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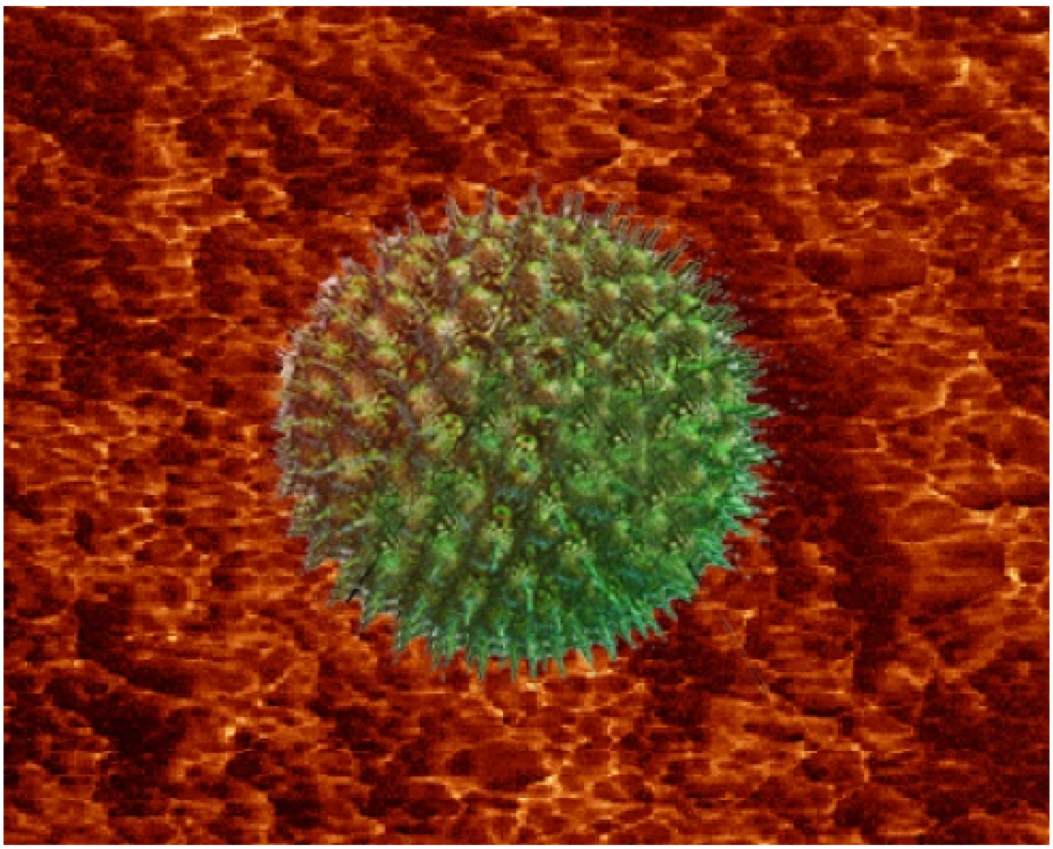
Searching for fractals may help cancer cell testing

July 6 2011, By Phillip F. Schewe



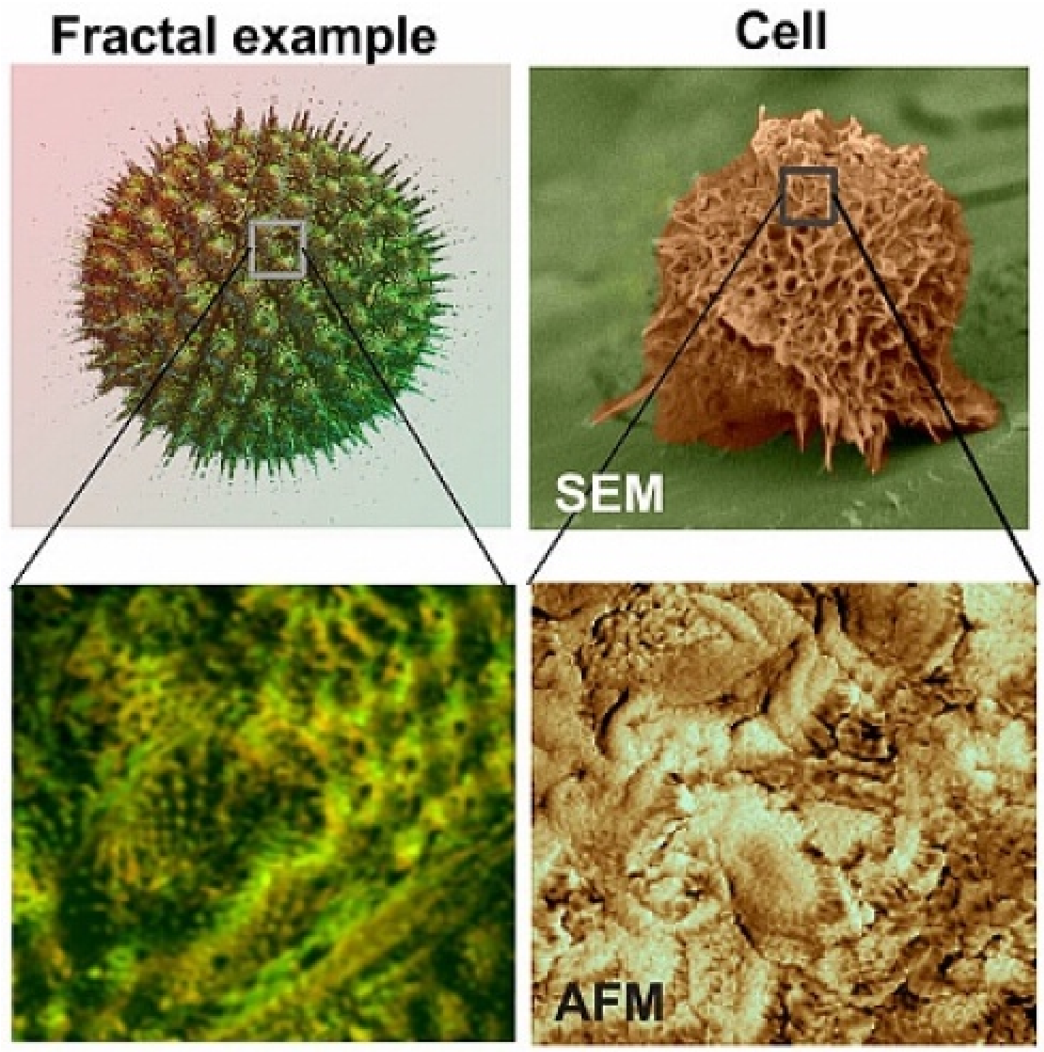
Researchers were able to determine a cell's ability to cling onto nearby objects and mapped the adhesion points of certain cells.Credit: Victor Sokolov

Scientists have long known that healthy cells looked and behaved differently from cancer cells. For instance, the nuclei of healthy cells -- the inner part of the cells where the chromosomes are stored -- tend to have a rounder surface than the nuclei in cancerous cells.

A new experiment looks at the shapes of healthy and cancerous cells taken from the human cervix and has attempted to quantify the geometrical differences between them. The research, carried out at Clarkson University in Potsdam, N.Y. finds that the cancerous cells show more fractal behavior than healthy cells.

Fractal is the name used for heavily indented curves or shapes that look very similar over a variety of size scales. For example, the edge of a snowflake, when observed with a microscope, has a lacelike structure that looks the same whether at the level of a millimeter, or a tenth of a millimeter, or even a thousandth of a millimeter. The position of galaxy clusters in the sky seems to be fractal. So does the snaking geometry of streams in a river valley, or the foliage of leaves on a tree. The shape of coastlines and clouds reveals a fractal, "self-similar" geometry. Even the "drip" paintings of Jackson Pollack are fractal.

Fractal geometry apparently also appears in the human body. The pattern of heartbeats over long intervals looks fractal. How about the geometry of cells? And could the observation of fractal geometry be used to identify cancer cells?



The above figure shows a cell imaged by SEM (scanning electron microscope) and AFM (atomic force microscope). Credit: Victor Sokolov

Igor Sokolov and his Clarkson colleagues used an atomic force microscope to view cells down to the level of one nanometer, or a billionth of a meter (one-millionth of a millimeter). Just as the needle on a record player rides over the groove of a rotating vinyl record to read out the music stored on the record's surface, so the sharp needle forming the heart of an atomic force microscope rides above a sample reading out the contours of matter just below at nearly atomic resolution.

Previous studies of cells at the microscopic level produced two-dimensional maps of the cells' surface. The new study produces not only three-dimensional surface maps of geometry. But with their atomic force microscope device the Clarkson scientists can also map properties such as the rigidity of the cells at various points on its surface or a cell's adhesion, its ability to cling to a nearby object, such as the needle probe of the atomic force microscope itself.

The Clarkson measurements show that cancerous cells feature a consistent fractal geometry, while healthy cells show some fractal properties but in an ambiguous way. The fact that the adhesive map is fractal for cancerous cells but not for healthy cells was not known before.

Being able to differentiate clearly between healthy and cancerous cells would be important step toward a definitive diagnosis of cancer. Can a fractal measurement of cells serve as such a test for malignancy?

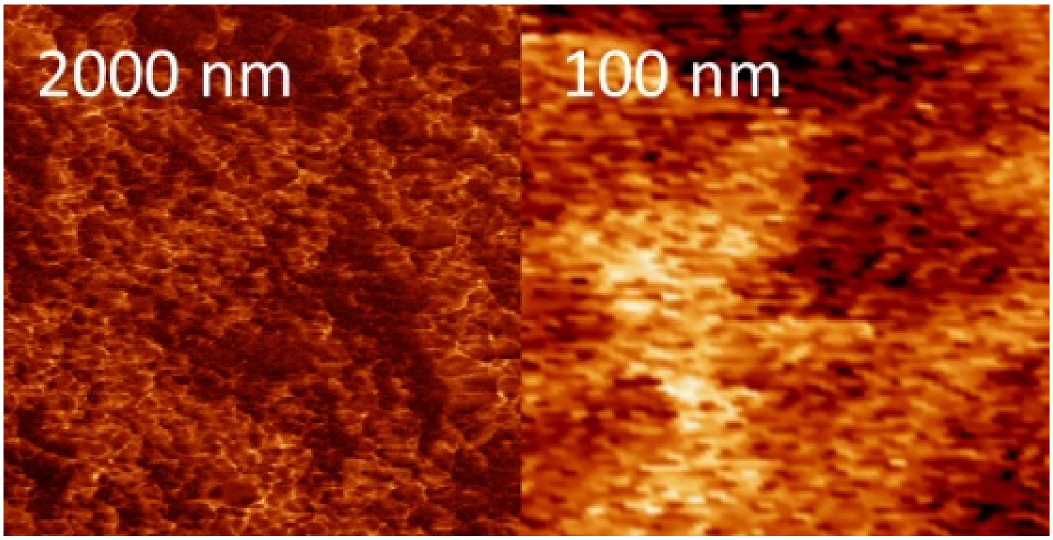
Sokolov believes it can.

"The existing cytological screening tests for cervical cancer, like Pap smear, and liquid-based cytology, are effective and non-invasive, but are insufficiently accurate," said Sokolov.

These tests determine the presence of suspicious abnormal cells with sensitivity levels ranging from 80 percent all the way down to 30 percent, for an average of 47 percent.

The fractal criterion used in the Clarkson work was 100 percent accurate in identifying the cancerous nature of 300 cells derived from 12 human subjects, Sokolov said. He intends now to undertake a much wider test.

"We expect that the methodology based on our finding will substantially increase the accuracy of early non-invasive detection of cervical cancer using cytological tests," Sokolov said.



The above image shows a side-by-side comparison of the adhesion for the surface of a cancer cell -- in this case, the cell attached to the needle probe of the atomic force microscope itself. Credit: Victor Sokolov

Sokolov asserts that physics-based methods, such as his atomic force microscope maps of cells, will complement or even exceed in detection ability the more traditional biochemical analysis carried out at the single cell level.

"We also plan to study how fractal behavior changes during cancerous transformation, when a normal cell turns into a fully developed malignant cell, one with a high degree of invasiveness and the ability to reproduce itself uncontrollably," Sokolov added.

Robert Austin, an expert on biological physics at Princeton University in N.J., believes it is important to learn more about the properties that make cancer cells lethal, such as their ability to metastasize, to invade new parts of the body. About the Clarkson paper, which is appearing in the journal Physical Review Letters, Austin said "Perhaps this is a step in the direction of connecting physical aspects of cancer cells with the biological reality that their proliferation and invasiveness is what makes them deadly."

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