Jelinski/Cornell

Artificial Spider Silk

By RICHARD LIPKIN

The gold-colored dragline silk of the spider Nephilia clavipes *encircles these paper rings.*

Scientists vie to synthesize the precious strands of the golden orb weaver

"In the spring of 1881 I was a few feet distant from a couple of individuals who were quarreling," George Emery Goodfellow, a physician in Tombstone, Ariz., scribbled in his diary more than a century ago.

"They began shooting."

Two bullets pierced the breast of one gunman, who staggered, fired his pistol, and crumpled onto his back.

Examining the body, Goodfellow found that, despite fatal injuries, "not a drop of blood had come from either of the two wounds.

"From the wound in the breast a silk handkerchief protruded," he noted. But when he tugged on the handkerchief, he found the bullet wrapped within it. Evidently, the bullet had torn through the man's clothes, flesh, and bones but had failed to pierce his silk handkerchief, Goodfellow recounted in his "Notes on the Impenetrability of Silk to Bullets."

Fascinated by this, he documented other cases of silk garments halting projectiles—including one incident in which a silk bandanna tied around a man's neck kept a bullet from severing his carotid artery. "The life of this man was, presumably, saved by the handkerchief," Goodfellow wrote.

The strength, toughness, and elasticity of silk continue to intrigue scientists, who wonder what gives this natural material its unusual qualities. Finer than human hair, lighter than cotton, and—ounce for ounce—stronger than steel, silk tantalizes materials researchers seeking to duplicate its properties or synthesize it for large-scale production.

Visions of wear-resistant shoes and clothes; stronger ropes, nets, seatbelts, and parachutes; and rustfree panels and bumpers for automobiles all dance through researchers' minds. So do improved sutures and bandages, artificial tendons and ligaments, and supports for weakened blood vessels. Soldiers and police long for bulletproof vests of spider silk.

While many insects secrete silks of varying quality, the dragline silk of the golden orb-weaving spider, *Nephila clavipes*, has attracted the most scientific attention. Researchers marvel at its high tensile strength and ability to stretch without snapping. It is tougher, stretchier, and more waterproof than the silkworm's strands used today in fine garments.

Spider dragline silk "exhibits a combination of strength and toughness unmatched by high-performance synthetic fibers," says David A. Tirrell, a materials scientist at the University of Massachusetts at Amherst.

Even though it's lighter, dragline silk has proven itself in many ways superior to Kevlar, the strongest synthetic polymer, agrees Lynn W. Jelinski, a biophysicist at Cornell University. "The question is whether we can use our understanding of dragline silk proteins to produce a bio-inspired material."

Dragline silk provides a frame for spiderwebs and enables a dangling spider to plummet down and nab its prey. Because the orb weaver's survival depends on dragline silk, some 400 million years' of evolution have fine-tuned a "remarkably tough and versatile material," says John M. Gosline, a biologist at the University of British Columbia in Vancouver.

Now, several research groups are vying to spin the first artificial spider silk, a feat that requires a three-pronged approach, says Jelinski. One must determine the fiber's molecular architecture, understand the genes that yield silk proteins, and learn how to spin the raw material into threads.

Working with chemist Alexandra H. Simmons and physicist Carl A. Michal, both at Cornell, Jelinski proposed in the Jan. 5 SCIENCE a model to explain dragline silk's strength and elasticity.

Scientists had known for years that, of the 20 natural amino acids, only 7—alanine and glycine, with lesser amounts of glutamine, leucine, arginine, tyrosine, and serine—serve as silk's primary constituents. Their exact sequences and structural relationships, however, had remained elusive.

Jelinski and her colleagues have used nuclear magnetic resonance (NMR) to show how the natural silk fiber's main components hang together. The fiber is made up of two alanine-rich proteins embedded in a jellylike polymer. Jelinski's group found that the crystalline structure of one of the proteins is highly ordered and the structure of the other is less ordered. These proteins stick to the glycine-rich polymer, which makes up about 70 percent of the material.

Based on the NMR studies, Jelinski argues that dragline silk's strength and elasticity derive from a blend of ordered and disordered components. The silk's amorphous polymer, resembling a "tangle of cooked spaghetti," makes the fiber elastic, while the two types of protein give it toughness.

Moreover, Jelinski holds that the synthetic silk of the future shouldn't be "too regular" in its molecular patterning. "Nature's randomness," she says, "would give the material extra strength."

For the spider dragline silk, scientists believe they have identified the entire genetic sequence, which measures more than 22,000 base pairs. But they disagree about how much of that sequence needs to be cloned to make proteins good enough to spin into top-quality synthetic threads.

Long stretches in the sequence may be inconsequential to the material itself, functioning as regulatory genes for the spider's own purposes. Some scientists believe that as few as 300 base pairs may suffice to make a good silk, but others hold that several thousand or even the entire sequence is needed.

Randolph V. Lewis, a molecular biologist at the University of Wyoming in Laramie, has identified genes for dragline silk's two main proteins. His team recently cloned portions of those genes and implanted them in the bacterium *Escherichia coli.* He has coaxed the bacterium into producing silk protein in solution, which he squeezes through a fine tube to make synthetic silk fibers.

"I think soon we'll be able to make a close analog of spider silk," says Lewis. "Will it be identical to silk? Probably not. But it may still be an excellent fiber."


Lewis/Univ. of Wyoming

N. clavipes *spins a wicked web and awaits its prey.*

Lewis says he doubts there's anything "magical" about the way spiders spin silk. "They're not even good at making fibers," he says. "Spiders vary the silk's consistency too much. A manufacturer wouldn't tolerate so much variation."

Ideally, he wants to do more than just replicate natural silk strands. "I want to control silk's properties," Lewis says.

At the U.S. Army's Natick (Mass.) Research, Development & Engineering Center, David L. Kaplan and his colleagues also have set up a program to fabricate spider silk.

Using techniques similar to those of Lewis, Kaplan's team has identified what they believe are the critical portions of the dragline silk genes, then fashioned polymer fibers based on those several hundred base pairs. They're banking on the idea that they don't need to replicate the entire set of genes. Rather, by focusing on just the portions of proteins believed to make silk tough, they think they can produce silklike threads.

Plants and fungi, as well as bacteria, could serve as hosts for artificial genes. Kaplan says that if a robust plant could express a dragline silk gene, perhaps silk proteins could be harvested in vast quantities, processed into a liquid polymer, and spun in factories.

"Now we're spinning silk fibers from the synthetic proteins," he says. The Army's interest in artificial silk lies in making durable and protective clothing, parachutes, and war paraphernalia—perhaps even bulletproof vests to replace existing Kevlar ones.

"We want a biologically inspired synthetic fiber with many uses," he adds. "It should be as tough as natural silk but easier and cheaper to make."

Cloning the entire silk protein is not necessary, agrees John P. O'Brien, a chemist at DuPont Co. in Wilmington, Del. "We think we can mimic most of natural silk's properties with much simpler polymers and produce them large-scale.

"Silk has a lot in common with reinforced rubber," he adds. "This allows us to use theories of rubber elasticity to design the synthetic fiber's architecture."

To reduce the length and complexity of the synthetic protein, DuPont chemist Stephen R. Fahnestock says his group has homed in on four short amino acid sequences from one of the two major proteins. By implanting a synthetic gene for those sequences, his team has coaxed bacteria and yeast into producing a novel protein, which DuPont is spinning like conventional polymers into fibers.

"They're not quite like natural spider silk," says O'Brien, "But they're still good when woven into multifilament yarns."

Kenn H. Gardner, a biophysicist at DuPont, points out that spider silk, both the natural and new synthetic versions, is essentially a form of nylon. "That's our business," he says.

"What's particularly interesting to us is the way these organisms make silk nylons in environmentally benign ways," O'Brien says. "They process proteins from water-based solutions, without using petroleum products or organic solvents. From a manufacturing point of view, this is very attractive."

Given the "consumer love affair with natural fibers," he adds, "we want to offer substitutes for natural fibers that are free of associated problems, such as poor wash-wear performance, stretching, wrinkling, and shrinkage.

"Ideally, we're aiming for a better-than-natural alternative fiber."

Taking a different approach, chemists Glenn R. Elion of Plant Cell Technologies in Chatham, Mass., and Richard M. Basel of Lebensmittel Consulting in Fostoria, Ohio, are going for the entire silk gene.

They're working with what they believe is the full dragline silk gene sequence. Using a technique for which they have a patent pending, they have moved that sequence of 22,000 base pairs into bacteria and obtained enough raw spider silk to begin spinning fibers, they claim.

Elion says that his group also is aiming to insert the whole dragline silk gene into high-protein plants, like soy, to produce large yields of silk protein more efficiently.

The researchers are also attempting to alter the silk's color, he says. Spun into threads, natural dragline silk glistens in glorious golden tones. By tinkering with regulatory genes that spiders use for camouflaging their silk, Elion believes that he may be able to generate other colors.

Many species of spiders produce up to seven kinds of silk, with different strength, flexibility, stickiness, and translucence. "Spiders adjust their silk's properties by expressing different genes in different glands," says Gosline. "We're still not quite sure how they do it." In his efforts to quantify the mechanical properties of different silks, Gosline is toying with spider silk genes to find out how to fine-tune the material's quality for specific applications.

In addition to the genes for the dragline silk proteins of the golden orb weaver, Gosline's group has gone after four related genes in another spider, *Araneus diadematus,* that produces an unusual silklike protein. Gosline's team is manipulating these genes to figure out how to vary the silk's qualities.

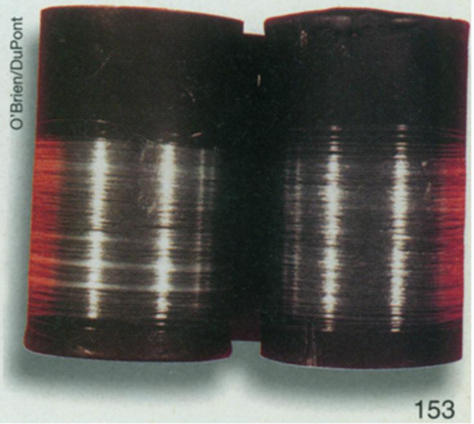
"We're finding that different genes produce proteins containing differing amounts of crystalline material," Gosline says. "Somehow, spiders use this to modulate silk's properties."

Gosline says that he's searching for the rules governing silk's structure. "If we can change silk's properties in predictable ways, then we can use those rules to tailor its production to specific applications.

"Maybe through genetic engineering we can make silk proteins that have never gotten expressed through natural evolution," he adds.

The practical and economic potential of generating artificial spider silk sings a siren's song to biotechnologists. Globally, as much as 60 percent of the threads used to weave clothing come from natural fibers, including cotton, wool, and silk. "We're talking about billions of dollars," says Elion. "This is a major market."

"Bio-inspired materials are providing a new frontier for the fiber business," Jelinski says. "Someone's going to hit a home run in this field. But I'm not sure yet who it will be." ☐


O'Brien/DuPont

Spider dragline silk served as a model for these silver synthetic fibers.