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CELL MIGRATION

Determined to move

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The development and maintenance of our body depend on the ability of cells to move through physical barriers, such as tissues and pores. Moreover, migration through confined environments is a key feature of metastasizing cancer cells. Now, reporting in *Nature Physics*, Chase Broedersz and colleagues apply a data-driven modelling approach to find a stochastic equation of motion that describes confined cell migration, revealing qualitative differences in the migration dynamics of cancerous and non-cancerous cells.

Unconfined motility of cells on 2D surfaces can be described by persistent random motion. However, a theoretical model of confined cell migration consistent with experimental observations remains elusive. To quantitatively analyse confined cell migration, Broedersz and colleagues designed a micropattern with two square islands coated with adhesive ligands that are connected by a thin bridge, representing a constriction. "We found that single cells seeded on the adhesive islands first spread and then repeatedly hop back and forth along the bridge between the two islands," says Broedersz. By measuring nuclear trajectories, the researchers showed that the time it takes for a cell to hop across the bridge is highly variable. Therefore, the hopping behaviour of a cell can be described as inherently stochastic.

To capture these experimental observations, Broedersz and colleagues generalized the equation of persistent random motion, and described the dynamics as a function of cell position and velocity by a simple stochastic equation of motion. "A key advantage of our approach is that it enabled us to disentangle the dynamics into distinct components of cell motion: a deterministic component, which tells us what the cells do on average, and a stochastic term, which quantifies the inherent fluctuations in cell dynamics," explains Broedersz. "Using this method, we discovered that cells generate a deterministic drive to move across the constriction." Such a dynamical systems approach has been widely used to understand gene regulatory networks and signal transduction pathways in cells, but is a new way of thinking about confined cell migration.

The researchers then tested their theoretical framework for cancerous and non-cancerous cell lines. Interestingly, breast cancer cells exhibit qualitatively different dynamics to non-cancerous breast cells. Cancerous cells perform deterministic oscillations described as limit cycles in a 2D plane of cell position and velocity. By contrast, non-cancerous cells are excitably bistable: they deterministically relax to either of the two fixed points on the adhesive islands. This distinct motility phenotype could potentially provide a tool for quantifying and diagnosing the differences in the motion of different cell types.

Broedersz and colleagues would also like to apply their approach to 3D microenvironments. "Our next challenge is to develop controlled 3D environments that mimic the local properties of an actual extracellular matrix," comments Broedersz. Furthermore, they want to study the impact of the geometry of the confinement on cell migration and investigate how system-level dynamical laws are linked to the microscopic dynamics of cellular cytoskeletal components.

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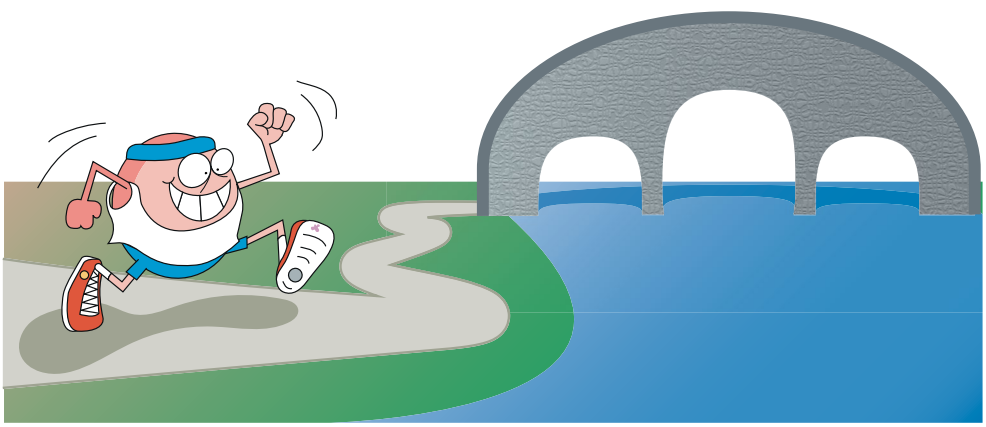

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