excerpts from
Our 86 Billion Neurons: She Showed It
Steven Mithen, November 24, 2016 Issue, The New York Review of Books
Reviewed:
The Human Advantage: A New Understanding of How Our Brain Became Remarkable
by Suzana Herculano-Houzel

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The best science often depends on asking the most basic questions, which are often the hardest to ask because they risk exposing fundamental limitations in our knowledge. Herculano-Houzel asked one of those questions soon after being hired as an assistant professor at the Federal University of Rio de Janeiro in 2002: How many neurons are there within the brain? [...]

She was inspired to do so by the pervasive myths about the brain she kept encountering, such as that we use only 10 percent of our capacity. Moreover, none of the distinguished neuroscientists she asked could tell her the source for the claim that there were 100 billion neurons in the brain, which they all believed.

Prior to devising brain soup, the only method available for counting neurons was stereology. This involves placing probes into thin slices of brain tissue, counting the number of cells, and then extrapolating to the entire brain structure being examined or the whole brain itself. The problem with this is heterogeneity within the brain: different parts of the brain have quite different densities of neurons, varying up to a thousand times across small areas. As such, it is very difficult to extrapolate accurately from neurons counted in thin sections to those within a structure of the whole brain.

Brain soup was the method Herculano-Houzel devised to deal with the problem of a brain’s heterogeneity. Her procedure was to dissolve a brain of whatever species, with its millions or billions of cell membranes, in detergent to create a homogeneous distribution of free-floating cell nuclei. She could then sample the suspension, use a blue dye to stain the nuclei, count them up, and confidently extrapolate to the number of cells in the entirety of the brain, or whatever part of the brain she had begun with.

Those cells would be of three types—neurons, glial cells, and endothelial cells. Glial cells are crucial to the synaptic transmission of information across neurons, while endothelial cells form the walls of the capillaries that take oxygen and nutrients to the brain via the blood. Fortunately, the neurons could be distinguished by tagging them with a red-colored neuron-specific antibody, one that attaches to the NeuN protein within the cell nuclei. By counting the number that turned from blue to red once the antibody was added to the suspension, she could establish the proportion of the total cell count that was neurons.

Not only is this method quite simple, it can be applied quickly. Within a single day, we are told, one can take a whole brain, divide it into its principal parts—normally the cerebral cortex, the cerebellum, and “the rest”—chop each part into small chunks, dissolve them, sample the suspension, add the dye and antibodies, and make the counts. Validating the method was a challenge—how can one check such counts when no other method exists? Fortunately, there had been sufficient stereological research undertaken on the rat cerebral cortex and cerebellum to indicate that the brain soup estimates were accurate—as least for the brains of rodents. [...]

Within ten years of devising brain soup, Herculano-Houzel and her colleagues had published data for forty-one species and were able to find some striking patterns. Primate brains were indeed constructed quite differently from those of all other types of mammals—they had many more neurons packed into the same quantities of brain mass. This is the case for both the cerebellum and the cerebral cortex, with the former containing about 80 percent of the neurons for any type of mammals—with an exception that I will come to. [The exception: Moles and shrews were found to pack neurons into their cerebellums at the same linear rate in relation to mass as nonhuman primates, i.e., they have a more primate-like density of neurons.]. For instance, the [non-primate mammal] capybara and [primate] bonnet monkey have a cerebral cortex of the same size, just over forty-eight grams, but the former has 306 million neurons while the latter has 1.7 billion. [...]

The evolutionary punch line is that when the primates branched off from the ancestor they had in common with nonprimates, around 65 million years ago, this led not only to distinctive traits such as stereoscopic vision, prehensile hands, and larger brains, but also to a new way of building the brain: no longer did an increase in the number of neurons require an increase in the average size of the neurons (although some larger ones were still required). As such, primates could pack their brains with many more neurons for the same brain mass. This delivered the primate advantage: by keeping the overall volume relatively low, signals were able to quickly propagate within the brain, enabling the integration of information. [...]

What about the human advantage? [...]

Here are the numbers she found: the average human brain has 16 billion neurons in the cerebral cortex, 69 billion in the cerebellum, and slightly fewer than one billion in the rest of the brain.

Letters
It’s Not All Neurons December 1, 2016

It’s Not All Neurons
Christof Koch
Are we really 86,000 times smarter than honeybees?
December 22, 2016 issue

In response to:
Our 86 Billion Neurons: She Showed It from the November 24, 2016 issue

To the Editors:

I would like to provide some perspective on the numerology of neurons as expressed by Steven Mithen in his review of Suzana Herculano-Houzel’s book The Human Advantage [NYR, November 24].

First—unlike physics, in which constants such as the speed of light can be determined with an accuracy of one in a billion, biological systems are characterized by a high degree of variability. Thus, brain size and number of neurons in most species vary by a factor of two. Thus, the 86 billion nerve cells counted by Herculano-Houzel’s method is not a universal hallmark of Homo sapiens but an average of the brains of four elderly Brazilian men.

Second—the adult male brain is about 150 grams heavier than the female one. For the neocortex, responsible for perception, memory, language, and reasoning, this disparity translates to about 23 billion neurons for men versus 19 billion for women; yet there is no difference in their average IQ.

Third—the relationship between intelligence and number of neurons is weak within and across species. Thus, the neocortex of the long-finned pilot whale contains an estimated 37 billion neurons, twice as many as the human neocortex. Consider honeybees for an even less mammalian-centric point of view. They recognize faces, communicate the location and quality of food sources to their sisters via the waggle dance, and navigate complex mazes with the help of cues stored in short-term memory. Yet they do this with fewer than one million neurons. Are we really 86,000 times smarter?

Christof Koch
President and Chief Scientific Officer
Allen Institute for Brain Science
Department of Biology
University of Washington
Seattle, Washington

COMPLETE REVIEW

Our 86 Billion Neurons: She Showed It
Steven Mithen
We evolved and learned a clever trick in our evolutionary past in order to find the time to feed our neuron-packed brains.
November 24, 2016 Issue
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Reviewed:
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by Suzana Herculano-Houzel
MIT Press, 256 pp., $29.95

[photo credit] Fabio Motta/Estadão
[photo caption] Suzana Herculano-Houzel, head of the Laboratory of Comparative Neuroanatomy at the Federal University of Rio de Janeiro, August 2015

Reading about the brain is as fascinating as it is demanding. During the last decade we have had a steady stream of books purporting to explain how the brain works and its relationship to mind, consciousness, creativity, and many other qualities that might give us humans an advantage over other types of animals. Is human distinctiveness attributable to mirror neurons, quantum mechanics, or the inferior frontal gyrus (or fold) in the cortex? What a relief to have a book that provides an answer as simple as it is convincing. Suzana Herculano-Houzel suggests that the human advantage lies in the 86 billion neurons that are packed into a mere 1,400 grams of matter in the human brain.

What is perhaps more astounding than that number itself, one that is actually less than the often assumed 100 billion neurons, is that 86 billion makes us an entirely typical primate for our size, with nothing special about our brain at all, so far as overall numbers are concerned. When one draws a correlation between body mass and brain mass for living primates and extinct species of *Homo*, it is not humans—whose brains are three times larger than those of chimpanzees, their closest primate relative—that are an outlier. Instead, it is the great apes—gorillas and the orangutan—with brains far smaller than would be expected in relation to their body mass. We are the new normal in evolution while the great apes are the evolutionary oddity that requires explanation.

But we remain special in another way. Our 86 billion neurons need so much energy that if we shared a way of life with other primates we couldn't possibly survive: there would be insufficient hours in the day to feed our hungry brain. It needs 500 calories a day to function, which is 25 percent of what our entire body requires. That sounds like a lot, but a single cupful of glucose can fuel the brain for an entire day, with just over a teaspoon being required per hour. Nevertheless, the brains of almost all other vertebrates are responsible for a mere 10 percent of their overall metabolic needs. We evolved and learned a clever trick in our evolutionary past in order to find the time to feed our neuron-packed brains: we began to cook our food. By so doing, more energy could be extracted from the same quantity of plant stuffs or meat than from eating them raw.

The role of cooking in human evolution has previously been championed by Richard Wrangham in his book *Catching Fire: How Cooking Made Us Human* (2009),[*] while long before Claude Levi-Strauss had identified that the raw and the cooked have something fundamental to do with being human. Herculano-Houzel argues that cooking was not simply a bonus for prehistoric *Homo* but an essential requirement for the brains to become larger. This was also Wrangham's view, but *The Human Advantage* certainly provides further reasons to believe that this is the case—86 billion of them.

While the cooking of food arises only toward the end of this "brain by numbers" book, the making of "brain soup" is its main concern. In 2004, Herculano-Houzel devised a way of reducing brains to liquid as a means to count the number of neurons in them. It is technically known as the "isotropic fractionator." The method and its findings have been debated and discussed within neuroscience and now come to a wide readership with this fascinating book, one that conveys the huge passion of a scientist on a quest to understand the brain.

Prior to Herculano-Houzel's research, scientists simply assumed (we are told) that the brains of all mammals were built in the same way and hence that the overall brain mass as compared to body mass was the critical determinant of cognitive ability. This was exemplified by Harry Jerison's concept of the "encephalization quotient" (EQ) in the 1970s (encephalization as used here is an evolutionary increase in the relative size of the brain to the body). Jerison suggested that the human brain was 7.5 times larger than would be expected for a generic mammal of our body size. Humans, in this view, are an evolutionary outlier.

Although the EQ is still widely cited, it is open to significant concern: if some species have brains larger than expected, and hence a capacity for activities that go beyond simple survival, a statistical requirement is that there must be species with brains smaller than expected. How could they possibly survive if their brain cannot provide for standard bodily functions? Moreover, after humans, the most encephalized species—i.e., the one with the largest brain relative to body mass—is the capuchin monkey: Is that tiny creature with an EQ of two really more intelligent than the great apes, which with EQs of less than one would have a questionable ability to survive at all?

If not the EQ, then perhaps absolute brain size is the determinant of intelligence. If so, why are chimpanzees cleverer than cows (however cleverness is measured), when both have brains of around 400 grams? And if sheer size is important, why aren't African elephants and sperm whales, with brains of five and nine kilograms respectively, getting ready to vote for the next president of the US rather than humans, with our mere 1.4 kilograms of brain? It was to resolve these conundrums about brain mass, body mass, and intelligence that Herculano-Houzel turned to chainsaws, butchers' knives, and kitchen blenders to make brain soup.

The best science often depends on asking the most basic questions, which are often the hardest to ask because they risk exposing fundamental limitations in our knowledge. Herculano-Houzel asked one of those questions soon after being hired as an assistant professor at the Federal University of Rio de Janeiro in 2002: How many neurons are there within the brain? Perhaps she was able to ask such a simple but surely vital question because of her training in science communication and the diversity of her previous studies, a lesson to any young scientist today. She had started at the Federal University in Rio with undergraduate studies in virology, undertook graduate studies in the nervous system at Case Western Reserve in Cleveland, and then completed a Ph.D. in visual neurophysiology at the Max Planck Institute for Brain Research in Frankfurt before returning to Rio.

That was initially at the Museum of Life, where she devised science games for children and wrote a popular book on neuroscience. She then returned to her alma mater to train young scientists in communication—with an allowance to pursue research if she were so inclined. She was inspired to do so by the pervasive myths about the brain she kept encountering, such as that we use only 10 percent of our capacity. Moreover, none of the distinguished neuroscientists she asked could tell her the source for the claim that there were 100 billion neurons in the brain, which they all believed.

Prior to devising brain soup, the only method available for counting neurons was stereology. This involves placing probes into thin slices of brain tissue, counting the number of cells, and then extrapolating to the entire brain structure being examined or the whole brain itself. The problem with this is heterogeneity within the brain: different parts of the brain have quite different densities of neurons, varying up to a thousand times across small areas. As such, it is very difficult to extrapolate accurately from neurons counted in thin sections to those within a structure of the whole brain.

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Those cells would be of three types—neurons, glial cells, and endothelial cells. Glial cells are crucial to the synaptic transmission of information across neurons, while endothelial cells form the walls of the capillaries that take oxygen and nutrients to the brain via the blood. Fortunately, the neurons could be distinguished by tagging them with a red-colored neuron-specific antibody, one that attaches to the NeuN protein within the cell nuclei. By counting the number that turned from blue to red once the antibody was added to the suspension, she could establish the proportion of the total cell count that was neurons.

Not only is this method quite simple, it can be applied quickly. Within a single day, we are told, one can take a whole brain, divide it into its principal parts—normally the cerebral cortex, the cerebellum, and “the rest”—chop each part into small chunks, dissolve them, sample the suspension, add the dye and antibodies, and make the counts. Validating the method was a challenge—how can one check such counts when no other method exists? Fortunately, there had been sufficient stereological research undertaken on the rat cerebral cortex and cerebellum to indicate that the brain soup estimates were accurate—as least for the brains of rodents.

Once Herculano-Houzel had developed the protocol, the next step in her research—and, I suspect, her life, because surely such research would be extremely demanding—was acquiring brains to turn into soup. She had easy access to the brains of the laboratory mainstays—the mouse, rat, guinea pig, and hamster—but needed more and bigger brains. She put the word out. Two capybara (large rodent) heads soon arrived in a Styrofoam box floating in paraformaldehyde, swiftly followed by a couple of agouti brains. This sample of six rodent species was compared with the first primate brains available, those from a marmoset, a galago (or bushbaby), and an owl monkey. The results immediately showed that primates were packing much larger numbers of neurons into their brains than were the rodents.

Other brains were acquired. When “rummaging” in a colleague’s cold storage, Herculano-Houzel found four large cerebellums, three from orangutans and one from a gorilla. These had been left in a bucket of paraformaldehyde, apparently forgotten about, for over a decade. She writes that being given these cerebellums was like Christmas. In 2009 another colleague in South Africa agreed to provide a complete hemisphere, or half brain, of an elephant, a (literally) huge asset because of its greater size than that of a human and hence an opportunity to discover whether it also had more neurons. But that elephant brain ultimately proved impossible to export through South African customs, although a number of other African brains from bats, rodents, a giraffe, and an antelope passed through without difficulty.

Elsewhere in South Africa she was able to buy the brains she needed. This was from a legitimate business that provided a maximum-security facility for wildlife either seized from poachers or caught legally in the wild and then returned to the wild or sold to zoos—or to scientists needing brains (she wasn’t the only one). Herculano-Houzel was given a list of animals available and their prices; she made her choice and persuaded her funding bodies to pay the cost. Veterinarians euthanized the animals and then she and her students removed the brains; she describes how she quickly learned to undertake precision work with a chain saw. The meat was fed to the big cats in the facility and its workers were allowed to cure and keep the furs for themselves.

Within ten years of devising brain soup, Herculano-Houzel and her colleagues had published data for forty-one species and were able to find some striking patterns. Primate brains were indeed constructed quite differently from those of all other types of mammals—they had many more neurons packed into the same quantities of brain mass. This is the case for both the cerebellum and the cerebral cortex, with the former containing about 80 percent of the neurons for any type of mammals—with an exception that I will come to. For instance, the capybara and bonnet monkey have a cerebral cortex of the same size, just over forty-eight grams, but the former has 306 million neurons while the latter has 1.7 billion.

Nonprimate brains are described as inflationary in size because as they gain neurons their mass increases at an exponential rate of +1.6 compared to a linear one-to-one relationship between the increase in neurons and the increase in mass in primates. It is similar with the cerebellum, although in that case the exponential increase for brain mass with neurons is rather less inflationary, at +1.3. One exception: the group of mammals known as eulipotyphlans (moles and shrews) were found to pack neurons into their cerebellums at the same linear rate in relation to mass as nonhuman primates.

The proximate cause for this difference between nonprimates and primates relates to the average size of neurons, which increases exponentially as the number of neurons increases in nonprimates but not in primates. As the cortex of a nonprimate acquires ten times more neurons, its neurons become on average four times larger and hence the cortex forty times larger in mass; if the cortex gains a hundred times more neurons, the neurons are on average sixteen times larger and hence the cortex become 1,600 times larger. Among primates, the average size of neurons remains constant as the neurons increase in number, staying roughly equal to the size of neurons within the cortex of a small rodent.

The evolutionary punch line is that when the primates branched off from the ancestor they had in common with nonprimates, around 65 million years ago, this led not only to distinctive traits such as stereoscopic vision, prehensile hands, and larger brains, but also to a new way of building the brain: no longer did an increase in the number of neurons require an increase in the average size of the neurons (although some larger ones were still required). As such, primates could pack their brains with many more neurons for the same brain mass. This delivered the primate advantage: by keeping the overall volume relatively low, signals were able to quickly propagate within the brain, enabling the integration of information.

What about the human advantage? Herculano-Houzel's initial attempts with human brains were unsuccessful. These came from a pathology department and had been too strongly fixed with formaldehyde for her procedure to be effective: no amount of stewing in citric acid, bleaching under colored lights, and cooking in the microwave would enable the stained antibodies to distinguish the neurons within her human brain soup from the other cells. Fortunately another source became available from the School of Medicine at São Paulo, which used a gentler method for fixing donated brains, leaving them ideal for cutting up with a slicer and dissolving in detergent.

Here are the numbers she found: the average human brain has 16 billion neurons in the cerebral cortex, 69 billion in the cerebellum, and slightly fewer than one billion in the rest of the brain. This fitted almost perfectly with the neuronal scaling rules derived for nonhuman primates: we have a perfectly normal primate brain, just the right number of neurons for the mass of our brain and also our body size.

That finding flew in the face of conventional wisdom, which argued that when correlations are drawn between body size and brain size for living primates (including the great apes), humans appear to have a brain size three times larger than expected. But Herculano-Houzel argues that it is the great apes, not humans, that are the exception. While the great apes also conform to the neuronal scaling rules—i.e., the average size of their neurons doesn't increase exponentially as they gain more neurons—their brains are much smaller than should be expected for their body size.

The evolutionary story she tells by way of explanation is one of choosing between brain and brawn. Being restricted to eight hours of foraging a day, the ancestral great apes chose brawn (which, of course, means they underwent natural/sexual selection for a larger body size): the amount of energy that could be acquired was invested in building a bigger body rather than a bigger brain. At seventy-five kilograms a 30 billion–neuron brain was the maximum size that could be fueled. Ancestral *Homo* went a different way: it increased the energetic uptake from foraging by increased scavenging and hunting while maintaining a relatively small body size, enabling its brain to expand to an estimated 40 to 50 billion neurons for *Homo habilis* two million years ago. But that was the limit: there was no time left in the day and no other sources of food to exploit. Further expansion of the brain required securing more energy from the same type and quantity of foodstuffs. As from 1.5 million years ago that is just what our ancestors achieved by cooking their food.

What was it about all of those extra neurons in the human brain that provided the human advantage? A starting point is to assume it has something to do with expansion of the cortex, this being a long-established view about the human advantage, with particular regard to the prefrontal cortex where planning complex cognitive behavior occurs. But even though the human cerebral cortex constitutes 82 percent of the total brain mass, the largest when compared to all mammals, it was found to contain only 19 percent of the total number of neurons in the brain, the same percentage as in the guinea pig and capybara, and midway in the 15 to 25 percent range found in most mammals.

How can the human cerebral cortex have expanded so greatly in comparison to the rest of the brain while maintaining a proportion of neurons equivalent to that found in the cerebral cortex of other small-brained primates? Herculano-Houzel's answer lies partly in the absolute number of neurons in the human cerebral cortex and partly in the fact that different scaling rules apply to the cerebral cortex and the cerebellum.

These rules are constant across all primates: when additional neurons are added to the brain, the cerebral cortex increases in mass at a much faster rate than does the cerebellum. This is because the cerebral cortex requires larger neurons than the cerebellum—neurons that have long-range connections of several centimeters to link different cortical areas; neurons in the cerebellum need to span no more than a few millimeters. As a result, the cerebral cortex becomes proportionally larger even though the ratio of cortical to cerebellar neurons remains the same. So with humans, the 16 billion neurons in the cerebral cortex result in its forming 82 percent of the total brain mass, despite the human brain's remaining entirely typical for a primate with regard to the proportions of neurons in the cerebral cortex and in the cerebellum.

Neither is the human advantage found in an expanded frontal or prefrontal cortex; both of these are of a standard mass with a standard number of neurons for a primate of our size. Nor does the human advantage appear to arise from increased connectivity: the volume of white matter in the prefrontal cortex is also quite normal for a primate of our size. As far as can be established, the nature of connections—the wiring diagram—of the human brain is also much the same. All that seems to be left is the absolute number of neurons.

Although we have a standard number of neurons for a primate of our size, other primates of approximately our size such as the bonobo and the orangutan have, as I have mentioned, much smaller brains than one would expect from their body mass. We therefore have a very high total number of neurons compared both to great apes of our size and to primates smaller than we are: the 8 percent of cortical neurons in the human prefrontal cortex constitutes 1.3 billion neurons, compared to 230 million in the baboon, 127 million in the macaque, and 20 million in the marmoset. The human advantage comes from no more than strength in numbers.

What about the much bigger brains of elephants and whales? At the time of writing, Herculano-Houzel had yet to analyze a cetacean brain but she had managed to secure that African elephant's hemisphere. Cutting this up provided a further challenge, one undertaken with a new set of butchers' knives and an army of students to make elephant brain soup by the gallon. And then a surprise: the elephant brain had more neurons than the human brain, not just a few more but three times as many: 247 billion to our 86 billion. But 98 percent of these were located in the cerebellum at the back of the brain, leaving a mere 5.6 billion in the 2.8-kilogram cerebral cortex compared to the 16 billion in the 1.2-kilogram human cerebral cortex. What are all those neurons doing in the elephant cerebellum, ten times more than one would expect? Most likely controlling that other exceptional feature of the elephant, its 100-kilogram and highly sensory muscular trunk.

If a new neuronal scaling rule gave us the primate advantage at 65 million years ago, and learning to cook provided the human advantage at 1.5 million years ago, what, one might ask, gave us the "*Homo sapiens* advantage" sometime around 70,000 years ago? That was when our ancestors dispersed from Africa, to ultimately replace all other humans and reach the farthest corners and most extreme environments of the earth. It wasn't brain size, because the Neanderthals' matched *Homo sapiens*. My guess is that it may have been another invention: perhaps symbolic art that could extend the power of those 86 billion neurons or maybe new forms of connectivity that provided the capacity for language.

This is a book written with passion, about a scientific quest pursued with passion—a quest to answer a simple question that a child might ask but that the most distinguished neuroscientists had ignored. It's given my own neurons the best workout they've had for a very long time, which is perhaps why I'm now feeling ready for a cooked dinner.