CONCLUSION

1. INTRODUCTION TO CONCLUSION

The crux of the present work is the inclusion of the "sector of change" with its diverse methods and mechanisms, including random mutations, as an endogenous part of the biological system, similar to the R&D sphere organically intertwined as an endogenous part of the economy.

The reason I dwell so much on this notion of change is because this phenomenon defines life. Other conditions being equal, the waning of the organism's capacity for change may result in painless death. Recent discoveries concerning the possible link between telomeres and the process of change seem to validate this statement. It goes without saying that other factors may cause the death of an organism long before its capacity for change is exhausted. Pathological disorders in the mechanism of change are one cause of death, especially when they assume such devastating form as cancer (just as malfunctions in the R&D mechanism can lead to the disintegration of a social system).

The spotlight in the present work was on the somatic mechanism of change. The fact that change in individual somatic cells takes place is not contested. What is not clear is whether or not there is a *multi-stage* process of change based on somatic cells. General evolutionary considerations suggest an affirmative answer since the phenomenon of biological change existed prior to the appearance of specialized germ cells. Even if somatic change does take place in developed organisms, it may represent some archaic mechanism that may or may not interact with the germ cells that pass on hereditary information.

In my opinion, biological science is just beginning to probe into the normal process of organism restructuring through the internal somatic mechanism of change. Research on the subject could enrich our understanding of disorders incorporated in the more general process of biological change. Furthermore, the paradigm that regards a disease as a break-down of some otherwise normal mechanism points to new ways of reconstructing the normal mechanism through these manifest deviations.

All these considerations went into my definition of cancer as an *extreme form of a pathological attempt to reconstruct an organism via the somatic mechanism of change.*

My ruminations into the mechanism of somatic change, its pathology, and some related issues are encapsulated in the following quasi-hypotheses".

1.1. Quasi -Hypotheses Concerning the Normal Mechanisms of Change

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

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

3. It is quite plausible that the genetic system incorporates the so called tunnel process. In other words, change is initiated both at the end, i.e., induced by the environment which can directly affect the zero-level program with chemicals, radiation, etc., as well as at the beginning, i.e., 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. The development of specialized germ cells, prior to sexually differentiated cells, and the germatic mechanism of change that succeeded the somatic one (on the evolutionary time 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.

6. While the somatic mechanism of change plays a secondary role perhaps it continues to fulfill the following functions: a) it complements the germ mechanism in situations where relatively minor and slow changes are required by the organism; b) it fulfills specific functions not covered by the germatic mechanism; c) it acts as a back-up ensuring that such a critical evolutionary task as change is not neglected; d) finally, it may be an anachronism.

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

8. Sexes can be defined based on the role of the organisms directly partaking in the act of crossing and change implementation, unlike classification based on the inherited unchangeable function in a group, such as workers and soldiers among insects.

9. In principle, crossing could involve more than two sexes. By analogy with the separation of power in the realm of social systems, 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 formation of organisms that fail to conform to the basic laws of development.

If one were to seek out the third sex in nature, one should probably do so among developed organisms (such as insects) where the population density is rather high making it easier to meet representatives of all sexes needed for reproduction.

If the third sex is not found in nature, one could set up computer simulation of the evolutionary process under the assumption of trisexual reproduction and see what kind of results are obtained.

10. It is quite possible that under 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, meaning profound changes in the structure of the organism. This does not prevent each sex from engaging in the functions specialized in by the other sex.

Perhaps, the above hypothesis could 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?" The answer proposed in the books does yield to experimental verification.

11. In trying to reconstruct the normal mechanism of somatic change through its pathological manifestation, in this case metastasis, one could hypothesize migration of normal somatic cells (perhaps, some emigrant cells even return to the original organ). Moreover, cell migration, apart from embryonic cells, blood and lymphatic cells, is not chaotic, meaning it is governed by the logic of the process of change. The fact that even sporadic migration of normal somatic cells has not been documented does not mean it is non-existent. A number of biologists have confirmed that the hypothesis of somatic cell migration does yield to experimental verification.

12. Since activation of the telomerase involves all cells undergoing change, natural death or fading away of an organism could be due to the termination of the process of change. Some scholars have entertained the idea of extending the organisms' life span by direct manipulation of the telomerase. It seems that this method which leaves out the mechanism that excites telomerase under normal conditions may upset the balance of related physiological processes.

1.2. Quasi -Hypotheses Concerning Cancer

1. Cancer is a disorder at the second level of a hierarchically organized internal mechanism of change (the zero level genetic program controls development, the first level program changes the zero-level one, and so on).

2. The frequency of cancer is directly proportional to the species' predisposition toward change and inversely to the defense afforded by the immune system.

3. Making one strong assumption that certain types of somatic change do transfer to germ cells, it seems cancer occurs most frequently during the period when the organism begins to age, but prior to deep old age. The reproductive system through which changes are passed on and which triggers the mechanism of change begins to grow weak but does not fade away completely as does the mechanism of change. The immune system which ought to prevent the formation of pathological changes suffers a similar decline.

4. The frequency of cancer of specific organs is directly proportional to the organ's predisposition to change and inversely proportional to its defense by the immune system.

5. In one particular case of male and female reproductive organs that produce germ cells the difference in the respective frequency of cancer

stems from the functional role of the two sexes. Male characteristics are geared toward assimilation of changing environmental conditions while the female system is structured to accommodate major changes in the organism.

6. It is quite plausible that the powerful barriers preventing cancer cells from penetrating the testes and a lack of such protection in the ovaries attest to the following phenomenon. The anachronism of somatic change is more pronounced in the females since profound changes initiated at the beginning require a more thorough testing of the parts, at least at the informational level, and their subsequent integration - the task that is better suited for the somatic mechanism.

The difference between the somatic mechanism of change in males and females is correlated with the following puzzling fact: there exist powerful barriers in the way of cancer cells penetrating the scrotum but none for the ovaries.

7. Metastasis take root in organs that are "suppliers/consumers" of the organ in which the malignancy originates. The extent of infiltration depends not so much on the capacity of the vascular/lymphatic system to carry the cells but the scope of change demanded of the "consumer/supplier" organ. Another possibility is that organs susceptible to metastasis are morphologically related. Finally cancer may strike organs that are formed according to the sequential logic of the genetic program.

8. Assuming cancer cells are of the dissident type, rather than destroy them treatment should aim to limit the scope of their activity, possibly by isolating them temporarily. Under extreme circumstances when the danger posed by cancer cells is lethal and their proliferation cannot be curbed, they must be removed from the organism.

To summarize the ideas expounded in the book, I would say that the book paints an apparently contradictory picture of my theory of the mechanism of biological change, bothnormal and pathological. In other words, ideas submitted for readers' judgment conflict with the prevailing neo-Darwinist precepts (mutations generated by the minor random nature of changes in the DNA program bombarded by external factors and tested for viability through natural selection. I do not discard the neo-Darwinist conception. It is not in my character to reject outright all the previous scientific achievements. I believe, following Bakhtin's footsteps,[1] that new theories do not annul the old but merely limit the scope of their applicability.[1] I always try to stipulate the precise conditions under which old theories are valid. However, even mathematics that has excelled at linking the final conclusions with all the initial conditions is full of

pitfalls.[2] Of course, I am unable to specify the conditions under which the neo-Darwinist views on the mechanism of change are true. Based on some general considerations and by analogy with economics I would say that these conditions reflect the case of organism modification. On the other hand, my approach underscores the process of change related to the emergence of new species, orders, and classes.[3]

I would also like to note the concept presented in the book makes no claim for immediate acceptance on the part of biologists or for a prominent place in the textbooks. My goal is much more modest, namely for the book to become part of the library of ideas regarding the evolution of the biological system. This too imposes certain conditions that must be met in the book. They are that the ideas advanced should not be generally known, obvious, or outright wrong.

Some people I talked to disagree, maintaining that the necessary condition for an idea which aspires to scientific validity to be admitted into the library of ideas is that it be accompanied by hypothesis which yield to experimental verification. This approach to science is the cornerstone of the Anglo-Saxon tradition. The great advantage of this empirical tradition is that it prevents idle and unconfirmed scientific speculation. Its drawback is that peculiar scorn for vague ideas that are not yet ripe for direct experimental testing. I believe this attitude is rooted in the notion that new ideas are easy to concoct and that any scholar can come up with new ideas at will. Or perhaps, it is held that any new idea needs to be elaborated and this requires money which, in turn, requires that the proposed theory be corroborated, at least to some extent; and if the theory advances no experiment-amenable hypothesis, foundations will not even consider the proposal... and so on and so forth.

Whatever the reasons behind this skepticism toward new ideas, I believe the Anglo-Saxon tradition does have its Achilles' heel. The scholarly tradition of continental Europe is different. It certainly holds ideas amenable to experimental verification (not to speak of those corroborated by experiment) in high esteem. However, the continental tradition shows appreciation for the initial, oftentimes feeble steps in the development of new ideas even if there is no clear-cut method of experimental testing.

The reader might well guess that I am a disciple of the continental European tradition [4], at least as far as keeping the ideas from sinking into oblivion. Nevertheless, I did formulate a number of preliminary hypotheses which do yield to experimental testing. The three aforementioned prerequisites for preserving the idea are certainly insufficient for its positive assessment or for initiating research. Practical implementation

stipulates many other conditions, not the least of which is finding "devotees" willing to undertake research based on this idea.

I would again remind the reader that my only claim is for the ideas expressed here to be included in the library of ideas. It is very difficult to judge an idea at an early stage and only time will tell whether or not my ideas will attract readership.

It is very tempting to try to assess the importance of these initial stages in terms of investing in subsequent research. However, it is very difficult, if not impossible to *objectively* evaluate innovative theories.

Nevertheless, it has been tried. Perhaps, the most famous attempt is the Science Citation Index devised by Eugene Garfield in 1963. The crux of his recipe was to measure the publication's worth by the number of times it has been cited. This method was widely accepted both among scientists as well as agencies which allocate research money. This formula is unlikely to produce many admirers for my ideas. However, I am optimistic because the above method has recently been subjected to some harsh criticism. Take, for instance, an article which appeared in Science. It quotes Garry Schuster, the head of the University of Illinois chemistry department, as saying:

> "You have to wonder what kinds of papers get the most citations and what that really means. Papers that report useful techniques, for example, will be cited more often than papers that present a new concept, particularly a very new one and one that not many people in a field have thought about. And then review articles in a field can garner a lot of citations and really make no original contribution to the science."[2]

Therefore, the important thing in assessing innovative ideas is not to try to evaluate them objectively, but to create conditions for their preservation. And in case there are people interested in these ideas, these people will have a chance to pursue them based on their own subjective judgment.

Naturally, this final conclusion is an attempt to justify my ambitious incursion into biology, and some of the most intricate and fundamental biological phenomena, the mechanism of evolutionary change and (!) cancer. Moreover, I have made clear my intention to link these two phenomena by viewing cancer as a pathology of the mechanism of evolutionary change.

However, my hope is to find an appreciative reader who will discover some useful information and will be forgiving toward my ambitions.

NOTES TO CONCLUSION

[1]. "The rise of the computing's new order will be anything but painless. Since mid-1950's the computing world has been overthrown twice: minicomputers broke the monopoly of mainframes in the late 1960's and early 70's, and in the mid-70's personal computers began edging minicomputers out of the spotlight. Each time, the older machine survived, but it no longer ruled."[3]

[2]. My now deceased friend Boris Moishezon told me of certain pitfalls befalling algebraic geometry. At the end of the 19th century a group of Italian geometers proved a number of important theorems.When their proofs were reevaluated in the middle of this century based on the new developments in algebraic geometry many proofs were found faulty in the sense of the final conclusion not being rigidly derived from the initial assumptions. Some of the theorems were salvaged by stipulating the precise conditions under which they are true.

[3]. In a sense, my views recall Løvtrup's[4] concept that new species emerge as a result of macromutations that are independent of other mutations.

[4]. In the extreme case, the dream of speculative-writers is to write in the spirit of socialist realism. I would like to present one real-life example so that an uninitiated reader might understand the essential nature of this style.

In the early 1930s a Soviet journalist, Elena Mikulina,[5] published a brochure about the socialist competition. Stalin wrote an introduction to this brochure because he exalted socialist competition as an antidote to its capitalist counterpart. Mikulina's brochure was written in the notorious tradition of socialist realism, i.e., the material was largely contrived while claiming to describe reality - real life socialist competition. At that time Stalin had a firm, but not an absolute grip on power. So, it was still possible for one Russova, who was unable to criticize Stalin directly for supporting such a superficial article with contrived facts, to do so indirectly by accusing Mikulina "of misleading comrade Stalin". Wishing to shield comrade Stalin from unworthy publications, Russova suggested that this brochure be withdrawn from the shelves. A well-known communist at the time, Felix Kohn, who was the head of the Union Radio Committee and deputy chief of the International Control Commission gave Russova's review to Stalin. In his reply to Kohn Stalin wrote that he realizes that "There is no spinner by the name of Bardin in this world and there is no a spinning factory in Zariadie". However, he (Stalin) still thinks that Mikulina's brochure holds merit because it "**popularizes** the idea of competition and **instills** in the reader the spirit of competition. That is what really counts, not some minor misconceptions."[6]

[1]. M.BAKHTIN, Problems of Dostoyevsky's Poetics (University of Minnesota Press, Minneapolis, 1984).
[2]. G.TAUBES, Science, **260**, 5110 (1993), 884-886.
[3]. J.MARKOFF, N. Y. Times, January 8, 1995.
[4]. S.LØVTRUP, Rivista di Biologia, **75**, 2 (1982), 231-272.
[5]. E.MIKULINA, Socialist Competition of the Masses (Cooperative Pub., Moscow,1932).
[6]. J.STALIN, in Collected Works, **12**, (Gospolitizdat, Moscow, 1951), 112-115.