Homeostatic Mechanisms

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It is the role of the biologist to find a system or systems of explanation within the bounds of which one might arrange myriads of empirical data to reside comfortably. In this sense, a single unified theory for all of biology would be the ideal situation. In the same way, it is the role of the biology teacher to find and use those principles, concepts, or systems which allow biological information to fall easily into place. The idea of homeostatic mechanisms is just such an idea.

Homeostasis as derived from the etymology is a condition of similar static activity. *The American College Dictionary* defines homeostasis as a condition describing an organism in physiological equilibrium. The cognitive act is exchange. The result is maintenance of life and evolution.

The concept of homeostasis[1] can probably be traced back to Hippocrates or even earlier in history, but Walter Cannon, the father of the term, quotes the German physiologist, Pflinger, who said in 1877 that "The cause of every need of a living being is also the cause of the satisfaction of the need." In a sense Isaac Newton expressed this in the 17th Century with his third principle: "To every action there is an equal and opposite reaction."

Again quoting Cannon from his *Wisdom of the Body*[2] where he quotes Leon Fredericq (1885): "The living being is an agency of

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[1] See L. L. Langley's book, Homeostasis, Rheinhold Publishing Corp., New York, 1965, for a splendid development of the subject.

[2] New York: W. W. Norton and Company, Inc., 1963.

such sort that each disturbing influence induces by itself the calling forth of compensatory activity to neutralize or repair the disturbance. The higher in the scale of the living beings, the more numerous, the more perfect and the more complicated do these regulatory agencies become. They tend to free the organism completely from the unfavorable influences and changes occurring in the environment."

The statement above really refers to an evolutionary development so that within the great period of geologic time during which organisms have inhabited the earth, it postulates a gradual but continuous development of steady state systems. A frog, not too lowly a creature, has not yet developed the means to prevent rapid evaporation of water from his body and reactions to drying are still centered above the medulla and not yet committed to reflex action so that a frog with an anesthetized brain can sit next to a pan of water and dry out to the point of death. This absence of a physiological or an anatomical homeostatic mechanism must result in a behavior homeostasis to continue existence, i.e., the frog must live in water or hibernate in a mud hole as far from environmental harshness as is consistent with its ability to return to its natural habitat without undue loss of time or energy.

Walter B. Cannon uses and defines homeostasis perhaps for the first time as a condition within the organism which may vary but which for the most part remains relatively constant.

George E. Palade says in *The Scientific Endeavor* that at the cellular and subcellular level "life depends on an extensive organization in depth, on a superposition of patterns which amount to infinitely more order than matter usually tolerates. This thermodynamically improbable situation is achieved by continuously supplying energy to a preexisting structural framework." This is one *key* to understanding much of biology. The organism finds itself in an environment with almost limitless potential energy supplies to maintain its organization including that which is bound up in other organisms. Conquering the dilemma of abundance of *energy potentially available* in space and time to *energy immediately available* in space and time is the story of biological evolution now and in the future.

Fundamentally the concept of homeostasis *is* the concept of the battle of the organism to maintain its organization against all the odds of entropy tending toward its eventual breakdown.

The story of homeostasis is an admixture of contradictory terms. Guyton[3] says that "the term *homeostasis* is used by physiologists to mean *maintenance of static,* or constant, *conditions in the internal environment.* Essentially all the organs and tissues of the body perform functions that help to maintain these constant conditions." While most scientists speak of steady state systems which seems more or less *static* as stated above, other scientists speak of a *dynamic* equilibrium. The proteins of the liver are thus said to be turning over every 60 days; the blood every 40 days. This concept of continuous turnover of body constituents has been eminently revealed by the work of Schoenheimer and his colleagues. Much misunderstanding in scientific knowledge was the result of the unbelievable speed of synthesis of for example protein in animals or sugar in plants. In both cases the synthesis occurs in many steps in less than a minute. Research workers thus missed many of the intermediate steps. The dynamics of the situation is self evident.

"Nothing" is really static. At the molecular level, if a reversible reaction *is* occurring (which implies the equilibrium) the rate may be exceedingly slow like that at the interface between a bar of silver and a bar of gold or extremely rapid as at the interface of oxygen and nitrogen. In both instances there is an equilibrium. The first could be said to be *static,* the second *dynamic*—the terms are relative.

However, except for organisms at extremely low temperature or parts of organisms like spores in a rather dry, cool state, the molecular activities within cells or of whole organisms are extremely dynamic.

There are other factors besides energy *per se* for which the steady-state system appears necessary for greatest efficiency of operation.

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[3] Guyton, Arthur C., The textbook of medical physiology, 2nd Ed., Philadelphia: W. B. Saunders Co., 1961.

They are maintenance of essential building blocks, maintenance of optimal operating temperatures, pressures and pH, maintenance of oxidizable compounds, maintenance of an eat or be eaten stance, maintenance of an oxygen supply, maintenance of an at-ready system of nerves, etc.

Thus in the words of Nason, homeostasis is " . . . the unique and remarkable ability of many animals, despite extreme changes in external conditions, to maintain a stability or constancy of their internal environment. . .".[4]

"The living state is synonymous with adaptations that stir our amazement because they form a remarkable chainlike sequence of dependent events which function harmoniously to maintain the system in a steady state of equilibrium. Changes may occur in a system of this kind, but only within narrow limits; they are quickly annulled and the system returns like a spring to its initial condition under full control. Every disruption sets up forces which initiate the processes for restoring the normal state."[5]

The idea of homeostasis can be extended to any level of organization within the biotic world from the molecular to the societal in which there exists a state of dynamic equilibrium which by one operational mode or another involving *feedback mechanisms* the cell organelle or society attempts to maintain this state of equilibrium.

The steady-state when more or less static requires the smallest expenditure of energy and as the state deviates from the established low energy equilibrium, the energy requirement increases. It is logical to assume that inasmuch as the two components of the universe, *matter* and *energy,* are the components of the struggle for existence of any form of life, any upset in the equilibrium system will necessitate capture or release of more energy to restore the sensitive balance to the steady state of structure and event.

The simplest steady-state system involves two components, A and C, in a relationship where A goes to C: $A \longrightarrow C$; and C goes to A: $C \longrightarrow A$; or $A \rightleftarrows C$.

A biological need stimulates the onset of a reaction. A is the reactant; C is the product. If too much of the product accumulates beyond the needs of the biological system, the reaction reverses back to A or C is shunted off into storage form. In chemistry, this "simple" system of reactant and product can be illustrated by

$$N_2O_4 \rightleftarrows 2NO_2$$

where in the early stages of the reaction in a closed system the reaction goes to the right until the increased pressure (two molecules from every one) will push the reaction to the left until an equilibrium sets in. If however NO_2 is used or removed the reaction continues toward the right as long as reactant is available.

All of this acts in accordance with Le Chatelier's rule which states that: if a system of equilibrium is subjected to any stress, a change which reduces or tends to reduce the stress will occur. Thus by understanding this rule and the fact that ammonia can be produced by synthesis of nitrogen and hydrogen as

$$N_2 + 3H_2 \rightleftarrows 2NH_3$$

one can deduce that because less molecules are available in the system on the right than on the left (2 compared to 4 (3+1)) one can produce more ammonia by increasing the pressure of the system. This does happen and this is the technique of ammonia production.

A slightly more regulated system might have three components:

$$A \overset{\overset{E}{\downarrow}}{\rightleftarrows} C$$

Here E is a component which speeds up the reaction so that equilibrium is arrived at sooner. If however C continues to be used up, then the end result is a continued reaction A to C. E is a *catalyst* in the reaction (obviously known as an enzyme in biology).

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[4] Nason, Alvin, Textbook of modern biology, New York: John Wiley and Sons, Inc., 1965.

[5] Graubard, Mark, The foundations of life science, New Jersey: D. Van Nostrand Co., Inc., 1958.

A still more tightly regulated system might have four components:

$$\begin{tikzcd} & E \arrow[d] & \\ A \arrow[rr, shift right] & {} & C \arrow[ll, shift right] \\ & I \arrow[u] & \end{tikzcd}$$

E could be a stimulator to the system, *causing* it to speed up and I could be an inhibitor *causing* it to slow down.

In biological systems an enzyme is said to act as a template where a reaction is speeded up because two or more *reactants* are placed in juxtaposition to one another, and thus it appears that the minimum units in the biological model are:

$$\begin{tikzcd} & E \arrow[d] & \\ A + B \arrow[rr, shift left] & {} & C \arrow[ll, shift left] \\ & I \arrow[u] & \end{tikzcd}$$

It is clear of course that a simple chemical system, $A + B \rightleftarrows C$ will have inherent controls based upon the simple (?) regulatory device of concentration change (again see mass-action law and Le Chatelier's principle in general chemistry). Chemical equilibrium is the result of a balance of opposing rates. At a given temperature there is a fixed driving force for forward and reverse reactions. This driving force is generally expressed as $\triangle F$ (i.e., in terms of free energy).

If a reaction moves to the right with a relatively large release of free energy, it will tend to continue to move in that direction. If on the other hand, the reaction to the right requires energy to continue the reaction to the right, it will tend to revert to the opposite direction. Coupled reactions are common in biology where the net end result is a release of some free energy. Here one reaction using energy is coupled to one releasing energy.

If there is a great increase in the concentration of A, the reaction would tend in the direction of the removal of A although B would be necessary to maintain the reaction and would thus become the *limiting* factor to the reaction. If on the other hand there was an accumulation of product C, the reaction would tend toward lowering of its concentration, i.e., $C \longrightarrow A + B$.

An example of a two reactant, two product system is as follows:

$$A + B \rightleftarrows C + D$$

An example of this sort of reaction is that which takes place when acetic acid is esterified by ethyl alcohol to ethyl acetate and water:

$$CH_3C00H + C_2H_50H \rightleftarrows CH_3C00C_2H_5 + H_20$$

Starting with an equimolar proportion of acid and alcohol, the reaction will proceed to the right until about ⅔ of the reactants are converted to ester and water. At this point, the reaction begins to move to the left but dehydration can continue to pull the reaction to the right.

In engineering, the elements of an automated or steady state[6] system consist of four distinct but closely interlocked parts:

(1) the processing system;
(2) the mechanical handling system;
(3) the sensing equipment; and
(4) the control system

The living organism is similar to the most advanced engineering system which is best illustrated by L. London Goodman as follows (Fig. 1):

When the hand reaches out to pick up a ball, an analysis of the system at the organism level reveals the same elements of the system as in engineering.

First, the $\boxed{\text{program}}$ is established by the brain—in this case a desire to pick up the ball. This desire is then translated into a $\boxed{\text{control}}$ system within the brain making

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[6] An excellent description is given by L. London Goodman (1956), "Automation is the technology of automatic working in which the handling methods, the processes, and the design of the processed material are integrated to utilize as is economically justifiable the mechanization of thought and effort in order to achieve an automatic and in some cases a self-regulating chain of processes." Encyclopaedia Britannica, Vol. 2. p. 558, 1965 ed.

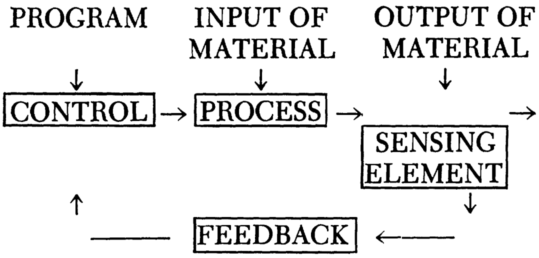

Fig. 1

connections through the various nerves to the various muscles, the process or prime mover finally gathering the ball in. If however the child's grasp is inaccurate, both sense organs, sensing element, in the hand and eye feedback information that corrects the action via the control mechanism. Feedback permits a degree of self-regulation in organism and machine.

As another example of operation at the organism level, Cannon stated that if there were no temperature regulator in the human body, the heat produced in 20 minutes of muscular effort would cause the albuminous materials within the blood to coagulate like the white of an egg after boiling.

Temperature regulation allows for the hands and face of man to be exposed at two extremes such as 130°C or minus 35°C without significant change in body temperature. At the slightest rise in body temperature, a series of operations goes into effect. The blood vessels dilate in surface tissues and constrict in interior tissues thus diverting blood from the internal organs to the surface. Fluid eluted from the tissues enters the blood and thus increases the blood volume and further cooling occurs. At the same time sweat glands are activated and release perspiration to the skin surface which upon evaporation produces a further cooling effect. The heart rate goes up and the speed of circulating blood brings a larger volume of blood to the surface per unit time. The respiration rate goes up and more heat is removed by exhaled air from the lungs.

Still at the organism level, the medulla of the brain acting as an acidity regulator, reacts to increase of $C0_2$ or lactic acid in the blood following twenty minutes of vigorous exercise which increase, if unabated, would result in convulsions and finally death. The resultant increase of respiration rate lowers blood acidity.

At the cellular level, a large number of metabolic reactions proceed toward a steady state of events. A micro-structure within the cell may "demand" glucose, phosphate, and oxygen and after a long chain of reactions produce ATP molecules. These reactants must be drawn from the immediate vicinity of the mitochondrion within the cell. If the cell is the total *organism* then its reactant requirement is satisfied by probing and collecting from the immediate external environment surrounding the unicellular organism. If on the other hand, the cell is deep within a multicellular organism, the reactant requirement may be drawn from the surrounding tissue fluid. It may be delivered to the tissue fluid from the external environment to the organism by a simple or elaborate transport system as the case demands. If the reactants are not in the immediate environment of the organism, the organism like a jellyfish must move to the reactants or conversely an organism like a sponge must move the reactants to it.

The organism operates in a system which is one of *least energy* whereby reactants are brought into the system and *waste* products removed from the system with the least expenditure of energy. This implies the steady state.

The most efficient steady-state system also requires a store of energy or reactants that is "immediately" at hand. If the time required to move a store of energy or reactants into the system is great, then the steady state begins to breakdown or the energy state drops to a lower level of efficiency, e.g., fermentation. Thus if the oxygen supply to a system has diminished, energy comes off at a different level. Complete oxidation of glucose slows down and then upon fulfillment of reaction needs, it speeds up at an accelerated rate.

Large deviations from the steady state may entail greater expenditures of energy than *maintenance* of the steady-state. Engineers recommend keeping air conditioning systems, heating systems, or electronic systems operating all the time. The degree of inefficiency would tend to be eliminated in the process of evolution where in every instance the struggle for existence which is essentially a struggle for energy would eliminate the "luxury" program and would favor the "austerity" program or at least favor damping off the reactions with high peaks and valleys to a low fluctuating state of higher frequency.

In the same way, release of energy from glycogen, starch, or glucose in small quantum leaps the size and magnitude of ATP molecules (7,000 calories per mole) in a series of stepwise reactions is "preferred" to the "catastrophic" leap from glucose to $C0_2$ and H_20 (685,000 calories per mole) as in oxidative burning which would provide much more energy than is needed at any moment and at a destructive temperature.

Thus, molecular components within a cell are in a steady-state with each other both in terms of energy and structure. New molecules are constantly replacing old molecules within any structure. Whole cells die and are replaced by others. Tissues are in a steady-state within their own system, i.c., new cells replace old ones regularly. If a large part of a liver is excised, the normal rate of liver cell reproduction would shift to a high rate of liver cell reproduction. If a blood loss occurs, the bone marrow would shift its production of red blood cells until the equilibrium number was restored. On the other hand if the reactants of the body decreased, for example by a shift to a higher altitude where oxygen tensions were lower, there would be a corresponding increase in blood tissue to compensate, i.e., to maintain a steady-state of oxygen supply. A temporary (physiologic) increase in breathing rate would occur until structural compensatory reactions took over.

At lower levels of social organization, aggregates of organisms in some ways maintain a steady-state system or homeostatic condition wherein environmental poisons are absorbed by each organism in such minute amounts as to leave insufficient concentration to do any damage. Symbiotic organisms constitute a simple biotic homeostasis, the best example of which is green hydra wherein *Chlorohydra viridisma* live in a steady-state system with *Zoochlorellae,* a green algae. The algae allow the hydra to live in a normally low external oxygen environment by providing a rich, immediate oxygen medium. The algae provide energy to hydra.

Societal insects such as bees "regulate" the environment by such means as clustering whereby bodies piled one on top of the other hold a certain amount of warmth in the immediate environment on a cold day. Maintenance of fungi gardens and aphids by termites is a mutually beneficial arrangement provides a steady-state system for all species involved.

Specialization of cells, tissues, organs, or individuals provides increased efficiency (again in terms of energy) in a system of functions which is in homeostatic balance. In any one population or species as indicated earlier, those individuals capable of operating with increased efficiency in terms of energy expenditures would tend to survive under circumstances of duress. Thus over vast periods of time, organisms with the most efficient and most harmonious (i.e., homeostatic) relationship with each other and the environment would tend to survive.

An organism, structure, substructure, or function immune (in the above sense) from the immediate and often violent changes of the external environment would thus have *survival value.* Biological organization will then continue to survive and will thrive provided that environmental change is not too sudden and not too catastrophic. Homeostatic systems can only operate within the spark of life. Death is a steady-state but albeit too steady and too permanent.

Essentially the organism is in conflict sometimes with itself, sometimes with other organisms in or out of the community and constantly with the abiotic environment. The dynamics of conflict are in reality the province of the political scientist who studies states, or the sociologist who studies communities, or the psychologist who studies people, but they rarely reach the levels of organization where the subunits are at work —organisms, systems, organs, tissues, cells, and molecules. This is the province of the biologist.

The steady state system is conflict under control. Change is ever with us—there is no peace for any living organism. Each species must be at-ready to cope with the new enormously complex conflicts that arise daily or from time to time.