Hybrid Quorum sensing in *Vibrio harveyi*-two component signalling

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# Table of Contents

1 INTRODUCTION ................................................................................................................. 3

1.1 THE MULTI CHANNEL LUX CIRCUIT IN VIBRIO HARVEYI........................................... 4
1.2 FEEDBACK CONTROL IN HYBRID QUORUM SENSING ............................................ 6

2 REFERENCES ......................................................................................................................... 7

2.1 LITERATURE REFERENCES ......................................................................................... 7
2.2 VIDEO LINK ....................................................................................................................... 7
1 Introduction

Though distantly related bacteria show LuxI/R systems similar to that of *Vibrio fischeri*, two notable forms of bacteria *Vibrio harveyi* and *Vibrio cholerae* do not conform to the LuxR/I mediated quorum sensing pattern. These two bacteria do not possess the LuxI or LuxR genes similar to *Vibrio fischeri*. *Vibrio fischeri* the free living marine bacterium is a notable pathogen of marine organism while *Vibrio cholerae* is the etiological agent for cholera whose life cycle alternates between human host and aquatic environment while *Vibrio harveyi* shows bioluminescence and production of metalloproteases repressing type three secretion, *Vibrio cholerae* uses quorum sensing to repress biofilm formation, activate protease production and to produce virulent factors. *Vibrio cholerae* cells employ quorum sensing to promote genetic exchange between them in the presence of chitin.

*Vibrio harveyi* uses quorum sensing approach reminiscent of both Gram-negative and Gram-positive bacteria as shown in Fig 1. *Vibrio harveyi* responds to acyl-Homoserine Lactone like Gram-negative bacteria and also employs a signal transduction system involving a two component circuit, hence making the system a hybrid quorum sensing circuit. In addition to these two signalling cascades *Vibrio harveyi* also employs a second autoinducer AI-2 in its circuit. The structure of this autoinducer is unknown though the gene required for its production has been identified in several Gram-negative and Gram-positive bacteria.

![Fig 1. Hybrid quorum sensing exhibited by Vibrio harveyi](image-url)
1.1 The multi channel Lux circuit in Vibrio harveyi

In *Vibrio harveyi*, two autoinducer response systems function in parallel and control the expression of the luciferase structural operon luxCDABE, as described in Fig 2. Each of these systems comprises a sensor (sensor-1 or sensor-2) and its cognate autoinducer AI-1 or AI-2. In this case, the autoinducer-1 is the N-(3-hydroxybutanoyl)-homoserine lactone whose synthesis does not involve the LuxI like protein as in *Vibrio fischeri*. AI-1 is produced by Lux M protein which shares no homology with the LuxI family of proteins although it may be thought that the biosynthetic pathways are identical. As stated earlier, the structure of the second autoinducer is not known. These autoinducers AI-1 and AI-2 are detected by LuxN (sensor 1) and LuxQ (sensor 2) cognate sensors which are the two component proteins of the hybrid sensor class. LuxN and LuxQ comprise a sensor kinase domain and a response regulator domain. A periplasmic binding protein LuxP, similar to the ribose binding protein of E. coli in conjunction with LuxQ initiates a signal transduction in AI-2. Phosphorylation and dephosphorylation events transduce information from both systems to LuxU, a shared signal integrator protein. Since LuxU is a phosphotransferase, it transfers the signal to a response regulator protein called LuxO.

![Fig 2. The lux circuit in Vibrio harveyi comprising of two autoinducers Al-1 and Al-2](image)
At lower cell densities, in the absence of the autoinducers the sensors get autophosphorylated, undergo a series of intra and intermolecular phosphor transfer events, phosphorylating LuxO. The phosphorylated LuxO represses luxCDABE. At higher cell densities in the presence of the autoinducers sensors LuxN and LuxQ, transition from kinases drive phosphate towards LuxO to phosphatases that remove phosphates from the circuit. Unphosphorylated LuxO does not activate the expression of the repressor. Hence luxCDABE is transcribed leaving to a phenotype of bioluminescence. The expression of luxCDABE also requires a transcriptional activator LuxR which is different from the LuxR employed by *Vibrio fischeri* quorum sensing system.

In species like *Salmonella typhimurium* and *E.coli*, the genes regulated by the second autoinducer AI-2 code for an ABC transporter called Lsr (LuxS-regulated) whose diagrammatic representation is shown in Fig 3. Inside the cellular space the autoinducer is phosphorylated by LsrK and is hypothesized to interact with LsrR, a transcription factor involved in repressing the lsr operon. The complexation of lsr to AI-2 prevents repression of lsr. The LsrB Ligand proposed to be the autoinducer-2 was identified to be 2R, 4S-2-methyl-2, 3, 3, 4-tetrahydroxytetrahydrofuran and not the furanosyl borate diester.

![Diagram of LsrB and LsrR interaction](image)

**Fig 3.** Hybrid quorum sensing exhibited by *Salmonella typhimurium*
1.2 Feedback control in Hybrid Quorum sensing

Quorum sensing networks extensively use positive feedback for phenotypic expression. In the LuxI/R systems employed by Gram-negative bacteria the expression of this autoinducer synthase is positively controlled by the LuxR protein which is bound to the AHL. This feedback loop accelerates AHL production synchronizing organizational behaviour of quorum sensing. Peptide based Gram-positive bacteria also employ positive feedback loops. The response regulator in these systems act as auto activators of the operon in the system. This wiring through auto regulation improves positive feedback through which the levels of the peptide Ligand, membrane receptor and response regulator increase drastically with threshold accumulation of the autoinducer required for detection. The following feedback loops have been identified in Vibrio harveyi and Vibrio cholerae as in Fig 4.

1. Hap-R, LuxR auto repression loop
2. Hap-R/LuxR-Qrr feedback loop
3. LuxO auto repression loop
4. LuxO-Qrr feedback loop

Fig 4. Feedback loops in Vibrio harveyi and Vibrio cholerae
The feedback loops in *Vibrio harveyi* and *Vibrio cholera* have been proven to function together to minimize variations in the levels of individual components of the quorum sensing circuit. Such feedback loops ensure synchrony in the quorum sensing response over the population of cells ensuring collecting behaviour.

2 References

2.1 Literature References


2.2 Video Link

Bonnie Bassler (Princeton) Part 1: Bacterial Communication via Quorum Sensing

http://www.youtube.com/watch?v=saWSxLU0ME8