Bacterial gangs: United and strong by means of quorum sensing

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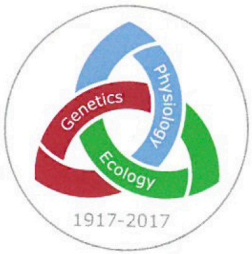

Laboratory of Microbiology

Mighty Microbes

The amazing world of microorganisms

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Contributors

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Bacterial gangs: United and strong by means of quorum sensing

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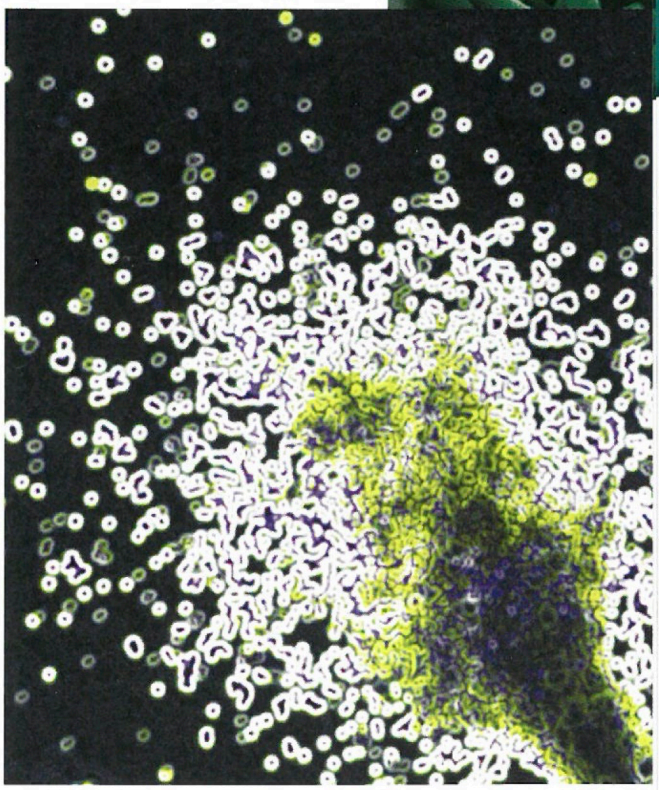
Microorganisms can effectively communicate with each other. They share information about their community size (quorum), and thereby their nutrient requirement, then take appropriate action such as moving away. They use signalling molecules to coordinate their behaviour. These compounds, like similar molecules in humans, are called pheromones.



Light-emitting *Vibrio fischeri* bacteria isolated from the "light-organ" of the Hawaiian bobtail squid.

Signalling molecules

When neighbouring cells secrete signalling molecules, the pheromones accumulate in the vicinity of the cells. This stimulates production, causing an exponential rise in the concentration of signalling molecules at sites where there are many microorganisms. At a critical cell concentration where the threshold of the number of signalling molecules is just exceeded, a regulator protein will be activated. This will stimulate further synthesis of the pheromones as well as the synthesis of proteins that could be useful at that moment in that environment. This might involve processes such as the emission of light, swarming of cells, biofilm formation, development of antibiotic resistance or developing of virulence (the ability to infect human cells by pathogenic bacteria such as *Salmonella* or pneumococci). Several of these responses commonly occur simultaneously. For microbes that develop antibiotic resistance, it is quite effective to form a tight layer of bacteria (biofilm) that is hard to penetrate by antimicrobials and enzymes. This is the first line of defence.

Around 1994, the term "quorum sensing" was coined, but the phenomenon had been known for some time. In the 1970s, researchers added supernatant from a dense culture of the light-emitting marine bacterium *Vibrio fischeri* to a non-light emitting group of related bacteria which began emitting light. They had picked up the signal in the supernatant. This signalling molecule was a pheromone known as N-acyl-homoserinelactone, denoting a whole family of similar compounds that occur mainly in Gram-negative bacteria. These pheromones can be taken up from the environment by bacteria other than the producers and will activate the regulator protein in the recipient cells.

Gram-positive bacteria also do it!

Quorum sensing is also employed by Gram-positive bacteria. However, they usually make use of different pheromones, peptides. This is related to the difference in the

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This squid from Hawaii has a clear light spot at its back that is caused by a large number of light-emitting *Vibrio fischeri* bacteria which live closely together and stimulate each other to produce light. They benefit from nutrients provided by the squid, while the animal benefits from the light because it confuses possible predators. Many other examples of quorum sensing have been identified, including in pathogenic bacteria from genera such as *Pseudomonas, Burkholderia,* and *Yersinia*.

structure of Gram-positive (one membrane) and Gram-negative (two membranes) cell envelopes. There is a big difference in the ability of particular molecules to penetrate them and reach the cell cytoplasm.

A nice example of quorum sensing by peptides was described in the early 1990s. The production of the natural antimicrobial peptide nisin, widely used in the food industry as a natural preservative, relies on its own production rate. When cells start growing, a small amount of this peptide is produced. When the extracellular peptide is detected by a sensor protein in the membrane, a signal is sent to an intracellular regulator which enhances the transcription of the genes needed for its own biosynthesis and the cell's immunity. This initial tiny amount of signalling peptide is not detected by neighbouring cells, just by the producer. Only once production increases there is sufficient peptide to induce production in neighbouring cells as well.

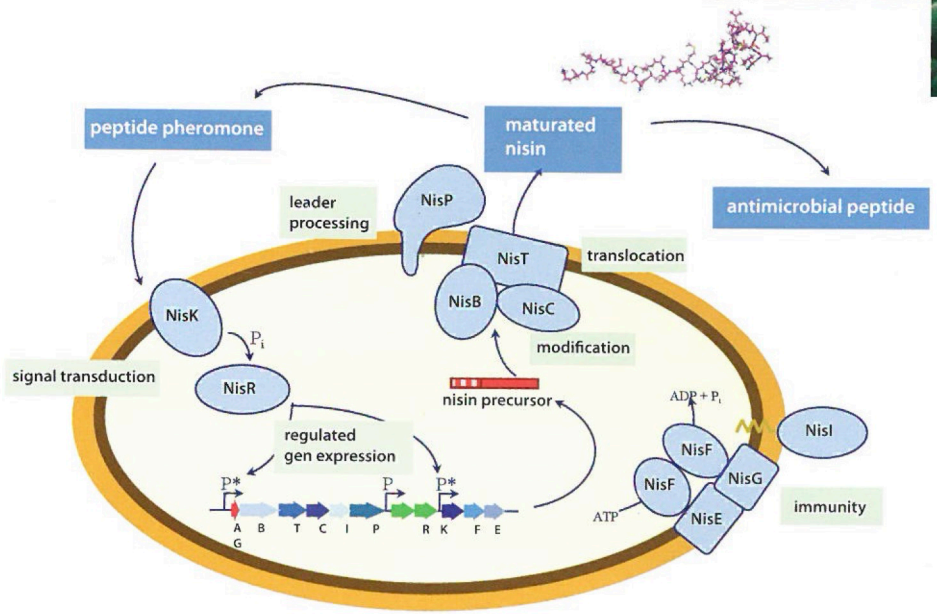
Miscommunication

Because quorum sensing signalling molecules play such an important role in the communication that initiates the production of harmful and toxic compounds or in the formation of biofilms, they are also the Achilles heel of the system. Competing microorganisms can secrete enzymes that degrade the signalling molecules, preventing correct communication between cells. This makes the bacteria vulnerable, and can even lead to their premature death, a phenomenon known as "quorum quenching". Notably, such a strategy can also be used to kill pathogenic bacteria. Novel quorum quenching strategies can be developed on the basis of information about the enzymes acting on the signalling molecules. The enzymes must be precisely delivered so they only act where the infection has occurred. One interesting possibility is to include

these enzymes in small droplets of biodegradable material, which will open to deliver their contents when they reach their target.

The purpose and advantages of quorum sensing

Some behaviour only makes sense when the whole group participates. Performing a solo Mexican wave at a football match has little effect. A party attended by only one or two people is not much fun. In the bacterial world, it is exactly like that. When competing for the best niche with plenty of food and optimal conditions, bacteria perform best in a group. It is then also profitable to share energy-costly processes such as light emission, virulence, biofilm formation or the production of antimicrobials. With a small team, such endeavours are doomed to fail.



The biosynthesis of the antimicrobial peptide nisin.

Communicating supporters perform a Mexican wave.