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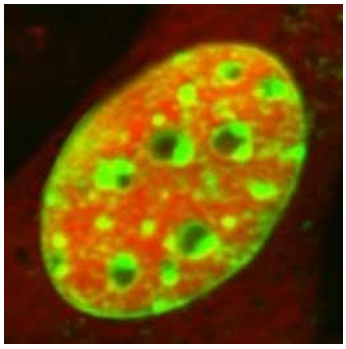
News

Cells go fractal

Mathematical patterns rule the behaviour of molecules in the nucleus.

Claire Ainsworth

The maths behind the rugged beauty of a coastline may help to keep cell biology in order, say researchers in Germany. Fractals — rough shapes that look the same at all scales — could explain how the cell's nucleus holds molecules that manage our DNA in the right location.



A cell displays chromatin (green) and a molecule used for tracking (red).

J. ELLENBERG

In new experiments, Sebastien Huet and Aurélien Bancaud of the European Molecular Biology Laboratory in Heidelberg, Germany, tracked the movement of molecules within cells in a lab dish, then compared the pattern of movement against mathematical models. Large molecules, they found, moved according to the same rules as small molecules — suggesting that their environment was truly fractal. The team reported their findings this week at the EMBO meeting in Amsterdam.

"It's a really interesting approach," says Angus Lamond, a cell biologist at the University of Dundee, UK. "It's very promising that the fractal model appears to be able to describe the [molecular] behaviour in this way."

Crowd control

To stop important biochemical reactions going awry, cells must make sure that the correct molecules meet and interact with each other at the right time and in the right place. Cells mostly achieve this by corralling molecules into cellular compartments bound by fatty membranes. However, such membrane barriers do not occur in the cell nucleus, which instead contains several distinct regions, each with different properties.

One example is the structure of chromatin, the combination of DNA, RNA and proteins that forms chromosomes. Some areas of the nucleus contain heterochromatin, in which DNA is packed tightly around proteins called histones. Other nuclear areas contain euchromatin, which is more loosely packed. Genes in euchromatin tend to be active, whereas those in heterochromatin are usually inactive. The mystery is how the cell maintains these distinct compartments of gene activity, despite the highly dynamic behaviour of the proteins that regulate DNA.

Previous work by other researchers had suggested that the sheer concentration of molecules crowded together in different areas of the nucleus can change the way they interact with each other. Chromatin itself is responsible for most of the crowding, and researchers have imagined it as a sponge, with holes allowing or blocking access to the different-sized molecules that regulate DNA. Until now, however, no one knew if this actually happened in living cells.

By tracking fluorescent molecules injected into live mouse cells in a lab dish, Huet and Bancaud found that the molecules did indeed move as if they were having to navigate obstacles. Surprisingly, when the team looked at the behaviour of different-sized molecules, they saw that large molecules were obstructed to the same degree as small ones. The result suggested that these molecules were 'seeing' the same crowded environment, regardless of scale. In other words, the environment seemed to be fractal: a system of branched channels resembling a coastline, says lab head Jan Ellenberg.

Fractal dimensions

The team then watched how different kinds of proteins moved around and bound to euchromatin and heterochromatin. Intriguingly, this suggested that the two forms of chromatin were fractal in different ways. Euchromatin seems to have a higher fractal dimension, which means it takes up more three-dimensional space, exposing a large and rough surface to the molecules interacting with it. Heterochromatin's low fractal dimension makes it flatter and smoother, with a smaller surface area.

This could help to explain how the cell tweaks the behaviour of the proteins that control DNA, says Huet. The proteins that activate a gene do so by binding to particular DNA sequences that are scattered sparsely along chromosomes. The bulky fractal structure of euchromatin could encourage proteins to hop around over large stretches of DNA, making it easier for them to scan for their target sequences. Proteins that help to keep genes inactive, by contrast, often do so by altering histones — and because histones are plentiful, the inactivating proteins need to move more systematically. The flatter fractal structure of heterochromatin should encourage them to stick close to be able to do this.

So the nucleus might be able to switch the behaviour of different areas of DNA simply by altering the fractal structure of chromatin. "This would be an indication that you can tune the way you search for these targets," says Huet, "by changing the structure of these targets."

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