Ray Peat's Newsletter

The future cannot be predicted, but futures can be invented. **Denis Gabor**

Intention, Learning, and Health

Everyone recognizes that changes occur when we adapt to a new climate, a new diet, a new sport, or a new kind of work; the idea of "body building" is based on the understanding that choices of activity can cause major changes in appearance and abilities. However, the exact nature of adaptive change has been poorly defined, and has been influenced by ideological and dogmatic commitments, especially related to inheritance.

The idea that individual cells might, in a purposeful and useful way, change their functions and structures in response to something in their environment . . . has been, for more than 100 years, something to deny and to discourage to protect the reductionist-mechanistic model of reality.

Even Charles Darwin acknowledged the existence of inheritance of acquired traits, and proposed that cellular changes in the body produced by interactions with the environment were transmitted through the blood to the gonads and germ cells as particles he called gemmules. One reaction against that idea was that the apparatus of heredity exists only in the nuclei of the germ cells, and that the nuclear material is absolutely impervious to the effects of the environment.

For more than 100 years the dogma of the isolation of the "germ line" from the "soma" influenced every aspect of thinking in biology and medicine. One of the derivative ideas was Crick's Central Dogma of molecular biology, that information flows from (nuclear) DNA to (cytoplasmic) protein, and never in the reverse direction. Another derivative dogma was that the nucleus is "the brain of the cell." Supporting that idea was the dogma that the cytoplasm of the cell consists of a membrane-enclosed fluid in which things occur only by random diffusion—random interaction of solutes could hardly have a guiding brain-like function. Some people who couldn't accept the "nuclear brain" idea decided that the cell membrane (constructed according to the nuclear blueprint) must be the source of the cell's meaningfully organized behavior.

When a person chooses a new kind of activity their cells cooperate by changing their nature, "behaving" differently. More than 100 years ago, some of the best known and best financed biological research was designed to prove that cells don't "behave," since behavior implies intrinsic awareness and purposeful action; their reactions were called "tropisms," implying a purely mechanical change in reaction to a stimulus. Shortly after the doctrine of tropisms was established for single cells such as amebas and paramecia, the Behaviorist movement in what had been psychology, following J.B. Watson's false description of the meaning of Pavlov's work, began claiming that human life operated similarly, and that consciousness and purpose didn't exist. Later, B.F. Skinner argued that ideas of moral autonomy, freedom, and human dignity were hindrances to understanding human nature.

Researchers (such as Beatrice Gelber) who demonstrated that single cell organisms can learn purposefully were sidelined, and written out of science, but a few people have continued to produce evidence of intelligent, purposeful behavior, and deliberate useful changes in their DNA, even by bacteria (James A. Shapiro).

The conditions that evoke the formation of exosomes that are appropriate for the problem caused by stress are continually changing, and are different in different parts of the body.

Many practical biologists, plant and animal breeders, kept the idea of adaptive inheritance alive, and the idea of cytoplasmic inheritance began developing as an alternative to nuclear inheritance. Starting in the 1930s and '40s, Tracy Sonneborn's work with unicellular paramecia began to show that inheritance isn't just nuclear. When cytoplasmic inheritance could no longer be denied, its real meaning was denied by arguing that it operated through the same kind of genes as nuclear inheritance, "plasmids" floating in the formless cytoplasm, containing some DNA that had either escaped from the nucleus, or that had originated from symbiotic bacteria. Interest in Sonneborn's work was effectively redirected, either by seeing it as just more Mendelian genetics, or, when that wasn't possible, to declare that paramecia were no longer suitable organisms for studying inheritance.

One of Sonneborne's experiments that undoubtedly contributed to the declining interest in paramecium research involved microsurgery, in which he cut out and reversed a section of the organism's surface, so that the cilia that normally beat in a direction that propelled the cell forward would beat in the reverse direction. The animal survived, and the cilia in that area always beat in the wrong direction for the rest of its life. When it divided, the daughter cells, and all the following descendants had the same patch of reversed cilia. It was obvious that the "body plan" of the paramecium isn't under the control of the genes.

When research in a wide range of animals, and humans, began making it impossible to deny that environmental conditions can cause transgenerational effects, the reality of "epigenetics" was accepted by mainstream biologists as a non-Mendelian form of inheritance, but they detoxified and denatured it, by finding mechanisms that could account for it, but only in a very limited and temporary way, that didn't have any influence at all on their basic doctrine, that the "germ line" is ultimately impenetrable by adaptive changes in response to new environmental situations. The changes they accept do nothing more than influence which of the inherited eternal DNA genes will be expressed for a while, allowing the original, species-defining traits to be restored when the suppressive effects are removed. For them, "epigenetics" refers to a change in the state of cellular differentiation that persists through cell division; an early source of the word was Waddington's use of "epigenesis" to refer to the changes of gene expression that produce stable changes in cell differentiation during the process of development of the organism.

Experiments have made it clear that experience is always modifying our being, and that our continuous processes of adaptation and development can't be separated from our understanding of the world.

The belief in genetic determinism has had a strong influence on the understanding of an organism's adaptation to its environment. The differentiated state of the cells in our body is usually considered to be terminal, and occurs when an undifferentiated precursor or stem cell receives specific influences that cause a particular pattern of gene expression, which then persists in non-dividing cells. During the development from stem and precursor cells, the "epigenetic" factors, DNA methylation, histone acetylation, formation of micro-RNA, etc., stabilize the differentiated state of the cell.

This view of cellular differentiation is convenient for the medical doctrine of incurable

diseases—the state of differentiation follows an orderly plan, and that plan changes only by changing something in the cell's nucleus. When tumor cells are formed, it's because something has randomly interfered with the plan, disrupting the genes, in a manner that can only get worse.

The idea that individual cells might, in a purposeful and useful way, change their functions and structures in response to something in their environment, without having to go through a series of differentiating cell divisions, has been, for more than 100 years, something to deny and to discourage to protect the reductionist-mechanistic model of reality.

For a long time, the changes of aging were explained as the result of accumulation of random somatic mutations, irreversibly destroying genes and the tissue functions that depend on them. That idea was proven to be contrary to the evidence, and it was replaced by the idea of irreversible cell differentiation, a pattern of gene transcription that strongly resists change, held in place by epigenetic modification of the genes (Nacarelli, et al., 2017; Nacarelli and Sell, 2017; Lopes-Paciencia, et al., 2019). The origin of the problem is always in the genes, and the general picture has hardly changed from the time when random somatic mutations explained aging, degeneration, and cancer.

Exosomes, virus sized particles emitted by cells, especially when they are under stress, are known to transmit information to other cells within an organism, and to modify their state of differentiation (Hayashi and Hoffman, 2017). There is now good evidence showing that they, like Darwin's gemmules, can transmit information from somatic cells to germ cells. Their functions within the organism are now widely considered to be an agent of epigenetic adaptation. They carry many different substances, including microRNA and other factors that modify DNA methylation and histone acetylation. Current attention is directed to understanding the way that exosomes modify gene expression, the state of differentiation, in the cells that receive them, emphasizing the stability of the changes.

I think the crucial question is how the cell that produces them has organized their composition so that their effects in the organism will achieve an adaptive effect, often a restorative effect that corrects harmful conditions that have been produced by stress. This is intelligent purposive behavior, usually beneficial for the organism. In the case of cancer cells, the changes they cause are good for the survival of the cancer, but bad for the organism.

In the process of optimizing our interactions with our environments, we need to continually improve conditions, rather than reducing our needs to match poor environments.

The conditions that evoke the formation of exosomes that are appropriate for the problem caused by the stress are continually changing, and are different in different parts of the body. Environmental conditions elicit quick, intelligent, evaluative reactions from the cells. In a chronically bad environment, these changes that are the best that can be achieved at the moment, will continue to accumulate, and the accumulation of contextually appropriate reactions will lead to harmful degenerative effects, as long as the environment presents stressful conditions.

Rather than blaming the cells, as in the current doctrine of aging as an accumulation of cells with the "senescence-associated secretory phenotype," SASP, we might consider the effects of eliminating the harmful features of the environment. If cells are purposefully and perceptively adaptive, we would expect cells in a more suitable environment to begin to re-adapt, eliminating their adaptations to a harmful environment, including SASP cells and fibrotic tissues with depressed oxidative metabolism, and to begin producing fully vital cells adapted to life at a higher energy level.

The experiments that showed learning in single cells, which obviously can't involve changes in synapses, conflicted with the theories of learning based on a computer model in which synapses correspond to transistors, and axons correspond to wires. In the last 75 years there have been great advances in understanding how awareness might exist in living substance, disregarding the schemes in which awareness consists

of abstract information, resting on a foundation of a network of synapses, and instead viewing it as a direct physical interaction between the perceiver and the perceived.

Our society has invented some institutions that powerfully negate our basic need to understand and to develop coherently.

Rather than the digital basis of information theory, this approach is analogic, and functions primarily with wholes, rather than parts that gain their meaning only indirectly. Luca Turin's studies of odors and chemical perception provide a good introduction to this view of the brain.

In the 1940s, Denis Gabor worked out the physical theory of holography, in which 3-dimensional images can be stored in a solid substance, in a non-localized way. Around the same time Karl Lashley was trying to find where "memories are stored" in the brain (the "engram"), by destroying parts of the cortex after the animal had been trained. By the 1950s, he had determined that memories weren't stored in particular locations, but that the whole cortex of the brain was involved in every memory. Later, Karl Pribram, who worked with Lashley, realized that Gabor's hologram was at least a good metaphor for the way the brain works, with a particular memory distributed throughout a mass of tissue, rather than being localized in an "engram."

Although Pribram didn't question the basic doctrine of on-off, digital function of nerve impulses, he proposed that the fields created in complex networks of synapses might be able to store experience in a holographic manner. Recognizing that perception is organized in whole patterns, or Gestalts, he proposed that similar principles might organize behavior—he called these behavioral programs "Images of Achievement." Unfortunately, even while assembling the ideas of others constructively, he didn't discard the mechanistic methods and beliefs of Behaviorism.

Decades earlier, in the 1930s, P.K. Anokhin had worked out an alternative to the mechanistic theories of behavior based on reflexes, and developed a cybernetic and holistic view of intelligent behavior. The organism's perception and behavior were described as unified "Functional Systems," which included metabolic, endocrine, and adaptive-developmental processes, as well as awareness and action. Anokhin called the model of the world, including the organism's needs and actions, the "Action Acceptor," which was always being revised according to the success of the action, which validated the organism's understanding of the situation. Information from proprioceptors as well as external senses was continuously renewing this model of the world.

Anokhin understood the holistic nature of perception, and, having avoided the atomizing assumptions that broke behavior down into stimuli and reflexes, he also avoided the assumption that nerves conducted only "on-off" information, binomial digital messages, and he described examples in which a single nerve transmitted complex signals. If a single-celled organism can "mentally model," or imagine, itself in a world, why should we imagine that our nerve cells can't deal with anything more complex than "on-off" information?

Every cell in the body, except blood cells and cancer cells, contains a "primary cilium," which has an internal structure similar to the cilia that are used for propulsion, except that it lacks the parts needed for movement. These cilia are the cells' sense organelles; they have different specializations—they can detect the movement of fluids, pressure, sounds, odors, and light. Every brain cell contains one of these sensory organelles. In the hippocampus, the primary cilia are involved in contextual memory (Rhee, et al., 2016). They also allow cells to align their polarity according to their position in the body.

If the olfactory cell can, as Luca Turin describes, identify the complex vibratory patterns of chemicals, why would other nerves be unable to recognize and transmit the same information to other parts of the brain? In the eyes and auditory nerves, why would the specific qualities sensed by the primary cilia have to be reduced to on-off signals for transmission? If the signals transmitted by nerve axons are complex, then the issue of "distributed" knowledge is explained—each part is aware of its place in a Gestalt, in the Action Acceptor, allowing it to align its functions with

the purposeful future-oriented activity of the whole organism.

In the case of muscle cells, endocrine cells, cytokine producing cells, etc., this alignment is what the Functional Systems consist of. Cell dissolution and cell multiplication, as well as re-differentiation, are elicited by the needs of the functional system. The form, function, and being of the organism are governed by the Functional Systems, in a continuously adapting process.

In the 1950s, when most psychologists believed that only vertebrates were capable of learning, James McConnell demonstrated that flatworms, planaria, could be trained to change their behavior. These worms are able to regenerate a whole body, including the brain, from any part of the organism. McConnell found that worms regenerated from a part, such as the tail, of a trained worm retained the knowledge that had been acquired by that worm. He also found that when trained worms were ground up and fed to untrained worms, those worms learned the behavior more easily. He suggested that RNA molecules synthesized following the worm's training might be responsible for distributing the learned behavior throughout the whole organism. During the 1960s, several other researchers found that extracts from the brains of other animals, including insects, fish, and rats, could transfer learned behavior to untrained animals. In 2013, experimenters confirmed McConnell's work, by demonstrating that after being decapitated, the regenerated flatworms retained their training.

These experiments have made it clear that experience is always modifying our being, and that our continuous processes of adaptation and development can't be separated from our understanding of the world.

In the process of optimizing our interactions with our environments, we need to continually improve conditions, rather than reducing our needs to match poor environments. The brain is always the organ that maintains the Acceptor of Action and organizes the Functional Systems to guide our development, and with each success the achievement is institutionalized in our metabolism, improving the intensity and range of our understanding, and increasing the power and efficiency of the brain.

Simply realizing the absolute importance of the environments that we are constantly adapting to can lead to learning how to adapt more appropriately, and how to make our environments more life-supporting.

Biologists have recognized this process in all animals—"cephalization," the process of development of bigger and better brains operating in more complex and appropriate environments. Improved nutritional and hormonal support can increase the brain's size, complexity, and learning ability. An enriched environment improves brain function, thickness of the cortex, and longevity, while reducing inflammation and increasing immunity (Carughi, et al., 1989; Laviola, et al., 2004; Arranz, et al., 2010; Jurgens and Johnson, 2012; do Prado, et al., 2016; Pusic, et al., 2016). Impoverished, boring, stressful environments have the opposite effects.

Our society has invented some institutions that powerfully negate our basic need to understand and to develop coherently. The professionalization of medicine, for example, has contributed to a weakening of the population's ability to perceive its needs and to imagine appropriate solutions. Authoritarian attitudes throughout the culture create distrust of autonomous understanding and of independent choice of goals. "Science," especially medical science, has become life's greatest danger, when its goal has become the empowerment of "artificial intelligence," centralizing control, institutionalizing the reductionist view of knowledge, and displacing actual intelligence.

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