# Wormwholes: A Commentary on K. F. Schaffner's "Genes, Behavior, and Developmental Emergentism"*

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Although *Caenorhabditis elegans* was chosen and modified to be an organism that would facilitate a reductionist program for neurogenetics, recent research has provided evidence for properties that are emergent from the neurons. While neurogenetic advances have been made using *C. elegans* which may be useful in explaining human neurobiology, there are severe limitations on *C. elegans* to explain any significant human behavior.

**1. Introduction.** The Bristol N2 strain of *Caenorhabditis elegans* is an organism constructed for the genetic analysis of behavior. It has an invariant cell lineage (the cell divisions which occur between the fertilized egg and the adult are largely identical and always produce the same set of tissues), an invariant nervous system whose 302 neurons have reproducible synaptic connectivity, and an invariant genotype. Moreover, this strain of *C. elegans* has a repertoire of behaviors that it performs on a very limited environment, a flat agar surface supplied with a uniform pad of identical bacteria. The very richness of life that the Developmentalist Challenge claims engenders diversity have been hunted down and eliminated from *C. elegans* research.

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Ken Schaffner has now turned to this organism—an organism "designed" to show that the basis for behavior lies in the genes—to ask whether it supports the precepts of the Developmentalist Challenge. The main issues of the debate can be distilled to the following five questions:

1) Are discrete behaviors determined by single genes?
2) Is behavior an emergent property?
3) Will genetic analysis in *C. elegans* reveal the origin of behavioral variation?
4) How does knowledge gained from *C. elegans* bear on human behavior?
5) Do genes regulate "higher' behaviors unique to animals like humans?

**2. Are Discrete Behaviors Determined by Single Genes?** *In the context of a whole organism*, a single gene can determine a behavior. In *C. elegans*, the most compelling examples (and those discussed by Schaffner) are the genes encoding the mechanosensory receptors and the odorant receptors, for example, the *odr-10* gene. This gene encodes the odorant receptor for diacetyl. In the absence of a functioning copy of the *odr-10* gene, the animal simply does not show movement (chemotaxis) to diacetyl. Thus, in this sense, *odr-10* determines attraction to diacetyl (Sengupta et al. 1996).

That genes affect behavior and in some sense determine behavior is obvious in humans, as well as in *C. elegans*. Children with Angelman syndrome generally have inappropriate laughter, while children with Prader-Willi Syndrome have an insatiable appetite. Boys lacking the gene for hypoxanthine phosphosphoribosyl transferase have an uncontrollable urge towards self-mutilation, while those with William's Syndrome tend to be gregarious and empathetic. As yet, we do not understand how the genes involved in these syndromes confer these personality traits to the afflicted individual.

Still these genes do not determine a behavior. The HPRT gene of Lesch-Nyhan syndrome encodes a purine-salvage enzyme, not a compulsion. Genes do not act in a vacuum, and genetic analyses measure the effect of the loss or gain of gene function in an intact organism, that is, where all other genes are intact and functioning. Mice lacking the HPRT gene do not share the human behavioral phenotype. Thus, the geneticist determines the function of a gene by analyzing the difference between an intact individual and a second "identical" individual which only differs at this single locus. Thus, a gene may be an essential component of any behavior, but it does not "determine" it.

**3. Is Behavior an Emergent Property of Many Genes?** While *odr-10* may encode a protein essential in binding diacetyl, more complex behavior, such as the actual *movement* of the worm toward the source of diacetyl, is diffusely encoded. This movement requires the products of a myriad of genes to construct and operate a motor circuit. (Here it is important to identify the level of the behavior, and Schaffner sometimes suggests that it is the worm's ability to detect diacetyl; at other times he suggests it is the ability of the worm to move towards the source of this compound.)

One would have to conclude that behavior is an emergent property from the levels of the gene or the neuron. Certainly there is nothing in the nature of the gene or of the neuron which could allow us to predict the nature of behavior that arises from it. We already know almost the entire DNA sequence of the *C. elegans* genome, but the predicted behavior of the animal does not emerge from this knowledge. We also know the complete neural connectivity of the worm, but the behaviors of the animal cannot be read from the patterns of neuronal connections.

A behavior such as chemotaxis occurs in a network or field in which the interactions of several genes and gene products are occuring. Thus the knocking out of any one of them—the genes involved in forming the odorant receptor, the genes encoding the proteins that transmit this signal to the cell body of specific neurons, the genes involved in allowing other neurons to form synapses with particular muscles, the genes involved in neuromuscular adhesion and muscular contraction—would prevent the behavior. To say that a particular gene "controls" a complex behavior is akin to saying that a person scored the "winning" basket in a 100-point basketball game (see Wheeler 1991, Gottlieb 1992). Similarly, to partition a behavior into its genetic and environmental components is akin to saying that the player scoring that goal was acting independently of his or her teamates and the opposing team.

**4. Will Genetic Analysis in *C. elegans* Reveal the Origin of Behavioral Variation?** The behavioral biologist cares about variability in a population, why certain individuals act differently from one another. Darwin's interest in inheritance focused on these subtle variations in the behaviors in a population. On the other hand, these subtle variations in behavior are just the sort of thing that a good Mendelian geneticist abhors. The Darwinian concept of the gene was incremental in nature; many genes are thought to act in concert to produce a behavior. By contrast, the Mendelian concept of the gene was discrete, each gene regulating a defined trait and has an invariant relationship between an allele and phenotype. (Neither Darwin nor Mendel used the term "gene," nevertheless each had a concept of the unit of inheritance). In

the creation of model organisms for the study of genetics, *the variability which is so important to the evolutionary biologist is bred out.* With this standard reagent, the geneticist can look at genes in a "+" or "−", or normal or abnormal, manner. To a geneticist, genes have discrete outputs, they are digital in nature. This is largely for practical reasons: we cannot follow, map, and clone a gene unless there is a discrete trait associated with its presence and absence. For this reason, screens for behavioral mutants preordain an outcome which indicates that each gene regulates a discrete behavior. But this may be a fallacy of the technique and not reflect reality. Moreover, when mutations emerge with complex phenotypes (such as the inability to move towards any compound), we tend to discard them.

Thus, *C. elegans* research will tend to indicate a discrete relationship between genes and behavior. The behavioral biologist cares about subtle variations that can be as diffuse as personality traits, just the sort of thing that a geneticist abhors. For the behavioral biologist, the behavior is the output of developmental history, the physical environment, one's status in a population, contingent personal history, and the sum inheritance of one's genotype. This is unsatisfying to the reductionist behavioral geneticist because behavior becomes simply descriptive of what is observed. It becomes a historical study. If a worm had personality, a *C. elegans* behavioral geneticist would most certainly ignore it, and the reasons for this obstinancy are valid: the genetic inputs into behavior have not yet been determined. We first need to define the limitations on behavior imposed by genetics. Then, perhaps, future generations can fix an input on the more difficult phenomena of environmental variability and chance.

**5. How Does Knowledge Gained from *C. elegans* Bear on Human Behavior?** Work in *C. elegans* has shown that genes can have very discrete effects on simple behaviors. But the behaviors in which we are most interested are complex human behaviors—consciousness, attention, agency—and these we will never understand these by studying *C. elegans*. With *C. elegans* we have a hope of understanding the relationships of genes to neurons, from neuron to circuit, from circuit to behavior. Certainly, principles concerning simple behaviors learned in *C. elegans* will obtain in humans. We expect that the mechanisms underlying even more complex behaviors such as learning or the emergent properties of circuits will be shared in worms and humans. Although the principles distilled from such studies will obtain in humans, it does not follow that we will understand human behavior at the level that concerns the philosopher. The dangerous assumption here is that the behavior of *C. elegans* translates to humans; but in fact many of the

behaviors we are exploring are no more complicated than the knee jerk reflex in humans which only involves 3 neurons. Similarly in *C. elegans* most behaviors only encompass neurons at three levels: the sensory neurons, interneurons, and motor neurons. *C. elegans* offers a bewildering richness of behavior with only 302 neurons, and the behaviors of genetically identical nematodes on an isotropic environment are often different. One of us (E.J.) has mutants in which most worms lie straight in a paralyzed manner; but a fraction of them will consistently take on a quite different "curly" posture. A "cloned" animal does not breed true in relationship to this posture but reproduces the original distribution of phenotypes. There is a stochastic influence. In organisms with the same inheritance, a small set of neurons with identical connections, and the same environment, there are still behavioral differences as a result of chance events during development. What complexity does the human offer with $10^{12}$ neurons, some of them having thousands of connections with other neurons? What complexity is then added by having some neurons which respond to the rich abiotic, biotic, and social environments given to humans?

So what have we learned from *C. elegans* that will bear on humans? We have learned that genetic differences can affect behavior. The question is not "do genes control behavior"? Yes, they can. But rather, "to what extent do genes control behavior?" In fact, in some sense, we already know that genes can control consciousness and free will. There are several human mental retardation and behavioral syndromes (such as those mentioned earlier) wherein conscious behavior is altered by the loss of individual genes. Does this explain consciousness or free will? No. Or at least no better than atomic structure and quantum physics explain the emergence of life.

**6. Do genes regulate "higher' behaviors unique to animals like humans?** If genes clearly affect behavior, what is all the fuss about? The issue that upsets certain scientists is raised by the popular press: do our genes *determine* our behavior? Are we meaty marionettes jerked about by our genes? We agree with Lewontin that it is very dangerous to ascribe complex behaviors solely to genotype. A deterministic philosophy is dangerous for an organism with consciousness, agency, and different environments. If homosexuality were genetic, then why aren't all Greeks practicing bisexuals today? If our genotype determines our behavioral phenotype, how can there be people who undergo major personality changes within their lifetime?

Another fallacy of these debates is the Nature vs. Nurture dichotomy. First, measures of heritability are not fixed. Heritability is a measure of the degree a trait is inherited in a certain environment. It need

not even be a genetic parameter (Lewontin 1970, Block 1995). In *C. elegans* research, we attempt to keep variations in the environment to a minimum and thereby maximize the heritability of a trait. In humans, a particular allele of a gene could be exposed to similar or radically different environments and the heritability will vary as a consequence. Second, the variance seen in such measures is often attributed to the environment—specifically, the contribution that does not come from inheritance must come from the environment—but this is not necessarily so. Differences in connectivity could be caused by stochastic developmental effects during development (see Schnabel 1997). The nervous system also seems to encourage such differences by the "winner takes all" mechanisms caused by Hebbian rules of neuronal connections. Thus, differences in neural connections and their strengths may emerge from developmental noise, respecification by stimuli, and by selective mechanisms that occur in development.

A third fallacy is that animal studies can reveal the entire human behavioral repertoire. While humans are definitely animals, animals are not humans. Darwin noted the domestication of animals as evidence that behavioral traits have a genetic basis, and breeders have noted that single-gene inheritance can account for differences in the behaviors of domesticated mammals. This is to be expected, since there is an obvious endocrine component to certain behaviors. But human behaviors also have more complex levels. If you wish to curb aggressive behaviors in a bull, you can castrate him. If you wish to curb aggressive behaviors in a man, *threat* of castration is often sufficient. And these two mechanisms can act through different pathways (i.e., threat of castration need not reduce testosterone levels, etc.). Moreover, there will be variations in the responses to threats, and these responses also are a component of behavior.

Between the gene and the behavior there are multiple levels. Having a gene does not mean that it is necessarily transcribed, and transcribing the gene does not necessarily mean that the mRNA will be processed and translated into an active protein. If the protein is active in a neuron, it does not mean that it will contribute to the function of the neuron, and if the neuron functions, it can act differently in different networks. Like certain genes that synthesize enzymes in the liver or crystallins in the lens (the same protein having different functions), the properties of a gene product depend upon its context. The deletion of the *fosB* genes from mice will change the nursing behavior of the mother (Brown et al. 1996), but nursing is not the "function" of the transcription factor encoded by this gene. The idea that development is not a simple conduit but an interactive maze that modulates what genes "do" has become a major component of *C. elegans* neurobiology.

**7. So Why Do Genes Sell?** Ken Schaffner has admirably catalogued eleven theses of this Developmental Critique, but on whose door should he nail them? Two churches on which to post the theses would be those housing behavioral geneticists and journalists. These two groups interact synergistically, each positively feeding back on the other. The newspapers trumpet that behavioral geneticists have identified such things as the "gay gene," the "alcoholism gene," and the "depression gene." Afterwards, when other laboratories cannot replicate these findings and the scientific reports are quietly withdrawn, the public is not told about the withdrawal (see Mann 1994, Nelkin and Lindee 1995, Harris 1997). Our culture subscribes to a molecular phrenology, and genetic causation sells. Why do people "want" to hear that genes are responsible for behaviors? (The null hypothesis is to say that this behavior is encoded into the genome, presumably as an evolutionary adaptation; but we won't say that). On one level, genetic determinism becomes a useful way both to avoid responsibility and to define certain groups or individuals as being naturally bad (or good). On a deeper level, genetic causation appears so compelling because that many people believe that genes are the essence of our identity and ethnicity. They have become our "soul" (Nelkin and Lindee 1995, Haraway 1997).

**8. Summary.** In summary, do genes control behavior? Yes. But can we predict behavior from genes: no more than we can predict the evolution of mosquitos from understanding particle physics. But neither are we faced with anarchy. Behavior is limited by genes. There is a behavioral repertoire associated with each organism. Schaffner is quite right that *C. elegans* neurobiologists will obtain the simple solutions: "a necessary condition," those elements that are the uniquely required components, but not the complete set. It is doubtful that we will understand the relative contribution of each gene to a specific behavior. By using *C. elegans*, neurobiologists have been able to document the complexity that is inherent in a very simple neural system. And here may be the place where the developmental critique of the simple reductionist approach to behavior is receiving its best evidence.

REFERENCES

Block, Ned (1995), "How hereditability misleads about race", *Cognition* 56: 99–128.

Brown, Jennifer R., Hong Ye, Roderick T. Bronson, Pieter Dikkes, and Michael E. Greenberg (1996), "A defect in nurturing in mice lacking the intermediate early gene *fosB*", *Cell* 86: 297–310.

Gottlieb, Gilbert (1992), *Individual Development and Evolution*. New York: Oxford University Press.

Haraway, Donna J. (1997), *Modest Witness@Second Millenium*. New York: Routledge Press.

Harris, Richard F. (1997), "Journal journalism", *Current Biology* 7: 458.
Keller, Evelyn F. (1992), "Nature, Nurture, and the Human Genome Project", in D. J. Kevles, and L. Hood (eds.), *The Code of Codes*. Cambridge, MA: Harvard University Press.
Lewontin, Richard C. (1970), "Race and intelligence", *Bulletin of the Atomic Scientists* 26(3): 2–8.
———. (1992), *Biology as Ideology*. New York: Harper.
Mann, Charles C. (1994), "Behavioral genetics in transition", *Science* 264: 1686–1689.
Nelkin, Dorothy and M. Susan Lindee (1995), *The DNA Mystique: The Gene as Cultural Icon*. New York: W. H. Freeman.
Schnabel, Ralf (1997), "Why does a nematode have an invariant cell lineage?", *Seminars in Cell and Developmental Biology* 8: 341–349.
Sengupta, Piali, Joseph H. Chou, and Cornelia I. Bargmann (1996), "*odr-10* encodes a seven transmembrane domain olfactory receptor required for responses to the odorant diacetyl", *Cell* 84: 899–909.
Tauber, Alfred I. and Sahotra Sarkar (1992), "The Human Genome Project: Has blind reductionism gone too far?", *Perspectives in Biology and Medicine* 35: 220–235.
Wheeler, Samuel C. III. (1991), "True figures: Metaphor, social relations, and the sorites," in David R. Hiley, James F. Bohman, and Richard Shusterman (eds.), *The Interpretive Turn*. Ithaca: Cornell University Press, pp. 197–217.
Whitney, Glayde (1995), quoted in "Specter at the feast", *Science* 269: 35.