Leeah Rergyamdee

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Cell Biology

Professor Steel

Cell Maze Paper

A study in August 2020 was published by a group of scientists, led by Luke Tweedy, to see how cells would respond to being placed in a variety of mazes. The cells used in this experiment were *D. discoideum*, which is a soil-dwelling amoeba (single-celled organism), and pancreatic cancer cells, as both of these cell types typically need to navigate over long distances. In order for these cells to navigate to where they need to go, they use the process of chemotaxis, in which cells move in response to changing chemical stimuli in their environment (Specktor, 2020). Thus, the researchers in this experiment wanted to test these cell types' efficiency of using chemotaxis in order to find their way out of these mazes, in which some of them (such as the replication of the Hampton Court Palace maze) were relatively large. In order for *D. discoideum* to find their way through the maze, they used a combination of chemotaxis and amoeba movement, which is the main source of movement for amoebas and occurs when the cytoplasm of the cell protrudes and forms pseudopodia, which are basically fake feet (Wikipedia contributors, 2020a). The chemical attractant used and observed in the experiment is known as cAMP (cyclic adenosine monophosphate), and acts as a signaling chemical in amoebae. Amoeba release cAMP signals, which attracts other amoebae. This process ultimately results in amoebae clustering together and releasing cAMP signals in waves. This creates a concentration gradient, allowing for other amoebae to move toward and find the main source, which is the amoeba releasing the most cAMP chemicals (Wikipedia contributors, 2020b).

From the scientist's findings, it can be concluded that the *D. discoideum* were faster than the pancreatic cancer cells at solving the mazes. Figure 2 from (Tweedy, et al., 2020) shows 3 different mazes in increasing complexity. The figure also shows the two cell types and time intervals of where they end up in the maze. For all 3 mazes, the *D.discoideum* cells reached these intervals and finished the maze consistently faster than the pancreatic cancer cells. For the simplest maze, the *D. discoideum* were about 39x faster than the pancreatic cells, 48x faster for the intermediate maze, and 64x faster for the complex maze. However, it is important to note that although the pancreatic cancer cells took longer to complete the maze, they had a similar success rate in finding the right path(s) compared to the *D. discoideum*. This means that a faster completion rate does not equate to a lesser success rate, and that the *D. discoideum* cells were more efficient in completing the maze faster and more accurately than the pancreatic cancer cells.

To compare the pathing of *D. discoideum* cells and pancreatic cancer cells, the scientists developed a computer simulation on what they expected to happen, which is also shown in Figure 2. For the simple maze, the computer simulation was very accurate; it predicted that most cells would always choose the right path, which was reflected in the real data. The results were about the same for the intermediate maze, showing great accuracy between the computer

simulation and the real data. The complex maze was relatively accurate, but less accurate compared to the simple and intermediate maze. This brings up an interesting point, as this shows how most of the cells are not randomly choosing which path to take. This is shown best in the complex maze simulation, as it shows for the first interval, about 50% of cells will go up, and the other 50% of cells will go down (the down path being the incorrect path). This decision was found to be the one with the most error because it was the very first decision being made; the longer the dead end, or wrong path, the harder it would be for the cells to differentiate it from the correct path. However, after the first decision, there seems to be a slight preference for which path the cells would take, despite the split being relatively close to 50% for each branch. In both the *D. discoideum* and pancreatic cancer cells, there is a slight increase in the number of cells that choose the correct path at each interval. This is especially shown in the last branch, where most of the cells choose the correct path. This slight difference hints that it is not completely random choice, and that there is a force driving the cells to down the correct path, i.e. the chemical attractant(s).

The chemical attractant thus has an important role in impacting the cell's ability to pick the correct path. More specifically, the diffusion rate of the chemical attractant has the greatest impact on the accuracy of the cell's decisions to choose the right path. The researchers used two types of chemical attractants – cAMP (faster diffusion rate – 17,500 μm/min) and LPA (slower diffusion rate – 1,580 μm/min) in a computer model to predict which would result in a greater accuracy. They predicted that using a faster-diffusing chemical attractant (cAMP) should result in more accurate decision-making by the cells, which is shown in Figure 4 (Tweedy, et al., 2020). When they performed their experiment, they created 3 mazes in which there was a "fake" reservoir and a "real" reservoir, shown in Figure 5 (Tweedy, et al., 2020). For each maze, there was a dead-end length, which led to the fake reservoir, and an approach length, that led to the real reservoir. Maze A had a short dead-end length and a short approach length (150 μm). Maze B had a short dead-end length (150 μm) and a longer approach length (450 μm). Maze C had a dead-end length and approach length of 600 μm. They predicted that shorter approach and dead-end length would yield the most error, as the cells would not have enough time to clear away the chemical attractant due to the short length of both. They also predicted that a longer approach and shorter dead-end length would result in some error, but due to the shortness of the dead-end length, the cells could correct this error and correctly identify the right path. Lastly, the predicted that a long approach length and long dead-end length would result in the least amount of error, because if the dead-end length is long, the signal of the chemical attractant will be weaker, thus it will not attract as many cells towards it. Their hypotheses were proven correct through experimental data, proving that the diffusion rate of the chemical attractant really does make a difference.

References

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