to act as phosphate donors for response regulators, which then function as transcription factors that regulate gene expression. In the vast majority of gram-positive bacteria, these quorum-sensing autoinducing peptides exhibit a characteristic Arg-Pro motif. Additionally, they contain various post-translational modifications that can include amidation, phosphorylation, cyclization, and the formation of disulfide or thioether bridges, all of which contribute to the stability and functionality of these signaling molecules. [9]

Acanthamoeba castellanii is a species of amoeba distributed worldwide that preys on a variety of microorganism types, including bacteria and fungi. Lawrence et al. reported that A. castellanii secretions can interfere specifically with bacterial gram-negative QS-based signalling and can reduce the production of virulence factors in Pseudomonas aeruginosa. However, it remains unclear whether the secretions of A. castellanii can interfere with the QS of gram-positive bacteria such as Staphylococcus aureus. Staphylococcus aureus exhibits high adaptability and has a wide distribution, ranging from food contamination to medical diseases, as a common pathogenic bacterium. [10]

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3.2. Gram-Negative Bacteria

Different bacterial species employ a wide variety of signaling molecules and communication strategies for quorum sensing (QS). In general terms, Gram-negative bacteria utilize a signal synthase, complemented by a cytoplasmic regulator that becomes active once a critical threshold of the QS signal is attained. Within the realm of Gram-negative bacteria, the QS systems of genera such as Photobacterium, Vibrio, Aeromonas, and Enterobacteriaceae are comparatively well documented and are primarily based on acylated homoserine lactones (HSLs) that serve as their signal molecules. In several instances, one can observe multiple LuxI-LuxR-type pairs existing within the same organism, underscoring the complex nature of these systems. Importantly, QS does not always show a direct correlation with bioluminescence, as evidenced by the diverse array of QS genes found in the genus Aliivibrio. In stark contrast, the QS systems seen in Pseudomonas species display significant differences from those of the other Gram-negative species mentioned previously; specifically, they depend on a LasR/LasI pair along with a second regulatory system, RhlR/RhlI, that further enriches their signaling capabilities. Furthermore, the QS systems present in the genera Rhizobium, Sinorhizobium, and Mesorhizobium also feature multiple LuxR as well as LuxI genes. This complexity equips these organisms with highly adaptable regulatory circuits capable of integrating and responding to various environmental signals, thereby enhancing their environmental interactions and survival strategies. [11]

3.3. Archaea and Quorum Sensing

Quorum-sensing communication in Archaea relies on signaling molecules that remain largely unidentified, as investigations have yet to yield conclusive results. Early attempts to detect acyl-homoserine lactones—common Gram-negative autoinducers—in species such as Methanothrixsoehngenii and Methanothrixharundinacea were unsuccessful [3]. Similarly, efforts to identify gamma-butyrolactones, used in Streptomyces signaling, in halophilic Archaea failed to isolate these compounds in either pure or mixed cultures of Haloarcula or Halobacterium species. Signals known to operate at elevated salt concentrations remain unknown, suggesting Archaea may employ distinct molecules for cell–cell communication [2].Nevertheless, some Archaea, including Methanosaetaharundinacea, Thermococcus coalescens, Sulfolobussolfataricus, and Halobacterium salinarum, appear to possess communication systems, as indicated by genomic data; their genomes contain genes putatively involved in quorum sensing and several predicted gene clusters resembling the DedA family, known for participation in cell-to-cell signaling.

IV. EVOLUTIONARY PERSPECTIVES

A comparative examination of the major quorum-sensing gene systems illustrates the evolutionary dynamics among bacterial strains that display diverse phenotypes and genetic characteristics. Investigations into the phylogenetic relationships of autoinducer and autoinducer-receptor genes reveal occasional horizontal gene transfer events that contribute to the emergence of novel quorum-sensing systems [3]An evolutionary model accounting for these relationships is proposed, and analyses of selective pressure suggest that the diversification of quorum-sensing systems is driven by adaptive processes [6].

4.1. Phylogenetic Analysis

Phylogenetic analysis reveals that most QS species form coherent clades at the species and family levels. MeZmbers of the same genus typically cluster together, consistent with the Vertical Inheritance Hypothesis, which posits that genes within a particular group have a common evolutionary origin. However, some AHL genes branch outside their expected taxonomy; for instance, strains of Serratia, Pantoea, Enterobacter, Klebsiella, and Erwinia—despite belonging to the Enterobacteriaceae family—appear across different clades. Similarly, Burkholderia, from the Burkholderiaceae family, is found in three separate clades. Evidence of horizontal gene transfer (HGT) is observed, particularly among AHL genes within the LuxI–LuxR system. To assess this, the consistency index (CI) and retention index (RI) of AHL QS genes were compared to those of housekeeping genes from the same strains. The AHL QS genes generally yield smaller CI values but larger RI values, Despite variations among related QS systems in different strains, they all function as communication systems within coexisting bacterial populations, underscoring their adaptive significance and the conservation of key regulatory mechanisms. ([11]

4.2. Horizontal Gene Transfer

Quorum sensing (QS) systems appear to have been spread among several bacterial strains by horizontal gene transfer (HGT) processes. For example, LuxI/R type genes have been detected in virulence plasmids of Pseudomonas savastanoipv.

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savastanoi NCPPB 3335 and in the Ti plasmid of Agrobacterium tumefaciens strain C58. It is also evident in a strain of Roseobacter sp. CIM8-4 isolated from a coral sponge, supporting the expected occurrence of HGT during co-habitation of these strains. Further, it has been suggested that genes responsible for the synthesis of N-acyl-homoserine lactone (AHL) molecules were acquired through HGT in Pseudomonas aeruginosa. The spectral tuning of N-acyl-homoserine lactone synthases in gram-negative bacteria may have been shaped through adaptive evolution. In P. aeruginosa, the production of virulence factors is regulated by QS signals transmitted through the interaction of two-component systems. This TCS pathway is inferred to have evolved through HGT during its long history. [12]

In the case of Vibrio harveyi, there is an intricate QS system consisting of multiple receptors for different autoinducers; LuxN is an example that is sensitive to AI-1 (HAI-1). LuxN appears to be derived from HGT of the luxQ and cqsS genes. Clearly, the entire QS system has a massive history of HGT, cooperative interactions, and selection practices that have shaped its present role in maintaining a very high level of complexity.[13]

4.3. Adaptive Evolution of Quorum Sensing

Quorum sensing (QS) is a fascinating phenomenon that describes the remarkable ability of bacterial populations to communicate effectively through the release and subsequent detection of specific signal molecules that are known as autoinducers. As the abundance of these autoinducers increases within the environment, they bind to specific receptors on the bacterial cells, ultimately leading to the activation of gene expression in a highly coordinated manner that is dependent on the density of the cell population. Two main classes of active signals emerge from these interactions: the N-acyl-homoserine lactones typically found in Gram-negative bacteria, and the processed oligopeptides which are characteristic of Gram-positive bacteria. The evolutionary dynamics involving genetic mixing and clonal exploitation create a scenario in which distinct signal-response strategies are selected. [14]

Clonal populations, which arise from the same ancestral cell, are capable of accurately tuning both their signal and response thresholds. This fine-tuning allows them to adapt their behavior in accordance with local population density, ensuring that cooperative behaviors are only initiated when the population reaches a sufficient threshold known as a quorum. On the other hand, genetic mixing tends to favor strategies that are more coercive in nature; these strategies are marked by an increased level of signal production and generally higher response thresholds. Such traits compel greater cooperation among the bacteria, especially when they are mixed with strains that are more responsive to the signals. Despite this complex interplay, these coercive strategies remain adaptive in the context of clonal populations, allowing them to thrive even under variable conditions. [3]

5.Comparative Overview of Quorum Sensing Systems and Regulatory Genes in Bacterial Species

Table(1) of Quorum Sensing Genes in Selected & Additional Bacteria

Bacterium	Signal Type \ System	Key Genes / Elements	Notes	Citation (Author, Year)
Vibrio fischeri	AHL (LuxI/LuxR); AHL (AinS/AinR)	luxI, luxR; ainS, ainR	Bioluminescence QS model—Lux is main, Ain upstream.	[15]
Pseudomonas aeruginosa.	AHL (LasI/LasR, RhlI/RhlR); HAQs/PQS	lasI, lasR; rhlI, rhlR; pqsA-E, pqsH, pqsR, pqsE	Multi-tiered hierarchy; PQS coordinates secondary metabolites	[16]
Vibrio cholerae	CAI-1 (CqsA/CqsS); AI-2 (LuxS/LuxPQ)	cqsA, cqsS; luxS, luxP, luxQ	CAI-1 dominates; QS affects biofilm formation/dissociation.	[17]
Vibrio harveyi	AI-1; AI-2; CAI-1-like	luxM, luxN; luxS, luxPQcqsA, cqsS	Three parallel pathways converging on LuxO	[18]

Staphylococcus aureus	AIP/Agr (agrBDCA); RNAIII	agrB, agrD, agrC, agrA; RNAIII	Controls virulence factors; multiple agr types	[19]
Staphylococcus epidermidis.	AIP/Agr (agrBDCA)	agrB, agrD, agrC, agrA	Regulates biofilm maturation and immune evasion in device-related infections	[20]
Bacillus subtilis	ComQXPA + Rap/Phr	comQ, comX, comP, comA; rapA–H, phrA–H	Regulates competence, surfactin production, cellular differentiation.	[21]
Streptococcus pneumoniae	CSP/ComCDESigX	comC, comD, comE; sigX	Mediates genetic competence	[22]
Streptococcus mutans	CSP/ComDE; ComRS; SigX	comC, comD, comE; comS, comR; sigX	ComRS directly regulates sigX	[23]
Klebsiella pneumoniae	AI-2 (LuxS); QseBC	luxS; qseB, qseC	Affects capsule synthesis, iron acquisition, and virulence gene regulation	[24]
Enterococcus faecalis	GBAP/fsr	fsrA, fsrB, fsrC, fsrD	Controls gelatinase; therapeutic target	[25]
Enteropathogenic E. coli (EPEC) / EHEC	AI-3/epinephrine/ norepinephrine (QseC/QseB)	qseC, qseB	Regulates attaching–effacing lesions and motility.	[26]
Burkholderiacenocepacia	AHL (CepIR, CciIR)	cepI, cepR; cciI, cciR	Two interacting systems	[27]
Agrobacterium tumefaciens	AHL (TraI/TraR)	traI, traR	Controls Ti plasmid transfer	[28]
Sinorhizobiummeliloti	AHL (SinI/SinR/ExpR)	sinI, sinR, expr	Regulates EPS II, motility, and alfalfa symbiosis	[29]
Helicobacter pylori	AI-2 (LuxS)	LuxS	Influences motility, colonization, and biofilm-like microcolonies in gastric mucosa.	[30]
Acinetobacter baumannii	AHL (AbaI/AbaR; + AbaM)	abaI, abaR, abaM	Motility, biofilm, virulence	[31]
Clostridium perfringens	Agr-like + AI-2 (LuxS)	agrB, agrD; luxS	Agr-like QS controls toxin production and gas gangrene pathogenicity.	[32]

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Haemophilus influenzae	AI-2 (LuxS)	LuxS	Controls biofilm density and competence; linked to chronic infections like otitis media	[33]
Neisseria meningitidis	AI-2 (LuxS)	LuxS	Influences biofilm formation, competence, and immune system evasion.	[34]
Salmonella enterica	AI-2 (LuxS); AI-3/QseBC	luxS; qseB, qseC	Modulates virulence, motility, stress response in host gut environment	[35]

The table(1) show presents a comparative analysis of quorum sensing (QS) genes among several bacterial species, emphasizing the diversity of signaling molecules, regulatory mechanisms, and their biological significance.

1. Diversity of signaling molecules:

The information shows that bacteria use a broad range of QS signals. AHLs (N-acyl homoserine lactones) are mostly used by gram-negative bacteria, such as Vibrio, Pseudomonas, and Agrobacterium. Conversely, gram-positive bacteria, such Staphylococcus and Enterococcus, mostly depend on AIPs (autoinducing peptides). Vibrio cholerae, Salmonella, Haemophilus, and Neisseria are among the genera that exhibit the AI-2 signal as a more "universal" communication molecule. It is noteworthy that certain intestinal infections, like Salmonella and E. coli, have developed the capacity to react to host-derived chemicals like norepinephrine and adrenaline, demonstrating cross-kingdom signaling.

2. Levels of regulation and complexity:

QS systems range in complexity from simple to quite complicated. For example, Pseudomonas aeruginosa has a multi-layered hierarchy (Las, Rhl, and PQS) that coordinates virulence and secondary metabolite production, whereas Vibrio fischeri has a comparatively simple LuxI/LuxR system. Three parallel routes that converge on LuxO, a key regulator, are integrated by Vibrio harveyi. This implies that ecological adaptability and pathogenic potential are frequently correlated with the complexity of QS networks.

3. Functions in pathogenicity and survival:

The table emphasizes how important QS is in controlling disease virulence. QS directly regulates the generation of toxins in Clostridium perfringens and Staphylococcus aureus. QS controls biofilm formation in Acinetobacter baumannii and Klebsiella pneumoniae, increasing resistance to antimicrobial agents and immunological responses. QS is used by Helicobacter pylori and Neisseria meningitidis to create colonies that resemble biofilms and circumvent host defenses. On the other hand, QS promotes symbiosis with plants in non-pathogenic species like Sinorhizobiummeliloti, demonstrating that QS is not just virulent but also promotes advantageous interactions and environmental adaption.

4. Implications for genetics and therapy:

A number of genes linked to QS, including luxS, qseBC, and comDE, seem to be species-specific, which makes them attractive targets for anti-QS treatments. It might be feasible to reduce virulence and biofilm formation by blocking these pathways without applying the same selective pressure for resistance as conventional antibiotics. The potential of quorum quenching techniques as innovative antibacterial treatments is thus highlighted in the table.

V. TRANSMISSION OF GENES GOVERNING QS

5.1 Transmission Vertically

The term "vertical transmission" describes how genes are passed down from parent cells to daughter cells during regular cell division.

Through this mechanism, a species' QS systems are guaranteed to remain stable and conserved across many generations.

Among the examples are:
In Vibrio fischeri, luxI/luxR
In Staphylococcus aureus, agrBDCA,
Streptococcus comDE.

5.2 Horizontal Transfer of QS Genes

Since these genes are crucial to the organism's ecological success, they are frequently maintained.

Despite great evolutionary gaps, AHL-based systems are extensively found in Gram-negative bacteria, indicating widespread horizontal gene transfer.

Burkholderiacenocepacia'sCepIR/CciIR system exhibits similarities to Pseudomonas QS systems, suggesting gene exchange.

The luxS gene, which produces AI-2, is found in several unrelated genera, including Vibrio, Helicobacter, Salmonella, and Haemophilus. It is believed that this wide distribution is caused by both vertical inheritance and recurrent horizontal transfers.

VI. IMPACT OF ENVIRONMENTAL FACTORS

The environmental context greatly influences the evolutionary dynamics of quorum sensing (QS) systems across bacterial strains. The capacity to produce, detect, and respond to QS signals is tightly connected to immediate surroundings, which in turn impose selective pressures shaping the behavior of natural isolates. One critical factor lies in the availability of limiting nutrients. Bacteria often link QS to the production of metabolically expensive factors that maximize growth only when certain chemicals become scarce. For example, Pseudomonas aeruginosa integrates iron limitation with QS control of siderophore production [3].Temperature and pH also modulate QS evolution by affecting the stability of AHL-type signals and the efficacy of molecules designed to interfere with QS behavior

The physical structure of bacterial communities further contributes to the surrounding milieu for QS evolution. Bacteria most commonly reside within spatially-structured groups such as biofilms or flocs that tend to accumulate multiple species from the ambient environment. Many strains have an enhanced capacity to generate sufficient extracellular concentrations of QS signals only within dense, mixed groups. Conversely, some isolates such as Vibrio harveyi require high cell density while growing in free-floating groups—a condition believed to generate the Milky Sea phenomenon in the ocean. Clearance and perception of signals necessarily differs between structured and unstructured populations, while diffusion across boundaries depends on ecific chemical properties [36]

A final overarching influence arises from the presence of other species within mixed communities. Members often detect heterologous signals that perturb group behavior, leading to complex networks of mutual exploitation and signaling interference. Antibiotics and secondary metabolites found in the ambient environment can prevent signal transmission or influencemolecular features, providing fertile ground for evolutionary innovation. Numerous environmental variables engage the balancing act between the cost of producing QS signals and the benefit of enhanced cooperation. Understanding how natural selection shapes behavioral variation in light of such factors represents a continuing challenge in isolating definitive principles guiding QS functionality. [37]

6.1. Nutrient Availability

Rising bacterial populations encountered in pooled culture (indicating inhibited growth and signaling interference). Failure of charidialide to inhibit Arthrobacter QS suggests selective targeting. Alternative mechanisms, possibly nutrient limitation, might regulate QS. Disputing the previous model, evidence favors a hypothesis where coalitions secrete factors limiting nutrient availability to isolate and dominate resources[2].

6.2. Temperature and pH

Environmental conditions such as temperature and pH directly influence the evolution of quorum sensing (QS) systems. In the case of Streptococcus pyogenes, a two-pronged sensory mechanism was identified whereby a bacterial quorum-sensing regulator responds to both environmental pH and population density to modulate virulence-factor production. During invasive soft-tissue infections, the specific induction of genes involved in virulence and tissue destruction correlates with a combination of extracellular acidification and signaling-peptide accumulation[38].. The pro-peptide precursor is secreted and processed to produce an active heptapeptide pheromone (SIP) that binds and activates the Rgg2 regulator, thereby upregulating virulence-related gene expression. Subsequently, SIP-dependent upregulation of the speB gene results in secretion of the SpeBZ zymogen. The acidified extracellular environment promotes rapid maturation of SpeBZ to the active SpeBM protease form, facilitating disease progression by cleaving various host and bacterial proteins. This integrated QS circuitry endows the bacterium with the ability to synchronously regulate protease production in response to both population density and pH. The convergence of environmental pH and peptide-signaling cues offers insights into bacterial signaling and suggests potential pH-based therapeutic interventions. [39].

6.3. Presence of Inhibitors

Quorum sensing (QS) is the process by which microbial cells sense and respond to the presence of other microbial cells through gene regulation, mainly via autoinducers (AIs). Bacteria use QS to regulate processes such as biofilm formation, virulence, motility, antibiotic production, and sporulation. In vibrios, three QS systems are known, involving different autoinducers: AHL (e.g., HAI-1), AI-2, and CAI-1, which regulate physiological functions like biofilm formation, swarming, and bioluminescence. Disruption of QS can reduce virulence in bacteria such as V. cholerae and V. parahaemolyticus, or quench bioluminescence in V. harveyi, indicating QS inhibition[40].

Cross-species QS interactions are generally synergistic among Vibrio species, affecting biofilm formation, pathogenicity, and resuscitation from non-culturable states. However, no prior reports have described QS inhibition among Vibrio species; describe for the first time a quorum-sensing-associated inhibition upon contact with another Vibrio species. The widespread use of antibiotics has led to bacterial resistance, biofilm formation, and drug efflux mechanisms. Because QS is involved in virulence and drug tolerance, it is a target for antibacterial agents, and various QS inhibitors have been identified, showing promise in infection models [41].

Bacteria communicate through diffusible chemical compounds, a process known as sociomicrobiology. They use autoinducers such as acyl-homoserine lactone (AHL) in Gram-negative bacteria, oligopeptides in Gram-positive bacteria, and autoinducer-2 (AI-2) for interspecies communication. AI-2 signals are considered non-species specific, mediating communication among many bacterial species, though their structures remain largely unknown.

VII. CLINICAL IMPLICATIONS

Many bacteria use quorum sensing to coordinate population density-dependent behaviors, including virulence and pathogenesis [6]. Quorum sensing enables communication both within and across species and cellular domains and regulates cooperative and competitive social behavior that affects the structure and function of mixed microbial communities. The significant roles of quorum sensing in bacterial survival and infection indicate that the development of the next-generation antibiotics targeting quorum sensing systems remains a viable, innovative therapeutic strategy.

7.1. Quorum Sensing in Pathogenesis

Quorum sensing (QS) facilitates coordinated bacterial responses, enabling regulation of processes such as swarming motility, competence, biofilm formation, conjugation, antibiotic production, symbiosis, and virulence factor secretion [6].QS is also essential in regulating the formation and dispersal of bacterial biofilms. Because the acquisition and maintenance of QS systems require tight selective pressures, the investigation of the evolution of these signaling networks and comparison of the QS regulon across related species and strains should provide additional insight into the complex functionalities regulated by QS

QS plays a pivotal role in bacterial pathogenesis. The formation of biofilms is involved in more than 65% of all bacterial infections and is highly correlated with the failure of antibiotic treatment of these infections. The regulation of pathogenic factors through QS has been reported for several human, animal, and plant pathogens belonging to genera such as Pseudomonas, Vibrio, Ralstonia, Erwinia, Enterobacter, Staphylococcus, Salmonella, and Burkholderia. Examples of species with established QS-dependent pathogenesis include Pseudomonas aeruginosa, Vibrio anguillarum, and Vibrio vulnificus. [42]

The identification of compounds capable of targeting bacterial virulence as a therapeutic alternative has resulted in a growing interest in the development of compounds interfering with the QS signaling cascades. This strategy is considered less susceptible to driving the evolution of resistance mechanisms that limit the utility of classical antibiotics and provides an approach to address the increasing challenge of antibiotic resistance. [43]

7.2. Targeting Quorum Sensing for Antibiotic Development

Bacterial pathogens govern virulence through a diverse range of mechanisms. Among the top candidates for next-generation antibiotics is interference with the bacterial cell-to-cell signaling process known as quorum sensing. Quorum sensing is a bacterial communication system involved in virulence and drug tolerance; since its discovery in marine bacteria forty years ago, systems have been identified in numerous organisms and are now considered promising targets. Various natural and synthetic inhibitors have been isolated that display antibacterial efficacy in infection models [41].

Bacteria communicate via diffusible chemical compounds known as autoinducers. Three classes of molecules have been described: acyl-homoserine lactone in Gram-negative bacteria, oligopeptides in Gram-positive bacteria, and autoinducer-2 (AI-2), which mediates interspecies communication. Antibiotic resistance has become a serious global health threat, and researchers are pursuing strategies that target bacterial virulence factors as alternatives to conventional antibacterial drugs. Quorum sensing represents a particularly attractive target, because several bacterial virulence factors are controlled by this mechanism [44].

VIII. FUTURE DIRECTIONS

Recent advances in sequencing techniques and synthetic biology are expected to facilitate in vitro studies on microbial systems [6]. The evolutionary investigation of conserved QS genes in phylogenetically diverse bacteria will enhance understanding of the early development of intercellular communication. Beyond the natural applications of the QS process, the innovative business of QS-based biotechnology may provide additional insight into important future directions[3].

8.1. Emerging Technologies in Research

Quorum sensing (QS) is one of the most important bacterial communication systems and has been extensively studied primarily in murine and clinical isolates. However, only a small proportion of naturally isolated strains have been included in previous research. To detect evolutionary dynamics in QS, it is necessary to isolate new strains and screen for QS activities. Various molecular reporters can be used to identify QS signals, and 16S rDNA sequencing can determine the genotype of these strains.[45]

QS, or cell-density-dependent gene regulation, appears in almost all bacterial populations. It relies on chemicals known as autoinducers—oligopeptides in Gram-positive bacteria, acyl-homoserine lactones in Gram-negative bacteria, resultant oligopeptides, and carbon dioxide in archaei. Some bacteria, such as Vibrio harveyi, employ both oligopeptides and a derivative of vitamin B6 as autoinducers. In most cases, the sequence of regulating factors depends on the bacterial origin. Because QS relies on the communication of bacteria within a population, different environmental factors, such as nutrient levels, temperature, pH, inhibitors, and antibacterial agents, affect bacteria and exert selective pressure on QS evolution. The emergence of new strains, illustrated here using Pseudomonas aeruginosa, Staphylococcus aureus, and Vibrio harveyi, has also influenced the evolution of QS systems. [10]

8.2. Potential Applications in Biotechnology

Evolving QS systems offer promising biotechnological prospects in food, agriculture, and nanomedicine. Modulating AHL production by engineering LuxI synthases currently represents the principal method for deploying QS-regulated processes [46]. No alternative enzymatic routes for controlling AHL generation exist yet, despite the variety of AHL signals. Strategies targeting AHL activity can be broadly classified into inhibitors (i.e., molecules affecting QS-regulated molecular functions) and quorum-quenching agents (enzymes driving the hydrolysis or cleavage of QS signal molecules). Quorum-quenching mechanisms operating on AHL molecules occur naturally and influence bacterial QS[3]. Ensuring robust synthesis of chosen signals throughout application periods remains challenging. Inverting typical QS processes to achieve decreased yields at high cell densities might be beneficial in certain contexts. To date, applications under development do not separate QS synthesis from regulation. combined these aspects by overexpressing LuxI AHL synthase and introducing mammalian miRNAs targeting the transcriptional activator LuxR, demonstrating significant reduction in antimicrobial peptide production, as illustrated in the case of recombinant Lactococcus lactis.

IX. CONCLUSION

This study presents an evolutionary analysis of quorum sensing (QS) systems among various bacterial strains. By examining the evolutionary trajectories and variations of QS genes across numerous strains, the research offers insights into the evolutionary dynamics and inter-strain differences shaping bacterial QS mechanisms.

This analysis explores the evolutionary pathways, underlying mechanisms, and inter-strain variations of QS systems in an extensive

e collection of diverse bacterial strains. By clarifying the evolutionary dynamics of QS genes, it provides a foundation for understanding the origins and diversification of bacterial QS processes.

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