Surface Tension Drives Cancer Cell Migration

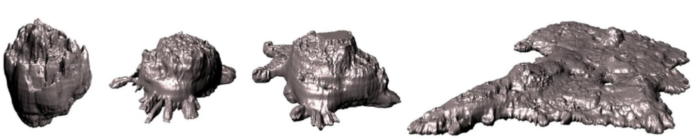
A model used to explain the wetting of drops can also describe cell migration driven by variations in a surface's stiffness, a finding that could help in understanding how cancers grow.

By **Katherine Skipper**

Cell migration drives the development of embryos, the response of our immune system, and the spread of cancer. This migration can be driven by mechanical cues, such as the stiffness of the surface over which the cells move. Scientists have long known that some cells migrate toward stiffer environments, a process called durotaxis, and that groups of cells can perform collective durotaxis even when the individual cells don't. Yet, researchers remained in the dark on aspects of what causes this response. Now results show that collective durotaxis may be driven by surface tension, a finding that may be relevant to understanding the growth of cancers [**1**].

When it comes to motion, cells—like humans—find it easier to gain traction on stiffer surfaces. This trend is thought to be behind collective durotaxis, with cells overlying a stiffer region of a surface finding it easier to move and thus easier to pull the rest of a cluster along.

To investigate this hypothesis, Macià Esteve Pallarès of the Barcelona Institute for Science and Technology, Irina Pi-Jaumà of the University of Barcelona, and their colleagues studied the behavior of clusters of cancer cells as they traveled over surfaces with different stiffnesses. Measuring the speed at which the clusters moved, they found that the speed initially increased with growing surface stiffness, before peaking and then decreasing. They also observed that the clusters took on different shapes depending on the surface: clusters on softer surfaces had outlines reminiscent of those of spherical water drops dewetting hydrophobic surfaces, while those on stiffer surfaces resembled the flat pancakes of water drops wetting hydrophilic surfaces.



Three-dimensional renderings of cell clusters on substrates of different stiffness. The cell cluster in the left image sits on the lowest stiffness substrate and the cluster in the right image on the highest.
Credit: M. E. Pallarès *et al.* [1]

The plateauing speed behavior observed for high-stiffness substrates fits with the predictions of existing models; there is a physical limit to the traction force each cell can exert, so at some point the speed stops increasing and will either level off or decrease. The models, however, don't make predictions for the shape of the cluster. Because of the similarities between the cluster shapes and drop shapes, Pallarès, Pi-Jaumà, and their colleagues turned to theories developed for drops to see if they could gain insight into what was going on.

The team developed a model for the system's behavior based on an "active" version of the so-called Young–Dupré equation, which relates the contact angle of a liquid drop on a surface to the surface tension of that drop. In this active version, opposing traction and contraction forces from the cells are transmitted across the cluster, inducing an effective surface tension, which determines the contact angle with the substrate. Using their model, the researchers showed that they could reproduce the experimentally observed cluster shapes.

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The team says that this finding shows that a wetting framework provides a way to model cell migration without having to factor in the complexities of cell–cell communication. "What we propose is that this process, durotaxis, that was defined in the field of cell biology, can be explained or accounted for quite precisely with the physics of wetting," says Xavier Trepat of the Barcelona Institute for Science and Technology and one of the researchers on the study.

"This work contributes to our understanding of the mechanisms underlying durotaxis," says Elias Barriga who studies the mechanisms of morphogenesis at the Instituto Gulbenkian de Ciência, Portugal. Roeland Merks a mathematical biologist at the University of Leiden, Netherlands, adds, "It is really elegant work."

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REFERENCES

1. M. E. Pallarès *et al.*, "Stiffness-dependent active wetting enables optimal collective cell durotaxis," **Nat. Phys. (2022).**