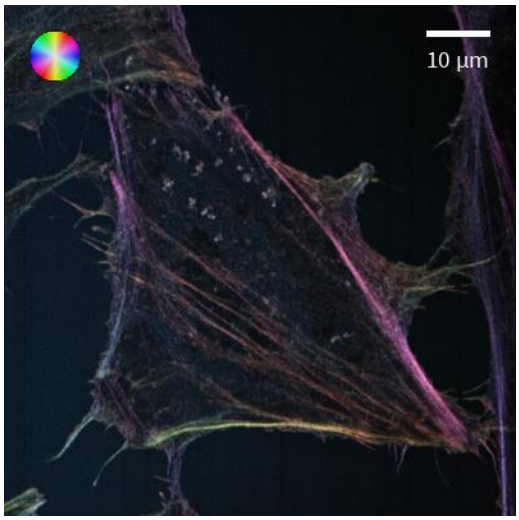
Wouter Duverger

When cells run astray

Developing light polarisation microscopy for research into cell migration diseases.

Cell migration is the process by which a cell can travel throughout the body of its own accord. It can be dangerous if this gets out of control, but it is not completely understood why or how the cell migration machinery in a cell can be damaged. For example, cell migration is the leading cause of cancer death: 90% of all cancers are only deadly when the cancer cells start spreading through the body. Issues with cell migration can also cause chronic inflammation and even birth defects.



Polarisation image of a cell's actin skeleton.

For these reasons, a lot of effort has been put into understanding cell migration better. A promising way to do that is to study *Y. pestis*. *Yersinia pestis* is a species of bacteria that caused the plague, responsible for wiping out almost a third of the European population in the 14th century. Nowadays, vaccines and treatments are available, but these bacteria are still worth a look because the way they work is quite fascinating. To kill a cell, they break down its actin network. The actin network is the cell's skeleton, and is therefore essential for many things, including its ability to migrate. Actin fibres ("bones") are composed of small actin molecules like a tower of Lego blocks. But when these are broken down, scientists have discovered that actin can also form very small structures like stars and rings all without help. If we understand how they form, we might get new insights about the cytoskeleton that help us understand cell migration better.

A single actin molecule has a diameter of about 5 nanometres (nm). To get a sense of how small that is, consider an actin molecule is about 100 000 000 times smaller than a football. And a football is about 100 000 000 times smaller than the planet Jupiter. That is the scale on which molecular biology works. Scientists often use fluorescence microscopy to locate different molecules in a cell by measuring the light intensity in different pixels. Until the 2000s, the pixel size of a microscope was not limited by the quality of its lens but by the wavelength of the light used (that gives you a pixel size of about 200 nm). Recent inventions have brought that down to about 50 nm for biological samples, which is a huge deal, but not enough to be able to resolve every single actin molecule in the cell.

In my thesis, I not only measured the intensity of light in every pixel, but also the polarisation of light at that point. That can tell us about the orientation of the actin molecules in a pixel, even if we cannot see their rotation directly. For an example of what that looks like, see the figure. Like the wavelength limit I mentioned before, there is also a limit to the "polarisation resolution". In my thesis, I have improved the angular resolution of this method, which has never been done before.

All in all, my thesis had a strong focus on implementing new microscopy methods at our lab, but I am excited about applying these to biological research and to find out what we can learn about these peculiar small actin structures in the cell skeleton.