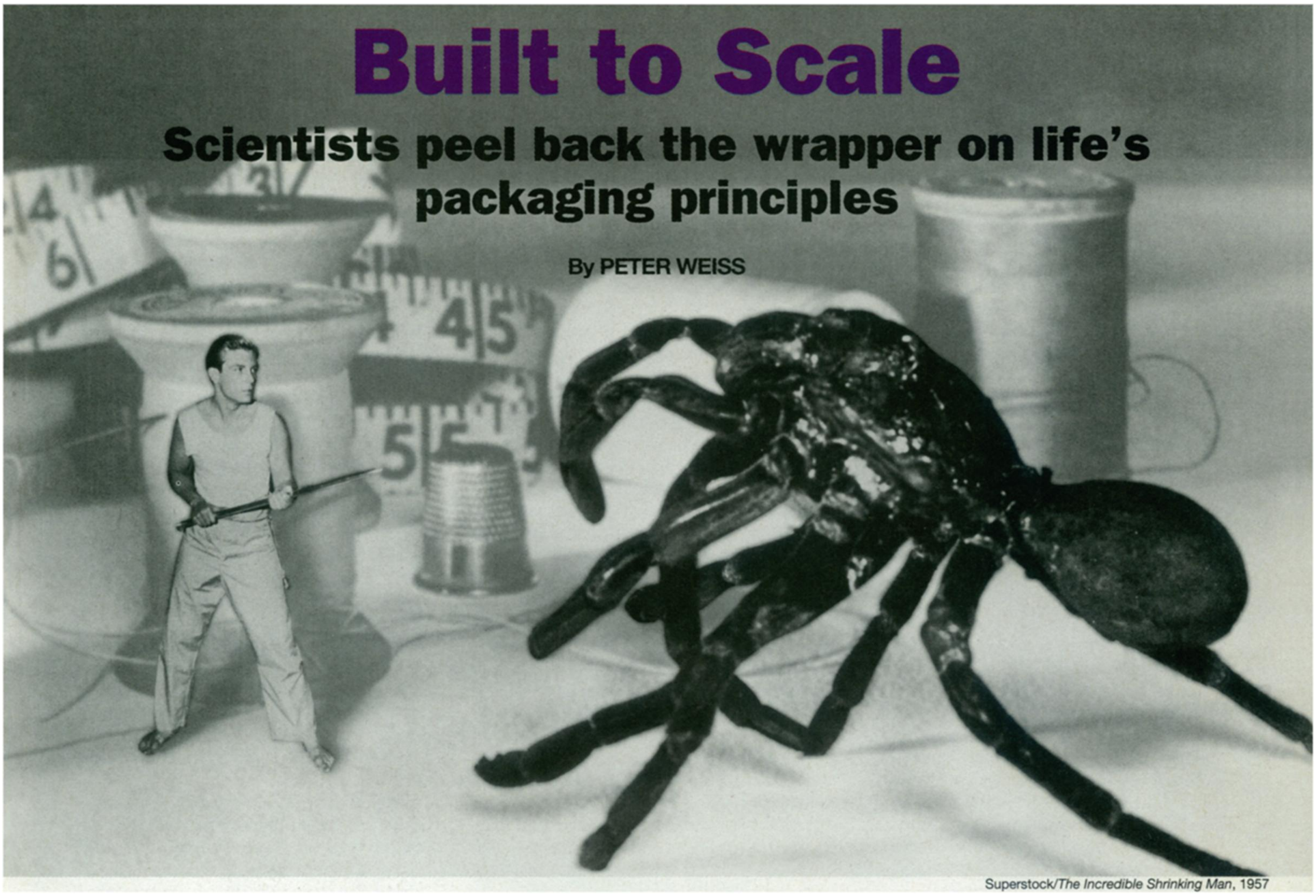
Built to Scale

Scientists peel back the wrapper on life's packaging principles

By PETER WEISS



Superstock/*The Incredible Shrinking Man*, 1957

There's no better way to make someone's flesh crawl than to put the person face-to-face with a bug of monstrous proportions.

Makers of science fiction and horror films have been resorting to the trick for decades. Mothra, a moth as big as three football fields, for instance, terrorized Tokyo in the 1961 movie of that name. In the more recent *Starship Troopers*, the creepy-crawlers are similar to arachnids. Ranging from bus-size spiders to 70-metric-ton ticks, the aliens impale, slash, and mash earthlings during a gory interplanetary war.

Luckily for us all, such gargantuan arthropods are pure fantasy. The reason they can't exist in the real world is well known to biologists, who have made countless comparisons between large and small organisms. Broad, widely accepted laws of biology govern the way traits of organisms vary with size. The laws dictate that you can't simply triple the linear dimensions of a spider and expect it to attack with three times greater strength, eat triple helpings of flies, and make a web three times as long.

Rather, most characteristics—such as strength, life span, frequency of reproduction, and rate of using up nutrients—correlate with size according to far-from-obvious mathematical relationships. Their formulas tend to include exponents that are multiples of 1/4. Because spiders as large as houses violate those so-called 1/4-power laws, they would collapse under their own weight and suffer other mortal defects.

What's the physical basis of the 1/4-power laws? Until recently, no one has been able to say.

"The nature of these laws is not just that they are quantitative, but they have this remarkable universal quality to them. They seem to apply to all of life at all scales," says Geoffrey B. West of Los Alamos National Laboratory and the Santa Fe Institute, both in New Mexico.

Biologists arrived at the laws empirically from arduous observations, measurements, and analyses of animals and plants. Only a few researchers have attempted to look for the deeper principles of biology and physics that give rise to the relationships.

Recently, however, West and biologists James H. Brown of the University of New Mexico in Albuquerque and Brian J. Enquist of the University of California, Santa Barbara have come up with what they believe may be general structural principles of organisms that can explain why 1/4-power laws rule.

Their findings, if they are borne out, may have broad implications for how living beings and their communities grow, function, interact, age, and die.

"What's so stunning about the whole area is that the good general rules—which are the ones they're focusing on—must have good general explanations. They're attempting to produce them," comments Paul H. Harvey of the University of Oxford in England. "It seems to me really good science."

Although filmmakers continue to ignore scaling laws, scientists have known about them for hundreds of years. Four centuries ago, Galileo observed that when you compare large and small animals, the bones from large animals are thicker than one would predict from the increase in length.

Until the 1930s, scientists expected traits of an organism to scale in proportion to the cube root, or 1/3 power, of the organism's mass. They made the simple geometrical argument that a creature's size can be described by a certain length. Because mass, or volume, is proportional to length cubed, traits related to size were to be proportional to the 1/3 power of mass.

Mammal metabolism, they argued, is proportional to the surface area of the animal's skin because skin area determines how fast metabolic heat is shed. Since skin area grows with the square of length, or the 2/3 power of mass, metabolism would scale in proportion to the 2/3 power of mass.

Max Kleiber, a Swiss-American animal physiologist, upended those expectations in 1932. His extensive studies of metabolic rates of different mammals versus their sizes produced exponents closer to 3/4 than the expected 2/3. Subsequently, researchers found that many other traits of animals and plants scale with mass by baffling multiples of 1/4. "Since the 1930s, there's really been this puzzle of, Why 1/4 powers?" Brown says.

In 1995, Brown and Enquist decided to try their hand at solving the mystery, especially after a study by Enquist, then a graduate student at the University of New Mexico, showed that plant metabolism also obeys a 1/4-power law.

Recognizing that they were facing a problem entwined with the physics of how organisms are built, the two sought a physicist to help them unravel it. When they found out that West, a theoretical particle physicist, was already contemplating similar questions, they teamed up with him.

The trio's collaboration bore its first fruit in 1997. The theory that the researchers published that spring explains 1/4-power scaling as a consequence of the inner architecture of organisms.

The team focused on nature's tendency to distribute energy, in the form of nutrients, within organisms via networks of branching tubes. In mammals, the blood vessels carry the energy-bearing molecules. A similarly branching internal architecture controls the flow of nutrient-laden water throughout plants and gives order to the tracheal tubes of insects, they noted. These observations lent credence to the idea that a universal principle is at work.

"Almost all of life, at all scales, is sustained by hierarchical branching networks. They are not necessarily branching tubes, but some sort of hierarchy," West says.

The researchers' study yielded a connection between organism size and the nature of its treelike network structure. They observed that in living creatures, such networks branch in an orderly, repetitive manner typical of a family of patterns known as fractals (SN: 3/1/97, p. S13).

Comparing the radii and lengths of the tubes from one generation of branching with those of the generation above or below it in size, they noted that the ratios stay roughly constant, as in a fractal. From aorta to capillary in a dog, for example, vessels branch about 15 times, diminishing at each generation by a factor of 0.58 in radius and 0.69 in length.

Consequently, the appearance of the network deep into many levels of branching is nearly identical to its appearance at a depth of only a few levels. In the lingo of fractal mathematics, the pattern is self-similar.

Fractal-like patterns appear frequently in nature and some human arenas (SN: 1/6/96, p. 8). Coastlines, cloud formations, river networks, leaf shapes, even urban growth, all present a characteristic appearance at whatever scale they are viewed.

The New Mexico researchers showed that the arcane exponents of the 1/4-power laws pop up naturally in equations that relate body size to the features of such fractal-like networks. The relationship reflects the number of generations of branching, ratios of tube dimensions, and the total volume of fluid in the network.

"One of the things that we've stumbled upon here is a very fundamental principle of design," Brown asserts.

Focusing mainly on mammals, the New Mexico researchers predicted 32 scaling exponents for different aspects of circulatory and respiratory systems. They found that their predicted values matched observed ones well. For instance, the model showed that blood volume expelled from the heart should vary in direct proportion to mass, giving an exponent of 1. The measured exponent relating mass to blood volume is 1.03, they note.

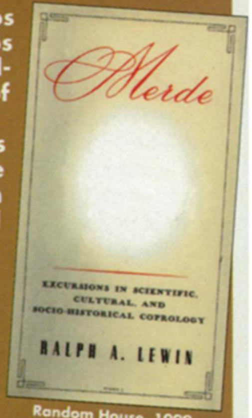
Satisfied with the power of their model to predict traits of mammals, the team recently made 28 predictions of scaling exponents for plants. The predictions, which appear in the Aug. 12 NATURE, compared well with the few values measured for plants.

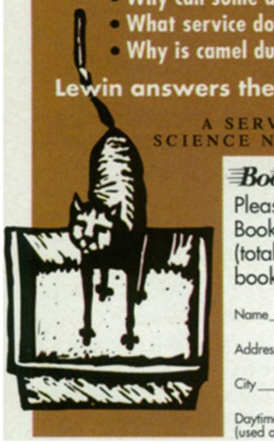
West, Brown, and Enquist "have produced new testable explanations. I think they have to be given enormous credit for that," Harvey says.

Since the theory's 1997 introduction, the New Mexico scientists have come to believe that their ideas rest on deeper foundations than they had originally thought. The traits of organisms that give rise to 1/4-power laws include hierarchical branching networks but aren't limited to them, they argued in the June 4 SCIENCE. What matters on a more fundamental level is whether the "effective surface area" of the organism is as great as it can possibly be.

Effective surface area accounts for not merely an organism's skin but also the surfaces, inside and out, through which nutrients and energy pass. It includes, for example, leaf area in plants and the total internal area of capillaries and gut surfaces in animals. Maximizing effective area with respect to body size makes it possible for an organism to nourish its cells most efficiently, which translates into fitness to win the survival battle, the researchers argue. A fractal pattern is one way to achieve extremely dense packing, the researchers note.

However, other factors also figure into the scientists' arguments. Organisms, for instance, develop in a configuration that minimizes the distance nutrients must travel and thus the energy expended in transport, they argue. Moreover, they postulate that the smallest of the volume-filling structures, the capillaries, for ex-





ample, are roughly the same size no matter how big the organism is. Justifying that assumption, they note that among multicellular organisms of all sizes, the cells themselves are of roughly the same dimensions.

In the smooth, simple, Euclidean geometry of lines, planes, and solids, scaling rules are easy to follow: Area increases in proportion to the square, or second power, of length. Volume scales according to the cube, or third power.

In the fractal realm of living tissue, however, where crumpled-up surfaces practically fill the organism's volume, it turns out that area, not volume, scales as the cube of some characteristic length, the researchers argue. Therefore, if volume can be considered as length times area, it ends up scaling as the fourth power of length. In terms of physiology and anatomy, the researchers conclude, organisms don't live in just three dimensions.

"Internally, we are four-spatially-dimensioned creatures," West says. Simply put, it's the "4" from four dimensions that explains the "4" in 1/4-power scaling relations, he and his colleagues assert.

Has the New Mexico group solved the riddle of life's scaling rules? Perhaps, say some scientists, but there's still a lot of testing that must be done.

"Good science benefits from the yin and yang of theory and experiment. Now, we have what seems a very robust theory. What we need now are some very robust experiments," says Karl J. Niklas of Cornell University.

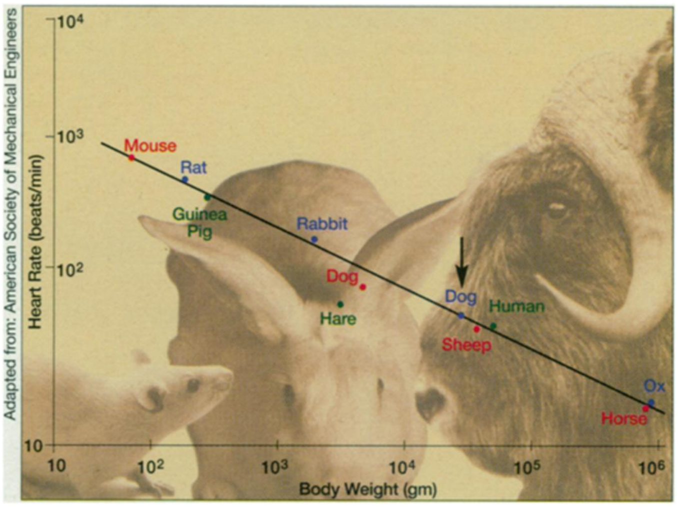
Even if the New Mexico team's model is essentially valid, 1/4-power laws spring from even deeper circumstances than the model suggests, argues physicist Jayanth R. Banavar of Pennsylvania State University in State College. The model by West and his colleagues is actually a special case, he says.

Banavar and Italian researchers Amos Maritan of the International School for Advanced Studies in Trieste and Andrea Rinaldo of the University of Padova have presented their more general finding. In the May 13 NATURE, they demonstrated mathematically that a 1/4-power law arises naturally whenever any transport network fulfills just one condition: Its flow moves from source to final destination by the most direct path.

The 1/4-power rule for such transport networks relates flow rate to network size, which makes it analogous to biology's 1/4-power law relating metabolism to body mass. Unlike in the New Mexico researchers' theory, however, the telltale exponent shows up without requiring hierarchical branching, fractals, or a living creature, Banavar says.

"Our approach has been to step back a little bit and focus on the central point that leads to this rather intriguing phenomenon," he says.

A cautionary note comes from a pair of Polish scientists, who even before the New Mexico group published their first article were arguing that researchers shouldn't take too seriously any 1/4-power laws that are supposed to hold across species boundaries. "Within species, their [1/4-power] model may work," comments Jan Kozlowski. However, "they should not extrapolate this result between species levels," he says.



Adapted from: American Society of Mechanical Engineers

Small mammals live fast and die young compared to big ones. Because heart rate tracks weight by a 1/4-power law, a dog (arrow) about 1/16 as heavy as a horse has a pulse about twice as fast as the horse's, not 16 times faster.

Kozlowski and January Weiner, both of Jagiellonian University in Krakow, argue that natural selection operates within species. Their computer simulations suggest that the between-species scaling laws are a statistical accident.

What's more, Kozlowski says, in many instances, circulatory systems don't resemble branching trees but are more reminiscent of roadway networks containing loops. Capillaries, on the other hand, look like collections of interconnected pores, as in a sponge.

In response, West agrees that the last few branchings of nutrient-supplying networks may transform into a tangle of vessels. However, modifying the model accordingly has no effect on the predicted scaling exponents, he says.

Both Brown and Enquist, in turn, disagree further with the Polish scientists. The physical constraints of being a certain size hold regardless of species, they say, so expecting an influence of scaling laws across species is as legitimate as expecting the laws to hold within them.

Although the New Mexico researchers haven't been convinced there are any fundamental flaws in the theory, it requires some fine-tuning, they say. The three scientists would also like to extend their work in many directions.

"Right now, it's sort of like we've opened Pandora's box," Brown says.

One goal is to strengthen their claim that the theory can explain power-law behavior even within single cells. Since the researchers revised it in the June 4 SCIENCE, the theory no longer formally requires a hierarchical branching network—which cells lack—to give rise to power laws. Accordingly, West and William H. Woodruff, a Los Alamos chemist, have begun studying subcellular details, hoping to predict power-law relationships from first principles there, as the group has done for mammals and plants.

West is also hoping the theory will answer important questions about aging and life span. "The question that intrigues me perhaps most deeply is, Why do we live on the order of 100 years, not 1 million years or 3 months? We know that everything is guided in some way by the molecules, but where did 100 years come from in the molecules?" he asks.

Brown and Enquist, who are both now also with the Santa Fe Institute, are bringing the new theoretical tool to bear on ecology, too. They are applying it, for instance, to the relative growth rates of plants in their natural community.

Scientists have known that small animals populate an area more densely than large animals do. A 1/4-power law links a species' density to the animal's body mass and metabolism.

Last year, Enquist and his colleagues used their model to study the size and population density of plants. They demonstrated that the mathematical relation described for animals also holds for plants. That was a surprise to plant ecologists—and a blow to a long-standing rule that density determines plant size according to a 1/3-power law.

The researchers have plenty of other ideas for using the 1/4-power theory. For instance, could it perhaps help scientists evaluate evidence of extraterrestrial life collected from meteorites or other planets? They could look for clues to the networks that provide a common denominator among earthly creatures.

Brown says someone has even suggested that the group exploit its theory to make a better kidney-dialysis machine.

Although none of the trio mentioned it, there's always the possibility that a good movie plot could come out of their work. How about this? When genetics experiments go wrong, insects find a way around the 1/4-power laws of nature, grow as big as dirigibles, and run amok. . . . □