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Instant insight: The soft cell

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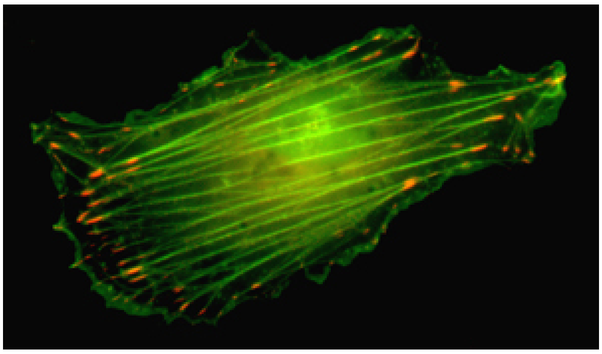
Ulrich Schwarz, soft matter researcher at the University of Heidelberg in Germany, explains why softness matters for cells

At the interface between chemistry, physics and biology, a new field of research has established itself during the last three decades or so, which by its followers is simply and lovingly called *soft matter*.

> **"Understanding soft matter is essential for many biomedical applications."**

Common examples of soft matter are liquid crystals, colloidal suspensions and polymer gels. These are all governed by weak intermolecular interactions, the key property leading to softness. The systems are widely used in technology, for example for computer displays, food, cosmetics and paint, because, in every case, it is essential that the material can be processed and manipulated easily. Cells and tissues, whose mechanical properties are determined mainly by polymer networks and lipid bilayers, also fall into this category.[1] Understanding soft matter is essential for many biomedical applications, including physiological and artificial tissue, which is a soft composite material made from cells embedded in a polymer matrix.



A cell pulls on its surroundings by contracting protein filaments (green) attached to the extracellular environment at cell-matrix contacts (red). Image courtesy of Patrick Heil and Joachim Spatz, University of Heidelberg, Germany.

The importance of softness in cellular systems does not stop at noting that the material properties of cells make them soft matter. Cells are complicated creatures, with sophisticated genetic programmes and all kinds of biochemical control structures, which react to a large variety of different signals impinging on the cell. Therefore, it came as a real surprise when a simple but somehow neglected physical parameter, the softness of the extracellular environment, was found to make a big difference to cellular behaviour and fate. Until then, cell adhesion had been studied mainly on stiff glass or plastic dishes, but using an elastic substrate for cell culture is actually neither difficult nor expensive. The standard choice here is polyacrylamide, which is available in many labs anyway, due to its use in gel chromatography.

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While the first studies with cells cultured on soft elastic substrates showed that cell morphology is quite different on soft *versus* hard substrates, very quickly it was realised that many more aspects of the life of cells are affected by extracellular stiffness, including cell migration, cell growth and division, cell death and cell differentiation. One dramatic example is the recent finding that the differentiation of stem cells into tissue-like cells resembling those from brain, muscle and bone can be accomplished simply by tuning the extracellular stiffness.[2]

If the rigidity of the environment matters so much in cell adhesion, we need to learn more about the way in which cells actually measure it. Rigidity is a passive property of the environment and cells have to actively pull in order to learn something about this aspect of their surroundings. Indeed, stiffness effects, including stem cell differentiation on soft elastic substrates, are abolished if a cell's ability to contract its environment is impaired.

"...evidence suggests that mechanotransduction, where a mechanical stimulus is converted into a biochemical signal, takes place mainly at cell-matrix contacts."

Theoretical arguments suggest that the cell uses internal stiffness to calibrate its measurement of external stiffness. A growing body of evidence suggests that mechanotransduction, where a mechanical stimulus is converted into a biochemical signal, takes place mainly at cell-matrix contacts. Here the forces can be transmitted between the cell interior and the extracellular matrix. The exact nature of the mechanosensor at the contacts is still not understood, but one attractive possibility is that the internally generated force pulls open adjacent proteins in a way that depends on extracellular stiffness. This could explain how biochemical function, physical force and extracellular stiffness are coupled at cell-matrix contacts.

It is clear that soft matter *matters* both inside and outside of the cell, and to a much larger extent than formerly appreciated.

Read Ulrich Schwarz's highlight 'Soft matters in cell adhesion: rigidity sensing on soft elastic substrates' in the special issue of Soft Matter on Proteins and Cells at Functional Interfaces.

References

1 U Schwarz, *Soft Matter*, 2007, **DOI:** 10.1039/b606409d

2 AJ Engler, S Sen, HL Sweeney and DE Discher, *Cell*, 2006, **126**, 677.