STM JOURNALS

Research & Reviews: A Journal of
Microbiology & Virology

https://journals.stmjournals.com/rrjomv/

ISSN: 2230-9853 (Online)
ISSN: 2349-4360 (Print)
Volume 14, Issue 3, 2024
September–December
DOI (Journal): 10.37591/RRJoMV

Review RRJoMV

Whispers of the Microbial World: Unveiling Bacterial Dialogues Through Quorum Sensing

Arnab Chattopadhyay[1], Arpan Das[1,*]

Abstract

Quorum sensing is a special way of bacteria by which they can regulate their own gene expression as per the population density of the bacteria. It is basically a type of cell-to-cell communication pathway used by the microbes. The signal molecule which helps in this mechanism are called auto inducer (AI). As the mechanism depends by changes in the cell density, so when the cell density reaches to the threshold cell density then the inducer molecule becomes activate to the corresponding gene regulation like biofilm formation, gene transfer, virulence, and competence formation etc. Vibrio fischeri is the marine bacteria in which the mechanism first discovered. In general, both types of bacteria like gram positive and gram negative show the quorum sensing, but they use different auto inducer like in case of gram-positive bacteria they use oligo peptides and to the opposite gram-negative bacteria they use acylated homoserine lactones as auto inducer in this case. This process depends upon the number of bacteria present in the environment. If the bacteria present individually in the environment, the process will be less beneficial as compared to the bacteria present in cluster form. Apart from this, now-a-days, Quorum sensing is considered as a unique source of novel target for antimicrobial therapy to the drug resistance mechanism as it may be multi or all drug resistance infection. Here the gram-negative bacteria are called Pseudomonus aeruginosa, a best example for studying the effect of virulence in quorum sensing.

Keywords: Quorum sensing (qs), gram-positive and gram-negative bacteria, auto inducer (ai), cell signaling, ohhl, *vibrio fisheri, p aeruginosa,* biofilm, anti-drug resistance

INTRODUCTION

Quorum sensing (QS) is basically a communication process among bacterial cells that involve the detection, production, and response to the extracellular signaling molecules which are known as auto inducers (AIs). AIs start accumulating in the environment with the increase in the bacterial population density, and the bacteria surveys this information to track alterations in their cell numbers and collectively alter their gene expression accordingly [1, 2]. QS controls genes that direct activities which are beneficial when performed by colonies of bacteria acting in harmony, i.e., in a synchronous way. Processes controlled by QS include sporulation, bioluminescence, competence, biofilm formation, antibody production, and virulence factor secretion [3–5].

***Author for Correspondence**
Arpan Das
E-mail: arpan432001@gmail.com

[1]Student, Department of Biotechnology, Haldia Institute of Technology, Haldia, West Bengal, India

Received Date: July 20, 2024
Accepted Date: August 06, 2024
Published Date: August 27, 2024

Citation: Arnab Chattopadhyay, Arpan Das Whispers of the Microbial World: Unveiling Bacterial Dialogues Through Quorum Sensing: A Journal of Microbiology & Virology. 2024; 14(3): 1–8p.

Regardless of the contrasting molecular mechanisms and regulatory components, all known QS systems in bacteria depends mainly on three basic principles. First, the members of the same populace produce autoinducers, which are the signaling molecules. At low cell density (LCD), AIs disperse, and, henceforth, are located at concentrations below the threshold required for their detection. On the contrary at high cell density (HCD), the accumulative production also induces a local high concentration, implementing activities, such as detection and response [6]. In the second

one, AIs are detected by using receptors that exist in the cytoplasm or in the membrane. Lastly, in addition to the activating gene expression which is necessary for cooperative behaviors, the detection of AIs on the other hand results in the activation of AI production [9–18]. In this way, the feed-forward auto-induction loop seemingly promotes concurrency or synchrony in their population. Flow diagram of Quorum Sensing in bacteria has been depicted in Figure 1.

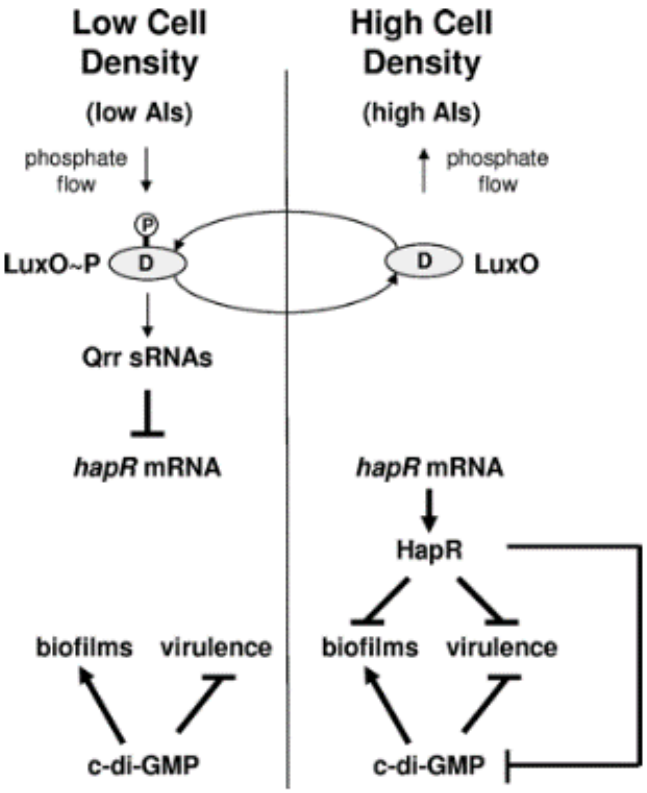

Figure 1. Overview of quorum sensing in bacteria.

QUORUM SENSING IN GRAM POSITIVE BACTERIA

There are mainly two pathways are seen for quorum sensing in gram-positive bacteria. In first case the auto-inducing peptides (AIP) are synthesized from ribosome as pro peptides and then modified post translation occurs. The AIPs are secreted from the presenting ABC transporter and then it undergoes to cleavage through the protease secreted so that it will be getting matured into the AIPs. When the concentration of the AIPs is reaching to a maximum point then the cell surface receptor kinase recognises the AIPs at the same time kinase activates through phosphorylation on the present conserved his residue. Then a downstream intracellular regulatory receptor is activated by kinase and transfers to the phosphoryl group to an Asp residue. After getting activation of the intracellular regulatory receptor goes for transcription of the specific genes. This above-mentioned pathway contains two key elements, one is His kinase, present in the membrane and another one is intracellular regulatory receptor, this pathway is known as two component pathways [7]. *Lactococcus lactis* and *Streptococcus pneumoniae* are the two organisms where the above-mentioned pathways were observed first [8]. Figure 2 depicts the mechanism of QS in gram positive bacteria.

QUORUM SENSING IN GRAM NEGATIVE BACTERIA

As the gram-positive bacteria and the gram-negative bacteria both perform the quorum sensing mechanism, specifically mentioned *Pseudomonus aeruginosa* a common example of gram-negative bacteria which shows this mechanism effectively. It is found in soil and water. The main reason to use these specific bacteria as a part of experiment is that it produces one kind of virulence factor which mainly contains exoproteases, lipases, exotoxins and siderophores. Many of the mentioned factors

regulate the quorum sensing in the mentioned bacteria. But the interesting thing is that the bacteria does not secret the factor always. It secrets it when the critical amount of population present there. In the genetic studies on *P. aeruginosa* say that there are two factors present which also regulate this system, one is LasR-I and RhlR-I where they have linked R and I genes. They are a part of quorum sensing system. Among the two factors the LasR is a transcription regulator, and it responds to the LasI-generated signal. On the other side Rhlr also a transcription regulator and it responds to the RhLl-generated signal. Depending on the density of population LasI secrets different factors. Like when there is a low density it secrets 3OC12-HSL, at the same time if there is a high density of population it secrets 3OC12-HSL in such a critical concentration so that it can be able to interacts with LasR [9]. Figure 3 depicts the mechanism of QS in gram-negative bacteria and Figure 4 depicts Quorum sensing circuit in *P. aeruginosa*.

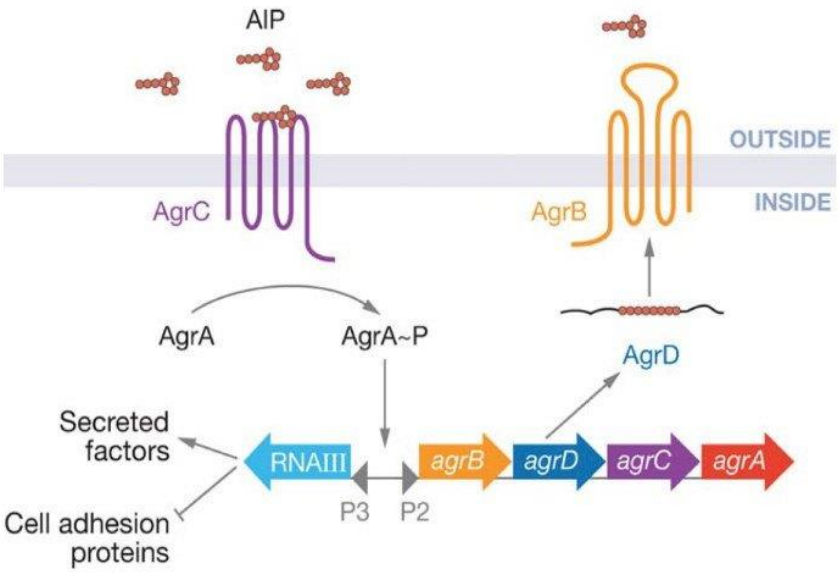

Figure 2. QS in gram positive bacteria [14].

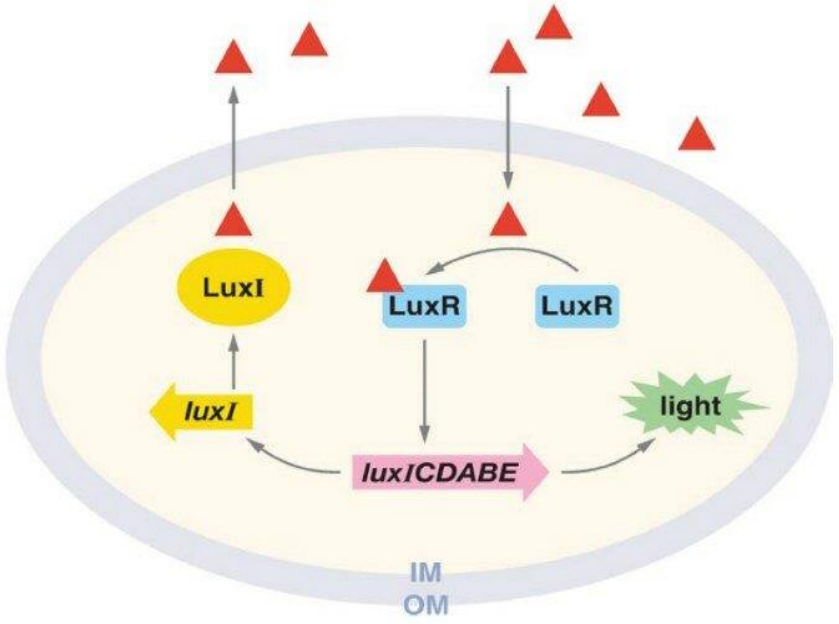

Figure 3. QS in gram-negative bacteria [16].

QUORUM SENSING IN *VIBRIO SPECIES*

Now-a-days, to study the mechanism of quorum sensing few specific species of the bacteria are cultivated in-vitro condition to observe the regulation and other properties of quorum sensing. So, *Vibrio sp* are one of them. The genus vibrio, mostly found in the marine. They are rod shaped in nature and all are gram-negative bacteria. It causes epizootic bacterial disease in marine organisms [20]. Mostly, Vibrio sp is "*Vibrio harveyi", Vibrio fischeri*. It is mostly used in in-vitro condition. The vibrio and luminescent are very much important for aquaculture and can affect all most all types of animals. They have a high frequency of ability to antibiotic resistance [21]. Acyl-homoserine lactone (AHL) are the main component for the occurrence of bioluminescence in *Vibrio sp*. The most interesting thing is that the *Vibrio sp* causes infectious disease in marine animals. For example, luminescent vibriosis in lobsters and shrimp is caused by *Vibrio harveyi, Vibrio crassostreae* causes infection in oysters. Apart from that many sp named *V. anguillarum* and *V. alginolyticus* infect several marine animals [22]. The genus contains membrane bound autoinducer receptor. That helps to find them. Apart from that Lux-R homologs acts as master regulator. Depending on the density of the environment the autoinducer secrets in nature and bind to the receptor along with it the phosphor-transfer protein Lux-U does the phosphorylate from kinase [23]. Then the regulator Lux-O gets response by transferring phosphate from Lux-U and activates the transcription of sRNAs [23]. Lux-R and AphA are the two master transcription factors, from whereby the translation processes the desired protein structure is produce [24].

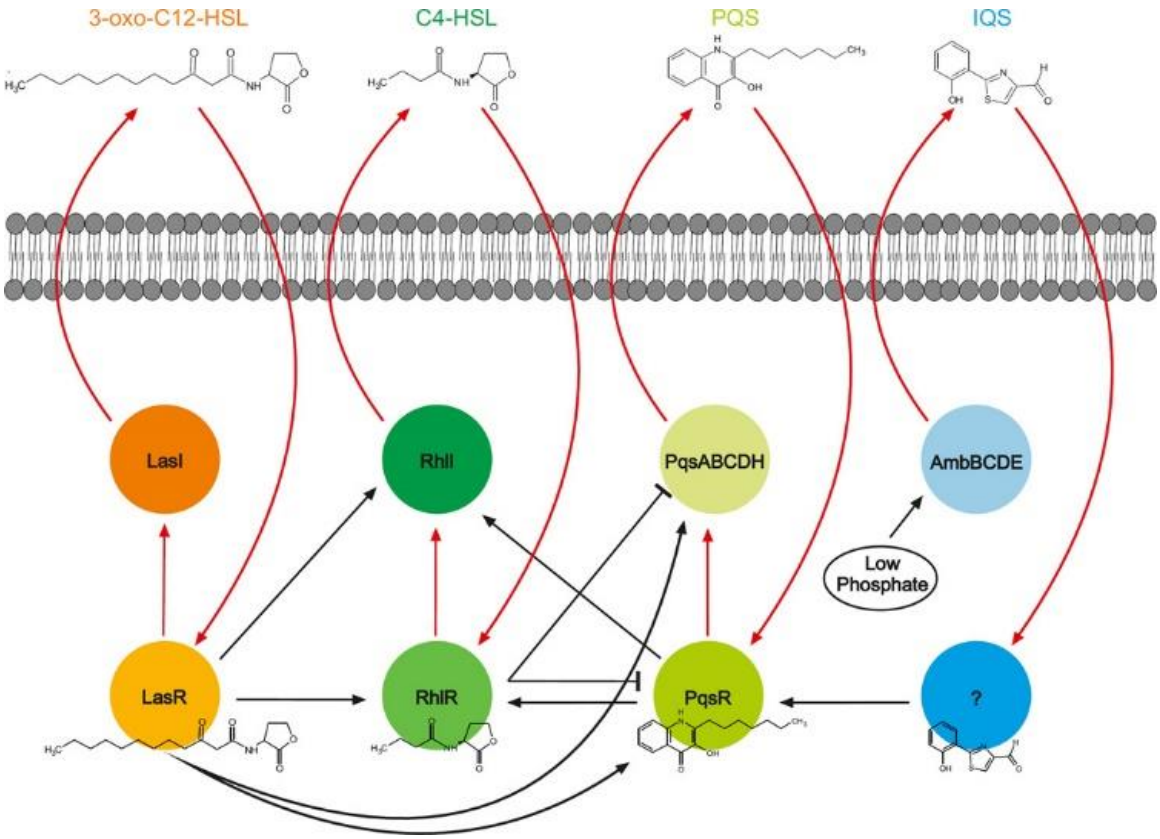

Figure 4. Quorum sensing circuit in *P aeruginosa* [12].

MOLECULAR INTERACTION BEHIND QUORUM SENSING

The molecular interaction behind the quorum sensing was first discovered by the mid of 1980 on *V. fischeri.* At the same time Greenberg et al. also showed the regulation of the sensing on marine species. But it is not all, still some regulations of the bacterial species are under observation. The marine bacteria are basically esoteric light emitting marine bacterial species. But during 1990s this proposal was changed. After this many individual research groups tried to find out the regulatory systems in gram-negative bacteria involved that is homologous to Lux-RI system of *V fischeri*. The above mentioned sy

stems basically used proteins that shared sequence similarly to Lux-RI and signaling molecules that are into the same division of chemicals as OHHL. Though there are 20 Lux-R and LuxI homologues from different microorganisms. These proteins are effectively involved in quorum sensing regulation of assorted physiological functions [10]. Molecular level of interaction in Quorum sensing is depicted in Figure 5.

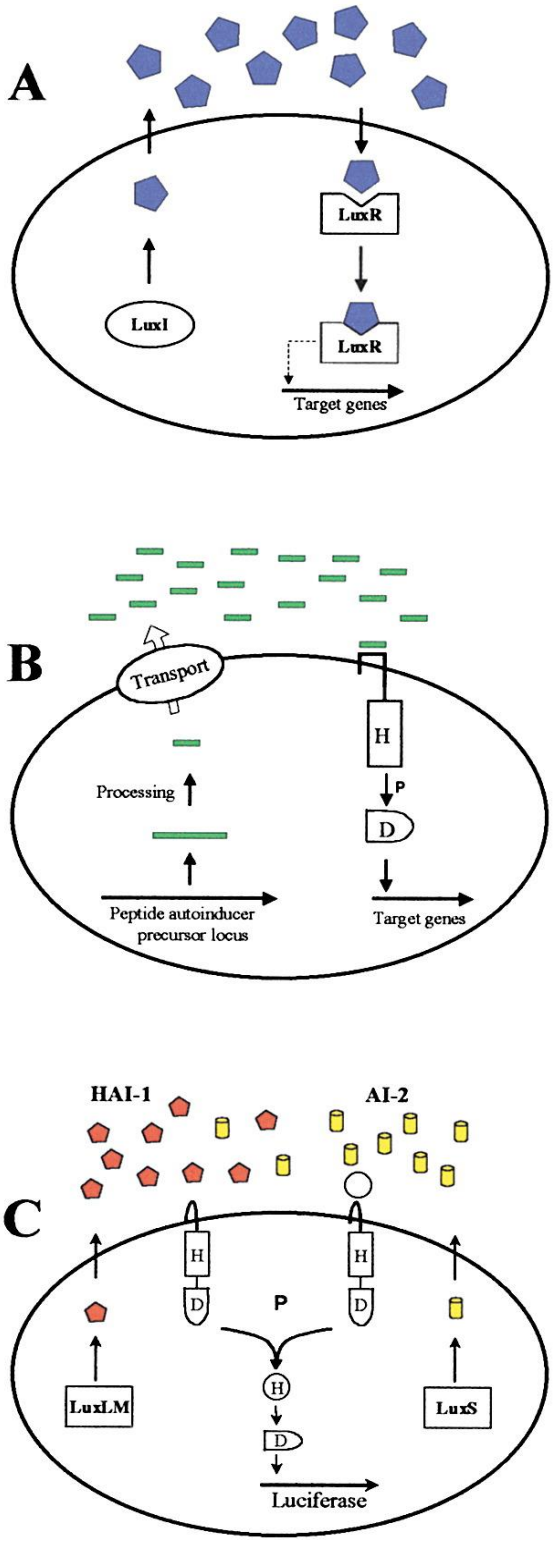

Figure 5. Molecular level of interaction in quorum sensing [15].

NOVEL QUORUM SENSING MOLECULES

Now, molecules belong to two different families of quorum sensing. The molecules are identified and isolated from spent culture of *P. aeruginosa*. The first group molecules known as diketopiperazines. This molecule is synthesized from various microorganism like *P. luorescens*, *P. Alcaligenes*, *Citrobacter freundii, P. aeruginosa* and *Enterobacter agglomerans*. Interestingly as the DKPs are a novel quorum sensing molecule but sometimes it also acts as an inhibitor for quorum sensing and sometimes also activate the quorum sensing. It's like that DKP interacts with Lux-R homologues to exert the positive and negative effects. However, the concentration also plays a significant role to express or inhibit quorum sensing like mechanism. The protein called Lux-S, produced by autoinducer-2 involved in quorum sensing system. It is expected that to catalyse the dissociation of S-ribosylhmocystein to homocysteine and the autoinducer molecule 4,5-dihydroxy-2,3-pentadione. The crystal structure of Bacillus subtilis was clearly visualized at 1.2Å resolution. Both in a binary complex of Lux-S with s-ribosyl-homocysteine and homocysteine at 2.2 to 2.3 Å. From this above-mentioned structure, it can be clearly defined that Lux-S shows a homodimer with a novel fold based on an eight stranded β barrel flanked by six α-helices [11].

ROLE OF QUORUM SENSING IN PATHOGENICITY AND ANTIMICROBIAL RESISTANCE

Antibiotics are used to make a resistance against the bacteria. It may be specific or multi uses. To get relief and survive from the antibiotic the bacteria follow a unique mechanism that is called the antibiotic mechanism. In case of antibiotic resistance mechanism, the bacteria follow quorum sensing process. The antibiotics are made to directly kill the bacteria or to stop the formation of protein membrane present in the outer layer of the bacteria, So, the amounts of bacteria can easily be stopped. The common example of antibiotic is Penicillin. Basically, it degrades the outer protein layer of bacteria. So, the bacteria become die. But now-a-days, a factor, called 'superbugs' is used by the bacteria to resist themselves against the antibiotic. So that the factor is becoming a problematic for human health. The common example is *Staphylococcus aureus* has an ability to degrade the penicillin by producing β-lactamase, which can easily inactivate the effect of Penicillin [13]. Figure 6 shows range of pathogenicity in *Staphylococcus aureus*.

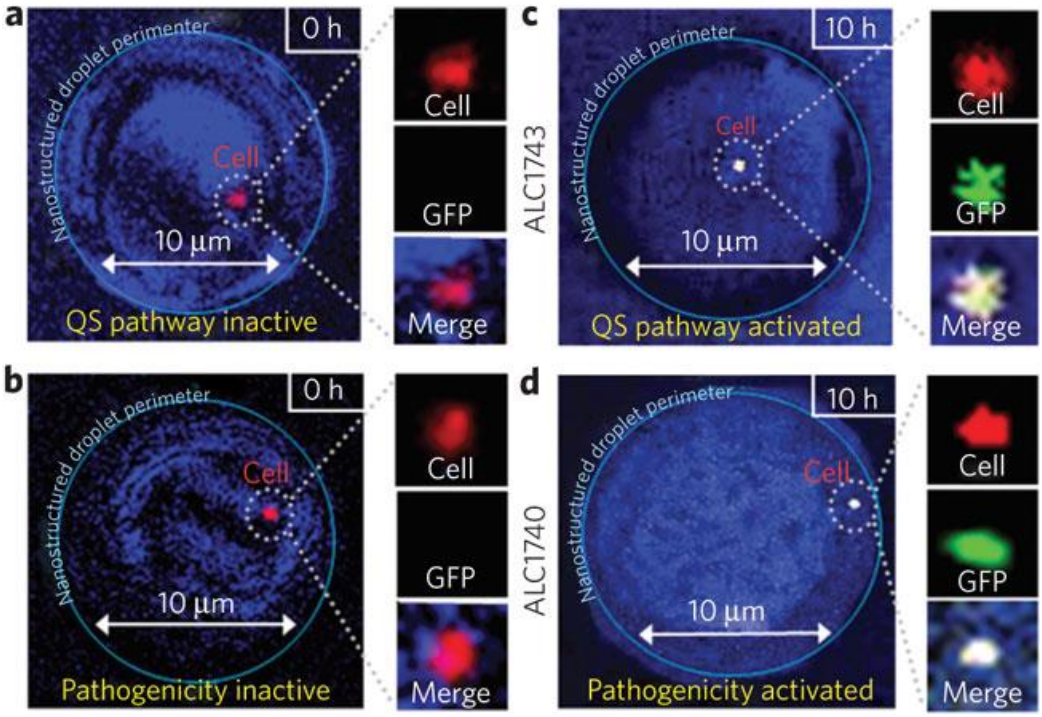

Figure 6. Range of pathogenicity in *Staphylococcus aureus* [17].

BIOFILM FORMATION AND WASTEWATER TREATMENT

Biofilm formation is a process where bacteria form a colony and make a layer to survive or adapt themselves in different environmental in conditions. It helps to grow the tolerance and stress, and it also makes the bacteria infectious for other species. This group behaviour of bacteria, which causes the formation of biofilm reveals the ability of regulation of quorum sensing. Few molecules or series of compounds that are involved in the biofilm formation are autoinducer-2(AI-2), indole, auto-inducing peptide, diffusible signal factor, N-acyl-homoserine lactone and these are interspecific and intraspecific signal molecule with regulatory function of formation of biofilm [25]. Besides being the infectious in nature biofilm has an important role in wastewater treatment. A population of microbes in its various forms like granules, flocs etc. are used in the wastewater treatment. Mostly gram-negative and gram-positive both are used simultaneously. Basically, the biofilm reacts with the nitrogen, dissolved oxygen and nitrate and other organic compound present in the water to maintain the BOD. Commonly known quorum sensing signal i.e., AHL is produced from pseudomonas, Agrobacterium, significantly contribute to the water treatment [26–28].

CONCLUSION

Quorum Sensing (QS) is a fundamental regulatory mechanism used by many bacteria to curb traits collectively that allows bacteria to accomplish niches. For example, the QS enables symbionts to get access to the nutrient-rich environments in hosts. By using Quorum Sensing bacterial populations control biofilm formation, which then provides the members of the population superior access to the nutrients and, therefore, enables them to out-compete the non-biofilm-producing neighbors. Eventually, as discussed earlier in the above-mentioned examples, the bacterial populations that make their living by leveraging eukaryotic hosts have integrated production of the virulence factors fundamental for a pathogenic lifestyle, for their ability to encounter changes in cell population density.

It is very clear that QS gene regulatory function is the outcome of regulatory networks that has been layered onto the basic autoinducer production and detection appliances. Because of the global genetic programs controlled by QS, the reason by which these additional regulatory mechanisms likely assure that the altered gene expression occurs only under the precisely defined circumstances is because of the global genetic programs which are controlled by this Quorum Sensing mechanism. Next, it is very interesting that QS plays a role in dictating the biofilm production process by which the members of the biofilm communities are certainly benefitted although the mechanism and timing of production differ for different species. Considering the similar conditions, the bacterial communication is likely more robust when the cells are in close association provided by biofilms. Researches regarding this are very promising in the upcoming future.

REFERENCES

1. Miller MB, Bassler BL. Quorum sensing in bacteria. Annu Rev Microbiol. 2001;55(1):165–199.
2. Waters CM, Bassler BL. Quorum sensing: cell-to-cell communication in bacteria. Annu Rev Cell Dev Biol. 2005;21:319–346.
3. Novick RP, Geisinger E. Quorum sensing in staphylococci. Annu Rev Genet. 2008;42:541–564.
4. Ng WL, Bassler BL. Bacterial quorum-sensing network architectures. Annu Rev Genet. 2009;43:197–222.
5. Williams P, Camara M. Quorum sensing and environmental adaptation in Pseudomonas aeruginosa: A tale of regulatory networks and multifunctional signal molecules. Curr Opin Microbiol. 2009;12:182–191.
6. Kaplan HB, Greenberg EP. Diffusion of autoinducer is involved in regulation of the Vibrio fischeri luminescence system. J Bacteriol. 1985;163:1210–1214.
7. Sturme MHJ, Kleerebezem M, Nakayama J, Akkermans ADL, Vaugha EE, de Vos WM. Cell-to-cell communication by autoinducing peptides in gram-positive bacteria. Antonie Van Leeuwenhoek. 2002;81(1–4):233–243.
8. Bhatt VS. Quorum sensing mechanisms in gram-positive bacteria. In: Implication of Quorum Sensing System in Biofilm Formation and Virulence. 2018;297–311.

9. Parsek MR, Greenberg EP. Acyl-homoserine lactone quorum sensing in gram-negative bacteria: a signaling mechanism involved in associations with higher organisms. Proc Natl Acad Sci U S A. 2000;97(16):8789–8793.
10. Whitehead NA, Barnard AM, Slater H, Simpson NJ, Salmond GP. Quorum-sensing in gram-negative bacteria. FEMS Microbiol Rev. 2001;25(4):365–404.
11. Ruzheinikov SN, Das SK, Sedelnikova SE, Hartley A, Foster SJ, Horsburgh MJ, et al. The 1.2 Å structure of a novel quorum-sensing protein Bacillus subtilis LuxS. J Mol Biol. 2001;313(1):111–122.
12. Papenfort K, Bassler BL. Quorum sensing signal-response systems in gram-negative bacteria. Nat Rev Microbiol. 2016;14(9):576–588. doi: 10.1038/nrmicro.2016.89.
13. Zhao X, Yu Z, Ding T. Quorum-sensing regulation of antimicrobial resistance in bacteria. Microorganisms. 2020;8(3):425.
14. Deep A, Chaudhary U, Gupta V. Quorum sensing and bacterial pathogenicity: from molecules to disease. J Lab Physicians. 2011;3(01):004–011.
15. Bassler BL. Small talk: cell-to-cell communication in bacteria. Cell. 2002;109(4):421–424.
16. Lamine TS, Zaixiang L, Kaba MA, Johny CB, Waleed AA. Quorum Sensing Inhibitor and its Inhibition Mechanism: Mushroom Derived Agents. IJAIR. 2019;7:2319–1473.
17. Carnes EC, Lopez DM, Donegan NP, Cheung A, Gresham H, Timmins GS, et al. Confinement-induced quorum sensing of individual Staphylococcus aureus bacteria. Nat Chem Biol. 2010;6(1):41–45.
18. Novick RP, Projan SJ, Kornblum J, Ross HF, Ji G, Kreiswirth B, et al. The agr P2 operon: An autocatalytic sensory transduction system in Staphylococcus aureus. Mol Gen Genet. 1995;248:446–458.
19. Seed PC, Passador L, Iglewski BH. Activation of the Pseudomonas aeruginosa lasI gene by LasR and the Pseudomonas autoinducer PAI: An autoinduction regulatory hierarchy. J Bacteriol. 1995;177:654–659.
20. Liu H, Srinivas S, He H, Gong G, Dai C, Feng Y, Wang S. Quorum sensing in Vibrio and its relevance to bacterial virulence. J Bacteriol Parasitol. 2013;4(172):3.
21. Defoirdt T, Boon N, Sorgeloos P, Verstraete W, Bossier P. Quorum sensing and quorum quenching in Vibrio harveyi: lessons learned from in vivo work. ISME J. 2008;2(1):19–26.
22. Kim BS, Jang SY, Bang YJ, Hwang J, Koo Y, Jang KK, et al. QStatin, a selective inhibitor of quorum sensing in Vibrio species. MBio. 2018;9(1):10–1128.
23. Freeman JA, Bassler BL. Sequence and function of LuxU: A two-component phosphorelay protein that regulates quorum sensing in Vibrio harveyi. J Bacteriol. 1999;181(3):899–906.
24. Tu KC, Bassler BL. Multiple small RNAs act additively to integrate sensory information and control quorum sensing in Vibrio harveyi. Genes Dev. 2007;21(2):221–233.
25. Wang Y, Bian Z, Wang Y. Biofilm formation and inhibition mediated by bacterial quorum sensing. Appl Microbiol Biotechnol. 2022;106(19):6365–6381.
26. Sahreen S, Mukhtar H, Imre K, Morar A, Herman V, Sharif S. Exploring the function of quorum sensing regulated biofilms in biological wastewater treatment: A review. Int J Mol Sci. 2022;23(17):9751.
27. Ruby EG. Lessons from a cooperative bacterial-animal association: The Vibrio fischeri-Euprymna scolopes light organ symbiosis. Annu Rev Microbiol. 1996;50:591–624.
28. Nadell CD, Bassler BL. A fitness trade-off between local competition and dispersal in Vibrio cholerae biofilms. Proc Natl Acad Sci USA. 2011;108:14181–14185.

