

A Well-Hung Horse: Sired by Knowledge and Imagination

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For more than a century, historians of science have been spinning a philosophical roulette wheel, pondering which is more important in the creative process: imagination or knowledge. The most original scientists (and artists) in our day discover newness by blending existing knowledge with imaginative thinking.

Knowledge versus Imagination

The opening salvo in the imagination versus knowledge debate goes back to the Dutch chemist Jacobus van't Hoff, who was awarded the first Nobel Prize in Chemistry in 1901. van't Hoff is credited with two original achievements. The first is his proposal that atoms in a molecule are arranged in a three-dimensional space—a hypothesis that led to the discovery of the asymmetrical carbon atom and to the founding of a new field of physical chemistry. And the second is that the speed of a chemical reaction is related to temperature and the concentration of components in the reaction. Thus, two fundamental concepts—molecular shape and reaction kinetics—originated with this one individual.

van't Hoff believed that the key to scientific creativity was not facts and knowledge, but imagination. Imagination, in his view, is the essential building block of scientific inquiry. In 1878, van't Hoff assembled his ideas into an essay entitled *Imagination in Science*, in which he pointed out that many of the world's most original scientists like Newton, Galileo, Davy, and Boyle possessed lifelong strange imaginings and superstitions that influenced their approach to science (Springer, 1967). Most creative scientists, according to van't Hoff, were a bit “crazy”—with “crazy” being shorthand for bold thinking and being free to try new things that less-creative colleagues would deem ridiculous.

Although van't Hoff was the first to emphasize the value of imagination in science, it was Einstein who put imagination on the philosophical map. In a 1929 interview in *The Saturday Evening Post*,

a journalist asked Einstein “How do you account for your discoveries? Through intuition or inspiration?” Einstein replied, “Both. I'm enough of an artist to draw freely on my imagination, which I think is more important than knowledge.” He explained that knowledge is limited to what we already know and understand, while imagination leads to all there ever will be to know and understand (Viereck, 1929).

Einstein and van't Hoff were exceptional rarefied thinkers who viewed imagination and knowledge as horses of a different color. To them, imagination was the domain of scientists and artists; knowledge was for curators and accountants. In Einstein's universe, there was neither space nor time for the most imaginative of accountants—even those who could cook the books and never get caught.

In the real world of today, the most creative scientists possess a special knack for asking the right question, framed in the context of existing knowledge, which is then used as a stepping stone to imaginative thinking. A wonderful example of the creative blending of knowledge and imagination is illustrated by a portrait in Room 34 of the National Gallery in London. Room 34 contains famous 18th century British society portraits by Thomas Gainsborough and Joshua Reynolds, who painted their aristocratic subjects on a grand scale in the European manner. But the portrait that I will tell you about is not one of a famous English nobleman; rather, it's a horse of a different color; in fact, it's actually a portrait of a horse—a real Arabian horse named *Whistlejacket*, the star racehorse of his day in 18th century England (Figure 1, left). *Whistlejacket* was named

after a popular cocktail containing gin and molasses that was golden colored like *Whistlejacket's* flanks.

Whistlejacket: A Historic Painting by George Stubbs

The oil-on-canvas painting of *Whistlejacket* was completed in 1762 by the British artist George Stubbs (1724–1806) (Warner and Blake, 2004). There are 2,300 paintings in the National Gallery's collection, which includes famous works by Caravaggio, Rembrandt, Rubens, Velasquez, Van Gogh, and Cezanne. In terms of viewer popularity and museum shop sales, *Whistlejacket* is the National Gallery's equivalent of The Louvre's *Mona Lisa*. The National's museum shop sells 32 different *Whistlejacket*-designed items, including the usual postcards, posters, scarfs, umbrellas, etc. But one of these items is unique for a museum shop—a bottle of Sloe Gin, a modern-day recreation of the 18th century *Whistlejacket* cocktail containing 27% alcohol (www.nationalgallery.org.uk).

Whistlejacket is monumental in size—9.5 feet by 8 feet—the size of an actual horse. *Whistlejacket* occupies pride of place in its location in the National Gallery (Longmuir, 1997). It is hung at one end of the Gallery's long main corridor in such a way that the museum-goer sees an enormous horse through multiple glass doorways as he or she wanders through ten intervening rooms that connect one end of the Gallery to the other (Figure 1, right). The painting is a true traffic-stopper and a powerful magnet, attracting and pulling people to it from remote parts of the museum. As a museum curator might say, *Whistlejacket* is a well-hung horse!



Figure 1. A Well-Hung Horse

(Left) *Whistlejacket* by George Stubbs, 1762. Oil on canvas. 9.5 × 8 ft. The painting hangs in London's National Gallery at one end of the museum's long main corridor and can be seen through ten intervening rooms that connect one end of the museum to the other. (Upper-right) *Whistlejacket* is seen through the door in Room 35 that leads directly to Room 34, where *Whistlejacket* hangs. (Lower-right) *Whistlejacket* is seen through the door in Room 9, which is located at the opposite end of the museum's long corridor from Room 34. <http://nationalgallery.org.uk/visiting/virtualtour/>.

So what makes *Whistlejacket* such a remarkable painting? The answer lies in the creativity of George Stubbs, whose deep knowledge of the anatomy of horses stimulated his imagination in a unique way. Stubbs began his career as a scientist, studying human anatomy at a medical school where he also taught himself to draw and paint. His first job in 1750 was to illustrate an anatomy book on human fetal development. He then switched his anatomical interests from humans to horses.

The Anatomy of a Horse: A Scientific Masterpiece by George Stubbs

For the next two years, Stubbs carried out grueling dissections and experiments on dead horses. To familiarize himself with the animal's anatomy and physiology, he suspended the dead horses from his stable roof, stripped away their muscles, injected their veins with wax, and positioned them in various poses so that he could make meticulous drawings and engravings (Rott, 2012).

Stubbs' studies of equine musculature and skeletal structure were published in 1766 in a graphic masterpiece, *The Anatomy of the Horse* (McCunn and Ottaway, 1976). The horse is presented in 36 large plates and 18 tables, with depictions of the skeleton alone, all of the muscle layers, and the ligaments, nerves, veins, glands, and cartilage. Stubbs' equine drawings are memorable for their life-like quality and exceptional anatomical precision—on par with Leonardo da Vinci's anatomical drawings of the human body. Stubbs' reputation as an expert on horses attracted the attention of the landed gentry whose passion in 18th century England was horse breeding and racing. Members of the Jockey Club of London commissioned him to paint portraits of their favorite horses.

Stubbs' portrait of *Whistlejacket* is a milestone in art history, making a radical break with convention and representing a prime example of the blending of knowledge with imagination. This was the first time that an animal was painted on a

scale reserved for a king. Unlike previous paintings involving horses, *Whistlejacket* is depicted alone with no people, no landscape, no battlefields, no saddles, no bridles, no whips—just one horse that is free to gallop in empty space with no noisy distractions. The only areas in the canvas where space is suggested are the two small shadows cast by the rear hooves. Stubbs' innovative use of empty space as a background focuses our attention on the subject's individuality—his flying mane, his shiny golden flanks, his taut muscles, and his terrified eye looking at us. Why is *Whistlejacket* so terrified?

When the portrait was nearly finished, an extraordinary event occurred. After Stubbs had removed the canvas from the easel and placed it against the stable wall, the portrait was glimpsed by the real *Whistlejacket*. The real *Whistlejacket* so believed that he was confronting a raging stallion that he began “to stare and look wildly at the picture, endeavoring to get at it to fight and kick it.” This must surely have been the moment when Stubbs realized that he had created a masterpiece of realism—one that was recognized by his living subject (Warner and Blake, 2004; Longmuir, 1997).

Although George Stubbs painted *Whistlejacket* 250 years ago, he and his work are a reminder of a famous line by William Faulkner: “The past is never dead. It is not even past.” Stubbs' passion for horses influenced all subsequent painters of horses, including Delacroix, Gericault, Degas, and Picasso. According to the art critic Robert Hughes (1984), *Whistlejacket* prefigured Picasso's famous horse in *Guernica*, the horse that thrusts “its outraged neck toward the indifferent sky of the 20th century.”

Gift Horse: A Contemporary Sculpture Inspired by Whistlejacket

The most recent reminder of George Stubbs' past is a contemporary sculpture of a strutting horse that was recently installed on top of the Fourth Plinth in London's Trafalgar Square, situated just in front of The National Gallery where *Whistlejacket* hangs (Figure 2, top). The new equine sculpture was created by Hans Haacke, a 78-year-old German-born artist who has lived in the United

States for the last 50 years (London Gov. UK, 2015). Haacke is one of the fathers of Conceptual Art whose followers make minimalist sculptures from industrial materials and found objects. Lately, Haacke has led a new art movement called Institutional Critique in which artists use their art to draw attention to hidden connections between politics, business, and established organizations such as museums and churches (Grasskamp, 2004).

Haacke's new bronze sculpture is 15-feet tall, twice the size of a real horse, and weighs 4,000 pounds (Figure 2, middle). It is attracting wide public attention not because it is a horse of enormous size but because it is a skeletal sculpture of a horse. The sculpture was inspired by George Stubbs' *Whistlejacket* painting and is based on one of the skeletal drawings in Stubbs' classic book *The Anatomy of the Horse* (Figure 2, bottom). Haacke titled his bronze skeleton *Gift Horse*. Apropos of its name, one of the skeleton's front legs is wrapped with a large ribbon tied in a pretty bow like on a present (Figure 2, middle). The ribbon displays a ticker-tape transmitting live electronic data from the London Stock Exchange. Why would Haacke decorate a dead horse from the 18th century with live stock quotes from the 21st century?

The answer lies in Haacke's knowledge of the historical background of Trafalgar Square combined with his imagination in using art as a platform to comment on established institutions. The Square's name commemorates the 1805 Battle of Trafalgar, the spectacular British naval victory over France dur-

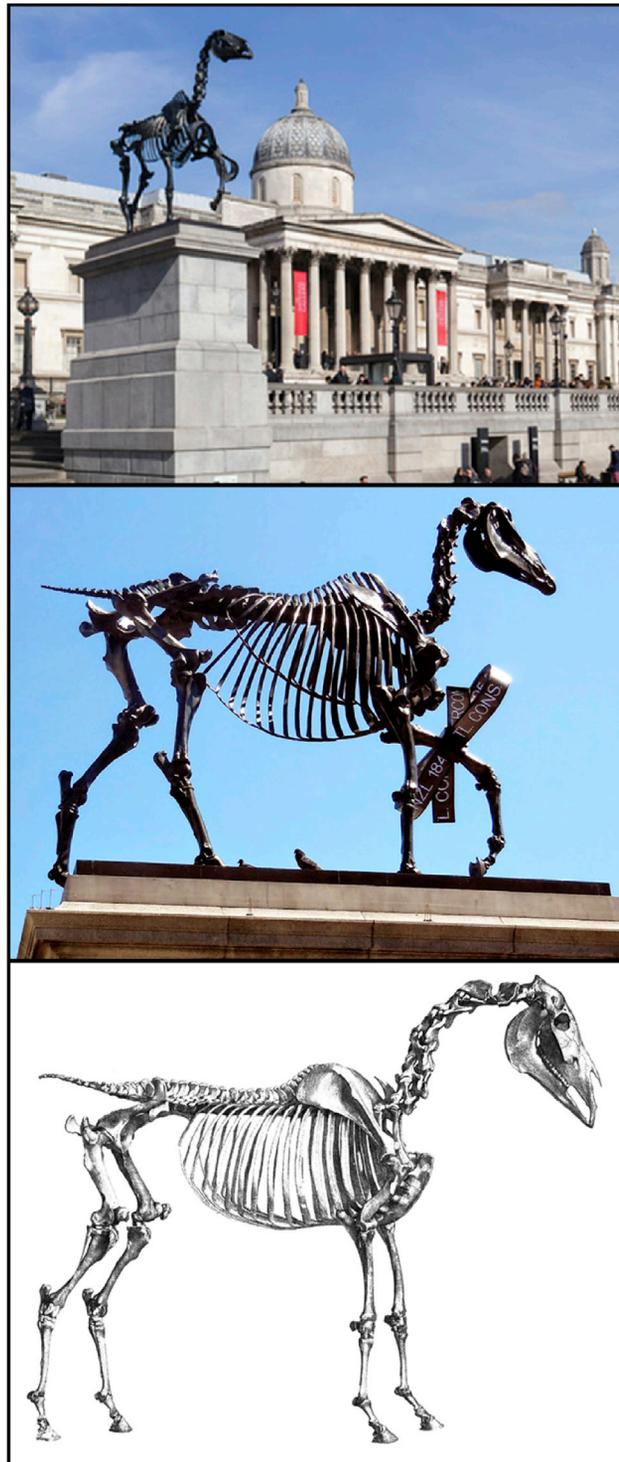


Figure 2. Haacke's Contemporary Bronze Sculpture Is Inspired by Stubb's Anatomical Horse

(Top) View of the north side of Trafalgar Square, showing the Fourth Plinth and the National Gallery from left to right. (Middle) Hans Haacke, *Gift Horse*, 2015. Bronze. Height, 15 ft. Exhibited on the Fourth Plinth at Trafalgar Square, London, 2015–2017. The tied ribbon bow on the right front leg of the horse skeleton displays a ticker-tape transmitting live electronic data from the London Stock Exchange. (Bottom) George Stubbs, *First Skeleton Table*, 1766. Copper plate drawing (McCunn and Ottaway, 1976).

ing the Napoleonic Wars (Hood, 2005). At the center of the Square stands a tall column on top of which sits a statue of Lord Horatio Nelson, England's greatest naval hero, who was killed at Trafalgar. Surrounding the Nelson Column are four large stone pedestals, which the British call the Four Plinths. Three of the four plinths carry equestrian sculptures of kings or military heroes.

The Fourth Plinth, erected in 1841, was intended to display a statue of King George IV on horseback, but the cost was so exorbitant that it was never completed, and it remained bare for 150 years until the British government decided to use it as a public platform for displaying a contemporary sculpture that could be viewed by the 40,000 people who visit Trafalgar Square each day. Every 1 to 2 years, 100 leading artists from around the world are invited to enter a competition. Since 1999, ten artists have been selected to showcase their artwork on the Fourth Plinth.

Combining Knowledge and Imagination to Create *Gift Horse*

Hans Haacke's *Gift Horse* is arguably the most deeply researched of all the sculptures to have appeared on the Fourth Plinth. As already mentioned, it is steeped in art history, reaching back to the anatomical work of George Stubbs. There is also the historical connection to the British and their passionate love for horses, which raises the question as to why Haacke would sculpt the skeleton of a horse rather than the real thing. I think he is teasing the British, reminding them of the precariousness of their Empire and of their poor financial situation 150 years ago, which left

the Fourth Plinth empty and bare. And now Haacke, a German-American, has come to the rescue—not with a sculpture of a real horse, but with the bare bones of King George's horse.

In addition to the historical references, there is a political bite to *Gift Horse*. The ticker-tape on the skeleton's leg is a reminder that money is the power that drives both the good and the bad in the world and the dynamic behind modern-day income inequality. Then there is the provocative title of *Gift Horse*. It is almost certainly an allusion to the Greeks' Trojan Horse that led to the saying "Beware of Greeks bearing gifts." Is Haacke telling us to "Beware of brokers bearing hot tips"?

George Stubbs and Hans Haacke produced their art in two different centuries. Yet, they achieved greatness by a similar route: both used existing knowledge as a stepping stone to imagination. Stubbs' knowledge of the anatomy and physiology of horses stimulated him to unite science and art in creative ways that resulted in his becoming one of our great portrait painters. Haacke's knowledge of complex contemporary social and financial systems stimulated him to expose in original ways those things in the world that need to be brought to public attention.

2015 Lasker Awards: A Marriage of Knowledge and Imagination

Like Stubbs and Haacke, the 2015 Lasker Awardees possess an intuitive talent for creating something new by blending knowledge with imagination. This special knack for newness allowed them to make discoveries that opened new fields of biomedical science. In much the way that Stubbs redefined portraiture by imaginative choice of subject matter and innovative elimination of background noise, this year's medical research laureates have produced original portraiture that explicitly and distinctly illustrates how our cells respond to DNA damage and how our immune system deploys a powerful strategy to fight cancer.

Basic Award

The Lasker Basic Research Award honors two scientists, Evelyn M. Witkin (Rutgers

University) and Stephen J. Elledge (Brigham and Women's Hospital), for discoveries concerning the DNA damage response—a mechanism that protects the genomes of all living organisms. The maintenance of genome integrity is a daunting task, owing to the constant assault on DNA by external agents (e.g., chemicals, radiation, UV light, etc.) and errors occurring during normal DNA replication. Witkin's groundbreaking research in the 1960s on UV radiation in bacteria led to the identification of the SOS response, a global response in which DNA damage leads to the expression of diverse gene products that not only enhance DNA repair and cell survival, but also increase mutagenesis and genetic variability. The mechanism mediating the bacterial SOS response involves the activation of about 30 unlinked but coordinately regulated genes, each controlled by a bacterial operon involving the same repressor (LexA) and inducer (RecA).

In the late 1980's, 25 years after Witkin's classic work in bacteria, Elledge began his studies of the DNA damage response in more complex organisms, working first in yeast and subsequently in mammalian cells. He discovered that eukaryotic cells sense and respond to DNA damage by a fundamentally different mechanism than bacterial cells even though the two systems share the same overarching theme. The eukaryotic mechanism is mediated by a signaling system involving a protein kinase cascade that senses damaged DNA. Once activated, the kinases produce multiple cellular responses, including changes in cell-cycle control, DNA repair, apoptosis, autophagy, and telomere maintenance as well as pathways involving RNA processing and modulation of energy metabolism. Human mutations in key components of this signaling cascade, such as those disrupting the function of ATM kinase, cause genome instability and cancer, as occur in patients with Ataxia Telangiectasia.

Clinical Award

The Lasker~DeBakey Clinical Research Award honors the scientist James P. Allison (University of Texas MD Anderson

Cancer Center), who pioneered a monoclonal antibody approach that unleashes the immune system to treat cancer, as first exemplified by the clinical success of CTLA-4 antibody therapy for metastatic melanoma. Allison's discovery of immune checkpoint blockade has now been extended to other T cell inhibiting pathways (e.g., anti-PD-1) for treatment of not only melanoma, but of other malignancies, including lung cancer.

Public Service Award

In much the same way that Haacke's knowledge of complex contemporary social and financial systems stimulated him to expose those things in the world that need to be brought to attention, this year's Lasker~Bloomberg Public Service Award honors Médecins Sans Frontières, an organization renowned for its bold and innovative responses to leadership in health emergencies, as recently exemplified by its frontline response to last year's Ebola crisis.

For a more detailed account of this year's Lasker awardees, please refer to the Lasker website at www.laskerfoundation.org and to the articles in this issue of *Cell*.

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