tions and the ordering of localized atoms will be antiferromagnetic, like the crystal created by the Munich group when $\varphi = 90°$. Absorption probe experiments by the Paris group showed that the vibrational energy levels were independent of direction in the plane, indicating that the potential wells are circularly symmetric. The measured potential depths varied as $\sqrt{Intensity/Detuning}$ in good agreement with theory.

The Paris group also demonstrated three-dimensional crystallization using four traveling-wave fields in a tetrahedral geometry. Three of the fields were linearly polarized in the plane perpendicular to the direction of propagation of the fourth beam, which was circularly polarized. The fourth beam breaks the symmetry between σ_+ and σ_- potential wells due to the other three beams. In particular, if the fourth beam is σ_+ polarized, the σ_+ wells will be deeper. In this case, the potential minima are located on a body-centered-cubic lattice, and the trapped atoms are primarily in the $m_j = J$ state. Thus, unlike the one- and two-dimensional cases which were antiferromagnetic, the three-dimensional crystal is analogous to a ferromagnetic medium. The broken symmetry between the three dimensions also results in an asymmetry in the potential wells. The crystals were again probed using absorption, but in this case the vibrational energy levels varied with direction because of the ellipsoidal shapes of the potential wells. Finally, the Munich group reports that they also have preliminary results of three-dimensional crystals.

The wealth of experimental possibilities created by these two- and three-dimensional crystals is yet to be explored. The density limits and role of atom-atom interactions are still unknown. In addition, transferring this two-dimensional order to a solid surface would present considerable experimental challenges, but may offer very narrow dots that can be used for lithography. The possibility of confining several cold atoms in a single potential offers the hope of observing interesting collective effects and may present a suitable system for observing Bose-Einstein condensation.

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A New Twist on Integrins and the Cytoskeleton

Steven R. Heidemann

The movement, shape, and polarity of cells depend on the close cooperation of proteins outside the cell [the extracellular matrix (ECM)], proteins on the surface of the cell (cell adhesion molecules, that is, integrins), and proteins inside the cell (the cytoskeleton). In this issue of *Science*, an elegant biophysical study by Wang and co-workers (*1*) confirms a mechanical connection among ECM components, integrins, and the cytoskeleton, which are responsible for changes in cell form and function. Indeed, their new result suggests that integrins are part of a group of cooperating molecular elements that are organized according to tensegrity (tensional integrity) architecture, the building concept of R. Buckminster Fuller that underlies geodesic domes.

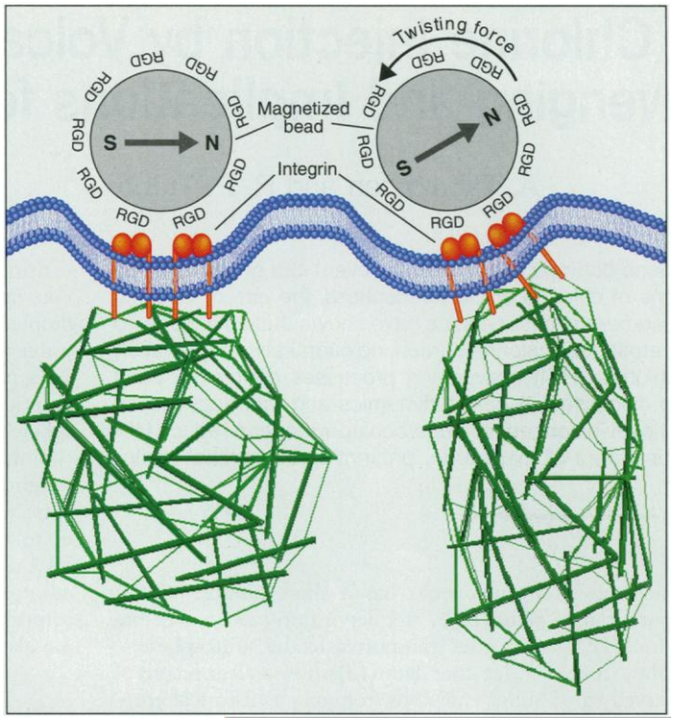
Cultured cells lose their characteristic flattened shape and become round when their adhesion to the culture dish is loosened by the protein degrading enzyme trypsin or when their cytoskeleton is disrupted by drugs. Current thinking about this interplay between cell adhesion and the cytoskeleton is strongly influenced by the structure of focal adhesions (*2*). These regions of very close contact (approximately 15 nm) between the plasma membrane of cells and their underlying substratum appear to represent direct mechanical linkages from the outside to the inside of the cell. In the now classic model, proteins of the ECM, including collagen, laminin, and fibronectin, bind to the extracellular region of a plasma membrane receptor, an integrin. Integrins are a superfamily of integral membrane proteins that are heterodimers of α and β subunits (*3*). Many integrins have an affinity for the amino acid sequence arginine-glycine-aspartate (RGD) in their ECM ligand. The integrins also have a small cytoplasmic region that binds to elements of the actin cytoskeleton: Immunofluorescent images of focal adhesions show co-localization of integrins with the termini of actin bundles and with actin-binding proteins. Also, integrins bind in vitro to actin-binding proteins such as talin and α-actinin (*2*, *3*).

These biochemical studies have been advanced considerably by the work now reported by Wang and co-workers. They have used a sophisticated application of magnetometry, a method for investigating the mechanics of cells and cytoplasm that goes back at least as far as Crick's only (I believe) experimental report (*4*). Magnetic microbeads were coated with different ligands and used in combination with external magnetic fields to exert controlled mechanical stresses on integrin receptors without changing the shape of the cell. For example, beads coated with synthetic RGD peptides or antibody to the b_1 integrin subunit would be expected to bind specifically to integrins, whereas beads coated with acetylated low density lipoprotein (LDL) or bovine serum albumin (BSA) would bind to other membrane proteins not involved in cell adhesion. The beads were allowed to attach to capillary endothelial cells in culture dishes. Earlier experiments from the same lab showed that fibronectin, an RGD-containing ligand for several integrins, regulates the assembly of these cells into blood vessel–like tubes (*5*). The attached ferromagnetic beads (which remain magnetized after withdrawal of an external magnetic field) were magnetized in a uniform dipole orientation by application of a strong, very brief, homogeneous magnetic field. A second, longer and weaker homogeneous magnetic field was then applied perpendicular to the first, thus producing a mechanical twisting force. The extent of bead rotation was measured by an in-line magnetometer that detected the original magnetic field vector that persisted during twisting. In the absence of any mechanical restraints on the beads, the second pulse would be expected to completely reorient the beads to the new magnetic field, that is, twist the beads through 90° and completely eliminate the original magnetic field vector. Indeed, beads coated with BSA or LDL twisted nearly this much. In contrast, beads coated with RGD peptide or antibodies to integrin twisted through less than 30° at the highest reported forces, indicating a significant mechanical constraint on the twisting of integrin-bound beads. The constraint is evidently due to cytoskeletal linkages to integrins. Addition of poisons directed against the three principal cytoskeletal filaments—microfila-

The author is in the Departments of Physiology and Microbiology, Michigan State University, East Lansing, MI 48824.

ments, microtubules, and intermediate filaments—reduced the mechanical constraints, and combining the drug directed against microfilaments (actin) with one of the other drugs virtually eliminated the resistance to twisting.

An exciting feature of this method is that it provides the opportunity to quantitatively investigate the molecular mechanics of the cell adhesion—cytoskeleton interaction. In this first report of this technique, the authors investigate the most fundamental relation in the mechanics of any material, the ratio between the force (stress) and the resulting deformation (strain). This relation is a measure of the stiffness of the material and is familiar as the spring constant of springs and other elastic solids. Unlike most nonbiological materials, the integrin-attached beads showed progressively increased resistance to twisting with increasing force. That is, the integrin-cytoskeletal complex continually stiffens with stress, as do other biological structures such as mesentery, lung tissue, and relaxed muscle.



Twisting beads. Magnetic beads attached to integrins are restrained by the cytoskeleton in their twisting response to a magnetic force field. The relationship between twisting force and the extent of bead twisting suggests tensegrity structure in the cytoskeleton. [Based on illustration by Deborah Moulton]

The research presented in this new report comes from the lab of Ingber, who has long championed the view that cells reflect tensegrity architecture (6), in which a continuous network under tension is supported by discrete compressive struts. This complementary force interaction among structural elements underlies the architecture of tents, domed stadiums, and the increasingly familiar stick-and-wire toy models and sculptures. The authors use one of the toy models to show that the stress stiffening of the integrin-cytoskeletal complex is consistent with tensegrity structure. In addition to providing a possible explanation for the mechanical response of cells and tissues, this building principle can help explain unusual cell shapes (7), morphogenetic changes (5), control of cytoskeletal assembly (7, 8), and nuclear responses to cell shape and attachment (9).

The notion of cellular tensegrity, however, does not meet with universal acclaim; many find it too tidy. Yet the cytoskeleton of many cell types exhibits the basic tensegrity force interaction: An actin network under tension is supported, in part, by compression of microtubules (6, 7, 10). At the same time, mechanical force has attracted increasing attention as a quite general regulator of cell function. Among many possible examples: The initiation and elongation of neural axons can be regulated directly by tension (11). Vascular endothelial cells exhibit a complex pattern of responses to shear stress (12). Differentiating myoblasts in culture respond to experimentally applied forces by forming well-organized muscle with parallel arrays of fibers and tendons (13). Mechanical force also affects classical signal transduction mechanisms such as second messengers and ion fluxes (14). This wide array of cytoplasmic responses to external forces fits well with tensegrity architecture, in which the structural elements are interconnected in a global fashion; stretch one part and the force is transmitted throughout the entire structure.

Regardless of one's enthusiasm for the cellular tensegrity hypothesis, however, it currently lacks the sort of molecular specificity we have come to expect in understanding cellular mechanisms. Our understanding of cytomechanics has come from pushing and pulling on and in whole cells or on molecules and mixtures in vitro. Often, cytomechanical inferences have been derived from experiments without any mechanical measurements, such as observations of cytoskeletal changes. By directly investigating the mechanics of an identified protein in the living cell, the method used by Wang and colleagues (1), and others like it, will open the field by providing more molecular details for both the established and more speculative aspects of cytomechanics. Are the other basic types of adhesion molecules—cadherins, selectins, and immunoglobulin-like proteins (15)—also connected to the cytoskeleton? A simple change of bead treatment should answer this question. Which of the many actin-binding proteins play a mechanical role? Talin, for example, binds rather weakly to integrins in vitro; is it truly a mechanical link? One can easily imagine the current method being combined with specific probes for actin-associated proteins to answer such questions. With the exception of stretch-sensitive ion channels, it is unclear how mechanical force is transduced into a biochemical signal. Integrins, for example, are increasingly seen as chemical signal transducers (16). Is signal transduction related to the cell adhesion function of integrins and are cytoskeletal forces involved? The answer might be obtained by twisting integrin-attached beads and measuring protein phosphorylation in the presence and absence of cytoskeletal poisons. In any case, cytomechanics and detailed biochemistry have flirted with one another long enough. The current report can be taken as a serious proposal of marriage.

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