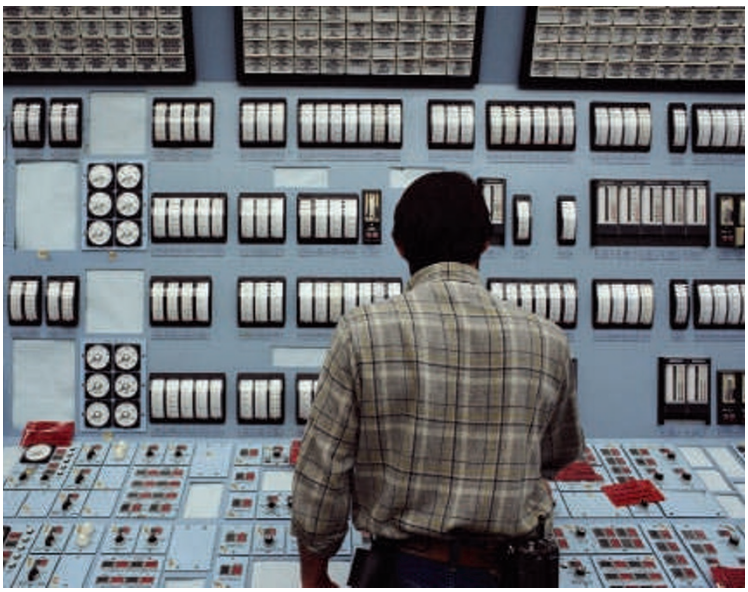
QUORUM SENSING

Setting the threshold

A negative regulator that controls the activation threshold for quorum sensing in *Pseudomonas aeruginosa* has been identified, according to a new report from Richard Siehnel, Pradeep Singh and colleagues.

Quorum sensing allows bacteria to communicate with each other through the production and perception of small extracellular signal molecules such as acyl homoserine lactones (HSLs). In batch culture, genes controlled by quorum sensing show a sigmoidal expression curve, with expression triggered when the bacterial cell density passes a specific threshold. A key unanswered question, until now, has been how this threshold is achieved.



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The authors were interested in investigating the idea that a negative regulator might be responsible for setting the threshold by inhibiting the expression of quorum sensing-regulated genes in the pre-quorum period. The authors used an inducible expression screen to identify repressors of quorum sensing-controlled genes, and from 20,000 transposon mutants only one candidate gene was identified. This insertion was mapped to a position upstream of the gene PA2593, which encodes a protein the authors have named QteE (quorum threshold expression element). QteE is present in all sequenced *P. aeruginosa* strains but not in other bacterial species.

Expressing *qteE* in *P. aeruginosa* repressed many quorum sensing-dependent phenotypes. But how does this repression work? In *P. aeruginosa*, the best characterized quorum-sensing systems are the LasI–LasR system (in which the synthase, LasI, produces a 3-oxo-C_{12}-HSL and LasR is the signal receptor) and the RhlI–RhlR system (in which the synthase, RhlI, produces a butanoyl HSL and RhlR is the receptor). The authors analysed the effect of QteE on both signal molecules and found that *qteE* expression eliminated the activity of both molecules but had no effect on their production or degradation. The authors then turned their attention to LasR and found that when *lasR* was over-expressed QteE no longer repressed the transcription of *rhlA*, a quorum sensing-regulated gene. Expressing *qteE* had no effect on the levels of *lasR* transcription or translation, but it did significantly reduce the stability of the LasR protein and was also found to independently reduce the stability of RhlR. Finally, the authors demonstrated that inactivation of *qteE* eliminated the activation threshold for several quorum sensing-regulated genes.

The post-transcriptional mechanism by which QteE reduces LasR and RhlR stability remains to be determined, but the authors present a provisional model in which the stoichiometry between QteE and LasR is the key factor. At low cell densities, the relative activity of QteE is greater than that of LasR and so quorum sensing-controlled genes are repressed; once a quorum is reached, the balance shifts in favour of LasR and quorum sensing-controlled genes are switched on.

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ORIGINAL RESEARCH PAPER Siehnel, R. *et al.* A unique regulator controls the activation threshold of quorum-regulated genes in *Pseudomonas aeruginosa*. *Proc. Natl Acad. Sci. USA* **107**, 7916–7921 (2010)