

Primordialization:

The Way

New Living Organisms

Emerge

Mirabotalib Kazemie

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Contents

| | |
|--|-----------|
| INTRODUCTION | VI |
| PRIMORDIALIZATION | 9 |
| Reproduction, growth, communication with the environment, signal transmission, and the potential for association are the basic functions of urprimordial cells | 9 |
| Creation of multicellular organisms requires primordialization: changing of an urprimordial cell into a primordial cell | 10 |
| Form designs are encoded by the invariant proteins during the process of primordialization | 11 |
| The sources of urprimordial cells | 13 |
| Functions in multicellular organisms derive from cell's functions in urprimordial cells | 18 |
| Embryonal development requires memorization of the design program by the cells of the developing embryo | 19 |
| Reasons for the existing similarities between living organisms | 19 |
| Forms cannot be transformed | 21 |
| FORMS IDENTITIES ARE PRESERVED THROUGH THEIR POTENTIAL FOR ADAPTABILITY | 24 |
| Adaptability helps the living organisms to survive, and preserve their identities..... | 24 |
| Adaptability is not dictated by the environment..... | 26 |
| PRIMORDIALIZATION THEORY IS IN CONFORMITY WITH FINDINGS IN COMPARATIVE ANATOMY AND EMBRYOLOGY | 29 |
| Similarities between organs of different animals as interpreted by evolutionists | 29 |
| The limbs of land vertebrates' embryos are not fin-like structures | 31 |
| The presence of cartilaginous gill arches in land vertebrates' embryos is not evidence of their evolution from fish | 31 |
| The presence of notochord in land vertebrates' embryos is not evidence of vertebrates evolution from cephalochordates..... | 32 |
| Some cells in multicellular organisms with more than one function | 34 |
| MUTATIONS OF DNA DO NOT AFFECT THE DESIGNS OF THE BIOLOGICAL FORMS | 35 |
| Mutations in germ cells if left unchecked can lead to malfunctioning, monstrosity and death | 35 |

| | |
|---|-----------|
| Mutations do not lead to evolution of one living organism into another..... | 37 |
| THE EXISTENCE OF A DNA DAMPING MECHANISM | 39 |
| DNA has a passive role in cell affairs | 39 |
| DNA plays a passive role during development | 41 |
| DNA has no role during cell division..... | 42 |
| The high content of nonfunctional DNA in multicellular organisms may be the result of dumping nonfunctional DNA sequences .. | 42 |
| FOSSILS FROM PERSPECTIVE OF PRIMORDIALIZATION | 46 |
| The gaps between fossil finds and the problems associated with them..... | 46 |
| No evidence of Phylogenetic relation among chordates, fishes, amphibians and reptiles | 47 |
| The assumptions of evolutions of birds and mammals from reptiles are erratic | 50 |
| Primordialization theory rejects the evolution of man from any other creature | 53 |
| The facts and fictions about australopithecines..... | 54 |
| Neither upright walking nor free use of hand can influence the size of the brain; all three must occur simultaneously through primordialization | 56 |
| Who are Neanderthals ? | 58 |
| DIVERSITY IS NOT RELATED TO THE DIFFERENCES BETWEEN ORGANISMS PROTEINS..... | 60 |
| Similarity of sequence between homologous proteins provide no evidence of phylogenetic relationships | 60 |
| The estimates of rates of amino acid substitutions in proteins lack any significance | 62 |
| “FORM” SHOULD REPLACE “SPECIES” AS FUNDAMENTAL BIOLOGICAL CLASSIFICATION | 65 |
| The present choice of criteria for classification of living organism are very subjective | 65 |
| THE ORIGIN OF SEXUAL REPRODUCTION..... | 69 |
| The potential for sexual reproduction rests in urprimordial cells ... | 69 |
| Sex differentiation | 72 |
| Sexual way of reproduction may reduce the harmful effects of mutations..... | 73 |

PROTEIN INTELLIGENCE.....75

Protein molecules have the innate ability to recognize events,
 memorize their sequence, and respond to them..... 75

Protein molecules can program and reprogram the events
 inside the cell..... 77

**BEHAVIOR IN MULTICELLULAR ORGANISMS IS
 PROGRAMMED DURING PRIMORDIALIZATION.....80**

The relation between survival strategies of unicellular
 organisms and instincts or learned behavior
 in multicellular organisms 80

Some examples of instinctive behavior with foresight..... 82

Instincts and the level of developmental maturity at birth 84

Humans learn the means of survival from
 animals through mimicking85

Nervous systems in multicellular organisms are the restructured
 versions of urprimordial cell's communication and
 decision-making systems..... 86

**PRIMORDIALIZATION THEORY AND THE EVOLUTION
 THEORY FACE TO FACE88**

The arguments behind Darwin-Wallace theory of evolution..... 88

The anatomy of giraffe, humming birds, penguins, ostrich, and man
 all are fixed through primordialization 91

SUMMARY OF THE PRIMORDIALIZATION THEORY:94

CONCLUSION.....96

FOOTNOTES..... 100

REFERENCES..... 104

Introduction

In this book I describe for the first time a comprehensive biological theory which I believe to be able to show that the designs of biological organisms are determined by regulatory programs which are encoded by proteins that are invariant, and that changes in the sequences of DNA molecules are not involved in generation of new forms of living organisms. I name this theory “the theory of primordialization”. Its development is based upon careful evaluation of numerous scientific data published in particular in recent years in the fields of biological sciences, such as developmental biology, comparative anatomy, molecular biology, biochemistry, zoology, paleontology, etc. As the reader will recognize, the theory of primordialization takes a reasonable approach to help differentiate between the mechanisms which are involved in development and those which are in charge of biological diversity.

In connection with the theory of primordialization one of the new notions which has been discussed in this book is the concept of cellular and protein intelligence. Protein intelligence is the supreme kind of intelligence that is shared by all living organisms. Protein intelligence is the basis of cellular intelligence which in turn is paramount for the development of both instincts and learning faculties in multicellular organisms. Another fundamental

issue dealt with in this book is a new concept about the purpose behind adaptability and variability of the living organisms. Under primordialization theory adaptability and the tendency for variability are defined as innate potentials in living organisms which serve not only the survival of the organisms, but also the integrity of their identities. The nature of these two potentials, as described in this book, opposes the evolutionary version about them as means of transformation of forms.

In this place for the convenience of the reader I consider appropriate to make beforehand a brief remark about some terms used in this book. The use of word “species” is avoided throughout the book, except in one occasion when this term itself is the subject of discussion. Instead, I use the word “form” to distinguish biological organisms according to their distinct body designs. A form, however, can contain many species. “Urprimordial cells” is referred to the very first living cells appeared on earth, and to any other cells which share the same quality with those very first living cells. “Primordial cells” I call the living cells which carry programs for the design of the forms to which they develop. Primordialization is the process of turning an urprimordial cell into a primordial cell. This brief description, however, is not a replacement for detailed handling of these terms inside the book.

Primordialization

Multicellular organisms differ from each other by virtue of their body designs. An organism with a distinct body design is a “form”. The design of a multicellular form is determined by its primordial cell. A primordial cell is a cell which in addition to the basic functions and potentials of an urprimordial cell also contains regulative programs that determines the layout of the form structures during its embryonal development. A form cannot be transformed into another form.

Reproduction, growth, communication with the environment, signal transmission, and the potential for association are the basic functions of urprimordial cells

Life on earth would have ended quickly soon after it emerged, if the first living cells (I refer to them as urprimordial cells) had not been able to reproduce their own kind. In addition, those cells must have been able to grow, otherwise, after a few generations the daughter cells at some point would have reached extreme reduction in size, exhaustion of their resources, and eventually ceased to exist. They would have died also, if they were not been able to communicate with their environment. In order to accomplish this, they must have been equipped with some cell-surface

proteins that could mediate contact with the environment, and with some other proteins, located on the surface and inside the cells, that could transmit the signals from the cell surface toward the inside and in reverse direction.

With regard to the creation of multicellular organisms, it is important to realize that the urprimordial cells had not been able to succeed in this, if they had not possessed the potential to associate with each other. Thus, for those single-celled organisms the first step toward becoming a multicellular organism was that after cell division their daughter cells, under favorable conditions, were also able to stay together, instead of moving apart. In addition, for becoming a multicellular organism, the pores of their daughter cells at the moment of their association must have been able to join end to end and establish intercellular connections.

Creation of multicellular organisms requires primordialization: changing of an urprimordial cell into a primordial cell

The final step for the emergence of a multicellular organism is the integration into an urprimordial cell of a primordial program, that is a program which determines the design of that form and regulates its development within the context and boundary of its design. Without such a program multicellular organisms would have been nothing more but masses of undifferentiated cells. In order to distinguish those cells which are furnished with primor-

dial programs from the normal urprimordial cells, I call them primordial cells. The process of changing an urprimordial cell into a primordial cell I name primordialization. Thus, primordialization is the process by which multicellular organisms are being designed directly from urprimordial cells, or cells equivalent to them, as I will explain below.

Form designs are encoded by the invariant proteins during the process of primordialization

What kind of molecules are encoding the primordial programs? To answer this question I propose the following model: primordial programs are encoded by the invariant proteins in urprimordial cell, so that primordial cells differ from one another by the differences in the pattern in which their invariant proteins are combined and arranged during the primordialization process. In each primordial cell its primordial program contains the information for the ultimate appearance, function, and behaviour of the form to which it develops, including the executive power which regulates its development. The invariant proteins used for making the programs may constitute only a small fraction of urprimordial cells' proteins, but they can encode thousands of different primordial programs depending on the number, sequence of their alignment, and conformation with which they encode each single program. At this place, I want to point out that based on the understanding that the number of invariant proteins in an urprimordial

cell is limited, it is reasonable to conclude that among living organisms there exists no protein which on its own alone can determine the design and identity of a form. In other words, there are no form-specific proteins among living organisms.

In any primordial cell if the sequence of the proteins involved in the primordial program is altered the program will be destroyed and the primordial cell and/or the organism will die. In *Drosophila*, the proteins which determine the initial polarity of the egg, apparently, belong to the group of invariant proteins which contribute to their primordial program. Changes introduced in the sequences of those proteins disrupt the design of the embryo and are lethal ⁽¹⁾. In mouse zygote it has been shown that the first cleavage occurs 17-20 hr. after fertilization, and no mRNA synthesis occurs during this period. This fact indicates that the whole process concerned with the basic design of the organism and the strategy of the subsequent development is controlled by the proteins already present inside the egg. In *Drosophila* and *Xenopus* the very rapid cycles of DNA replication at the beginning, too, hinder transcription, so that up to the cellular blastoderm stage development depends on proteins present in the eggs before fertilization ⁽²⁾. Egg cells are replicates of primordial cells. It seems that they must obtain those proteins which are essential for the design of their respective forms always in the same composition and sequence in order to get the green light for starting the development of the organism.

The sources of urprimordial cells

From what has been described above it is evident that for the creation of multicellular organisms the existence of urprimordial cells is needed. This makes it necessary that these cells must be available at all times since the beginning of life on earth. However, free-living original urprimordial cells are unlikely to be available on earth for billions of years. Therefore, there must exist other sources where cells equivalent to original urprimordial cells could be produced for primordialization. As a matter of fact such cells can be produced by disruption of the pattern of an existing primordial program by means other than affecting the amino acid sequences of its invariant proteins. This can lead to disintegration of a form into undifferentiated cells. These cells can be reprogrammed with a new design (reprimordialization), that is the invariant proteins can be rearranged to redesign a new form.

Cells equivalent to urprimordial cells can be produced through partial or total disintegration of a multicellular organism under a process which is called, incorrectly, metamorphosis. For example, the egg laid by a *Drosophila* fly grows into a form which is totally different from the one which produces the egg, namely into an organism called larva. The fly, in its turn, is not the result of further development of the larval structures; it has its own independent design programmed in the imaginal cell⁽³⁾. These cells are disintegrated epidermal cells which are cleared from their original program, which means they become equivalent to urprimordial

cell; then they are reprogrammed, i.e. reprimordialized and reorganized into imaginal discs, from which the fly structures develop.

The production of urprimordial cells is very obvious by nauplius larvae of parasitic copepod *Haemocera danae*, when they become parasite in a polychaete worm. Inside the host the life of nauplius larva reaches an end; its structures disintegrate, leaving no sign of a larva behind. What is left is an ovoid mass of small undifferentiated cells. Since these cells give rise to a new form, a free-swimming organism within the host, a form very distinct from the previous ones, they must be reprogrammable with the program for the design of this new form. This is possible only if these cells were cleared from design program of the previous form, thus becoming urprimordial.

That any organism named larva is representing an independent form is evident from the facts that they have no resemblance with the so-called adult organism, whether it is an insect, or any other living organism for that matter. With some exceptions, they live independently, are active, and feed. In addition, their characters as independent forms can be supported by the extreme differences between the environments under which they and the “adult” forms live. They may be parasitic, when the “adult” is free-living (e.g., Gordioidea), or free-living when the adult is parasitic (e.g., parasitic copepods). Finally, many larvae, instead of leading to the so-called adult organisms, can reproduce, independently, other larvae either asexually (e.g., *Cecidomyia*), or sexually (*Cetenophora*).

Darwin himself admitted that organisms that develop one after the other during metamorphosis are independent forms, when he wrote, "No one probably will dispute that the butterfly is higher than the caterpillar." In making this comparison, implicitly he recognized the fact that the two are independent living organisms. He, however, did not realize that in this process there has been no indication for any accumulation of slight modifications or evolution of one form into another, let alone an indication for an evolution of a lower organization into a higher organization.

Creation of medusas from a hydroid polyp also based upon urprimordial cells which are produced through disintegration of parts of the polyp. The polyp usually buds other polyps. One of these buds behave differently. It disintegrates and form a gametangium. During this disintegration process two things must happen, in order to lead from a polyp to a medusa. First, the program responsible for the design of the polyp must be cleared, thus leading to generation of urprimordial cells. Second, these cells must be reprimordialized to establish a program for the design of the medusa as a new form different from the polyp.

Cells equivalent to urprimordial cells seems also to be generated from embryonic cells: in vertebrates embryos at 8-16-cells stage (the merula) the external cells become trophoblast leading to the formation of placenta. From this I infer that in order for the external merula cells to be able to lead the formation of placenta, first of all, their original program must be abolished; in other

words, they must first become urprimordial. Then through reprimordialization these cells acquire a placenta program and become primordial cells, which then develop into placenta. This structure is not an organ of the organism which continue to grow after birth, because if it were an organ it must be integrated into the anatomy of that organism, on the contrary, it is an independent organism which is attached to the other organism by the umbilical cord. One of the two organisms is designed in such a way to undergo extensive differentiation with organ building, and the other one, the placenta, remains as a less differentiated mass of tissues. Though there are some embryos which are known to have the ability to reproduce themselves (in larvae belonging to Trematoda, for example), in case of placenta interesting is, however, the fact that the embryonic cells are not producing embryos of the same organism, but that they are reprimordialized to produce a new form.

In addition, I consider processes such as the one which turns the unicellular amoeba *Dictyostelium discoideum* into a multicellular slug reprimordialization. When starved the amoebae collect into multicellular mounts. The cells within the aggregates turn into undifferentiated cells, which then reorganize and lead to the formation of a multicellular slug. The undifferentiated cells must have been cleared from the design program of an amoeba, otherwise the design of a multicellular slug cannot be established. They aggregate, apparently, in the same way as the original urprimordial

cells did more than a billion years ago and created the first multicellular organism.

In a recent study the production of embryonic cells from human blastocytes has been reported. These cells are said to be undifferentiated, pleuropotent, and resembling human embryonic carcinomas. Furthermore, it is worth mentioning that in experiments conducted in mice it has been shown that if a normal early embryo is grafted into the kidney or testis of an adult mouse, it rapidly become disorganized and the normal control mechanisms of cell proliferation break down, resulting in a disorganized mass of differentiated tissues mixed with undifferentiated cells. What happens here seems to be a disruption of the primordial program, so that for the cells, despite the fact that they can divide, grow, and differentiate, there is no more form design to follow. Carcinogenesis seems to be another situation where the cells fail to recognize the boundaries of the form and grow out of the context of form's design. Both cases of the undifferentiated cells mentioned, and the cancerous cells may well be regarded, to some degree, as cells equivalent to urprimordial cells.

Functions in multicellular organisms derive from cell's functions in urprimordial cells

The next question which arises and has to be answered is how the primordialization theory explains the emergence of functions in multicellular forms. The answer is this: upon development of a multicellular form from a primordial cell the functions of the newly formed multicellular organism take their origin from that of an urprimordial cell, redesigned for that form during primordialization. In the example of slug mentioned before, this organism at the anterior end of its body has light sensitive structures. These light sensitive structures must be considered as a result of reorganization and reprogramming of the light sensitive molecules and structures present in the undifferentiated cells of the mounts and their placement at the anterior end of the body, when these cells form the slug.

The development of sight in invertebrates and vertebrates seems to be based on the same principle. The eyes of these organisms differ from each other only with regard to the design and morphological details. In this sense, in none of those organisms it can be said that its eyes are evolved from another kind of eyes, or they are more or less advanced than the eyes of any other organism. In each case, eyes are built in a way to best fit the design of the form.

Embryonal development requires memorization of the design program by the cells of the developing embryo

A further problem which needs to be discussed, is how the information on the design of the form passes from an egg cell to many cell generations in a developing embryo. The answer I propose is this: when an egg cell divides it transfers the information on the design of the form to its daughter cells through encoding it in the spatial arrangement of the secondary regulatory proteins the daughter cells receive. In other words, while the job of the primordial program is to code the design of the form and preset its boundary, the functions of the secondary regulatory programs are to lead the organs to develop within this preset boundary. In *Drosophila*, for example, the egg-polarity proteins define the spatial coordinates of the embryo. The segmentation and homeotic selector proteins then serve to interpret the positional information provided by the first group. Passing of information will continue in this manner from one cell generation to the other until the structure of the form is complete. This is how the cells memorize the design of the form and function accordingly during development.

Reasons for the existing similarities between living organisms

The similarities and differences found between the sequences of homologous proteins in living organism do not reflect the differences they show with regard to their basic forms designs. For example, the difference between the amino acid sequences of corresponding proteins from apes and man seems to range, according to the type of protein, from zero to less than one percent. Despite this small difference, they are recognizable as two different biological forms. The reasons are at hand:

Structural proteins are not made to fit a specific purpose, for example, formation of a specific tissue or organ. On the contrary, the same structural protein can be used for making totally different structures. For example, in *Drosophila*, the same structural proteins seem to be used for making antenna or leg, halteres or wings, depending on the position of the body. In experiments where the loss of function of some other homeotic proteins result in changes of thoracic parts of the body into structures appropriate to abdominal segments, and vice versa, it seems that both visceral and thoracic organs can be built from the same structural proteins.

The structural and numerical chromosome changes also cannot explain the reason for similarities or differences between living forms. On the contrary, long ago, in experiments where the effects of change in the number of chromosomes were studied in salamanders, it was found that animals with haploid and pentaploid set of chromosomes were of the same size and appearance; they also

did not differ with regard to the morphology of their internal organs ⁽⁴⁾.

As we know, living organisms to various degrees share similar regulative mechanisms which determine the sequence of their development; this, too, also seems not to be able to explain the existence of similarities or differences between the morphologies of the biological organisms.

According to primordial theory, the reason for similarities and differences among living organisms is explainable: although, living organisms differ from each other with regard to their primordial programs, however, it does not mean that the structural elements of the forms each time must be newly reinvented. Primordial programs uses the same elements, but it shapes them in such a way to fit the designs of many different forms.

Forms cannot be transformed

The most important consequence of primordialization is that one form of a living organism cannot be transformed into another form. Nonetheless, deregulation of a regulatory system subordinate to the one which determines the design of a form can lead to alteration of some anatomical structures of the form. Such changes may well be disfiguring and/or incompatible with the general features and proper functioning of the form. They, however, have no

consequences on the design of the form; they are not transformations of different biological organisms into one another; they are just monstrosities. For example, an anencephaly that is caused by a defect in a subordinate regulative system responsible for the formation of head structures is a monstrosity in vertebrates and invertebrates alike, because none of those animals born with anencephaly will represent a new form. Very different from this kind of anencephaly is the anencephaly in chelicerates which is not a monstrosity, because their primordial cells are so programmed that these animals have no heads, and that the organs which are operating in head section in other arthropods are located in prosoma in these animals. As reminder, the bodies of chelicerates are subdivided into two portions, the prosoma (front) and the opisthosoma (back). The prosoma contains segments that bear the chelicerae (spider' fangs), pedipalps and four pairs of walking legs. It carries the main feeding, sensory, and locomotor apparatus. To underline the fact that morphological changes caused by alterations of the subordinate regulatory systems does not mean transformation of one form into another, in the following I elaborate on mutations which displace body structures.

In *Drosophila* the decision as to whether an antenna or leg should develop in its head region depends from the presence or absence, respectively, of a protein known as *Antennopedia* protein⁽⁵⁾. The observation that in the absence of this protein leg sprouts in the head instead of antenna is generally misunderstood and misinterpreted. Replacement of an antenna by a leg, for ex-

ample, was easily taken as an evidence that insects are evolved from multipeds. Against this notion it can be argued that if antennae were evolved from legs located in the same positions, why the subordinate program for making legs in these locations in multipeds should still exist in *Drosophila*. One expects that it should have been replaced completely by the program which makes antennae. According to the primordialization theory the reason for the simultaneous presence of both subordinate regulative system is at hand. Apparently, the cells at the antenna growth areas of the head of this fly have the potential to develop in both directions. Normally, the design regulative program instructs the responsible subordinate regulative system of antenna to build and put antenna in the specified spots of the head. If this regulative system is intact the cells build antenna. However, in the absence of the latter system leg regulative system put automatically legs in those spots of the head. In other words, a loss of function of proteins responsible for making antenna triggers automatically proteins in charge of making legs to develop legs, instead, in those positions of the head. Despite this change, the form remains the same: it is still a *Drosophila* fly. The same is true for observations in which due to a loss of function of some other homeotic proteins in segments belonging to thorax region abdominal organs develop, and reversely in segments belonging to abdominal region thoracic organs develop. These alterations, however, do not mean that thoracic organs are evolved from abdominal ones, or conversely.

Forms identities are preserved through their potential for adaptability

Adaptability is a biological potential which allows living organisms to undergo functional, behavioral, and morphological changes within the boundaries of their forms. Organisms utilize this potential to encounter the impact of the environmental changes and to survive as distinct biological forms.

Adaptability helps the living organisms to survive, and preserve their identities

The potential for adaptation is common among all living organisms. This ability is recognizable in the flexibilities and variations the organisms show with regard to their behavior, anatomy, and functions in response to changing environmental conditions. At the molecular level, adaptability means autonomous rearrangement and reorganization of the cell's macromolecules in response to the environmental factors which affect the organism. This involves, for example, repair of damaged DNA sequences, the conformational changes of protein molecules on the surface of a living cell, reshuffling of a cell's cytoskeletal elements, readjustment of a cell's metabolism, changes of sexual behavior, and a

cell's redesigning of its own protein molecules. One form of DNA manipulation under cell control is DNA rearrangements using mobile DNA elements. This includes single nucleotide substitutions, insertions or deletions of large and small nucleotide sequences, and translocations of DNA sequences. In fact, living organisms not only have the ability to alter its DNA sequences, but also they can produce new ones, even at a very fast rate. The best known example for this is the production of new DNA blueprints for the variable regions of immunoglobulin molecules in vertebrates as part of their precaution to respond to the enormous number of antigens, most of them had never been encountered by the former generations of the organisms in the past ⁽⁶⁾.

Since these changes do not pertain to invariant proteins which are involved in encoding the designs of the forms, they serve not only the survival of the organisms, but their survival as distinct forms. It is adaptability which helps the living organisms to survive and preserve their identities as independent forms in an ever-changing environment, unless the environmental conditions become so harsh that the organism fails to have a chance to mobilize this potential effectively. As a matter of fact, a biological organism which fails to put at work this potential will die.