SCIENCE NEWS of the week

3-D Atomic View of Muscle Molecule

Scientists have known for decades that two proteins called actin and myosin interact to make muscles contract. In muscle cells, these proteins bundle into filaments, with myosin overlying actin and pulling itself along actin to shorten muscle fibers. Myosin obtains the chemical energy needed to fuel this shortening by breaking phosphate off adenosine triphosphate (ATP) molecules.

Now, researchers can take an in-depth look at how this molecular motor transforms chemical energy into motion, says Ivan Rayment, a crystallographer at the University of Wisconsin-Madison. In the July 2 SCIENCE, he, Wisconsin colleague Hazel M. Holden, and their collaborators present a detailed, three-dimensional picture of myosin. They then combine their findings with earlier results from the Scripps Research Institute in La Jolla, Calif., and from the Max Planck Institute for Medical Research in Heidelberg, Germany. "What this work does is tie [previous results] together," says Rayment.

The synthesis confirms current ideas about actin and myosin and fills in some missing details, comments Edwin W. Taylor of the University of Chicago.

"Now you have the 3-D structures of the two major players [actin and myosin]," adds Ralph G. Yount, a protein biochemist at Washington State University in Pullman. "You can begin to figure out how they work on a molecular basis."

Until now, the actual structure of the myosin molecule had eluded scientists, Rayment says. Try as they might, they could not grow crystals of this very soluble protein, a necessary first step for doing X-ray diffraction studies to pinpoint the location of the atoms in the myosin molecule.

Then, a decade ago, Rayment modified dissolved myosin by adding methyl side groups to some of the amino acids that make up the protein, thus obtaining crystals. He and his colleagues spent the next six years working out a way to make each myosin molecule in the solution take up the same number of methyl side groups in the same places to ensure that a pure crystal formed.

Myosin consists of two interwoven protein fragments, or "heavy chains." Each fragment has a fat "head," with two smaller peptide chains attached, and a tail. Rayment's group made crystals of single head fragments.

The new data confirm that one side of myosin's head contains a binding site for ATP. Actin attaches on the opposite side of the head. The structure also shows that the head's two peptide "light chains," each about 150 amino acids long, cling tightly to the head. Unexpectedly, however, the amino acids in the head also fold to form a cleft along the middle.

Rayment et al./Univ. Wis.

Computer graphic shows myosin fragment's light chains (yellow, magenta) wrapped tightly about its heavy chain "head," which contains an ATP binding site (green) separated by a horizontal cleft from where actin attaches at lower right corner.

"You can now see how the atoms can be interacting and what changes are taking place to [cause] tension," says Richard W. Lymn, a muscle biophysicist at the National Institute of Arthritis and Musculoskeletal and Skin Diseases in Bethesda, Md.

Rayment and his colleagues think that when ATP attaches, it causes the narrow cleft to widen. This motion splits the binding site for actin and loosens myosin's hold on actin. Then myosin bends, encircles the ATP, and chops off a phosphate. This causes yet another shift in myosin's structure so actin can reattach.

"[This shift] closes the cleft, squeezes out phosphate, and the molecule pops open," Rayment explains. The initial bending strains the molecule — like stretching a rubber band. The reclosing of the cleft releases that strain, and the rebound of about 5 nanometers causes myosin to slide over actin, creating the "power stroke" for contraction. The light chains extend the distance of this shifting in the cleft, making a longer lever, he adds.

"It's landmark research," comments Yount. "It's the sort of thing that will wind up in every biology textbook."

— E. Pennisi

Pesticides in produce may threaten kids

Many fruits and vegetables sold in the United States contain one or more pesticides. In general, these residues are low and within concentrations allowed by law. However, because the foods they taint make up such a large proportion of a young child's diet, children may be ingesting unsafe quantities of toxic agricultural chemicals. Or so conclude a pair of reports issued this week.

"If you eat, you eat pesticides," asserts Richard Wiles of the Environmental Working Group (EWG) in Washington, D.C., a new, nonprofit spinoff of the Center for Resource Economics.

For *Pesticides in Children's Food,* the report EWG issued Monday, Wiles examined previously unpublished residue data on 17,000 food samples tested at Food and Drug Administration (FDA) laboratories nationwide and 3,000 samples analyzed for supermarkets by independent labs. He then coupled these data — all for foods available between 1990 and 1992 — to federal estimates of children's consumption patterns and compared the resulting exposure estimates with health-risk data.

The analysis suggests that more than one-third of a child's lifetime exposure to and cancer risk from some pesticides will accumulate by age 5. Indeed, by his or her first birthday, the average American child's exposure to some carcinogenic pesticides will exceed the federal government's lifetime acceptable-cancer-risk threshold, calculated to result in one malignancy in every million individuals.

Though Wiles says this exposure is "completely unacceptable," he says the risk involved is small and does not warrant avoiding fruits and vegetables.

"We're not talking about a food panic here," agrees Philip J. Landrigan of Mt. Sinai School of Medicine in New York City, chairman of a National Academy of Sciences (NAS) panel that reviews related issues in another report issued this week. "Parents should continue to emphasize fruits and vegetables in their children's diets."

However, the NAS panel's investigation of federal practices to limit pesticide contamination of food indicts the regulatory status quo.

The main problem, Landrigan says, is that the government has taken a "one size fits all approach," basing pesticide-risk evaluations on the diet of a typical adult. But "children differ substantially from adults, not only in size but also in metabolism and in what they eat — and therefore in the pesticides to which they are exposed," he points out. To account for that, he says, "basic changes are needed in the current regulatory system."

To improve regulations, the NAS committee advocates that the government:

- conduct food consumption surveys of children to establish diets typical of spe-