Squares, triangles: Regardless of their form, bacteria can figure out where to split with a little help from Alan Turing

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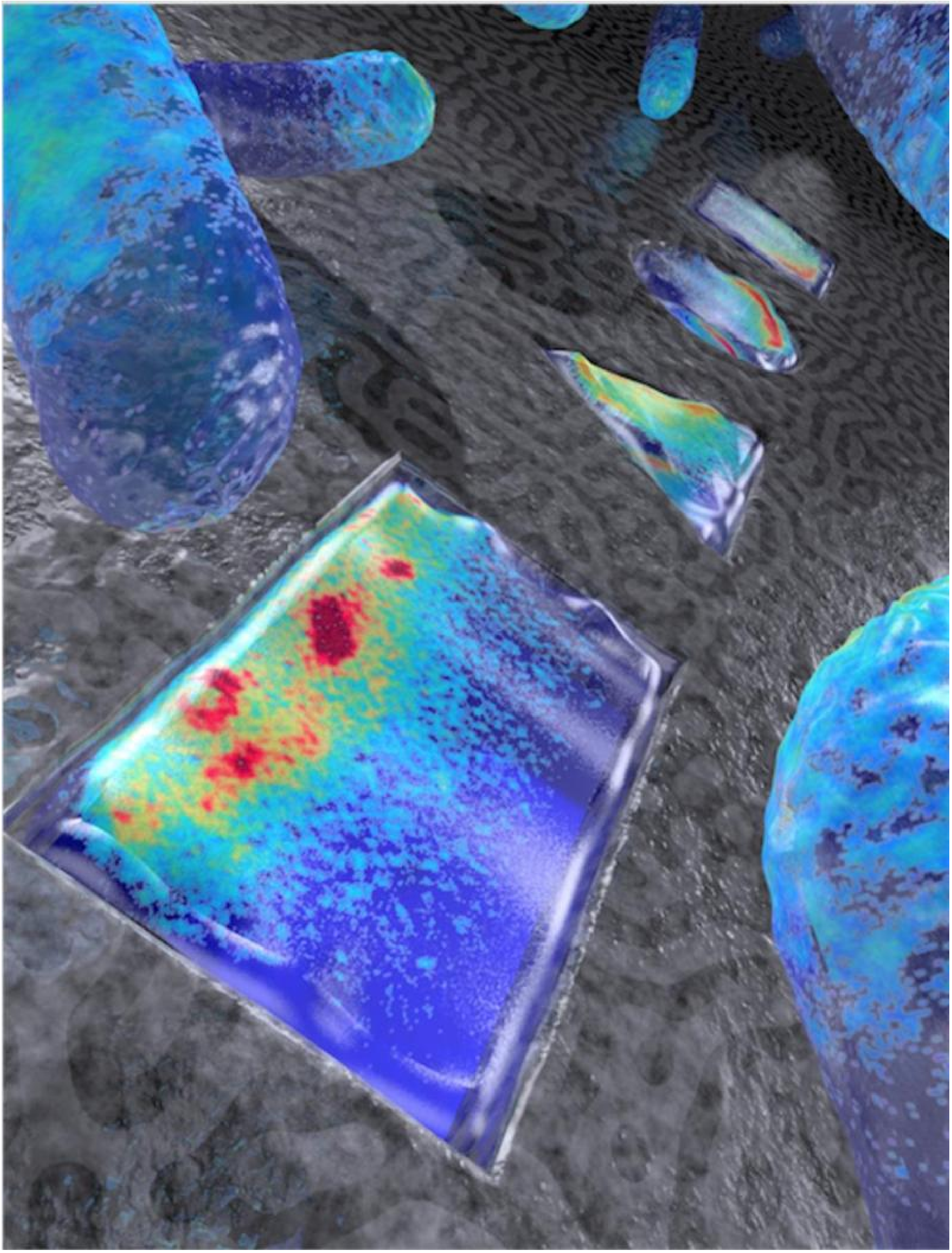


Artistic rendering live E.coli bacteria that have been shaped into a rectangle, triangle, circle, and square (from front to back). Colors indicate the density of the Min proteins that represent a snapshot in time (based on actual data), as these proteins oscillate back and forth within the bacterium, to determine the mid plane of the cell for cellular division. Credit: Cees Dekker lab TU Delft / Tremani

The E.coli bacterium, a very common resident of people's intestines, is shaped as a tiny rod about 3 micrometers long. For the first time, scientists from the Kavli Institute of Nanoscience at Delft University have found a way to use nanotechnology to grow living E.coli bacteria into very different shapes: squares, triangles, circles, and even as letters spelling out 'TU Delft'. They also managed to grow supersized E.coli with a volume thirty times larger than normal. These living oddly-shaped bacteria allow studies of the internal distribution of proteins and DNA in entirely new ways.

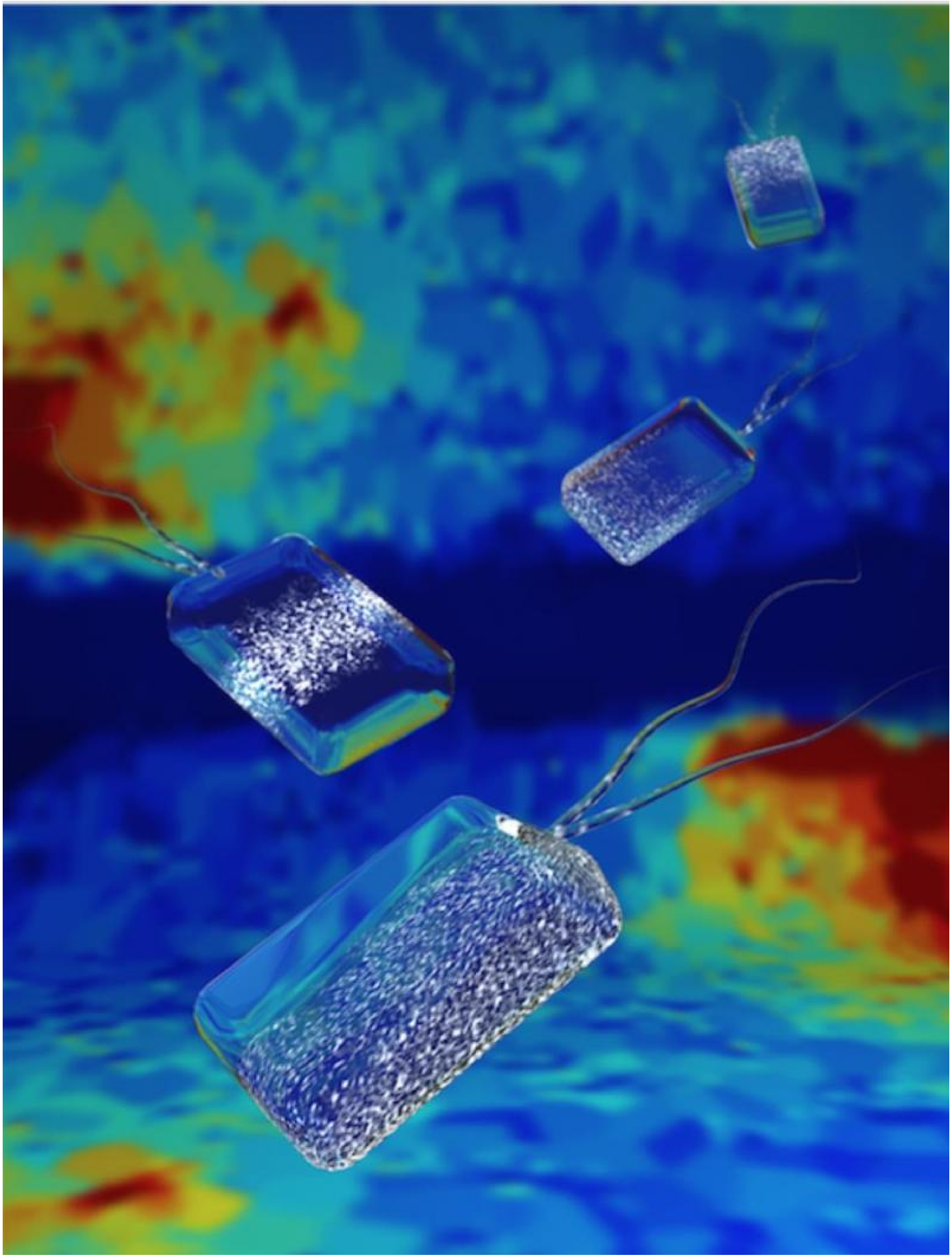
In this week's *Nature Nanotechnology*, the scientists describe how these custom-designed bacteria still manage to perfectly locate 'the middle of themselves' for their cell division. They are found to do so using proteins that sense the cell shape, based on a mathematical principle proposed by computer pioneer Alan Turing in 1953.

Cell division

"If cells can't divide properly, biological life wouldn't be possible. Cells need to distribute their cell volume and genetic materials equally into their daughter cells to proliferate.", says prof. Cees Dekker, "It is fascinating that even a unicellular organism knows how to divide very precisely. The distribution of certain proteins in the cell is key to regulating this, but how exactly do those proteins get that done?"

Turing

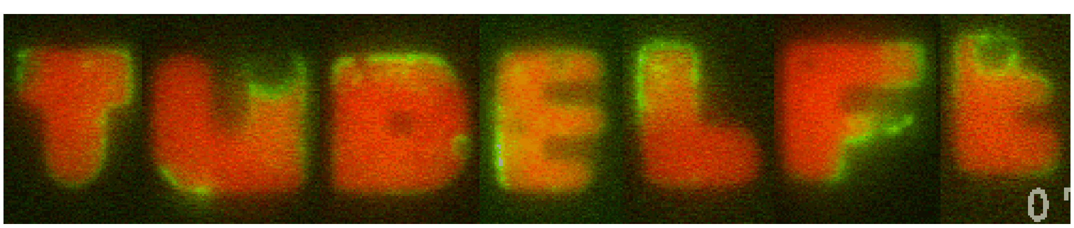
As the work of the Delft scientist exemplifies, the key here is a process discovered by the famous Alan Turing in 1953. Although Turing is mostly known for his role in deciphering the Enigma coding machine and the Turing Test, the impact of his 'reaction-diffusion theory' on biology might be even more spectacular. He predicted how patterns in space and time emerge as the result of only two molecular interactions – explaining for instance how a zebra gets its stripes, or how an embryo hand develops five fingers.



Artistic rendering live E.coli bacteria that have been shaped into rectangles. White dots indicate the Min proteins that oscillate back and forth within the bacterium, to determine the mid plane of the cell for cellular division. Credit: Erik Major, Fabai Wu and Cees Dekker lab at TU Delft

MinD and MinE

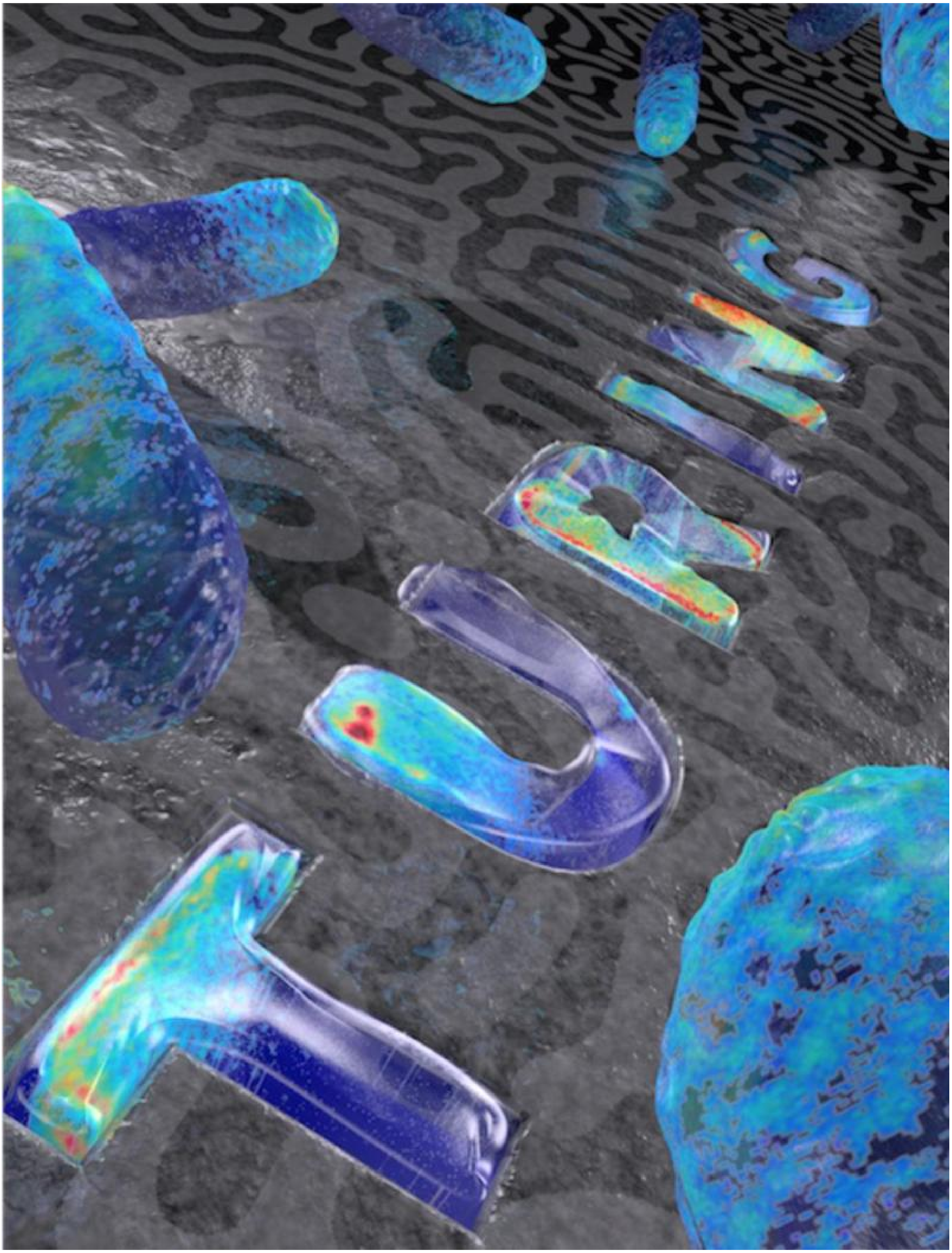
Such a Turing process also acts with proteins within a single cell, to regulate cell division. An E.coli cell uses two types of proteins, known as MinD and MinE, that bind and unbind again and again at the inner surface of the bacterium, thus oscillating back and forth from pole to pole within the bacterium every minute. "This results in a low average concentration of the protein in the middle and high concentrations at the ends, which drives the division machinery to the cell center", says PhD-student Fabai Wu, who ran the experiments. "As our experiments show, the Turing patterns allow the bacterium to determine its symmetry axes and its center. This applies to many bacterial cell shapes that we custom-designed, such as squares, triangles and rectangles of many sizes. For fun, we even made 'TUDelft' and 'TURING' letters. Using computer simulations, we uncovered that the shape-sensing abilities are caused by simple Turing-type interactions between the proteins."



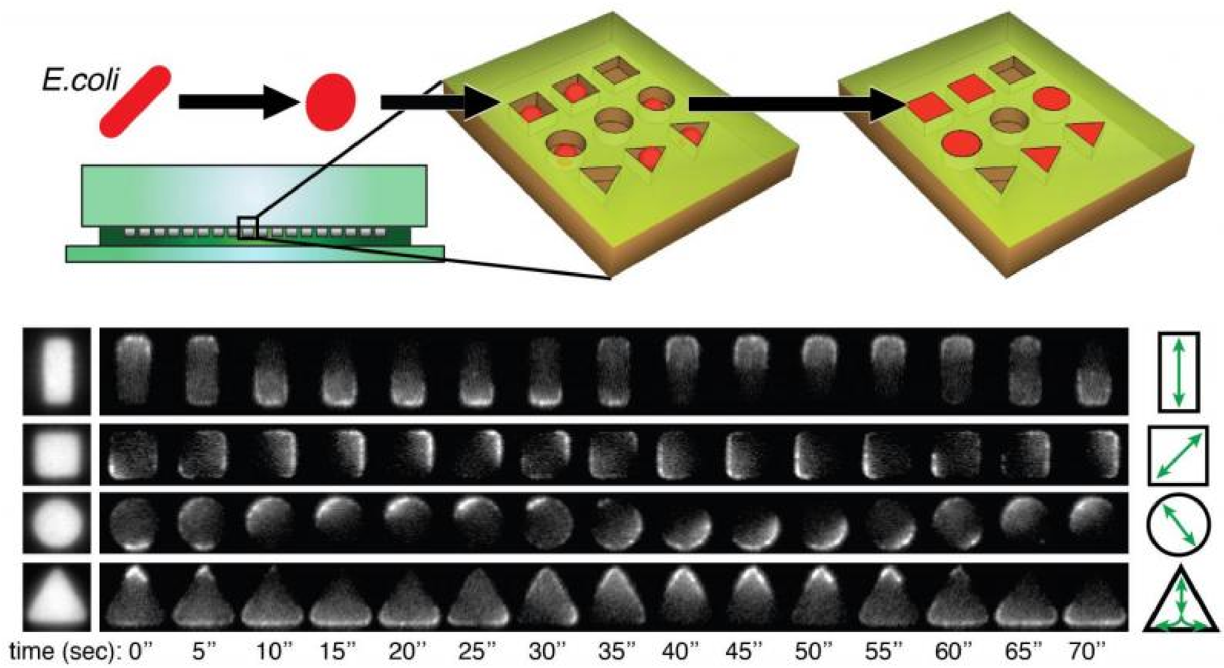
Actual data for live E.coli bacteria that have been shaped into the letters TUDELFT. The red color shows the cytosol contents of the cell, while the green color shows the density of the Min proteins, representing a snapshot in time, as these proteins oscillate back and forth within the bacterium to determine the mid plane of the cell for cellular division. Credit: Fabai Wu, Cees Dekker lab at TU Delft

Spatial control for building synthetic cells

"Discovering this process is not only vital for our understanding of bacterial cell division – which is important in developing new strategies for antibiotics. But the approach will likely also be fruitful to figuring out how cells distribute other vital systems within a cell, such as chromosomes", says Cees Dekker. "The ultimate goal in our research is to be able to completely build a living cell from artificial components, as that is the only way to *really* understand how life works. Understanding cell division – both the process that actually pinches off the cell into two daughters and the part that spatially regulates that machinery – is a major part of that."


TURING

Actual data for live E.coli bacteria that have been shaped into the letters TURING. Top image shows the cytosol contents of the cell. Bottom show the density of the Min proteins, representing a snapshot in time, as these proteins oscillate back and forth within the bacterium to determine the mid plane of the cell for cellular division. Credit: Fabai Wu, Cees Dekker lab at TU Delft



Images of E.coli bacteria in various shapes, with proteins oscillate back and forth within the bacterium to determine the mid plane of the cell for cellular division. Credit: Delft University of Technology

More information: Symmetry and scale orient Min protein patterns in shaped bacterial sculptures, *Nature Nanotechnology*. Advance Online Publication (AOP), DOI: 10.1038/nnano.2015.126

Provided by Delft University of Technology