Adam Shriver, a doctoral student in philosophy/neuroscience/psychology at Washington University. He is concerned about the pain that veal calves and gestating sows suffer as a result of their unnatural diets and feedlot conditions. And so, in a *New York Times* Op-Ed piece (Feb. 19, 2010), he urged that the animals be genetically engineered to remove the awareness of pain. "If we cannot avoid factory farms altogether, the least we can do is eliminate the unpleasantness of pain in the animals that must live and die on them. It would be far better than doing nothing at all."

Shriver's proposal was directed at the professional research community. But there are now various organizations, such as BioCurious and DIYbio, whose aim, in part at least, is to encourage the general public to indulge their taste for imposing their own fantasies upon other organisms. There's also an International Genetically Engineered Machine competition for undergraduates. The sponsoring organization writes: "Student teams are given a kit of biological parts at the beginning of the summer from the Registry of Standard Biological Parts. Working at their own schools over the summer, they use these parts and new parts of their own design to build biological systems and operate them in living cells."

By now the trend has, it seems, accelerated altogether beyond control—if control was ever even possible. And while professional researchers in molecular biology have some ethics guidelines and protocols for preventing the unwanted release of engineered organisms into the environment, the same is hardly true of do-it-yourselfers laboring away in their kitchens.

What can one say in response to this chaotic mixture of noble aspirations, utter pettiness, hell-bent recklessness, and cavalier experimental curiosity—all marked by an apparently total disinterest in the living organisms being manipulated? Nothing much, I'm afraid, in just a few words. Perhaps you, like me, are rendered temporarily speechless by the kind of thing described above. There is, however, at least this: it all says something about why an organization such as The Nature Institute is needed in today's world! (Beyond that, I do hope before long to post a major essay on our website, which I've written for a book on bioethics to be published by the Hastings Center.)

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A Modest Champion of the Whole Organism

Whenever I hear it said that "the whole is greater than the sum of its parts," I find myself wondering (rather uncharitably, perhaps) whether the speaker has any more understanding than I do of what the words might actually mean—or whether (as it often sounds to my ears) the cliché is merely an expression of feel-good, more holistic-than-thou sentiment. Why, if the thought is so important, do we almost never hear its meaning spelled out—or at least not spelled out in a way that makes much sense?

I readily grant that I, too, have always believed the phrase to conceal something important, despite my inability to do justice to its meaning. One offhand remark that stimulated my thought on the matter came from physicist Arthur Zajonc a few years ago, when he said something roughly to this effect:

> If people really believe a whole is greater than the sum of its parts, we should ask them to identify the "greater" reality that remains to be recognized once all the parts have been summed up.

I did in fact occasionally pose that question to others, but without promising result. While I had my own vague intuition of the matter, it never gained the clarity I would have liked.

You can imagine my delight, therefore, when I encountered a straightforward and decidedly non-clichéd interpretation of the phrase from a leading cell biologist of the twentieth century — an interpretation proffered in reassuringly dry, matter-of-fact language unlikely ever to become the clarion call of a New Age. In fact, the author of the interpretation often put his meaning into a mathematical formula—one surely never destined for the fame of $E=mc^2$, but perhaps fully as important once we realize its implications for our understanding of living organisms:

$$V_S < (v_a + v_b + v_c + \ldots v_n)$$

Don't worry, however. There's no need to consider the formula here. The whole matter can be explained without a formula, and with clear examples. For those interested, I'll save the explanation of the formula itself (which will require all of a sentence or two) for later.

Paul Weiss, Scientist of Distinction

Shortly after his student days in Vienna, where he studied mechanical engineering, physics, and biology, Paul Alfred Weiss met the man who would become a founder of general systems theory. It was in the early 1920s. As Weiss tells the story: "A sparkling Viennese student, a little more than three years my junior, approached me for a meeting—Ludwig von Bertalanffy. We met in coffeehouses and 'milked' each other. I soon found that his thinking and mine moved on the same wave-length—his coming from philosophical speculation, mine from logical evaluation of practical experience" (1977).

At the other end of his life, in the 1970s, Weiss found himself in association with the likes of Arthur Koestler, editor of the book, *Beyond Reductionism* (to which Weiss had contributed a chapter), and the Frensham Group, which included ethologist Konrad Lorenz, psychologist Jean Piaget, developmental biologist C. H. Waddington, chemist and philosopher Michael Polanyi, neurophysiologist John Eccles, and other notable researchers seeking a broad philosophical and interdisciplinary understanding of the living world.

In light of these connections, what is remarkable about Weiss' life is the degree to which he pursued his wide understanding without ever taking up, or even showing much interest in, philosophy as such. Throughout his long career he remained a scientist's scientist, rigorous, focused on practical research, and with a mathematical cast of mind. As he himself put the matter with regard to Bertalanffy, "And so it remained for half a century, each of us hewing his separate path according to his predilection. That is, I kept on as the empirical experimental explorer, interpreter, and integrator, for whom the 'system' concept remained simply a silent intellectual guide and helper in the conceptual ordering of experience, while he, more given to extrapolations and broad generalizations, and bent on encompassing the cosmos of human knowledge, made the theory [general systems theory] itself and the applicability of it to many areas of human affairs his prime concern" (1977).

However, all profound observation must be at least implicitly open to the widest possible realms of thought, and Weiss was nothing if not a profound observer. His objection to much of the science he encountered in his day centered on what he found to be an uncomfortable constriction of observation and understanding by abstraction, machine-like linear notions of cause and effect, and the ignoring of context.

In his doctoral thesis of 1922, Weiss studied the response of butterflies to light and gravity. He argued, according to his biographer, that "the nervous system cannot be reduced to a rigid tropistic machine, but that the elementary steps in behavior are subordinated to the state of the whole," a view he later found fruitful in his studies of the vertebrate nervous system (Overton undated; quotations below are from this source unless otherwise indicated). He subsequently experimented with limb transplantation in newts and other organisms. While doing this work at a clinic in Bier, Austria, he discovered a frog with two extra limbs at the nearby Hungarian railway station. The limbs were fully functional, confirming some of his own experimental findings. “The frog was featured in his European lectures and the idea of the ‘natural experiment’ became a teaching device and later found its way into his text and teaching lectures.”

Weiss went on to engage in a wide range of research, but he never found himself too far from questions relating to the development and functioning of the nervous system, and to embryology and organismal development in general. He would eventually write a leading textbook, *Principles of Development*, along with many other books and numerous technical papers. In 1930 he came to the United States, where he spent many years at the University of Chicago. In 1947 he was elected to the National Academy of Sciences, and in 1954 he became one of the first professors at the new Rockefeller University in New York, where he directed a laboratory specializing in wound healing, cancer, and development and repair of the nervous system. During World War II, he worked on techniques for nerve regeneration, some of which were later applied in Army and Navy hospitals. He would eventually serve as visiting professor at ten universities, and become dean of the graduate school of biomedical sciences at the University of Texas.

Once, when asked why he worked so hard, he “was overheard to reply that his reason for wishing to be a good embryologist was that by doing so he might repay the United States for what it had done for him.”

Weiss always emphasized the importance of language, devoting lectures to the changing meaning of embryological terms over time, or the differences in usage among contemporary investigators. He originated terms such as “neurobiology” and “developmental biology” as part of an effort to overcome the compartmentalization and fragmentation of the life sciences. He worried that, in his words, “While scientific workers are more and more constrained into narrower and narrower confines in which to pursue their specialties, science as a whole cannot develop into a healthy and proportionate organism unless specialists will leave their burrows on periodic occasions and meet on common ground.”

Finally, much like E. S. Russell of an earlier generation (see *In Context* #22), Weiss objected to the dominance of gene-centered explanation long before such complaints were widely considered respectable. “What is misleading in the term ‘genetic determination’,” he wrote, “is that it conveys the notion that the development of an organism is simply the mechanical product of a bundle of linear ‘cause-effect’ chain reactions, reeling off in rigid sequence according to a minutely predesigned plan of clockwork precision. That notion, reinforced by the anthropomorphic language that endows genes with the powers of ‘dictation’ and ‘control’, rests on a basic misconception of the nature of biological processes in general and of developmental dynamics in particular” (1973). And again:

“A ‘cause’ (or gene) is something *without* which some ‘effect’ (or character) which you expect *fails* to occur, while something else occurs instead. To turn the sum of such negative statements around and fashion from them a positive doctrine of of plenipotency (of causes or genes) seems to me a reprehensible somersault of logic” (1973).

Weiss’ contributions have, in recent decades, been largely overlooked amid the intense enthusiasms and one-sided technical developments of the era of molecular biology. But if I am not mistaken, there is now a growing opportunity for his voice to be heard. Perhaps the reaction of an Italian molecular biologist, after reading a paper in which I mentioned Weiss, is a pointer to the future: “I went on Google Scholar to download relevant articles of Dr. Weiss. Wow! I spent more than three hours reading very clear and neat scientific prose underlining exactly the same problems we are facing today.”

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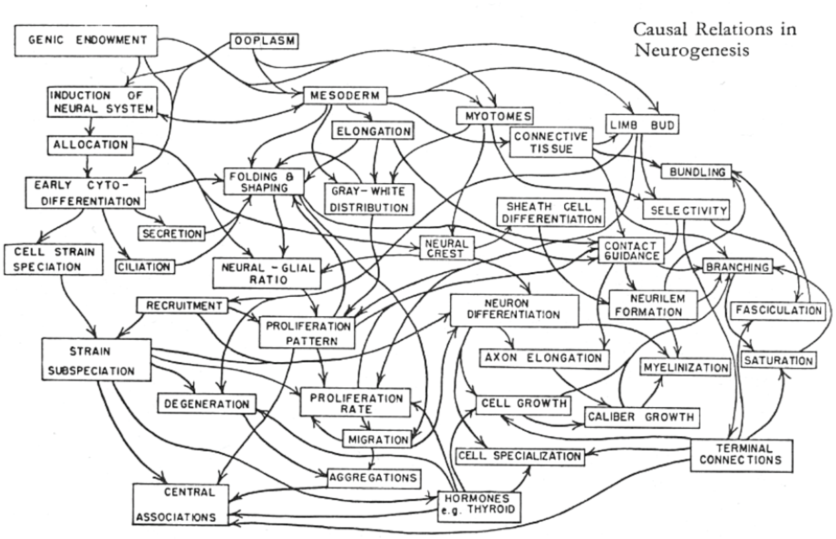
Of Contexts and Coordination



Causal Relations in Neurogenesis

Paul Weiss, born in Austria in 1898, began his research in the early 1920s and migrated to the U.S. in 1930, where he spent most of his distinguished, several-decades' long research career—a career capped by receipt of the National Medal of Science from President Jimmy Carter. (See the accompanying box for biographical details.) Throughout his career he devoted a great deal of time to the observation of embryonic development and the behavior of cells both *in vivo* and in tissue cultures, often using techniques he himself pioneered. Interested in cell differentiation, morphology, and the development of patterns, especially at the cellular level, he elucidated the ways in which physics and chemistry play out in specific processes. He even developed mathematical models for some of these processes.

As prolific and important as these contributions were, Weiss was convinced by his observations almost from the beginning that the usual machine-like explanations of living processes were grossly inadequate to capture what was going on—and could easily be shown to be inadequate as soon as one took the larger context into account. That context was seething dynamism. "In contrast to a machine," he wrote later in life, "the cell interior is heaving and churning all the time; the positions of granules or other details in the pictures, therefore, denote just momentary way stations, and the different shapes of sacs or tubules signify only the degree of their filling at the moment" (1973).

He liked to point out how misleading are the pictures of stable cellular structures we see in textbooks; in reality, even the two-dimensional surfaces and cellular membranes, the three-dimensional cytoskeleton, and various fiber systems are subject to more or less continuous dissolution and reconstitution. Particular structures are only snapshots of flow. Life is a dynamic process, he would say, and "the elements of a process can be only elementary *processes*, and not elementary *particles* or any other static units" (1962).

Not only are there countless processes vital to life in every cell of the body, but these processes, in addition to having their own apparent goals, are in cooperative interdependence, or in tension, or in some cases in a kind of opposition to each other. But the sum total of interactions, for all their differing natures and tendencies, "hold together" in a striking way. "The only thing that remains predictable amidst the erratic stirring of the molecular population of the cytoplasm and its substructures is the overall pattern of dynamics which keeps the component activities in definable bounds of orderly restraints" (1973). The context, in other words, possesses a certain stability amidst all the surging movements of the part-processes with their varying degrees of freedom.

This principle of the rule of the context over its part-processes holds at all scales, not only at that of the cell. In order to appreciate what it means to achieve a reliable and stable overall result from myriad part-processes, consider the accompanying figure, showing (in an extremely simplified way) some of the interdependencies and interactions during the development of a mature nervous system from a fertilized egg.

Weiss liked to point out that no two limb buds in a developing embryo are ever exactly the same; the formative cells (mesenchyme cells) are growing and moving in a different way in each specific case. Yet the end result of their growth is a "standard," fully formed limb of the right sort. More dramatically, the same cell group in a limb bud can form the asymmetric pattern of a right limb or, if transplanted to the opposite side, the contrary pattern of left-handed asymmetry (1971).

Clearly, the molecular substances (including the genes) in those cells at the beginning of the process are not by themselves determining the outcome of growth. Beside its full complement of "genetic information," each cell needs additional "topical information" derived from the structure of the collective mass. How otherwise, Weiss asks, could any unit know just what scrap of information to put to work at its particular station in order to conform to the total harmonious program design? Left solely to their own devices, individual cells and their entrapped genomes would be no more capable of producing a harmonious pattern of development than a piano with a full keyboard could render a tune without a player (1973).

In sum, "overall regularity in the gross is attained and maintained not as a mechanical result and a reflection of a corresponding underlying regularity of rigidly stereotyped behavior of the component elements down to the smallest detail, but on the contrary, in spite of a high degree of vagrancy among the latter. The individual component does not 'know' where and in what specialty it will end up until it has been well on its way and given a defining 'cue'" (1973).

Returning to the "churning" sea of protoplasm mentioned earlier: it is remarkable that, not only must all the cellular processes and features support each other in a cooperative way despite their individual divergent tendencies, but this cooperation must occur in an extremely fluid context without tight compartmentalization or mechanical linkages (1963): "Small molecules go in and out, macromolecules break down and are replaced, particles lose and gain macromolecular constituents, divide and merge, and all parts move at one time or another, unpredictably, so that it is safe to state that at no time in the history of a given cell, much less in comparable stages of different cells, will precisely the same constellation of parts ever recur . . . Although the individual members of the molecular and particulate population have a large number of degrees of freedom of behavior in random directions, the population as a whole is a system which restrains those degrees of freedom in such a manner that their joint behavior converges upon a nonrandom resultant, keeping the state of the population as a whole relatively invariant" (1962). This "nonrandom resultant" is exactly what we lose sight of when we study the members of a population as separate entities.

All this, then, provides an explanation of the formula given above. Put very simply, this is what the formula says: the variability of a cell as a whole is less than the sum of the variabilities of its component parts. (Weiss actually uses the more technical and mathematical term, *variance*.) The same principle works at many levels, from organelles, to cells, to tissues and organs, to organisms—and even to the collection of organisms within an ecological setting. In the case of the cell, according to Weiss, the formula "represents an 'operational' description of what it is that makes the cell as a unity 'more than the sum of its parts'. In order that this formula be satisfied, one must evidently postulate that the component processes, when operating in the common integral system, are *interdependent* in such a manner that as any one of them strays off the norm in one direction, this entails an automatic counteraction of the others" (1963).

So it's a bit ironic: the whole is *more* than the sum of its parts because it varies *less* than would be suggested by a consideration of all the separate part-processes. A principle of coordination works from the whole into the parts, from the larger context into the subcontexts.

Of course, answering one question often raises additional questions. Weiss characterizes a relation between the whole and its parts that gives reasonable meaning to "The whole is greater than the sum of its parts," but this leaves us wondering about the nature of a whole that is able to achieve such coordination of its parts. The issues are subtle, and subject to a great deal of confusion in today's scientific environment. They cannot be treated here, but I have dealt with them at length in Talbott 2010 and 2011, and you will find all the related papers at http://natureinstitute.org/txt/st/mqual.

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