PART TWO:

Evolutionary Mechanisms of Change: Normal Case

The set of biological objects, together with their mode of interactions, make up the biological system. Just like many other systems, biological systems are dynamic in the sense that they change over time. Considering the stability of an organism as far as its adaptability is to the environment, including its ability to "repair" itself, an organism can easily turn into a very conservative system incapable of change. However, organisms manage to overcome this conservatism, which is really a challenging feat. Ernst Mayr [1] has noted that

> "The real problem of speciation is not how differences are produced but rather what enables populations to escape from cohesion of the gene complex and establish their independent identity. No one will comprehend how formidable this problem is who does not understand the power of the cohesive forces in a coadapted gene pool." (p.297)

Let us examine the general characteristics of the mechanisms of biological change from the systems multi-dimensional perspective, i.e., function, structure, process, operator, genesis.

CHAPTER 3

THE MECHANISM OF BIOLOGICAL CHANGE – GENERAL CHARACTERISTICS

1. CATEGORIES OF BIOLOGICAL DYNAMICS

In keeping with the spirit of the present book, I shall distinguish the following categories of biological dynamics: its sources, its course, and the methods of representation which correspond to the various mechanisms of implementation.

1.1. Activeness and the Course of Development

Biological objects are *active*, meaning that they possess internal mechanisms which allow them to shape the environment as well change their own performance, depending on the signals received from the environment.

Under ideological monism instituted by those in power, the conflict between the active and the passive approaches to the behavior of biological systems may assume rather violent form.

In the Soviet Union, at the end of the 1940s, Pavlov's theory of animal behavior, with its emphasis on the passive mode of animal, as well as human, response through the development of reflexes to external stimuli, became the ruling ideological dogma in biology. The proponents of the opposing theory, which endowed animals and especially human beings with more capacity to control one's behavior,[2] experienced severe hardship. Only after Stalin's death were Pavlov's teachings dethroned as the only true theory and relegated to one of many important approaches to the study of animal (human) behavior.

Active systems, picked for methodological purposes as those determining biological dynamics, can be represented as having *random* or

directed development. In the present context, the term random does not preclude the usefulness of local actions as long as these actions are not ordered.

1.2. Survival, Viability, Growth, and Development

The course of development of any system is defined by such categories as *survival*, *viability*, *growth*, and *development*. Survival connotes the preservation of a given organism *per s*e. Viability is the preservation of a given organism via reproduction.[1] Growth implies a quantitative rate of change different from just one (one represents survival or viability); development involves qualitative shifts where each step is associated with a qualitatively new phenomenon requiring new methods of operation. By analogy with physics, compounds undergo phase transitions to assume qualitatively distinct states. The category of development as it pertains to biology must be qualified to distinguish development in the sense of "construction" (development of a biological entity based on a given program*)* from development which incorporates changes in the program itself. The first case is commonly known as *embryonic* development. The second type of development shall be called *innovative development***.**

Along with Russell Ackoff and Jamshid Gharajedaghi,[3] I am a proponent of the primacy of development, with growth, viability, and survival allotted a subordinate role required to support development. Within this conceptual framework, the global formulation of the dynamics of biological systems becomes crucial. The view that the key objective of living creatures is survival is widespread. Survival, being a prerequisite for all else, is essential. However, if survival is deemed the ultimate goal, *local* needs tend to dominate, since survival today overshadows all other concerns. In principle, viability, growth and development can be viewed in terms of long-term survival, but it makes our analysis very cumbersome.[2]

Another factor affecting the assignment of priorities among the many alternative objectives of system's dynamics is the decision-maker's mind-set.

Perhaps an example will clarify my point. Some years ago I happened to meet some leading executives from the Clark Corporation. At the time, the firm was facing a crisis, it was, in fact, on the verge of bankruptcy. Under the circumstances, survival would seem the most pressing concern of the firm’s top executives who were focusing the elimination of all unnecessary current expenditures. However, the mind-set of the firm’s leader, James Rinehart, a man who has successfully combined

academic training and practical thinking, was geared toward development; survival was viewed as a precondition. The corporate slogan became**:** *"Cut expenditures; don't cut your future."* As a result, cutbacks initiated by the firm were carefully screened so as not to hurt the firm's future. Many corporate leaders recognize this, but it takes a special gift to implement the idea of development and make survival and growth subsidiary, especially when the firm is threatened with bankruptcy.

1.3. Directedness and Goal

The terms *directedness* and *goal* are not identical. If all we were concerned with was the *course* of the system's dynamics, it would be sufficient, by definition, that there exist states sufficiently remote from the initial state. In Greek *tele* means 'remote'. Thus, an exclusive emphasis upon the direction of development could be termed a *telelogical* approach. Once a *telological* component is incorporated into the above scheme, we have a goal, *telos* in Greek, representing a terminal state toward which the system gravitates. Here, the category of a goal may appear implicitly, i.e., as a manifestation of the system's trend of development, or it can be formulated explicitly as one option within the set of available alternatives.

The two terms introduced by Ernst Mayr[4] in relation to biological systems - *teleonomic* and *teleomatic* processes - reflect these two methods of setting goals. In general, the term *teleological* is reserved for situations where directedness also incorporates the component of a goal.

While the study of biological systems claims to based upon causal rather than telological approach, it is implicit that the analysis is largely teleological, in the sense that *directedness* is postulated as the *struggle for survival.* It is this tenet which equates the performance of any biological entity, e.g., cell, organism, species, with its *eternal existence* that is implicitly assumed to direct the energy of the living system.

1.4. Representation of a System

Let us consider the various ways in which the course of biological dynamics can be represented.

The course of biological dynamics can be inferred phenomenologically via the *extrapolation* of past trends, in which case we search for the *laws* of development of a biological system represented as a *black box*. The implicit goal is to relate inputs and outputs, ignoring the

actual mechanism of transformation formed by the established rules of interaction, e.g., physical, chemical reactions; technologies, among the objects comprising the system. It is further assumed that the link between inputs and outputs is represented in the most compact form, by a formula, meaning that the need to *select* subsequent course of development from *alternatives* at each step of the procedure does not arise.

The course of development can also be deduced based on non-random mechanisms of operation of biological systems, subject to some basic principles of interaction of biological objects comprising the system.

There are at least two ways to represent these principles of interaction. One representation of a biological system is based on the basic principles of interaction of its constituent elements that, given the initial state of the system, ultimately attain equilibrium via forces, attractors and repulsors, that define the system's dynamics. The second approach is predicated upon the assumption that system's dynamics obeys certain criteria of optimality that reflects the totality of forces acting upon the system, subject to constraints on the initial state and the rules of interaction. The first approach corresponds with models of equilibrium; the second one yields an optimality-driven representation of a system.

It is important not to confuse the method of representation of a biological system with its mechanism of operation. The latter falls into at least two categories: *horizontal* mechanisms based on the interaction of equal biological elements, and *vertical* ones predicated upon a governing body. Generally speaking, each mechanism of operation can be combined with each of the aforementioned modes of representation.

I would like to note in this connection that certain contrived artifices, when used *heuristically* may be conducive as well as obstructive to the development of a given field. The concept of God who rules the universe not only impeded the progress of science, but facilitated the development of certain great ideas, such as the extremal principle in mechanics characterized by treating system's dynamics as a search for a optimal trajectory.

As far as biological systems are concernd, the proponents of the scientific approach often attempt to create models of dynamic ecological equilibrium[5], while the adherents of the Divine origins of the universe, *creationists*, devise models with an explicit and well-defined criteria of perfection. Biological models complying with the rigid requirements of hard science may also incorporate the principle of optimality. An example are models of blood circulation.[6] Both approaches represent methodological devices for representing the system, and they should not be confused with the actual mechanism of operation built into the system.

As the history of physics and economics has shown, the confusion between the representation of a system and its mode of operation can wreak great havoc.

The proponents of the equilibrium model in physics thought they were describing a world of cause and effect with no God; the advocates of the extremal principle insisted on God's creating a perfect world that is governing by a certain criterion of optimality. Considering the time when the church in Europe was not separate from the state, this kind of ideological interpretation of the universe was perceived by scientists-atheists as not so innocuous. It took a long time before the affinity between the two concepts was understood mathematically. Then the conflict subsided. As a result of the separation of church and state, the discussion eventually shifted to the realm of science. Its ideology-free agenda was concerned with the various methods of representing the physical world.

In economics, the equilibrium representation was seen as a manifestation of spontaneous, chaotic, market-type development driven by many participants interacting with each other via the price mechanism. Optimization models were associated with a centrally planned economy governed by a central body which allocates economic resources according to the selected criterion. I do not think it is necessary to dwell on the damage caused to economic science by this kind of confusion, especially in former communist countries with a plan-based system rooted in the Marxist economic doctrine.[7]

It should be noted that even to this day some professors in Catholic universities maintain a keen interest in the extremal principle in mechanics. In fact, the Catholic church has expressed enthusiasm toward the active modes of representation of economic systems. The Papal Academy of Sciences published a two-volume set compiled from works presented at a scientific conference on the problems of economic planning.[8] The conference was held from December 7 –13, 1963. It was attended by most economists from around the world who were involved in the problems of state control of the economy. The Pope himself appeared before the gathering.

Let us not, however, ignore the history of science and reject creationism outright. If we choose to interpret it non-literally, it could hint at some interesting new ideas.

The next problem to consider is the basic mechanism of the implementation of biological development.

2. FUNCTIONAL ASPECT: WHAT IS THE COURSE OF BIOLOGICAL CHANGE?

A telelogical framework seems to be an appropriate methodological tool for a related question: "What is a plausible course of development of a biological system?"

1.1."Apart From Trying to Survive, Every Species Strives to Create A Species More Perfect Than Itself"

We can construe a scheme to guide the development of the biological world that manifests itself in the following principle: *"Apart from trying to survive, every species strives to create a species more perfect than itself."*

This principle resembles the design approach to biological systems, and it has been discussed by a number of scholars in the field.[9] The approach is not all that absurd and, apart from its methodological significance, as a metaphor, it is helpful from the ontological perspective. In the light of recent discoveries in molecular biology, we now recognize that embryonic development is based on a program very similar to those governing the design of complex objects. This program incorporates the idea of a hierarchical procedure of constructing an organism. It was discovered that many different creatures, from *Drosophile* to man, possess the so called *Hox genes*[10] whose number fluctuates between 8 and 36; distant related genes have been found in plants, fungi, and molds. Hox genes are active at the early stages of embryonic development. They determine an organism's basic structure by telling the various cells their destination: where the head is, the chest, etc. Hox genes function by producing proteins called transcription factors. These proteins clamp onto the chromosomes and trigger, in a wave-like fashion, the action of subordinate genes. These genes operate in a manner of simple information signals, that is they produce a strong biochemical reaction induced by a rather weak impulse. The subsequent development of individual organs is another problem with its own long history.

Let us return to this paradigm that, "Apart from trying to survive, every species strives to create a species more perfect than itself."

Assuming that evolution is progressive, one observes that living creatures have undergone certain improvement. However, it seems impossible for a species to be more perfect that another species if all relevant parameters are taken into account. Some obsolete species which have given birth to a new species, might still not perish. Considering the

fact that the environment is far from stable preserving the new species as well as the old provides considerably more space for living creatures to develop. Naturally, the ratio between the old and the new species comprising the manifold of creatures changes over time; most species disappear altogether.

Once we accept the above paradigm, the struggle for survival - the guiding hand of evolution - as well as growth (in the sense of change, with positive or negative signs, in the size of the population) become necessary conditions for the process of development.

Man might very well not be the crowning or the end point of development and just as Man evolved from an ape-like primate, so a new species springing from Man may appear in the future.

These are the thoughts articulated by Nietzsche, through Zarathustra in his speech to the people:

> "I teach you the overman. Man is something that shall be overcome. What have you done to overcome him?
> All beings so far have created something beyond themselves; and do you want to be the ebb of this great flood and even go back to the beasts rather than overcome man? What is the ape to man? A laughingstock or a painful embarrassment. And man shall be just that for the overman: a laughingstock or a painful embarrassment. You have made your way from worm to man, and much in you is still worm. Once you were apes, and even now, too, man is more ape than any ape.
> Whoever is the wisest among you is also a mere conflict and cross between plant and ghost. But do I bid you become ghosts or plants?
> Behold, I teach you the overman. The overman is the meaning of the earth. Let you will say: the overman shall be the meaning of the earth!"[11]

1.2. How Can one Create an "Overman"?

There are at least two ways to proceed: one is by continuing the course of biological evolution, and the second is by artificial means.

Let us consider the first route. Its mere feasibility is important for my purposes: allowing for future biological changes justifies my hypothesis of an active mechanism of change instilled in human beings.

Philosophy aside, let us see what biologists and non-biologists have to say about the future evolution of man.

Scholars most firmly entrenched in the current scientific mindset, which limits their horizon to about 50 years, are rather circumspect in predicting the future of man. They do not expect any major changes in the human species in spite of drastic changes in the environment. Some scholars express more concern with such factors as the food supply to feed the exploding global population. Many prominent scholars came to Dublin in 1993 to discuss these issues at the conference entitled "What is Life?". A brief synopsis of the conference was presented in O'Neill, *et al.*[12]

Free of the shackles of the current state of science, I am going to let my imagination run wild and look at the distant future of the human race.

Practically all scientists believe that man will continue to evolve perhaps eventually creating a new race. A famous French astronomer Camille Flammarion (1842-1925), had the following thoughts on the subject:

> "A new race, intellectually more developed, shall take our place on Earth, and who knows if you, my pensive and dreamy readers, and I are not destined to meet in an office of some scientist of the 276-th century as pallid and magnificent skeletons with name tags on our brows... We'll be looked upon as rather curious specimens of some long extinct race, fairly crude and vicious but possessing certain rudiments of culture and civilization and exhibiting a mildly pronounced proclivity for science."[13]

While most scientists acknowledge that there is still room for change, some suggest that human evolution has come to an end, at least as far as morphology is concerned. This claim is supposedly corroborated by the fact that man has become an absolute master of the animal kingdom and has therefore overcome the need to struggle for survival. In other words, while the possibility of future change is there, the proponents of the above theory would not classify these changes as evolutionary, in the sense that these changes are not dictated by an unyielding struggle for survival and subsequent selection.[14, 15]

I believe this kind of rejection of enduring evolution is due to a rather superficial notion of evolution reduced to the struggle between man and animals. It ignores the fact that man still struggles with a myriad of

microorganisms and the victor is by no means certain, as well as with the inorganic world which continues to wreak havoc in the form of earthquakes, floods, and other tribulations. There is really no end to the human struggle for survival as long as man is what he is. The external aspect of survival is really just one side of the coin. Man also strives to improve his performance in order to grow (multiply) or otherwise develop within the limited resources available to him.[3]

The great majority of scholars believe that man will continue to evolve. This view is really based on the extrapolation of phenomenologically observed changes in human beings over time – from Pithecanthropus - Neanderthal - Cromagnon - to modern man. Extrapolation is also applied to individual body parts/organs showing that they may disappear[16], [17]or undergo structural changes, at least in quantitative terms, over time. Interesting in this respect are the observations made by the paleontologist S. Williston, whose findings were subsequently generalized by W. Gregory into what is known as "Williston's Law." Essentially the assertion is the following: as the organism evolves, polyisomerism (large number of elements comprising some part of the body) is replaced by anisomerism, or a small number of elements. Consider the monkey's tail. Man has retained four-five semi-reduced vertebrae of the coccyx and the number is sometimes as low as three.[18](p.78)

Within the phenomenological framework, the study of the various deviations from the norm found in modern man reveals interesting possibilities for predicting man's future. Pathologists have accumulated a much data on the variability of human body parts. It turns out that "under close inspection every single organ reveals some kind of deviation from the so called normal structure."[19] (p.77)

The major problem of the phenomenological approach is the time frame within which changes take place. Changes in the population as a whole are extremely slow, but frequently they manifest themselves in the anomalies found in individual beings:

> "...the human organism is not an immutable or finished product. It is but a stage in the continuing evolution of man. Changes are slow. They take place over long periods of time and therefore do not yield to direct observation. It is only through anomalies and deformities - the key milestones - that evolutionary changes reveal themselves to us. At the present time, the course of human evolution is unclear. It is our job to provide a detailed description of all the anomalies and

> deformities that we find. Armed with this raw data future scholars will be able to know exactly, rather than just guess, the course followed by the philogenetic changes in our bodies."[20]

This methodological device (the role of abnormalities) will be helpful when I examine the mechanism of change itself.

The phenomenological approach to human evolution branches into many different mechanisms of change which I shall touch upon in the next chapters.

A new Man who will appear in the course of biological evolution might, at the very least, possess a much greater capacity to fulfill those functions that are intrinsic to man. One way to create such beings is by developing the already existing organs, provided it does not interfere with other functions. However, this course of human evolution is slow; in fact, it is significantly slower than in other primates and mammals.[4]

More radical ways of human evolution - ones not necessarily rooted in biology - are also plausible. Improvements might be achieved by combining artificial and natural organs. Biological evolution characteristically replaced or strengthened certain organs with external means; for instance, a natural shell replaced by some artificial cover; the use of sticks, stones and other artifices, instead of strengthening the body parts themselves.

In this respect Man has come a long way compared to other animals. Man has created rather powerful devices to improve his extremities (arms, legs) and to be able to do things for which he lacks specialized parts altogether, flying, for instance. Man has also begun to create artificial devices capable of improving or even replacing certain internal organs, e.g., kidneys, heart. It seems that this process of substitution is boundless, and, eventually, Man, made up entirely of artificial internal and external parts, could be created. The new type of artificial Man really represents a new species, since he will reproduce based on principles completely unlike those underlying human reproduction. One name for this new species is *Kiberhomo*. It is a combination of cybernetic technology and human structure.[5]

Thus, a new species superior to Man could be created on the substratum of Man. The creation of a new species on the substratum of another species with previous evolutionary experience taken into account is characteristic of biological evolution. However, it might be rather painful and slow in terms of evolution to create a new "improved" species based on the same principles as those underlying human machinery.

Perhaps the most effective way to create a new species is to invent new principles completely unlike those governing human development. Such a species could be created by Man outside of himself, as an artificial system. Man-made technology based on the new principles could eventually turn into a self-developing autonomous system having considerably greater creative powers.

Two questions arise in this respect: 1) Is an artificial system capable of formulating its own goals?, and 2) Can Man assign goals and constraints to this system so that the side effects of its operation will not cause him too much suffering?

There is no definite answer to these questions. People with the so called Western system of values continue to develop artificial systems capable of being superior to Man. They assume that the point of irreversibility, in terms of the welfare of mankind, is still very remote. In this sense, the disciples of Western civilization, no matter what local benevolent goals they advocate, are in a global sense, following the teachings of Zarathustra: "What is great in man is that he is a bridge and not an end: what can be loved in man is that he is an overture and a going under." [21] (p.27)

These thoughts stimulated me to propose the following interpretation of the Old Testament: God is not an absolute, but rather a developing entity; Man was created by God in order to augment God's greatness. We can further surmise that Man can increase his own power and eventually create a force superior to himself and increase God's might at the same time. This way God's might grows faster than that of any of his creations (or the creations of his creations), preventing them from ever becoming greater than God. Here, it is time to stop, for these deliberations fall far outside the scope of the Old Testament.

As we examine the *structural* aspect of the mechanisms of change it is important to pinpoint the type of cells we are talking about, namely germ and/or somatic cells. Whether or not changes in the somatic cells are heritable is another sensitive issue.

Much of my discourse regarding the mechanisms of change pertains to both somatic and germ cells; in case certain ideas apply to one type of cell only it shall be so stipulated). The reader is warned to shy away from assuming that changes associated with somatic cells must necessarily pass on as hereditary information. I realize this temptation, for, I, myself, would not rule out that under certain conditions changes in somatic cells do affect germ cells.

3. STRUCTURAL ASPECT: THE STRUCTURE OF THE "GENERATIVE SYSTEM"

3.1. "Generative System"

Biological mechanisms of change are usually associated with genes. To analyze this fallacy, I need to revert to the definition of the vertical and horizontal mechanisms discussed above. These categories, presented in the context of economics, have general systems significance. Equally relevant to our discussion of the biological realm,[22] these categories will help devise an adequate representation of the general structure and dynamics of the process of change.

It can be reasonably surmised that, at the very beginnings of the evolution of life, nature operated with a rather limited number of primary biochemical compounds and (bio)chemical reactions. The main problem under the circumstances was to augment the set of chemical compounds and methods of their interaction. Here, the horizontal mechanisms seem to have predominated. They reflected direct interaction of various elements and biochemical compounds without the intervention of a specialized coordinating program. This perspective on horizontal mechanisms operating in biological systems is characteristic of the theories of self-organizing systems, such as the theory of autopoiesis.

Just a passing note based on general considerations on the development of the universe and the evolution of living creatures: it quite plausible that survival, growth, and even the development of living creatures, of which change is an integral part, could unfold via basic chemical reactions without such specialized informational background as RNA and, subsequently, DNA.

As living system became increasingly more complex (greater variety of biochemical compounds and methods of their interaction), the evolution of life was driven by new combinations of existing primary compounds as well as methods of their interactions. The huge number of possible combinations necessitated some kind of a systematic procedure of selection aimed at eliminating large parts of inherently ineffectual genetic combinations. This is where vertical mechanisms, initially, perhaps, operating, from the structural point of view, through the hormones [6] and subsequently through the genes, come in as programs governing the creation of new organisms.

The emergence of the informational substrate (*the genetic system*) marked a tremendous step in the evolution of the organic world. It made

several things possible including the capacity to preserve "memory" of the past in a very compact form, to assimilate incoming information, and to simulate the situation by means of built in programs. An informational profile introduced anticipatory techniques to regulate the behavior of compounds that form living creatures and to send signals that organize the behavior of living creatures.

It should be noted that the concept of a genetic system is more general than that of the "*genome*."

As a rule, the process of change is associated with the genome as one complete haploid set of chromosomes, which carries a program of the creation of an organism. However the set of genes involved in the development of an organism is not necessarily limited to the genome. In fact, active genes may be housed outside of the cell's nucleus - in organelles, including mitochondria, or they may scattered in the cell's cytoplasm in the form of viruses [7] and similar structures.[8] The term "*genetic system*" encompasses the entire set of genes be they in the nucleus or the cytoplasm. Our discussion of biological change will be limited primarily to the genome. I should note that there are two kinds of changes in the genome, which I call operational and structural. The operational case implies that certain genes are suppressed or activated with the structure of the genome remaining intact; under structural changes the structure of the genome itself is altered.

The above model of the genetic system reveals that in spite of "verticality" it is not completely centralized. There are independent genes located in parts of the cell other than the genome.

The notion of vertical genetic mechanisms in the genome predominating in the process of change does not rule out the existence of other mechanisms.[9] As is the case with any innovation, the informational profile does not nullify direct interaction of chemical compounds but merely limits its scope.[10] Horizontal mechanisms are manifest in biological innovations being driven not only by changes in the genes but independently by changes in the cytoplasm.

Theories of the hereditary function of cytoplasm, along with chromosomes, have a history that is more than a century-old and is well known in the literature. Although chromosomal heredity has maintained its primacy and many attempts to explain heredity through cytoplasm have been rejected, the general concept of cytoplasmic heredity (non-Mendelian inheritance), as Ernst Mayr mentioned[23] (pp. 786-790), is still very fertile.

As early as 1950, T.Sonneborn published a paper entitled "Partner of the Genes." He elaborated upon his ideas in an article published much

later in 1979.[24,25] S.Løvtrup analyzed non-Mendelian inheritance in the book Epigenetics.[26] Other interesting findings in the vein of non-Mendelian inheritance were presented by P.Sheppard; one such discovery revealed the impact of cytoplasm on the resemblance of cuckoos' eggs.[27]

The latest advances in biology impelled Brian Goodwin to state unequivocally that the totality of the organism and the environment take part in the creation of a new organism. "The position I am taking in biology could be called organocentric rather than genocentric."[28]

To sum up, the mechanisms of change incorporate both vertical and horizontal structures that include genes as well as other components. The totality of all these elements could be termed a "generative system". This totality is founded upon horizontal mechanisms, but it incorporates powerful vertical ones as well.

3.2. The Hierarchical Level at Which Changes Take Place

Another aspect of the mechanism of change is the level of the hierarchy, i.e., the degree of aggregation, at which changes take place whether they are induced by internal or external sources, or are random or ordered.

We can distinguish at least three levels of the hierarchy: genes, chromosomes, and cells. Each of these structures represents an aggregate, meaning that changes in each respective structure do not necessarily affect any other structures. In present work, I am more concerned with the genes, but I shall touch upon other levels as well.

The source of change within an aggregate can be external or internal. Internal sources of change are associated with a mechanism of change that is self-induced, i.e., triggered by internal forces; external sources, by definition, affect a given aggregate from the outside. Each source is sufficient to induce change in an organism. My primary interest is with the internal sources of change, but I shall briefly discuss the external case as well as the combination of the two.

The process of change within an aggregate can be random or ordered (of course, this dichotomy ignores the degree of order). My focus here is primarily on the ordered sources of change.

The boxes in the table below correspond to different combinations among the levels of the hierarchy, the sources of change, and the binary degree of order of the process of change.

TABLE 3.1. Sources of change and degree of order.

Structure	Process of change	The source of change	
		External	Internal
Genes	Random	Chemicals, radiation, break downs in the cell	Damage
	Ordered	Viruses, regular fluctuations in radiation	Program-changing program
Chromosomes	Random		
	Ordered		Transposons
Cells	Random		
	Ordered		Crossing
Tissue	Random	Infection	Damage
	Ordered		

Some clarification is in order.

The gene level. This level actually comprises the primary subject matter of the book. At this point, I would like to note that viruses also count as structures that induce change at genome level.

These genetic strands merit a digression based almost entirely on the work by Konstantin Umansky.[29]

The term *virus* carries a negative connotation because of its association with various diseases. The leitmotif of Umansky's book is the positive role of the viruses, which manifests itself primarily in helping organisms to adapt. The diseases associated with viruses ought to be treated as a pathology of their positive functions in helping with adaptation.

> "...one feature shared by all respiratory virus infections is that they are seasonal and correspond to changes in the environment (Fall/Winter and Spring seasons). It is important to note that these outbursts are not "calendar specific" but correspond to the extremum points of the changing environment, i.e., time frames when adaptive reorganization is most urgent, especially so for respiratory organs. These observations lead us to conclude that certain respiratory viruses are factors that partake in the organisms' adaptive acclimatization." (p. 30)

For instance, the virus *Fignia* is a genetic factor that controls the sensitivity of certain types of *Drosophila* to carbon dioxide. When this virus penetrates the fly's genetic structure, it allows the fly to adapt its breathing habits to that particular environment. Characteristics thus acquired are passed on, establishing continuity so crucial for survival.

The feature that makes it possible for viruses to partake of the process of adaptation to changing conditions is their "omnipresence." It is rooted in the universal structure of the viruses, i.e., the ability to penetrate any living creature, including plants, animals, and man, and to migrate from one to another.

As a result "...viruses constitute the public genetic pool that can be used by any biological entity." (p. 12)

In other words, the diversity of viruses both inside and outside the organisms represents a gene pool; genes fusing with certain structures of the host cell lead to changes in the organism.[11]

The chromosome level. Changes at the chromosomal level are less explored than changes at the gene level. Here, I would like to quote from a work by Nikolay Vorontsov:

> "It is important to note that chromosomal rearrangements of the Robertsonian type (2Afi1M), and chromosomal inversions (i.e., rotation of an individual segment by 180º) do not alter gene composition; here, evolution does not effect the structure of genes and takes place without gene mutations. Consider the following analogy: gene mutation involves changes in hereditary constitution, which can be compared to changes in the content of a tape recording; chromosomal mutations, on the other hand, are like changes in the construction of the cassette carrying the tape. Chromosomal mutation changes the dispersal of hereditary information, because information flow (‘gene flow’) between tape recorders with differently constructed cassettes is bound to be limited."[30] (p.181)

More recent research on chromosomal mutations is linked to telomeres. This topic is discussed in greater detail in Chapter 6.

The cell level. See Chapter 6.

The tissue level. Change at the tissue level has multiple appearances. One of the more interesting forms of change is metaplasia. "The term metaplasia denotes a form of regeneration which ultimately

produces a new tissue that is morphologically and functionally distinct from the original tissue."[31]

3.3. The Temporal Hierarchy of the Mechanisms of Change

We have looked at the structure of the genetic system from the *spatial* perspective. Mechanisms of change also have a *temporal* aspect, i.e., the time span of the change relative to the life span of a given organism. The temporal dimension can be roughly divided into three segments: current, mid-term, and long-term.

Current refers to shocks, sudden changes, short-term changes in temperature, etc. The common method of adaptation, or adjusting an organisms for homeostasis, to short-term changes is through flexibility incorporated into the various organs, i.e., by quantitatively varying the magnitudes of parameters governing the operation of the existing organs. These changes can also be induced by viruses which alter the DNA or the RNA of the cells.

Mid-term changes are accommodated in a more complex manner, possibly requiring restructuring of certain organs with corresponding changes, at least operational changes, in the performance of the genetic system. Structural changes in the genetic system are possible, although they might not become genetically fixed and would thus not pass on.

Finally, long-term changes in an organism can be tied to its development achieved through an active conquest of the environment and adaptation to some of the more consistent fluctuations. This kind of change is usually associated with major structural shifts in the genetic system, including the creation of new families, orders, classes, etc., with new genetic information being passed on to the progeny. Perhaps long term changes are implemented by means of an internal mechanisms of change at the level of genes and chromosomes.

The present work focuses on this last type of change. Current and mid-term types of changes ought not to be slighted, since their mechanisms of implementation might be similar in some respects to the mechanism of long-term change. For example, changes that take place through germ cell recombination can be important any time.

In generalizing what I have said regarding the temporal and the spatial hierarchy of the mechanisms of change, we have to look at the following structures:

Frst, the mechanism of change operating at each level of this spatial/temporal hierarchy, i.e., the interaction among the various structures of both the temporal and the spatial hierarchy;

Second, the mechanism linking the various levels of the spatial and temporal hierarchies, i.e., aggregation and disaggregation[12]; and,

Third, the mechanisms for changing all of the mechanisms described above.

4. PROCESSIONAL ASPECT: A POSSIBLE LINK BETWEEN THE MECHANISMS OF CHANGE AND SELECTION

The prevailing philosophy of the mechanisms of change postulates that all change is random, induced by external factors. Subsequently, forces, also external to the genetic structure, carry out the selection of the generated mutations.

Let the starting point of our analysis of the mechanisms of change be such elementary components as molecules and biochemical reactions which give rise to an organism. Under these assumptions, the entire problem of evolution is reduced to ordering the process of *selection* of living creatures from the possible combinations of these building blocks.

Kauffman writes: "We have come to think of selection as essentially the only source of order in the biological world. If "only" is an overstatement, then surely it is accurate to state that selection is viewed as the overwhelming source of order in the biological world."[32] (p.6)

By encompassing a wide array of modern discoveries in such areas as mathematics, physics, chemistry, and biology, Kauffman makes a strong case for the idea that evolutionary selection can be viewed as *self-organizing.*[13] This innovative approach questions the undue emphasis, prevalent among biologists from the time of Darwin, on the random nature of evolutionary change produced by external factors.[14]

Taking Kauffman's framework as our starting point (the primary objects of a system are exogenous, i.e., determined by an outside world and the rules of their interaction are given), the problem of development does reduce to uncovering the laws of selection, or "algorithms" of selection based on certain criteria. Thus, selection determines which discrete objects (living organisms) shall exist in time and in space and which shall perish.

We can approach selection as a hierarchical process, meaning that it takes place at the innerlevel (among parts of a single organism) as well the interlevel (among different organisms). This hierarchy of selection forms a single chain, but the sequential nature of the process (selection at

one level of the hierarchy preceding selection at other levels) suggests we use two terms - *change* and *selection* - to underscore the peculiarities of each stage. The term change will be reserved for the process of selection within the discrete entity. It is the first link of the selection process. Selection proper denotes interaction between the discrete entities and the environment.

The greatest progress in biology has been in the theory of selection, with heredity a close second. Mechanisms of change within the organism are relatively less explored.

A brief remark on the relationship between change and selection. The emphasis is placed upon constituent elements and random processes of transformation, while the actual selection of genetic combinations that generate a given organism is secondary. This approach would make sense if the number of possible combinations were relatively small, i.e., if all the combinations could be constructed and tested through selection. However, if the number of combinations is large, this kind of mutation mechanism is rather resource and time consuming. The other problem encountered in connection with the above approach is the creation of intermediate combinations in the absence of an end-goal – merely a vague course of development. I have touched upon this situation in connection with the tunnel process.

I shall illustrate this speculative point regarding the role of change and selection with an example from the field of artificial intelligence as applied to music.

The structures of a number of music genres, such as fugues and certain dances, have been formally dissected to such an extent as to yield to computer generation. By randomly varying certain parameters defining the structure of the musical piece, a computer can create a multitude of musical

mutations. All of these mutations comprise *feasible space*, meaning that they conform to the criteria defining a given genre. The problem is how to select from this a practically infinite number of mutations. There are two ways to carry out the selection process.

One way is to have a *law* that governs musical composition. The law implicitly incorporates both the composer's taste, and, indirectly, listeners' taste, and external constraints such as technical characteristics of the instruments, accessible decibel range, etc. However, it is very difficult to formulate such a law. For one thing, the audience's taste is subject to change, and forecasting shifts in taste is virtually impossible.

In the absence of such a law governing musical composition, we can employ a criterion of selection, so that there are established priorities of one type of musical mutation. Presently, neither the composer nor the listener is able to formalize these criteria for selecting musical works of choice. Naturally, these criteria are employed at the intuitive level of the composer/ listener.

Assume for the moment that the composer knew the criterion for selecting the best musical work in a given genre. By conducting an exhaustive search of all possible mutations within that genre, the composer would be able to choose the best one. One limitation of this approach is that it is too time-consuming, especially if the number of "mutations" is very large, for example, all variations distinguishable by man. In other words, the criterion, even if known, is insufficient to select among a huge number of variations. This situation is similar to solving optimization problem: one also needs an algorithm of selection which deletes branches that will undoubtedly miss the sought after solution. It is well known that the ordered procedures of shrinking the feasible space containing the solution can be combined with random techniques such as the Monte Carlo method. In fact, strictly optimal solutions are not always attainable, if only because of temporal or spatial constraints of existing algorithms. Herbert Simon coined the term *satisficing* to denote this kind of given the constraints solution. In any case, unlike the listener, the composer does possess an algorithm of selection. This algorithm is generally intuitive and indeterministic. Of course, knowledge of musical theory introduces some order to this process, with some parts of the musical work possibly produced in a deterministic manner.

Let us now return to biological systems. By analogy with music, imagine a mechanism of change which generates a certain number of new mutations within a given genetic structure. It is quite possible that the genetic structure has a hierarchy of levels marking the difference among the species, genus, family, class, phylum. Within each level there is room for considerable change and variation. Moreover, within this space, nature seeks satisficing (rather than optimum) mutations either through a law or some criterion combined with an algorithm. These search techniques may well incorporate random mutations similar to Monte Carlo. Of course, random variations thus produced should be distinguished from the random mutations resulting from damage to the genetic structure.

The following table illustrates in a systematic fashion the relationship between selection and change.

TABLE 3.2. Ordering methods within the genetic structure.

Search method	Random element included	
	Yes	No
Random	11	-
Ordered according to:	21	22
Law	211	221
Algorithm	212	222
Exhaustive Search	2121	2221

It is reasonable to assume that whatever the actual mechanism of implementation of the process of change (through somatic cells or germ cells) may be, the cell's genetic structure is *selective* in creating new forms.

NOTES TO CHAPTER 3

[1]. "There are two common misunderstandings of evolution that should be mentioned explicitly. The first is that evolution promotes survival. This is only indirectly true. What evolution promotes is reproduction. Survival is obviously important to reproduction..." [33] (p.22)

[2] Compare the Ptolemean geocentric and Copernican heliocentric views of the solar system. Both theories have "prophetic powers" to predict the position of the sun and the planets, but, while Copernican system does so directly and elegantly, the Ptolemean framework is rather artificial and cumbersome.

[3] Similar views argued somewhat differently (for instance, ecological changes due to industrial production) are expressed in the article by C.Wills.[34] The article was written as a rebuttal to J.Jones, a British geneticist. The latter published an article in the New York Times in the mid-1992s in which he claimed that human evolution has come to an end because of a significant decrease in evolutionary pressure.

[4]. However, this course of human evolution is slow; in fact, it is significantly slower than in other primates and mammals. The relative pace of evolution was pointed out as early as 1961 by a molecular evolutionist, Morris Goodman. The hypothesis was confirmed by recent research in this field reported in the conference commemorating Goodman's 70th birthday: "Molecular Anthropology: Toward a New Evolutionary Paradigm", March 12-14, 1995, Wayne State University, School of Medicine, Detroit."
More on this in A.Gibbons. [35]

[5]. The term is not my invention. I read about it or heard it many years ago from a friend of mine in the Soviet Union, Leonid Grinman.

[6]. The relevance of this comes to the fore in the light of recent discoveries purporting that the development of organisms depends not only on the informational structures

such as DNA or RNA, but also on the equally important hormones which probably preceded the informational substrata in terms of the evolutionary timetable.

One of the champions of this approach to the evolution of life is Fernando Nottebohm, a prominent American behavioral ecologist and neurobiologist, who has explored the behavioral aspects of animals in an ecological community.

Let me quote the following passage from an article written by Natalie Angier:

"In the era when genetics and the glories of DNA reign supreme, and most molecular biologists are fixated on discovering the genes for everything from senility to shyness, researchers of a more naturalist bent are suggesting a different tack.

Genes are only a part of the story of any animal's profile, they say, and other influences, like hormones, can contribute to, complicate and in some cases override the innate program inscribed in a creature's genes. And although researchers have long appreciated that a fetus's own steroid hormones, produced by its growing sex organs - testes in a male, ovaries in a female - will in turn help shape the growing animal's body and brain, only recently have they paid significant attention to hormonal contributions from the mother or, in the case of litters, the other siblings in the uterus."[36]

[7] Viruses in the cytoplasm are interesting for exploring the link between non-nuclei genes and the process of change. There is indirect evidence, based on the rather contradictory claims concerning the causes of viruses, which suggests that viruses possess powerful structures capable of influencing the process of change. "Three hypotheses have been advanced to explain the origins of viruses: 1) viruses come from primitive pre-cellular forms of life; 2) viruses are degenerated microorganisms; 3) viruses are by-products of cell components that have escaped from under the cell's control." [37] p. 62.

[8]. "Suppressor gene called DCC (for deleted in colon cancer) may be as far from the nucleus as it's possible to be: at the cell's outer membrane, where it could be involved in cell-cell adhesion."[38]

A similar phenomenon occurs in other types of suppressor genes. The development of genetic engineering has reaffirmed the fact that the genetic system might incorporate structures outside the genome. For example, Duchenne's muscular dystrophy results from a damaged gene responsible for producing a certain protein. Once the damaged muscle cells were injected with DNA luciferase expression vector the protein was produced. Moreover, the "transplanted" gene did not need to be in the cell's genome; it could have been part of the nucleus or even cytoplasm.[39,40]

[9]. The following fact may serve to reinforce this statement. The crossover between a mare and an ass produces a mule, while the crossover between a stallion and an ass produces a hinny. These two different mutations belong to the same species that is, in fact, infertile (only reversible fertile). Taking into account that the male germ cell contributes only the chromosomes during fertilization of female germ cell, while the female germ cell features an entire array of hereditary structures, the decisive role of the chromosomes in defining the species comes to the fore; distinguishing features result from the structures in the female germ cell.

[10]. n this connection, I recall a conversation with my friend, a physiologist involved in the study of trophic ulcer. His research into the link between the nervous system and the humoral mechanism at tissue level is pertinent to the study of genetic programs and self-organization at the cell level.One argument in favor of one particular method of treating trophic ulcer was based on the assumption that the phase of development of a tissue is correlated with the engagement of the nervous system in regulating the tissue. Trophic ulcer represents degenerated tissue, so its incessant regulation by the nervous system may be inadequate and actually impede recovery. This approach suggested a new method of treatment: to arrest the nervous system using Novocain and induce natural self-organization within the tissue; meanwhile, administer artificial feeding to the tissue using various lotions. Once the process of self-regeneration reaches a certain level of organization the novocain blockade is suspended reactivating the control by the nervous system (the tissue reverts to its normal metabolic mode).

[11]. These considerations regarding the positive role of the viruses in the process of change apply to many different kinds of viruses, including retroviruses."Based on morphological, virological, biochemical and molecular biological data, it is proposed that the presence of endogenous retrovirus particles in the placental cytotrophoblasts of many mammals is indicative of some beneficial action provided by the virus in relation to cell fusion, syncytiotrophoblast formation and the creation of the placenta. Further, it is hypothesized that the germ line retroviral infection of some primitive mammal-like species resulted in the evolution of the placental mammals."[41]

[12]. In a large scale system such as economics, changes occurring at different levels of aggregation is a key problem. Macroeconomic changes, i.e., changes in highly aggregated sets of indicators, must be represented differently at lower levels where the actual integration of these aggregates takes place. A lot of ingenuity was required to develop constructive aggregation/disaggregation techniques.[42]

[13]. There is a great deal of literature on self-organizing systems. I am, however, surprised that Kauffman's above mentioned book fails to mention any literature on the subject which was pioneered by Heinz Von Foerster.[43] It was further elaborated and applied to biological systems in the works of Humberto Maturana and Francisco Varela,[44] Milan Zeleny,[45] and others.

The other source of ideas in this field is the theory of automata developed by Michail Tseitlin,[46] Victor Varshavsky and Dmitry Pospelov.[47]

It seems to me that whatever Kauffman's own opinion of the aforementioned works is, he should have made it known, since the thrust of his own work follows similar themes.

[14]. Kauffman also applied his concept to economic issues and attempted to link internal mechanisms of technological development, which belongs in the realm of engineering, with the selection of the actual technologies, which is subject of the economic science proper.

CHAPTER 4

TWO CLASSES OF EVOLUTIONARY MECHANISMS OF CHANGE

1. MECHANISMS OF SURVIVAL, VIABILITY, GROWTH AND DEVELOPMENT

One way to classify biological mechanisms is according to the objectives pursued whether they are aimed at sustaining an organism (survival), or at an organism's growth and development.

There exist two different mechanisms for sustaining an organism. One aims to keep the entire organism alive by repairing or replacing its malfunctioning parts. Such common biological phenomenon as repair, particularly in cells, and regeneration of certain body parts attest to the viability of this mechanism. While the repair methods are not the main tool in preserving the species, they are still of paramount importance. Assuming that the task of the living organisms at some stage of the evolution was limited to self-preservation (as opposed to quantitative growth or development), this class of repair mechanisms could have played a leading role. It is entirely possible that, looking at the evolution of the physical world as a whole, living creatures who lack the capacity to expand (in number) but have internal mechanisms of self-preservation, might turn out to be more durable.

The other mechanism of survival is predicated upon the mortality of living creatures, meaning that the organisms have, for whatever reason, a finite life span. Here, organisms possess a very special mechanism which allows them to reproduce.

If the biological system were aimed exclusively at survival, these two mechanisms would be competing on a par with each other. However, since living creatures also strive to *expand*, the only feasible alternative is

the second mode of survival. The regeneration method, while not extinct, is relegated to a subordinate role.

Population growth assumes two different forms. The first one is known as division. This method is associated with, but not limited to, single-cell organisms that split into two parts. However, only the most simple of multicellular organisms, such as weeds, reproduce by division. Evolution has produced an interesting subclass of division-based reproduction where a new organism springs from a small part of its parent. What makes this offshoot technology possible is that each part of an organism contains a program which defines its offspring. This type of reproduction is called *fragmentation*; it occurs in flatworms, sea stars, sea urchins.

The advantage of division as a reproductive method is its economy of means: it utilizes the organism itself as the substrate upon which new organisms are formed. But this method also has its drawbacks. As C. Duddington mentioned,[48] (pp.135-136), in plants, for instance, this mode of reproduction would make it impossible for a new organism to develop at a large distance from its parent, or for the plant to survive under strong fluctuations in temperature (a spore is preserved much more effectively). Generally speaking, division-based methods seem ill-suited for complex organisms when new creatures would have to originate from rather specialized parts of a developed organism. Instead, nature has devised specialized germ cells which develop into a new organism. Over the course of a complex multi-stage process of development which starts out with a single cell, a new multicellular organism is formed.

Because reproduction by division is based entirely on somatic cells let us call this kind of reproduction *somatic*. By analogy, reproduction by means of specialized germ cells will be called *germatic*. Why did I pick this rather unusual term for reproduction based on specialized cells? In the literature on the subject, asexual methods of reproduction are usually opposed to sexual reproduction. A single parent is deemed the distinguishing feature of asexual reproduction which includes division as well as development from a single specialized cell, such as a spore. For my purposes, the crucial criteria in classifying reproductive methods is whether or not reproduction takes place directly using the substance of the parent (somatic cells) or by means of specialized cells, be they germ cells (i.e., cells belonging to two or more sexes) or asexual cells, such as a spore. The term germatic is used to emphasize reproductive modes based on specialized germ cells.

In nature we also observe combinations of two germ cell reproductive methods - sexual and asexual. Ferns are very interesting in this respect.

> "The sporophyte, which is the fern plant, reproduces asexually by means of spores, which germinate to produce the prothallus, a tiny plant no more than a quarter of an inch across. The gametophyte bears the sex organs, and the product of its sexual reproduction is the fern plant."[49] (p. 114)

The table below presents different combinations of organism types and methods of reproduction.

TABLE 4.1. Organisms having/lacking specialized germ cells.

Type of organism	Sex	Presence/lack of specialized germ cells	
		Present	Lacking
Single-cell	Asexual	-	Amoebae
Multicellular	Asexual	Spores	Many types of weeds
	Two sexes	Animals	

If the sole objective of the living creatures were quantitative growth, reproduction by division would be given top priority, at least for simple multicellular organisms, because it seems to be a more economical and expedient way to procreate - it is simpler and works with the already existing structures.

Once nature had introduced such phenomenon as development and its steadfast companion change, the hierarchy of the various mechanisms of biological dynamics had shifted dramatically. Living creatures must not only survive and grow, but also change in order to become more effective at conquering the environment, with adaptation being one particular case.

An in-depth probe into the somatic and germatic mechanisms of change is discussed in the next chapter. At this point, I would like to note that the somatic mechanism seems more cumbersome, because changes in one set of cells must be transmitted and coordinated with other cells. On the other hand, a germ-cell based mechanism of change allows all changes to take place at one location, using a compact set of elements comprising the specialized cell. Although some features are mechanism-specific, the

somatic and germatic mechanisms are not separated by a Chinese Wall. On the contrary, they interact and complement one another.

2. EVOLUTION OF THE MECHANISMS OF EVOLUTIONARY CHANGE

Division-based reproduction makes somatic cells the only source of change. Under germ-cell reproduction, two mechanisms of change are possible: a joint germ/somatic cell mechanism and a germ-cell mechanisms only. I shall focus on the first case of joint operation.

2.1. Combinations of Germatic and Somatic Mechanisms of Change

With two types of cells, we have the following variables: the vehicle of change can be somatic or germ cells and the source of change can be internal or external. The above parameters can be combined in logical modes either/or as well as and/and. The nine alternatives linking the various mechanisms of change are shown in the following table.

TABLE 4.2. Possible mechanisms of change.

Cells in which change takes place	Sources of change		
	External	Internal	Internal and external
Somatic	11	12	13
Germatic	21	22	23
Somatic & Germatic	31	32	33

I shall list three examples to illustrate the above table. The first reflects combination 11, i.e., change takes place through somatic cells only and results from external factors only. In keeping with the "11" framework , germ cells that partake in reproduction may form as a result of somatic cells producing certain ingredients. This is precisely the view espoused by Charles Darwin in his theory of pangenesis.[50]

The second example reflects the currently prevailing theory of evolution -combination 21 assumes that reproduction is carried out only through the germ cells, and the source of change is primarily the environment.

Third, one can assume that change, which includes both somatic and germ cells, results from a combination of internal and external sources

– this is combination 33. I am proponent of this concept, and I shall elaborate it below.

The ruling theory of biological change prior to the 20th century is encapsulated in the first example (combination 11). The 11 camp was not without internal conflicts. For instance, Lamarck and Darwin disagreed as far as the mechanism of change: Lamarck deemed goal-oriented active change possible (the famous example of giraffe's neck), while Darwin emphasized change as adaptation to the environment.

In the 20th century the theory of change exemplified by the second case (combination 21) has become dominant.

2.2. Some Hypothetical Examples of the Mechanisms of Change

Let us begin by looking at the general characteristics of the somatic and the germatic mechanisms of change. Some hypothetical examples of the growing developmental complexity of living creatures should clarify the link between these two mechanisms. As far as the sources of change are concerned, in single-cell organisms the somatic and the germ mechanisms of change are one.

Imagine a *two-cell* organism. Each cell is a microcosm, in the sense of being able to divide and produce a new organism. Specialization and exchange of resources improve the performance of both cells. In a two-cell organism, a change in one cell would probably call for appropriate changes in its partner cell. One way for all the needed changes to be implemented is through the transfer of ingredients that would cause change in the partner cell: this is the *aftereffect* method. The process of change can also be accommodated by the mechanism of *prevention*. It entails an iterative process with feedback: the second cell that has undergone change induced by the first cell sends certain cues to the genome of the first cell in order to qualify changes that are taking place in the first cell. In principle, this process might converge to a new well-defined organism.

When change occurs as an aftereffect, there is another way a new two-cell organism might be formed, provided the populatio*n* as a whole exhibits sufficient diversity. Two-cell organisms, or some subset of organisms, that are part of the population split up into single-cell organisms which then become autonomous (less specialized), with some of them adjusting to some changed cell when they merge to form a new organism.

In the case of a preventive mechanism, the function of change can be implemented via the genome of each pair of cells, meaning that change

takes place in the specialized sector of the genome without affecting the more stable sectors of the cell responsible for its daily operations. Following all the mutual adjustments between the changing genomes of the two cells, an organism might actually switch to some new mode of operation.

A transition from a two to a three-cell organism creates new opportunities for change without sacrificing the advantages of specialization. One cell could assume the reproductive functions, i.e., become the germ cell. The problem of origins of the germ cells has a long history. As Claude Villee mentioned[51] (p.12), the current view holds that reproductive cells are formed from non-specialized somatic cells. While one cell could become a germ cell, the other two cells that remain somatic support the germ cell. This scheme opens up new options. For instance, one alternative is for the two somatic cells to reproduce only, thus ensuring that the dead cells are replaced with new ones. Change would be limited to the germ cell. Another alternative is for changes to occur first in the somatic cells and eventually migrate to the germ cell, which will reproduce a changed organism. Another scenario represents a combination of the first and second alternatives, when change takes place in both the somatic and the germ cells.

The above considerations remain valid for multicellular organisms, except that the process of the creation of new organisms involves complex hierarchical structures.

One can also imagine a complex organism in which change is limited only to the somatic cells: the majority of somatic cells support the already existing structures, while some designated subset is involved in innovation. The changing somatic cells coordinate the changes and then gather in one place specially designated for the purpose of producing a new organism.

This kind of somatic mechanism of change might be cumbersome and time-consuming because of the many steps required to harmonize all the changes. The duration of this process hinges on the organism's life-span. The longer the process of innovation transfer among the somatic cells and the shorter the organism's life span, the more vulnerable is the mechanism of somatic change. Its drawbacks would be reduced if we were to relax the assumption that all changes must be completely harmonized with each other or if *partial* changes in the somatic cell were allowed to be transferred to the germ cells. The germ cells, having some special free space in their genome, would slowly accumulate information regarding somatic changes, and this information would somehow be fused with the programs already in the germ cell.

2.3. Analogy Between Machine and Organism Design

Before we proceed with our analysis of the advantages of the germ-cell based mechanism of change, especially for complex organisms, I would like to propose an analogy between methods of creation of new organisms and complex machines. The analogy follows the outlined framework regarding the methodology of design of new organisms.

Consider, for example, an engineer who wants to modernize an existing piece of machinery based on the "substrate" of the machine itself. Modernization would be limited to a particular aggregate, with some parts being replaced by new ones. If the to-be-modified aggregate requires no changes in the adjoining aggregate, the problem of modernization is solved. However, in the general case, changes in other blocks are required. The secondary changes to be introduced might not agree with the initially modified aggregate. An engineer will pursue this iterative process in order to attain maximum compatibility between the original aggregate and its co-workers. Eventually this process of integration of all the changes in the various parts of the machine might well improve its overall performance.

The example reveals some problems associated with major modernization based on keeping the fundamental blocks intact. The described method becomes unsuitable altogether in the construction of machines based upon new principles of design and operation; new machines require many new types of aggregate that must be integrated. Of course, new aggregates could be built, regarding this as a sequential multi-stage process, upon relatively universal principles of design modifying them as we go from one stage to another.

As engineering advanced, it became clear that the creation of new machines, as well as major modernization of the old ones, called for a hierarchical process of design based on one informational field, namely the blueprints. Blueprints are nothing but a substrate used to design new models fast and efficiently or to modify and then integrate the units with relative ease.

The key task of such a hierarchical process might be the design of a new aggregate - the heart of the new principle of operation. The general architecture of the machine could then be adjusted to the key unit. Under this approach, it is possible to use standard versatile aggregates that are amenable to modernization. One way to modernize a machine is to use/idle, as the circumstances dictate, certain capabilities of the versatile aggregate.

The hierarchical multi-stage process of design takes advantage of sequential as well as parallel techniques. As new aggregates are designed

and various parts modified, inconsistencies might surface. This would call for changes in the blueprints of individual aggregates as well as the overall machine architecture. It would not make sense to have the complete technology of manufacturing the machine from the very beginning. Rather, one ought to focus on the design of individual aggregates and their basic units as well as the technology to implement the next immediate stage. This information would not only provide clues about the ways to proceed at the given stage, but also design and technological guidance for subsequent stages, including ways to alter the information as the process unfolds and the actual results become available.

2.4. The Relationship Between the Somatic and the Germatic Mechanisms of Change

The above analogy reveals the advantages of the germ-cell based mechanism of change as compared with the somatic one. In the germ-based mechanism, change takes place at a *holistic* informational level where it is easier to carry out a hierarchical integration of programs governing the development of individual parts of an organism. Under the somatic procedure, the informational profile would change within the individual organs and information would then migrate and be coordinated with the associate organs, finally passing unto the germ cells.

Whatever the structure of the somatic mechanism of change, it is too cumbersome when it comes to restructuring the entire complex organism, and inadequate altogether for organisms based upon new principles of design. On the other hand, a mechanism of change implemented via the germ cells is concentrated in *one place*, so integration of these changes is faster and easier. Moreover, if, as in the previous example, the time required to harmonize the changes is longer than the organism's life span, the intermediate changes can be preserved in the genome and passed on. Apart from housing an established program of development, the genetic structure of a changing germ cell might allocate a special place for storing and creating new programs. This factor is important in understanding the role of heredity in passing on genetic changes. Information that is passed on is not limited to characteristics already expressed in the phenotype, but encompasses newly acquired genetic features as well. I would like to mention here that uncovering these new invisible genetic changes may prove beneficial for an early diagnosis of a pathology.

The somatic mechanism of change, however, should not be ignored when it comes to modifying specific parts of an organism rather than undertaking major restructuring. Here, the somatic mechanism of change may well complement the germatic one, with changes taking place in the organism itself without waiting for a new one to inherit and express the changes, as is the case with the germatic mechanism of change. Whether or not changes in the somatic cells pass on to the progeny, the somatic mechanism complements the germatic one.

Our discussion of the somatic and the germatic mechanisms of change suggests a positive correlation between the role of the germ mechanism and organisms' complexity. Perhaps the somatic mechanism is retained, but a) it complements the germatic mechanism when relatively minor and immediate changes are called for, b) it fulfills specific functions not covered by the germatic mechanism of change, c) it supports the germetic one in order to support such vital evolutionary process as change, and d) finally, it may simply be an anachronism.

If the somatic mechanism of change is an anachronism, it would be similar to an appendix. In herbivorous animals the appendix played an important function. In man its functions are unknown. As long as the appendix is calm, it is not harmful. But, once inflamed, it leads to a pathological condition fraught with death. Outside intervention is required and, if administered on time, pathology can be overcome.

CHAPTER 5

INTERNAL MECHANISMS OF CHANGE

1. BRIEF COMMENTS ON THE RELATIONSHIP BETWEEN INTERNAL AND EXTERNAL MECHANISMS OF CHANGE

1.1. Adaptation, Proadaptation, and Preadaptation

The current reigning doctrine in biology purports that all the different factors external to the genome, regardless of whether the affected changes are induced in somatic or germ cells, produce change in the genome *directly*.

Essentially, external mechanisms are thought to behave randomly via chemical substances, radiation, and similar factors, and semi-ordered operation of these mechanisms is manifest in gene recombination resulting from crossing (assuming, of course, there is some kind of order in selecting one's mate).

The importance of various external factors in driving biological change is beyond doubt. Most theories, other than Lamarckism, assume there is no connection between the actual mutations and the demands of the environment. An interesting theory of so called *adaptive mutations* elaborated in the 1980s tried to break away from this dogma. Its basic thesis is that cells possess mechanisms for selecting appropriate mutations, provided certain preconditions for selecting these mutations are met and no cell growth takes place.[52,53] This theory was vehemently opposed by most biologists. However, the proponents of the "adaptive mutations" theory continued to collect supporting evidence and discovered far-reaching disparities between the mechanism of random mutations and that of adaptive mutations.[54-5556] The adaptive mutations hypothesis is still inconclusive, but it warrants further investigation.[57-5859]

By generalizing the notion of adaptive mutations, we can distinguish among *adaptive*, *proadaptive*, and *preadaptive* processes.

Adaptive is used denote a process by which an organism prepares itself to respond to changes in the environment whatever these changes may be. This kind of adaptation is predicated on the flexibility of the organs, i.e., their ability to shift from one mode of operation to another, diversity of tools at the organism's disposal (such as different antibodies), etc.

Proadaptation represents a change-specific process by which an organism gets ready for changes in the environment. The currently used biological term, "adaptive mutations", corresponds (my terminology) to proadaptive mutations. The following passage was written by James Shapiro:

> "Neo-Darwinists teach that mutations arise independently of biological needs. Physical insults, chemical fluctuations, and replication errors lead to stochastic changes in DNA sequences. Random mutations mean that the evolutionary watchmaker is blind. To bolster their argument, neo-Darwinists cite an experiment by Luria and Delbruck in which bacterial mutations occur prior to selection for the mutant phenotype. However, this neo-Darwinist position has been challenged for over a decade by the discovery that certain mutations occur much more frequently when they are selected, and thus adaptively useful, than they do during normal growth. The principal difference between these so-called "adaptive mutations" and the phage resistance mutations studied by Luria and Delbruck is that selection for adaptive mutations is not lethal. Thus, nonmutant cells can survive to undergo DNA changes under selective conditions. Not surprisingly, the evolutionary significance of adaptive mutation is highly controversial, and there is great curiosity as to its mechanism..."[60]

Preadaptation commonly refers to "the existence of a prospective function prior to its realization."[61] (p. 86). According to this definition, preadaptation encompasses changes in an organism that were not previously utilized, but which can be utilized in a new environment as well as changes not directly associated with any shifts in the environment.[62] The latter class of changes actually represents the initial stage in a multi-

stage process which may eventually bridge these initial stages with changes in the environment. Many,[63,64] but not all, biologists recognize the preadaptive process as it is expounded above.[65]

While the proadaptive process is definitely induced by the environment, adaptive and preadaptive processes are more ambiguous. We cannot rule out that these processes are affected by external factors that are somehow correlated with changes in the genetic program. However, it is more likely that these processes are driven by an internal mechanism of change which supports a dynamic, rather than static, conception of the genome (see section 4 in this chapter).

1.2. The Tunnel Process and Preadaptation

An event in an organism that starts from the beginning and fails to serve any purpose in terms of the current conditions is deemed either an atavism, a feature important at some time in the past, or a deformity. However, the problem could be reformulated in the following way: structures without any immediate adaptive purpose are beginning to emerge; the need for them is totally obscure and, in fact, the development of some new structures may never lead directly to any one specific characteristic. The development of these structures may undergo numerous stages of transformation prior to the emergence of a structure which might give rise, relatively quickly, to pragmatically useful characteristics, that is, characteristics that reflect development from the end.

Change from the beginning - the creation of potential for development [1] – seems to have arisen with the emergence of (bio)chemical innovations; however, the origins of this process are clouded in mystery [2]. It seems that changes from the beginning derive not from the morphological creation of potential, but from changes in karyotype, i.e., the set of chromosomes typical of that species in terms of size, number, constituent elements, etc. As Ernst Mayr[66] mentioned, "closely related species often differ more conspicuously in their karyotype than in their morphology."(p. 310)

Over the course of subsequent development, changes in karyotype are expressed morphologically as a new characteristic whose initially obscure purpose emerges, ultimately linking up with the end.

One final comment regarding the tunnel process concerns the relationship between the mechanisms of change and heredity (even if the phenomena are limited to the germ cells). It is essential to take into account the amount of time required for genetic changes initiated at the beginning

to reach a stage where the structures generated by these changes can be bridged with the end, in effect, the demands imposed by the environment. Assuming that change from the beginning proceeds rapidly, i.e., these changes link up with the process of change from the end over the reproductive life of the organism in question, the problem of the tunnel process and heredity is resolved within the traditional scheme of change and heredity. However, the time required for beginning-induced changes to prove their worth might be so long that no organism can utilize these changes to its competitive advantage over its reproductive life. Therefore, changes from the beginning will also be passed on genetically, but their purpose in terms of adaptation might come to light only after many generations. This time lag explains the appearance of characteristics that do not seem to conform to the demands imposed by the environment. It is important to keep track of the changes in the genetic structure that manifest themselves only after several generations. Diagnostics based on this kind of hidden long-term changes could be called *very early* diagnostics.

Our discussion of the tunnel process and heredity raises one of the most formidable problems in biology, namely, the emergence of new species via a multi-stage process of change. The most perplexing issue in this field is the possibility that at some intermediate stage of this process a genetic state(s) may emerge that is actually useless or even detrimental to the organism in the context of a given environment. Of course, in the ideal case, any change within an organism aimed at (eventually) creating a new species is also conducive to its adaptation in a given environment. This mode of development, or the process of change, unfolds slowly, and paleontological evidence is expected to corroborate it.

The emergence of a new species, however, does not always follow this mode of evolution. An organism's intermediate states may divert considerable resources for its development to the detriment of the already tested structures, and may actually hinder the organism's hard-earned capacity to adapt to a given environment. This paradigm of development of new species, which parallels the creation of macroevolutionary diversity, raises major but rather poorly explored problems.[67] The most notable exceptions to the rule are the work of Ernst Mayr and the theory of *punctuated equilibria* elaborated by N. Elridge and Steven Gould.[68]

It is no accident that the problem of the emergence of a new species under a multi-stage process of development has been neglected by biologists. Indeed, if one rejects the notion of an internal mechanism of change and the possibility of a tunnel process, it becomes rather agonizing to explain the emergence of unnecessary or even harmful (in terms of a

given environment) changes in the genome that are expressed in the phenotype, with all the ensuing (possibly negative) consequences.

Acknowledging the possibility of an internal mechanism of change and the tunnel process opens up new approaches. Changes in the organism aimed at creating a new species may accumulate in some internal structures of the genome and materialize in the phenotype only when these changes are reconciled with the environment. Consequently, the lack of paleontological evidence for intermediate forms heralding the emergence of a new species may be due to the fact that the phenotypes expressing this kind of intermediate change never actually existed. These intermediate changes are also not found in the genes governing the development of a given organism.

Thus, the emergence of a new species via a multi-stage process could also be analyzed in terms of the tunnel process. The implied distinction between changes in the genome and changes in the phenotype extends to changes in the part of the genome connected to the internal mechanism of changes, i.e., the selfish genes.[3]

More detailed examples of the tunnel process may be found in the literature, with many examples that can be analyzed from the standpoint of tunnel process. An interested reader may benefit from learning about one fascinating methodological cue that is presented below.

1.3. Origami

Origami is defined in Webster's New World Dictionary as "a traditional Japanese art of folding paper to form flowers, animal figures, etc." The general discussion and the quotes concerning origami are based on a book by Isao Honda[69]. A theoretical analysis of certain aspects of origami is referred to my paper.[70]

I remember my mother's teaching me to construct origami, but I was never taught to invent new origami. The Japanese approach to origami is rooted in an entirely different vision. The child is taught certain basic operations for transforming the initial piece of paper. For traditional origami , these operations are fixed.

> "Almost all traditional origami constructions rely on the manipulation of certain regulated and fixed folding methods. Creative unregulated folding lines play a part only when the origami process is near completion."(p.27)

> "There are certain origami works that are the accidental result of the addition of a few auxiliary folds to a basic fold during an attempt to develop something else."(p.29)

These random events are still limited, since they are based on the geometric folds.

> "Though there are many other works which develop accidentally when the man folding was actually groping around for some other form, because all of these accidental creations rely on established origami folding lines, their construction is always geometrical." (p.29)

A student of origami first learns how to make certain objects from beginning to end. The next stage is to learn intermediate forms, which in and of themselves do not suggest any final object, but which possess vast potential for subsequent development. Having mastered these lessons, the pupil must then continue on his own. However, the choice of intermediate forms does depend on the final image:

> "...we must first decide what shape we want to make. After various folding attempts we arrive at a number of basic fundamental forms." (p.29)

This approach to constructing origami is not a carbon copy of the biological process of mutation, but perhaps there are some useful parallels: the established folding lines correspond to a fixed number of types of biochemical reactions. The construction of a geometric network of folding lines and intermediate forms representing the potentials for development which give rise to new origami is akin to the development in living creatures of a somewhat ordered network of cells which serves as a foundation for subsequent processes of cell specialization, choice of cell location in the organism, cell interaction, and the creation of intermediate forms which are rather remote from the final organism. One major distinction between origami and biological development is the lack of a preconceived image on the part of the latter, an image that is correlated with the choice of intermediate forms. Perhaps, when it comes to the creation of new living creatures on the basis of an ordered network of cells and intermediate forms, random processes (to some degree) in the internal hierarchy play a more significant role.

In summing up our discussion of external and internal mechanisms of change, we may safely assume that internal and external sources of change interact with each other; it is only natural that there would be some kind of a feedback among programs at different levels. For instance, assuming that the second-level program is linked with the first level one via a feedback mechanism, then an internal mechanism of change would be affected by environmental factors that, even if they have no direct bearing on the second level, do affect the first level program.

Another feature of the interplay between external and internal mechanisms of change is that it allows the process to be not completely ordered. In fact, random perturbations may be conducive to its overall progress. This is not unlike a combination of a completely ordered simplex method with the random Monte Carlo method used in linear programming to solve optimization problems.

In effect, the two sources of change - from the beginning and from the end - should not be opposed to each rather. The only case where this polarization is justified is when all change is end-induced, i.e., when new structures arise to serve some immediate purpose of growth or survival. Assuming that the mechanism of change incorporates different phases/structures of varying proximity to the immediate demands imposed by the environment, the two types of change would seem to compliment each other. The first phase aims at the creation of *predispositions* toward development. In other words, the intermediate states that are selected ought to have the potential to transform into beneficial structures, although there may be no immediate need for them in terms of survival in a given environment. Characteristics that are directly conducive to the survival of the organism/species in a given environment are formed at the second stage.[4] This approach to the relationship between external and internal mechanisms of change suggests an answer to the question posed in the previous chapter in connection with the non-random formation of intermediate genetic combinations over the course of development of an organism having a large number of constituent units (which makes an exhaustive search of all possible variations cumbersome and unmanageable).

I would like to quote an example given by Sydney Brenner regarding the development of worms. Brenner surmises two levels in the genome which control the growth of an organism.

> "The first layer is a noisy, inaccurate set of processes that generates a "sort-of-worm." And the second is a set of refinement processes that tames the unruliness of the first and

> yields a real and recognizable worm. There is in fact the potential for many types of worm locked up in the genome, but the one that comes out is determined by the refinement genes. Of course, in this process many changes will have 'unpredictable' consequences..."[71]

2. PHENOMENOLOGICAL REPRESENTATION OF THE INTERNAL MECHANISM OF CHANGE

In chapter 3, I pointed out two ways to represent a system via a law (analytically) or via a mechanism that coordinates the system's constituent elements, subject to certain constraints on the principles of their interaction.

Biologists conducting phenomenological research into organisms' internal mechanisms of change have been guided by the traditional search of natural scientists for *laws* with the organism itself, regarded as a black box. These laws pertain to such variables as the shifts in the ratio between different mutations, as well as the development of specific mutations or even resulting individual organs.

It has been verified at the phenomenological level that there is a pattern to the distribution of random mutations[72].

The laws allegedly governing the evolution of individual organs will be discussed below.

The reader should now to refer back to Table 3.2 (Chapter 3). *Law-based* theories of biological change, which Ernst Mayr would call *telenomic*, are not homogeneous. Some of them are intertwined in a strange manner with classical Darwinism, in the sense that they presume change from the end, using the tunnel process framework, meaning the demands imposed by the environment.

According to Ludwig Doderlein,[73] the initial development of a species follows the classical struggle for survival: a species asserts itself in the world by accumulating changes in the various organs; subsequently, these changes are passed on and reinforced/preserved through the process of selection. However, this mode of development changes once the species has displaced its competition. The changed organs which have ensured survival by utilizing the experience of previous generations continue to change by themselves as a result of inertia.[5] At first, such changes might be merely useless, but eventually they become detrimental and lead to the demise of the species. Doderleine illustrates his theory with such examples as the saber toothed tigers, mammoths, giant deer, and *Babirussa* boars

living on the island of Celebes. Once this species of boars was free of competition, their fangs continued to grow, in some cases penetrating the scull. Doderleine's theory can be summarized as follows: the evolution of a species follows a bell-shaped curve.

Leo Berg produced a variation on Doderleine's evolutionary theme.[74] Berg's concept introduces an explicit assumption that changes evolve from the beginning, meaning that changes unfold according to some internal laws that are independent of the environment. Moreover, these laws are not necessarily driven by inertia. Berg illustrated his concept with numerous examples from the plant and animal kingdoms.

One of the most interesting schemes belonging to this class of "law-based" theories of evolution is the concept of aristogenesis advanced by Henry Osborn.[75] It claims that certain aristogenes, whose function is rather obscure, appear in the germ cells. As aristogenes evolve, they generate very important organs. Osborn ascribed the emergence of aristogenes to environment-induced factors. Later, he claimed, that aristogenes develop on their own accord.

What fascinated me about Osborn's concept was the idea that, not only is change initiated at the beginning, but the purpose of the various structures formed at these early stages is not clear. Therefore, while the environment does exert some obscure pressure upon the formation of aristogenes , there is no direct program-like connection between the final demands of the environment and the initial changes. Also, once aristogenes are formed, they evolve on their own.

Using my terminology, aristogenes could be compared to potentials, which are capable of developing in different directions within some feasible space. In fact, as potentials evolve based on some internal principles of development, they reach a transition phase, at which point they might actually begin to assimilate signals from the environment.

3. STRUCTURAL REPRESENTATION OF THE INTERNAL MECHANISM OF CHANGE

3.1. Preliminary remarks

Most biologists reject the notion of an internal genetic mechanism of change. This controversy has a long history. It seems to me that the aversion on the part of the biological community toward research into the internal mechanisms of change is due to the fact that their own

investigations, fueled by the rapid technological advances in molecular biology, are focused on the study and search for genes responsible for the development, operation, and interaction of specific organs. In addition, they seek to uncover flaws in the mechanisms regulating these genes - flaws that give rise to certain pathologies such as cancer.

A number of biologists, however, have advocated a different approach to the genome as a dynamic system - a thesis which runs contrary to the prevailing view of a genome as a static system subject to random external fluctuations.

One of the leading scholars in this group is James Shapiro. He very early was aware of the importance of McClintock's work.[76] Shapiro constructed a theoretical as well as an experimental framework for the concept of the genetic system as an information-processing dynamic system rather than a mechano-chemical one. In his article[77], he even called genomes "smart systems."

> "Our thinking about genetic systems needs to become much more sophisticated before we will be in a position to comprehend the contents of massive DNA sequence data bases and use the information effectively. Instead of the basically mechano-chemical view of the genome inherited from neo-Darwinism and the early years of molecular biology, we need to think of genomes as information-processing systems."

In the same article, Shapiro also underscored the existence of non-traditional mechanisms responsible for restructuring the genome (beside the well-known ones such as damage repair).

> "Complementary studies have examined how genetic change comes about, either in germ line, through the action of transposable elements or recombination and mutator functions, or in somatic tissues during developmental DNA rearrangements. The results show quite clearly that many (perhaps the vast majority) of DNA alterations are not due to chance chemical events or replication errors. Rather, they result from the action of highly sophisticated biochemical systems which may be thought of as genome reprogramming functions."[6]

My working assumption also recognizes the existence of an internal mechanism of change.

The key to my approach to biological change is recognizing the importance of the internal mechanisms of change which I assume are based on the existence of a program within the genetic structure which affects programs of development regardless of whether the affected changes are occuring, in somatic or germ cells, and whether their are induced endogenously or exogeneously.

Current research in developmental biology is slowly becoming receptive to the idea of genetic programs that alter lower level genetic program.[78] This line of research is also being pursued by biologists at the molecular level. For instance, whereas previously research was focused on the genes responsible for the formation and interaction of the various organs - first-level program - in more recent years, the emphasis has shifted toward the second-level program which involves transposons, etc. All this basically conforms to the concept of a dynamic genome introduced by Barbara McClintock[79]

Molecular research into the higher order genetic programs that affect the code does not repudiate classical biology, with its emphasis upon the phenomenological course of development of different species. The two branches complement each other, but fusing them into a unified vision still must be accomplished.[80]

According to the tunnel process, internal mechanisms of change can proceed from the end as well as from the beginning. In the first case, the program-changing program in the genome is triggered by external factors; and, in the latter case, the program-changing program is governed by its own internal principles.

Having programs at just two levels, i.e., organism-structuring program and program-structuring program, suggests the autonomous workings of the internal mechanism of change. The second-level program can modify the first level program and if the genome possesses a third level program. There is even more room for change due to internal causes because the first level program is potentially affected by the third and the second level programs.

We can safely assume that internal and external sources of change interact with each other: it is only natural that there should be some kind of a *feedback* among programs at different levels. For instance, assuming that the second-level program is linked with the first level one via a feedback mechanism, an internal mechanism of change would be affected by environmental factors that, even if they have no direct bearing on the second level, do affect the first level program.

Although these assertions regarding an internal mechanism of change are hypothetical and unconfirmed, there is evidence that attests to the existence of the necessary preconditions, including:

1) pronounced predominance in the genome of selfish genes (also called *junk* or *trash* DNA) whose function is unknown (so called C-value paradox) and which probably partake of the internal mechanism of change;

2) certain regularity exhibited by the selfish genes;

3) the presence of transposons that partake directly in the process of change;

4) the presence in the genome of a powerful mechanism of ordered search through numerous possible combinations.

3.2. The C Value Paradox

What is the so called C-value paradox? Essentially, it states that the amount of DNA in the genome is much greater than the amount needed to code for the various proteins which form an organism.

> "The **C value paradox** takes it name from our inability to account for the content of the genome in terms of known functions. It expresses the existence of two puzzling features:
>
> There may be large variations in C values [the total amount of DNA in the (haploid) genom of each living species] between certain species whose apparent complexity does not vary much. In amphibians, the smallest genoms are just below 10^9 bp, while the largest are almost 10^{11}bp. It is hard to believe that this could reflect a 100-fold variation in the number of genes needed to specify different amphibians.
>
> To reinforce this skepticism, some closely related species show surprising variations in total genome size. For example, two amphibian species whose overall morphologies are very similar may have a difference of, say, 10 in their relative amounts of DNA. It seems unlikely that there could be a tenfold difference in their gene number. Yet if the gene number is roughly similar, most of the DNA in the species with the larger genome cannot be concerned with coding for protein: what can be its function?
>
> There is an apparent excess of DNA compared with the amount that could be expected to code for proteins. Indeed,

> this is often referred to as the problem of excess eukaryotic DNA. We now know that some of the excess is accounted for because genes are much larger than the sequences needed to code for proteins (principally because of the intervening sequences that may break up a coding region into different segments). We do not know yet whether this form of organization is sufficient to resolve the problem."[81] (p. 67)

Research into selfish genes seems to confirm that some of these genes are involved in genome repair or regulation,[82] but the nature of this class of genes remains a mystery.

One possible scenario underlying the C value paradox is that selfish genes are employed in the internal transformation process that generate new organisms.[7] One indirect confirmation of this hypothesis is the varying size of the genome of different organisms. It is interesting to note that the largest genome belongs to plants and amphibians (up to 10^{11}), rather than complex mammals whose genome is of the order of 10^{9}. In fact,

> "Mammals have genomes that fall into a particularly small range of DNA contents, with a C value usually of 2-3 picograms ($2\text{-}3 \times 10^{9}$ base pairs). Amphibia, by contrast, vary very much more widely, from less than 1 picogram to almost 100 picograms. Even closely related amphibia may have greatly different content of DNA in the haploid genome."[83] (p. 88)

This gap in the C value bears an intriguing correlation with completely independent statements by biologists regarding the origins of the species.

> "New species do not evolve from the most advanced and specialized forms already living, but from relatively simple, unspecialized forms. Thus mammals did not evolve from the large, specialized dinosaurus but from a group of rather small and unspecialized reptiles."[84] (p. 751)

It is quite plausible that this correlation reflects some kind of a causal connection. It would seem that the greater the C value (other conditions being equal), the more room there is for radical changes in an organism, including changes that lead to the birth of new species. However, "room for change" is not a sufficient condition. It is necessary to have sufficient variety of building blocks and biochemical processes to ensure subsequent

dynamics within this space. A very simple organism, even one whose C value is high, has relatively little opportunity to develop. It is deficient in the number of ready blocks-organs and lacks sufficient variety of biochemical processes, particularly their combinations, that all contribute to the process of creation. On the other hand, an organism that is overly complex is not too amenable to change, because change is limited by all the different combinations of the already existing block-organs. It follows that these intermediate (complexity wise) organisms, such as amphibians, have the greatest opportunity to change.[8]

The C value paradox is unlikely to be resolved within biology's traditional frame of reference. Most mainstream biologists refer to excess genes as junk, trash, etc. - terms that reflect the negative attitude of biologists toward the role of these components in the process of evolution.

Richard Dawkins was one of the first scientists to attempt to link the function of these excessive genes with their evolutionary significance.[85]

He put forth a definite concept of selfish genes in which the unit of evolutionary selection was not an organism but a gene, i.e., selection bears directly upon the genes, and their struggle for survival is essential in and of itself. The question then arises regarding the link between the autonomous behavior of the genes and the development of the organism's phenotype, or at least the host cell in which these genes reside.

According to one rather extreme point of view

> "When a given DNA, or class of DNAs, of unproved phenotypic function can be shown to have evolved a strategy (such as transposition) which ensures its genomic survival, then no other explanation for its existence is necessary. The search for other explanations may prove, if not intellectually sterile, ultimately futile."[86] (pp. 601-603).

Less radical opinion purports to reconcile the autonomous evolutionary development of the genome with some beneficial function fulfilled by these excessive genes (by analogy, even moderately harmful parasites can form a symbiosis with the host organism). This autonomous development of the genome might become detrimental if it exceeds a certain threshold by diverting too many nutrients and energies into sustaining the genome itself. Excessive uncontrolled expansion of the genome is sometimes compared with *genome cancer*.[87]

Even biologists who endeavored to look for the functions of these unknown genes have managed to come up with what are, at best, only partial hints inspired by the prevailing dogma.

In 1992, for example, a group of European scientists made outstanding discoveries in decoding the structure of the DNA. They were able to complete a project aimed at uncovering the sequence of a complete eukaryote chromosome: the 315,357 base pairs of chromosome III of the yeast Saccharomyces cervisiae. Along the way, they uncovered an entire class of genes which comprised more than half the chromosom and whose function is completely obscure. In generalizing the results, the author of the project report wrote: "Searching for the function of the new genes is going to be a time consuming business-far tougher than the original sequencing."[88]

Project coordinator, Piotr Slonimsky, who was responsible for the functional analysis of the data, lists a number of specific factors which might trigger the functions of these functionally mysterious genes – for instance, morphology, temperature sensitivity, etc. However, there is no allusion to the idea that these genes might partake of the internal mechanism of evolution.

4. STRUCTURAL REPRESENTATION OF THE INTERNAL MECHANISM OF CHANGE (CONTINUATION)

4.1. Patterns exhibited by selfish DNA

It has been established that the genome is comprised of predominantly selfish DNA whose role is unclear. Assuming that these sequences embody the internal mechanism of change, they must be organized.

The last few years have witnessed the emergence of strong evidence attesting to the orderly nature of this class of genes. A group of Boston scientists have uncovered a linguistic pattern in the selfish genes.[89] Using sophisticated techniques borrowed from linguistics, ranking the words in order of frequency, text redundancy, these scholars "have shown fairly clearly that the 'junk' has all the features of a language". Interestingly, the same tests applied to familiar coding segments with known functions determined that these parts lacked linguistic features. My interpretation of this discovery is the following: since coding segments represent a set of instructions, like all instructions, they make insipid the creative features (as outlined above) of a living language that are generally directed at serving creative purposes.

The Boston group in its article concludes that whatever the function of these selfish genes is, the discovered regularity signifies that these genes do send meaningful messages:

> "We extend the Zipf approach to analyzing linguistic texts to the statistical study of DNA base pair sequences and find that the noncoding regions are more similar to natural languages than the coding regions. We also adapt the Shannon approach to quantifying the "redundancy" of a linguistic text in terms of a measurable entropy function, and demonstrate that noncoding regions in eukaryotes display a smaller entropy and larger redundancy than coding regions, supporting the possibility that noncoding regions of DNA may carry biological information."[90]

In fact, new data suggests that the messages produced by selfish genes pertain to the process of change which does not exclude other regulatory or repair functions of these genes.

4.2. Transposons

I believe that the starting point for any discussion concerning the role of the selfish genes should be Barbara McClintock's research into transposons.[91] McClintock's research in corn mutations demonstrated the presence of an internal mechanism of change which allows transposable genes - transposons (first called *jumping genes*, and then *mobile genes*) and multi-factor biochemical systems to reconstruct DNA molecules.[92] Reconstruction takes place at the chromosome level, meaning that the jumping genes had transposed from one chromosome to another. This transposition was "fixed" along the chromosome, thus passing on to the next generation. McClintock began to explore the jumping genes phenomenon as early as 1944, and that time she was the sole advocate of this idea.[93] Public accounts of her jumping-genes concept date to the early 1950s and in the early 1960s the existence of these genetic components was rigorously documented. More advanced work focusing on the molecular structure of these elements began in the mid-1970s.[94]

From its very inception, McClintock's concept of jumping genes was rejected by most biologists who opposed the very idea of an internal mechanism of change. In spite of the fact that by the time her ideas became public McClintock was a well-known and respected geneticist (in 1939 she

was elected Vice President of the Genetics Society of America, in 1944 she became a member of the National Academy of Sciences, and in 1945 the President of the Genetics Society), her reputation among her colleagues was that of a "crazy old woman." There were many reasons why McClintock's revolutionary ideas ran against the grain of conventional biological theory: First and foremost was the discovery of DNA in the 1940-50s as the vehicle of genetic information, the double helix structure of the DNA, the launching of the central dogma of molecular biology (purporting a rigid sequence: DNA-RNA-proteins, precluding any feedback), shift in the target of experimental molecular biology from multicellular organisms (McClintock's corn experiments) to a single cell, as well as many other reasons. However, following the initial excitement over all these great discoveries, there was a renewed interest in exploring McClintock's ideas, now at the molecular level. This renewed fascination was sufficient for McClintock to be awarded the Nobel prize in 1983 for "Discovery of mobile genes in the chromosomes of a plant that change the future generations of plants they produce."

However, this was not a happy end to an otherwise rocky road, but only an *intermediate event*. While recognized by some biologists, including James Shapiro, McClintock's ideas did not receive universal acceptance in the biological community. Even today, many biologists have a poor understanding of her achievements. In 1983 Evelyn Fox Keller wrote in her book devoted to the life and work of Barbara McClintock: "Barbara McClintock remains in crucial respect an outsider."[95](p.xii). Little has changed since then as far as the attitude espoused by the leading biologists toward McClintock. For instance, in 1990 a conference was held devoted to new trends in evolutionary theory. It brought together many leading American evolutionists. The name of Barbara McClintock was missing. It was not to be found in the Index of names listed in the conference proceedings.[96] The sole exception was a paper devoted to the behavior of jumping genes in *Drosophila*.[97] The paper mentions in the introduction that the development of the concept of the dynamic genome based on mobile elements (as opposed to the prevailing static concept) ranks among the most important recent discoveries in genetics. The authors pay tribute to the work Mobile Genetic Elements, edited by J. Shapiro. There is a single sentence to the effect that about 40 years earlier Barbara McClintock discovered transposable elements and that this discovery was met with great skepticism, and it was only in the last two decades that these elements were found in abundance in living organisms. No reference was made to any of McClintock's work.

While most evolutionists are somewhat condescending to ward McClintock's ideas, a number of molecular biologists are beginning to recognize her achievements.

In his obituary statement James Shapiro wrote the following words about McClintock: "One day, she may well be seen as the key figure in the 20th century biology."[98]

His praise is based not only on McClintock's discovery of mobil elements, but also on her global vision of the biological mechanisms of change, vision which might prove influential in the 21 century.

> "...standard theories are still framed in terms of independent genetic units, whereas McClintock thought of the genome as a complex unified system exquisitely integrated into the cell and the organism.
> ...There is good reason to believe that McClintock's integral view of the genome will prove to be prophetic."

At the same time, a number of biologists continue the work on transposons conducted by Barbara McClintock, endorsing the idea that the selfish genes are the source for transposons and, in general, a vehicle of an internal mechanism of change.

John McDonald organized a conference on "Transposable Elements and Evolution" held on June 27 and 28, 1992, at the University of Georgia in Athens.

Molecular biologist Rene Herrera of Florida International University in Miami spoke at the conference:

> "The concept of useless DNA is now obsolete“, [adding *A.K.*] that the selfish DNA theory, which holds that the only function of the elements is to reproduce themselves and spread throughout the genome, might have been acceptable a few years ago when little was known about transposable elements, but is no longer."[99]

Claims were made at this conference, corroborated by preliminary experimental data, to the effect that transposable genes can explain changes not only within a single organism, but also the origins of new species. Moreover, these genes are able to function outside a given organism, moving from one species to another.

The work of Richard M. von Sternberg *et al.*[100] elaborated upon some very interesting results regarding the inner mechanism of change in

connection with transposable genes and their interaction with Interspersed Repetitive Elements.

I am enthusiatic about all of the discoveries linked with internal evolutionary mechanisms of change. At the same time, I feel the greatest limitation of research in this area is the small number of specific types of internal mechanisms which have been shown to cause change. Only one such mechanism, namely mobile genes, has been studied in depth. The champions of this mechanism try to use it to explain as broad a spectrum of changes in the organism as possible (as seemed to be the case at the aforementioned Meeting on "Transposable Elements and Evolution").

5. STRUCTURAL REPRESENTATION OF THE INTERNAL MECHANISM OF CHANGE: COMPUTER BASED ON DNA-MOLECULE

Assuming that selfish genes incorporated into DNA and the transposons partake of the internal mechanism of change, then one precondition for this mechanism to perform successfully is that the structure of the DNA molecule must incorporate an elaborate mechanism of searching through and selecting from the myriad of possible combinations of constituent elements. In other words, an internal mechanism of change signifies that the genome is not merely a set of instructions for coding RNA and respective proteins; the mechanism must also perform recombinations on the elements comprising the genome. In fact, it could be stipulated that, in the event the initial structure of the DNA is somehow ordered, the mechanism also generates ordered combinations.

The computer, recently invented by an outstanding American scientist Leonard Adleman, based on the DNA molecule confirms unequivocally the presence of a genetic mechanism of selection[101]. Adleman proved experimentally that the computer he created has the capacity to solve the so called *seven cities* problem. (In effect, there are seven cities interlinked via one-way or two-way routes. Determine whether it is possible to travel from any one city to any other city without traversing the same path.) This important problem, known as the directed Hamilton path problem, embraces many different problems including the search for optimal solutions, some logical problems (Boolean logic satisfaction), and basically all search problems where the number of combinations grows exponentially with the number of variables.[102]

Adleman's computer could be classified as an analog device, since the computations are performed using natural processes, in this case,

biochemical ones rather than some artificial informational program. (In principle, the criteria distinguishing between digital and analog devices are whether the operations are discreet or continuous). The data are entered by using techniques of genetic engineering to form the required sequence of basis amino acids. The solution is also represented by the resulting configuration of the DNA molecule.

In comparison with conventional computers, the performance of the DNA computer is astounding; its advantage in speed is abillion-fold, while its energy and space requirements trillions of times less. While each individual operation performed by the DNA machine takes considerably more time than its conventional counterpart, the fantastic speed is achieved via an incredibly high degree of parallelism. Adleman's computer is not universally superior for all applications. It suffers from numerous drawbacks, and only more research will determine its scope of application.[103]

The important point in terms of our discussion is that Adleman's computer is an experimental verification of the genome's incredible propensity for ordered processing of information. Its implications for biology are best summarized by David Gifford:

> "For biologists, the results indicate that simple biological systems have the ability to compute in unexpected ways. Such new computational models for biological systems could have implications for the mechanisms that underlie such important biological systems as evolution and immune system".[104]

A number of biologists choosing not to ignore "Adleman's computer" have essentially acknowledged that the genome does incorporate a performance mechanism, implying that it is more than just a set of DNA coding instructions. Still clinging to the prevailing notion of the random nature of mutations, however they insist that the genome operates in a random mode.

Let me quote Kevin Kelly known for his work on the applications of new biology to machines, social systems, and economics.

> "When we understand that computation is a very broad term that includes a range of calculations as different as the way a test tube of DNA finds a sequence of letters or the way an adding machine tallies a sum, then we can see something else: the DNA in our cells also computes. Over thousands of generations, the DNA in human cells can produce a new body-and-mind form that will be better adapted to our

> environment. It does this by trying a billion different versions all at once. You are one possible answer. So am I. This may not be the smartest way to modify a design, but then again, we know it works."[105]

In summary, a definitive internal mechanism of change has not been established but numerous discoveries in biology have laid a firm foundation for the possibility of its existence. Positive evidence includes: the predominance in the genome of order-exhibiting surplus genes with unknown functions (so called C value paradox); a linguistic pattern in the selfish genes; the presence of transposons among the selfish genes; and, finally, a powerful mechanism of search incorporated into the genome.

One other benefit of hypothesizing an internal mechanism of change is to become open to *assimilate* new discoveries in molecular biology pertaining to selfish genes. All too often, proponents of the traditional approach, especially evolutionary biologists, tend to deny or simply ignore these discoveries, while the less militant ones mold new data to fit it into the orthodox framework.

NOTES TO CHAPTER 5

[1]. The term *evolutionary potentials* does appear in the literature. In a sense it is synonymous with the generic term *potential for development*: "one has to admit that the immense comprehensiveness of the hierarchy of life proves that the first organisms that occurred on the globe must have been provided with great developmental possibilities. An adequate term for these possibilities is evidently "evolutionary potentials"."[106]

[2]. "Chemical inventions on the cellular level are the prerequisite of some the most important adaptive shifts. Alas, our knowledge of comparative biochemistry is still far too rudimentary to tell us whether or not it was a biochemical invention that gave the mollusks, crustaceans, and other now dominant groups of marine invertebrates their ascendancy over eurypterids, trilobites, graptolites, and brachiopods, once the rulers of the seas."[107] p. 62.

[3]. Similar ideas (unrelated to the tunnel process scheme) regarding the emergence of new species were expounded by S. Gould and E. Vrba: "Perhaps repeated copies (of DNA, *A.K.*) can originate for no adaptive reason that concerns the traditional Darwinian level of phenotypic advantage.... Some DNA elements are transposable, if they can duplicate and move, what is to stop their accumulation as long as they remain invisible the phenotype (if they become so numerous that they begin to exert an energetic constraint then natural selection will eliminate them)? Such "selfish DNA" may be playing its own evolutionary game at a genic level, but it represents a true nonadaptation at the level of the phenotype. Thus, repeated DNA may often arise as a nonadaptation. Such a statement in no way argues against its vital

importance for evolutionary futures [that is, for subsequent phenotypical adaptation of repeated DNA]. When used to great advantage in that future, these repeated copies are exaptations."[108]

Note. "Exaptation is Gould's neologism, one introduced to distinguish structures whose current functional role is not part of the explanation of their origin from those whose roles are."[109] (p. 244)

[4]. By analogy, this pair of biological structures might be compared to the left and the right hemispheres of the brain. The latter forms a artistic image which creates predisposition to a solution; the left side is responsible for rigid logical manipulations.

[5]. A particular case of Doderleine's general theory is the concept elaborated by Othenoi Abel.[110] The only recognized source of changes in living creatures is inertia. This constitutes the so called "Abel's Law", deduced from the assumption that the organic world is based on the laws of physics, which includes mechanics and the law of inertia.

[6]. J. Shapiro in his note reiterated his approach to the internal mechanism of change. "Molecular genetics has revolutionized our understanding of cellular mutational mechanisms. The new information alters some of our underlying assumptions. On the one hand, we now know that elaborate repair regimes take care of accidental genomic damage (for example, radiation and chemical insults, replication errors). Thus, these random events diminish as potential sources of evolutionary variation. On the other hand, it is now clear that cells contain multiple, sophisticated, natural genetic engineering systems (nucleases, ligases, topoisomerases, recombinases, transposons, retrotransposons, plasmids, viruses), and we increasingly appreciate these cellular biochemical activities as important mutagenic agents. The versatile operations of these systems include insertion, deletion, inversion, fusion, amplification, dispersed and tandem reiteration, and other DNA rearrangements.

... I find it more reasonable to think of mutational events (which may involve many precise biochemical reactions) as resulting from the concerted action of dedicated cellular machines than as accidents or "pathologies." My argument is that these "high-tech" natural genetic engineering systems serve an adaptive function by generating the hereditary variability needed for short and long-term survival. They provide the biochemical activities that account for evolutionary patterns of genome organization unanticipated by conventional theory shuffling of sequences encoding protein domains, assembly of regulatory regions containing multiple transcription factor binding sites, duplication and dispersal of sequences among gene families, and amplification of repetitive DNA elements."[111]

[7]. In a developed society the proportion of people involved in R&D sector increases dramatically. Just compare a primitive society in which all members are involved in routine tasks with a modern society where new ideas and their implementation draw upon people in numerous research organizations.

[8]. This approach to development bears an affinity to origami. When its structure is extremely simple, initially, a flat piece of paper, there is plenty of potential room for development. However, it is impossible to produce complex origami at the initial stages of the process because of a lack of intermediate structures as well as allowable operations upon these structures; for instance, one cannot use twisting out

until certain intermediate structures amenable to this operation are created. Once a complex origami is created, change is limited by the large number of rather rigidly interconnected constituent parts. It turns out, that the greatest room for creativity is at the intermediate stages. Here, we have a sufficient variety of units which allows many different transformations to be performed upon them.

CHAPTER 6

SPECIAL FEATURES OF THE SOMATIC MECHANISM OF CHANGE

This chapter presents a broader picture of the somatic mechanism of change outlined in previous chapters. In going through this chapter, the reader should keep the following things in perspective: 1) The great majority of biologists today reject outright the notion of the somatic mechanism of change. As a result, literature that might examine the subject in any sort of systematic fashion is lacking. Therefore, our subsequent discussion, although corroborated by some empirical evidence, is primarily the fruit of my own deliberations; 2) Almost every stage of the hypothesized process of somatic change is inconclusive, since it is postulated on comparing and contrasting it to the development of cancer; 3) My aim was to outline a general approach to the mechanism of biological change, therefore, the discussion of each stage of somatic change is brief; and 4) I am not claiming that the changes induced by the somatic mechanism of change are transferred to the germ cells; for my purposes, the mere existence of the somatic mechanism of change is sufficient. If it is determined that somatic cells exert influence over germ cells, that would make the pathological expression of somatic change ever more complex, if only because these changes are passed on to future generations. With all these qualifications, my discussion of the somatic mechanism, is rather sketchy.

I shall begin by outlining the stages of the somatic mechanism of change and then proceed to discuss each stage individually.

1. THE STAGES OF THE PROCESS OF SOMATIC CHANGE

One general characteristic of the mechanism of somatic change is that it represents a multi-stage process. It incorporates a wide array of tools responsible for changing the genetic program that forms an organism as well as for regulating the pace and depth of these changes. This change is

carried out primarily by means of horizontal mechanisms, i.e., via interactive behavior of changing cells.

The process of somatic change may consist of the following stages:

1. When considered from different perspectives the sources of change may be quite diverse:

The temporal aspect, meaning at which stage of the organism's development (starting with the embryonic stage) do changes take place;

The hierarchical aspect - changes that take place in the organism range from changes in individual genes to changes in the organism as a whole;

The genesis of the sources of change which range from external factors such as chemicals, radiation, and viruses, to self-induced internal processes.

2. The more critical the change, i.e., the more sectors of the genetic code that are affected, the less differentiated the cell must be in order to free itself of the forces hindering its diverse genetic capacities. It is quite plausible that a cell undergoing a major change would initially act as if it were degenerating (negative differentiation) or that less mature, and thus less differentiated cells, would be involved in the process of change. These features are characteristic of the *stem cells* that have the capacity to develop into different specialized cells (within certain limits). For instance, in the blood producing system of mammals, stem cells can develop into erythrocytes, trombocytes or leukocytes. The versatility of the stem cells varies from unipotent cells, which can develop into only one type of differentiated cells, to oligopotent cells that can evolve into a few types of differentiated cells, and to pluripotent cells, that are capable of developing into many different types of differentiated cells. Moreover, stem cells can grow unchecked, opting to remain stem cells or become irreversibly differentiated.[112,113]

3. A less differentiated cell behaves according to changes in its genetic structure: within the existing genome by activating the suppressed genes/suppressing active genes, or by incorporating new components in the genome (this takes place when a virus enters the genome), or through cell fusion (mentioned in connection with Paramecium reproduction).

4. Less differentiation is also related to the need on the part of an innovator cell to be independent economically from the governing mechanism. Economic autonomy allows the innovator cells to acquire nutrients by bypassing the controls imposed by the established mechanism of resource allocation. To achieve this end, the innovator cell must simplify

its metabolism. It can be done by, switching from oxygen metabolism, characteristic of highly developed cells, to primarily anaerobic, or by reducing the number of receptors linking it with other cells, etc. Under certain conditions, the reverse tactic is exercised, i.e., when an innovator cell augments its link with the organism (still preserving its high degree of differentiation and a complex system of oxygen metabolism) by increasing the number of receptors, by greater mutability (assuming some mutations are more readily adopted by the organism than the existing ones), etc. Augmented ties may make it easier for the cell (taking into account its population size) to acquire the additional nutrients it needs for rapid development.

5. Changes in the cells vary in scale, i.e., the scope of changes is very wide. A rough classification gives us three arbitrary categories: minor, intermediate, and major changes.

By definition, a cell which has undergone minor change is able to *localize* its development to a given organ. This typically occurs when adaptation to changes in the environment calls for temporary, not inherited, changes in cell operation. (See in Chapter 3 the role of the viruses in an organism's adaptation to changing conditions.)

Intermediate changes mean that the cell must be capable of *interacting* with other cells thus paving the way for the creation of a new organ or changes in the existing organs.

A cell with major innovative tendencies must be capable of coordinating the proposed changes with cells in other organs. Eventually all of the information must find its way into the germ cells thus passing on to the progeny.

6. At the early stages of cell development (M1 and M2), changes in the cell are linked to different mechanisms, particularly to telomeres, since telomeres also act to preserve chromosome structure (more about telomeres in section 2 of this Chapter).

7. Each DNA type possesses its own damage-repair mechanism that solves very elegantly problems which, at first glance, seem insurmountable; in a sense, this mechanism acts to prevent sporadic break-downs.[1] Presumably, changes of an innovative nature need not trigger the repair mechanism which either fails to react to innovations or possesses genes that block its actions. The existence of such a selective mechanism of repair is indirectly confirmed by different segments of the gene having a different propensity for repair.[114]

One theory claims that the death of a cell is also preprogrammed, meaning that cell interaction activates some internal mechanism that leads to a kind of suicide (*apoptosis*).[115] A recent scientific discovery found two

genes in Drosophile (ced-3, ced-4) whose joint action results in the death of a normal cell.

It is well known that apoptosis normally surfaces during the course of embryonic development. Perhaps apoptosis takes place when the incurred damage cannot be repaired. In other words, the process of apoptosis may weed out poorly mutated cells, including those that may pose a threat to the organism.[2]

8. Following its renewed specialization, the cell must resume its reproductive cycle. Telomere recovery is crucial, since a cell that has exhausted its telomeres may not be able to reproduce.

9. The changed cell must reproduce faster in order to have time to influence the development of its host organ or other organs and, in the case of germ cell reproduction, possibly even the germ cells.

10. The mechanism of accelerated cell growth suggests the presence of its counterpart - a mechanism that impedes cell growth. This widespread duality is due to the fact that, to get the process of accelerated growth started, more effort (greater pace) is required than is necessary for the process to continue at its regular pace. Brakes are used to slow the process to its normal pace.[3]

The discovery of gene *p.16* by D.Beach confirms that normal cells possess such a suppressor gene – a gene that halts cell multiplication and causes the cell to revert to a calm state.[116]

11. As changed cells develop, they may form new structures that are precursors of new organs; of course, the degree of novelty will vary. These new formations may require an infrastructure, including the blood supply system, to ensure the necessary supply of nutrients to its cells. Organisms possess an intricate mechanism to ensure the creation of such an infrastructure in the tissue. This mechanism incorporates growth factors (fibroblast growth factor and VEGF) as well as inhibitors (trombospondin and platelets). Heparin, in turn, controls both the growth factors of the new blood supply system and the inhibitors.[117]

12. One way for a cell to convey information to other cells is to excrete respective genetic information; the other mode is for the entire cell to penetrate other organs.

In order for a cell to travel from one organ to another, there must be a mechanism of cessation from the living tissue of the host organ. Such a mechanism is part of the genetic code, i.e., the code contains genes governing cell separation from the tissue.[118]

13. One might assume a certain regularity or pattern in cell migration. Perhaps the changed cells spread throughout the organism, but they take root primarily in those organs that are somehow related. Perhaps

they consume/supply nutrients to the target organs or are morphologically related to them. Finally, they may be linked to organs that are formed sequentially as the genetic program unfolds.

Another plausible scenario is that the process of coordination in the hereditary somatic mechanism is of iterative nature, meaning that the changed cells from a given organ that have traveled to other organs come back to the original organ more informed.

14. Political independence of an innovator cell means that the immune system should not put excessive pressure on it. One can also assume that an immune system operating under the conditions of equilibrium would be too rigid, suppressing or preventing dissident cells from taking root. It is quite plausible that the immune system itself possesses a mechanism that weakens it somewhat (but only somewhat) in order to allow new entities to develop. This mechanism is probably turned on as the process of change unfolds.

2. SOME COMMENTS ON CELL DIVISION AND THE PROCESS OF CHANGE

2.1. Telomeres.[119, 120]

The role of telomeres was first uncovered by Hermann Müller. He showed that a *Drosophila* chromosome without an end is unable to recover.[121] Barbara McClintock, in her work with unstable corn chromosomes, hypothesized the existence of normal structures that ensure chromosome unity.[122] It was discovered that telomeres fulfill this function. This fact was widely acknowledged in the late 1970s, early 1980s.[123] It was also shown that the chromosome segments closest to the telomeres are especially prone to change. This is evident in chromosome mixing which can be observed, for instance, in the formation of sperm cells.

Telomeres are structures situated at both ends of each chromosome. Besides their role in preserving chromosomal structure, other important features of telomeres were discovered. In the early 1970s , A. Olovnikov advanced a hypothesis that telomeres are crucial in cell division - they send division-controlling signals to the cell. With each division, a part of the telomeres breaks away and the cell ages, a process known as cellular senescence. Eventually, the chromosome runs out of telomeres, the cell can no longer divide, and it dies.[124]

This discovery seemed to open the door to understanding the process of aging and death. However, the situation turned out to be more complex. First, it was discovered that the results attained concerning telomere behavior did not apply to cancer or to sperm cells, the latter two are kind of immortal because telomeres are constantly replenished.[125] At the more advanced stages of the developmental-tumor, this waning of telomeres may terminate and they may even begin to recover. Telomere restoration is due to the activation of a cell factor or enzyme called telomerase. It contains the RNA structure which codes for respective new links of telomeres. In a normal adult cell telomerase is inactive.[126]

All of these characteristics of telomere behavior are not exclusively responsible, either directly (terminating cell division) or indirectly (the growth of telomeres in cancer cells), for an organism's death. As previously noted, biologists have recently uncovered two genes (ced-3, ced-4) in a drosophile cell whose joint action can result in a cell's death.[127] There might be a fascinating link between these genes and telomeres and telomerase!

However, my hypothesis regarding the internal somatic mechanism of change would lead one to think that telomerase activation observed in cancer and sperm cells pertains to all cells undergoing change. It is no surprise that cancer and sperm cells exhibit increased telomerase activity; these cells are most amenable to change. Cancer cell changes, almost by definition, and the changeability of the sperm, as I hope to show in the next chapter, is related to their role in the biological mechanisms aimed at development (rather than just survival or growth).

The aforementioned function of male and female gametes in the process of change and the difference in their respective volume of production are also related to the way these cells are formed (process). At the embryonic stages of development, ova are formed through mitosis of immature cells called oögonia. After a short while (in human beings by the third month), they turn into oöcytes which are the result of the meiosis process. At birth the ovaries house up to 400,000 *oöcytes*. As the organisms develops, these oöcytes merely mature. On the other hand, male gametes undergo several stages of mitosis, and by the time they reach puberty they turn into mature spermatazoons. Based on the data presented by James Crow, University of Wisconsin, by the time an organism is physiologically ready for mating, the male gametes have undergone 36 divisions, at the age of 20 - 200 divisions, and by 30 - 430 divisions, and at 45 - 770 divisions.[128] Normal human cells divide from 50 to 100 times.

It would seem that the necessary, but insufficient, condition for the life of an adult organism is the normal process of change, while a sufficient condition for death is either termination of change or pathological change.

The above statement may sound rather trivial - it is part of folk wisdom. Note, however, that widespread among businessmen is the notion that terminating a firm's development change is a sure way to bring about its demise.

Pursuing the idea that a cell undergoing normal transformation restores its chromosome telomeres to ensure continual reproduction, I believe that promoting normal change in an organism serves to increase its life span. This kind of approach differs from the one espoused by most scholars dealing with the problems of aging who advocate direct manipulation of telomerase.[4] Direct activation of telomerase is bound to disturb the balance of contingent physiological processes if the mechanism which turns it on under normal circumstances is ignored. I would also like to note that the idea of activating telomerase and increasing an organism's life span by supporting the mechanism of change bears in a very practical way, upon our attitude regarding cancer.

2.2. Possible Migration of Somatic Cells

The mechanism of somatic change, as described in the previous chapter, suggests that an innovator cell must coordinate its activities with cells of other organs.

This aim can be accomplished by dispatching cells containing new genetic information to other organs. One method to implement this kind of information exchange is by means of viruses that are, possibly, an intrinsic part of the information contained in the genome. This phenomenon is especially prominent in pathological cases (see the following Chapter).

On the other hand, this kind of limited information exchange might be inadequate, especially when the changes in the innovator cell are profound. Perhaps it takes total contact if the information to be transferred transcribes not only much of the genome, but also the cell's cytoplasmic structures.

Assuming that cell contact is required, there must be a mechanism of cell migration, i.e., separation of innovator cell from the host tissue and its penetration into other organs whose cells must undergo respective changes. Moreover, cell migration is probably non random, because the original host organ and the target organs are either morphologically linked

or linked by the genetic sequence governing the development of a new organism.

At this point in time, this rather nebulous picture of normal cell migration is a fruit of my imagination. The prevailing opinion among biologists is that such a phenomenon does not take place. The study of the migration of cells in multicellular organisms was limited to such normal cells as embryonic, blood, lymphocyte cells and, in the pathological case, to the metastasizing cells. One special degenerative case of cell migration is the discharge of dead cells from the tissue. This case also involves a mechanism of cell cessation.

Generally speaking, the problem of cell migration remains largely a mystery [5], and it has not been proved that migration of normal tissue cells is impossible. In fact, in keeping with my approach of reconstructing the normal mechanism of somatic change based on its pathological manifestations, I would to say that cell migration could take place among innovator cells. Indeed, the phenomenon of metastasis suggests the existence of a mechanism that allows a cell to disengage from the host tissue and migrate to other organs. What prevents this mechanism from engaging when it comes to at least innovator-type cells?

One complicating factor in staging an experiment to test this hypothesis is determining the specific conditions under which the mechanism of cell migration becomes active. Moreover, this mechanism may affect only deviant cells, which would create an even more formidable task of distinguishing between innovator cells and the cancer cells.

2.3. Age-Specific Features of the Mechanism of Change

It appears that the nature of changes in cell structure differs with different stages of life.

During the embryonic stage of fetus development, the main concern is with the formation of an organism according to the inherited genetic code and the environment, including the womb, in which the fetus is developing.

During childhood, prior to puberty, the focus is on growth, basically within the framework of the inherited genetic information.

The process of cell change, especially a major change, belongs to the period following puberty, but prior to the start of the aging process. It is probably during this period that changes within the cells, as well as the interplay between the cells and the immune system including the transfer of new information to the germ cells, is best coordinated.

As the organism begins to age (perhaps excessive stress has a similar effect) break-downs in the mechanism of cell change, in the immune system and in the coordination between the two, become more aggravated. We cannot rule out that some negative consequences of aging are also due to the failing mechanism of cell change. In keeping with Dilman's theory of aging and major non-infectious diseases,[129] it is quite plausible that aging, like such ailments as high blood pressure, diabetes, cancer, etc., reflects an organism's inability to cope with the persistent flow of various nutrients needed at some point in time for the organism's growth. This inability may be due to the deteriorating mechanism of cell change.

Perhaps, in very old age, the mechanism of change ceases to function and cells that fail to change simply die out.

3. QUASI-HYPOTHESES STEMMING FROM THE MATERIAL PRESENTED IN THIS CHAPTER

1. The genetic system of a cell possesses a hierarchically organized internal mechanism of change. The program that codes the organism's development is denoted as the zero level program; the program that changes it represents the first level program; and the program that changes the first level program is termed the second level program.

2. Taking into account the intricate nature of the genetic system and the resources required to sustain it (see, for example, the C-value paradox in Chapter 3) an organism's development raises the problem of resource allocation between creating and nourishing a dynamic genetic system, on the one hand, and, on the other hand, faster cell growth (in conjunction with greater quantity) governed by a routine genetic program.

3. It is quite feasible that the genetic system incorporates the tunnel process. In other words, change is initiated both at the end, meaning it is induced by the environment that can directly affect the zero-level program via chemicals, radiation, etc., as well as at the beginning, i.e., the internal changes in the second or first level programs.

4. With changes initiated at the beginning, there ought to be structures in the genome that minimize those genetic combinations that lead nowhere or to a dead end.

5. While the somatic mechanism of change plays a secondary role, perhaps it continues to fulfill the following functions: a) complements the germ mechanism in situations where relatively minor and slow changes are required by the organism, b) fulfills specific functions not covered by the

germ mechanism, c) acts as a back-up ensuring that such crucial evolutionary function as change is not neglected, and d) finally, it may be an anachronism.

6. Minor changes unfold primarily from the end, while major changes originate at the beginning.

7. In trying to reconstruct the normal mechanism of somatic change through its pathological manifestation, in this case metastasizing, one could hypothesize the migration of normal somatic cells; perhaps some emigrant cells even return to the mother organ. Moreover, cell migration is not chaotic in the sense that cells from one organ get attached to those organs that are logically connected by the process of change. The fact that even sporadic migration of normal somatic cells has not been documented does not mean that such a phenomenon does not exist. A number of biologists have confirmed that somatic cell migration does yield to experimental verification.

8. Presumably, if the changes in the cell are of innovative nature, the repair mechanism could be turned off – it either ignores innovations or activates genes that block the repair mechanism.

9. Since activation of the telomerase pertains to all cells undergoing change, natural death or fading away of an organism is possibly due to the termination of the process of change. A number of scientists have entertained the idea of extending an organism's life span through direct manipulation of the telomerase. It seems that direct activation of telomerase, without touching the mechanism which triggers it under normal conditions, may derail other related physiological processes.

NOTES TO CHAPTER 6

[1]. Shapiro classifies the repair mechanism as a mechanism of change.[130] In seems to me that it should be assigned to damage-type changes (break downs, mistakes).

[2]. There can arise other situations when a cell sacrifices itself in the name of the overall development. In this context, apoptosis may be regarded as a manifestation of a cell's altruism. The phenomenon of apoptosis (similarly to self-sacrifice in the social realm) is limited to a small number of cells. Just a note in passing: there is not a single instance in the Torah describing self-sacrifice, for whatever noble purpose.

[3]. Presumably biochemical processes need both catalysts and inhibitors. Generally speaking, both accelerators and brakes are needed to keep any strong fluctuations under control (as in the whip and the reins used to control a horse). I have applied this generalization to economics, suggesting that faster growth of the economy requires both income growth - a catalyst, as well as price increase - an inhibitor (within reasonable limits, of course). More in my article.[131]

[4]. "...if manipulation of cellular life span were technically possible through regulation of telomerase, it might be possible to decrease morbidity or increase life span of the organism."[132]

[5] "How cells migrate has been the subject of much scrutiny and model building for many years, but is still not understood."[133]

CHAPTER 7

SOME FEATURES OF THE GERMATIC MECHANISM OF CHANGE: THE ORIGINS OF SEX DIFFERENTIATION

To reiterate, the leitmotif of the present book is the mechanism of change incorporated in the somatic cells. Allow me to digress and pick up a parallel motif reflecting the external mechanisms of change implemented via the germ cells. I believe the digression is justified for I shall bridge this minor theme with the leitmotif in the later part of the book.

The subject I want to touch upon is one particular mechanism of change based on the germ cells - the mechanism of sexual reproduction.

There are many ways to classify methods of reproduction. Interesting in this connection is the typology proposed by A. Kondrashov. His approach was based on population genetics which he regards as a crucial element of evolution. His classification distinguishes two methods of reproduction: amphimixis and apomixis:

> "amphimixis - that is, a life cycle with alternating syngamy and meiosis - advantageous over apomixis - or production of offspring from single mitotically derived cells. Amphimixis is used instead of the potentially confusing term "sexual reproduction" because sexes are exogamous classes of gametes. In some cases of "sexual reproduction", any pair of gametes can form a zygote (e.g. homothally in fungi), and there are no sexes. Similarly, apomixis is used instead of "asexual reproduction" because the latter also sometimes includes vegetative reproduction when a progeny appears from many cells."[134]

The proposed taxonomy of crossing is based on their chronological evolution of reproductive methods. My initial criteria generates two categories - somatic (based on fragmentation) and germatic (based on

specialized germ cell). Germatic reproduction is further classified based on the number of cells partaking in the reproductive process (one cell (*spore)* or cell crossing). The cross-over category is further subdivided based on the following criteria: are the cells homogeneous or heterogeneous (sexual) in terms of function. Finally, heterogeneous cells split into two classes depending on whether they are contained in a single organism (hermaphrodite) or carried by different organisms.

Presumably at the early stages of evolution simple multicell organisms lacked germ cells and reproduced by means of fragmentation. The process of change in such organisms was rather cumbersome since change in some cell(s) had to be harmonized with changes in other cells of the organism, whether these changes were induced internally or by environmental conditions including hybridization.

It seems the evolution "realized" that change can be implemented more effectively via the germ cells if only because the genetic material which defines the development of a new organism is collected in one compact space. Over the course of evolution, reproduction via germs underwent fundamental shifts. Evolution initially devised germs and then separated the hosts of these cells, i.e. creating genders. The process of evolution has not ended and new forms of crossing may emerge in the future.

While there is no general agreement among biologists as to the origins of the sexes one major benefit of sexual differentiation advanced by biologists is the increase in diversity of genetic combinations generated by crossing. Thus, *compatibility* of the crossing organisms represents a necessary condition for the emergence of the sexes.

In my opinion, however, the above condition is not sufficient for the emergence of sexes. I have tried to elaborate a general approach to sexual differentiation, not necessarily limited to two sexes, and to show that distinct functional attributes of crossing organisms represent another necessary condition in the definition of the sexes.

It should also be noted that the crossing mechanism is geared toward greater diversity, or at least toward preserving diversity, and may well come in conflict with population growth. This may occur, for example, when the number of sexes that partake in crossing exceeds or equals the number of offspring.[135]

Indeed, for population expansion purposes reproduction, when germ-cells are present, parthenogenesis would be most appropriate in terms of the above objective, and in case germ-cell fusion does take place, all the constituent genetic components should belong to one host organism (hermaphrodism). No matter how virile a given organism is, meaning

whatever its capacity to bring new creatures into the world through a single act of crossing, all other conditions being equal, the method of crossing sexes produces less offspring than if the act was carried out by a single organism. Reproduction via a single organism produces at least one new offspring and the total population will be two, i.e., the proportion between the total population and the originators of offspring is 2:1. Now, even if only two organisms cross to produce a new one, then a progeny of one will generate a total of only three organisms, i.e., the proportion between the total population and the originators of offspring is 3:2.

The arithmetic simply underscores the fact that crossing via sexes is really geared toward the creation of diversity. Naturally, diversity itself may prove conducive to survival and growth if only because it gives rise to creatures that might be better adapted to changing conditions.

1. SEXUAL TYPES AND HOW THEY EVOLVED OVER THE COURSE OF EVOLUTION

1.1. Definitions

Greater diversity of life forms, being a necessary condition of biological evolution, can be attained via changes within a given organism as well as via mutation and recombination of genes. The passing of changes in a given organism to the progeny is accomplished by means of fragmentation or germ cells (for single-cell organisms the notion of a germ cell and an organism is one and the same). In turn, each germ cell is ether a spore, or a carrier of gametes, complete hereditary information. Organisms' recombination under fragmentation (division) is carried out by means of hybridization. With sex cells present this function is fulfilled by crossing (and sometimes by hybridization.)

Whatever definition of sex we pick, a necessary condition for sexual differentiation is the compatibility of the crossing cells. At this juncture it does not matter whether these cells fulfill different functions, whether crossing takes place in one or more organisms, or whether the offspring is fertile or sterile.

I would like to elaborate on the above statement and examine the crossing mechanism in some of the simplest organisms (which replicate via fragmentation) that lack functional differentiation but whose structure incorporates certain physiological variations (examples of such organisms are given below). In fact, these simple organisms must be compatible and

not every member of the species can cross with any other member. The actual compatibility may hinge upon the effectiveness of crossing of physiologically different organisms even if we assume that they can cross with each other, at least in theory. It is quite plausible that what we observe here is a very characteristic phenomenon in biological systems, namely, prevention of less effective solutions.

To sum up, we want to isolate from the manifold of organisms that change by means of crossing a subgroup which shall be termed compatibles.

Another *necessary* condition for sexual differentiation (for now omitting the explanation) is for the cells involved in recombination to be functionally distinct. Thus, a cell's affiliation with a particular sex would depend on the specific qualities attached to the "compatibles", i.e., the functions assigned to each sex other than just the capacity to cross. Therefore, functionally different germ cells are compatibles but not vice versa.

One more important point is that the presence of different germ cells is not sufficient for the emergence of the sexes since germ cells may be produced by a single organism. By definition sex refers to organisms that carry a single type of germ cell (gametes).

1.2. Examples

The significance of this definition of sex may be illustrated with other relevant combinations between the germs and their hosts. The combinations incorporate the following parameters: the number of organisms that produce different germ cells, the number of organisms that take part in producing offspring immediately after the germ cell is produced, and the number of organisms that partake in crossing. The table below presents different types generated by the various combinations of these characteristics.

TABLE 7.1. Germ cells and their hosts.

The number of producers of different germ cells	The number of producers of new organisms immediately after germs are produced	The number of organisms partaking in the crossing act		
		One		Several
		Parallel	Sequentially	
One	One	Full hermaphrodite	X	Symbion pandora
	Several	X	Pseudo-intersex	Hermaphrodite of herms type
Several	Several	X	X	Sexes

Let us examine the various types of organisms presented in the table.

1.3. Hermaphrodite

A "hermaphrodite" is an organism that contains different gametes. The term "full hermaphrodite" shall be reserved for self-fertilizing organism that produces progeny (not to be confused with parthenogenesis when there is no self-fertilization; simply one female sex is sufficient to produce an offspring). This kind of full hermaphrodism is characteristic of relatively simple forms of life such as snails.

This suggests that even full hermaphrodites are merely a stage in the development of sexes.

Interesting in this respect is the classification of hermaphrodite types proposed by Anne Fausto-Sterling.[136] Between what I termed "full hermaphrodite" and sexes there are at least three other groups, all incapable of self-fertilization, united in the medical literature under the term "*intersex*". Fausto-Sterling includes in the first group called *herms* that have one testis and one ovary. She purports that in principle herms could

perform as both fathers and mothers but their system of ducts and tubes prevents the fusion of sperm and egg. The second group is comprised of male pseudohermaprodites called *merms* that have testes and incomplete female genitalia but no ovaries. The third group of female pseudohermaprodites called *ferms* possess ovaries and some features of male genitalia but no testes.

Together with the male and female sex all these hermaphrodites comprise, according to Fausto-Sterling five sexes.

Fausto-Sterling's work is interesting in that she focuses on the diversity and special features of hermaphrodites, an area which is rather obscure. However, aforementioned arguments supporting my definition of sex conflict with her classification that matches various hermaphrodites to different sexes.

Our examination of hermaphrodites provides a new insight into the origins of the sexes, including male and female sexes. Biological literature on the subject (as does mythology) frequently raises the question of primacy, i.e., which sex originated from which. This issue is still unresolved with contrasting views being expressed even when it comes to the origins of male and female sexes.

> "In the organizational concept the female is the default sex and the male the organized sex, imposed on the female by the action of hormones. In my alternative scenario, the female is the ancestral sex and the male the derived sex."[137]

Our discussion of evolution suggests that sexes emerged as a result of a single germ cell splitting up into two functionally distinct cells both housed in the same self-fertilizing organism (full hermaphrodite); subsequently hermaphrodites gave rise to sexes, meaning functionally specialized hosts of specialized germ cells. Attesting to the plausibility of this course of development of the reproductive system are the vestiges of hermaphroditic phenomenon still present in sexually differentiated organisms.

1.4. "Sex-convertible Organisms"

The spectrum between full hermaphrodite and sexes contains so called *sex-convertible organisms*. In terms of sexual differentiation, organisms that belong to these intermediate forms have no special functional features although theoretically they that can fulfill the functions of either sex. Such sexual transformation is observed among some species of fish that can alternate between male and female sexes depending on the circumstances.

Sex-convertible organisms, as well as ordinary sexes, are capable of fulfilling the functions of one of the sexes in a single act of crossing. At the same time, they differ from sexes in that the latter are specialized while sex-convertible organisms are universal. By the same token, sex-convertible organisms, as well as hermaphrodites, are capable of fulfilling different functions in the act of crossing. But, while hermaphrodites can do so, at least in principle, in parallel, the sex-convertible organisms can do so only in sequence, i.e., after undergoing the necessary transformation.

1.5. Symbion pandora

This organism attaches itself to lobster's lips and alters its mode of development as it evolves. At the asexual stage, *Symbion pandora* is a larva which produces both male and female cells similarly to hermaphrodites. The larva evolves into a midget male organism replete with spermatozoids and housing a developing female organism. Subsequently, the female leaves its host, and, as the female dies, it discharges a fertilized cell which develops into a new larva. The old larva does not die after the sexes are formed but continues to develop until it reaches a stage at which it discharges males. Perhaps this intricate fusion of sexual and asexual stages of reproduction suggested to D. Ackerman, the author of an article about *Symbion pandora*, the term "trisexual, it will try anything".[138]

It seems that this mode of reproduction represents a peculiar combination of sexual and asexual processes rather than true trisexual reproduction. This class of organisms is very interesting and could be termed *chimera*.

The list of possible combinations between the germ cells and their hosts that partake in crossing has not been exhausted. But my key point is to state a sufficent condition for the definition of developed sexual types, namely the emergence of functionally specialized germ cells carried by specialized hosts.

As revealed in the next section many biologists reduce the problem of sexual types to genetic recombination.

2. THEORIES OF SEXUAL TYPES THAT FOCUS ON THE IDEA THAT CROSSOVER TAKES PLACE VIA VARIATIONS OF GERM CELLS

The functional diversity of germ cells is usually ignored, meaning most theories fail to recognize that the capacity for cross-over is just one necessary condition for the definition of sex and that other criteria are no less relevant. "Sex is the process whereby a cell containing a new combination of genes is produced from two genetically different parent cells."[139] (p.87)

Thus, whatever definition of sex is picked by biologists, from the functional point of view, the origin of different sexes is identified with greater genetic diversity within the species with little or no importance assigned to the functional specifics of the organisms involved in crossing. Still, it is not denied, in fact, it is presumed that the ultimate aim of diversity is quantitative growth of the species.[140]

This approach to sexual types is well presented in a famous work by Edward Wilson Sociobiology**.** Interestingly, Wilson preludes his discussion of the origins of sexes with what seems at first glance a very paradoxical remark. "Sex is an antisocial force in evolution"[141] (p.314).

He goes on to say that

> "Perfect societies, if we can be so bold as to define them as societies that lack conflict and possess the highest degrees of altruism and coordination, are most likely to evolve where all of the members are genetically identical. When sexual reproduction is introduced, members of the group become genetically dissimilar.
> ... The inevitable result is a conflict of interest.
> ... It has always been accepted by biologists that the advantage of sexual reproduction lies in much greater speed with which new genotypes are assembled." (p.314-315).

An example of the notion of recombination being confused with different sexual types is the recently discovered process of reproduction in Fungus.[142] A more complex case is reproduction in *Paramecium*. It was observed that *Paramecium* engage in cross-over which ensures greater genetic diversity. It has also been established that under relatively stable conditions *Paramecium* reproduce by division. Under changing conditions they begin to mate thereby merging and exchanging genetic information (primarily through nuclear fusion; afterwards the "compound" *Paramecium*

stretches out and forms a dumb-bell; finally it splits and forms two *Paramecium* with new genetic traits which then reproduce by division).

However, Paramecium do exhibit selectivity - not every organism mingles with any other. I quote T. Sonneborn, a pioneering specialist in the field of *Paramecium* reproduction.

> "We have studied the inheritance of three kinds of traits in *Paramecium*. In all three respects the two mates of a pair do, in fact, produce unlike cultures. One of these traits is sex, or mating type. Although the two individuals that mate are functionally hermaphroditic, they differ physiologically: mating can occur only between physiologically diverse cells, that is between different mating types."[143]

In stressing the role of the sexes in preserving diversity, the theory of mating types advanced by H.Bernstein, *et al*,[144] is actually a particular case of the general approach rooted in genetic diversity.

Their theory states that the female sex is actually sufficient for reproduction. However, there is a multitude of external factors such as radiation, chemicals, etc. that exert a damaging effect on the ovum. The function of doubling the number of chromosomes through fusion with the male germ cell is an effective restoration of the damaged genetic structure of the ovum.

However, the need to repair damage through genome doubling does not warrant the emergence of such complex interaction between different mating types. First of all, the cell itself possesses a mechanism of self-repair. Even if this mechanism is not adequate, chromosome doubling, as means of repair of the genetic structure of the ovum, could be achieved in a simpler manner through the fusion of germ cells belonging to similar organisms, not to mention the fact that the germ cells of organisms having asexual reproduction, such as certain species of lizards, have significantly more chromosomes than developed mammals. Moreover, all the chromosomes in the cell come in pairs, so for repair purposes, asexual reproduction would perform just as well.

The functional aspect of mating types is linked with the structural aspect, which is predicated on structurally differentiated organisms. Of course, structural differences range from minor genetic variations to major differences that define the function of the mating organisms. In speaking of the sexes I want to emphasize the differences in the reproductive system of

the organisms directly partaking in mating (unlike differentiation based on the organism's function in a colony - workers and soldiers among insects).

From the process-oriented point of view, sexual differentiation depends on the number of participants involved in cross-over. In nature we observe mainly one particular case of pair-wise crossing (mating).

> "Why are there usually just two sexes? The answer seems to be that two are enough to generate the maximum potential genetic recombination, because virtually every healthy individual is assured of mating with a member of another (that is, the "opposite") sex."[145] (p. 316).

Whith other conditions being equal, mating may indeed produce the greatest number of new genetic combinations given the size of the population. However, taking other factors also conducive to genetic diversity into account, it may turn out that the act of crossing could well involve more than two organisms. I shall come back to this question in a later part of the paper. At this point I just wish to note that the general notion of sex as a compatible creature with different genetic make-up would point to multi-sexual reproduction among flu viruses. These viruses were observed in genetic recombination that involved two or more viruses.[146]

Let us now look at the category of sexual types in terms of genesis. Interesting in this regard is the theory advanced by two Canadian scholars, Michael Rose and Donald Hickey. They claim that the emergence of sexes did not provide any evolutionary advantage. In fact, they portray sexes as a mechanism that promotes the spread of parasite segments of the DNA; these DNA sequences found in many cells are similar to viruses and are commonly found in many types of cells."In this context, males can be seen as parasitic DNA made manifest at the organismal level."[147]

The authors further contend that while sexes originated as parasites they evolved into biologically useful entities.

In the light of my concept of the tunnel process and sexual types (see section 3) the above theory gains a new dimension. Perhaps, the authors' contention that sexes evolved from the beginning rather than from the end is correct. In that case the initial stages of innovation (here, the sexes) ought to be carefully tested, meaning the novelty which at first seems useless or parasitic may, in fact, turn out to be beneficial. If we make the opposite assumption regarding random mutations, i.e., if we rule out that there are mechanisms in nature that form biological potential, then nature's verdict on these pragmatically obscure states will, at least initially,

be negative. Of course, positive evaluation of biological potential is a very complex task as revealed in our discussion of the tunnel process.

Now I want to examine in detail three theories of sexual types, the last of which is my own.

3. THEORIES OF SEXES THAT FOCUS ON THE IDEA THAT CROSSOVER TAKES PLACE VIA FUNCTIONALLY DISTINCT GERM CELLS

3.1. Laurence Hurst's and William Hamilton's Theory of Sexual Types

One contemporary theory on the nature of sex links the emergence of sexual types with conflict prevention in the zygote between different gamete parts that contain genetic information.[148] This concept incorporates the idea that structural elements bearing genetic information are not limited to the cell's nuclei but are contained in organelles (e.g., mitochondria) and other cytoplasmic structures.

Just as any other theory the above theory has undergone its own evolution, most comprehensively expounded in the works of Lawrence Hurst and William Hamilton.[149,150,151,152]

Essentially this theory states that sexes differ based on the extent to which an organism directly partaking in crossing via its germ cells is able to shed its cytoplasmic genetic structures including organelles. According to the authors, the importance of organelle shedding as a sexual characteristic stems from the fact that the zygote is not some idyllic system but an active and inner-conflicting one. This turbulence is a result of different parts of the germ cells competing with each other when they fuse because each cell pursues its own interest. One special threat to zygote development is posed by the competition from the organelles which, unlike the chromosomes, are not integrated with the zygote.

The outlined theory purports that "sexes" appear when the zygote is formed through a complete fusion of germ cells belonging to different organisms. For example, this process takes place in common green algae *Chlamydomonas*.

On the other hand, according to the above theory, sexes are non-existent when the interaction between germ cells is limited to the exchange of nuclei. According to the authors, sexual differentiation in many species is predicated upon one sex sacrificing its organelles in order to form a

zygote. The most widespread phenomenon is the hierarchy of two sexes when one of the two partners, usually the male sex, gives up its organelles.

The authors contend that their criteria allows for multi-sexual reproduction. Certain species of slime mold, e.g., *Physarum polycephalum,* could have as many as 13 sexes. This approach to sexes is based on a multi-level hierarchy of organisms. Under fusion, the organelles of the higher organism are passed on; the lower ranking organism gives up its organelles. As I see this case, what we are dealing with is not 13 different sexes but a more selective kind of crossing among compatibles. However, from the evolutionary perspective this intricate mode of crossing is not expedient. Employing his definition of sexes, Hurst notes :

> "For any particular sex the cytoplasmic genes sometimes will be inherited, and sometimes won't be inherited depending on who you mate with, so it's got an inherent vulnerability to cheats; what happens if one mutant set of mitochondria refuses to shut down?"

The authors thus conclude that two sexes are optimal.

In lieu of the recent discoveries pertaining to gamete recombination Hurst had to revamp his theory on the origins of sexual types.[153] It was discovered that complete fusion of male and female gametes was observed not only in mussels (*Mytilis*) but also in mice and *Drosophila*, although in a less developed form. In fact male and female offspring of mussels are endowed with different mixture of father's and mother's mitochondria. For example, daughters usually inherited just the mother's mitochondria while the sons primarily inherited a combination of mother's and father's mitochondria.

As is the fate of many theories, subsequent discoveries not so much invalidate their predecessor theories as limit the scope of their application to a more narrow range than was at first suggested by the author. Hurst has said that his original theory of sexual types was no exception.

3.2. V. Geodakian's Theory of Sexual Types

There are other approaches to the definition of the sexes and their role in evolution. The theory of two sexes proposed by Geodakian emphasizes the benefits of mating which is claimed to produce an optimal combination

between population size and genetic diversity within the population.[154] The key to Geodakian's theory is the general cybernetic notion that organized systems exhibit:

> "Separation between the task of preserving (conservative body) aimed at keeping things as they are and the task of changing (operative body).
> ...the implications for biological systems are the following: females in the population exhibit stronger tendency for hereditary continuity, while males - for change.
> ...to use cybernetic terminology, females represent the virtual memory of the species and the males manifest the operational (temporary) memory of the species."

Within the outlined framework Geodakian attempts to explain certain facts related to the number of males in a population. For example, it was observed that under favorable conditions very simple creatures having sexual reproduction such as water fleas and aphids exhibit a strong tendency for parthenogenesis. At the same time, in a more turbulent (changing) environment some females begin to produce males who then fertilize the females. Moreover, the observed difference in male and female roles sheds light on the accelerated turnover of males in the population, i.e., their higher rate of birth and death under changing conditions.

Geodakian notes that the number of males in a population may increase as a result of some females turning male, a hypothesis supported by some recent research in the West. It was observed that fresh water hermaphrodite African snails alter their pattern of reproduction depending on the density of parasite organisms in the water. If the water is free of parasites the snails fertilize themselves. However during intense infestation some snails grow a male organ and engage in sexual intercourse[155].

Unlike Hurst and Hamilton, Geodakian's theory of the sexes is oblivious to cell structure. In other words, the cell function is not linked in any way to cell structure. This omission was the result of the following considerations:

> "...differentiation into two sexes ensures the production of two kinds of gametes or germ cells: tiny and mobile spermatozoons whose task is to come in contact with a relatively large but stationary ovum that provides nutrition for the future embryo."

Geodakian's stance on the subject basically falls in line with another theory that links the origins of different sexes to differences in gamete type: one type is relatively simple therefore behaving as attractor gametes; the other type is complex acting as attracted gametes.[156] I agree with Geodakian that sex differentiation is not rooted in these differences. Rather the fact that these cells exhibit different levels of activity is a consequence of their functional role, a topic discussed below.[1]

It seems that the theory of sexual types developed by Western scholars is similar to the one proposed by Geodakian: it basically emphasizes the need to eliminate the impact of parasitic entities.[157] However the authors of all these theories based on the emergence of the sexes as a response to changes in the environment fail to mention Geodakian's name.

Both theories of sexual types (Geodakian's and Hamilton's/Hurst's) are impressive if only because each theory distills certain important empirical facts and suggests a plausible explanation. By emphasizing different aspects of sexual reproduction the two theories seem to complement each other.

4. MY THEORY OF SEXUAL TYPES

4.1. Multisexual reproduction

My approach to the concept of sex is based on the role of individual participants of the crossing act in fulfilling the function of change (this is different from classification based on unchangeable specific function inculcated in the organisms, e.g., workers and soldiers among insects).

The outlined approach to sexual types allows for more than two organisms to partake in cross-over. Most theories of sexual types, as it was mentioned above, postulate only two sexes. The reason I question this particular assumption is because its revision gives us a broader view of the problem of mating and the sexes.[2]

Other conditions being equal, mating is optimal for implementing crossing between functionally distinct organisms because it minimizes the number of such organisms. However, other mechanisms of crossing involving more than two organisms can be construed.

As I have noted above, under mating population size is sacrificed (relatively to hermaphrodism) for the sake of greater genetic diversity. Similarly, with three or more organisms required to produce a new one,

population size and even the number of genetic combinations may well decline, but the "quality" of the combinations actually produced may ultimately prove more conducive to the development of the species.

On May 3, 1984 I was invited to give a talk at a "crazy ideas" seminar held at the Benjamin Franklin Research Institute in Philadelphia. The subject of my lecture was "Multi-sexual reproduction," meaning reproduction involving more than two organisms.[3] I chose to use an analogy with political systems where the birth of a new social institution calls for a deep-wrought separation of powers. Using the above analogy, we could imagine at least three sexes.

The first sex, counterpart of the legislative branch, would elaborate programs of strategic development with long-term significance. By analogy with the executive branch, the second sex would elaborate tactical programs within the framework established by the first sex. (Presumably, adjustments to current conditions – "operative management" – is carried out by the organism using the means at its disposal, such as reserves, organs for adjusting to temperture fluctuations, etc.) Finally the third sex, the "judicial branch", would confirm that the programs followed by the other two sexes are in accord with the fundamental programs of development, thus preventing the birth of organisms violating basic precepts of development. The idea of prevention in biological development is quite plausible: it is unlikely that "quality control" over new structures is performed exclusively by hindsight, i.e., through natural selection.

So, my approach to the definition and classification of the sexes implies that the organisms directly partaking in crossing must play different roles, analogous to different functions fulfilled by the governing bodies. In this respect my approach resembles that of Geodakian. In fact, the role he ascribes to the male sex is essentially the same as the second sex,"executive power", in my scheme. However, the function of the first sex,"legislative", which might correspond to the female sex is vastly different from the role ascribed to the female sex by Geodakian. He deems female the conservative sex - it preserves what has been attained. In my opinion, the female sex takes on development geared toward profound long-term changes (I shall elaborate on this point later on).

As far as the third sex is concerned, I am not familiar with its equivalent in nature. However, the existence of the third sex with its respective functions is quite plausible. If one was to seek out the third sex in nature one should probably do so among organisms where the population density is rather high making it easier to meet representatives of all the sexes needed for reproduction. Even if not found in nature we can

set up computer simulation of the evolutionary process with tri-sexual reproduction and see what kind of results are obtained.

4.2. The Tunnel Process and the Sexes

To reiterate the point made in our previous discussion of the R&D process in economics, the process of innovation represents a multi-stage process which can start at the final stage (end of the tunnel) that reflects the immediate concerns of the environment, or it can start at the initial stage that echoes the immediate concerns of internally-driven development of basic science. Still owing to the mutual feedback among its various stages, R&D represents a single unified process .

I have also noted that an analogous tunnel process phenomenon is observed in biological systems. This approach might help explain the splitting of specialized germ cells which occurred over the course of evolution as gametes and sexes appeared, first and foremost among the developed mammals. One working assumption is that under mating the male sex voices change associated with the final stage of the process of development, i.e., it reflects the demands of the environment. The female sex, on the other hand, is the vehicle of change characteristic of the initial stage, i.e., it implements profound internal shifts in the structure of an organism. The above scheme does not preclude the male sex having any connection with the initial stage or vice versa for the female sex.

The following puzzling question served as the impetus for these speculations: "Why is it that in developed species the testicles are outside the body and the ovaries hidden deep inside the body?" The first part of the question is well explored. The common explanation is that sperm production takes place at temperatures below the so called normal body temperature. In my opinion, this explanation can be challenged. For one thing, being outside the body makes testicles, a rather delicate organ so vital for procreation, rather vulnerable.[4] As far as the temperature factor, an organism could have easily created a cooler niche inside itself to accommodate sperm production. We know that various parts of the body exhibit a wide range of temperature and in some species of mammals, e.g., elephants, whales, dolphins, the testicles are hidden inside.

It seems to me, that this kind of fragile construction of the male body is justified if, by being outside, the testicles would be more susceptible (responsive) to changes in the environment and especially such a global parameter as radiation. It has been determined that changes in earth's radiation level (sometimes as a result of sun spots) are linked with

certain biological phenomenon such as migration of lemmings, crop yields, etc. The fact that female ovaries are well hidden under the skin protects them from some kinds of current external factors allowing them to focus on the other mechanism of change.

All these speculative deliberations can be reformulated into experimentally verifiable hypotheses. For instance, the following experiment could be set up: a small dose of radiation could be applied to the testicles to see whether that affects the sperm. The females could be subjected to a similar small dose of radiation and then the ovaries and the ova checked for the aftereffects. If this kind of radiation exposure produces different results in the reproductive organs of male and female animals then my hypothesis regarding higher absorbency of environmental factors by the male gains credibility.[5]

Still, there is other evidence supporting the notion of functional differentiation of the sexes. I want to emphasize that the mutation rate is much higher in the human male germ line than in the female germ line [6] and, to bolster the claim, there are profound dissimilarities in the reproductive systems of males and females so strongly expressed in humans. With each ejaculation the human male releases up to 300 million sperm, while ovaries of a new born female contains about 400,000 ova and no new ones are produced.[158]

General principles of evolution point to at least three factors that allow species to develop: 1) capacity for quick reproduction; 2) organisms' ability to rapidly adapt its structure to the new conditions; 3) active individual performance.

There is a strong correlation between these factors and an organism's complexity. The more complex an organism, the more pronounced is the third factor and the less critical are the first two.

Indeed, for viruses, microbes, bacteria, etc. a typical organism is relatively simple. Owing to its simplicity these organisms are able reproduce at a very fast pace and some are able to alter their structure within a short period of time (viruses can do this literally within years). On the other hand, each individual organism may easily perish in the course of its life cycle. As organisms become more complex the reproduction rate wanes and the time required for structures to change increases. Nevertheless, these parameters are respectively considerably greater/less in insects, for instance, than they are in mammals. Each mammal is relatively complex. Its reproduction cycle is rather long and changes in its structure are very slow. At the same time, each individual creature is extremely adept and endowed with a variety of means to fulfill its function.[159]

Comparing sperm and ova one observes certain correlation between their complexity, factors supporting their functional role, and the coordination between their function and other aspects of their system's performance. From the functional point of view, the primary role of the spermatozoid is to convey changes in the environment to the succeeding generations by doubling the number of chromosomes, triggering the development of the fertilized cell, etc. If the sperm's structure was a complex one (i.e., instead if millions of sperm there was one very complex one) it could still function as far as interaction with the female members of the species. However, the creation of such a complex sperm would not agree with its alleged function of rapid change. The fact that the sperm is structurally similar to viruses is precisely the feature which allows it to change rapidly.[7] The process of sperm production entails multiple divisions of the sperm. This kind of behavior promotes diversity since many changes take place during cell division. Perhaps, the genesis of sperm formation over the course of evolution can be traced by observing the process of sexual differentiation as the embryo develops.

Assuming the primary function of the ovum is to support major changes in the organism, passing on the genes to the progeny is a necessary condition for this function to be fulfilled. The cell's structure would have to be complex to fulfill this function.

Quite possibly, internal genetic changes experienced by the ovum as it forms (process dimension) occur at the initial stages when the cell is not yet mature (oögonia). The cell undergoes multiple divisions; external changes (but still within the organism) take place at a stage when the already indivisible ovum begins to mature (oöcytes). As far as the genesis facet of cell dynamics, prior to the emergence of different sexes the germ cell absorbed both the environmental factors as well as the internal changes. Perhaps, over the course of evolution the task of responding to current external factors was shed and assumed by the specialized cells of the male sex. Nevertheless, the ovum has kept all of its former functions. Parthenogenesis attests to the idea that unlike the sperm the ovum is, in principle, sufficient to ensure reproduction. Vestiges of parthenogenesis have recently been discovered even in humans[160,161]

All these speculations regarding the germ cells, assuming mutations can occur at different stages of their development, is corroborated by J. Haldane's hypothesis that the ovum and the sperm of different species exhibit very different mutation patterns.[162] The mutation frequency pattern of male and female gametes of different species is the following: two in rodents, six in primates, and ten in humans.[163]

What is the significance of male gamete mutability, especially among the more developed animals?[8] A number of biologists have offered the following explanation for the reasonably high rate of mutation of the male gamete: this process makes up for the epistatic selection (selection where one gene acts to suppress another gene) which reduces diversity as well as the formation of harmful mutations. However, since excessive mutation rates may generate too many new harmful combinations, the task is to find some optimal number of mutations that will serve to promote the evolutionary process.[164] An interesting model to simulate optimal mutation frequency ratio between males and females was undertaken by R. Redfield[165] The results obtained are not conclusive since the model could have failed to take certain factors important to the evolutionary process into account. A large percentage of male gamete mutations may turn out to be harmless or useless because variation is limited to the so called "selfish" genes whose role is still obscure.

4.3. Characteristics of Sexual Types and Information Transfer Between the Somatic and Germ Cells

The above discussion of the relation between the tunnel process and sexes has lead me to another topic, the transfer of information from somatic to germ cells.

Suppose the migration of somatic cells in multicellular organisms does take place. In the extreme case a changed somatic cell might even try to invade the germ cells in order to pass on changes to the progeny. This whole notion is rejected by the great majority of biologists who hold that evolutionary changes are due to external factors affecting DNA of germs. Of course, in view of the grave danger of introducing untested changes in the established genetic program there must be strong barriers in the way of somatic cells penetrating germ cells. Perhaps, these barriers make it difficult to observe somatic cell penetration even if the phenomenon does take place. In principle, it could take place in a physiologically modified form through viruses going from innovative somatic cells into germs. It is fascinating to find out how viruses manage to accomplish this task.[166, 167]

Direct penetration by innovator somatic cells is more complex. The process might turn out to be quite different in males and females. In the light of such phenomenon as parthenogenesis it would be reasonable to suppose that change unfolds primarily though the female medium. My assumption that females impart major beginning-induced changes and males convey changes from the end seems to imply that in males positive

change unfolds primarily through the germ cells. Perhaps, in the female sex the archaic somatic mechanism of change has been preserved to a greater extent than in the males: profound changes originating at the beginning might require more testing of the various components (at least at the informational level) and their subsequent integration - something the somatic mechanism of change accomplishes more thoroughly.

These speculations regarding the roles of the somatic and germatic mechanism of change agree with the following facts. There exist mysterious biological barriers in the way of foreign cells invading the scrotum but no such barriers exist for ovaries. As a result, secondary cancer of male testicles is non-existent (and primary cancer is rather rare) while ovaries (and the female reproductive system in general) are a favorite spot for secondary as well as primary cancer. It goes without saying that these facts establish a certain correlation rather than a proof of my supposition that innovator somatic cells should have an easier time penetrating the female reproductive system.

5. CONCLUSIONS

1. The development of the germ cells, prior to sexually differentiated cells, and the germatic mechanism of change that succeeded the somatic one on the evolutionary scale was dictated by the advantages of implementing the process of change within one type of cells - *in one place* where it is much easier and faster to coordinate all the changes.

2. Sex can be defined based on the role of specialized germ cells directly partaking in the act of crossing by means of specialized hosts.

3. A question that frequently comes up is which sex originated from which. It seems that sexes emerged as a result of a single germ cell splitting up into two functionally distinct cells both carried by the same self-fertilizing organism (full hermaphrodite); subsequently hermaphrodites gave rise to sexes.

4. Crossing may involve many sexes. By analogy with the separation of power in the social domain, there could be at least three sexes: the first is a counterpart to the legislative branch, the second to the executive branch, and the third to the judicial branch. The last sex would oversee that the programs introduced by the other two sexes agree with the fundamental program of development. This prevents the creation of organisms that fail to conform to the basic precepts of development. Before the third sex is found in nature, one could set up and observe the results of

a computer simulation of the evolutionary process under the assumption of trisexual reproduction.

5. It is quite feasible that in reproduction by mating the male expresses primarily the end phase of the process of development (i.e., he is the vehicle of environment-induced changes). The female sex is primarily involved with the beginning phases, i.e., profound changes in the structure of the organism. This does not preclude each sex from incorporating functions specialized in by the other sex. Perhaps the above hypothesis ought to be rephrased: Why is it that among developed animals, the testicles are outside the body and the ovaries are hidden deep inside under the skin?

6. Assuming for the moment that females bear deep changes from the beginning and males drive end-induced current changes would seem to imply that in males the germ cells are quite important in implementing change and change in somatic cells is more of an anachronism. Perhaps the mechanism of change in somatic cells is more pronounced in the females. It grapples with on-going environmental fluctuations, freeing the ovum to handle more systemic beginning-induced transformations.

7. The difference between the somatic mechanism of change in males and females points to the possibility of somatic changes being transmitted to germ cells (with the hereditary potential). What lends plausibility to this hypothesis is the following unexplained fact: there exist powerful barriers in the way of foreign cells penetrating the scrotum but none for the ovaries.

8. I would like to note that my comments regarding male and female gametes in no way contradict the theory of sexual types proposed by Lawrence Hurst and William Hamilton. However, the differences in the gametes pinpointed by these authors were used to explain in rather general terms the emergence of different sexual types over the course of evolution. In my opinion, these differences in gamete behavior represent a subordinate evolutionary trait which makes genetic crossing more effective.

NOTES TO CHAPTER 7

[1]. It seems to me that the greater activeness of the males as compared with females, a widespread phenomenon in the animal kingdom, is determined by the difference in the production of gametes. Females are basically born with a certain number of eggs (ova). In principle, an ovum can produce an offspring without male participation. Ova are fertilized and can be relatively passive, theoretically always ready to bond. It is another matter that females can pick the best time for mating and under certain

conditions reject mating attempts on the part of the male (for example, a pregnant bitch refusing a male dog's overtures). Males, on the other hand, produce sperm on a continuos basis. Only upon reaching a certain level of sperm content is the male ready to actively seek out a mate. In more developed animals the ability of the male to mate is also controlled by erection. Perhaps, this feature is aimed at preventing males lacking a sufficient amount of sperm from attempting to mate since intercourse is so attractive in itself.

[2]. Mating does not imply that the progeny will consist of just two sexes. The reproductive process may give birth to many different types of organisms that do not partake in mating but have special functions in the community. For instance, "The queen honey bee is inseminated by a male just once in her entire lifetime, during the "nuptial flight." The sperm she receives are stored in a little pouch connected with her genital tract and closed off by a muscular valve. As the queen lays eggs, she can either open this valve, permitting the sperm to escape and fertilize the eggs, or keep the valve closed, so the eggs develop without fertilization.
... The fertilized eggs become females (queens and workers); the unfertilized eggs become males (drones)."[168] p. 609.

[3]. I first made my ideas on multi-sexual reproduction public in Moscow at a "duck dinner" organized by a wonderful woman Galina Karpelevich-Poliack. These lines are dedicated to her.

[4]. The exposure of the male organ (partially the female one also) is particularly dangerous when walking erect. Perhaps the Biblical legend concerning the ramifications of Adam and Eve tasting the fruit from the tree of knowledge was fueled by these considerations. "And the eyes of them both were opened, and they knew that they were naked; and they sewed fig-leaves together, and made themselves girdles." (*Pentateuch*, Genesis, 3:7).
Interestingly this legend leads me to speculate that the cardinal difference between man and animal is not really the making of tools (some animals have tools also) but the invention of artificial things to cover his body as called for by changing circumstances (in this case walking erect).

[5]. It seems an experiment of this sort has been performed on real human beings. I want to recount a story told to me by a Russian doctor who came to the US. The doctor was unfamiliar with my hypothesis regarding the mechanism employed by the two sexes to fulfill their function. The story has to do with the aftermath of the Chernobyl accident. Men who happened to be in the area affected by radiation, but not in the epicenter, and who then left the area and got married to local women had a statistically significant percentage of deformed children. Women who happened to be within the affected area, but not the epicenter, and who then left the area and got married to local men had a significantly lesser percentage of deformed children.
I have merely relayed a story as told to me by one doctor. I have no documented evidence to corroborate these findings. In fact, I could have been blinded by my subconscious desire to hear evidence supporting my hypothesis and this could have distorted my perception. As my now deceased friend, mathematician Boris Moishezon liked to say, if you really want to prove a theorem and its seems like you have succeeded in proving it, the proof is probably flawed.

There is major work being conducted in the former Soviet Union to study the aftermath of the Chernobyl disaster. Foreign scientists have access to the area and scholars interested in the subject could verify the story told above. Even if the results prove negative, the findings of such a study could be quite informative.

[6]. Based on the mutation rate of sperm and eggs in different species, W.-H. Li, *et al.*[169] conclude that the evolution of DNA sequences is driven by the male sex. From my perspective this conclusion is rather rash. There are mutations and there are mutations. Perhaps the authors' approach is valid for minor mutations whose number far exceeds the number of major mutations; the latter are perhaps driven primarily by the female sex.

[7]. It is well known that there are four types of viruses produced by a combination of DNA and RNA on the one hand, and a single or double spiral on the other. Spermatozoon is a kind of virus which has DNA and double helix structure.

[8]. The impulse that inspired me to address this question was provided by Natalie Angier article. [170]

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