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ORIGINAL CONTRIBUTION

On Reductionism in Biology: Pillars, Leaps, and the Naïve Behavioral Scientist

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Neurobiologists (Neurons) versus the Cognitive Neuroscientists (Cognition)

Cell Biologists (Cells) versus the Physiologists (Organs/Organ Systems)

Geneticists (Genes) versus the Biochemists (Metabolism)

Molecular Evolutionists (Gene/Protein) versus Paleontologists (Organism/Fossils)

Listed above are simplified descriptions of several past and current debates in the biological sciences. The points of departure in these conflicts lie not only in defining what the appropriate question is, but also in differences in approach to understanding certain phenomena. Such debates involve politics, can become personal and, consequently, can accumulate baggage that has little to do with the science itself. Notwithstanding, debate is understood to be an integral part of scientific progress, and a product of different perspectives and areas of expertise converging on large scientific questions. What the listed debates have in common are differences in the sizes of the units of study (the unit in parentheses) — in each scenario the first group of scientists study phenomena at a smaller scale than their opponents.

REDUCTIONISM'S MAIN EVENT

The flagship example of a scientific debate is perhaps the most visible debate in the history of science, that surrounding the origins of life on earth and, more contentiously, the origin of *Homo sapiens*. This debate is commonly labeled with terms such as "Creationism" and "Darwinism," but those who investigate further find that some of the most sophisticated arguments regarding evolution occur not between evolutionists and non-evolutionists but between the differing evolutionist factions engaged in a major sub-debate over how to study biological evolution most effectively.

In one corner of this sub-debate lie the "Ultra-Darwinists," comprised of biologists who generally point to natural selection as being responsible for the vast majority, if not all, of the variation we observe in organisms, both extant and in the fossil record. Their strategy involves

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identifying a characteristic of an organism followed by the construction of a model to explain how that characteristic evolved by natural selection, meaning that the trait conferred a reproductive benefit to that species in an ancient environment. John Maynard Smith and Richard Dawkins have been two of the many famous participants in this branch of evolutionary thinking and have put forth decades of convincing arguments on its behalf. Those who practice the more modern field of evolutionary psychology borrowed from this branch of evolutionary thinking [1].

The opposing side does not possess a readily identifiable label, but it's fair to say that their views are in stark contrast to those of the Ultra-Darwinists. Interestingly, they are every bit as evolutionist as the Ultra-Darwinists in their belief in the omnipotence of natural selection in explaining the origin, expansion, and existence of life on earth in lieu of any supernatural force. What they disagree on is the amount of biological variation that natural selection has crafted, as they often emphasize that other non-Darwinian forces can be very instrumental in creating the observable traits in many organisms. The late Stephen Jay Gould and many others popularized this wing of evolutionary polemic [2].

What is noteworthy in this example is the underlying similarity between this and many other debates, including those summarized at the introduction. They find a common theme, that of the appropriateness in the application of reductionism — the belief "that the higher levels of integration of a complex system can be fully explained through a knowledge of the smallest components" as expressed by Ernst Mayr [3].

THE "LEAP" METAPHOR

Reductionism works best when the problem needing reduction isn't intuitively far removed from the modern methods and understanding needed to solve the problem. When a sickle cell anemia patient undergoes a characteristically painful episode, we "reduce" the episode by switching on a microscope and observing the abnormal shape of the patients' erythrocytes. We further "reduce" the episode by observing properties of the hemoglobin molecule responsible for the abnormal function of diseased erythrocytes. We are successful in this instance because the answers we seek are clear and conspicuous. This is much different than describing sickle cell anemia symptoms in terms of quarks or superstrings, for instance. Trying to describe erythrocyte structural abnormalities in these terms would be nonsensical, because the "leap" between sickle cell anemia and quantum physics is, at the present time, too large. The intuitive connection between sickle cell anemia and a genetic mutation, on the other hand, is well within the scope of our current technology and understanding.

We use the metaphor of the "leap" to describe the connection between phenomenon and mode of explanation, because that is exactly what an effort at "reducing" a scientific explanation involves: taking a step from one place to another. We know how to walk and where each step will land, how it will feel, and because of this sureness we can estimate how far each step will go. The suspenseful aspect of a leap is that the further the distance, the more uncertain one is about landing effectively.

As illustrated in Figure 1, knowing one's footing, leaping capability, and exactly where one needs to leap, increases the probability for a successful leap. For instance, our thorough understanding of the structure and properties of hemoglobin and our knowledge of the symptoms that the sickle cell anemia patient suffers increases the chance that the connection drawn between the two is a valid one.

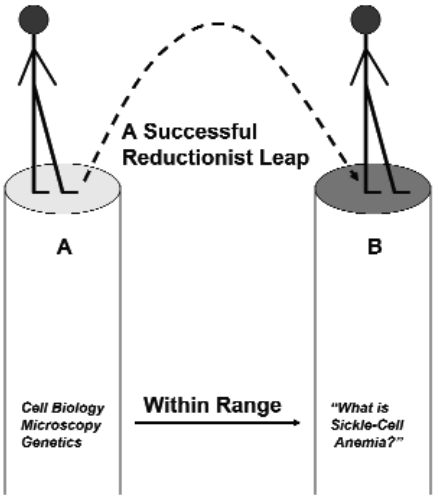

Figure 1. A successful Reductionist leap. The scientist in the figure has a clear understanding of what he/she is asking: in this case: "What is Sickle Cell Anemia?" Sickle cell anemia is a disease with conspicuous symptoms that follows a Mendelian pattern of inheritance. The tools used to answer a question comprise the footing of the reductionist leap. The leap distance is how close pillar **A** is to pillar **B**, meaning how well the acumen in pillar **A** can answer the question posed in pillar **B**. The closer the distance, the better chance for a successful reductionist leap.

Reductionist thinking is particularly subject to this "weakest link" syndrome: Charles Darwin, despite understanding the role of heredity in natural selection, misunderstood genetics, which was responsible for his inability to complete the link between genetics and evolution [4]. As intrigued as many of us are by superstrings, physicists barely know enough about them to describe sub-atomic particles, let alone sickle cell anemia. When we don't agree on the avenue towards explanation, we cannot arrive at an explanation. This is depicted in Figure 2.

HUMAN BEHAVIOR AND REDUCTIONISM: FRIENDS OR FOES?

A classically contentious area of science where reductionism has simultaneously gained champions and detractors is in the realm of human behavior and, more specifically, behavioral genetics. Some might argue that we as a society, for example, feel far more comfortable discussing why a young girl "has her mother's eyes," than we do the possibility that she has her "father's temper." The discomfort is often blamed on societal efforts of being "politically correct," a fear that biology might tell us something contrary to our assumptions, how we view ourselves, and how society is currently run [5]. This is the result of an overall ugly scientific past in the science of human behavior, a field of science that has harbored some of history's most vaunted exercises in scientific foolery.

This questionable past has caused many to approach modern behavioral science with heavy suspicion. Some might argue that it is time for us, as both a scientific community and society at large, to move ahead and embrace the biological frontiers of the behavioral sciences, because ultimately we benefit in countless ways from knowing how our biology impacts our behavior.

Reductionism applied to behavior does have some merit. Strikingly, we are learning more about the biological and genetic roots of diseases like schizophrenia and possibly autism [6]. Several studies once argued that carrying an extra Y chromosome led to relatively aggressive behavior in the some of the carriers [7]. In other behavioral abnormalities, the "leap" between agent and behavior can be even simpler; we understand why cocaine is

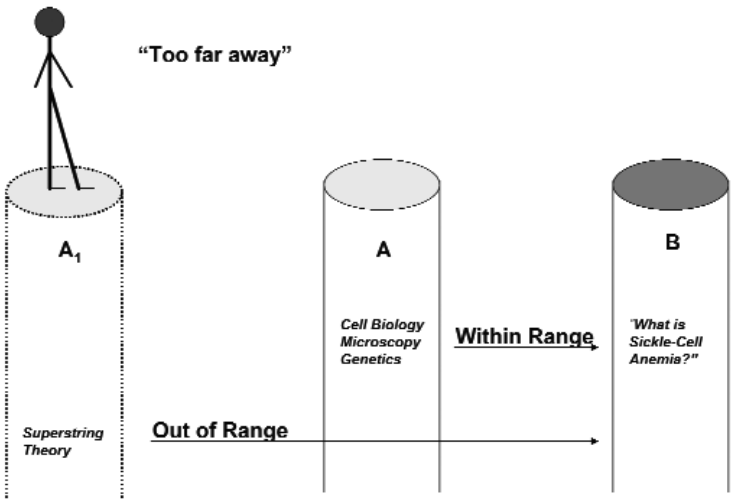

Figure 2. "Too far away." This occurs when the means to understanding a problem is too removed, intuitively, to lead to a helpful explanation. In this example, superstring theory is called upon to explain a medical condition. Superstring theory has come a long way in sophistication, but not nearly enough to explain macro phenomena like sickle cell anemia.

addictive and why too much ethyl alcohol can contribute to drunkenness through the study of receptors and neural synapses. We know how *Homo sapiens* behave when they have too much to drink. If inebriation presented as mild fatigue, we wouldn't know what to look for, which would muddy the preciseness of its study.

Impreciseness of study has higher stakes in the biology of behavior than in other fields of science. While a misstep in application of superstring theory can lead to the incorrect calculation of the physical properties of a subatomic particle, a misstep in the behavioral sciences has ramifications far greater. Society looks to the behavioral sciences for insight, because it is here that society searches for a ground zero of moral judgments, which often are crystallized into its laws. For example, if biology refutes the claim that "refrigerator mothers" are the cause of autism, then no longer can society, or the law, confidently blame mothers for that condition [8]. Indeed, in the behavioral sciences, overzealous applications of reductionist thinking deserve special attention and, where it is abused, heavy criticism.

THE NAÏVE BEHAVIORAL SCIENTIST

The reality is that most human behavioral disorders don't present with symptoms as conspicuous as hallucination. The vast majority of behavioral disorders have symptoms that are so subjective that one would be wise to question the existence of a specific "behavior" at all. We'll construct a hypothetical example that illuminates this problem: a young scientist interested in the existence of a gene or set of genes for "deviant behavior." The problem arises in defining what exactly "deviant behavior" is and exactly where one looks for people with this gene.

Let us place ourselves in the shoes of this behavioral researcher as he battles his conscience. We'll outline his thought process and demonstrate how hubris leads

to frustration in attempting to sort out how to study a "deviance gene." This example is not intended to serve as a straw man to debate against the specific case of a gene for deviant behavior but instead to provide a detailed example of the ways in which reductionist thinking is vulnerable to missteps.

We, the behavioral scientists, understand that in most large-scale genetic studies a substantial sample size of affected and unaffected individuals is required to trace the origin of a gene. Our first task then is to isolate a population where our "deviance gene" might be present in higher frequency than normal. This is similar to a scenario where, if we were interested in genetic determinants for high blood pressure, we might survey several cardiology clinics because carriers of a "high blood pressure gene" should be more prone to suffer from heart problems than the average person. In the case of deviance, the world provides us a parallel to the cardiology clinic in the prison system, which is populated by people whose behavior deviated from that which their larger society deems appropriate.

This logic appears sound until we notice that the deviant behavior leading to incarceration runs the gamut of the human behavioral spectrum. One could argue that the only connection between an incarcerated murderer and a marijuana peddler is their presence in prison. We continue that train of thought and ask ourselves what these other groups of criminals might have in common: rapist and a petty thief; a repeat DWI offender and a computer hacker; a con man and an inner-city gang member. The only common gene one might find in this population would be a gene for violating a federal, state, or local law. That being the case, Leona Helmsley would have the gene and apparently so would Martha Stewart. Obviously, the search for a deviance gene in a broad sense is unhelpful. We need to be more specific.

We convince ourselves that the "deviance gene" shouldn't be present in people who commit their acts for scrupulous purposes. We sigh in relief because we've escaped the first potentially confounding hurdle and now have a rationale to eliminate, for example, politicians who break the law, from our study. We say to ourselves: *Maybe the gene we are in search of codes for behavioral disloyalty towards a larger society? Is it a gene for low moral threshold, societal non-conformity? It certainly seems to make sense. Criminals, after all, did do a poor job of conforming.*

We take this thinking to a county jail and interview incarcerated young people who speak, amongst other things, of the gang structure that exists in prisons and in America's cities. Many incarcerated persons are members of gangs in prisons and some of the most disturbing violence is on account of gang rivalries [9]. We decode to focus on gangs because they exist both within and outside of prisons, and therefore, could be a target population for our study. We interview several prisoners and urban gang members and think we are on the right track. Many of those we interview seem deeply disturbed and have taken part in destructive violence. We think we've isolated our target group for deviance.

A disturbing thought overcomes us as we ponder our interview data, pertaining to what the data communicate about the gang structure that many incarcerated young people are a part of — we seem to have underestimated the sophistication of gang structure. We ask ourselves: *Are gangs the appropriate place to search for "deviant" behaviors? Aren't the inner-city gangs of the United States troubling institutions specifically because the kids who join them are loyal? Aren't gangs a large problem because kids do conform to them and their rules? Isn't that what makes them bad? Is it the fact that they are col-*

lectives, with hierarchies, with codes and laws of their own? Members often pay duty and will give and take a life in the name of their institution [9]. If anything, gang members are too loyal. Violence often occurs on the basis of this loyalty to their peer group.

We stumble through this apparent hurdle, but are rescued when we tell ourselves the following:

The gang members' loyalty is not for constructive purposes, but for destructive purposes. So maybe our gene is for "destructive deviance" and not solely for deviance.

But further discomfort follows this declaration, as we admit that *most of the people in prison, including many who have committed violent crimes, involve behavior and crimes committed in pursuit of wealth. Much of the imprisoned population simply used illegal means to attaining the wealth. Crack cocaine dealers don't seem to risk their freedom and lives on inner-city corners because it's fun, they likely believe the risk worth the financial return.*

With our pride still intact, we attempt to move forward. We try to localize our search, to eliminate Martha Stewart from our study as we note that *obviously she is different than the inner-city drug dealer.* We think we've found an escape by saying that perhaps violent criminals are what we are looking for. The problem is that focusing on violence eliminates nearly half of the imprisoned population in many states who are incarcerated for non-violent crimes [10].

We decide to pursue the violent aspects to deviance, as it seems a bit more conspicuous, and, therefore, more amenable to study. In the process, we are forced to admit several things: *Yes, the gang member from East Los Angeles does display loyal behavior, and yes, this loyal behavior might be at the root of the gang problem in American inner-cities. They are loyal. They kill, and are willing to be killed, for a purpose. They kill not in the name of dollars alone, but in the name of a gang, which is often a street or section of some neighborhood, a highly immaterial entity requiring manufactured allegiance.*

Unfortunately, we realize that the same adjectives could easily be applied to a soldier fighting in any given war, people who are not incarcerated, not criminals, and by most standards, not deviant.

We elaborate on this thought. *A private in the United States Marines fights and kills on orders from persons with higher authority, people who are generally not family members, with allegiance that is manufactured. A motivation other than monetary gain drives many brave deeds, but respect, honor, and belief in the cause being fought are necessary; hence, the discipline and drilling involved in most military training.*

We become uncomfortable with this parallel, because sadly, we cannot tease apart the urban gang member from the fictional "Private Ryan." We continue: *Both gang members and Marine privates commit startling acts of bravery. The difference lay in that the private's acts are legal under the United States Constitution, while the gang members' acts are illegal under local and federal law.*

Unless there is a gene for obeying the United States Constitution we are forced to admit that, cognitively, the Marine Private and gang member might engage in very similar behavior. We speak on the perspective of the brain:

As far as the brain is concerned, unloading a Glock-9 at a rival gang member who is on one's "turf" might not be much different than a soldier firing rounds from an AK-47 at platoon of Vietcong guerillas during the Vietnam War. In both cases the goal is to end the life of another person, in the name of an allegiance to some entity, group, or collective. Neither the gang member nor the U.S. soldier is

hunting for food, but rather killing on principle, because they were told to and because they feel that the killing has a moral justification.

With this understanding, we return to the original focus of our study, the "deviance gene." We remember, however, that we were misled earlier, because if "deviance" is defined by breaking the law, then Pete Rose might be just as likely to carry the gene as the modern day Al Capone. This isn't a comforting thought.

We tell ourselves *no, Pete Rose does not have the "violent" aspect to the "deviance gene*" and begin to suspect that the gene we are in search of is a "violence-deviance" hybrid. We sit on that thought for a minute but soon realize that we are beginning to make a fatal logical error common in biology: trying to craft the genes around what we are trying to prove and not crafting what we are trying to prove around the actual existence of genes responsible. At this rate of lazy intra-polemic we'll need a "bank-robber gene," right next to the "drug dealer on Linden Boulevard gene," with the "con man gene" on the next chromosome. We are forced to chuckle at our hubris, and move on.

In the course of our study, we are finding that the search for a "deviance gene" is loaded with many other contradictions and confounding loopholes. What we are also finding is that in studies like these, separating the moral from the scientific isn't easy; an oil tycoon and a cocaine drug kingpin might actually have a lot in common, cognitively. The fact that one gains wealth legally and the other illegally says nothing for a biological and, therefore, genetic difference between the two of them. Reluctantly, we decide to put the study aside for a few days and go back to the drawing board.

REDUCING REDUCTIONISM

The situation in Figure 3 below outlines an error in misidentification of the parent problem in a reductionist appeal. In this case we have no idea where to look for a "deviance gene" and which populations to screen, because we realize that the notion of "deviant behavior" is far too sub-

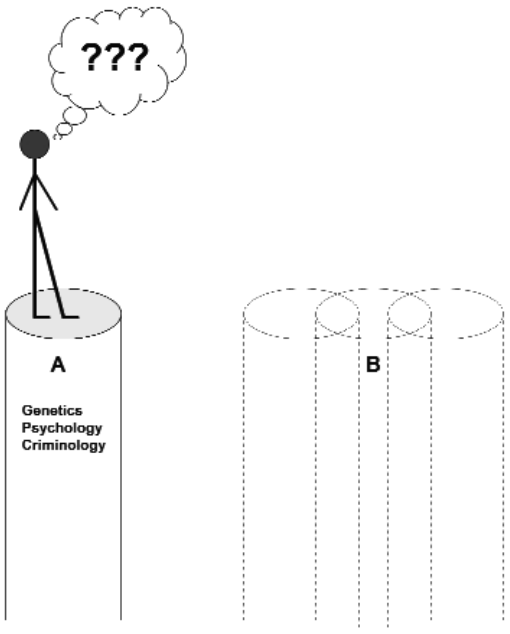

Figure 3. "Imprecise destination." The behavioral scientist in the figure is unsure of where to leap. The pillar **A** contains the tools that will be called upon to answer the question in pillar **B**. In this situation, the acumen in pillar **A** can be infinitely sophisticated, yet the question posed in pillar **B** cannot be properly located and, therefore, cannot be answered.

jective to merit a helpful genetic study, as our genes don't magically fit behaviors for the sake of publication. Interestingly, deviant behavior is hardly the only behavior where searching for a genetic source runs into the outlined roadblocks. Deviance is no more prone to the outlined missteps than any other well studied human behavior. Intelligence, the prince of debated human behavioral characteristics, finds at least as many barriers to a consensus understanding. Both deviance and intellect were, after all, two of the cornerstone targets of the eugenics movement, and thousands of people were sterilized on the suspicion or belief that they harbored biology that predisposed them to deviant behavior or inferior intellect [11].

The truth is that there are likely very few labs in the world dedicated to studying the genetics of "deviance" specifically, and amongst those, it is likely that they have a better grasp on the problem than the outlined "Naïve Behavioral Scientist." That example was used solely to illustrate how the study of human behavior is particularly vulnerable to overzealousness, the type that is typical of misappropriated reductionist thinking.

One could trace the abuse of reductionist thinking to societal and professional pressures; any amount of data linking large complex phenomena to smaller, more manageable phenomena is going to be explored because in the dynamic institutions that are human societies, we appreciate anything that can be written in stone such that we can feel comfortable making a moral judgment. For example, in the case of autism, the "refrigerator mothers" explanation was simpler to understand, and perhaps easier to deal with, than a complex gene-environment interaction that we are still likely decades away from fully decoding.

With its potential for error, one might ask about the future of reductionist thinking in the behavioral sciences — are its flaws just a necessary outgrowth of its successes? Recently, the same genetic mutations have been shown to play a role in vastly different psychiatric disorders, further clouding the relationship between genetics and psychopathology [13]. Surely, if the genetic boundaries are unclear between behaviors that appear as different as manic depression and schizophrenia, we can expect behaviors that we diagnose legally, like deviance, to be at least as complex in biological underpinning, assuming there is a specific biological underpinning.

Indeed, questioning existing dogma can only improve our understanding, but we certainly don't want a world totally bereft of reductionist thinking. Successful reductionist "leaps" have benefited humankind and the world in countless ways. It's not reductionism, per se, but the distance between the pillars that might need re-evaluation. Maybe science can learn that, in addition to being humbling, complexity is as intriguing as simplicity. This is a lesson that the human genome project has taught the world. Only a few years, ago many believed that a complete human genome sequence was the crown jewel of biology and that the sequence alone was the key to understanding life. This is no longer the case, as the scientific community now speaks of a "transcriptome," "proteome," and "kinome," all representing pillars of understanding between an inert sequence of nucleic acids (the genome) and us as living, metabolizing, human beings. This has engendered a paradigm shift in the way biology is discussed: simply screaming out "A Gene for Cancer," for example, no longer means very much. Biomedical research now understands the importance of what goes on in between the gene and the cancer, between the genes and phenotypes. And as far as the behavioral sciences go, moral judgments might have to be made without the aid of biology. Maybe science simply

isn't equipped to fill all of the gaps, make all the "leaps" we want it to make.

Making moral judgments without the aid of biology is a not a task that society should fear, as this apparent quandary highlights one of the defining characteristics of our species: the ability to craft a seemingly infinite array of personalities and psychologies from a finite genetic palette. Society needs only to learn to be satisfied with the very modest, yet enormously helpful, "leaps" that scientific knowledge can provide us, that do not build our world for us, nor tell us what is right from wrong, but give us a foundation, however small, upon which to build society.

REFERENCES:

1. Gould, SJ. Darwinian fundamentalism. NY Rev Books. June 12, 1997.
2. Stearns SC. Less would have been more: Review of *The Structure of Evolutionary Theory* by S.J. Gould. Evolution 2002;56: 2339-45.
3. Mayr E. *What Evolution Is*. New York: Basic Books; 2001: p. 290.
4. Silver BL. *The Ascent of Science*. New York: Oxford University Press; 1998.
5. Pinker S. *How the Mind Works*. New York; W.W. Norton; 1995.
6. Varma SL and Sharma I. Psychiatric morbidity in the first degree relatives of schizophrenic patients. Br J Psych. 1993;162:672-8.
7. Geerts M, Steyaert J, and Fryns JP. The XYY syndrome: a follow-up study on 38 boys. Genet Couns 2003;14:267-9.
8. Cohen S. *Targeting Autism: What We Know, Don't Know, and Can Do to Help Young Children with Autism and Related Disorders* (updated edition). Berkeley: University of California Press; 2002.
9. Schneider EC. *Vampires, Dragons, and Egyptian Kings: Youth Gangs in Postwar New York*. Princeton, New Jersey: Princeton University Press; 1999.
10. BJS. *Sourcebook of Criminal Justice Statistics, 2000*. Washington, DC: USGPO; 2001.
11. Virginia governor apologizes for eugenics law. USA Today; May 2, 2002
12. Buervenich S, Carmine A, Arvidsson M, et al. NURR1 mutations in cases of schizophrenia and manic-depressive disorder. Am J Med Genet. 2000;96:808-13.
13. Keenan K, and Wakschlag LS. Are oppositional defiant and conduct disorder symptoms normative behaviors in preschoolers? A comparison of referred and nonreferred children. Am J Psych. 2004;161:356-8.