

Signal and Silence: The Language of Microbes

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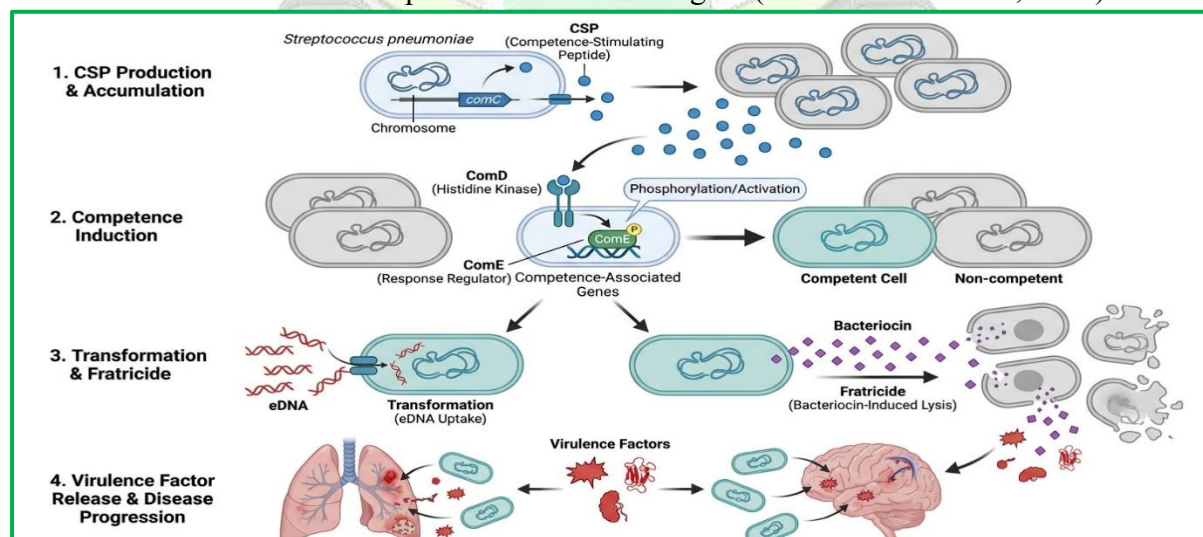
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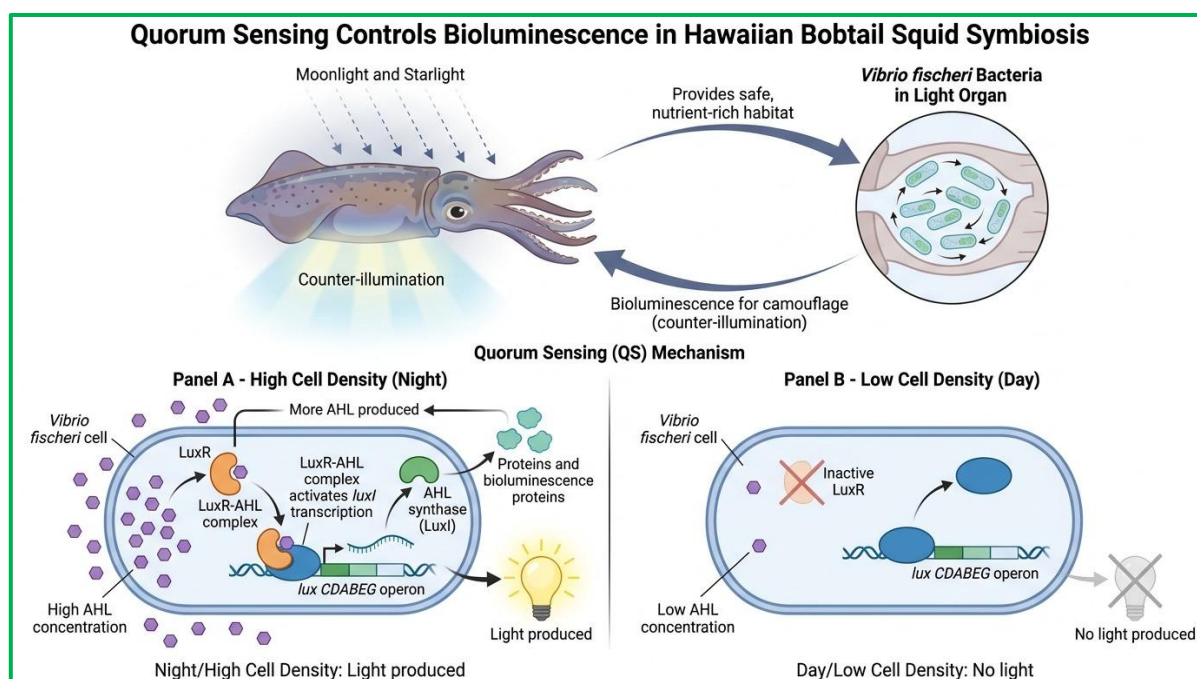
Quorum Sensing (QS) is cell to cell communication. Bacterial cells communicate among themselves using molecular signals in a density dependent manner i.e., bacteria coordinate gene expression according to population density. QS results in bioluminescence, pathogenicity, biofilm formation (Liu *et al.*, 2025). QS is different in gram positive and gram negative bacteria. Gram positive bacteria uses AI (autoinducers) like AHL (Acyl homoserine lactone) which are smaller in size and can pass easily, whereas gram negative bacteria uses peptides much bigger in size and needs a special two component sensor system (Sikdar and Elias, 2020; Liu *et al.*, 2025). Quorum quenching (QQ) is the inhibition mechanism may be biological or chemical. It can occur through inhibition of signal synthesis, degradation or modification of signalling molecules, obstruction of signal reception, or disruption of downstream signal transduction. QQ has attracted interest as an antivirulence strategy because it may reduce pathogenic behaviour without necessarily killing the bacteria directly (Boban *et al.*, 2023; Liu *et al.*, 2025)

Mechanisms

Gram positive bacteria: QS is first observed in *Streptococcus pneumoniae* which produces peptides into environment. ComCDE quorum sensing system is seen in *S. pneumoniae*. The precursor encoded by comC is processed and exported as the competence stimulating peptide (CSP). As the bacterial population grows, extracellular CSP accumulates and binds to ComD, a membrane associated histidine kinase. ComD then activates the response regulator ComE, initiating the expression of competence-associated genes (Wei and Havarstein, 2012). Due to the high population amount of peptides also increases which makes cells competent. Competent cells take up extracellular DNA (eDNA) present in the surrounding through transformation. While taking up the eDNA, competent cells release bacteriocin that lyses the cells which didn't become competent. Lysed cells release virulence factors that helps competent cells invade host tissues and cause diseases like pneumonia and meningitis (Wei and Havarstein, 2012).



Gram negative bacteria: Gram negative bacteria possess diverse circuits involving AHLs, AI-2, diffusible signal factors and other signalling molecules (Sikdar and Elias, 2020) but most commonly used is luxI/luxR system. Popular example is Hawaiian bobtail squid and *Vibrio fischeri* bioluminescence. Bacterial bioluminescence helps the squid match downwelling moonlight and starlight, reducing its silhouette when viewed from below. This phenomenon is called counter-illumination (Septer, 2024). It have a flashlight effect countershading and protecting squid from predation as it hunts at night, inreturn *V. fischeri* gets safe and nutrient enriched habitat. This QS mechanism is operated by AHL which is catalysed by AHL synthase, the product of luxI gene. The luxI gene encodes an AHL synthase that produces primarily 3-oxo-C6-homoserine lactone. Transcription of luxI increases when there is higher accumulation of AHL, this is accomplished through transcriptional activator luxR which becomes active when AHL binds to it forming a simple positive feedback loop (Septer, 2024; Liu et al., 2025). At higher cell density, during night AI diffuses into the cell which binds to luxR. Active luxR stimulates transcription of luxI which inturn produces AHL and RNA polymerase reads the light producing genes like lux CDABEG thus producing light. At lower cell density, AHL doesn't bind to luxR since there is no or less AHL in cell which stops RNA polymerase from reading the operon hence no light is produced.



Quorum quenching mechanisms

QQ can be achieved through enzymatic degradation of AI compound or by blocking of AI production or reception through the addition of compounds named as inhibitors that can mimic them (Sikdar and Elias, 2020; Boban et al., 2023)

- Blockage of signal synthesis:** In this mechanism synthesis of AI is inhibited. BuT-DADMe-ImmA is an analog of MTAN, which will disrupt QS even at low conc by blocking AHL signal formation without affecting bacterial life. Triclosan can also inhibit AHL signaling (Gutierrez et al., 2009).
- Interference with signal molecules:** QQ can also be achieved by using inhibitors with structure similar to AHL's making them to bind to AHL receptor protein and inhibit gene expression. These chemicals are known as antagonists which interferes with native AHL's and disturbs its binding to AHL receptor. Streptomycin an Azithromycin acts as antagonists (Liu et al., 2025).
- Inactivation of signal molecules:** QQ is achieved by degraded of AHL signal molecule leading to inactivation of their effect. It happens in two mechanisms namely chemical degradation or lactonolysis and enzymatic degradation (Sikdar and Elias, 2020; Ryu et al., 2022).

Chemical degradation: Process of opening of AHL ring, it will takes place at pH above 7. Enzymatic degradation: Enzymes like lactonase, acylase, AHL oxidoreductase, decarboxylase and deaminase are responsible for AHL's degradation. AHL lactonases hydrolyse the ester bond of the homoserine lactone ring and produce the corresponding open ring acyl homoserine. AHL acylases cleave the amide bond between the acyl chain and the homoserine lactone moiety. This reaction produces a fatty acid and homoserine lactone and is generally irreversible. AHL oxidoreductases oxidise or reduce chemical groups on the acyl side chain. They modify rather than necessarily destroy the signal, reducing or altering its affinity for its receptor. Other enzymes, including some paraoxonases and specialised signal modifying enzymes, may also contribute to QQ, although their substrates and biological roles vary.

QQ applications

Human health care field:

a) Treatment of human infections: With the rising issue of drug resistant bacteria which will communicate and increase the virulence through qs, there is a need to decrease their virulence by qq (Uroz, S. and Oger, P.M. 2016).

Ex: Garlic oil to control cystic fibrosis (Smyth *et al.*, 2010).

b) Medical device applications: QS induced bacteria such as *P. aeruginosa*, *Proteus* and *Serratia* are closely related to health care associated infections caused by infected catheters or ventilators. Furanone, Acylase, combination of acylase & amylase are some of the qq enzymes coated on catheters or ventilators to reduce the spread of microbes (Lade *et al.*, 2014).

c) Dental Plaque biofilms: Many oral bacteria can be affected using qq mechanisms. Periodontal infections can be reduced resulting in better oral hygiene with the help of qq (Uroz, S. and Oger, P.M. 2016).

d) Cancer therapy applications: Qs has been linked to cancer therapy where the signals of *P. aeruginosa* disrupts breast cancer cell proliferation (Uroz, S. and Oger, P.M. 2016).

Agriculture field: Pathogenicity of tobacco, potato, chinese cabbage and cauliflower plants is reduced by engineered production of qq enzyme lactonase and AiiA enzyme by plant associated microbe *Erwinia carotovora* (Dong *et al.*, 2000).

Aquaculture: Pathogenic effect of *Vibrio* isolates in shrimp culture are inhibited by brominated furanone synthesized by an algae (Sudan *et al.*, 2026).

Environmental field: Interference with qs reduces microbial adhesion and thus biofouling. Enzymatic qq technology is used to inhibit the biofilm formation by bacteria through AHL degradation (Köse-Mutlu *et al.*, 2019).

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