You've Got Soul

the science of individuality

By David Bochner

"...Animals are taking into account tiny signals of fundamental individuality when they choose mates. It gives a whole new meaning to the phrase 'liking someone for who they are.'"

Human beings have had millennia of experience in telling one another apart. Perhaps we take it for granted that we can distinguish one individual from another because it occurs so naturally that we barely have to think about how it works. But when two identical twins are standing next to each other, how do you tell them apart? Religious traditions have long recognized that there is a difference, hidden from the naked eye, that sets people apart. Many call it the soul. Albert Einstein, a man who straddled the realms of science, religion, and philosophy, also believed that the soul is a quality that belongs distinctly to a single human being. In an address to the Princeton Theological Seminary on May 19, 1939, he said, "It is only to the individual that a soul is given" (1).

Today, researchers are only just beginning to investigate these visceral notions of individuality. Scientific tools are becoming more precise and more focused, and genetic information about the human species has become available to any researcher who wants it. Now that the Human Genome Project has gone so far in finding how we are all the same, science is beginning to delve into how we are truly different. Where religion sees the individuality of the soul, we are now able to let science examine the individuality of the human being. As researchers draw closer to the sources of these perceived differences, perhaps the religious and scientific explanations will not be as different as we think.

Being Unique

In discussing the science of individuality, we would be remiss if we failed to mention genetics. Every person's DNA codes for every protein in their body, from those found in the eyes to those in hair to those in fingers. But let us return to the example of identical twins: their eyes, hair and fingers have been made according to the same genetic blueprint. However, they are distinct individuals who often have different tastes and personalities. At the most fundamental level, we can recognize not only that they are different, but how are they so. Nevertheless, the question remains: what are we seeing when we "see" individuality? Recently, a marriage of a genetics and neuroscience has offered a surprising discovery that brings us closer to understanding human individuality.

Transposons, or jumping genes, are tiny pieces of DNA that contain only enough information for them to copy themselves. As tiny, parasitic pieces of information, they are able to cut themselves out of the genome, copy themselves many times, and then randomly reinsert themselves into new locations (2). If they are inserted into a gene, they can interfere with the expression of that gene, changing the way the cell operates. Transposons were first discovered

credit: Jennifer Ang, HSR.

in Indian corn, where they inserted themselves into various color-determining genes to give the corn its distinctive mosaic appearance (2).

Both the laws of evolution and tests for transposon activity suggest that transposons are active in only a small subset of rapidly dividing cells (3). But researcher Allison Muotri and her colleagues wondered: can neuronal progenitor cells (NPCs), which give rise to neurons, which themselves are known for not replicating, still harbor actively replicating transposons? By implanting an artificial form of a transposon called LINE-1 into rat NPCs, they found that these cells can readily support such a process. The artificial transposon they used had been encoded with a special, interrupted form of the gene for green fluorescent protein. Only after the transposon had been copied, spliced, and re-inserted into the genome would it encode a functional product, making the cell fluoresce with a green color (Figure 1). Indeed, many of the cells glowed with a bright green color when transfected with LINE-1 (4).

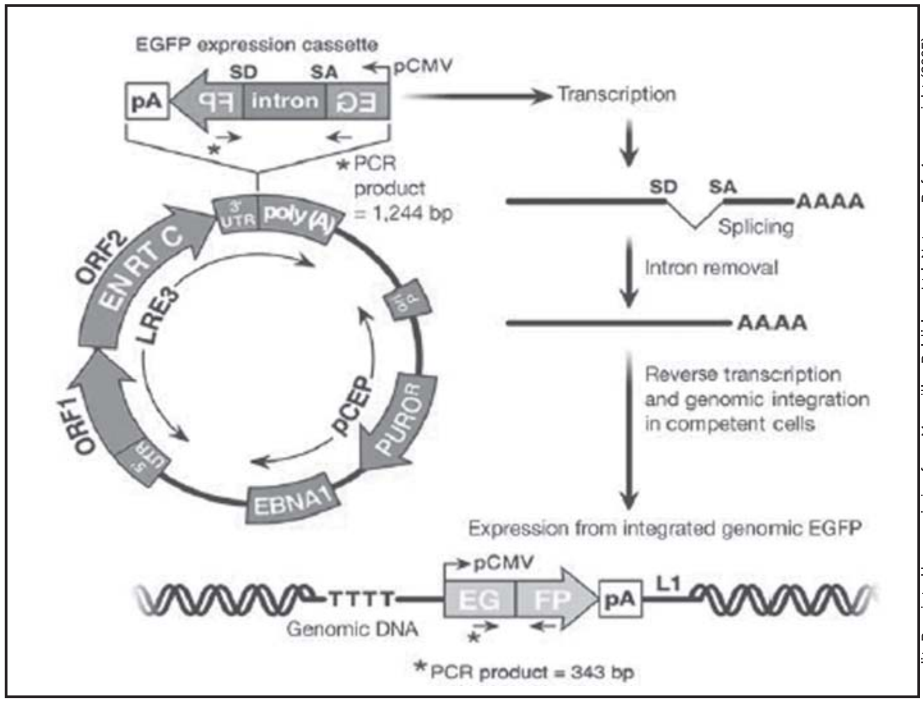

Figure 1. A diagrammatic representation of how Muotri demonstrated the insertion of LINE-1 elements into neuronal genomes. The transposon construct contained a green fluorescent protein (GFP) gene that was interrupted by other DNA. Only when the LINE-1 element was removed, modified, and copied, and re-inserted would the cell actually fluoresce in green (4).

But this procedure had an interesting effect on the cells: every so often, a cell that showed green fluorescence also showed abnormal behaviors that are associated with changes in the expression of various genes. The most common effect was the rapid differentiation and maturation of an NPC into a cell resembling a fully developed neuron (4). By analyzing these cells, Muotri found that every so often, the LINE-1 transposon could insert itself into a gene that the neuron was expressing and change the way in which the gene was expressed. In several cases, the insertion of LINE-1 resulted in the overexpression of a gene associated with cell maturation, making the cell mature far faster than normal (4).

This observation raised the question: if LINE-1 transposons can insert themselves into the DNA of NPCs, and if these insertions can change the way neurons behave, does this phenomenon occur in the cells of a complete organism? To answer this question, Muotri used the same transposon construct as before, but placed it into the DNA of mouse embryos such that all of the embryo cells would have the potential for the transposon to copy itself. As expected, these embryos possessed occasional cells in their brains that fluoresced with a brilliant green color, indicating that the transposon was actively being copied (4). By combining these results with those from the previous experiment, Muotri reasoned that these cells are likely to have undergone changes in gene expression (4). If transposons were to insert themselves with sufficient frequency into the genes of neurons, they could make the entire brain a genetic mosaic as unique as Indian corn.

Although there is still a great deal of work to be done, Muotri and her colleagues have suggested that these slight, random changes in gene expression might be sufficient to make the brain operate in a unique manner in different people (4). If a person's brain is changed even slightly by this phenomenon, it could be a key contributor to human individuality. This individuality could constitute a part of why we perceive human beings as being distinct and of what sets them apart in our eyes. This notion of distinctness helps to form the basis of what some religions call the soul. For instance, ancient Egyptian mythology incorporated human distinctness into a soul-like quality called the Ba, the supernatural embodiment of what makes a person unique (5).

Finding That Special Someone

Individuality, however, does not lie only in being inherently unique. A large part of the notion that human beings are distinct from one another lies in the recognition of one person by another. An obvious example of this idea is mating. How do animals, including human beings, find the "right" partner? Intuitively, we assume that they take some idea of what makes that person special, of who that person fundamentally is, and see if it fits with their own sense of self. In this case, unlike with the NPC transposons, science and intuition both have it right.

For years, scientists have recognized the major histocompatibility complex (MHC) as one of the key proteins that makes an individual unique. The exact structure of the MHC is determined by a series of genes with so many possible variations that it is almost impossible for two people to have the exact same MHC (6). This uniqueness makes sense in light of the MHC's function: the MHC plays a key role in helping the immune system identify cells as "self" or "foreign." It represents both our body's sense of self and its defense against invaders (6).

The MHC consists of several parts, or domains, only a few of which contribute to its uniqueness. Several relatively constant domains anchor the MHC to the membrane of antigen-presenting cells (APCs), the watchdog cells of the immune system (6). What makes the MHC unique is the binding area that projects from the membrane. This area is responsible for holding an antigen, or a small section of a foreign protein, and presenting it to supervisory immune cells, which are known as T cells (7). T cells have a similarly variable receptor on their surface that recognizes not only what molecule is being presented, but also what molecule is *doing* the presenting. In this way, the body uses the MHC to induce a reaction to foreign proteins but not to normal ones. The binding area of the MHC has several grooves that it uses to hold both the T cell and the foreign protein; the shapes of these grooves are controlled by a number of highly variable genetic factors (6).

Recently, studies have shown that the MHC is not merely an internal signal, but also an external one. While it has long been known that the MHC is the "self" signal to our own immune system, it has recently been found that many species, including rats, fish, and humans, exude chemical information about the MHC that is picked up by the sense of smell (6). Scientists believe that the MHC's antigen binding domain occasionally breaks off from the cell membrane and binds to odorant molecules that carry it out of the body (Figure 2). Recent studies suggest that these smell-related signals are used by many animals, and perhaps even humans, to choose their mates.

Many of these species, the most notable of which is the stickleback fish, select mates by maximizing the number of potential variations on MHC genes that are passed on to their offspring (7). By maximizing these variations, the two parents strive to have a child with a unique, hard-to-mistake MHC. With such an MHC, the child's immune system would be robust and less likely to make a mistake and ignore harmful invaders (7). Thus, many animals take tiny signals of fundamental individuality into account when choosing a mate, giving new meaning to the phrase, "liking someone for who they are."

In and of itself, this process makes sense from an evolutionary perspective. If an invader were ever able to mimic some part of the parent's MHC, the offspring with the most unique MHC would be least susceptible to such a disease. More importantly, however, it reveals an important interplay between our unconscious senses and our perception of a unique, distinct individual. In a sense, partners are chosen on the basis of a fundamental signal of who that individual is. Nature selects for "soulmates" who, through their mating, can create something truly unique between them.

There's Something About You

We have already discussed how people might be inherently unique, and how that uniqueness might lead to the development of the idea of the soul. But what about the act of perception itself? While it is important to determine what distinguishes one person from another, it is equally important to look from the inside and find out how we separate our *perceptions* of one person from those of another.

In some severe forms of epilepsy, tiny electrodes are implanted into the brain in order to help control seizures. Modern technology allows these electrodes to record as well as treat brain impulses, often on the scale of a single nerve cell (8). As a result, it is possible to record the electrical activity of single

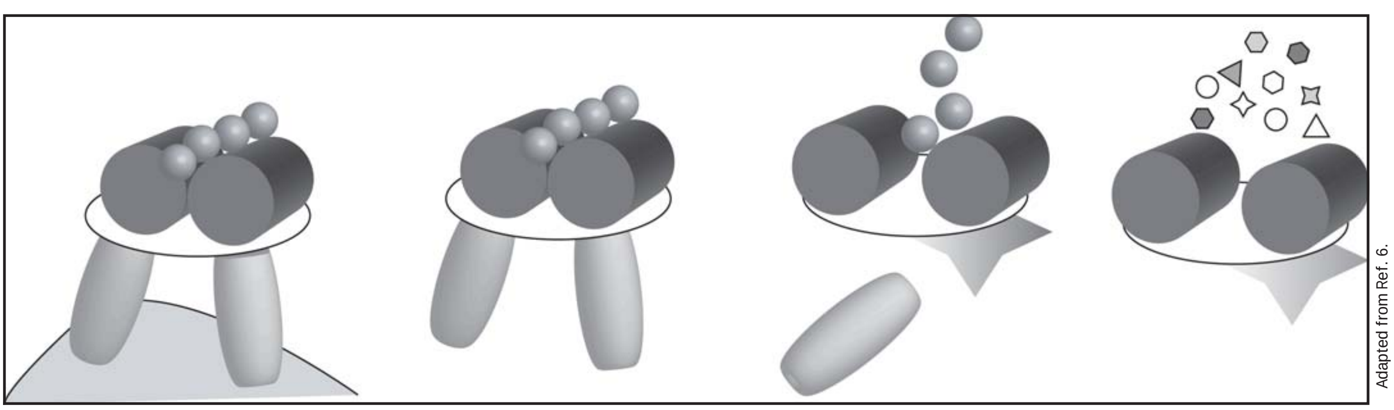

Figure 2. A diagram of how the MHC molecule might give off odorant signals. The MHC, which sits in the cell membrane, first breaks off from the membrane, leaving behind the membrane-bound domain. The binding portion (the flatter, top portion) is then free to bind to and travel with other molecules that eventually leave the body and become airborne (6).

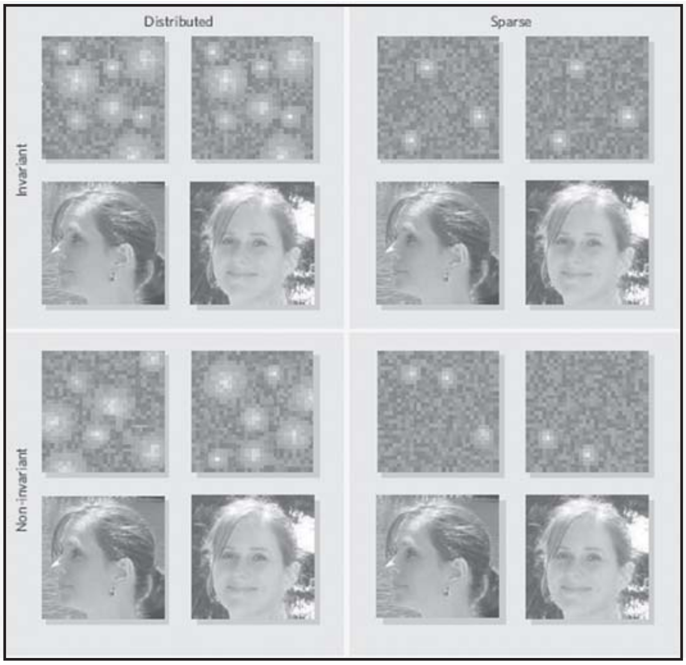

Figure 3. There are several possible ways in which visual information might be stored in nerve cells. These methods down into two intersecting categories: 1) whether the information is widespread across many neurons or sparsely given to a small number of cells and 2) whether the neurons that store and recall the information are the same every time. The diagram shows simulated responses to a familiar face, assuming each of the four combinations of these two categories (8).

neurons in response to various stimuli.

Computational neuroscientist Roderigo Quiroga and his colleagues chose a rather unconventional stimulus. They showed several individuals who had electrodes implanted into their brains photographs, names and drawings of famous people or places. They subsequently recorded their brains' reactions on a cellular level, focusing on a region called the medial temporal lobe, which plays an important role in visual processing (9). What they found was a surprisingly consistent pattern where specific cells fired off electrochemical signals at consistent rates, not just for particular faces, but for the entire identity of a person. Drawings, photographs, and even just the name in plain text of actresses like Jennifer Aniston and Halle Berry revealed specific, non-overlapping sets of cells that showed activity when the individual was exposed to one of these (9).

Part of what is remarkable about this perception is its consistency. It is well-established that certain neurons in various regions of the brain fire in response to various stimuli. But in Quiroga's experiments, the pattern according to which nerves fired for a certain celebrity involved a distinct, invariant set of cells (8). Neuroscientist J. Y. Lettvin once poked fun at the idea that there was one neuron assigned to recognize one person, coining the term "grandmother cell" to describe a cell specific for one's grandmother (8). But recent discoveries by Quiroga and his colleagues suggest that this notion may be closer to the truth than anyone had ever expected.

Simply put, it makes sense for neurons to store information in relatively small sets of active cells; it saves space and allows for an improved ability to pick important elements from visual information (8). But what is remarkable about Quiroga's work is, once again, the invariance of the pattern. Not only are there rare groups of cells storing information, there are also specific identities for which cells do the storing (9). The human brain is somehow able to parcel visual information off in such a manner that the same cells react to it, whether the picture is of Halle Berry in her Catwoman costume, or a pencil sketch, or even her name (Figure 3) (9). Impressively, these neurons do not fire for Jennifer Aniston, for whom a separate population of cells exists.

Although Quiroga's study gives us no clues as to what we see when we tell one person from another, it reaffirms the fact that our brains are seeing something which, even on the level of individual cells, is recognizable. The process of perceiving one human being as different from another is not merely an illusion that science can neither confirm nor deny; it is a reproducible, almost invariant pattern of cell behavior. Regardless of whether our nerve cells are detecting a soul, Quiroga's data shows that they are certainly recognizing some concept of an individual, independent from the means used to identify that person.

In many debates, religion and science often fall on opposite sides. But new discoveries occasionally demonstrate that the two sometimes agree. In some sense, human reasoning and intuition are important to both fields, and in the case of human individuality, their uses overlap. The same human intuition that senses something special or unique about a person can be used to determine what makes that person unique. For all the harsh logic of science, it can reaffirm the beliefs of human individuality even as it opposes others. Perhaps, by continuing to delve into the intuitions that tradition has brought to light, science can find its own version of the human soul, while still maintaining the scientific soul that has brought so much progress to mankind. H

—David Bochner '08 is a Neurobiology concentrator in Mather House.

References

1. "Albert Einstein: Religion and Science." 22 November 2005. URL: <http://www.sacred-texts.com/aor/einstein/einsci.htm>.
2. McClintock, B. "Controlling elements and the gene." *Cold Spring Harb. Symp. Quant. Biol.* 21 (1956): 197-216.
3. Ostertag, E. M. and H. H. Kazazian. "Genetics: LINEs in mind." *Nature* 435 (2005): 890-891.
4. Muotri, A. R., *et al*. "Somatic mosaicism in neuronal precursor cells mediated by L1 retrotransposition." *Nature* 435 (2005): 903-910.
5. Zabkar, L. V. *A Study of the Ba Concept in Ancient Egyptian Texts.* Studies in Ancient Oriental Civilization, 34. Chicago: University of Chicago Press, 1968.
6. Singh, P. B. "Chemosensation and genetic individuality." *Reproduction* 121.4 (2001): 529-539.
7. Milinski, M., *et al*. "Mate choice decisions of stickleback females predictably modified by MHC peptide ligands." *Proc. Natl. Acad. Sci. USA* 102 (2005): 4414-4418.
8. Connor, C. E. "Neuroscience: friends and grandmothers." *Nature* 435 (2005): 1036-1037.
9. Quiroga, R. Q., *et al*. "Invariant visual representation by single neurons in the human brain." *Nature* 435 (2005): 1102-1107.