Nanotechnology Muscles In

"Nanotechnology is an explosive technology that will see far greater application in biological research." So says Gerald Pollack at the Bioengineering Center of the University of Washington (Seattle, WA). Pollack and his colleague, Mark Fauver, along with other collaborators, have developed a nanofabricated force transducer to measure and understand the forces associated with muscle contraction. They suspend a rabbit myofibril, the smallest unit of skeletal muscle that still retains a structural organization characteristic of whole muscle, between a micromotor and the force transducer. The tip of the myofibril is expanded so that its striation pattern can be observed through a microscope (Figure 1). The force transducer is a lever made of silicon nitride, the deflection of which is detected by a photodiode array. The nanofabrication of the levers occurs at the Cornell University National Nanofabrication Facility (NNF, Ithaca, NY) using a semiconductor wafer-like manufacturing process. The devices (for which patents have been filed) are very cheap; several thousand can be manufactured for a few thousand dollars.

Pollack's work measuring the striation pattern during tension development and shortening of the myofibril has led to a rethinking of long-held views of muscle contraction. It has shown, for example, that less tension is developed when the myofibril is stretched out than when it contracts to its natural length. Being able to observe submicron structures such as the striations in the myofibril, there is little indeterminate about their spacing. Moreover, because the myofibrils are in series, their tension is similar and is measurable by the nanofabricated force transducers. As Pollack says, "By knowing how force development varies with striation spacing, and by resolving other of the field's controversial issues, our group has been able to narrow the possible mechanisms of contraction."

The next step in Pollack's work is to measure forces in individual molecules. This means working with a single actin filament of 7 nm in diameter (the myofibrils are about 1 μm in diameter) and with finer levers that will enable the detection of subpiconewton forces. The goal, according to Fauver, is to "measure the unitary events of contraction in a definitive, unambiguous manner, and thereby help resolve the underlying contractile mechanism with the use of nanotechnology."

The levers have utility that goes beyond research. Currently, a separate group at the Bioengineering Center of the University of Washington is developing devices to measure normal and shear stresses *in vivo* and to assist in refining prostheses design. Such devices could play key roles in measuring and monitoring other muscles in *in vivo* settings.

—M.M.

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Other work combines chemical and biochemical approaches to achieve organization at the nanoscale. In work aimed at developing biomimetic biosensors,[6] Jean-Marc Laval's group at the University of Compiègne (Compiègne, France) created a synthetic lipid bilayer by first putting a self-assembling octadecyl-trichlorosilane monolayer onto the surface of a porous aluminium oxide electrode and then depositing a phospholipid monolayer on top of that. The bilayer hosted a range of hydrophobic electron transfer molecules, such as ubiquinone and plastiquinone, and enzymes, such as pyruvate oxidase.

Nanotechnology in Basic Biology

Progress in nanotechnology has meant that there is now almost no clear border between (bio)chemistry and physics. Biotechnologists have depended, to a great extent, both in research and in the development of products, on their ability to constrain macromolecules. One only has to think of affinity chromatography, ELISA, and solid-phase synthesis or sequencing to understand how useful it is to be able to restrict the position of just one macromolecule in space. Now, through nanotechnology, biotech-nologists can start to control two (or possibly more) interacting entities. We can bring together two molecules, not by letting them wander randomly around in the same general three-dimensional space (as we do when mixing reagents), but by physically increasing their proximity.

This will bring a revolution in biochemistry. Nobody currently works with one molecule or one interaction (except those undertaking virtual biochemistry *in silico*). But through AFM, for instance, it would be possible to arrange and study directly the contact between a ligand and a protein structure. Traditional approaches in studying protein-ligand binding may become obsolete.

Another way of providing a direct link between interacting macromolecules is through the exploitation of the mechanical properties of some biological molecules. Consider, for instance, the work done by researchers at Stanford University School of Medicine (Stanford, CA) and King's College London (London, U.K.). They have been able to measure the nanometer displacements and piconewton forces involved when a single actin filament, stretched between two latex beads held in optical traps, interacts with a single (or very few) immobilized myosin molecule[7] (See also "Nanotechnology Muscles In"). Beyond what it tells us about the actin-myosin interaction, this study was important because it demonstrated coupling between a mechanical process and a biochemically well-defined process.

Nanotechnology can also provide considerable insights into catalysis. In 1993, a group at the University of Liverpool (Liverpool, U.K.) used STM to study the oxidation of carbon monoxide at the surface of an oxygen-covered rhodium surface[8] (the process is related to the catalytic removal of carbon