Chatting coordinates heterogeneity

July 26 2017

Bacterial cells communicate with one another by using chemical signal molecules, which they synthesize and secrete into their surroundings. By this means, the behavior of an entire population can be controlled and coordinated. Biophysicists led by Professor Erwin Frey, who holds the Chair of Biological and Statistical Physics at LMU, have now shown theoretically how this can be accomplished even when only a subset of cells actually emits the requisite signals. The new findings appear in the online journal *eLife*.

Once the concentration of the relevant signal molecule reaches a certain threshold level in the environment, bacteria can collectively respond by implementing a specific behavioral response, such as the production of bioluminescent compounds or formation of a biofilm. This mechanism is referred to as 'quorum sensing'. The term was derived from the initial belief that all the cells produced the signal, such that its concentration in the environment directly reflected the number of cells present. However, more recent investigations suggest that this is not always the case - even in genetically identical populations. "We were interested in understanding how such phenotypic heterogeneity can arise in situations in which the cells are genetically identical and are exposed to the same environmental conditions," says Johannes Knebel, one of the joint first authors of the new paper.

Frey and his colleagues made use of mathematical models to analyze the complex interplay between ecological factors and population dynamics, and were able to demonstrate that populations can indeed respond in a coordinated fashion to chemical information even when the signal molecules are generated by only a subset of the cells. "For that to occur, two preconditions must be met", says Knebel. "The first is that all the cells in the population must be capable of reacting to the actual level of the signal in the environment - in other words, they must be able to perceive the signal and increase their production. The second prerequisite is that synthesis and secretion of the signal reduce the fitness of producer cells. This would be the case, for instance, if signal production requires the expenditure of energy, which would inevitably reduce the division rate of producer cells."

Under these conditions, non-producing cells in the model always grow faster than producers. Since all the bacteria in the population can perceive the signal, non-producers may respond to its presence by becoming producers themselves. Bacteria already engaged in signal production, on the other hand, will not further increase its rate of synthesis. "Bacteria react to an environment that is shaped by themselves. This ecological feedback is what makes it possible for phenotypic heterogeneity to arise in genetically identical populations," says Frey. "Our mathematical analysis demonstrates that, once established, such heterogeneity can stably persist and is robust to perturbations."

It has been speculated that such heterogeneous production of signaling molecules could be advantageous for the whole population because it allows for a division of labor between signal producers and non-producers, or because the creation of phenotypic diversification provides greater evolutionary flexibility and enables populations to adapt more rapidly to environmental change. However, an understanding of the biological functions of phenotypic heterogeneity in such systems will require dedicated experimental studies, say the authors of the new paper.

More information: Matthias Bauer et al, Ecological feedback in quorum-sensing microbial populations can induce heterogeneous

production of autoinducers, *eLife* (2017). DOI: 10.7554/eLife.25773

Provided by Ludwig Maximilian University of Munich