Cell-cell signalling in unicellular organisms

How single-celled organisms use signals to communicate. Yeast mating types, bacterial quorum sensing, and biofilms.

Introduction

In multicellular organisms (such as yourself), cell-cell signalling allows cells to coordinate their activities, ensuring that tissues, organs, and organ systems function correctly. Does that mean that unicellular organisms, like yeast and bacteria, don't use cell-cell signalling pathways?

As a matter of fact, these organisms do still need to "talk" to one another. The cells may not be part of the same organism, but they belong to the same population, and – just like people in a human population – need ways to communicate about matters of interpersonal or community importance. Bacteria, for example, use chemical signals to detect population density (how many other bacteria are in the area) and change their behaviour accordingly, while yeast produce chemical signals that allow them to find mates.

Here, we'll take a closer look at how unicellular organisms "chat" with one another using chemical signals.

Quorum sensing in bacteria

For many years, it was thought that bacteria were mostly loners, making decisions at the individual rather than the community level. More recently, it's become clear that many types of bacteria engage in a mode of cell-cell signalling called **quorum sensing**.

In quorum sensing, bacteria monitor the density of the population (the number of other bacteria in the area) based on chemical signals. When the signalling reaches a threshold level, all the bacteria in the population will change their behaviour or gene expression at the same time.

Quorum sensing in symbiosis

Quorum sensing was discovered first discovered in *Aliivibrio fischeri*, a bacterium that has a symbiotic (mutually beneficial) relationship with the Hawaiian bobtail. *A. fischeri* form colonies inside the squid's "light organ." The squid gives the bacteria food, and in return, the bacteria bioluminescence (emit light). The glow of the bacteria prevents the squid from casting a shadow, hiding it from predators swimming beneath.

Image modified from "Euprymna scolopes," by Chris Frazee and Margaret McFall-Ngai (CC BY 4.0)[2] *.*

When *A. fischeri* bacteria are inside of a squid's light organ, they glow, but when they're free-living in the ocean, they don't. Through decades of work, scientists discovered that the bacteria use quorum sensing to decide when to produce bioluminescence. It would be a metabolic waste for a lone bacterium in the open ocean to carry out chemical reactions that emit light, since they provide no benefit without a squid host. When many bacteria are tightly packed in a light organ, however, glowing in unison provides an advantage: it allows the bacteria to fulfil their end of the symbiotic bargain, keeping their squid host (their food source) from being eaten by predators.

Mechanisms of quorum sensing

Quorum sensing is based on the production and detection of **auto inducers**, signalling molecules continually secreted by bacteria to announce their presence to their neighbours (typically, neighbours of the same species). Auto inducers let bacteria sense population density and change their behaviour in a synchronized fashion when the density reaches a certain threshold.

In some types of bacteria, the secreted auto inducers are small, hydrophobic molecules such as acyl-homoserine lactone (AHL). AHL is the auto inducer made by *A. fischeri*, the bacteria that occupy a squid's light organ. In other types of bacteria, the auto inducers may instead be peptides (short proteins) or other types of small molecules.

Because AHL is small and hydrophobic, it can diffuse freely across the membranes of the bacterial cells.

- When there are few cells in the area, the little AHL that's made will diffuse into the environment, and the levels of AHL inside the cells will remain low.
- When more bacteria are present, a larger amount of AHL will be produced (thanks to the greater number of contributors).
- If AHL levels get high enough, indicating a critical density of bacteria, the AHL will bind to and activate a receptor protein inside the cells.

- The active receptor acts as a transcription factor, attaching to specific sites on the bacterium's DNA and changing the activity of nearby target genes.

In *A. fischeri*, the transcription factor turns on genes that encode enzymes and substrates required for bioluminescence, as well as the gene for the enzyme that makes AHL itself (amplifying the response in a **positive feedback loop**).

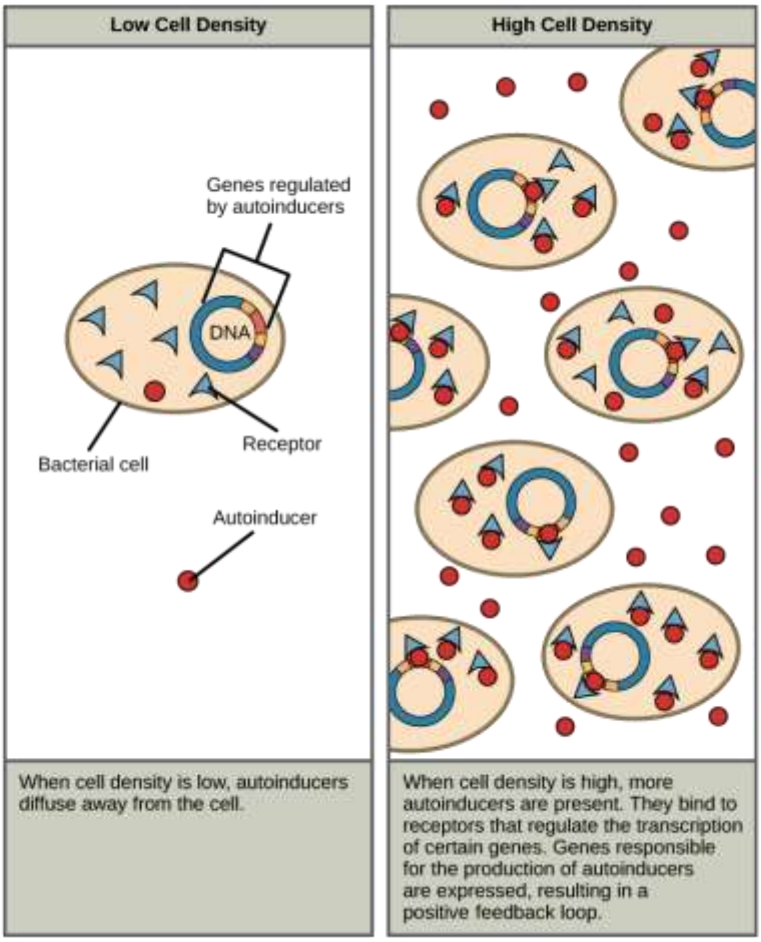


Diagram of quorum sensing.

First panel: low cell density. When cell density is low, auto inducers diffuse away from the cell.

Second panel: high cell density. When cell density is high, more auto inducers are present. They bind to receptors that regulate the transcription of certain genes. Genes responsible for the production of auto inducers are expressed, resulting in a positive-feedback loop.

Some kinds of bacteria use peptide (protein) auto inducers for quorum sensing. Like AHL, these auto inducers allow bacteria to detect population density and change their behaviour when density reaches a certain threshold. However, because they aren't small and hydrophobic like AHL, peptide auto inducers cannot diffuse freely across the membrane. Thus, they typically act through a different kind of signalling pathway than AHL. In this pathway:

- A peptide auto inducer doesn't enter the receiving cell, but instead binds to and activates a receptor on that cell's surface.
- Binding triggers a signalling cascade that activates a transcription factor.
- The transcription factor changes activity of target genes to increase production of auto inducer (a positive feedback loop) and alter cell behaviour.

Staphylococcus aureus, the bacterium that causes staph infections in humans, provides a good example of quorum sensing using a peptide auto inducer. At a threshold population density, *S. aureus* bacteria simultaneously shift to a more virulent, or disease-causing, mode. The shift takes place through a peptide auto inducer pathway, which changes gene expression and leads to production of toxins and other virulence factors.

In general, each species of bacteria has its own auto inducer, with a matching receptor that's highly specific (won't be activated by the auto inducer of a different bacterium). However, some types of auto inducers can be produced and detected by multiple species of bacteria. Scientists are investigating how these molecules may allow for between-species communication.

Quorum sensing and biofilms

Some species of quorum-sensing bacteria form **biofilms**, surface-attached communities of bacterial cells that stick to one another and to their substrate (underlying surface). Biofilms can be quite complex, with bacterial cells organizing to form ordered structures, and some biofilms contain multiple species of coexisting bacteria.

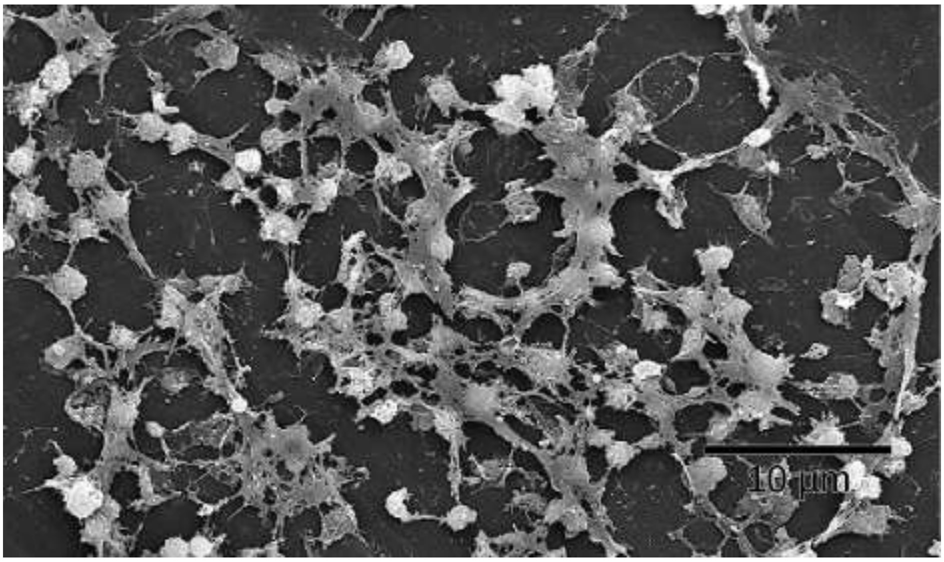


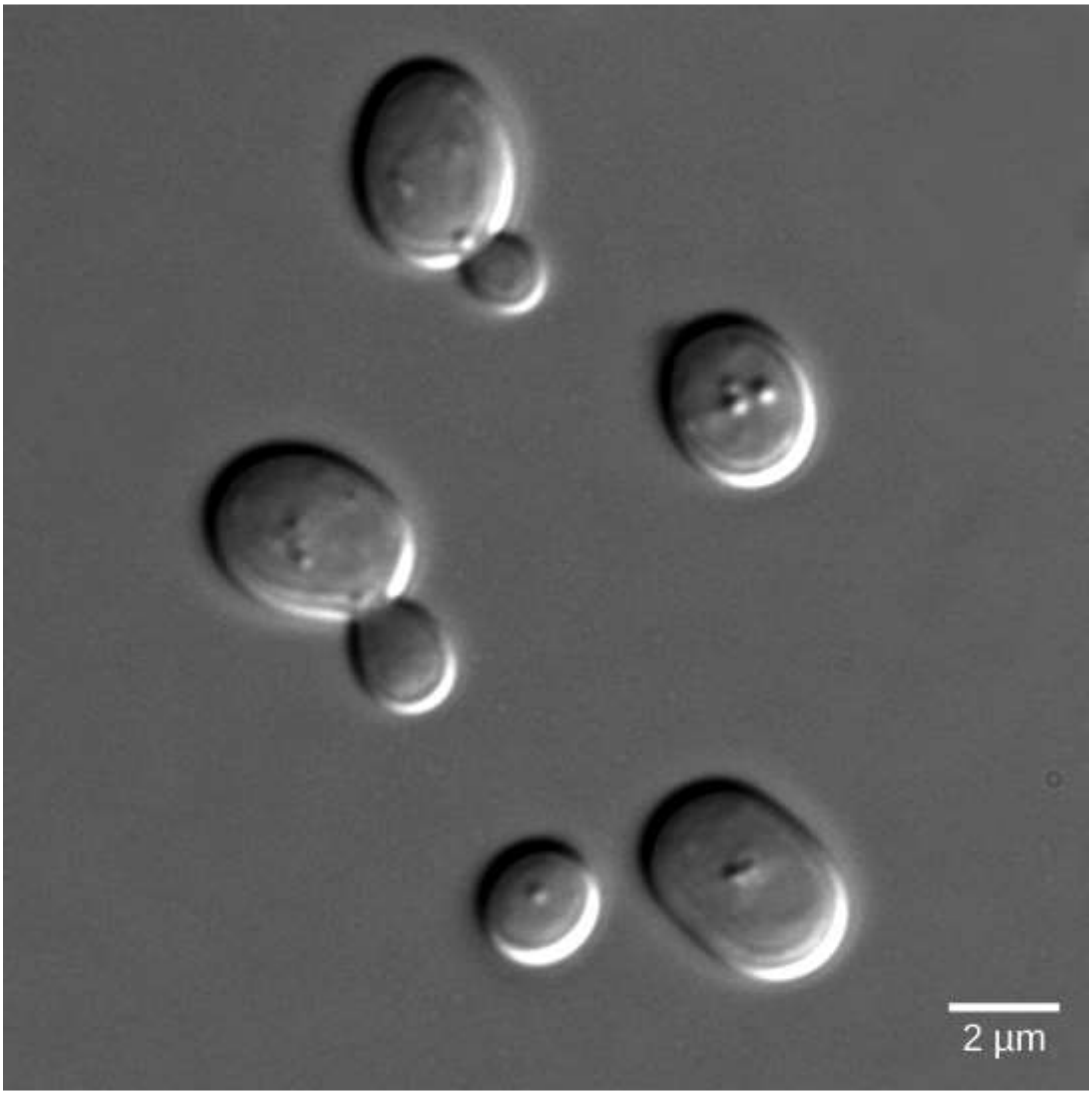
Image of a *Staphylococcus aureus* biofilm on the surface of a catheter.

Image modified from "Signalling in single-celled organisms: Figure 3," by OpenStax College, Biology (CC BY 3.0). Based on original image by Janice Carr, CDC.

Although much remains unknown about biofilms, it's increasingly clear that they play crucial roles in human health and disease. For instance, the *S. aureus* colonizing the surface of a catheter above are organized in a biofilm. Quorum sensing can play an important role in the formation, maintenance, and breakdown of biofilms.

Signalling in yeasts

The yeasts that ferment grapes into wine, or cause bread to rise, are single-celled eukaryotes. They're neither animals nor plants, but actually a type of fungus. (Yum!) Some baker's yeasts are shown in the microscope image below.



Micrograph of yeast cells.

Image credit: "Signalling in single-celled organisms: Figure 1," by OpenStax College, Biology (CC BY 3.0.

One of the best-studied signalling pathways in yeast is the mating factor pathway. Budding yeasts can mate in a process similar to sexual reproduction, in which two haploid cells (cells with a single set of chromosomes, like human sperm and eggs) combine to form a diploid cell (a cell with two sets of chromosomes, like human body cells). The diploid cell can then go through meiosis to make haploid cells with new combinations of genetic material.

To find another haploid yeast cell that is prepared to mate, budding yeasts secrete a signalling molecule called mating factor. Mating factor comes in two different versions, as does its receptor, and this system may help yeasts mate with other yeasts that are not close relatives. Binding of mating factor to a compatible receptor triggers a signalling cascade that causes the yeast to "shmoo," or produce an outgrowth so it can fuse with its mate. You can see the details of this pathway in the video on cell signalling in yeast reproduction.

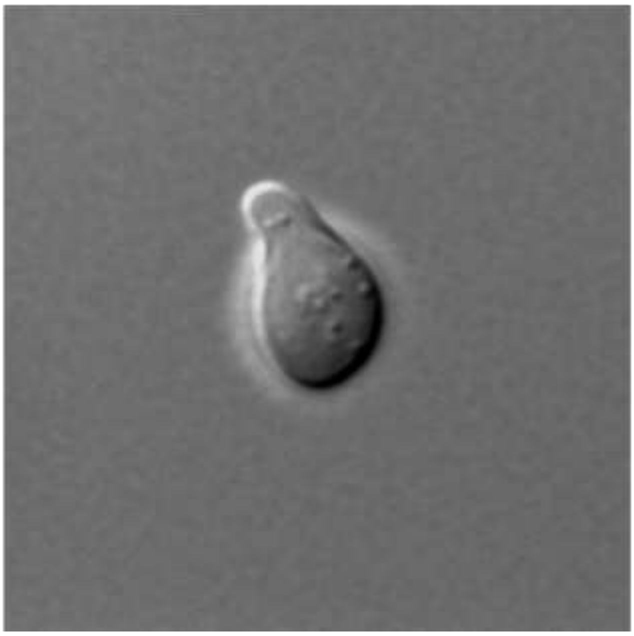


Image credit: "Shmoo yeast, S. cerevisiae," by Masur, public domain.

If you look closely at the mating factor signalling pathway, you'll find that it includes types of molecules familiar from humans. For instance, the mating factor receptor is a G protein-coupled receptor, and it acts through a MAP kinase signalling pathway like the one used in human growth factor signalling.