Future outlook. It is expected that future studies using genetically engineered gain- and loss-of-function mouse models will unravel the physiologic functions and mechanisms of actions of this fascinating family of secreted hormones. Elucidating the intertissue crosstalk mediated by CTRPs will enable a much better understanding of the endocrine circuits underlying the integrated control of whole-body energy homeostasis.

For background information *see* ADIPOSE TISSUE; AMP-ACTIVATED PROTEIN KINASE (AMPK); CYTOKINE; DIABETES; ENERGY METABOLISM; GLUCOSE; HORMONE; HUNGER; INSULIN; LEPTIN; LIPID METABOLISM; METABOLISM; OBESITY in the McGraw-Hill Encyclopedia of Science & Technology.

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Darwin's bark spider

Spiders are exceptionally diverse and abundant, being the primary predators of insects and other arthropods in many terrestrial ecosystems. Many spiders use silk traps to catch insects; in these cases, the familiar wagon wheel–shaped webs, or orb webs, are classical examples (**Fig. 1**). Spider orb webs are highly efficient and specialized traps that are thought to account for the success of web spiders. In the short term, orb webs allow spiders to catch flying insects that are not readily caught by many other kinds of predators, which may explain the ecological abundance of orb spiders. In the long term, the evolutionary origin of orb webs can explain a major radiation of spiders, resulting in the many thousands of orb spiders that are alive today. This diversity of orb spiders includes spiders that build webs of varying sizes: from webs as small as 1–2 cm (0.4–0.8 in.) in diameter, which are aimed at small flies such as fruit flies and mosquitoes, to webs that are more than 1 m (3.3 ft) in diameter, which can catch large insects and even small vertebrates. Among orb webs, however, none is larger than that of Darwin's bark spider (*Caerostris darwini*; a new species discovered in Madagascar), which can span up to 2 m (6.6 ft) across (Fig. 1). These webs are suspended along rivers and lakes, often crossing the water on bridge-lines that can span more than 20 m (66 ft). These large webs built over water allow access to prey that are not caught frequently by more typical terrestrial orbs. The prey include insects and possibly small vertebrates that use the rivers as passageways, as well as those that live part of their life in water, such as mayflies.

Exceptional spider silks. Orb spiders use extraordinary biological materials, spider silks, to spin their webs. An orb web contains two radically different types of silk threads. One is dragline silk, which is so named because most spiders use this kind of silk for safety lines that they constantly spin as they crawl about their habitats. Dragline silk is similar to steel in terms of stiffness and strength (**Fig. 2**), and forms the structural support threads, frame, and radial lines of orb webs (Fig. 1). The other type of fiber is capture spiral silk, which is used to build the adhesive spiral that sticks to prey when they hit the web. Capture spiral silk is relatively pliable and highly elastic, being almost like rubber (Fig. 2).

Among the many types of materials produced by living organisms, silks have an impressive combination of material properties. Silks are lightweight, strong, elastic, and durable fibers that readily compare to high-quality synthetic fibers in terms of desirable properties such as strength and resistance to breakage. In synthetic fibers, strength and elasticity are difficult to combine, that is, fibers can be either strong, such as steel, or elastic, such as rubber, but rarely both (Fig. 2). However, spider silks combine these typically divergent properties into fibers that can absorb more energy before breaking, a property known as toughness, compared to any other natural and most synthetic materials. Thus, the stiff dragline silks are about as strong as steel but much more elastic, and the pliable spiral silk is as stretchy as rubber but much stronger (Fig. 2). Both require about three times more kinetic energy to break per volume in comparison to high-performance synthetic polymers such as Kevlar™. However, even among spider silks, none is tougher than the silks of Darwin's bark

Fig. 1. A typical dense orb web (left), and a river-crossing web (right) of a female Darwin's bark spider, *Caerostris darwini* (inset). The riverine webs can reach 2 m (6.6 ft) in diameter.

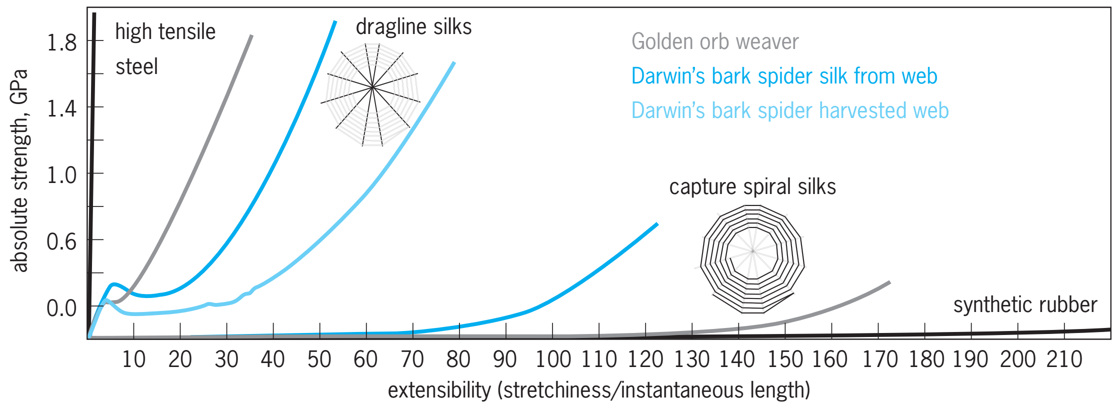

Fig. 2. Mechanical properties of the silks of Darwin's bark spider in comparison to the "standard" of spider silk research, that is, silks of the golden orb spider *Nephila*. The silks of both spiders are impressively strong and are comparable to synthetic materials like steel. However, spider silks are also very stretchy, such that they require much more energy to break, making them significantly tougher than steel. Darwin's bark spider dragline silk exhibits even more stretchiness than the dragline silk of other orb spiders like *Nephila*, which helps to explain why it is so incredibly tough. The highly elastic but much weaker capture spiral silks contain adhesive glues and are similar to rubber in their performance.

spider. The dragline silk of Darwin's bark spider is one of the strongest dragline silks spun by any species of spiders, being up to two times more elastic than typical dragline silk, which results in extraordinary toughness (Fig. 2).

Silk diversity and biomimetic fibers. Each spider produces a "tool kit" of different kinds of silks, with some female spiders producing up to eight distinct types of silk that are used for such functions as lifelines, egg protection, and web construction. Some of these silks are stiff, whereas others are pliable; some are strong and some are relatively weak; and some are highly elastic, whereas others do not stretch much at all. This variation also occurs for a single type of silk compared across spider species. Given that there are well over 41,000 known spider species on Earth, with many more to be discovered, and that each one of them can make several types of silk, nature has produced a virtual goldmine of probably more than 200,000 different silk fibers. Scientists have barely begun to sample this variation, with most silk research focusing on one silk type from a few spider species.

Much research on spider silk is ultimately driven by the desire to utilize these amazing materials for human benefit, whether using the spider silks directly or replicating the material properties of the silks in synthetic "biomimetic" materials. Spider silk and biomimetic fibers have many potential uses for humankind. By combining incredible strength and elasticity in a lightweight and durable fiber, spider silks or their synthetics could find use in many fields and industries, including those related to fabrics (lightweight superfabrics and tough ropes), medicine (bandages and ligaments), military equipment (ballistics), and robotics (sensors, activators, and artificial muscles). However, natural harvesting of spider silk is not feasible at commercial scales because spiders produce silk in relatively low quantities and spiders cannot be easily farmed (in contrast to silkworms). Unfortunately, biomimetic fibers so far do not approach spider silk's strength and elasticity. In part, this results from a lack of understanding of the detailed mechanism of silk spinning, as well as limited comparative work on the protein building blocks of different kinds of spider silks. Future progress likely lies in using the variation of natural spider silks to understand how structural and molecular differences in silks determine which silks are relatively weak and which perform the best. For such applications, Darwin's bark spider silk is important as representing the toughest known natural fiber; then, even if it is impossible to fully replicate the silk properties in synthetics, it might be possible to still achieve something exceptional with a product that is only half as good as the original.

Scientific significance of discovering Darwin's bark spider. Why is the discovery of *Caerostris darwini* or Darwin's bark spider important? The scientific significance lies not so much in Darwin's bark spider building the "biggest" web, nor in it spinning the "toughest" silk, because these are both simply extremes in the enormous diversity of spider webs and silks. Instead, the discovery of Darwin's bark spider is significant for at least three reasons. First, it has been hypothesized that fundamental changes in the silk properties of Darwin's bark spider enabled a novel ecology, that is, the spinning of webs across large bodies of water. Second, the correlation between the extreme silk toughness and the unique habitat of these spiders allows scientists to use the knowledge of the natural history of spiders to predict something about the biomechanical properties of their silks. Such "bioprospecting" can speed discovery of exceptional biomaterials in nature, providing a new tool in the race to inventory biodiversity under the threats of habitat loss and extinction. Third, discovering the molecular basis for the extreme toughness of Darwin's bark spider silk could help unravel key molecular features and building blocks for biomimetic silks. Comparative studies of silks that range from relatively weak to relatively tough are critical for understanding how the structural composition of spider silks relates to their material properties, and hence also to the development of biologically inspired synthetic fibers. Therefore, for future research, Darwin's bark spider holds many promises.

For background information *see* ARACHNIDA; ARANEAE; ELASTICITY; ENGINEERING DESIGN; MANUFACTURED FIBER; MATERIALS SCIENCE AND ENGINEERING; NATURAL FIBER; PREDATOR-PREY INTERACTIONS; SILK; SPIDER SILK; STRENGTH OF MATERIALS in the McGraw-Hill Encyclopedia of Science & Technology.

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Denotational semantics

Computer programs are complex, structured assemblies, as are buildings and television sets. However, programs are also linguistic assemblies, as are epic poems on the scale of Homer's *Iliad* or *Odyssey*. Even more so than with a building, television, or epic poem, a program must match its "blueprint" or specification exactly. For example, flight-control software or medical software must perform exactly as described; otherwise, someone might be harmed. Because of its linguistic aspect, a program's specification often looks like a mathematical formula, and a program's semantics (meaning) must be mathematical in nature to provably match the specification.

Programs are written in a language, just as poems are, and the semantics of a computer program are derived from the semantics of the language used to write it. Because computer languages are structurally simpler than human languages, techniques from linguistics and symbolic logic can state precisely what a language's constructions mean and therefore what a program written in the language means. This motivates the study of programming-language semantics.

The first attempts at stating precisely a programming language's semantics employed machine operations and computer hardware to describe what programs compute, but this approach was too detail-laden to be useful for proofs of mathematical correctness. In the mid-1960s, in Oxford, England, Christopher Strachey, himself a computer hardware designer and also a language designer, adapted techniques from mathematical logic to define the semantics of computer language. His approach, called denotational semantics, established a middle ground between computer-hardware detail and mathematical abstraction and permitted precise, yet intuitive, definitions of language constructions. Denotational semantics is the standard starting point for stating what computer languages mean.

Semantics of arithmetic. Here is a simple example of denotational semantics. The first programming language that people learn is arithmetic. It has a syntax (spelling laws) as well as semantics. First, we must state precisely the syntax, that is, how to write grammatically correct arithmetic:

A numeral, N, such as 0 or 1 or 2 or . . . , is an arithmetic expression.

If E_1 and E_2 are arithmetic expressions, then so are $(E_1 + E_2)$ and also $(E_1 \times E_2)$.

For example, 2, $(4 + 2)$, and $(2 \times (4 + 2))$ are all grammatically correct arithmetic; they are "programs" in the language of arithmetic. The syntax definition is often written in equational form, as a Chomsky-style grammar law:

$$E ::= N \mid (E_1 + E_2) \mid (E_1 \times E_2)$$

We compute on arithmetic using laws for addition and multiplication. Thus, a hand-held calculator is a computer that understands the arithmetic language. Like a spoken language, the words and phrases of arithmetic have meaning, and the meaning of an arithmetic expression is formed from the meanings of its subexpressions. This approach underlies its denotational semantics, which looks like this:

$$\begin{aligned} &\boldsymbol{E} : \text{Expression} \dashrightarrow \text{number} \\ &\boldsymbol{E}[\mathrm{N}] = N \\ &\boldsymbol{E}[(\mathrm{E1} + \mathrm{E2})] = \text{plus } (\boldsymbol{E}[\mathrm{E1}], \boldsymbol{E}[\mathrm{E2}]) \\ &\boldsymbol{E}[(\mathrm{E1} \times \mathrm{E2})] = \text{times } (\boldsymbol{E}[\mathrm{E1}], \boldsymbol{E}[\mathrm{E2}]) \end{aligned}$$

The first line states that $\boldsymbol{E}$ is the name of a function that converts arithmetic expressions to their meanings, which are numbers. (You can read $\boldsymbol{E}[.]$ as "the meaning of.") The second line says that the meaning of a numeral, N, is just the corresponding number, *N*. The next line says that the meaning of $\mathrm{E1} + \mathrm{E2}$ is the addition of the numerical meaning of E_1 to the numerical meaning of E_2. Multiplication is defined similarly. Here is how we determine the meaning of the program, $(2 \times (4 + 2))$:

$$\begin{aligned} &\boldsymbol{E}[(2 \times (4 + 2))] = \text{times } (\boldsymbol{E}[2], \boldsymbol{E}[(4 + 2)]) \\ &\boldsymbol{E}[2] = \textit{two} \\ &\boldsymbol{E}[(4 + 2)] = \text{plus } (\boldsymbol{E}[4], \boldsymbol{E}[2]) \\ &\boldsymbol{E}[4] = \textit{four} \end{aligned}$$

The equations expose the phrase structure within the expression. The expression's meaning follows the structure, and when we solve the equation family, we deduce that the program's meaning is twelve:

$$\boldsymbol{E}[(2 \times (4 + 2))] = \text{times } (\boldsymbol{E}[2], \boldsymbol{E}[4 + 2]) = \text{times } (\textit{two}, \text{plus } (\boldsymbol{E}[4], \boldsymbol{E}[2])) = \text{times } (\textit{two}, \text{plus } (\textit{four, two})) = \text{times } (\textit{two, six}) = \textit{twelve}$$

If there were a crucial correctness property of this program, it would be stated in terms of the structure of the program. (As an example, all numbers computed while totaling the meaning of this program are