MOLECULAR BIOLOGY

Cells Like It Soft

Cells behave differently in soft surroundings than on hard glass or plastic surfaces, on which they are usually investigated. Recent experiments show that forces at contact sites between cells and their surroundings influence the cells' development and behavior. Scientists at the Max Planck Institute of Colloids and Interfaces in Golm near Potsdam have now succeeded in explaining, modeling and predicting cell behavior on and in soft materials (PNAS, August 5, 2003).

The human body consists of about ten trillion (10^{13}) cells, which can be classified into more than 200 different cell types. To function properly, two apparently contradictory principles must be fulfilled: Cells must adhere to each other and simultaneously be able to reorganize rapidly – for example, to react to infection or injury. Nature has evolved different strategies to do so: Firstly, tissue cells build up a porous network of proteins, the so-called extracellular matrix, which binds the cells to each other, but also leaves them enough room to move. Secondly, cells permanently assemble new contacts and dissociate old ones. In this way, they dynamically pull on their "anchor ground" via hundreds of contact points. The resulting forces acting on the contacts also contain information about the mechanical properties of the environment. During recent years, it has become clear that these forces are converted into biochemical signals and finally into corresponding cellular reactions.

Ulrich Schwarz, head of an Emmy-Noether junior research group at the Max Planck Institute at Golm, in close collaboration with material scientists and cell biologists from the Weizmann Institute in Israel, demonstrated some time ago that the essential link between the environment's elastic properties and biochemical decision processes in the cell are the so-called focal contacts – relatively large protein aggregates at the cell membrane that connect the inner cellular protein skeleton with the extracellular matrix.

In this study, it was shown that the stronger the cellular force exerted on the surroundings at a focal contact, the larger the focal contact itself. In another study, the same group showed that external forces exerted on the cell also lead to enlarged focal contacts – a further indication that physical forces at focal contacts trigger increased protein aggregation and influence biochemical processes in the cell.

Using the mechanosensory function of focal contacts, cells gain information about the elastic properties of their surroundings. Particular cell types show optimal physiological behavior in an environment with relatively small stiffness – i.e. under conditions resembling those naturally occurring in the body. Furthermore, many cell types react in a characteristic way as soon as the elastic properties of their environment change. As a result, physiological cal processes in cells that depend on the elastic properties of their surroundings – such as maintaining the integrity of the connective tissue, wound contraction or cellular movement, in particular concerning cancer cells – can only be fully understood and eventually influenced if it is known how forces at focal contacts affect their behavior.

Schwarz and his coworker Ilka Bischofs have now succeeded in developing a theoretical model that, for the first time, can predict the behavior of a cell in soft materials. This model is based on two experimental findings. Cells preferentially show "normal" behavior in soft surroundings and orient themselves in the direction of largest effective stiffness. In other words, they seem to seek a stronger hold – probably because cells can then build up higher forces at their focal contacts.

Using calculations in elasticity theory, the researchers could predict how a cell reacts in certain situations, depending on external conditions. According to this model, in a soft environment, individual cells close to a rigid surface preferentially orient themselves perpendicular to the surface. In contrast, at freely deformable surfaces, individual cells orient themselves parallel to the surface, since in this case a perpendicular orientation would appear to be softer. In addition, the model predicts that, due to deformation of the elastic substrate located between them, several cells will preferentially line up in strings. In an external strain field, the cells strings will align with the direction of external stretch.

These predictions for cell orientation and positioning are in excellent agreement with numerous experimental observations that now find a unifying basis with the new theory. Many of the model's predictions are also new and need to be tested in future experiments. However, it is already clear that Bischofs' and Schwarz's model might lead to important applications in biotechnology and medicine – for example, concerning the behavior of cells in artificial tissues or close to interfaces to implants. ●

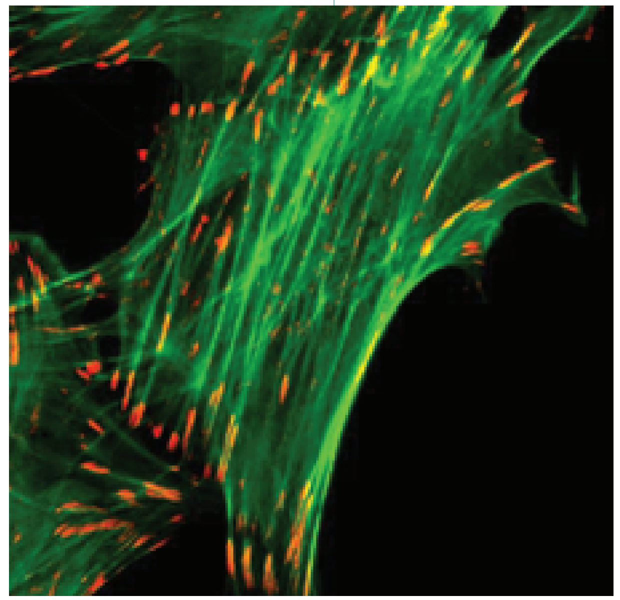
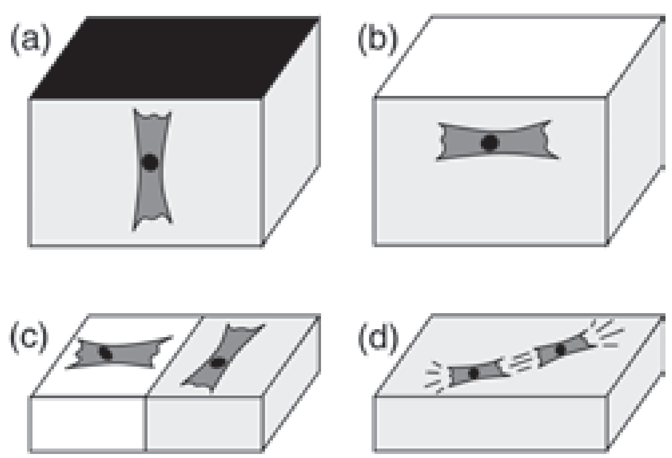


PHOTO: WEIZMANN INSTITUTE

View of a fluorescently labeled fibroblast cell: Bundles of actin filaments (green), which are part of the cell's inner skeleton, end at focal contacts (red) that connect the cell to its surroundings.



PICTURES: MPI FOR COLLOIDS AND INTERFACES

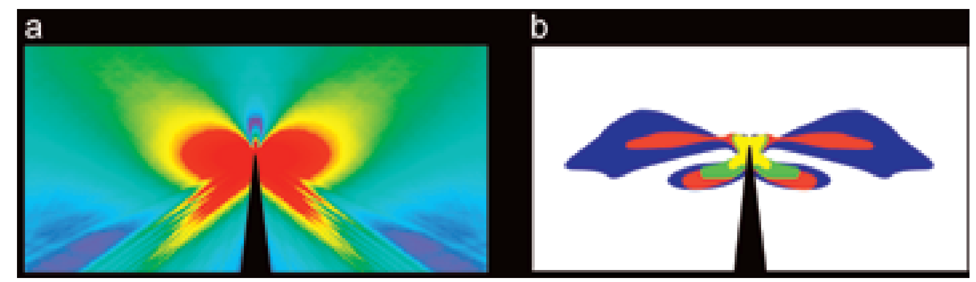
Predicting the cell's behavior in soft surroundings: (a) Cells prefer the direction of maximal effective stiffness in their environment, and so for example, orient themselves perpendicular to a clamped surface. (b) A parallel orientation is optimal with free surfaces. (c) A corresponding pattern arises on an elastic substrate close to a boundary between a soft (left) and rigid (right) region. (d) Several cells preferentially line up in strings because each cell stiffens the elastic environment at its ends.

@ Further information from:
DR. ULRICH SCHWARZ
Max Planck Institute
of Colloids and Interfaces, Golm
Tel.: +49-331/567-9610
Fax: +49-331/567-9602
e-mail: Ulrich.Schwarz@
mpikg-golm.mpg.de

MATERIAL SCIENCES

Supersonic Cracking

In brittle materials, cracks can spread at above the speed of sound – which is a lot quicker than classical theory allows. Scientists at the Max Planck Institute for Metal Research in Stuttgart and the IBM Almaden Research Center in San José (USA) have come to this conclusion on the basis of extensive computer simulations. Their studies can help to improve understanding of how cracks originate and propagate, which is important both for conventional technologies, such as in airplanes or spacecraft, as well as for novel nanoscale science and engineering (NATURE, November 13, 2003).



PHOTOS: MPI FOR METAL RESEARCH

Zone with high energy flow to the crack and extension of the hyperelastic regions. Image (a) shows the distribution of the local energy flow near the crack. The red-colored region defines a characteristic longitudinal scale for energy transport. Image (b) shows regions where material behavior is non-linear (hyper-elastic).

Glass breaks, steel tears and rubber bursts: materials can fail under stress in a variety of ways. Calculating when this happens is one of the most important tasks of construction or design engineers, who mostly still employ calculation procedures based on the classical physics of the so-called continuum: The calculation includes only the macroscopic material properties of the construction components under static or dynamic stress – and the microstructure or the fact that materials are made out of atoms is ignored. It has, however, now become clear that this "continuous" way of studying materials is not adequate – and that it is rather more important to understand a material's properties and behavior at the atomic level in order to assess its suitability for specific purposes. But when it's about dimensions in micrometers or even in the nanometer range, there is no longer any direct experimental approach to material-related phenomena: Computer simulations – which are often challenging – are the only way of finding out how materials respond in these tiny dimensions. Researchers at the Max Planck Institute for Metal Research in Stuttgart and the IBM Almaden Research Center have now used this approach to analyze the dynamics of cracks in brittle materials – and have established that conventional theories on the dynamic propagation of cracks neglect an important aspect: the fact that the elasticity of a solid depends on the extent of its deformation; the reason why metals become soft and, in contrast, polymers become hard when they are stretched to the limit of their strength.

Huajian Gao, Director at the Max Planck Institute for Metal